WORLD HEALTH ORGANIZATION
INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans

VOLUME 95

Household Use of Solid Fuels and High-temperature Frying

LYON, FRANCE
2010

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Household Use of Solid Fuels and High-temperature Frying

This publication represents the views and expert opinions
of an IARC Working Group on the
Evaluation of Carcinogenic Risks to Humans,
which met in Lyon,

10–17 October 2006

2010

IARC MONOGRAPHS

In 1969, the International Agency for Research on Cancer (IARC) initiated a programme on the evaluation of the carcinogenic risk of chemicals to humans involving the production of critically evaluated monographs on individual chemicals. The programme was subsequently expanded to include evaluations of carcinogenic risks associated with exposures to complex mixtures, lifestyle factors and biological and physical agents, as well as those in specific occupations. The objective of the programme is to elaborate and publish in the form of monographs critical reviews of data on carcinogenicity for agents to which humans are known to be exposed and on specific exposure situations; to evaluate these data in terms of human risk with the help of international working groups of experts in chemical carcinogenesis and related fields; and to indicate where additional research efforts are needed. The lists of IARC evaluations are regularly updated and are available on the Internet at http://monographs.iarc.fr/.

This programme has been supported since 1982 by Cooperative Agreement U01 CA33193 with the United States National Cancer Institute, Department of Health and Human Services. Additional support has been provided since 1986 by the Health, Safety and Hygiene at Work Unit of the European Commission Directorate-General for Employment, Social Affairs and Equal Opportunities, and since 1992 by the United States National Institute of Environmental Health Sciences, Department of Health and Human Services. The contents of this volume are solely the responsibility of the Working Group and do not necessarily represent the official views of the U.S. National Cancer Institute, the U.S. National Institute of Environmental Health Sciences, the U.S. Department of Health and Human Services, or the European Commission Directorate-General for Employment, Social Affairs and Equal Opportunities.

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Photograph of woman with child cooking over an open fire in Guatemala, courtesy of Nigel Bruce

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NOTE TO THE READER

The term 'carcinogenic risk' in the *IARC Monographs* series is taken to mean that an agent is capable of causing cancer under some circumstances. The *Monographs* evaluate cancer hazards, despite the historical presence of the word 'risks' in the title.

Inclusion of an agent in the *Monographs* does not imply that it is a carcinogen, only that the published data have been examined. Equally, the fact that an agent has not yet been evaluated in a *Monograph* does not mean that it is not carcinogenic.

The evaluations of carcinogenic risk are made by international working groups of independent scientists and are qualitative in nature. No recommendation is given for regulation or legislation.

Anyone who is aware of published data that may alter the evaluation of the carcinogenic risk of an agent to humans is encouraged to make this information available to the Section of IARC Monographs, International Agency for Research on Cancer, 150 cours Albert Thomas, 69372 Lyon Cedex 08, France, in order that the agent may be considered for re-evaluation by a future Working Group.

Although every effort is made to prepare the monographs as accurately as possible, mistakes may occur. Readers are requested to communicate any errors to the Section of IARC Monographs, so that corrections can be reported in future volumes.

IARC MONOGRAPHS ON THE EVALUATION OF CARCINOGENIC RISKS TO HUMANS

VOLUME 95
HOUSEHOLD USE OF SOLID FUELS AND HIGH-TEMPERATURE FRYING

Lyon, 10–17 October 2006

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[2] Each participant was asked to disclose pertinent research, employment, and financial interests. Current financial interests and research and employment interests during the past 3 years or anticipated in the future are identified here. Minor pertinent interests are not listed and include stock valued at no more than US$10 000 overall, grants that provide no more than 5% of the research budget of the expert's organization and that do not support the expert's research or position, and consulting or speaking on matters not before a court or government agency that does not exceed 2% of total professional time or compensation. All grants that support the expert's research or position and all consulting or speaking on matters before a court or government agency are listed as significant pertinent interests.

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PREAMBLE

IARC MONOGRAPHS ON THE EVALUATION OF CARCINOGENIC RISKS TO HUMANS

PREAMBLE

The Preamble to the *IARC Monographs* describes the objective and scope of the programme, the scientific principles and procedures used in developing a *Monograph*, the types of evidence considered and the scientific criteria that guide the evaluations. The Preamble should be consulted when reading a *Monograph* or list of evaluations.

A. GENERAL PRINCIPLES AND PROCEDURES

1. Background

Soon after IARC was established in 1965, it received frequent requests for advice on the carcinogenic risk of chemicals, including requests for lists of known and suspected human carcinogens. It was clear that it would not be a simple task to summarize adequately the complexity of the information that was available, and IARC began to consider means of obtaining international expert opinion on this topic. In 1970, the IARC Advisory Committee on Environmental Carcinogenesis recommended '...that a compendium on carcinogenic chemicals be prepared by experts. The biological activity and evaluation of practical importance to public health should be referenced and documented.' The IARC Governing Council adopted a resolution concerning the role of IARC in providing government authorities with expert, independent, scientific opinion on environmental carcinogenesis. As one means to that end, the Governing Council recommended that IARC should prepare monographs on the evaluation of carcinogenic risk of chemicals to man, which became the initial title of the series.

In the succeeding years, the scope of the programme broadened as *Monographs* were developed for groups of related chemicals, complex mixtures, occupational exposures, physical and biological agents and lifestyle factors. In 1988, the phrase 'of chemicals' was dropped from the title, which assumed its present form, *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*.

Through the *Monographs* programme, IARC seeks to identify the causes of human cancer. This is the first step in cancer prevention, which is needed as much today as when

IARC was established. The global burden of cancer is high and continues to increase: the annual number of new cases was estimated at 10.1 million in 2000 and is expected to reach 15 million by 2020 (Stewart & Kleihues, 2003). With current trends in demographics and exposure, the cancer burden has been shifting from high-resource countries to low- and medium-resource countries. As a result of *Monographs* evaluations, national health agencies have been able, on scientific grounds, to take measures to reduce human exposure to carcinogens in the workplace and in the environment.

The criteria established in 1971 to evaluate carcinogenic risks to humans were adopted by the Working Groups whose deliberations resulted in the first 16 volumes of the *Monographs* series. Those criteria were subsequently updated by further ad-hoc Advisory Groups (IARC, 1977, 1978, 1979, 1982, 1983, 1987, 1988, 1991; Vainio *et al.*, 1992; IARC, 2005, 2006).

The Preamble is primarily a statement of scientific principles, rather than a specification of working procedures. The procedures through which a Working Group implements these principles are not specified in detail. They usually involve operations that have been established as being effective during previous *Monograph* meetings but remain, predominantly, the prerogative of each individual Working Group.

2. Objective and scope

The objective of the programme is to prepare, with the help of international Working Groups of experts, and to publish in the form of *Monographs*, critical reviews and evaluations of evidence on the carcinogenicity of a wide range of human exposures. The *Monographs* represent the first step in carcinogen risk assessment, which involves examination of all relevant information in order to assess the strength of the available evidence that an agent could alter the age-specific incidence of cancer in humans. The *Monographs* may also indicate where additional research efforts are needed, specifically when data immediately relevant to an evaluation are not available.

In this Preamble, the term 'agent' refers to any entity or circumstance that is subject to evaluation in a *Monograph*. As the scope of the programme has broadened, categories of agents now include specific chemicals, groups of related chemicals, complex mixtures, occupational or environmental exposures, cultural or behavioural practices, biological organisms and physical agents. This list of categories may expand as causation of, and susceptibility to, malignant disease become more fully understood.

A cancer 'hazard' is an agent that is capable of causing cancer under some circumstances, while a cancer 'risk' is an estimate of the carcinogenic effects expected from exposure to a cancer hazard. The *Monographs* are an exercise in evaluating cancer hazards, despite the historical presence of the word 'risks' in the title. The distinction between hazard and risk is important, and the *Monographs* identify cancer hazards even when risks are very low at current exposure levels, because new uses or unforeseen exposures could engender risks that are significantly higher.

In the *Monographs*, an agent is termed 'carcinogenic' if it is capable of increasing the incidence of malignant neoplasms, reducing their latency, or increasing their severity or multiplicity. The induction of benign neoplasms may in some circumstances (see Part B, Section 3a) contribute to the judgement that the agent is carcinogenic. The terms 'neoplasm' and 'tumour' are used interchangeably.

The Preamble continues the previous usage of the phrase 'strength of evidence' as a matter of historical continuity, although it should be understood that *Monographs* evaluations consider studies that support a finding of a cancer hazard as well as studies that do not.

Some epidemiological and experimental studies indicate that different agents may act at different stages in the carcinogenic process, and several different mechanisms may be involved. The aim of the *Monographs* has been, from their inception, to evaluate evidence of carcinogenicity at any stage in the carcinogenesis process, independently of the underlying mechanisms. Information on mechanisms may, however, be used in making the overall evaluation (IARC, 1991; Vainio *et al.*, 1992; IARC, 2005, 2006; see also Part B, Sections 4 and 6). As mechanisms of carcinogenesis are elucidated, IARC convenes international scientific conferences to determine whether a broad-based consensus has emerged on how specific mechanistic data can be used in an evaluation of human carcinogenicity. The results of such conferences are reported in IARC Scientific Publications, which, as long as they still reflect the current state of scientific knowledge, may guide subsequent Working Groups.

Although the *Monographs* have emphasized hazard identification, important issues may also involve dose–response assessment. In many cases, the same epidemiological and experimental studies used to evaluate a cancer hazard can also be used to estimate a dose–response relationship. A *Monograph* may undertake to estimate dose–response relationships within the range of the available epidemiological data, or it may compare the dose–response information from experimental and epidemiological studies. In some cases, a subsequent publication may be prepared by a separate Working Group with expertise in quantitative dose–response assessment.

The *Monographs* are used by national and international authorities to make risk assessments, formulate decisions concerning preventive measures, provide effective cancer control programmes and decide among alternative options for public health decisions. The evaluations of IARC Working Groups are scientific, qualitative judgements on the evidence for or against carcinogenicity provided by the available data. These evaluations represent only one part of the body of information on which public health decisions may be based. Public health options vary from one situation to another and from country to country and relate to many factors, including different socioeconomic and national priorities. Therefore, no recommendation is given with regard to regulation or legislation, which are the responsibility of individual governments or other international organizations.

3. Selection of agents for review

Agents are selected for review on the basis of two main criteria: (a) there is evidence of human exposure and (b) there is some evidence or suspicion of carcinogenicity. Mixed exposures may occur in occupational and environmental settings and as a result of individual and cultural habits (such as tobacco smoking and dietary practices). Chemical analogues and compounds with biological or physical characteristics similar to those of suspected carcinogens may also be considered, even in the absence of data on a possible carcinogenic effect in humans or experimental animals.

The scientific literature is surveyed for published data relevant to an assessment of carcinogenicity. Ad-hoc Advisory Groups convened by IARC in 1984, 1989, 1991, 1993, 1998 and 2003 made recommendations as to which agents should be evaluated in the *Monographs* series. Recent recommendations are available on the *Monographs* programme website (http://monographs.iarc.fr). IARC may schedule other agents for review as it becomes aware of new scientific information or as national health agencies identify an urgent public health need related to cancer.

As significant new data become available on an agent for which a *Monograph* exists, a re-evaluation may be made at a subsequent meeting, and a new *Monograph* published. In some cases it may be appropriate to review only the data published since a prior evaluation. This can be useful for updating a database, reviewing new data to resolve a previously open question or identifying new tumour sites associated with a carcinogenic agent. Major changes in an evaluation (e.g. a new classification in Group 1 or a determination that a mechanism does not operate in humans, see Part B, Section 6) are more appropriately addressed by a full review.

4. Data for the *Monographs*

Each *Monograph* reviews all pertinent epidemiological studies and cancer bioassays in experimental animals. Those judged inadequate or irrelevant to the evaluation may be cited but not summarized. If a group of similar studies is not reviewed, the reasons are indicated.

Mechanistic and other relevant data are also reviewed. A *Monograph* does not necessarily cite all the mechanistic literature concerning the agent being evaluated (see Part B, Section 4). Only those data considered by the Working Group to be relevant to making the evaluation are included.

With regard to epidemiological studies, cancer bioassays, and mechanistic and other relevant data, only reports that have been published or accepted for publication in the openly available scientific literature are reviewed. The same publication requirement applies to studies originating from IARC, including meta-analyses or pooled analyses commissioned by IARC in advance of a meeting (see Part B, Section 2c). Data from government agency reports that are publicly available are also considered. Exceptionally,

doctoral theses and other material that are in their final form and publicly available may be reviewed.

Exposure data and other information on an agent under consideration are also reviewed. In the sections on chemical and physical properties, on analysis, on production and use and on occurrence, published and unpublished sources of information may be considered.

Inclusion of a study does not imply acceptance of the adequacy of the study design or of the analysis and interpretation of the results, and limitations are clearly outlined in square brackets at the end of each study description (see Part B). The reasons for not giving further consideration to an individual study also are indicated in the square brackets.

5. Meeting participants

Five categories of participant can be present at *Monograph* meetings.

(a) The Working Group is responsible for the critical reviews and evaluations that are developed during the meeting. The tasks of Working Group Members are: (i) to ascertain that all appropriate data have been collected; (ii) to select the data relevant for the evaluation on the basis of scientific merit; (iii) to prepare accurate summaries of the data to enable the reader to follow the reasoning of the Working Group; (iv) to evaluate the results of epidemiological and experimental studies on cancer; (v) to evaluate data relevant to the understanding of mechanisms of carcinogenesis; and (vi) to make an overall evaluation of the carcinogenicity of the exposure to humans. Working Group Members generally have published significant research related to the carcinogenicity of the agents being reviewed, and IARC uses literature searches to identify most experts. Working Group Members are selected on the basis of (a) knowledge and experience and (b) absence of real or apparent conflicts of interests. Consideration is also given to demographic diversity and balance of scientific findings and views.

(b) Invited Specialists are experts who also have critical knowledge and experience but have a real or apparent conflict of interests. These experts are invited when necessary to assist in the Working Group by contributing their unique knowledge and experience during subgroup and plenary discussions. They may also contribute text on non-influential issues in the section on exposure, such as a general description of data on production and use (see Part B, Section 1). Invited Specialists do not serve as meeting chair or subgroup chair, draft text that pertains to the description or interpretation of cancer data, or participate in the evaluations.

(c) Representatives of national and international health agencies often attend meetings because their agencies sponsor the programme or are interested in the subject of a meeting. Representatives do not serve as meeting chair or subgroup chair, draft any part of a *Monograph,* or participate in the evaluations.

(d) Observers with relevant scientific credentials may be admitted to a meeting by IARC in limited numbers. Attention will be given to achieving a balance of Observers

from constituencies with differing perspectives. They are invited to observe the meeting and should not attempt to influence it. Observers do not serve as meeting chair or subgroup chair, draft any part of a *Monograph*, or participate in the evaluations. At the meeting, the meeting chair and subgroup chairs may grant Observers an opportunity to speak, generally after they have observed a discussion. Observers agree to respect the Guidelines for Observers at *IARC Monographs* meetings (available at http://monographs.iarc.fr).

(e) The IARC Secretariat consists of scientists who are designated by IARC and who have relevant expertise. They serve as rapporteurs and participate in all discussions. When requested by the meeting chair or subgroup chair, they may also draft text or prepare tables and analyses.

Before an invitation is extended, each potential participant, including the IARC Secretariat, completes the WHO Declaration of Interests to report financial interests, employment and consulting, and individual and institutional research support related to the subject of the meeting. IARC assesses these interests to determine whether there is a conflict that warrants some limitation on participation. The declarations are updated and reviewed again at the opening of the meeting. Interests related to the subject of the meeting are disclosed to the meeting participants and in the published volume (Cogliano *et al.*, 2004).

The names and principal affiliations of participants are available on the *Monographs* programme website (http://monographs.iarc.fr) approximately two months before each meeting. It is not acceptable for Observers or third parties to contact other participants before a meeting or to lobby them at any time. Meeting participants are asked to report all such contacts to IARC (Cogliano *et al.*, 2005).

All participants are listed, with their principal affiliations, at the beginning of each volume. Each participant who is a Member of a Working Group serves as an individual scientist and not as a representative of any organization, government or industry.

6. Working procedures

A separate Working Group is responsible for developing each volume of *Monographs*. A volume contains one or more *Monographs*, which can cover either a single agent or several related agents. Approximately one year in advance of the meeting of a Working Group, the agents to be reviewed are announced on the *Monographs* programme website (http://monographs.iarc.fr) and participants are selected by IARC staff in consultation with other experts. Subsequently, relevant biological and epidemiological data are collected by IARC from recognized sources of information on carcinogenesis, including data storage and retrieval systems such as PubMed. Meeting participants who are asked to prepare preliminary working papers for specific sections are expected to supplement the IARC literature searches with their own searches.

For most chemicals and some complex mixtures, the major collection of data and the preparation of working papers for the sections on chemical and physical properties, on analysis, on production and use, and on occurrence are carried out under a separate

contract funded by the US National Cancer Institute. Industrial associations, labour unions and other knowledgeable organizations may be asked to provide input to the sections on production and use, although this involvement is not required as a general rule. Information on production and trade is obtained from governmental, trade and market research publications and, in some cases, by direct contact with industries. Separate production data on some agents may not be available for a variety of reasons (e.g. not collected or made public in all producing countries, production is small). Information on uses may be obtained from published sources but is often complemented by direct contact with manufacturers. Efforts are made to supplement this information with data from other national and international sources.

Six months before the meeting, the material obtained is sent to meeting participants to prepare preliminary working papers. The working papers are compiled by IARC staff and sent, prior to the meeting, to Working Group Members and Invited Specialists for review.

The Working Group meets at IARC for seven to eight days to discuss and finalize the texts and to formulate the evaluations. The objectives of the meeting are peer review and consensus. During the first few days, four subgroups (covering exposure data, cancer in humans, cancer in experimental animals, and mechanistic and other relevant data) review the working papers, develop a joint subgroup draft and write summaries. Care is taken to ensure that each study summary is written or reviewed by someone not associated with the study being considered. During the last few days, the Working Group meets in plenary session to review the subgroup drafts and develop the evaluations. As a result, the entire volume is the joint product of the Working Group, and there are no individually authored sections.

IARC Working Groups strive to achieve a consensus evaluation. Consensus reflects broad agreement among Working Group Members, but not necessarily unanimity. The chair may elect to poll Working Group Members to determine the diversity of scientific opinion on issues where consensus is not readily apparent.

After the meeting, the master copy is verified by consulting the original literature, edited and prepared for publication. The aim is to publish the volume within six months of the Working Group meeting. A summary of the outcome is available on the *Monographs* programme website soon after the meeting.

B. SCIENTIFIC REVIEW AND EVALUATION

The available studies are summarized by the Working Group, with particular regard to the qualitative aspects discussed below. In general, numerical findings are indicated as they appear in the original report; units are converted when necessary for easier comparison. The Working Group may conduct additional analyses of the published data and use them in their assessment of the evidence; the results of such supplementary analyses are given in square brackets. When an important aspect of a study that directly impinges

on its interpretation should be brought to the attention of the reader, a Working Group comment is given in square brackets.

The scope of the *IARC Monographs* programme has expanded beyond chemicals to include complex mixtures, occupational exposures, physical and biological agents, lifestyle factors and other potentially carcinogenic exposures. Over time, the structure of a *Monograph* has evolved to include the following sections:

1. Exposure data
2. Studies of cancer in humans
3. Studies of cancer in experimental animals
4. Mechanistic and other relevant data
5. Summary
6. Evaluation and rationale

In addition, a section of General Remarks at the front of the volume discusses the reasons the agents were scheduled for evaluation and some key issues the Working Group encountered during the meeting.

This part of the Preamble discusses the types of evidence considered and summarized in each section of a *Monograph*, followed by the scientific criteria that guide the evaluations.

1. Exposure data

Each *Monograph* includes general information on the agent: this information may vary substantially between agents and must be adapted accordingly. Also included is information on production and use (when appropriate), methods of analysis and detection, occurrence, and sources and routes of human occupational and environmental exposures. Depending on the agent, regulations and guidelines for use may be presented.

(*a*) *General information on the agent*

For chemical agents, sections on chemical and physical data are included: the Chemical Abstracts Service Registry Number, the latest primary name and the IUPAC systematic name are recorded; other synonyms are given, but the list is not necessarily comprehensive. Information on chemical and physical properties that are relevant to identification, occurrence and biological activity is included. A description of technical products of chemicals includes trade names, relevant specifications and available information on composition and impurities. Some of the trade names given may be those of mixtures in which the agent being evaluated is only one of the ingredients.

For biological agents, taxonomy, structure and biology are described, and the degree of variability is indicated. Mode of replication, life cycle, target cells, persistence, latency, host response and clinical disease other than cancer are also presented.

For physical agents that are forms of radiation, energy and range of the radiation are included. For foreign bodies, fibres and respirable particles, size range and relative dimensions are indicated.

For agents such as mixtures, drugs or lifestyle factors, a description of the agent, including its composition, is given.

Whenever appropriate, other information, such as historical perspectives or the description of an industry or habit, may be included.

(*b*) *Analysis and detection*

An overview of methods of analysis and detection of the agent is presented, including their sensitivity, specificity and reproducibility. Methods widely used for regulatory purposes are emphasized. Methods for monitoring human exposure are also given. No critical evaluation or recommendation of any method is meant or implied.

(*c*) *Production and use*

The dates of first synthesis and of first commercial production of a chemical, mixture or other agent are provided when available; for agents that do not occur naturally, this information may allow a reasonable estimate to be made of the date before which no human exposure to the agent could have occurred. The dates of first reported occurrence of an exposure are also provided when available. In addition, methods of synthesis used in past and present commercial production and different methods of production, which may give rise to different impurities, are described.

The countries where companies report production of the agent, and the number of companies in each country, are identified. Available data on production, international trade and uses are obtained for representative regions. It should not, however, be inferred that those areas or nations are necessarily the sole or major sources or users of the agent. Some identified uses may not be current or major applications, and the coverage is not necessarily comprehensive. In the case of drugs, mention of their therapeutic uses does not necessarily represent current practice nor does it imply judgement as to their therapeutic efficacy.

(*d*) *Occurrence and exposure*

Information on the occurrence of an agent in the environment is obtained from data derived from the monitoring and surveillance of levels in occupational environments, air, water, soil, plants, foods and animal and human tissues. When available, data on the generation, persistence and bioaccumulation of the agent are also included. Such data may be available from national databases.

Data that indicate the extent of past and present human exposure, the sources of exposure, the people most likely to be exposed and the factors that contribute to the exposure are reported. Information is presented on the range of human exposure, including occupational and environmental exposures. This includes relevant findings from both developed and developing countries. Some of these data are not distributed widely and may be available from government reports and other sources. In the case of mixtures, industries, occupations or processes, information is given about all agents known to be

present. For processes, industries and occupations, a historical description is also given, noting variations in chemical composition, physical properties and levels of occupational exposure with date and place. For biological agents, the epidemiology of infection is described.

(*e*) *Regulations and guidelines*

Statements concerning regulations and guidelines (e.g. occupational exposure limits, maximal levels permitted in foods and water, pesticide registrations) are included, but they may not reflect the most recent situation, since such limits are continuously reviewed and modified. The absence of information on regulatory status for a country should not be taken to imply that that country does not have regulations with regard to the exposure. For biological agents, legislation and control, including vaccination and therapy, are described.

2. Studies of cancer in humans

This section includes all pertinent epidemiological studies (see Part A, Section 4). Studies of biomarkers are included when they are relevant to an evaluation of carcinogenicity to humans.

(*a*) *Types of study considered*

Several types of epidemiological study contribute to the assessment of carcinogenicity in humans — cohort studies, case–control studies, correlation (or ecological) studies and intervention studies. Rarely, results from randomized trials may be available. Case reports and case series of cancer in humans may also be reviewed.

Cohort and case–control studies relate individual exposures under study to the occurrence of cancer in individuals and provide an estimate of effect (such as relative risk) as the main measure of association. Intervention studies may provide strong evidence for making causal inferences, as exemplified by cessation of smoking and the subsequent decrease in risk for lung cancer.

In correlation studies, the units of investigation are usually whole populations (e.g. in particular geographical areas or at particular times), and cancer frequency is related to a summary measure of the exposure of the population to the agent under study. In correlation studies, individual exposure is not documented, which renders this kind of study more prone to confounding. In some circumstances, however, correlation studies may be more informative than analytical study designs (see, for example, the *Monograph* on arsenic in drinking-water; IARC, 2004).

In some instances, case reports and case series have provided important information about the carcinogenicity of an agent. These types of study generally arise from a suspicion, based on clinical experience, that the concurrence of two events — that is, a particular exposure and occurrence of a cancer — has happened rather more frequently

than would be expected by chance. Case reports and case series usually lack complete ascertainment of cases in any population, definition or enumeration of the population at risk and estimation of the expected number of cases in the absence of exposure.

The uncertainties that surround the interpretation of case reports, case series and correlation studies make them inadequate, except in rare instances, to form the sole basis for inferring a causal relationship. When taken together with case–control and cohort studies, however, these types of study may add materially to the judgement that a causal relationship exists.

Epidemiological studies of benign neoplasms, presumed preneoplastic lesions and other end-points thought to be relevant to cancer are also reviewed. They may, in some instances, strengthen inferences drawn from studies of cancer itself.

(*b*) *Quality of studies considered*

It is necessary to take into account the possible roles of bias, confounding and chance in the interpretation of epidemiological studies. Bias is the effect of factors in study design or execution that lead erroneously to a stronger or weaker association than in fact exists between an agent and disease. Confounding is a form of bias that occurs when the relationship with disease is made to appear stronger or weaker than it truly is as a result of an association between the apparent causal factor and another factor that is associated with either an increase or decrease in the incidence of the disease. The role of chance is related to biological variability and the influence of sample size on the precision of estimates of effect.

In evaluating the extent to which these factors have been minimized in an individual study, consideration is given to a number of aspects of design and analysis as described in the report of the study. For example, when suspicion of carcinogenicity arises largely from a single small study, careful consideration is given when interpreting subsequent studies that included these data in an enlarged population. Most of these considerations apply equally to case–control, cohort and correlation studies. Lack of clarity of any of these aspects in the reporting of a study can decrease its credibility and the weight given to it in the final evaluation of the exposure.

Firstly, the study population, disease (or diseases) and exposure should have been well defined by the authors. Cases of disease in the study population should have been identified in a way that was independent of the exposure of interest, and exposure should have been assessed in a way that was not related to disease status.

Secondly, the authors should have taken into account — in the study design and analysis — other variables that can influence the risk of disease and may have been related to the exposure of interest. Potential confounding by such variables should have been dealt with either in the design of the study, such as by matching, or in the analysis, by statistical adjustment. In cohort studies, comparisons with local rates of disease may or may not be more appropriate than those with national rates. Internal comparisons of frequency of disease among individuals at different levels of exposure are also desirable

in cohort studies, since they minimize the potential for confounding related to the difference in risk factors between an external reference group and the study population.

Thirdly, the authors should have reported the basic data on which the conclusions are founded, even if sophisticated statistical analyses were employed. At the very least, they should have given the numbers of exposed and unexposed cases and controls in a case–control study and the numbers of cases observed and expected in a cohort study. Further tabulations by time since exposure began and other temporal factors are also important. In a cohort study, data on all cancer sites and all causes of death should have been given, to reveal the possibility of reporting bias. In a case–control study, the effects of investigated factors other than the exposure of interest should have been reported.

Finally, the statistical methods used to obtain estimates of relative risk, absolute rates of cancer, confidence intervals and significance tests, and to adjust for confounding should have been clearly stated by the authors. These methods have been reviewed for case–control studies (Breslow & Day, 1980) and for cohort studies (Breslow & Day, 1987).

(*c*) *Meta-analyses and pooled analyses*

Independent epidemiological studies of the same agent may lead to results that are difficult to interpret. Combined analyses of data from multiple studies are a means of resolving this ambiguity, and well-conducted analyses can be considered. There are two types of combined analysis. The first involves combining summary statistics such as relative risks from individual studies (meta-analysis) and the second involves a pooled analysis of the raw data from the individual studies (pooled analysis) (Greenland, 1998).

The advantages of combined analyses are increased precision due to increased sample size and the opportunity to explore potential confounders, interactions and modifying effects that may explain heterogeneity among studies in more detail. A disadvantage of combined analyses is the possible lack of compatibility of data from various studies due to differences in subject recruitment, procedures of data collection, methods of measurement and effects of unmeasured co-variates that may differ among studies. Despite these limitations, well-conducted combined analyses may provide a firmer basis than individual studies for drawing conclusions about the potential carcinogenicity of agents.

IARC may commission a meta-analysis or pooled analysis that is pertinent to a particular *Monograph* (see Part A, Section 4). Additionally, as a means of gaining insight from the results of multiple individual studies, ad-hoc calculations that combine data from different studies may be conducted by the Working Group during the course of a *Monograph* meeting. The results of such original calculations, which would be specified in the text by presentation in square brackets, might involve updates of previously conducted analyses that incorporate the results of more recent studies or de-novo analyses. Irrespective of the source of data for the meta-analyses and pooled analyses, it is important that the same criteria for data quality be applied as those that would be applied to individual studies and to ensure also that sources of heterogeneity between studies be taken into account.

(*d*) *Temporal effects*

Detailed analyses of both relative and absolute risks in relation to temporal variables, such as age at first exposure, time since first exposure, duration of exposure, cumulative exposure, peak exposure (when appropriate) and time since cessation of exposure, are reviewed and summarized when available. Analyses of temporal relationships may be useful in making causal inferences. In addition, such analyses may suggest whether a carcinogen acts early or late in the process of carcinogenesis, although, at best, they allow only indirect inferences about mechanisms of carcinogenesis.

(*e*) *Use of biomarkers in epidemiological studies*

Biomarkers indicate molecular, cellular or other biological changes and are increasingly used in epidemiological studies for various purposes (IARC, 1991; Vainio *et al.*, 1992; Toniolo *et al.*, 1997; Vineis *et al.*, 1999; Buffler *et al.*, 2004). These may include evidence of exposure, of early effects, of cellular, tissue or organism responses, of individual susceptibility or host responses, and inference of a mechanism (see Part B, Section 4b). This is a rapidly evolving field that encompasses developments in genomics, epigenomics and other emerging technologies.

Molecular epidemiological data that identify associations between genetic polymorphisms and interindividual differences in susceptibility to the agent(s) being evaluated may contribute to the identification of carcinogenic hazards to humans. If the polymorphism has been demonstrated experimentally to modify the functional activity of the gene product in a manner that is consistent with increased susceptibility, these data may be useful in making causal inferences. Similarly, molecular epidemiological studies that measure cell functions, enzymes or metabolites that are thought to be the basis of susceptibility may provide evidence that reinforces biological plausibility. It should be noted, however, that when data on genetic susceptibility originate from multiple comparisons that arise from subgroup analyses, this can generate false-positive results and inconsistencies across studies, and such data therefore require careful evaluation. If the known phenotype of a genetic polymorphism can explain the carcinogenic mechanism of the agent being evaluated, data on this phenotype may be useful in making causal inferences.

(*f*) *Criteria for causality*

After the quality of individual epidemiological studies of cancer has been summarized and assessed, a judgement is made concerning the strength of evidence that the agent in question is carcinogenic to humans. In making its judgement, the Working Group considers several criteria for causality (Hill, 1965). A strong association (e.g. a large relative risk) is more likely to indicate causality than a weak association, although it is recognized that estimates of effect of small magnitude do not imply lack of causality and may be important if the disease or exposure is common. Associations that are replicated in several studies of the same design or that use different epidemiological approaches or under

different circumstances of exposure are more likely to represent a causal relationship than isolated observations from single studies. If there are inconsistent results among investigations, possible reasons are sought (such as differences in exposure), and results of studies that are judged to be of high quality are given more weight than those of studies that are judged to be methodologically less sound.

If the risk increases with the exposure, this is considered to be a strong indication of causality, although the absence of a graded response is not necessarily evidence against a causal relationship. The demonstration of a decline in risk after cessation of or reduction in exposure in individuals or in whole populations also supports a causal interpretation of the findings.

A number of scenarios may increase confidence in a causal relationship. On the one hand, an agent may be specific in causing tumours at one site or of one morphological type. On the other, carcinogenicity may be evident through the causation of multiple tumour types. Temporality, precision of estimates of effect, biological plausibility and coherence of the overall database are considered. Data on biomarkers may be employed in an assessment of the biological plausibility of epidemiological observations.

Although rarely available, results from randomized trials that show different rates of cancer among exposed and unexposed individuals provide particularly strong evidence for causality.

When several epidemiological studies show little or no indication of an association between an exposure and cancer, a judgement may be made that, in the aggregate, they show evidence of lack of carcinogenicity. Such a judgement requires firstly that the studies meet, to a sufficient degree, the standards of design and analysis described above. Specifically, the possibility that bias, confounding or misclassification of exposure or outcome could explain the observed results should be considered and excluded with reasonable certainty. In addition, all studies that are judged to be methodologically sound should (a) be consistent with an estimate of effect of unity for any observed level of exposure, (b) when considered together, provide a pooled estimate of relative risk that is at or near to unity, and (c) have a narrow confidence interval, due to sufficient population size. Moreover, no individual study nor the pooled results of all the studies should show any consistent tendency that the relative risk of cancer increases with increasing level of exposure. It is important to note that evidence of lack of carcinogenicity obtained from several epidemiological studies can apply only to the type(s) of cancer studied, to the dose levels reported, and to the intervals between first exposure and disease onset observed in these studies. Experience with human cancer indicates that the period from first exposure to the development of clinical cancer is sometimes longer than 20 years; latent periods substantially shorter than 30 years cannot provide evidence for lack of carcinogenicity.

3. Studies of cancer in experimental animals

All known human carcinogens that have been studied adequately for carcinogenicity in experimental animals have produced positive results in one or more animal species

(Wilbourn *et al.*, 1986; Tomatis *et al.*, 1989). For several agents (e.g. aflatoxins, diethylstilbestrol, solar radiation, vinyl chloride), carcinogenicity in experimental animals was established or highly suspected before epidemiological studies confirmed their carcinogenicity in humans (Vainio *et al.*, 1995). Although this association cannot establish that all agents that cause cancer in experimental animals also cause cancer in humans, it is biologically plausible that agents for which there is *sufficient evidence of carcinogenicity* in experimental animals (see Part B, Section 6b) also present a carcinogenic hazard to humans. Accordingly, in the absence of additional scientific information, these agents are considered to pose a carcinogenic hazard to humans. Examples of additional scientific information are data that demonstrate that a given agent causes cancer in animals through a species-specific mechanism that does not operate in humans or data that demonstrate that the mechanism in experimental animals also operates in humans (see Part B, Section 6).

Consideration is given to all available long-term studies of cancer in experimental animals with the agent under review (see Part A, Section 4). In all experimental settings, the nature and extent of impurities or contaminants present in the agent being evaluated are given when available. Animal species, strain (including genetic background where applicable), sex, numbers per group, age at start of treatment, route of exposure, dose levels, duration of exposure, survival and information on tumours (incidence, latency, severity or multiplicity of neoplasms or preneoplastic lesions) are reported. Those studies in experimental animals that are judged to be irrelevant to the evaluation or judged to be inadequate (e.g. too short a duration, too few animals, poor survival; see below) may be omitted. Guidelines for conducting long-term carcinogenicity experiments have been published (e.g. OECD, 2002).

Other studies considered may include: experiments in which the agent was administered in the presence of factors that modify carcinogenic effects (e.g. initiation–promotion studies, co-carcinogenicity studies and studies in genetically modified animals); studies in which the end-point was not cancer but a defined precancerous lesion; experiments on the carcinogenicity of known metabolites and derivatives; and studies of cancer in non-laboratory animals (e.g. livestock and companion animals) exposed to the agent.

For studies of mixtures, consideration is given to the possibility that changes in the physicochemical properties of the individual substances may occur during collection, storage, extraction, concentration and delivery. Another consideration is that chemical and toxicological interactions of components in a mixture may alter dose–response relationships. The relevance to human exposure of the test mixture administered in the animal experiment is also assessed. This may involve consideration of the following aspects of the mixture tested: (i) physical and chemical characteristics, (ii) identified constituents that may indicate the presence of a class of substances and (iii) the results of genetic toxicity and related tests.

The relevance of results obtained with an agent that is analogous (e.g. similar in structure or of a similar virus genus) to that being evaluated is also considered. Such results may provide biological and mechanistic information that is relevant to the

understanding of the process of carcinogenesis in humans and may strengthen the biological plausibility that the agent being evaluated is carcinogenic to humans (see Part B, Section 2f).

(*a*) *Qualitative aspects*

An assessment of carcinogenicity involves several considerations of qualitative importance, including (i) the experimental conditions under which the test was performed, including route, schedule and duration of exposure, species, strain (including genetic background where applicable), sex, age and duration of follow-up; (ii) the consistency of the results, for example, across species and target organ(s); (iii) the spectrum of neoplastic response, from preneoplastic lesions and benign tumours to malignant neoplasms; and (iv) the possible role of modifying factors.

Considerations of importance in the interpretation and evaluation of a particular study include: (i) how clearly the agent was defined and, in the case of mixtures, how adequately the sample characterization was reported; (ii) whether the dose was monitored adequately, particularly in inhalation experiments; (iii) whether the doses, duration of treatment and route of exposure were appropriate; (iv) whether the survival of treated animals was similar to that of controls; (v) whether there were adequate numbers of animals per group; (vi) whether both male and female animals were used; (vii) whether animals were allocated randomly to groups; (viii) whether the duration of observation was adequate; and (ix) whether the data were reported and analysed adequately.

When benign tumours (a) occur together with and originate from the same cell type as malignant tumours in an organ or tissue in a particular study and (b) appear to represent a stage in the progression to malignancy, they are usually combined in the assessment of tumour incidence (Huff *et al.*, 1989). The occurrence of lesions presumed to be preneoplastic may in certain instances aid in assessing the biological plausibility of any neoplastic response observed. If an agent induces only benign neoplasms that appear to be end-points that do not readily undergo transition to malignancy, the agent should nevertheless be suspected of being carcinogenic and requires further investigation.

(*b*) *Quantitative aspects*

The probability that tumours will occur may depend on the species, sex, strain, genetic background and age of the animal, and on the dose, route, timing and duration of the exposure. Evidence of an increased incidence of neoplasms with increasing levels of exposure strengthens the inference of a causal association between the exposure and the development of neoplasms.

The form of the dose–response relationship can vary widely, depending on the particular agent under study and the target organ. Mechanisms such as induction of DNA damage or inhibition of repair, altered cell division and cell death rates and changes in intercellular communication are important determinants of dose–response relationships for some carcinogens. Since many chemicals require metabolic activation before being

converted to their reactive intermediates, both metabolic and toxicokinetic aspects are important in determining the dose–response pattern. Saturation of steps such as absorption, activation, inactivation and elimination may produce non-linearity in the dose–response relationship (Hoel *et al.*, 1983; Gart *et al.*, 1986), as could saturation of processes such as DNA repair. The dose–response relationship can also be affected by differences in survival among the treatment groups.

(*c*) *Statistical analyses*

Factors considered include the adequacy of the information given for each treatment group: (i) number of animals studied and number examined histologically, (ii) number of animals with a given tumour type and (iii) length of survival. The statistical methods used should be clearly stated and should be the generally accepted techniques refined for this purpose (Peto *et al.*, 1980; Gart *et al.*, 1986; Portier & Bailer, 1989; Bieler & Williams, 1993). The choice of the most appropriate statistical method requires consideration of whether or not there are differences in survival among the treatment groups; for example, reduced survival because of non-tumour-related mortality can preclude the occurrence of tumours later in life. When detailed information on survival is not available, comparisons of the proportions of tumour-bearing animals among the effective number of animals (alive at the time the first tumour was discovered) can be useful when significant differences in survival occur before tumours appear. The lethality of the tumour also requires consideration: for rapidly fatal tumours, the time of death provides an indication of the time of tumour onset and can be assessed using life-table methods; non-fatal or incidental tumours that do not affect survival can be assessed using methods such as the Mantel-Haenzel test for changes in tumour prevalence. Because tumour lethality is often difficult to determine, methods such as the Poly-K test that do not require such information can also be used. When results are available on the number and size of tumours seen in experimental animals (e.g. papillomas on mouse skin, liver tumours observed through nuclear magnetic resonance tomography), other more complicated statistical procedures may be needed (Sherman *et al.*, 1994; Dunson *et al.*, 2003).

Formal statistical methods have been developed to incorporate historical control data into the analysis of data from a given experiment. These methods assign an appropriate weight to historical and concurrent controls on the basis of the extent of between-study and within-study variability: less weight is given to historical controls when they show a high degree of variability, and greater weight when they show little variability. It is generally not appropriate to discount a tumour response that is significantly increased compared with concurrent controls by arguing that it falls within the range of historical controls, particularly when historical controls show high between-study variability and are, thus, of little relevance to the current experiment. In analysing results for uncommon tumours, however, the analysis may be improved by considering historical control data, particularly when between-study variability is low. Historical controls should be selected to resemble the concurrent controls as closely as possible with respect to species, gender and strain, as well as other factors such as basal diet and general laboratory environment,

which may affect tumour-response rates in control animals (Haseman *et al.*, 1984; Fung *et al.*, 1996; Greim *et al.*, 2003).

Although meta-analyses and combined analyses are conducted less frequently for animal experiments than for epidemiological studies due to differences in animal strains, they can be useful aids in interpreting animal data when the experimental protocols are sufficiently similar.

4. Mechanistic and other relevant data

Mechanistic and other relevant data may provide evidence of carcinogenicity and also help in assessing the relevance and importance of findings of cancer in animals and in humans. The nature of the mechanistic and other relevant data depends on the biological activity of the agent being considered. The Working Group considers representative studies to give a concise description of the relevant data and issues that they consider to be important; thus, not every available study is cited. Relevant topics may include toxicokinetics, mechanisms of carcinogenesis, susceptible individuals, populations and life-stages, other relevant data and other adverse effects. When data on biomarkers are informative about the mechanisms of carcinogenesis, they are included in this section.

These topics are not mutually exclusive; thus, the same studies may be discussed in more than one subsection. For example, a mutation in a gene that codes for an enzyme that metabolizes the agent under study could be discussed in the subsections on toxicokinetics, mechanisms and individual susceptibility if it also exists as an inherited polymorphism.

(*a*) *Toxicokinetic data*

Toxicokinetics refers to the absorption, distribution, metabolism and elimination of agents in humans, experimental animals and, where relevant, cellular systems. Examples of kinetic factors that may affect dose–response relationships include uptake, deposition, biopersistence and half-life in tissues, protein binding, metabolic activation and detoxification. Studies that indicate the metabolic fate of the agent in humans and in experimental animals are summarized briefly, and comparisons of data from humans and animals are made when possible. Comparative information on the relationship between exposure and the dose that reaches the target site may be important for the extrapolation of hazards between species and in clarifying the role of in-vitro findings.

(*b*) *Data on mechanisms of carcinogenesis*

To provide focus, the Working Group attempts to identify the possible mechanisms by which the agent may increase the risk of cancer. For each possible mechanism, a representative selection of key data from humans and experimental systems is summarized. Attention is given to gaps in the data and to data that suggests that more than one mechanism may be operating. The relevance of the mechanism to humans is discussed, in

particular, when mechanistic data are derived from experimental model systems. Changes in the affected organs, tissues or cells can be divided into three non-exclusive levels as described below.

(i) *Changes in physiology*

Physiological changes refer to exposure-related modifications to the physiology and/or response of cells, tissues and organs. Examples of potentially adverse physiological changes include mitogenesis, compensatory cell division, escape from apoptosis and/or senescence, presence of inflammation, hyperplasia, metaplasia and/or preneoplasia, angiogenesis, alterations in cellular adhesion, changes in steroidal hormones and changes in immune surveillance.

(ii) *Functional changes at the cellular level*

Functional changes refer to exposure-related alterations in the signalling pathways used by cells to manage critical processes that are related to increased risk for cancer. Examples of functional changes include modified activities of enzymes involved in the metabolism of xenobiotics, alterations in the expression of key genes that regulate DNA repair, alterations in cyclin-dependent kinases that govern cell cycle progression, changes in the patterns of post-translational modifications of proteins, changes in regulatory factors that alter apoptotic rates, changes in the secretion of factors related to the stimulation of DNA replication and transcription and changes in gap–junction-mediated intercellular communication.

(iii) *Changes at the molecular level*

Molecular changes refer to exposure-related changes in key cellular structures at the molecular level, including, in particular, genotoxicity. Examples of molecular changes include formation of DNA adducts and DNA strand breaks, mutations in genes, chromosomal aberrations, aneuploidy and changes in DNA methylation patterns. Greater emphasis is given to irreversible effects.

The use of mechanistic data in the identification of a carcinogenic hazard is specific to the mechanism being addressed and is not readily described for every possible level and mechanism discussed above.

Genotoxicity data are discussed here to illustrate the key issues involved in the evaluation of mechanistic data.

Tests for genetic and related effects are described in view of the relevance of gene mutation and chromosomal aberration/aneuploidy to carcinogenesis (Vainio *et al*., 1992; McGregor *et al*., 1999). The adequacy of the reporting of sample characterization is considered and, when necessary, commented upon; with regard to complex mixtures, such comments are similar to those described for animal carcinogenicity tests. The available data are interpreted critically according to the end-points detected, which may include DNA damage, gene mutation, sister chromatid exchange, micronucleus formation, chromosomal aberrations and

aneuploidy. The concentrations employed are given, and mention is made of whether the use of an exogenous metabolic system *in vitro* affected the test result. These data are listed in tabular form by phylogenetic classification.

Positive results in tests using prokaryotes, lower eukaryotes, insects, plants and cultured mammalian cells suggest that genetic and related effects could occur in mammals. Results from such tests may also give information on the types of genetic effect produced and on the involvement of metabolic activation. Some end-points described are clearly genetic in nature (e.g. gene mutations), while others are associated with genetic effects (e.g. unscheduled DNA synthesis). In-vitro tests for tumour promotion, cell transformation and gap–junction intercellular communication may be sensitive to changes that are not necessarily the result of genetic alterations but that may have specific relevance to the process of carcinogenesis. Critical appraisals of these tests have been published (Montesano *et al*., 1986; McGregor *et al*., 1999).

Genetic or other activity manifest in humans and experimental mammals is regarded to be of greater relevance than that in other organisms. The demonstration that an agent can induce gene and chromosomal mutations in mammals *in vivo* indicates that it may have carcinogenic activity. Negative results in tests for mutagenicity in selected tissues from animals treated *in vivo* provide less weight, partly because they do not exclude the possibility of an effect in tissues other than those examined. Moreover, negative results in short-term tests with genetic end-points cannot be considered to provide evidence that rules out the carcinogenicity of agents that act through other mechanisms (e.g. receptor-mediated effects, cellular toxicity with regenerative cell division, peroxisome proliferation) (Vainio *et al*., 1992). Factors that may give misleading results in short-term tests have been discussed in detail elsewhere (Montesano *et al*., 1986; McGregor *et al*., 1999).

When there is evidence that an agent acts by a specific mechanism that does not involve genotoxicity (e.g. hormonal dysregulation, immune suppression, and formation of calculi and other deposits that cause chronic irritation), that evidence is presented and reviewed critically in the context of rigorous criteria for the operation of that mechanism in carcinogenesis (e.g. Capen *et al.*, 1999).

For biological agents such as viruses, bacteria and parasites, other data relevant to carcinogenicity may include descriptions of the pathology of infection, integration and expression of viruses, and genetic alterations seen in human tumours. Other observations that might comprise cellular and tissue responses to infection, immune response and the presence of tumour markers are also considered.

For physical agents that are forms of radiation, other data relevant to carcinogenicity may include descriptions of damaging effects at the physiological, cellular and molecular level, as for chemical agents, and descriptions of how these effects occur. 'Physical agents' may also be considered to comprise foreign bodies, such as surgical implants of various kinds, and poorly soluble fibres, dusts and particles of various sizes, the patho-

genic effects of which are a result of their physical presence in tissues or body cavities. Other relevant data for such materials may include characterization of cellular, tissue and physiological reactions to these materials and descriptions of pathological conditions other than neoplasia with which they may be associated.

(*c*) *Other data relevant to mechanisms*

A description is provided of any structure–activity relationships that may be relevant to an evaluation of the carcinogenicity of an agent, the toxicological implications of the physical and chemical properties, and any other data relevant to the evaluation that are not included elsewhere.

High-output data, such as those derived from gene expression microarrays, and high-throughput data, such as those that result from testing hundreds of agents for a single end-point, pose a unique problem for the use of mechanistic data in the evaluation of a carcinogenic hazard. In the case of high-output data, there is the possibility to overinterpret changes in individual end-points (e.g. changes in expression in one gene) without considering the consistency of that finding in the broader context of the other end-points (e.g. other genes with linked transcriptional control). High-output data can be used in assessing mechanisms, but all end-points measured in a single experiment need to be considered in the proper context. For high-throughput data, where the number of observations far exceeds the number of end-points measured, their utility for identifying common mechanisms across multiple agents is enhanced. These data can be used to identify mechanisms that not only seem plausible, but also have a consistent pattern of carcinogenic response across entire classes of related compounds.

(*d*) *Susceptibility data*

Individuals, populations and life-stages may have greater or lesser susceptibility to an agent, based on toxicokinetics, mechanisms of carcinogenesis and other factors. Examples of host and genetic factors that affect individual susceptibility include sex, genetic polymorphisms of genes involved in the metabolism of the agent under evaluation, differences in metabolic capacity due to life-stage or the presence of disease, differences in DNA repair capacity, competition for or alteration of metabolic capacity by medications or other chemical exposures, pre-existing hormonal imbalance that is exacerbated by a chemical exposure, a suppressed immune system, periods of higher-than-usual tissue growth or regeneration and genetic polymorphisms that lead to differences in behaviour (e.g. addiction). Such data can substantially increase the strength of the evidence from epidemiological data and enhance the linkage of in-vivo and in-vitro laboratory studies to humans.

(*e*) *Data on other adverse effects*

Data on acute, subchronic and chronic adverse effects relevant to the cancer evaluation are summarized. Adverse effects that confirm distribution and biological effects at

the sites of tumour development, or alterations in physiology that could lead to tumour development, are emphasized. Effects on reproduction, embryonic and fetal survival and development are summarized briefly. The adequacy of epidemiological studies of reproductive outcome and genetic and related effects in humans is judged by the same criteria as those applied to epidemiological studies of cancer, but fewer details are given.

5. Summary

This section is a summary of data presented in the preceding sections. Summaries can be found on the *Monographs* programme website (http://monographs.iarc.fr).

(*a*) *Exposure data*

Data are summarized, as appropriate, on the basis of elements such as production, use, occurrence and exposure levels in the workplace and environment and measurements in human tissues and body fluids. Quantitative data and time trends are given to compare exposures in different occupations and environmental settings. Exposure to biological agents is described in terms of transmission, prevalence and persistence of infection.

(*b*) *Cancer in humans*

Results of epidemiological studies pertinent to an assessment of human carcinogenicity are summarized. When relevant, case reports and correlation studies are also summarized. The target organ(s) or tissue(s) in which an increase in cancer was observed is identified. Dose–response and other quantitative data may be summarized when available.

(*c*) *Cancer in experimental animals*

Data relevant to an evaluation of carcinogenicity in animals are summarized. For each animal species, study design and route of administration, it is stated whether an increased incidence, reduced latency, or increased severity or multiplicity of neoplasms or preneoplastic lesions were observed, and the tumour sites are indicated. If the agent produced tumours after prenatal exposure or in single-dose experiments, this is also mentioned. Negative findings, inverse relationships, dose–response and other quantitative data are also summarized.

(*d*) *Mechanistic and other relevant data*

Data relevant to the toxicokinetics (absorption, distribution, metabolism, elimination) and the possible mechanism(s) of carcinogenesis (e.g. genetic toxicity, epigenetic effects) are summarized. In addition, information on susceptible individuals, populations and life-stages is summarized. This section also reports on other toxic effects, including reproductive and developmental effects, as well as additional relevant data that are considered to be important.

6. Evaluation and rationale

Evaluations of the strength of the evidence for carcinogenicity arising from human and experimental animal data are made, using standard terms. The strength of the mechanistic evidence is also characterized.

It is recognized that the criteria for these evaluations, described below, cannot encompass all of the factors that may be relevant to an evaluation of carcinogenicity. In considering all of the relevant scientific data, the Working Group may assign the agent to a higher or lower category than a strict interpretation of these criteria would indicate.

These categories refer only to the strength of the evidence that an exposure is carcinogenic and not to the extent of its carcinogenic activity (potency). A classification may change as new information becomes available.

An evaluation of the degree of evidence is limited to the materials tested, as defined physically, chemically or biologically. When the agents evaluated are considered by the Working Group to be sufficiently closely related, they may be grouped together for the purpose of a single evaluation of the degree of evidence.

(*a*) *Carcinogenicity in humans*

The evidence relevant to carcinogenicity from studies in humans is classified into one of the following categories:

***Sufficient evidence of carcinogenicity*:** The Working Group considers that a causal relationship has been established between exposure to the agent and human cancer. That is, a positive relationship has been observed between the exposure and cancer in studies in which chance, bias and confounding could be ruled out with reasonable confidence. A statement that there is *sufficient evidence* is followed by a separate sentence that identifies the target organ(s) or tissue(s) where an increased risk of cancer was observed in humans. Identification of a specific target organ or tissue does not preclude the possibility that the agent may cause cancer at other sites.

***Limited evidence of carcinogenicity*:** A positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.

***Inadequate evidence of carcinogenicity*:** The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal association between exposure and cancer, or no data on cancer in humans are available.

***Evidence suggesting lack of carcinogenicity*:** There are several adequate studies covering the full range of levels of exposure that humans are known to encounter, which are mutually consistent in not showing a positive association between exposure to the agent and any studied cancer at any observed level of exposure. The results from

these studies alone or combined should have narrow confidence intervals with an upper limit close to the null value (e.g. a relative risk of 1.0). Bias and confounding should be ruled out with reasonable confidence, and the studies should have an adequate length of follow-up. A conclusion of *evidence suggesting lack of carcinogenicity* is inevitably limited to the cancer sites, conditions and levels of exposure, and length of observation covered by the available studies. In addition, the possibility of a very small risk at the levels of exposure studied can never be excluded.

In some instances, the above categories may be used to classify the degree of evidence related to carcinogenicity in specific organs or tissues.

When the available epidemiological studies pertain to a mixture, process, occupation or industry, the Working Group seeks to identify the specific agent considered most likely to be responsible for any excess risk. The evaluation is focused as narrowly as the available data on exposure and other aspects permit.

(*b*) *Carcinogenicity in experimental animals*

Carcinogenicity in experimental animals can be evaluated using conventional bioassays, bioassays that employ genetically modified animals, and other in-vivo bioassays that focus on one or more of the critical stages of carcinogenesis. In the absence of data from conventional long-term bioassays or from assays with neoplasia as the end-point, consistently positive results in several models that address several stages in the multistage process of carcinogenesis should be considered in evaluating the degree of evidence of carcinogenicity in experimental animals.

The evidence relevant to carcinogenicity in experimental animals is classified into one of the following categories:

***Sufficient evidence of carcinogenicity*:** The Working Group considers that a causal relationship has been established between the agent and an increased incidence of malignant neoplasms or of an appropriate combination of benign and malignant neoplasms in (a) two or more species of animals or (b) two or more independent studies in one species carried out at different times or in different laboratories or under different protocols. An increased incidence of tumours in both sexes of a single species in a well-conducted study, ideally conducted under Good Laboratory Practices, can also provide *sufficient evidence*.

A single study in one species and sex might be considered to provide *sufficient evidence of carcinogenicity* when malignant neoplasms occur to an unusual degree with regard to incidence, site, type of tumour or age at onset, or when there are strong findings of tumours at multiple sites.

***Limited evidence of carcinogenicity*:** The data suggest a carcinogenic effect but are limited for making a definitive evaluation because, e.g. (a) the evidence of carcinogenicity is restricted to a single experiment; (b) there are unresolved questions regarding the adequacy of the design, conduct or interpretation of the studies; (c) the agent

increases the incidence only of benign neoplasms or lesions of uncertain neoplastic potential; or (d) the evidence of carcinogenicity is restricted to studies that demonstrate only promoting activity in a narrow range of tissues or organs.

***Inadequate evidence of carcinogenicity*:** The studies cannot be interpreted as showing either the presence or absence of a carcinogenic effect because of major qualitative or quantitative limitations, or no data on cancer in experimental animals are available.

***Evidence suggesting lack of carcinogenicity*:** Adequate studies involving at least two species are available which show that, within the limits of the tests used, the agent is not carcinogenic. A conclusion of *evidence suggesting lack of carcinogenicity* is inevitably limited to the species, tumour sites, age at exposure, and conditions and levels of exposure studied.

(*c*) *Mechanistic and other relevant data*

Mechanistic and other evidence judged to be relevant to an evaluation of carcinogenicity and of sufficient importance to affect the overall evaluation is highlighted. This may include data on preneoplastic lesions, tumour pathology, genetic and related effects, structure–activity relationships, metabolism and toxicokinetics, physicochemical parameters and analogous biological agents.

The strength of the evidence that any carcinogenic effect observed is due to a particular mechanism is evaluated, using terms such as 'weak', 'moderate' or 'strong'. The Working Group then assesses whether that particular mechanism is likely to be operative in humans. The strongest indications that a particular mechanism operates in humans derive from data on humans or biological specimens obtained from exposed humans. The data may be considered to be especially relevant if they show that the agent in question has caused changes in exposed humans that are on the causal pathway to carcinogenesis. Such data may, however, never become available, because it is at least conceivable that certain compounds may be kept from human use solely on the basis of evidence of their toxicity and/or carcinogenicity in experimental systems.

The conclusion that a mechanism operates in experimental animals is strengthened by findings of consistent results in different experimental systems, by the demonstration of biological plausibility and by coherence of the overall database. Strong support can be obtained from studies that challenge the hypothesized mechanism experimentally, by demonstrating that the suppression of key mechanistic processes leads to the suppression of tumour development. The Working Group considers whether multiple mechanisms might contribute to tumour development, whether different mechanisms might operate in different dose ranges, whether separate mechanisms might operate in humans and experimental animals and whether a unique mechanism might operate in a susceptible group. The possible contribution of alternative mechanisms must be considered before concluding that tumours observed in experimental animals are not relevant to humans. An uneven level of experimental support for different mechanisms may reflect that disproportionate resources have been focused on investigating a favoured mechanism.

For complex exposures, including occupational and industrial exposures, the chemical composition and the potential contribution of carcinogens known to be present are considered by the Working Group in its overall evaluation of human carcinogenicity. The Working Group also determines the extent to which the materials tested in experimental systems are related to those to which humans are exposed.

(*d*) *Overall evaluation*

Finally, the body of evidence is considered as a whole, in order to reach an overall evaluation of the carcinogenicity of the agent to humans.

An evaluation may be made for a group of agents that have been evaluated by the Working Group. In addition, when supporting data indicate that other related agents, for which there is no direct evidence of their capacity to induce cancer in humans or in animals, may also be carcinogenic, a statement describing the rationale for this conclusion is added to the evaluation narrative; an additional evaluation may be made for this broader group of agents if the strength of the evidence warrants it.

The agent is described according to the wording of one of the following categories, and the designated group is given. The categorization of an agent is a matter of scientific judgement that reflects the strength of the evidence derived from studies in humans and in experimental animals and from mechanistic and other relevant data.

Group 1: The agent is *carcinogenic to humans*.

This category is used when there is *sufficient evidence of carcinogenicity* in humans. Exceptionally, an agent may be placed in this category when evidence of carcinogenicity in humans is less than *sufficient* but there is *sufficient evidence of carcinogenicity* in experimental animals and strong evidence in exposed humans that the agent acts through a relevant mechanism of carcinogenicity.

Group 2.

This category includes agents for which, at one extreme, the degree of evidence of carcinogenicity in humans is almost *sufficient*, as well as those for which, at the other extreme, there are no human data but for which there is evidence of carcinogenicity in experimental animals. Agents are assigned to either Group 2A (*probably carcinogenic to humans*) or Group 2B (*possibly carcinogenic to humans*) on the basis of epidemiological and experimental evidence of carcinogenicity and mechanistic and other relevant data. The terms *probably carcinogenic* and *possibly carcinogenic* have no quantitative significance and are used simply as descriptors of different levels of evidence of human carcinogenicity, with *probably carcinogenic* signifying a higher level of evidence than *possibly carcinogenic*.

Group 2A: The agent is *probably carcinogenic to humans*.

This category is used when there is *limited evidence of carcinogenicity* in humans and *sufficient evidence of carcinogenicity* in experimental animals. In some cases, an agent may be classified in this category when there is *inadequate evidence of carcino-*

genicity in humans and *sufficient evidence of carcinogenicity* in experimental animals and strong evidence that the carcinogenesis is mediated by a mechanism that also operates in humans. Exceptionally, an agent may be classified in this category solely on the basis of *limited evidence of carcinogenicity* in humans. An agent may be assigned to this category if it clearly belongs, based on mechanistic considerations, to a class of agents for which one or more members have been classified in Group 1 or Group 2A.

Group 2B: The agent is *possibly carcinogenic to humans*.

This category is used for agents for which there is *limited evidence of carcinogenicity* in humans and less than *sufficient evidence of carcinogenicity* in experimental animals. It may also be used when there is *inadequate evidence of carcinogenicity* in humans but there is *sufficient evidence of carcinogenicity* in experimental animals. In some instances, an agent for which there is *inadequate evidence of carcinogenicity* in humans and less than *sufficient evidence of carcinogenicity* in experimental animals together with supporting evidence from mechanistic and other relevant data may be placed in this group. An agent may be classified in this category solely on the basis of strong evidence from mechanistic and other relevant data.

Group 3: The agent is *not classifiable as to its carcinogenicity to humans*.

This category is used most commonly for agents for which the evidence of carcinogenicity is *inadequate* in humans and *inadequate* or *limited* in experimental animals.

Exceptionally, agents for which the evidence of carcinogenicity is *inadequate* in humans but *sufficient* in experimental animals may be placed in this category when there is strong evidence that the mechanism of carcinogenicity in experimental animals does not operate in humans.

Agents that do not fall into any other group are also placed in this category.

An evaluation in Group 3 is not a determination of non-carcinogenicity or overall safety. It often means that further research is needed, especially when exposures are widespread or the cancer data are consistent with differing interpretations.

Group 4: The agent is *probably not carcinogenic to humans*.

This category is used for agents for which there is *evidence suggesting lack of carcinogenicity* in humans and in experimental animals. In some instances, agents for which there is *inadequate evidence of carcinogenicity* in humans but *evidence suggesting lack of carcinogenicity* in experimental animals, consistently and strongly supported by a broad range of mechanistic and other relevant data, may be classified in this group.

(*e*) *Rationale*

The reasoning that the Working Group used to reach its evaluation is presented and discussed. This section integrates the major findings from studies of cancer in humans,

studies of cancer in experimental animals, and mechanistic and other relevant data. It includes concise statements of the principal line(s) of argument that emerged, the conclusions of the Working Group on the strength of the evidence for each group of studies, citations to indicate which studies were pivotal to these conclusions, and an explanation of the reasoning of the Working Group in weighing data and making evaluations. When there are significant differences of scientific interpretation among Working Group Members, a brief summary of the alternative interpretations is provided, together with their scientific rationale and an indication of the relative degree of support for each alternative.

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GENERAL REMARKS

This ninety-fifth volume of *IARC Monographs* considers household use of solid fuels for heating and cooking, a practice that can generate substantial quantities of indoor air pollution. The World Health Report 2002 identified indoor smoke from solid fuels as one of the top ten risks in terms of the global burden of disease (WHO, 2002). This health burden occurs almost exclusively in low-to-medium-resource countries, as solid fuels (e.g. wood, other biomass, and coal) are typically used only when other fuels are not available or not affordable.

An Advisory Group on priorities for future evaluations had recommended that IARC review indoor air pollution with high priority (IARC, 2003). This was reaffirmed and refined by a subsequent Advisory Group convened to plan a series of *Monographs* on air pollution. The first two volumes of this series, Volume 92 on polycyclic aromatic hydrocarbons and Volume 93 on low-solubility low-toxicity particles, evaluated these two major components of emissions from household use of solid fuels, and this volume builds on those reviews.

Some epidemiological studies of household solid-fuel use also reported data on cooking methods as a potentially confounding factor. Because many of these studies were conducted in countries where common cooking practices include stir-frying, deep-frying, and pan-frying, the results provide a basis for evaluating the potential carcinogenic hazard of high-temperature frying. Accordingly, this volume includes a second *Monograph* on the subject. High-temperature frying occurs in a wide range of populations living in low-, medium-, and high-resource countries.

Emissions from household use of solid fuels are complex mixtures containing thousands of chemical compounds at varying concentrations, and these may be admixed and adsorbed to particulate matter of widely varying dimensions. Accordingly, careful consideration must be given in using the available studies to make inferences about risks in other exposure circumstances. For example, do the results on household use of coal apply only to the specific sources of coal that were studied, or does other information make it reasonable to apply these results to other types of coal or even to other types of fuel? In making these determinations, it is necessary to consider the degree of similarity of the varying emissions mixtures, with respect both to composition and to biological activity. The Working Group spent much time discussing how narrowly or broadly to interpret the available studies. In doing this, data on the composition and the genetic toxicity of various mixtures were important in different ways.

The adverse health effects caused by household practices considered in this volume may be attributable primarily to products of incomplete combustion. In addition, the emissions from these solid-fuel stoves contain many chemical components known or likely to cause cancer in humans. Some of these are known to cause cancer outside the respiratory tract (e.g., benzene is causally associated with an increased risk of leukaemia). As the available epidemiological studies on household use of solid fuels did not examine these other cancers, the full burden of disease is not yet known and merits further investigation.

It is curious that although the most commonly used solid fuels are wood and other biomass, few epidemiological studies and cancer bioassays have investigated their potential cancer risks. The utility of further research is magnified by the high concentrations of emissions that can occur and by data showing that wood smoke is mutagenic in exposed humans.

A summary of the findings of this volume appears in *The Lancet Oncology* (Straif *et al.*, 2006).

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THE MONOGRAPHS

HOUSEHOLD USE OF SOLID FUELS

HOUSEHOLD USE OF SOLID FUELS

1. Exposure Data

1.1 Description and determinants of use of household fuels

1.1.1 *Introduction*

All over the developing world, meals are cooked and homes are treated with home-made traditional stoves or open fires. These stoves are fired with either biomass fuels, such as wood, branches, twigs or dung, or coal. When these are not available, agricultural residues or even leaves and grass are used. The smoke emitted from such stoves is made up of particles and gaseous chemicals. It is estimated that as many as 70% of households in developing countries use fuels such as wood, dung and crop residues for cooking (International Energy Agency, 2002; WHO, 2006). The seemingly 'free' availability of biomass fuels from nature makes them the primary fuel source for household purposes.

The problems related to the use of biomass as an energy source have been an issue of concern for more than three decades. The traditional stoves commonly used for burning biomass energy have long been found to be highly inefficient and to emit copious quantities of smoke due to the incomplete combustion of fuels. This inefficiency has also had consequences on the environment, since intense collection of fuelwood has resulted in deforestation in highly populated areas. The use of such fuels has also adversely affected health. In addition, the cost involved in terms of human energy and time required to collect and process such fuel has serious implications for productivity and gender equity.

Attempts to convert households from these fuels to modern fuels or from traditional stoves to more efficient and cleaner burning stoves through reform of the energy sector or indigenous innovative technology have been very effective in some countries, but dismal or non-existent in others. This section provides a description of the various fuels and some background on their energy content and the efficiency of their use. Thereafter, the current trends and the known determinants that explain the widespread use of biomass fuels and coal are reviewed. Since indoor air pollution from the use of biomass and coal in the

domestic sector is largely a phenomenon of the developing world, emphasis is mainly on these countries.

1.1.2 *Description of household fuels*

(a) Types of solid fuel

A wide variety of fuels are used in households in developing countries for cooking and heating. Solid fuels refer to both biomass fuels and coal. The most common fuel used for cooking and heating is wood, followed by other solid biomass fuels, such as charcoal, dung, agricultural residues and sometimes even leaves and grass. These fuels are often collected from the local environment in rural areas and are purchased through markets in urban areas.

In some rural areas, farmers who own or manage livestock have the option of using a digester to turn dung and agricultural waste into biogas, which is a fuel that can be used for both heating and/or lighting. Electricity is not commonly used in developing countries for cooking, but is often used for other purposes, such as lighting and powering appliances. In China and some coal-producing regions in India and South Africa, coal is used as a cooking and heating fuel, sometimes in combination with other biomass fuels. Raw coal may be used in many forms from lumps to briquettes to fine powders. Coal may be processed as simply as forming coal balls or cakes by hand followed by sun-drying, or may undergo a sophisticated procedure, such as being blended into a uniform mixture with binders to reduce sulfur and particulate emissions and formed into briquettes designed to burn efficiently and cleanly in special stoves.

Modern fuels include liquefied petroleum gas (LPG), kerosene and electricity.

(b) Energy density and efficiency of fuels

Fuels differ in their energy densities and efficiency (Table 1.1). Modern fuels such as LPG have the highest energy content per kilogram of fuel at approximately 45 MJ/kg. In contrast, crop residues and dung have energy densities of about 14 MJ/kg of fuel. The efficiency of a fuel is measured by the amount of energy used for cooking compared with that which escapes from the stove without actually heating the food. The efficiency of cooking with LPG is estimated to be approximately 60% compared with only 12% for agricultural residues burnt in traditional stoves. This is one of the reasons that commercial fuels such as LPG are considered to be superior to crop residue and dung (see below). Coal is a highly variable fuel, and ranges from anthracite with a high heating value anthracite through various forms of bituminous coal to lignite and peat. Each of these types of coal can contain different levels of moisture, non-combustible inorganic material (ash), sulfur and sometimes significant levels of other impurities, such as arsenic, fluorine, lead and mercury.

All fuels are burned in various types of device to provide the heat necessary for cooking. The device can be relatively efficient or inefficient and be associated with high or low levels of pollution. As indicated in Table 1.1, conversion efficiencies for kerosene

stoves range from 35% for wick stoves to 55% for pressure stoves; those for fuelwood stoves range from 15% for traditional stoves to 25% for improved stoves. Improved stoves have the potential to reduce indoor air pollution levels, to burn wood or other biomass more efficiently and sometimes to reduce average cooking times.

Table 1.1. Typical efficiencies at the final consumption stage of cooking

Fuel source	Energy content (MJ/kg)	Typical conversion efficiency[a] (%)	Useful energy at final consumption stage of cooking (MJ/kg)	Approximate quantity of fuel necessary to provide 5 GJ of useful energy for cooking (kg)
Liquefied petroleum gas	45.5	60	27.3	180
Natural gas	38 [MJ/m^3]	60		219 [m^3]
Kerosene (pressure)	43.0	55	23.6	210
Kerosene (wick)	43.0	35	15.1	330
Biogas (60% methane)	22.8 [MJ/m^3]	60		365 [m^3]
Charcoal (efficient stoves)	30.0	30	9.0	550
Charcoal (traditional stoves)	30.0	20	6.0	830
Bituminous coal	22.5	25	5.6	880
Fuelwood (efficient stoves), 15% moisture	16.0	25	4.0	1250
Fuelwood (traditional stoves), 15% moisture	16.0	15	2.4	2000
Crop residue (straw, leaves, grass), 5% moisture	13.5	12	1.6	3000
Dung, 15% moisture	14.5	12	1.7	2900

From Sullivan & Barnes (2006)

[a] The typical conversion efficiency for charcoal, fuelwood and kerosene is based on their respective stove types.

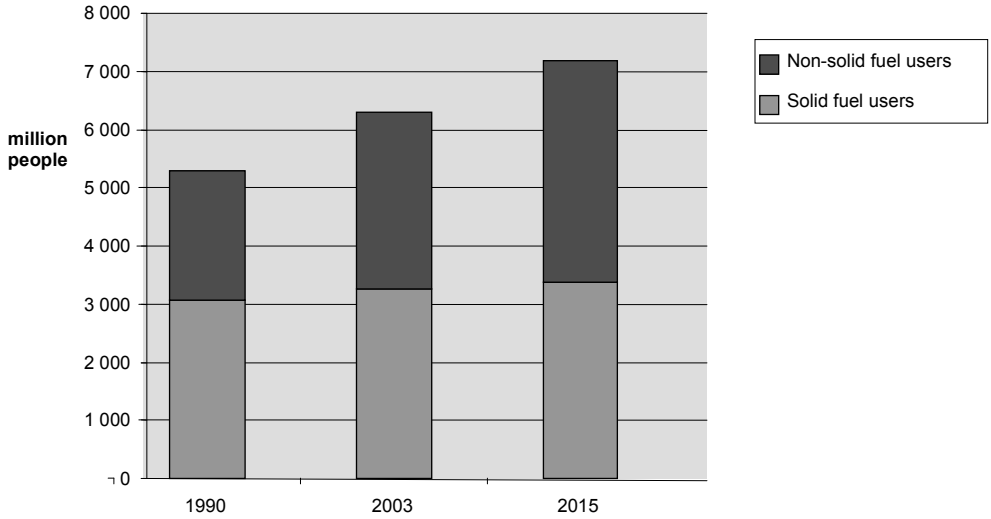
1.1.3 *Use of solid fuels worldwide*

Biomass is often the primary source of household energy in developing countries. Just over three billion people use biomass fuels for cooking and heating in developing countries and approximately 800 million people, mostly in China, use coal. As indicated in Figure 1.1, these statistics have been relatively stable over the last 15–20 years and are expected to continue into the future (WHO, 2006). Thus, it is anticipated that the use of solid fuels and especially biomass fuels will persist for many years to come.

Significant regional variations occur as well as differences between urban and rural areas. The findings that have been collected from national surveys conducted by the

Demographic and Health Surveys (DHS), the World Bank's Livings Standards Measurement Study (LSMS) and other similar studies are presented in Table 1.2. The estimates in Figure 1.2 are averages of main fuel use across the set of countries found in Table 1.2.

Figure 1.1. Population using solid fuels (millions) in 1990, 2003 (mid-point) and 2015



Adapted from WHO (2006) (Figure 14: Trends in solid fuel use)
Data for 2015 are based on:

- a business-as-usual scenario that applies the observed annual increase in the number of people with access to cleaner fuels from 1990 to 2003 to the period 2003–15;
- the voluntary Millennium Development Goal target proposed by the UN Millennium Project to halve the number of people without access to modern cooking fuels between 1990 and 2015.

Table 1.2. Household use of main cooking fuels in selected developing countries, national household surveys 1996–2003

Countries	% Solid fuels[a]			% Modern fuels[a]			Data[b]	
	Rural	Urban	National	Rural	Urban	National	Source	Year
AFRICA								
Benin	98.7	87.5	94.6	1.3	12.5	5.4	DHS	2001
Burundi	99.9	98.1	99.8	0.2	1.9	0.2	EP	1998
Cameroon	98.2	62.2	82.8	1.8	37.8	17.3	ECAM	2001
Eritrea	97.4	30.4	79.7	2.6	69.6	20.3	DHS	1995
Ethiopia	99.9	72.9	95.4	0.1	27.1	4.6	DHS	2000
Ghana	99.4	88.0	95.8	0.6	12.0	4.2	CWIQ	1997
Kenya	94.7	33.8	81.8	5.1	66.1	18.1	CWIQ	1997
Madagascar	98.8	96.2	98.2	1.1	3.7	1.7	EP	1999

Table 1.2. (contd)

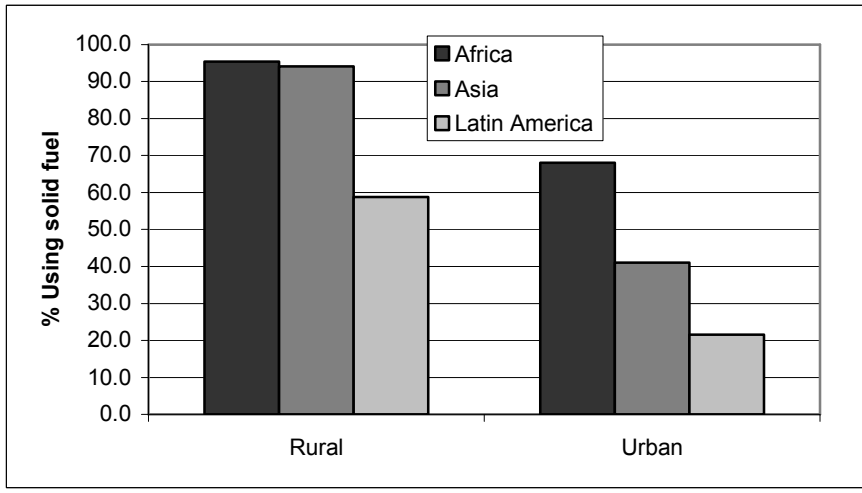
Countries	% Solid fuels[a]			% Modern fuels[a]			Data[b]	
	Rural	Urban	National	Rural	Urban	National	Source	Year
AFRICA (contd)								
Malawi	99.6	83.0	97.4	0.4	17.0	2.6	DHS	2000
Mali	99.8	98.4	97.9	0.2	1.6	0.4	DHS	2001
Niger	98.4	94.8	97.8	1.6	5.2	2.2	EPCES	1995
Nigeria (eight states)	94.2	57.4	85.7	5.9	42.6	14.0	CWIQ	2002
Rwanda	99.9	98.1	99.8	0.1	1.9	0.2	DHS	2000
Uganda	98.7	85.0	96.8	1.3	15.0	3.2	DHS	2001
Zambia	98.1	62.4	85.9	1.9	37.6	14.1	DHS	2001
Zimbabwe	93.6	4.7	59.7	6.4	95.3	40.3	DHS	1999
LATIN AMERICA								
Bolivia	80.4	7.1	34.4	19.6	92.9	65.6	DHS	1998
Brazil	38.3	2.7	9.3	61.7	97.3	90.7	PNAD	1999
Chile								
Colombia	48.2	3.4	19.5	51.8	96.6	80.5	ENH	2000
Costa Rica	23.9	3.6	11.8	76.1	96.4	88.2	EHPM	2000
El Salvador	71.7	17.6	37.9	28.3	82.4	62.1	EHPM	2000
Mexico								
Paraguay	71.3	22.0	43.3	28.7	78.0	56.7	EPH	2000
Uruguay	1.8	0.4	1.1	98.2	99.6	98.9	ECH	2000
Haiti	99.6	91.0	96.4	0.4	9.0	3.6	DHS	2000
Nicaragua	93.3	46.1	64.4	6.8	53.9	35.6	LSMS	2001
ASIA								
India	90.2	29.2	73.7	8.5	66.3	24.3	NSS	2000
Nepal	95.6	39.9	89.7	4.4	60.1	10.3	DHS	2001
Pakistan	95	28	76	5	72	24	HHS	2001
Cambodia	98.7	82.0	96.3	1.3	18.0	3.7	DHS	2000
Indonesia	83.2	20.4	72.2	16.8	79.6	27.8	Ag. Cens.	2003
Papua New Guinea	98.2	34.4	89.6	1.7	65.5	10.3	HHS	1996
Yemen, Republic of	53.1	3.0	41.6	46.9	97.0	58.4	HBS	1998

Ag.Cens., Agricultural Census; CWIQ, Core Welfare Indicators Questionnaire; DHS, Demographic and Health Survey; ECAM, Enquête Camerounaise Auprès des Ménages; ECH, Encuesta Continua de Hogares; EHPM, Encuesta de Hogares de Propositos Multiples; ENH, Encuesta Nacional de Hogares; EP, Enquête Prioritaire; EPCES, Enquête Permanente de Conjoncture Économique et Sociale; EPH, Encuesta Permanente de Hogares; HBS; Household Budget Survey; HHS, Household Survey; LSMS, Living Standards Measurement Study; NSS, National Sample Survey; PNAD, Presquisa Nacional por Amostra de Domicilios
No national survey for China, but other estimates suggest that 50% of urban households have access to LPG.
[a] Most households mix solid and modern fuels.
[b] Surveys involve average of main fuel used.

In Africa, use of biomass is common in both urban and rural areas (Table 1.2; Figure 1.2), and 89% of households in the countries surveyed depend on some type of

solid fuel, which includes both biomass and charcoal. In rural areas of Africa, virtually all households use biomass fuels.

Figure 1.2. Percentage use of solid fuel reported as main household cooking energy in national surveys, 1996–2003

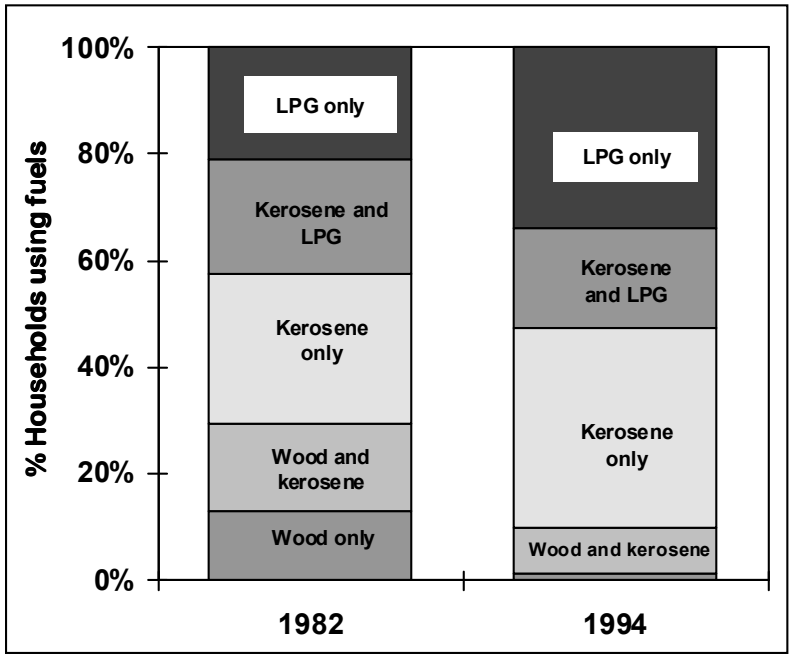


From World Bank (2003)
The figures are based on averages from the countries in Table 1.2.

In Asia, rural areas remain dependent on biomass energy, but many urban areas are increasingly switching to modern fuels (Figure 1.2). Overall, 74% of households in Asia report use of solid fuels, mostly in the form of biomass. However, in countries such as India and China, there are signs of significant change. In a case study in Hyderabad, India (World Bank, 1999; Barnes *et al*., 2005), most urban people in this large metropolitan area had switched to either kerosene or LPG for cooking in the 1990s (Figure 1.3). Recent national figures in India indicate that only about 20–30% of the urban population uses biomass energy, which is a significant change from 25 years ago. While rural areas are still dominated by biomass or other solid fuels, rising urban incomes and policies to facilitate the heterogeneity of modern fuel use in urban areas, including a significant conversion to kerosene and LPG in Asia, have been the main contributory factors to this trend.

The lack of regular national household energy surveys makes it impossible to quantify with confidence the state of household fuel use, but a variety of evidence can be used to establish estimates with some degree of confidence. For example, in China, the overall picture of household fuel use comes from the National Bureau of Statistics, which prepares national and provincial balances of commercial energy, excluding biofuels (e.g. National Bureau of Statistics, 2006), and the Ministry of Agriculture, which collects and occasionally publishes estimates of biofuel use by province (e.g. EBCREY, 1999). Published data do, however, show that more than 51% of urban households have access

Figure 1.3. Changes in choice of household cooking fuel in Hyderabad from 1982 to 1994



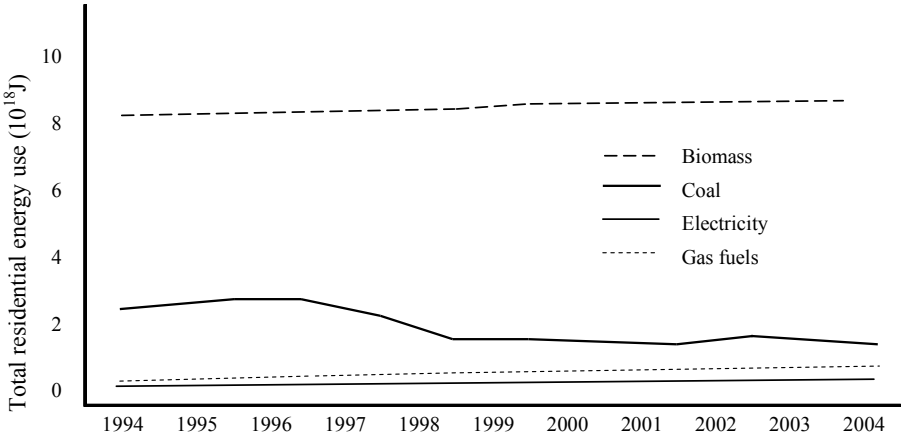
From Barnes *et al*. (2005)
LPG, liquefied petroleum gas

to gas fuels (National Bureau of Statistics, 2005). While access to gas in rural areas is growing, fewer than 10% of rural households use gas fuels as their main cooking fuel (Sinton *et al*., 2004a). All but about 1% of households have at least nominal access to electricity. Despite the rapidly growing availability of electricity and gas, coal and especially biomass remain the overwhelming energy sources for households nationwide (Figure 1.4).

In Latin America, although some extremely poor countries such as Haiti have fuel use patterns that are similar to those seen in Africa, many other countries are switching to modern cooking fuels such as kerosene and LPG (Table 1.2). With the exception of a few countries, less than 10% of the populations in most urban areas in Latin America use biomass energy for cooking (Table 1.2), and the use of modern fuels is also growing in rural areas. For instance, in rural Costa Rica, the use of biomass energy has declined to less than one-quarter of its population, the majority of which has switched to modern fuels.

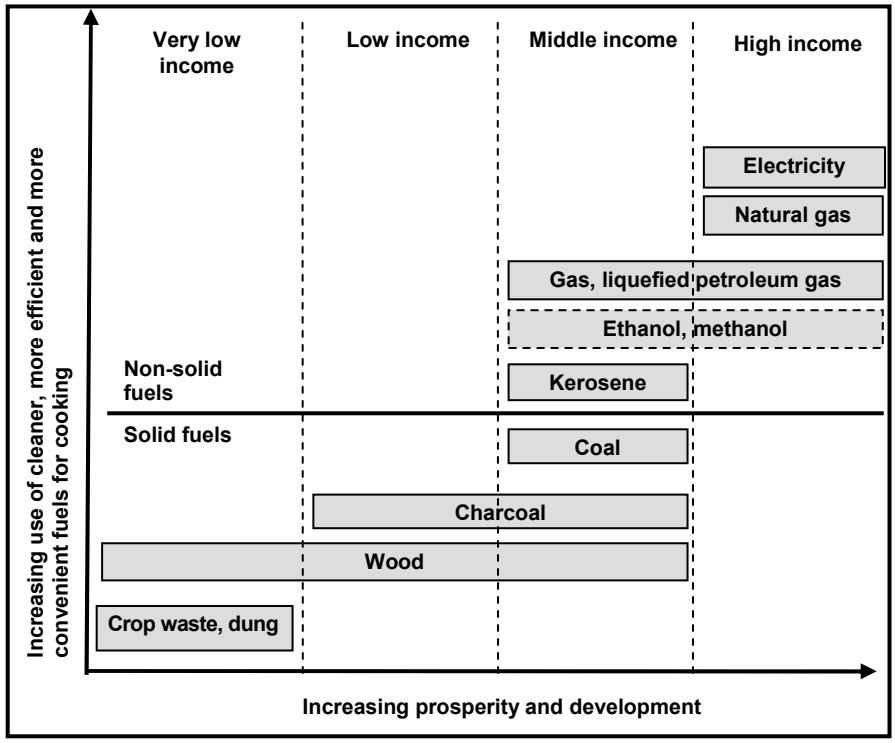
The transition from biomass fuels to modern fuels has been associated with improvement in economic prosperity and development (Figure 1.5). At very low levels of income or development, households depend on biomass fuels such as agricultural waste, dung or firewood. As incomes rise or the country becomes more developed, households

Figure 1.4. Total residential primary energy use in China



From International Energy Agency (2006a,b)

Figure 1.5. Transition from use of biomass fuels to use of modern fuels



From WHO (2006) (Figure 2: The energy ladder: household energy and development inextricably linked)
Note: Ethanol and methanol are rarely, if ever, used.
Dash: estimate

begin to convert to non-solid fuels such as kerosene, LPG or electricity. At middle income levels, households typically use both solid and non-solid fuels.

All over the developing world, significant variations in the use of biomass energy and coal are observed. Both rural and urban populations are switching to modern fuels. However, it is known that very poor countries generally can not afford to use modern fuels, and the richest of countries have already adopted them due to their convenience and cleanliness (see Section 1.4 on intervention and policies).

1.1.4 *Determinants of choice of fuel and energy use*

Most studies have found that three factors determine the choice of fuel (Leach, 1987; Leach & Mearns, 1988; Boberg, 1993; Barnes *et al*., 2005). The first is access to both modern fuels and to local biomass; the second involves affordability, as determined by household income, since modern fuels must be purchased on the market; the third is the policy options available, such as prices, subsidies and taxes, to reduce dependence on biomass.

(a) Availability and access to biomass and modern energy

The evolution of energy markets in developing countries is irregular. For modern fuels, the institutions that serve both urban and rural markets can be diverse: in some countries, government-run agencies control the flow of kerosene and LPG; in others, there is one dominant supplier that has a virtual monopoly; and in some others, a significant degree of competition exists among a limited number of private companies. In contrast, the supply of biomass is generally characterized by self production or collection of the fuel, local sales, or a market chain that spreads out from urban to rural areas. There is growing evidence that, if households have access to a variety of fuels, a greater acceptance of modern fuels occurs not only in urban (Barnes *et al*., 2005) but also often in some rural areas.

The type of biomass used in an area largely depends on what is available in the local environment. In Africa, wood is more readily available than in most other parts of the developing world. Most people rely on firewood in rural areas and both firewood and charcoal in urban areas to cook their meals. The use of wood, branches and, increasingly, brush is widespread in Asia and Africa. Dung cakes or balls are used more commonly in Asia and Latin America.

As wood becomes scarce due to deforestation, the use of agricultural residues as a source of energy increases. Crop residues are a very poor source of energy for cooking. In countries in Africa, charcoal is widely available and is thus used to almost the same extent as wood fuels. In China, coal is commonly used to cook and heat. In Bangladesh, a very densely populated country, the amount of local wood available to people is decreasing. A recent survey in Bangladesh (World Bank, 2006) indicated that people who live in areas where access to firewood from the local environment is minimal are turning towards

tree leaves, crop residue and dung (Table 1.3). In this situation, people are actually moving

Table 1.3. Consumption of energy in domestic activities: all divisions (per household/year: average over all households) in Bangladesh (2005)

Type of energy	All use	Heating		
		Cooking	Parboiling rice	Other
Biomass				
Firewood (kg)	1186	1065	29	93
Tree leaves (kg)	502	471	30	0.9
Crop residue (kg)	708	539	164	2.7
Dung cake/stick (kg)	524	504	16	4.2
Saw dust (kg)	8	8	0.02	0.02
Non-biomass				
Candle (piece)	16	–	–	–
Kerosene (litre)	29	1.8	–	0.07
Natural gas (Tk.)	10	10	–	–
LPG/LNG (litre)	0.05	0.05	–	–
Grid electricity (kWh)	144	0.25	–	4.00
Solar PV (kWh)	0.53	–	–	–
Storage cell (kWh)	0.55	–	–	–
Dry cell battery (piece)	15	–	–	–

From Asaduzzaman & Latif (2005)

down the energy ladder to lower and more polluting fuels. In Bangladesh, very little LPG is available in rural areas. In urban areas, the development of modern cities has resulted in a gradual decline in the use of biomass energy.

As seen in Table 1.4, when the population of a city reaches about 1 million, the use of biomass energy declines sharply, since access to local biomass energy becomes difficult. However, energy policies also play a role in the choice of household fuel. Thus, access to both biomass and modern fuels is an extremely important element in the choice of household fuel.

Table 1.4. Size and energy use in 45 cities in Bangladesh, 1980–88

City type	Population (in thousands)	Monthly income (US $ per capita)	Fuel (%)				
			Firewood	Charcoal	Kerosene	LPG	Electricity
Town	33	38	52	40	33	46	64
Small city	102	41	25	36	37	60	78
Middle city	526	35	47	53	64	23	69
Large city	3718	55	4	28	61	37	95

From World Bank (1988, 1989, 1990a,b,c,d, 1991a,b, 1992, 1993, 1996a, 1999) (hereinafter ESMAP Household Energy Surveys)
LPG, liquefied petroleum gas

(b) Income and affordability

Poverty is inextricably linked to the use of biomass. Most homes in developing countries use biomass energy, but there is a growing transition to modern fuels as well as a trend in the opposite direction. Modern fuels cost money–when households can afford to move up the energy ladder and access to modern fuels is not an issue, the transition is almost inevitable.

Affordability is only an issue if there is adequate access to modern fuels, which is often dictated by whether a household lives in an urban or a rural area. In many developing countries, an interesting pattern can be seen between income and fuel use. In the urban areas of India, Nepal, Guatemala and Nicaragua, for instance, the type of fuels used is dependent upon household income: solid fuels are more common among the poorer households and modern fuels are used by the rich. In some large urban areas, even the poor use kerosene and, in some instances, LPG for cooking. In contrast, in the rural areas of these countries, income has less influence on the type of fuel used. Across households of all income classes, solid fuels are common (World Bank, 2003).

In rural areas, affordability largely contributes to the widespread use of biomass energy. Households in rural areas are generally poor and biomass is often available to them from the local environment. The price of using biomass energy is simply the labour required in collecting it (World Bank, 1996a,b; WHO, 2006).

The amount of money spent by the poor on the small quantities of energy that they use is a very important portion of their overall household expenditure. The poor spend less on energy than the more wealthy households, but the percentage of income that they spend on energy is typically much greater. The urban poor spend between 10 and 20% of their income on energy, whereas the wealthy spend less than 5%.

In addition, the cost of energy services for the poor is also higher than that for the rich because cooking with fuelwood and lighting with kerosene are inefficient compared with cooking and lighting with modern fuels. Moreover, the poor often buy fuelwood and charcoal in small amounts, and the higher transaction costs of buying in small quantities inflate the price. Once the comparative efficiencies and transaction costs have been taken into consideration, the delivered energy for cooking often is more expensive for poorer people than for wealthy households.

Poorer people generally use biomass energy except under unusual circumstances. One study based on evidence from 45 cities has classified general points at which people switch from biomass to modern fuels (Barnes *et al*., 2005). Based on income figures given in 1980 US dollars, the study indicated that people start switching from wood at surprisingly low incomes–between US $12 and US $30 per person per month. However, where wood is inexpensive and readily available, people may continue its use at incomes of up to US $100 per person per month. The use of modern fuels, including electricity and LPG, generally intensifies at incomes of about US $40–50 per person per month. This suggests that definitive income 'cut-offs' for fuel substitution can not be identified precisely, only very broadly. The reason for this is the variation in access, pricing and

government policies. In addition, the study found that modern fuel consumption was higher than that anticipated among poorer households. This can reflect both the attractiveness of modern fuels and particular subsidy policies for some fuels; for example, subsidies for kerosene in Indonesia, coal in China and LPG in some countries.

1.1.5 *Conclusion*

The negative impact of biomass energy on the daily lives of populations (especially women and children) in the poorest parts of the developing world cannot be underestimated. Furthermore, evidence would strongly suggest that the persistent and widespread use of biomass energy largely depends on the factors of access, affordability and pricing policies.

1.2 Constituents of emissions

Wood consists primarily of two polymers: cellulose (50–70% by weight) and lignin (approximately 30% by weight) (Simoneit *et al*., 1999). Other biomass fuels (e.g. grasses, wheat stubble) also contain these polymers, although their relative proportions differ. In addition, small amounts of low-molecular-weight organic compounds (e.g. resins, waxes, sugars) and inorganic salts are present in wood. During combustion, pyrolysis occurs and the polymers break apart to produce a variety of smaller molecules. Even when they are intrinsically free of contaminants, biomass fuels and coals are difficult to burn in small simple combustion devices such as household cooking and heating stoves without substantial emissions of pollutants, principally due to the difficulty of completely pre-mixing the fuel and air during burning, which is easily done with liquid and gaseous fuels. Consequently, a substantial fraction of the fuel carbon is converted to products of incomplete combustion, i.e. compounds other than the ultimate product of complete combustion, carbon dioxide. For example, typical household coal and biomass stoves in China and India divert between more than 10% and up to ~30% of their fuel carbon into products of incomplete combustion (Smith *et al*., 2000; Zhang *et al*., 2000). Emissions of products of incomplete combustion from coal and biomass overlap largely depending on fuel species and stove types.

An individual product of incomplete combustion can be present in the gas phase, particle phase or both phases, depending on its volatility. Hence, products of incomplete combustion released from the combustion of biomass are a complex mixture of particulate and gaseous chemical species, including carbon monoxide, nitrogen dioxide and particulate matter (PM). Products of incomplete combustion also include a large number of hydrocarbons that are precursor components of photochemical smog and comprise ozone, aldehydes and particles (Tsai *et al*., 2003). Compared with biomass, many coals contain more intrinsic contaminants from their mineral deposits, such as sulfur, arsenic, silica, fluorine, lead and/or mercury. During combustion, these contaminants are not destroyed but are released into the air in their original or oxidized

form. Therefore, coal combustion tends to emit other pollutants in addition to products of incomplete combustion. In households that use sulfur-rich coals, for example, sulfur dioxide is present at elevated levels. Since the temperature of coal combustion is normally substantially higher than that of biomass combustion, higher emissions of oxides of nitrogen were measured for household coal combustion than for biomass combustion (Zhang *et al*., 2000).

Depending on the measurement and analytical methods used, the chemical constituents of biomass and coal smoke have been reported in different studies in the form of individual chemical compounds (e.g. carbon monoxide, benzene, formaldehyde), groups of compounds (e.g. total non-methane hydrocarbon, total organic carbon), elements (e.g. carbon, arsenic) or ions (e.g. fluoride, sulfate). The smoke constituents identified to date are summarized in Tables 1.5–1.7, by class of compound, element and ion, respectively. It should be noted that many of the wood smoke species reported in Table 1.5 were isolated from measurements of US appliances (e.g. woodstoves, fireplaces) and open-field combustion (e.g. wild fire, prescribed forest fire), because few studies have been conducted to characterize detailed chemical speciation for biomass stoves in developing countries. Compounds that are present in emissions from the combustion of wood or coal and have been evaluated by the IARC are listed in Table 1.8. One study has reported emission factors of some 60 hydrocarbons and ~17 aldehydes and ketones from ~28 commonly used fuel/stove combinations in China and emission factors of hydrocarbons from 28 fuel/stove combinations commonly used in India in the early 1990s (Smith *et al*., 2000; Zhang *et al*., 2000). In contrast, several hundred individual compounds have been detected in smoke samples of residential wood combustion, wildfire and prescribed burns (Rogge *et al*., 1998; McDonald *et al*., 2000; Oros & Simoneit, 2001; Schauer *et al*., 2001; Fine *et al*., 2002). Although less well characterized, many of the same chemicals were reported in smoke emissions from other types of biomass, including grasses, rice straw, sugar cane and ferns (Simoneit *et al*., 1993, 1999; Rinehart *et al*., 2002). Selected chemicals that are associated with carcinogenicity are discussed below.

Table 1.5. Constituents of biomass smoke and coal smoke, by chemical class

Compound	Wood smoke		Coal smoke	
	Species	References	Species	References
Inorganic compounds	Carbon monoxide	McDonald *et al*. (2006)	Carbon monoxide	
	Sulfur dioxide		Sulfur dioxide	
	Nitric oxide		Nitric oxide	
	Ammonia			

Table 1.5. (contd)

Compound	Wood smoke		Coal smoke	
	Species	References	Species	References
Hydrocarbons				
Alkanes	C_1–C_7	Rogge *et al*. (1998); McDonald *et al*. (2000); Schauer *et al*. (2001); Fine *et al*. (2002); McDonald *et al*. (2006)	C_2–C_{10}	Yan *et al*. (2002); Tsai *et al*. (2003)
Alkenes	C_2–C_7 (including 1,3-butadiene)	Rogge *et al*. (1998); McDonald *et al*. (2000); Fine *et al*. (2002); McDonald *et al*. (2006)	C_2–C_{10} (including 1,3-butadiene)	Yan *et al*. (2002); Tsai *et al*. (2003)
Aromatics	Benzene Xylene Toluene Styrene	Tsai *et al*. (2003) McDonald *et al*. (2006)	Benzene Xylene Toluene Styrene	Tsai *et al*. (2003)
PAHs and substituted PAHs	Acenaphthene Anthracene Benz[*a*]anthracene Benzo[*b*+*j*+*k*]fluorene Benzo[*ghi*]perylene Benzo[*a*]pyrene Benzo[*e*]pyrene Biphenyl acenaphthylene Chrysene Coronene 1,7-Dimethylphenanthrene Fluoranthene Fluorene Indeno[123-*cd*]pyrene 1-Menaphthalene 2-Menaphthalene 1-Methylphenanthrene Naphthalene Phenanthrene Pyrene Retene	Chuang *et al*. (1992); Rogge *et al*. (1998); McDonald *et al*. (2000); Oros & Simoneit (2001); Schauer *et al*. (2001); Fine *et al*. (2002); McDonald *et al*. (2006)	Acenaphthene Acenaphthylene Acephenanthrylene Anthracene Benz[*a*]anthracene Benzanthrone Benzo[*b*]chrysene Benzo[*a*]coronene Benzo[*b*]fluoranthene Benzo[*k*]fluoranthene Benzo[*b*+*j*+*k*]fluorene Benzo[*a*]fluorine Benzo[*b*]naphtha[2,1-*d*]thiophene Benzo[*pqr*]naphtha[8,1,2-*bcd*]perylene Benzo[*ghi*]perylene Benzo[*a*]pyrene Benzo[*e*]pyrene Chrysene Coronene Cyclopenta[*def*]-chrysene-4-one	Chuang *et al*. (1992); Wornat *et al*. (2001); Ross *et al*. (2002); Yan *et al*. (2002); Chen *et al*. (2004, 2005); Lee *et al*. (2005)

Table 1.5. (contd)

Compound	Wood smoke		Coal smoke	
	Species	References	Species	References
PAHs (contd)			Cyclopent[*hi*]acephenanthrylene Cyclopenta[*cd*]benzo[*ghi*]perylene Cyclopenta[*bc*]coronene Cyclopenta[*cd*]fluoranthrene Cyclopenta[*cd*]pyrene Dibenz[*a,c*]anthracene Dibenz[*a,h*]anthracene Dibenz[*a,j*]anthracene Dibenzo[*b,k*]fluoranthene Dibenzo[*a,e*]pyrene Dibenzo[*e,l*]pyrene Dicyclopenta[*cd,mn*]-pyrene Dicyclopenta[*cd,jk*]-pyrene Fluoranthene, Fluorene Indeno[123-*cd*]pyrene Naphtho[1,2-*b*]-fluoranthene Naphtho[2,1-*a*]pyrene 4-Oxa-benzo-[*cd*]pyrene-3,5-dione Phenanthrene Picene Pyrene Triphenylene Tribenzo[*e,ghi,k*]-perylene	
Total non-methane hydrocarbon		McDonald *et al*. (2000); Schauer *et al*. (2001); McDonald *et al*. (2006)		Tsai *et al*. (2003)
Unresolved complex mixture		Oros & Simoneit (2001); Fine *et al*. (2002)		

Table 1.5. (contd)

Compound	Wood smoke		Coal smoke	
	Species	References	Species	References
Oxygenated organics				
Alkanols	Methanol (+ methyl formate) Ethanol (+ acn + acrolein)	McDonald *et al*. (2000); Oros & Simoneit (2001); Fine *et al*. (2002); McDonald *et al*. (2006)		
Carboxylic acids	Heptanoic acid Octanoic acid Nonanoic acid Decanoic acid Undecanoic acid Dodecanoic acid Tridecanoic acid	Rogge *et al*. (1998); Oros & Simoneit (2001); Schauer *et al*. (2001); Fine *et al*. (2002); McDonald *et al*. (2006)		
Aldehydes and ketones	Formaldehyde Acetaldehyde Proponal Butanal Pentanal Octanal Nonanal (+ undecene) Glyoxal Acetone (+ propanal) 3-Buten-2-one Butanone 3-Methyl-3-buten-2-one	Rogge *et al*. (1998); McDonald *et al*. (2000); Schauer *et al*. (2001); Fine *et al*. (2002); McDonald *et al*. (2006)	Formaldehyde Acetaldehyde Acetone Acrolein Propionaldehyde Crotonaldehyde 2-Butanone Isobutyraldehyde Butyraldehyde Benzaldehyde Isovaleraldehyde Valeraldehyde *ortho*-Tolualdehyde *meta*,*para*-Tolualdehyde Hexaldehyde 2,4-Dimethylbenz-aldehyde	Miller *et al*. (1994); Zhang & Smith (1999)
Alkyl esters	Nonyl dodecanoate Decyl dodecanoate Undecyl dodecanoate Dodecadienyl dodecanoate Tridecyl dodecanoate	Oros & Simoneit (2001)		
Methoxylated phenolic compounds		Rogge *et al*. (1998); McDonald *et al*. (2000); Schauer *et al*. (2001); Fine *et al*. (2002); McDonald *et al*. (2006)		

Table 1.5. (contd)

Compound	Wood smoke		Coal smoke	
	Species	References	Species	References
Other organic compounds				
Other substituted aromatic compounds	*n*-9-Octadecenoic acid *n*-9,12-Octadecadienoic acid PCDDs PCDFs PCBs	Rogge *et al*. (1998); McDonald *et al*. (2000); Oros & Simoneit (2001); Schauer *et al*. (2001); Fine *et al*. (2002); Gullett *et al*. (2003); McDonald *et al*. (2006)		
Sugar derivatives	1,4:3,6-Dianhydro-R-D-Glucopyranose Galactosan Mannosan Levoglucosan Monomethylinosito	Oros & Simoneit (2001); Fine *et al*. (2002); McDonald *et al*. (2006)		
Coumarins and flavonoids	Coumarin tetramethoxyiso-flavone	Fine *et al*. (2002)		
Phytosteroids	Stigmasterol *â*-Sitosterol Stigmastan-3-ol Stigmastan-3-one	Rogge *et al*. (1998); Fine *et al*. (2002)		
Resin acids and terpenoids	Pimaric acid Isopimaric acid Abietic acid Levopimaric acid Neoabietic acid	Rogge *et al*. (1998); McDonald *et al*. (2000); Oros & Simoneit (2001); Fine *et al*. (2002)		
Unresolved compounds		McDonald *et al*. (2000); Schauer *et al*. (2001); Fine *et al*. (2002)		

PAH, polycyclic aromatic hydrocarbon; PCB, polychlorinated biphenyl; PCDD, polychlorinated dibenzo-*para*-dioxin; PCDF, polychlorinated dibenzofuran

Table 1.6. Elemental constituents of wood smoke and coal smoke

	Wood smoke (particle phase)		Coal smoke (particle phase)	
	Element	Reference	Element	Reference
	Carbon, including elemental carbon and organic carbon	McDonald *et al*. (2000); Watson *et al*. (2001); Hays *et al*. (2002)	Carbon, including elemental carbon and organic carbon	Watson *et al*. (2001) ; Ge *et al*. (2004)

Table 1.6. (contd)

	Wood smoke (particle phase)		Coal smoke (particle phase)	
	Element	Reference	Element	Reference
Metals	Na, Mg, Al, K, Ca, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Ga, As, Se, Br, Rb, Sr, Yt, Zr, Mo, Pd, Ag, In, Sn, Sb, Ba, La, Au, Hg, Tl, Pb	Kleeman *et al*. (1999); Watson *et al*. (2001)	Na, Mg, Al, K, Ca, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Ga, As, Se, Br, Rb, Sr, Yt, Zr, Mo, Pd, Ag, In, Sn, Sb, Ba, La, Au, Hg, Tl, Pb	Kauppinen & Pakkanen (1990); Watson *et al*. (2001) ; Ross *et al*. (2002); Ge *et al*. (2004)
Non-metals	S, P, Si, Cl, Br	Watson *et al*. (2001); Kleeman *et al*. (1999)	S, P, Si, Cl, Br	Watson *et al*. (2001); Ge *et al*. (2004)

1.2.1 *Particles as a whole versus particle components*

Particles emitted from biomass and coal combustion are fine and ultrafine in size (<1 μm in diameter) (Kleeman *et al*., 1999; Hays *et al*., 2002). Fresh coal or biomass smoke contains a large number of ultrafine particles, <1 μm in diameter, which condense rapidly as they cool and age. The smoke may contain some larger particles resulting from suspension of ash and solid fuel debris. Because combustion-generated particles and ash/debris particles have different chemical compositions and because particle size determines how deep the particles can travel within and beyond the respiratory tract, ascertaining size distribution plays an important role in the assessment of health impacts (see Section 4). For this reason, there has been a switch in recent studies to the measurement of inhalable (<10 μm, referred to as PM_{10}) or respirable (<2.5 μm, referred to as $PM_{2.5}$) particles rather than of total suspended particles (TSP) as in earlier studies.

A large number of chemical species are contained in combustion particles and many chemical species are not stable (Rogge *et al*., 1998). Although it is impractical to cover a large number of individual compounds in a single study, a component of a specific physicochemical property may be targeted. For example, total carbon content of particles is a measure of the carbonaceous aerosol. Total carbon may be further segregated into elemental carbon and organic carbon. Although approximately 5–20% of wood smoke particulate mass consists of elemental carbon, the composition of the organic carbon fraction varies considerably with the specific fuel being burned and with the combustion conditions. Elemental carbon has a characteristic carbon core onto which many metals and organic compounds can be readily absorbed or adsorbed.

Earlier studies also focused on different solvent extracts of particles (soot) emitted from biomass or coal combustion. For example, in Xuan Wei County, China, particles released from smoky coal combustion contained the highest amount of organic compounds extractable with dichloromethane, followed by particles released from wood

combustion and then by those released from anthracite (smokeless) coal combustion (Mumford *et al*., 1987). Some combustion emission particles carry stabilized free radicals. Very limited data have shown that free radicals of the semi-quinone type are present in wood smoke particles as well as diesel smoke and cigarette smoke, but not in coal smoke which may contain or carry free radicals of graphite carbon type (Tian, 2005).

Analytical techniques such as ion chromatography can measure chemicals in the extracts of combustion particles in their dissociated form (ions). Commonly identified ions are shown in Table 1.7. These are the most abundant ions in smoke particles.

Table 1.7. Ionic constituents of wood smoke and coal smoke

Ion	Wood smoke (particle phase)		Coal smoke (particle phase)	
	Species	References	Species	References
Anions	SO_4^{2-}	Watson *et al*. (2001); Hays *et al*. (2002); Kleeman *et al.* (1999)	SO_4^{2-}	Watson *et al*. (2001)
	Cl^-		Cl^-	
	NO_3^-		NO_3^-	
Cations	NH_4^+	Watson *et al*. (2001); Hays *et al*. (2002); Kleeman *et al.* (1999)	NH_4^+	Watson *et al*. (2001)
	K^+		K^+	
	Ca^{2+}	Hays *et al*. (2002)		

Table 1.8. IARC evaluations[a] of compounds present in emissions from the combustion of wood or coal

Agent	*IARC Monographs* evaluation of carcinogenicity			*Monographs* volume, year
	In animals	In humans	IARC Group	
Polynuclear aromatic hydrocarbons				
Benz[*a*]anthracene	Sufficient	Inadequate	2B	*92*, 2010
Benzo[*b*]fluoranthene	Sufficient	Inadequate	2B	*92*, 2010
Benzo[*k*]fluoranthene	Sufficient	Inadequate	2B	*92*, 2010
Benzo[*a*]pyrene	Sufficient	Inadequate	1	*92*, 2010
Dibenz[*a*,*h*]anthracene	Sufficient	Inadequate	2A	*92*, 2010
Chrysene	Sufficient	Inadequate	2B	*92*, 2010
Cyclopenta[*cd*]pyrene	Sufficient	Inadequate	2A	*92*, 2010
Indeno[1,2,3-*cd*]pyrene	Sufficient	Inadequate	2B	*92*, 2010
Naphthalene	Sufficient	Inadequate	2B	*82*, 2002

Table 1.8. (contd)

Agent	*IARC Monographs* evaluation of carcinogenicity			*Monographs* volume, year
	In animals	In humans	IARC Group	
Volatile organic compounds				
Acetaldehyde	Sufficient	Inadequate	2B	*S7*, 1987; *71*, 1999
Benzene	Sufficient	Sufficient	1	*29*, 1982; *S7*, 1987
1,3-Butadiene	Sufficient	Limited	2A	*S7*, 1987; *71*, 1999
Formaldehyde	Sufficient	Sufficient	1	*88*, 2006
Styrene	Limited	Inadequate	2B	*82*, 2002
Metals and metal compounds				
Arsenic	Sufficient	Sufficient	1	*84*, 2004
Nickel	Sufficient	Sufficient	1	*S7*, 1987; *49*, 1990

[a] Only those agents classified as Group 1, 2A or 2B are listed here.

1.2.2 *Polycyclic aromatic hydrocarbons (PAHs) and substituted PAHs*

Polycyclic aromatic hydrocarbons (PAHs) are formed during incomplete combustion of all carbon-based fuels and organic materials, including biomass and coal. At typical ambient temperature, lower-molecular-weight PAHs (with 2–4 aromatic rings) are present predominantly in the gas phase while higher-molecular-weight PAHs are present predominantly in the particle phase. Because PAHs of higher cancer potency are predominantly present in the particle phase (IARC, 2010), combustion particles have often been subjected to compositional analysis for PAHs and PAH derivatives. A detailed analysis of PAHs in the dichloromethane extracts of soot deposits from coal-burning stoves in several homes of Hunan Province, China, identified 32 individual PAHs ranging in size from three to eight fused aromatic rings. The PAHs found in the soot deposits included 20 benzenoid PAHs, six fluoranthene benzologues, one cyclopenta-fused PAH, one indene benzologue, three oxygenated PAHs and one sulfur-containing aromatic (see Table 1.5) (Wornat *et al*., 2001). Carcinogenic PAHs, methylated PAHs and nitrogen-containing heterocyclic aromatic compounds were detected in large abundance in the particles emitted from smoky coal combustion, as typically found in numerous households in Xuan Wei County,[1] Yunnan Province, China (Mumford *et al*., 1987; Chuang *et al*., 1992; Granville *et al*., 2003; Keohavong *et al*., 2003). In the aromatic fraction, coal combustion particles appeared to contain higher concentrations and more species of methylated PAHs than wood combustion particles (Chuang *et al*., 1992).

[1] Xuan Wei County is a site where decade-long studies have been conducted to examine lung cancer and household coal combustion.

However, profiles of specific PAHs and their abundance vary largely depending on the fuel types and combustion conditions. Between biomass smoke or coal smoke, it is difficult to discern which has the higher PAH content (Tian, 2005).

1.2.3 *Hydrocarbons and partially oxidized organic compounds*

Hydrocarbons identified to date include: in wood smoke—alkanes with 1–7 carbons, and alkenes with 2–7 carbons (including 1,3-butadiene); in coal smoke—alkanes with 1–10 carbons and alkenes with 2–10 carbons (including 1,3-butadiene); in both wood and coal smoke—aromatic compounds (e.g. benzene, xylenes, toluene, styrene) (see Table 1.5). Partially oxidized organic compounds identified in wood and/or coal smoke include alkanols, aldehydes and ketones (carbonyls), carboxylic acids, alkyl esters and methoxylated phenolic compounds. In addition, partially oxidized aromatic compounds and substituted aromatic compounds (e.g. aromatic organic acids, polychlorinated dibenzodioxins, polychlorinated dibenzofurans, polychlorinated biphenyls), sugar derivatives, coumarins and flavonoids, resin acids and terpenoids have been identified in wood smoke (see Table 1.5). Both biomass smoke and coal smoke contain gas-phase carcinogens (e.g. benzene, 1,3-butadiene, formaldehyde) in addition to particle-phase PAHs that have carcinogenic potential. A detailed analysis of organic wood smoke aerosol found nearly 200 distinct organic compounds, many of which are derivatives of wood polymers and resins (see Table 1.5; Rogge *et al*., 1998).

1.2.4 *Metals and other toxic substances*

Some carcinogenic substances in coal were found to be released into the air during the combustion of lignites used in Shenyang City of northern China and smoky coals used in Xuan Wei County, China. It was reported that lignites from a local Shenyang coal field had very high concentrations of nickel (75 ppm) and chromium (79 ppm) (Ren *et al*., 1999, 2004) when compared with the levels reported elsewhere in the world (0.5–50 ppm for nickel and 0.5–60 ppm for chromium) (Swaine, 1990). Microfibrous quartz has been found in some smoky coals from Xuan Wei County and the resulting coal smoke but not in wood smoke (Tian, 2005). Particles emitted from burning coals contaminated with toxic elements (e.g. fluorine, arsenic, mercury) in Guizhou Province of China and other areas have been reported to contain high levels of the corresponding elements (Gu *et al*., 1990; Yan, 1990; Shraim *et al*., 2003). As shown in Table 1.6, metal and non-metal elements have also been found in wood smoke particles, which reflects the intake of these elements from the soil by trees.

1.2.5 *Emission factors of some carcinogens*

The emission factor of a particular chemical species can be measured as the mass of the species emitted per unit mass of fuel combusted or the mass of the species emitted per unit energy produced or delivered through combustion. A very small number of studies

have been conducted to date to quantify emission factors of common pollutants for household stoves used in developing countries.

The available data for selected human carcinogens or probable carcinogens (benzene, 1,3-butadiene, formaldehyde and benzo[*a*]pyrene) are summarized in Table 1.9. The sum of PAHs, when ≥14 individual PAHs were measured, is also shown in Table 1.9. The cited studies measured PAHs most commonly reported in the literature: acenaphthene, acenaphthylene, anthracene, benz[*a*]anthracene, benzo[*b*]fluoranthene, benzo[*a*]-pyrene, benzo[*ghi*]perylene, benzo[*k*]fluoranthene, chrysene, dibenz[*ah*]anthracene, fluoranthene, fluorene, indeno[1,2,3-*cd*]pyrene, naphthalene, phenanthrene and pyrene.

Table 1.9. Emission factors of carcinogenic compounds in the smoke of solid fuel combustion in household stoves (and fireplaces)

Compound	Fuel type	Location (fuel source)	Emission factor[a] (mg/kg fuel)	Emission factor[a] (mg/MJ)	Reference
Benzene					
	Wood (1 type)	China	264–629	159–161[b]	Tsai *et al.* (2003)
	Wood (hardwood)	USA	1190		McDonald *et al.* (2000)
	Fireplace wood (2 types)	USA	225–312		McDonald *et al.* (2000)
	Coal (4 types)	China	2.71–1050	0.9–390[b]	Tsai *et al.* (2003)
1,3-Butadiene					
	Wood (1 type)	China	0.8–1.0	0.2–0.6[b]	Tsai *et al.* (2003)
	Wood (hardwood)	USA	197		McDonald *et al.* (2000)
	Fireplace wood (2 types)	USA	63–95		McDonald *et al.* (2000)
	Coal (4 types)	China	ND–21.3	ND–7.9[b]	Tsai *et al.* (2003)
Styrene					
	Wood (1 type)	China	ND	ND	Tsai *et al.* (2003)
	Wood (hardwood)	USA	117		McDonald *et al.* (2000)
	Fireplace wood (2 types)	USA	35–40		McDonald *et al.* (2000)
	Coal (4 types)	China	ND	ND	Tsai *et al.* (2003)

Table 1.9. (contd)

Compound	Fuel type	Location (fuel source)	Emission factor[a] (mg/kg fuel)	Emission factor[a] (mg/MJ)	Reference
Formaldehyde					
	Wood (2 types)	China	42–261	18–100[b]	Zhang & Smith (1999)
	Wood (hardwood)	USA	246		McDonald *et al.* (2000)
	Fireplace wood (2 types)	USA	113 –178		McDonald *et al.* (2000)
	Coal (3 types)	China	2–51	0.9–12[b]	Zhang & Smith (1999)
Acetaldehyde					
	Wood (2 types)	China	41–371	17–145[b]	Zhang & Smith (1999)
	Wood (hardwood)	USA	361		McDonald *et al.* (2000)
	Fireplace wood (2 types)	USA	301–450		McDonald *et al.* (2000)
	Coal (3 types)	China	0.8–81	0.3–20[b]	Zhang & Smith (1999)
Naphthalene					
	Wood (*Petocarpus indicus*)	Thailand	3.96		Kim Oanh *et al.* (2002)
	Wood (hardwood)	USA	28		McDonald *et al.* (2000)
	Fireplace wood (2 types)	USA	21–55		McDonald *et al.* (2000)
	Wood (eucalyptus chip)	Thailand	39.1		Kim Oanh *et al.* (1999)
	Charcoal	Thailand	7.48		Kim Oanh *et al.* (1999)
	Coal briquettes	Viet Nam	44.5		Kim Oanh *et al.* (1999)
Benzo[*a*]pyrene					
	Wood (*Petocarpus indicus*)	Thailand	0.41		Kim *et al.* (2002)
	Wood (eucalyptus chip)	Thailand	0.69		Kim Oanh *et al.* (1999)

Table 1.9. (contd)

Compound	Fuel type	Location (fuel source)	Emission factor[a] (mg/kg fuel)	Emission factor[a] (mg/MJ)	Reference
Benzo[*a*]pyrene (contd)					
	Wood (hardwood)	USA	0.20		McDonald *et al.* (2000)
	Wood (oak)	USA	0.56		Gullett *et al.* (2003)
	Fireplace wood (2 types)	USA	0.15–0.34		McDonald *et al.* (2000)
	Fireplace wood (3 types)	USA	0.31–0.58		Gullett *et al.* (2003)
	Charcoal (two types)	Kenya	0.01–0.12		Gachanja & Worsforld (1993)
	Charcoal	Thailand	0.17		Kim Oanh *et al.* (1999)
	Sawdust briquettes	Thailand	0.53		Kim *et al.* (2002)
	Coal briquettes	Viet Nam	0.30		Kim Oanh *et al.* (1999)
Benz[*a*]anthracene					
	Wood (hardwood)	USA	0.56		McDonald *et al.* (2000)
	Wood (*Petocarpus indicus*)	Thailand	0.62		Kim *et al.* (2002)
	Wood (eucalyptus chip)	Thailand	0.82		Kim Oanh *et al.* (1999)
	Wood (oak)	USA	0.73		Gullett *et al.* (2003)
	Fireplace wood (3 types)	USA	0.34–0.79		Gullett *et al.* (2003)
	Fireplace wood (2 types)	USA	0.31–0.45		McDonald *et al.* (2000)
	Charcoal	Thailand	0.06		Kim Oanh *et al.* (1999)
	Sawdust briquettes	Thailand	1.04		Kim *et al.* (2002)
	Coal briquettes	Viet Nam	0.11		Kim Oanh *et al.* (1999)

Table 1.9. (contd)

Compound	Fuel type	Location (fuel source)	Emission factor[a] (mg/kg fuel)	Emission factor[a] (mg/MJ)	Reference
Dibenz[*a*,*h*]anthracene					
	Wood (oak)	USA	0.04		Gullett *et al.* (2003)
	Wood (*Petocarpus indicus*)	Thailand	0.15		Kim *et al.* (2002)
	Wood (eucalyptus chip)	Thailand	0.6		Kim Oanh *et al.* (1999)
	Fireplace wood (3 types)	USA	0.03–0.08		Gullett *et al.* (2003)
	Charcoal	Thailand	ND		Kim Oanh *et al.* (1999)
	Sawdust briquettes	Thailand	0.24		Kim *et al.* (2002)
	Coal briquettes	Viet Nam	ND		Kim Oanh *et al.* (1999)
Sum of PAHs (≥14 individual PAHs)					
	Wood (*Petocarpus indicus*)	Thailand	66	0.97[c]	Kim *et al.* (2002)
	Wood (eucalyptus chip)	Thailand	110	5.6[c]	Kim Oanh *et al.* (1999)
	Wood (hardwood)	USA	75		McDonald *et al.* (2000)
	Wood (oak)	USA	147		Gullett *et al.* (2003)
	Fireplace wood (2 types)	USA	80–167		McDonald *et al.* (2000)
	Fireplace wood (3 types)	USA	31–144		Gullett *et al.* (2003)
	Charcoal	Thailand	24.7	0.8[c]	Kim Oanh *et al.* (1999)
	Sawdust briquettes	Thailand	260	6.3[c]	Kim *et al.* (2002)
	Coal briquettes	Viet Nam	102	4.4[b]	Kim Oanh *et al.* (1999)

ND, not detected (below method detection limit); PAH, polycyclic aromatic hydrocarbon
[a]The values are ranges of the means reported in individual studies
[b]Denotes milligrams per megajoule of energy delivered to the pot
[c]Denotes milligrams per megajoule of energy generated through combustion

Fuelwood combustion in two different Chinese cooking stoves generated 264 and 629 mg benzene for every kilogram of wood burned. Burning four types of household coal fuels (honeycomb coal briquette, coal briquette, coal powder and water-washed coal powder) in three different coal stoves generated a very wide range of benzene emissions (2.71–1050 mg/kg fuel) (Tsai *et al*., 2003). When the wood emission factors of benzene have been 'translated' into indoor concentrations for a typical village kitchen, benzene concentrations are expressed in parts per million (Zhang & Smith, 1996). As was the case for benzene, 1,3-butadiene emission factors had a wider range for coal combustion (see Table 1.9). However, wood combustion produced a higher formaldehyde emission factor than that obtained with coal combustion. Using the formaldehyde emission factors, Zhang and Smith (1999) predicted that a wood stove could produce sub-part-per-million and part-per-million peak formaldehyde concentrations in a typical village kitchen, depending on kitchen size and ventilation rate. Emission factors of benzo[*a*]pyrene for wood stoves appeared to be consistent across studies conducted in different countries, depending on fuel species (see Table 1.9). Interestingly, benzo[*a*]pyrene emission factors for fireplaces appeared to be similar to those for wood stoves and to depend on the wood species used. The benzo[*a*]pyrene emission factor for sawdust briquette was within the range of wood stove emission factors. In contrast, benzo[*a*]pyrene emission factors for coal and charcoal appeared to be lower. PAHs combined had the highest emission factor for sawdust briquette and the lowest for charcoal. Wood fuels/stoves (including fireplaces) and coal briquettes had overlaps in emission factor ranges for the PAHs combined. These emission factor patterns (wood versus coal) were, in general, consistent with indoor air concentration patterns measured in households that used coal and wood stoves (see Section 1.3).

1.3 Use and exposure

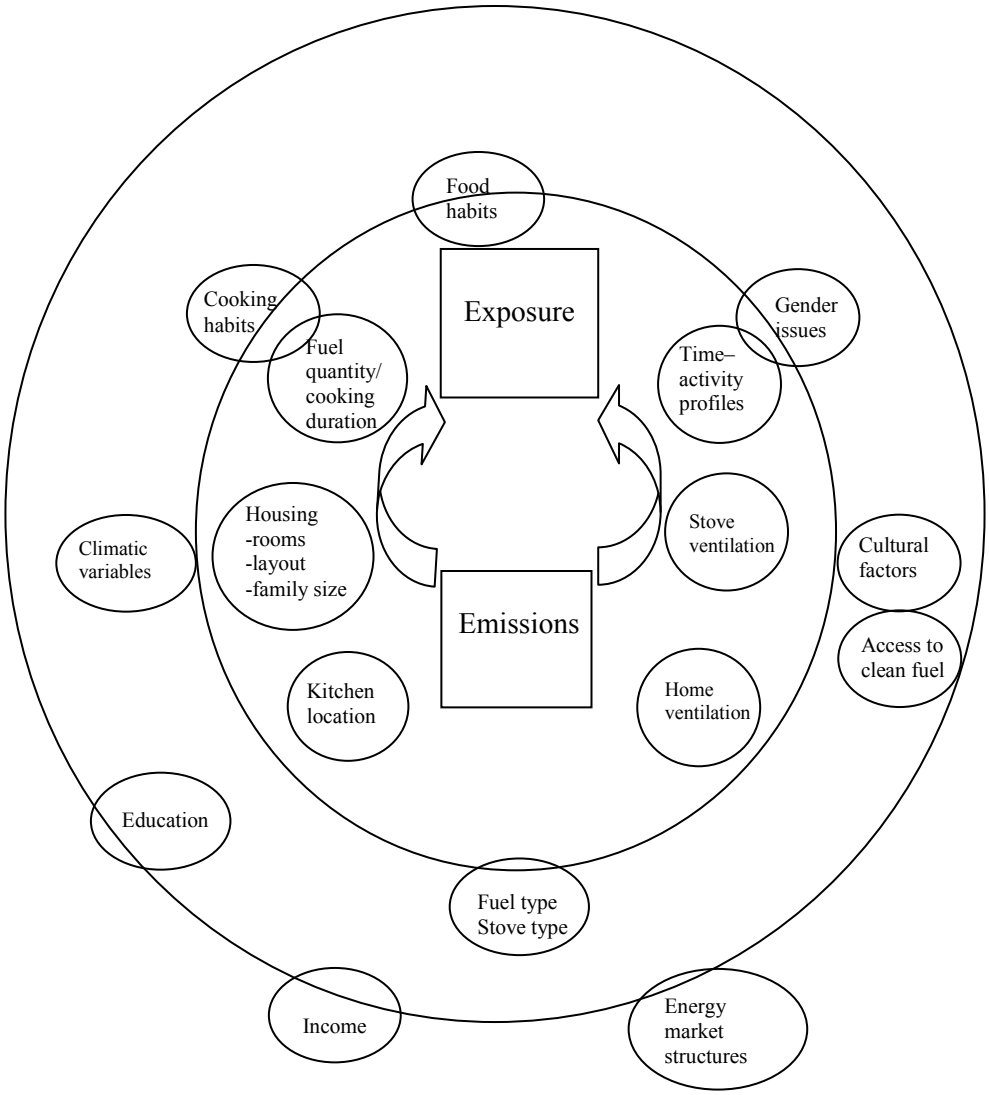
1.3.1 *General considerations on exposure to solid fuels*

(a) Determinants of exposure to indoor air pollution

Exposure to indoor air pollution resulting from the combustion of solid fuels is influenced by multiple factors. Individual exposure may be most directly influenced by the interaction of these factors with the source and the surrounding environment. However, many factors can contribute to this interaction indirectly. For example, the type of fuel and room dimensions may directly determine personal exposures but income, climatic conditions, cooking habits and family size may indirectly influence the type of fuel/stove (source) or the dimensions of the living space (surroundings). Determinants of exposure could therefore be described by classifying them broadly into 'proximal' (or 'microenvironmental') determinants that are directly in the exposure pathway and 'distal' (or 'macroenvironmental') determinants that contribute to differences in exposure through their effects on the systems that each of the proximal determinants may represent. Among the studies conducted in developing countries, there is a great deal of similarity in the

types of determinant that have been found to affect exposures. Hence, this section gives a general description of these determinants, while their specific contributions to population exposures may be found in individual studies described in Sections 1.3.2–1.3.5. A schematic illustration depicting the causal pathway and its interlinkage with some major classes of determinants is shown in Figure 1.6.

Figure 1.6. A schematic illustration of possible determinants of exposure to indoor air pollution related indoor cooking and heating with solid fuels. The outer circle represents distal determinants while the inner circle represents proximal determinants.



Drawn by the Working Group

(i) *Macroenvironmental (distal) determinants*

Socioeconomic (and demographic) determinants

These determinants operate largely through their influence on choice of fuel (one of the biggest contributors to indoor emissions and exposures, as described in Section 1.1). Income and education can also be expected to affect family size and type of housing that in turn affect fuel quantities or the number of rooms and/or location of the kitchen. Access to cleaner fuels may also be independently influenced by the prevalent national and regional energy market structures, which in turn would be linked to the gross domestic product of individual countries. Countries with a low gross domestic product per capita may experience greater gender inequities in terms of income, education, access to health care, social position and sociocultural preferences, all of which could potentially influence the exposures of vulnerable groups, such as women and children.

Geographic determinants

Although exposures result from indoor sources, external ecological variables can have a significant effect on the intensity and duration of pollution. Extreme temperature differentials between seasons, rainfall, altitude and even meteorological factors such as wind speed, wind direction and relative humidity, for example, could determine whether solid fuels are used for both cooking and heating and also affect aerosol dispersion and/or deposition. Patterns of vegetation (e.g. tropical rain forest versus scrub) could contribute to household decisions to seek alternative energy sources. Conditions of temperature and/or altitude that favour low dispersion (as may be commonly encountered in hilly/cold areas) may also favour higher ambient levels of pollution (resulting from indoor sources) which in turn contribute to increased exposure of the population.

(ii) *Microenvironmental determinants*

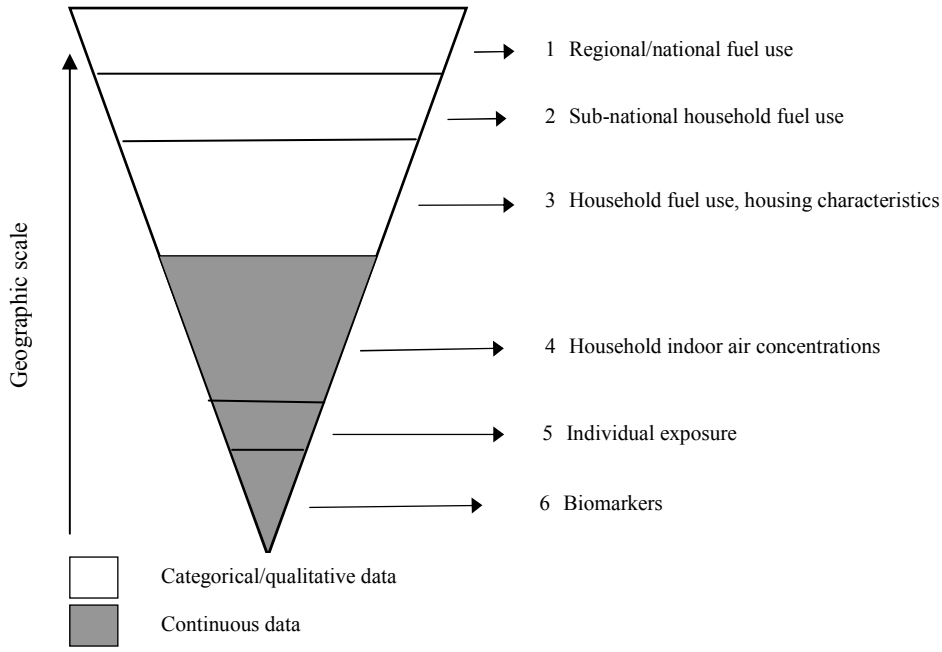
While the socioeconomic variables usually influence exposures indirectly through their effect on choice of fuel, several determinants directly influence spatial and temporal patterns of exposure within the household. Use and maintenance of improved stoves, household layout (including the location of kitchen), household ventilation, time–activity profiles of individual household members and behavioural practices (such as location of children while cooking) have been shown to influence pollution levels and individual exposures to them. Cultural habits may influence cooking practices which in turn may affect duration of cooking or the quantity of fuel used. While the available literature does not allow a detailed attribution of exposures to each of these variables, they can be expected to make varying contributions and must be considered when creating local or regional profiles of the exposure situation.

(b) Methods used to assess exposures

Exposures to indoor air pollutants that result from the combustion of solid fuels occur in the homes of millions of people on a daily basis. Multiple determinants affect these exposures directly or indirectly. While it would be impossible to create exposure profiles

by routine sampling of thousands of households, systematic assessments that use a combination of qualitative and quantitative methods have been necessary to identify the extent, levels and nature of exposures as well as to understand the relative contributions of specific determinants. An exposure pyramid that illustrates commonly applied approaches used in studies in developing countries is shown in Figure 1.7. As can be seen in the figure in general, as the geographic scale decreases, specificity increases, the availability of pre-existing or routinely collected data decreases and the cost of original data collection increases.

Figure 1.7. A schematic illustration of exposure assessment methods (tiers) used in studies in developing countries (adapted from Mehta & Smith, 2002; Balakrishnan *et al.*, 2004)



At the top of the pyramid are secondary data sources (tier No. 1). Some qualitative data on exposures, e.g. by primary fuel type, are routinely collected in national surveys such as the census and serve as readily available low-cost exposure indicators, but they often lack precision for estimating exposures at the household level. The influence of multiple household-level variables such as the type of fuel, type and location of kitchen and type of stove on actual household level concentrations/exposures is poorly understood in such assessments. However, this information has been very useful in estimating the proportions of people at risk for these exposures across multiple regions of the world and

also in tracking changes in the prevalence of some key determinants such as fuel and stove use in response to policy measures. More accurate (but more expensive) ways to measure exposures are actual household sample surveys of fuel use (tier No. 2). Indeed, this measure has been often used as the indicator of exposure in many epidemiological studies. Even better (but yet more expensive) methods include surveys not only of fuel use, but also of household characteristics such as type of construction material, stove type, number of rooms and windows and room ventilation (tier No. 3). The next stage, which is higher still in cost but more accurate, involves air pollution studies that use stationary air sampling devices set in one or more locations of the household over various lengths of time (tier No. 4). Some studies have been conducted in which people actually wore devices to measure their (personal) exposures to pollution, or in which exposures were reconstructed using concentration data and detailed time–activity–location records of individual household members (tier No. 5). Biological fluid or tissue biomarkers (tier No. 6) have not been applied in field settings, although some laboratory exposure chamber studies have been carried out. Finally, some methods that use a combination of qualitative information on a large number of households together with quantitative and qualitative information on a smaller subset of households have allowed the construction of models that predict levels of household exposure on the basis of qualitative information on selected determinants.

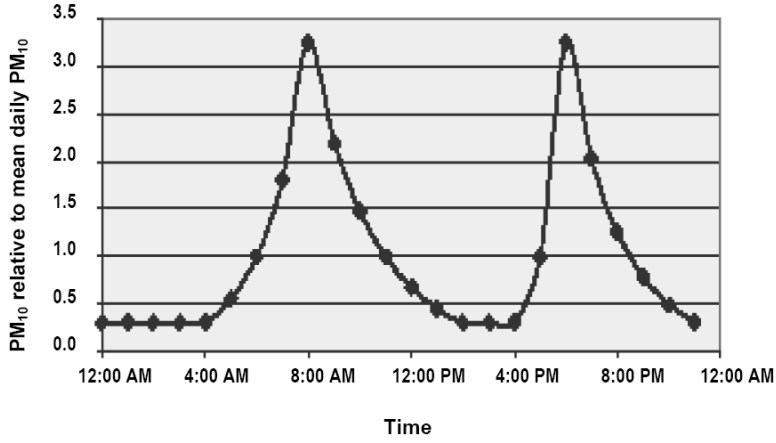
Using methods that collect primary data, a great deal of variation has been observed across studies that estimated either area concentrations or personal exposures (tiers 4 and 5). The choice of sampling locations, the time and duration of sampling, methods/instrumentation used for air sampling and exposure reconstruction coupled with a great deal of interhousehold variability in distribution of determinants such as fuel quantity, room dimensions, ventilation and stove type even within small geographical clusters make it difficult to compare quantitative estimates across studies directly. Of particular importance is the contribution of intense exposures over very short-term periods (i.e cooking periods) within a very small area (usually the kitchen) that often selectively target individual family members (usually women and young children). Figure 1.8 shows a typical distribution of pollutant levels over the course of a day within a single household and illustrates the importance of some of the factors mentioned above for exposures and measurements. The broad range in measurement results described in the following sections thus represents the variation that arises from differences in both exposure and sampling or study methodologies.

1.3.2 *China*

China had a population of nearly 1.3 billion in 2004 (National Bureau of Statistics, 2005). Approximately 757 million lived in rural households, most of whom were dependent on solid fuels for the bulk of their energy needs. Many urban residents also still rely on substantial amounts of coal; relatively few use biomass for occasional tasks. Although household coal is now officially discouraged or banned in all Chinese cities,

there is still significant but declining use in many, i.e. 5–10% of households, and a much larger proportion of usage in past decades. Thus, despite rapid urbanization and spread of the use of gas and electricity for cooking and heating, the majority of China's population depends mainly on solid fuels for household energy and is frequently exposed to the products of their combustion. A broad spectrum of information is available on population numbers that use different fuels under various conditions and their resulting pollutant levels (see for instance Impact Carbon (formerly CEIHD) at http://impactcarbon.org/). This information is not complete nor are all sources concordant with each other, but sufficient data exist to enable estimation of ranges of population exposures to a variety of pollutants.

Figure 1.8. Typical variations in PM_{10} level observed during the course of the day relative to daily means



From Mehta & Smith (2002)

(a) Use and determinants of use of solid fuels

(i) *Types and amounts of fuel*

The energy yearbooks published by the National Bureau of Statistics (Table 1.10) include some data from the Ministry of Agriculture on household use of biofuels (crop wastes, wood and biogas) by province, but the estimates of fossil fuel consumption in the National Bureau of Statistics' national and provincial balances (which estimate both urban and rural household energy use) differ substantially from those in the relatively rare publications from the Ministry of Agriculture that report the use of fossil fuels in rural households (Table 1.11). National Bureau of Statistics sources report the level of fossil fuel use for rural households to be only about 40% of that cited by the Ministry of Agriculture, possibly due to differences in allocating fuel use to agricultural and household purposes. While the levels of biofuel use are necessarily the same in both sources,

Table 1.10. Household energy use in China, 2004

Category		Original measurements		Conversion into PJ	
	Unit	Urban	Rural	Urban	Rural
Raw coal	Mt	17.33	45.65	409	1077
Washed coal	Mt	3.43	5.55	53	86
Briquettes	Mt	5.39	4.36	96	78
Coke	Mt	0.55	0.51	16	14
Coal gas	Bcm	13.70	0.11	155	1
Gasoline	Mt	2.24	0.63	96	27
Kerosene	Mt	0.02	0.25	1	11
Diesel	Mt	0.84	0.30	36	13
LPG	Mt	11.27	2.24	566	113
Natural gas	Bcm	6.69	0.03	261	1
Delivered heat	PJ	413.95	–	414	–
Electricity	TWh	148.33	98.10	534	353
Crop wastes	Mt	–	339.86	–	4273
Wood	Mt	–	210.92	–	3530
Biogas	Bcm	–	5.59	–	117
Total				2636	9694
Population	Millions	542.83	757.05		
Household size	Persons	2.98	4.08		

From National Bureau of Statistics (2005, 2006)
Mt, million tonnes; Bcm, billion cubic metres; LPG, liquefied petroleum gas; PJ, petajoules; TWh, terawatt–hours
N.B. Biofuel use published in National Bureau of Statistics (2006) is attributed to the Ministry of Agriculture. Data in the same categories as in this table are available from the same sources for nearly all of China's provinces and provincial-level municipalities.

Table 1.11. Rural household energy use in China, 1998

Category	Units		Conversion in PJ
Coal	163.45	Mt	3421
LPG	1.95	Mt	98
Oil products	4.51	Mt	189
Electricity	74.54	TWh	269
Crop wastes	286.24	Mt	3599
Wood	147.13	Mt	2462
Biogas	1.67	Bcm	35
Total			10 074

From EBCREY (1999)
Mt, million tonnes; Bcm, billion cubic metres; LPG, liquefied petroleum gas; PJ, petajoules; TWh, terawatt-hours

the difference between estimates of coal use mean that average dependence on biofuels could be approximately between 60% and 80%. Wood accounts for about two-fifths of biofuel use, and crop wastes make up the remainder; biogas use is still very small by comparison. Depending on the data source, coal use in rural households is either of the same order as that of crop wastes, or only a quarter as large.

Nevertheless, available data sources agree on at least one point: overall, rural households in China depend on solid fuels for about 95% of their energy needs. The corresponding proportion for urban households has fallen, and in 2004 was reported to be 22%. This percentage represented nearly 27 million tonnes of coal use. The assessment of the contribution of coal type in different areas of China has been complicated by the fact that the generic terms 'smoky coal' and 'smokeless coal' are widely applied in both rural and urban China. Generally, it appears that smoky coal is bituminous or sub-bituminous and smokeless coal is anthracite (For distinctions, see the glossary at http://www.eia.doe.gov/kids/energyfacts/sources/non-renewable/coal.html). The more smoky varieties have higher volatile contents, which makes them easier to ignite, but more difficult to burn cleanly in small combustion devices. Furthermore, household coal is frequently mixed with an earth or clay binder and produced as 'honeycomb' coal, i.e. in a cylindrical form of standard dimensions with vertical holes that facilitate lighting and combustion. Briquetting is also common. Such mixing has been associated with reduced indoor air pollution emissions, but no systematic testing across the many varieties under household conditions has been done. In addition to the honeycomb form, such mixed forms are variously known as 'coal cakes' and 'coal balls'. The same term probably has different meanings in different places. For example, the term 'coal cakes' is used both in rural Xuan Wei and urban Shanghai, although the specific composition of the coal cakes inevitably differs between the two locations and even within each location.

Gas fuels have become more widely available in many areas, and families spend relatively large amounts on their purchase. Government-sponsored projects at the household and village level have brought biogas into many homes, and some biomass gasification projects exist, but these serve a relatively small proportion of the rural population. Only the wealthiest families can afford to use LPG more than occasionally, and household digesters rarely produce enough to satisfy a family's entire cooking needs; thus, total use of gas fuels remains small.

Ad hoc household energy survey reports provide useful points of comparison in an attempt to establish the broader picture. Tables 1.12–1.15 present some of the information available on energy use at the household level. Survey methods, samples and locations differ among studies; therefore, comparisons of results need to be carried out with care. The information from the National Bureau of Statistics suggests that the average rural household energy use in 2004 was 52 GJ/household–year, or about 13 GJ/person–year. The range of figures in household surveys is spread widely around this average, as do provincial averages derived from statistical publications. Surveys of over 3200 households in six provinces in different regions conducted between 1987 and 1991 found annual household energy use ranging from about 7 to 24 GJ/person–year, compared

Table 1.12. Per-capita energy use in rural households in Liangshui County, Jiangsu Province, and Guichi County, Anhui Province (China), 2003

Location	End use	Energy source (MJ/year)							Total	Share
		Wood	Straw	Biogas	Coal	Kerosene	LPG	Electricity		
Liangshui County, Jiangsu (*n*=356)	Lighting			2		0.3		937	940	16%
	Cooking	1387	735	1258	363		53	109	3904	65%
	Animal feed	260	177	123	11		0.3		571	10%
	Water heating		169	345	46		2		561	9%
	Other		27	3	12				43	1%
	Total	1647	1107	1731	431	0.3	55	1046	6017	
	Share	27%	18%	29%	7%	0.005%	1%	17%		
Guichi County, Anhui (*n*=340)	Lighting							1059	1059	16%
	Cooking	3791		1384			269	13	5457	80%
	Animal feed	45		67					112	2%
	Water heating			197			2		199	3%
	Other			2					2	0.03%
	Total	3836		1650			271	1072	6829	
	Share	56%		24%			4%	16%		

From Wang *et al*. (2006)
LPG, liquefied petroleum gas
Electricity is converted from the value of fuel inputs to power generation.

with the average rural household energy use in 1990 of 11 GJ/person–year (Wang & Feng, 1996; Sinton *et al*., 2004b).

Wang and Feng (1997a,b, 2001) and Wang *et al*. (1999, 2002) have reported a large series of rural energy surveys in eastern China. In a detailed 2003 survey of nearly 700 rural homes in Anhui and Jiangsu in villages where rates of biogas use are very high (24% and 29%, respectively), Wang *et al*. (2006) showed that the level of use of commercial energy remains low (Table 1.12). Including biogas, biofuels accounted for 75–80% of average household energy. Observed energy use *per capita* in these villages which enjoy the mild climate of the central seaboard provinces was about half the national average for rural households. Unlike most surveys, this study also provided a breakdown by end-use which showed that, in these households where no space heating was recorded, cooking tasks far outweighed all others, even when families used large amounts of fuel for the preparation of pig feed. Households without biogas digesters used about 70% more energy—mainly solid fuels—than those with biogas digesters, which provides a basis for estimating the change in exposure resulting from adding gas to the household fuel mix. Notably, LPG use in households with biogas remained significant. An earlier study in Liangshui showed a similar result (Wang & Li, 2005).

In a 2003–04 winter survey of rural areas near Xi'an, in the northern province of Shaanxi, Tonooka *et al*. (2006) found that most of the households used a wide variety of fuels, but most relied mainly on biomass for cooking and heating (Table 1.13). Only 28% of the survey sample, located in a small village, depended mainly on coal. The use of LPG there was also widespread, but was mainly limited to the wealthiest families.

Table 1.13. Stoves and fuels used in rural households near Xi'an, Shaanxi, winter 2003–04

Main stoves and fuels	Cooking		Space heating	
	No. of households	Share	No. of households	Share
Crop residues-*kang*-traditional	110	50%	105	48%
Crop residues-traditional stove	9	4%	5	2%
Crop residues-*kang*-improved	18	8%	17	8%
Crop residues-improved stove	4	2%	0	0%
Twigs-*kang*	2	1%	4	2%
Twigs-traditional stove	5	2%	4	2%
Twigs-*kang*-improved	5	2%	7	3%
Twigs-improved stove	0	0%	0	0%
Coal	35	16%	72	33%
LPG	30	14%	0	0%
Electricity/unknown	0	0%	4	2%
Total	218	100%	218	100%

From Tonooka *et al*. (2006)
LPG, liquefied petroleum gas
A *kang* is a heated brick bed.

A 2002 survey of nearly 35 000 households in Shaanxi, Zhejiang and Hubei—a 10% subsample of which was monitored for indoor air quality (Sinton *et al*., 2004a,c)—documented the highly diverse fuel and stove use patterns that are typical throughout the country (Tables 1.14 and 1.15). For instance, in the database of households where indoor air quality was measured, 28 different fuel combinations were used in kitchens in winter and 34 different fuel combinations were used in summer (Sinton *et al*. 2004c). In the larger sample of the study, the survey results were generally in line with those arising from national statistics. In some areas, availability of LPG had made improved solid-fuel stoves obsolete, and some households had advanced from traditional solid-fuel stoves directly to LPG. In most cases, however, households used both gas and solid fuels for cooking. Most households in Shaanxi reported that they heated with coal in winter. In Zhejiang and Hubei, where nearly half of the surveyed households did not heat at all in winter, a surprisingly large fraction cooked with charcoal—which is illegal to produce and sell in many areas.

Table 1.14. Main cooking and heating fuels, rural households in Zhejiang, Hubei and Shaanxi, China, 2002

Fuel	Zhejiang		Hubei		Shaanxi	
Main cooking fuel (number of households)						
Wood	807	65.3%	490	43.9%	75	7.0%
Crop residues	300	24.3%	220	19.7%	276	25.9%
Coal	3	0.2%	318	28.5%	686	64.4%
LPG	109	8.8%	69	6.2%	25	2.3%
Electricity	11	0.9%	8	0.7%		
Biogas			6	0.5%	1	0.1%
Charcoal			1	0.1%	1	0.1%
Missing	6	0.5%	3	0.3%	1	0.1%
Total	1236		1115		1065	
Main heating fuel (number of households)						
Wood	231	18.7%	222	19.9%	49	4.6%
Crop residues	5	0.4%	8	0.7%	205	19.2%
Coal	19	1.5%	66	5.9%	750	70.4%
Charcoal	347	28.1%	324	29.1%	1	0.1%
Electricity	59	4.8%	2	0.2%	24	2.3%
LPG and kerosene	5	0.4%	2	0.2%		0.0%
No space heating/missing	570	46.1%	491	44.0%	36	3.4%
Total	1236		1115		1065	

From Sinton *et al*. (2004a)
LPG, liquefied petroleum gas
Wood includes logs, twigs and other woody biomass. Crop residues include other non-woody biomass and dung.

Table 1.15. Types of stove in rural households in Zhejiang, Hubei and Shaanxi, 2002

Stove type	Flue	Zhejiang		Hubei		Shaanxi	
		No. with stove type	Fraction of sample	No. with stove type	Fraction of sample	No. with stove type	Fraction of sample
Traditional biomass	Yes	235	18.9%	60	5.4%	166	15.6%
	No	6	0.5%	50	4.5%	1	0.1%
Improved biomass	Yes	684	55.0%	829	74.3%	212	19.9%
	No	7	0.6%	35	3.1%	6	0.6%
Coal	Yes	3	0.2%	141	12.6%	538	50.6%
	No	145	11.7%	671	60.2%	275	25.8%
LPG	No	723	58.1%	258	23.1%	173	16.3%
Biogas	No	2	0.2%	34	3.0%		
Open Fire	No			121	10.9%		
Other	Yes					90	8.5%
	No	4	0.3%	9	0.8%	85	8.0%

From Sinton *et al*. (2004c)
LPG, liquefied petroleum gas
Many households own more than one type of stove, so the numbers of stove types reported are larger than the household samples (n=3746). Many households also have more than one stove of the same type. In Shaanxi, 'other' stoves probably include some type of coal stove.

(ii) *Stove types, efficiencies and tasks (cooking and heating)*

Programmes to promote improved stoves have long been introduced in China (Smith *et al*., 1993; Sinton *et al*., 2004c). As the survey results in Sinton *et al*. (2004c) described, the complex fuel situation mirrors diverse patterns of stove ownership. Most households surveyed, typically had one or more coal and one or more biomass stoves, and commonly had a gas (LPG or biogas) stove as well. Households with improved biomass stoves commonly had portable coal stoves without flues. Nearly 12% of the households reported having four or more stoves. In the overall survey sample, 95% of the biomass stoves had flues (and 77% were classified as 'improved'); only 38% of the coal stoves were equipped with flues, although most coal stoves are of relatively recent vintage, often burn briquettes and often incorporate convenient and energy-efficient features such as water boilers and small steam/oven chambers.

More than half of the households surveyed used biomass stoves for their main cooking, and about half as many used coal stoves. Many more households had LPG

stoves than used them for their main cooking; many use the stoves only occasionally because of the cost of LPG and the ready availability of biofuels in many seasons. Although coal and biomass were commonly used for heating, many households in the sample (especially in Hubei) also used charcoal for heating. It is sometimes difficult to distinguish cooking from heating because cookstoves may be started earlier in the day and left to burn longer in the evening to provide some space heating. Moreover, air pollution and fuel-use surveys in China show a complicated situation in which several fuels and stoves are often in use in different parts of the house in different seasons. In addition to cookstoves and space-heating stoves, for example, the use of *kangs*, which are bed platforms heated from underneath by coal or biomass combustion, is common in different configurations: connected to a cookstove, with a special *kang* combustion chamber fueled from outside, or arranged such that a portable coal stove used during the day for heating and/or cooking is moved under the platform at night. In either case, *kangs* are connected to chimneys, but smoke can nevertheless leak into the bedroom. Most surveyed households—71% in Zhejiang, 80% in Hubei and 81% in Shaanxi—possessed an improved stove of some type. These proportions differed somewhat from the official figures of the Ministry of Agriculture on the wider adoption of improved stoves, but the latter are still indicative of the current predominance of improved stoves. Many small portable coal stoves still do not have chimneys, but are often ignited outside so that their smokiest stage of combustion does not occur indoors. There is also no assurance that the coal types in use today are the same as those used many decades ago in any particular area.

Improvements to biomass stoves have tended to focus on combustion efficiency and the venting of emissions outdoors. However, improved stoves can have higher emissions of pollutants per unit of delivered energy (Zhang *et al*., 2000). Improved coal stoves in China have been shown to increase exposure to pollutants dramatically since many are unvented (Sinton *et al*., 2004c).

(iii) *Regional and socioeconomic variation*

Region is highly correlated with socioeconomic status; per-capita income in eastern coastal provinces is typically two to three times higher than that in central and western provinces, for both rural and urban areas (National Bureau of Statistics, 2005). Provincial and national statistical data show that different patterns of fuel use are associated with different socioeconomic and geographical conditions (see Section 1.1). In wealthier provinces, use of electricity and LPG is highest. Where coal resources are richest—generally in the north—coal use is highest. In regions where coal is less readily available and incomes are low, biomass use is highest. In examining Ministry of Agriculture data for rural energy use by province, Wang and Feng (2005) found that, while electricity use was correlated with income, the fraction of total per-capita energy use from biomass was not correlated with income. The use of biofuels was higher in the Anhui households that had incomes more than double those of the Jiangsu households (Wang *et al*., 2006).

Recent survey results also showed patterns that suggest that solid fuel use does not necessarily decline with rising income, although the use of improved energy forms is positively correlated with income (Sinton *et al*., 2004c). In all three provinces, ownership of improved stoves was associated with lower incomes and, in Hubei and Shaanxi, they were significantly associated with lower levels of education. Fuels followed a similar pattern; the use of commercial fuels (coal, LPG and electricity) was generally associated with higher incomes.

(iv) *Variations between rural and urban locations*

No statistics have been published on biofuel use in urban areas, although a brief assessment of large coastal cities showed that a certain amount of biofuel continues to be used. Relatively large amounts of charcoal are used for cooking and winter heating in some areas according to anecdotal evidence. In terms of the total proportion of urban household energy use, however, the use of charcoal is probably small.

While studies generally reflect the fact that wealthier rural households use more gas and electricity than others and usually only the poorest burn solid fuels in pit stoves, there is a widespread lack of correlation between socioeconomic status and type of solid fuel used and type of stove (traditional or improved) used in rural areas. Tonooka *et al*. (2006) found this in Shaanxi, as did Sinton *et al*. (2004a,c). Wang and Feng (2003) found that, despite higher rates of LPG and electricity use, rural households in wealthy areas still depended on biomass for 50% or more of their energy, and sometimes up to 80%, i.e. to the same extent as households in poorer areas.

(b) Pollutant levels and exposures

Since the 1980s, many studies of indoor air quality in China have been published. The focus in the 1980s and early 1990s was on combustion-related pollutants (Sinton *et al*., 1995). Table 1.16 shows the range of values for particulates (TSP and PM_{10}), benzo[*a*]pyrene, sulfur dioxide, nitrogen oxide and carbon monoxide. For households that use solid fuels, average levels were often in excess of–sometimes several times over–levels set for ambient air quality standards.

In recent years, some attention has returned to combustion products as a result of projects with international participation. Some of these recent studies and a few from the early 1990s are summarized in Saksena *et al*. (2003).

The measured range of levels of particulates is quite wide; means start in the tens of micrograms per cubic metre, but more typically reach into the hundreds of micrograms per cubic metre, or even well into the thousands, as shown in Table 1.17—a sample of the many monitoring studies carried out. Most monitoring has focused on TSP, although PM_{10} is much more common now, and a few studies have examined PM_4 and smaller fractions. Studies of PM_{10} levels in kitchens during meal preparation indicate that cooks are exposed daily to levels of 600 $\mu g/m^3$ or even three times that much. A recent study examined winter levels of PM_4 in households in Guizhou and Shaanxi, in areas where

coal is contaminated with fluorine, and found that average levels in kitchen and living areas were from about 200 μg/m^3 to 2000 μg/m^3 (He *et al*., 2005).

Table 1.16. Indoor air pollution in Chinese residences: ranges of pollutant levels in research articles (1982–94) (arithmetic means)

Pollutant	Fuel	Urban (mg/m^3)	Rural (mg/m^3)	Standards[a] (Class II, mg/m^3)	
TSP	Coal	0.21–2.8	0.01–20	Daily average	0.3
	Gas	0.15–0.51	0.19	Max. at any time	1
	Biomass		0.17–2.6		
PM_{10}	Coal	0.16–2.7	0.12–26	Daily average	0.15
	Gas	0.14–0.45	–	Max. at any time	0.5
	Biomass		0.83–22		
CO	Coal	0.58–97	0.70–87	Daily average	4
	Gas	0.22–36	2.4	Max. at any time	10
	Biomass		0.5–16		
SO_2	Coal	0.01–5.8	0.01–23	Annual average	0.06
	Gas	0.01–1.3	0.02–0.07	Daily average	0.15
	Biomass		0.01–9.1	Max. at any time	0.5
NO_x	Coal	0.01–1.8	0.01–1.7	Daily average	0.1
	Gas	0.01–0.88	0.03–0.05	Max. at any time	0.15
	Biomass		0.01–.32		
BaP	Coal	0.3–190	5.3–19 000		
(ng/m^3)	Gas	4.7–93	–		
	Biomass		3.7–3100		

From Sinton *et al*. (1995)
BaP, benzo[*a*]pyrene; CO, carbon monoxide; Max., maximum; NO_x, nitrogen oxide; PM, particulate matter; SO_2, sulfur dioxide; TSP, total suspended particles
[a] Class II air quality standards are intended to protect human health and apply to residential areas.

Particulate levels are typically lower in summer, sometimes by an order of magnitude, but this is not the case universally. While differences in indoor pollutant levels between similar households that use solid fuels and gas fuels are clear, the differences between solid fuels are not always evident. Studies in Inner Mongolia and Gansu have shown that dung fuels lead to both higher and lower levels of PM_{10} than coal in similar households (Jin *et al.,* 2005). Furthermore, as can be seen in Figure 1.9, coal use in rural areas can apparently be cleaner than use of biomass. This alone could account for the large difference in the range of concentrations found between urban and rural households that

Table 1.17. Selected studies with quantitative measurements of particulates in indoor air pollution related to the use of solid fuel in China

Reference	Household location	No. of house-holds		Season	Fuel	Stove type	Parti-culate type	Mean[a] ($\mu g/m^3$)	CV	Range	Sampling location	Sampling duration	Method
Short-term (e.g. cooking)													
Zhao & Long (1991)	Baodong, Sichuan Province	Rural	4		Raw coal	No flue	PM_{10}	710		0.31–1.26	Kitchen	Cooking	
	Pengshui, Sichuan Province		3		Briquette			930		0.48–2.39			
	Qinjiang, Sichuan Province		4		Anthracite			970		0.43–2.04			
	Zigui, Sichuan Province	Rural	5		Anthracite			1120		0.11–2.23			
	Wushan, Sichuan Province		5 3		Raw coal Anthracite			1810 1260		0.61–4.55 0.22–3.29			
Gao *et al.* (1993)	Changsha, Hunan Province	Rural	5 4	Summer	Coal Wood		PM_{10}	640 1060	550 (SD) 1050 (SD)		Kitchen	Cooking (2–3 day avg)	

Table 1.17 (contd)

Reference	Household location	No. of house-holds		Season	Fuel	Stove type	Parti-culate type	Mean[a] ($\mu g/m^3$)	CV	Range	Sampling location	Sampling duration	Method
Smith *et al.* (1994)	Beijing	Urban	58		Coal	Improved	PM_{10}	1900	0.6			Meal	Cyclone
Longer-term													
Zhang (1988)	Gansu Province	Rural	4 4		Cow dung Coal		TSP	3020 3765	120 399	2558–3623 1876–5117		3-day avg	
Chang & Zhi (1990)	Inner Mongolia	Rural	15	Winter	Dung		TSP PM_{10}	1939 1674				Daily average	
				Summer			TSP PM_{10}	1061 830					
			6	Winter	Coal		TSP PM_{10}	1743 500					
				Summer			TSP PM_{10}	1559 393					
Qin *et al.* (1991)	Chengde, Hebei Province	Urban	15	Winter Summer	Coal	Traditional	TSP TSP	665 63			Breathing zone	24 h	Cyclone
	Shenyang, Liaoning Province	Urban	15	Winter Summer	Coal	Traditional	TSP TSP	651 125					
	Shanghai	Urban	15	Winter Summer	Coal	Traditional	TSP TSP	384 411					
	Wuhan	Urban	15	Winter Summer	Coal	Traditional	TSP TSP	291 112					

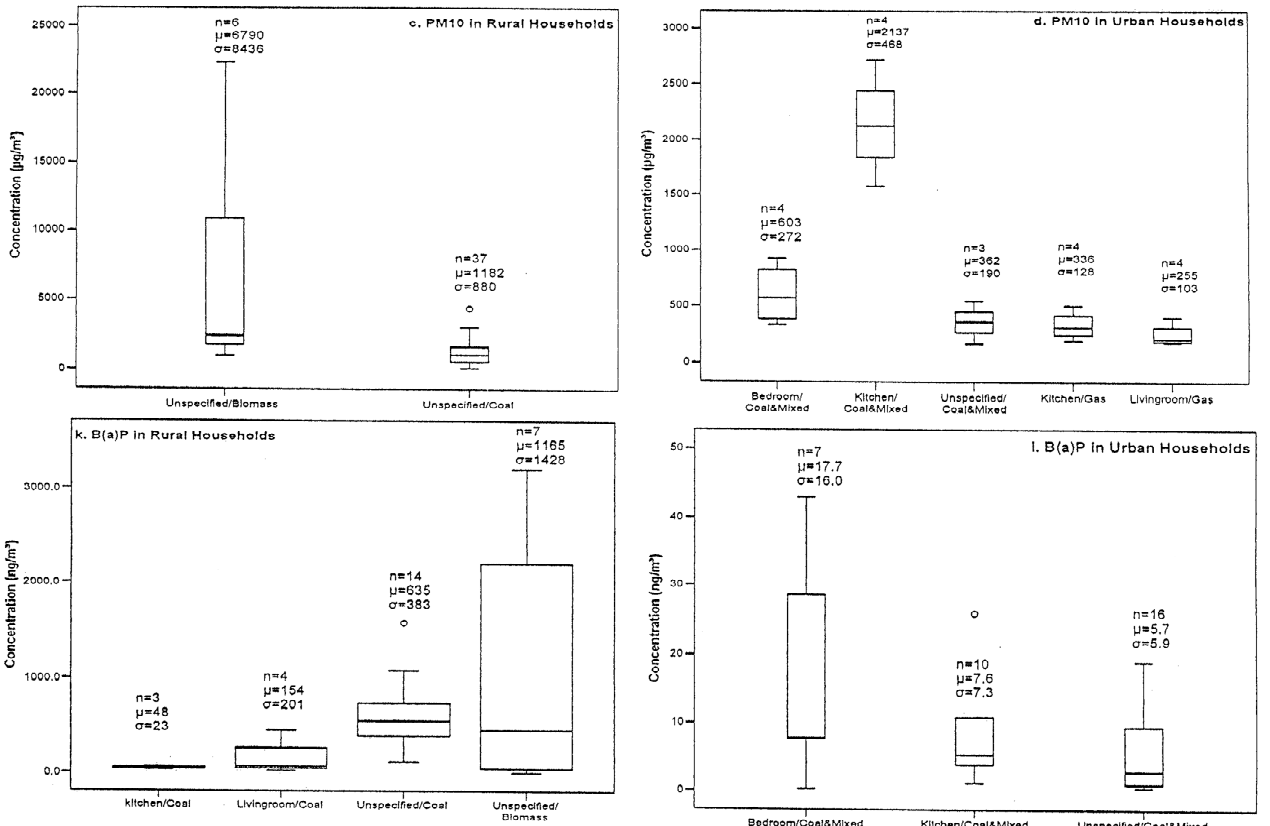
Table 1.17 (contd)

Reference	Household location	No. of households	Season	Fuel	Stove type	Particulate type	Mean[a] (μg/m^3)	CV	Range	Sampling location	Sampling duration	Method
Xu & Wang (1993)	Haidian, Beijing	Urban 31	Summer	Coal	Traditional	TSP	41	139		Bedroom	8 h	Gravimetric
	Dongcheng, Beijing	Urban 8	Summer	Coal	Traditional	TSP	90	110		Bedroom	8 h	
	Shijingshan, Beijing	Urban 10	Summer	Coal	Traditional	TSP	152	137		Bedroom	8 h	
Venners *et al.* (2001)	Anqing, Anhui Province	Rural 165	Summer	Wood		PM_{10}	248			Kitchen and bedroom		Gravimetric
Lan *et al.* (2002)	Xuanwei, Yunnan Province	Rural 15		Coal	traditional (*n*=2); improved (*n*=13)	PM_{10}	2080			1.2 m	24 h/day, 5 consecutive days	Gravimetric

[a] Data are arithmetic means.

avg, average; CV, coefficient of variation; PM, particulate matter; SD, standard deviation; TSP, total suspended particulates

Figure 1.9. Concentrations of pollutants measured in households that use solid fuel, China



From Sinton *et al*. (2004b)

The central line of each box plot indicates the sample median. The tops and bottoms of the boxes represent 75th percentiles, and the top and bottom horizontal lines represent the 95th percentiles.

B(a)P, benzo[*a*]pyrene; PM, particulate matter

use solid fuels. The former are exposed to much lower levels of PM_{10}, but the levels are still significantly higher in general than recognized ambient and/or indoor standards.

The impact on indoor air quality of improved stoves is similarly dependent on particular circumstances. For instance, improved stoves do not always have lower emissions factors (Zhang & Smith, 1999). Confounding factors such as differences in fuel combinations, shifting patterns of tasks and fuel use over time and use of multiple stoves may all influence exposure levels. The three-province survey (Sinton *et al*., 2004a) found that, taking smoking into account, in summer when stove use was dominantly for cooking, households that used coal experienced higher particulate (PM_4) levels than those that used biomass combinations, and traditional stoves emitted higher particulate levels than improved stoves (Table 1.18). Such differences disappeared during the winter heating season, however, when many households used unvented stoves; tobacco smoke was a confounding factor throughout. Even in summer and in households with no smokers, average PM_4 levels were in the range of 180–450 $\mu g/m^3$.

The same study (Sinton *et al*., 2004a) found that, in some cases, kitchens were not the sites with the highest average particulate levels. Those households that used coal or a combination of coal and biomass, unlike those that used biomass or a combination of biomass and gas, had higher particulate levels in living rooms than in kitchens. In living rooms, heating, smoking and perhaps other factors can result in levels over time that are higher than those in kitchens, despite the peaks associated with cooking. Among all the fuel combinations, average winter levels ranged from just under 100 to over 300 $\mu g/m^3$.

A recent survey of indoor air in households that used coal and biomass fuels in four provinces (Jin *et al*., 2005) showed that a variety of stove and fuel combinations in different seasons leads to average PM_4 levels in the hundreds of micrograms per cubic metre (Table 1.19). Differences between rooms with and without stoves were small.

A large number of studies that monitored benzo[*a*]pyrene were restricted to households in Xuan Wei County, Yunnan Province, but many others have reported assays performed elsewhere (Table 1.19). Measured indoor levels of benzo[*a*]pyrene were in a range spanning four orders of magnitude, from single digits (1.16 ng/m^3) to over 10 000 ng/m^3 in some of the studies in Xuan Wei County, in which bituminous coal led to much higher indoor levels than anthracite. In studies performed in other parts of the country, household averages rarely exceeded 40 ng/m^3. The relative preponderance in the literature of the Xuan Wei County studies may account in part for the difference observed in a comparison of the results of monitoring studies in urban and rural households that used solid fuels (Figure 1.9).

The combustion of wood fuels (using traditional stoves) emits levels of benzo[*a*]pyrene that fall within the range found in households that use coal (in improved stoves), and, in fact, have an upper range that far exceeds that found in the studies of coal. In the households in Xuan Wei County that used wood fuels (using traditional stoves), levels were often much higher than those in households that used coal (in improved stoves) in other parts of the country, which highlights the role played by stove type.

Table 1.18. Indoor air pollution levels in rural households in Hubei and Shaanxi, summer 2002

Room	Fuel	Smoking		PM_4 ($\mu/m^{3)}$	HOBO CO (mean ppm)	CO Dosimeter tube (ppm)
Living room	Wood twigs, agricultural residues, coal	Yes	N	15	5	5
			Mean	**316**	**1**	**38**
		No	N	8	2	2
			Mean	**235**	**0**	**23**
	Agricultural residues, coal	Yes	N	130	13	14
			Mean	**341**	**17**	**130**
		No	N	58	4	6
			Mean	**222**	**1**	**20**
	Coal products	Yes	N	79	15	16
			Mean	**301**	**11**	**85**
		No	N	51	8	8
			Mean	**284**	**17**	**73**
	Kruskal Wallis test		Asymp. Sig.	0.36	0.09	0.00

Table 1.18 (contd)

Room	Fuel	Smoking		PM_4 ($\mu/m^{3)}$	HOBO CO (mean ppm)	CO Dosimeter tube (ppm)
Kitchen	Wood twigs, agricultural residues, coal	Yes	N	15	4	5
			Mean	**478**	**4**	**38**
		No	N	8	1	2
			Mean	**191**	**0**	**23**
	Agricultural residues, coal	Yes	N	37	5	6
			Mean	**418**	**11**	**147**
		No	N	16	1	2
			Mean	**188**	**3**	**25**
	Coal products	Yes	N	29	3	4
			Mean	**263**	**8**	**125**
		No	N	15	2	2
			Mean	**451**	**35**	**125**
	Kruskal Wallis test		Asymp. sig.	0.29	0.06	0.00

From Sinton *et al*. (2004a)
Asymp. sig., asymptote significance; co, carbon monoxide; N, number; PM, particulate matter
N.B. Most households that use agricultural residues and wood also used some coal.

Table 1.19. Concentrations of PM_4 in rural households in four provinces in China, 2003

Province	Primary cooking fuel	Primary heating fuel	Indoor location	Month	No. of observations	Mean ($\mu g/m^3$)	95% CI
Gansu	Biomass	Biomass with some coal	Kitchen	March	96	518	364–671
				December	33	661	467–855
			Living/bedroom	March	96	351	205–500
				December	33	457	280–634
Inner Mongolia	Biomass	Coal and biomass	Single room (pt 1)	December	61	718	538–898
			Single room (pt 2)		61	719	480–958
Guizhou	Coal	Coal	Kitchen	March	96	352	224–480
				December	32	301	178–425
			Living/bedroom	March	96	315	186–443
				December	32	202	159–245
Shaanxi	Biomass and coal	Coal	Kitchen	March	100	187	143–230
				December	36	223	164–282
			Living room	March	25	215	136–293
				December	29	329	261–397
			Bedroom	March	98	186	132–241
				December	24	361	266–355

From Jin *et al*. (2005)
CI, confidence interval

Some time–allocation (time–activity) survey data have been published but they do not provide information regarding indoor environments (e.g. Ohtsuka *et al*., 1998; Jiang *et al*., 2006). A few studies of exposures to pollution and health impacts include the gathering of time–allocation information (Table 1.20). Pan *et al*. (2001), for instance, monitored indoor air quality in several locations from rural residents in Anqing, Anhui Province, and found that exposure to PM_{10} was dominated by the time spent indoors where levels were up to twice as high as those outdoors (Table 1.21).

1.3.3 *South Asia*

South Asia has nearly 1.5 billion inhabitants, who account for approximately a quarter of the world's population. Since nearly 70% of the population of this region lives in rural areas (WHO, 2005a) and approximately 74% relies on solid fuels for household energy requirements (Rehfuess *et al*., 2006), the region accounts for a major fraction of global exposure to indoor air pollution from smoke that is attributable to combustion of solid fuels. Recent estimates of disease burdens calculated by WHO indicate that nearly 4% of the disease burden in the region may be attributable to consequent exposures, and women and children under the age of 5 years bear the largest share of this burden (WHO, 2002,

Table 1.20. Selected studies with quantitative measurements of benzo[*a*]pyrene in indoor air pollution related to the use of solid fuel in China

Reference	Household location		No. of house-holds	Season	Fuel	Stove type	Mean[a] (ng/m^3)	CV	Range	Sampling location	Sampling duration	Method
Short-term (e.g. cooking)												
Yunnan Province Health Station (1984)	Xuanwei, Yunnan Province	Rural	6	1977	Bituminous coal	*Kang*	453.2		18.3–5992.4	Living room	Meal preparation	Fluorescence spectrometry
			6		Anthracite	*Kang*	69.1		17.7–191.7	Living room		
Yang *et al.* (1988)	Xuanwei, Yunnan Province	Rural	1		Wood		67.5				2 h	Fluorescence spectrometry
			1		Bituminous coal		399.1					
			1				295.5					
			1		Anthracite		8.5					
			1				25.5					
Longer-term												
Guo & Tang (1985)	Nanning, Guangxi Province	Urban	3	Autumn	Coal briquette		1.2			Kitchen	2-day averages	
			2				4.1					
			3				1.4					
Mumford *et al.* (1987)	Xuanwei, Yunnan Province		8	Autumn	Coal	Improved	13.4		4–21	1.5 m	12 h	GC/MS
		Rural	4	Autumn	Wood		3100	0.323				
			4		Bituminous coal		14 700	0.204				
			1		Anthracite		600					

Table 1.20 (contd)

Reference	Household location		No. of house-holds	Season	Fuel	Stove type	Mean[a] (ng/m^3)	CV	Range	Sampling location	Sampling duration	Method
Wang *et al.* (1989)	Harbin, Heilongjiang Province	Urban	13 4 4	Winter	Coal		34.0 43.1 23.4		10.6–59.8 26.7–51.1 10.6–39.9	Bedroom	3-day averages	Fluorescence spectrophotometry
Du & Ou (1990)	Guangzhou, Guangdong Province	Urban	20	4-season average	Coal		13	0.754				
He *et al.* (1991)	Xuanwei, Yunnan Province	Rural	27		Coal/wood/ smokeless coal different composition %	Traditional	76.1				12 h/day for 3 consecutive days	Fluorescence spectrophotometry
Xian *et al.* (1992)	Xuanwei, Yunnan Province	Rural			Wood Bituminous coal		25 110		6.3–75 69–180		24 h TWA	Personal monitoring
Guo *et al.* (1994)	Taiyuan, Shanxi Province	Urban	8 8 3	Winter	Briquette Briquette Briquette	F F F	7.9 10.9 7.3			Apartment bedroom Apartment kitchen Single-storey dwelling	3-day averages	
Liu *et al.* (2001)	Zhejiang Province	Urban	8	Summer	Coal	Improved	10		2–17	1.5 m	12 h	HPLC

Table 1.20 (contd)

Reference	Household location		No. of house-holds	Season	Fuel	Stove type	Mean[a] (ng/m^3)	CV	Range	Sampling location	Sampling duration	Method
Lan *et al.* (2002)	Xuanwei, Yunnan Province	Rural	15		Coal	Traditional (2); improved (13)	1660			1.2 m	24 h for 5 consecu-tive days	HPLC

CV, coefficient of variation; GC/MS, gas chromatography/mass spectrometry; HPLC, high-pressure liquid chromatography; L, living room; TWA, time-weighted average

[a] Data are arithmetic means

Table 1.21. Indoor air pollution in levels, time budgets and exposures in rural residences, Anqing, Anhui, China

Indoor pollutant levels (geometric means±SD)

Location	Sample size	PM_{10} (μg/m^3)	SO_2 (μg/m^3)	CO (mg/m^3)
Kitchen	373	518±27	12.4±36	2.0±9.9
Bedroom	504	340±9	10.9±18	1.6±6.0
Living room	366	287±9	11.0±19	1.6±4.5
Outdoor (among crops)	55	270±10	10.8±18	2.0±4.5

Time allocation (arithmetic means±SD)

Location	Male (n=245)	Female (n=222)
Kitchen	1.36±2.15	3.78±2.48
Bedroom	9.59±4.09	10.56±3.59
Living room	2.44±2.51	2.69±2.16
Outdoor (among crops)	0.84±2.66	0.62±1.49
Other	8.87±6.12	5.07±6.06

Personal average daily exposures

Pollutant	Sex	Sample size	Geometric means±SD
PM_{10} (μg/m^3)	Male	201	556±535
	Female	175	659±646
SO_2 (μg/m^3)	Male	194	23±67
	Female	170	25±70
CO (mg/m^3)	Male	193	2.25±1.6
	Female	169	2.5±2.4

From Pan *et al.* (2001)
CO, carbon monoxide; PM, particulate matter; SD, standard deviation; SO_2, sulfur dioxide

2005b). Nearly all countries in the region are classified as belonging to medium or low human development categories (UNDP, 2001) and the profile of several determinants of indoor air pollution that result from cooking and heating is similar within countries of the region.

Given the heterogeneous, decentralized nature of exposures across multiple geographical zones and the limitations of financial and technical capacity, few large-scale quantitative assessments have been possible in this region. Exposure assessments have involved multiple levels of accuracy and resolution and 'representative' exposures are therefore difficult to describe. Nevertheless, an attempt has been made to describe the levels of indoor air pollution in relation to specific determinants that operate at the

household (microenvironmental), socioeconomic and geographical (macroenvironmental) levels.

(a) Exposure data

Since they are currently outside the regulatory purview in most countries of the region, methods for the measurement of indoor air pollution have followed considerations of research as opposed to uniform protocols in adherence to national or international standards. Field logistics, contributions from multiple determinants and resource limitations have further contributed to additional challenges in making such measurements. Exposure assessments/estimations have thus been made on different scales with various levels of accuracy and resolution, in large part by individual research groups. As described earlier (Figure 1.9), the methods used in the region have ranged from fuel surveys to quantitative assessments of one or more pollutants under multiple exposure configurations. A few studies have also developed models to estimate exposure potentials. Accordingly, the results of exposure studies in the region are described below, by broadly classifying them as qualitative or quantitative assessments.

(i) *Qualitative studies of exposure*

Methods that rely on categorical qualitative variables collected from large populations can be expected to be less accurate and representative than those based on direct measurements of household or individual levels. However, as described below, every single quantitative measurement in this region unequivocally points to overwhelming pollution loads in homes that use solid fuel, which are often an order of magnitude higher than those in homes that do not use such fuels and several fold higher than commonly available exposure guidelines for specific pollutants. This has allowed 'reported solid fuel use' to be used quite reliably as a proxy for exposure in many epidemiological studies. Furthermore, the inclusion of information on the use of fuel in routinely administered population-based surveys, including national census surveys in many countries of this region, has allowed the generation of regional, national and sub-national estimates for percentages of total population at risk of such exposures to indoor air pollution. Exposure estimates recently generated by WHO (2002) for the purposes of assessing attributable (region-specific/global) disease burdens are an example of such an exercise. Results from selected recent studies that provided estimates of country levels are summarized in Table 1.22.

Information on several determinants (described in the previous section) other than the use of fuel has been collected in some national and many regional surveys. Many of these determinants are not independently associated with exposures to indoor air pollution and their contributions may be significant, but remain secondary to the type of fuel used. Many of these have, however, been found to be useful for extrapolation in models in which either data on fuel use have not been available (e.g. using data on income, education, energy market structures) or for further stratification of exposures on the basis

Table 1.22. Studies that reported percentages of solid fuel use in countries of South Asia as an indicator of the fraction of the population exposed

References	India	Pakistan	Thailand	Nepal	Sri Lanka	Bangladesh	Malaysia	Viet Nam	Indonesia	Korea
Mehta & Smith (2002); Desai *et al*. (2004); Smith *et al*. (2004)[a]	81	76	72	97	**89**	96	29	98	63	**68**
Rehfuess *et al*. (2006)[b]	74	72	72	80	67	88	<5	70	72	
Smith (2000)[c]	81	460 million people (~52% of the 1991 population) were estimated to be at risk of full exposure and nearly 252 million (~30% of the 1991 population) at risk of partial exposure in India								
Wickramsinghe (2005)[d]					83	15 million people (~83% of total and nearly 100% of the rural population in 1991) relied on solid fuels in Sri Lanka.				
Choudhari & Pfaff (2003); SCEA report (2006)[e]		67	86% of rural and 32% of urban households used solid fuels with a weighted average of 67% in Pakistan. The latter reference cites an 80% overall prevalence of solid fuel use based on routine data from a subset of 4800 households.							

[a] Global household fuel use database compiled using data from the national census, US Bureau of Census and UN Statistics Division wherever available and modelled (shown in bold) using demographic variables for other countries (as described in Mehta & Smith, 2002, Smith *et al*., 2004) using 1991 as the base year for census data.

[b] Global household fuel use database compiled using data from Demographic Health Survey (DHS, 2004), The World Health Survey (WHS, 2005) and The World Bank Living Standards Measurements Study (LSMS, World Bank 2006), wherever available and modelled using demographic variables, for other countries (as described in Mehta & Smith, 2002; Smith *et al*., 2004).

[c] Indian National Census data (1991) and data from The National Family Health Survey (1992), a population weighted national sample survey, was used to the extract information on household fuel use and related demographic variables.

[d] Data cited in a report compiled from the Food and Agricultural Organization (FAO) initiatives on Community Forestry and Regional Wood Energy Development Programme; no additional details are available.

[e] Data from Pakistan National Census Survey (1998) and The Pakistan Integrated Household Survey (PIHS, 1991) a national survey implemented jointly by the Federal Bureau of Statistics, Government of Pakistan and World Bank (as a part of the World Bank LSMS survey) was used to extract data on fuel use and related demographic variables. Census estimates were considerably lower than PIHS estimates.

of other quantitative studies (e.g. using data on stove type, ventilation, kitchen location, age, gender). Results from a selection of such studies are provided in Table 1.23.

Table 1.23. Studies that reported household survey/modelled data for potential exposures related to the use of solid fuel in South Asia

Country	Description of study results	Reference
Bangladesh	Quantitative measurement (of PM_{10}) results and determinant information from a stratified sample of 236 homes were extrapolated using regression models to predict air pollution levels in six regions within Bangladesh. Predicted levels in poorest, least educated households were found to be twice as high as those in the richest and most educated with significant geographical variations reflecting differences in distribution of fuel use and house construction materials. Exposures for young children and poorly educated women were found to be fourfold higher than those for men in higher income households with educated women (range of 24-h average levels measured, ~133–638 $\mu g/m^3$ PM_{10})	Dasgupta *et al*. (2004a,b)
India	Systematic laboratory measurements of particulates and greenhouse gas emissions from 26 fuel/stove combinations used in conjunction with a rural fuel use database and information on stove use from the relevant Government Ministry to generate state-level information on biofuel use, stove use, extent of improved stoves and emissions from solid fuel use. The emissions inventory shows major contributions to greenhouse gas and health-damaging pollutants from biomass-burning stoves. (Although several determinants intervene between emission and exposure, total emissions are largely driven by fuel type similar to concentrations and exposures across states making secondary data on total emissions a useful proxy for population exposure).	Smith *et al*. (2000)
India	Quantitative measurement (of respirable particulate matter) results from a stratified sample of 420 households and determinant information from 1032 households identified fuel type, kitchen configuration, ventilation, age and gender to be the most important determinants of exposures in three districts of the southern state of Andhra Pradesh. Evaluation of the national improved stove programme across six states found little evidence of sustained use and maintenance following distribution. Reported stove use currently remains a poor proxy for potential exposure reductions (range of 24-h average levels measured, ~73–732 $\mu g/m^3$ PM_4).	World Bank (2002a, 2004a)

Table 1.23. (contd)

Country	Description of study results	Reference
India	Quantitative data from ESMAP study above used to generate district level concentration and exposure profiles based on distribution of fuel use, kitchen configuration, age and sex distribution for the state of Andhra Pradesh. District level distributions largely driven by differences in fuel use. Differences were relatively modest compared with the high average exposures estimated for each district (range of modelled 24-h weighted average estimates for the district, ~350–450 $\mu g/m^3$ PM_4).	Balakrishnan *et al*. (2004)
India	Information on quantities of biofuel used compiled from food consumption statistics and specific energy requirements for food cooking for all major states and regions of India. Total biofuel consumption was estimated (with significantly lower uncertainties than that previously estimated using energy surveys) at 379 Tg/year with a national average biofuel mix of 74:16:10 for fuel-wood, dung and crop residues respectively. North and eastern regions of the country show higher biofuel consumption together with high per-capita food consumption and higher prevalence of dung and crop residue use. (Since consumption is linked to emissions and emissions to exposures, this represents a new measure to judge exposure potential related to cooking with biomass).	Habib *et al*. (2004)
Sri Lanka	Questionnaire survey of 1720 households from three villages in Sri Lanka used to prepare a profile of gender and poverty dimensions of energy access. Approximately 96% of surveyed households used biomass with 42% using some form of improved stoves and 67% of all stoves having chimneys. About 79% had attached kitchens and ~20% had kitchens well separated from the main house.	Wickramsinghe (2005)

(ii) *Quantitative studies of exposure*

While domestic combustion of solid fuel generates a mixture of pollutants, because of limited technical feasibilities and difficult field logistics, most studies in the region have restricted themselves to cross-sectional measurements of single pollutants (most often PM and/or carbon monoxide). However, a few large-scale studies (that mostly measured fractions of PM) carried out in India, Nepal and Bangladesh across multiple exposure configurations have provided considerable understanding of spatial, temporal and other determinants of population exposure related to solid fuel use in the region. A few have

also assessed levels of other gaseous pollutants including sulfur dioxide, nitrogen dioxide and select air toxics including PAHs and formaldehyde. Limited evidence is currently available to indicate (i) whether PM and carbon monoxide are representative indicator pollutants, (ii) whether the two are themselves consistently correlated under a wide range of exposure circumstances and (iii) how levels and proportions of other toxic constituents may vary with alternative distributions of determinants (most importantly with fuel type).

The following sections describe selected studies conducted within the region that measured levels of indoor air pollution to illustrate the scale and extent of exposures associated with the use of solid fuels for cooking and heating indoors. Several smaller studies have also been conducted, and, while an exhaustive listing of all studies conducted could not be compiled, Table 1.24 lists the major studies available in the published literature as well as in reports of projects available in the public domain. The global database of indoor air pollution studies maintained by the Department of Environmental Health Sciences, University of California Berkeley, USA (Saksena *et al*., 2003; WHO, 2005a), the bibliography of indoor air pollution studies maintained by The Energy Research Institute, New Delhi, India, and independent articles retrieved through internet search engines served as the basis for this compilation.

(iii) *Measurement studies in India*

Quantitative measurement studies have been conducted in India since the early 1980s. Many of the earlier studies only measured TSP matter during short cooking periods. One of the earliest large-scale studies of exposure assessment was conducted in the households of Garhwal, Himalayas (Saksena *et al*., 1992), and involved nearly 122 households in three villages across three seasons. Daily integrated exposure to TSP matter and carbon monoxide was assessed by personal and stationary sampling of air in six microenvironments. Concentrations of pollutants measured at the time of cooking were found to be very high (5.6 mg/m^3 and 21 ppm for TSP matter and carbon monoxide, respectively) but comparable with those measured in the Indian plains. The mean concentration in the kitchen while cooking often exceeded the concentration in other microenvironments, including the living rooms, and outdoors by an order of magnitude or more. Combining area measurements with individual time–activity records, the daily exposure of adult women to TSP matter and carbon monoxide was estimated to be 37 $mg•h/m^3$ and 110 $\mu g•h/m^3$, respectively.

More recently, two large-scale exposure assessment exercises for respirable particulates have been completed in India in the southern states of Tamil Nadu and Andhra Pradesh, respectively. In Tamil Nadu (Balakrishnan *et al*., 2002), a total of 436 rural households across four districts were monitored for respirable particulates (median aerodynamic diameter, 4 μm). Concentrations were determined during several cooking and non-cooking sessions in households and 24-h exposures were calculated on the basis of these concentrations in conjunction with time–activity records of household members. Concentrations of respirable particulate matter ranged from 500 to 2000 $\mu g/m^3$ during cooking in households that used biomass (geometric mean [GM], 1043–1346 $\mu g/m^3$)

Table 1.24. Major studies with quantitative measurement results for indoor air pollution related to the use of solid fuel in South Asia

Reference, location	No. of households	Season	Fuel	Stove type	Pollutant	Location[a]	Sampling duration[b]	Method	Range of levels reported (μg/m^3)[c]
Short-term exposure (<8 h)									
Aggarwal *et al.* (1982), India cited in GDB	5 urban homes		Wood	Traditional	TSP PAH (BaP)	Kitchen (1.5 m)	0.25 h (C)	Gravimetric TLC	7203 1270 (ng/m^3)
	4 urban homes		Dung	Traditional	TSP PAH (BaP)	Kitchen (1.5 m)	0.25 h (C)	Gravimetric TLC	15 966 8248 (ng/m^3)
	3 urban homes		Charcoal	Traditional	TSP PAH (BaP)	Kitchen (1.5 m)	0.25 h (C)	Gravimetric TLC	26 147 4207 (ng/m^3)
Smith *et al.* (1983), India	28 rural homes	Winter	Wood	Traditional	TSP BaP	Kitchen (breathing zone)	Meal duration	Gravimetric TLC	6400 4100 (ng/m^3)
	8 rural homes			Improved	TSP BaP			Gravimetric TLC	4600 2400 (ng/m^3)
Davidson *et al.* (1986), Nepal	18 rural homes	Winter	Wood	Traditional	TSP PM_{10}	Kitchen Kitchen	1–2 h (C) 1–2 h (C)	Gravimetric Gravimetric	880 (GM) 4700 (GM)
Reid *et al.* (1986), Nepal	60 rural homes	Autumn	Wood	Traditional Improved	TSP TSP	Personal exposures	1–2 h (C) 1–2 h (C)	Gravimetric Gravimetric	1750–3170 870–1370
Pandey *et al.* (1990), Nepal cited in GDB	20 rural homes at 1500 m	Summer	Wood/crop residue	Traditional	$PM_{2.5}$	Personal exposures	1 h (C)	Gravimetric	8200
				Improved	$PM_{2.5}$	Personal exposures	1 h (C)	Gravimetric	3000

Table 1.24 (contd)

Reference, location	No. of households	Season	Fuel	Stove type	Pollutant	Location[a]	Sampling duration[b]	Method	Range of levels reported (μg/m^3)[c]
Saksena *et al.* (1992), India	12 rural homes/6 micro-environments	Winter/ summer	Wood	Traditional	TSP CO	Personal exposures	Meal duration	Gravimetric TLC Electrochemical sensors	5600 21
Raiyani *et al.* (1993a), India	20 urban homes in each fuel category		Dung/wood/ charcoal	Traditional	TSP BaP	Kitchen (breathing zone)	Meal duration	Gravimetric TLC/HPLC	1190–3470 38–410 (ng/m^3)
Smith *et al.* (1994), India	61 urban homes		Wood/crop residue	Traditional	PM_{10}	Personal exposures	Meal duration	Gravimetric	900–1100
Smith *et al.* (1994), Bangkok	17 urban homes		Charcoal		PM_{10}	Personal exposures	Meal duration	Gravimetric	550
TERI (1995), India cited in GDB	20 homes with 18–20 measurements in each home		Wood	Traditional	PM_5	Kitchen (breathing zone)	Meal duration	Gravimetric	850–1460
Mandal *et al.* (1996), India cited in GDB	12 urban homes		Wood	Traditional	TSP	Kitchen (breathing zone)	4 h (C)	Gravimetric	646
Ellegard (1997), Viet Nam cited in GDB	35 urban homes		Wood		PM_{10}	Kitchen (breathing zone)	Meal duration	Gravimetric	770

Table 1.24 (contd)

Reference, location	No. of households	Season	Fuel	Stove type	Pollutant	Location[a]	Sampling duration[b]	Method	Range of levels reported (μg/m^3)[c]
Balakrishnan *et al.* (2002), India	436 rural homes from 4 districts stratified across four kitchen types	Summer	Wood/wood chips/crop residues	Traditional	PM_4	Personal exposures Living	1–2 h (C) 2–4 h (C)	Gravimetric	1307–1535 (GM) (wood fuel) 847–1327 (wood fuel)
Saksena *et al.* (2003)	40 urban homes		Wood	Traditional	PM_5	Kitchen (breathing zone)	Meal duration	Gravimetric	1200
Bhargava *et al.* (2004), India	10 rural homes	Summer/ winter	Wood Dung	Traditional	BaP	Kitchen (1.5 m) (C)	1 h	HPLC	700–1700 ng/m^3 980–1860 ng/m^3
Long-term exposure (8–24 h)									
Hessen *et al.* (1996), Nepal	34 rural homes		Wood	Traditional	TSP	Kitchen	24 h	Gravimetric	8420
Yadav *et al.* (1996), Nepal cited in GDB	39 rural homes at 2500 m	Winter	Wood	Traditional	TSP	Kitchen	8 h	Gravimetric	6400
				Improved	TSP	Kitchen	8 h	Gravimetric	4600
Balakrishnan *et al.* (2002), India	436 rural homes from 4 districts stratified across four kitchen types	Summer	Wood/wood chips/crop residues	Traditional	PM_4	Personal exposures	24 h	Gravimetric	172–226

Table 1.24 (contd)

Reference, location	No. of households	Season	Fuel	Stove type	Pollutant	Location[a]	Sampling duration[b]	Method	Range of levels reported (μg/m^3)[c]
Balakrishnan *et al.* (2004), India	412 rural homes from 3 districts stratified across four kitchen types	Summer	Wood/dung/ crop residues	Traditional	PM_4	Personal exposures Kitchen Living	22–24 h	Gravimetric and direct read out	431–467 297–666 215–357
Dasgupta *et al.* (2004a,b), Bangladesh	236 rural homes	Summer	Wood, dung, crop residues	Traditional	PM_{10}	Personal exposures Kitchen/living	22–24 h	Gravimetric and direct read out	196–264 60–1165

BaP, benzo[*a*]pyrene; CO, carbon monoxide; GM, geometric mean; HPLC, high-pressure liquid chromatography; PAH, polycyclic aromatic hydrocarbons; $PM_{2.5}$, particulate matter <2.5 μm; PM_4, particulate matter of 4 μm; PM_5, particulate matter of 5 μm; PM_{10}, particulate matter <10 μm; TLC, thin-layer chromatography; TSP, total suspended particulate matter

[a] Personal exposures usually refer to exposures of cooks.

[b] C denotes sampling during cooking. Meal duration refers to the sampling duration that covers the cooking period and typically ranges from 1 to 2 h.

[c] Most studies report arithmetic means unless otherwise specified. Distributions of levels have been found to be skewed in many studies but few report geometric means.

and average 24-h exposures ranged from 90±21 μg/m^3 for those not involved in cooking to 231±109 μg/m^3 for those who cooked; 24-h exposures were around 82±39 μg/m^3 in households that used clean fuels (with similar exposures across household subgroups).

The study in Andhra Pradesh (World Bank, 2002b; Balakrishnan *et al*., 2004) quantified daily average concentrations of respirable particulates (median aerodynamic diameter, 4 μm) in 412 rural homes from three of its districts and recorded time–activity data from 1400 household members. Mean 24-h average concentrations ranged from 73 to 732 μg/m^3 (GM, 61–470 μg/m^3) in households that used gas versus solid fuel, respectively. Concentrations were significantly correlated with fuel/kitchen type and quantity of fuel. Mean 24-h average exposures ranged from 80 μg/m^3 to 573 μg/m^3 among users of solid fuel. Mean 24-h average exposures were the highest for women cooks (GM, 317 μg/m^3) and were significantly different from those for men (GM, 170 μg/m^3) and children (GM, 184 μg/m^3). Among women, exposures were highest between the ages of 15 and 40 years (most likely to be involved in cooking or helping to cook), while among men, exposures were highest between the ages of 65 and 80 years (most likely to be indoors). The exposures were also characterized by dramatic temporal differences between cooking and non-cooking periods. Large peaks in concentrations during cooking accounted for most of the exposure potentials. Fuel type, type and location of the kitchen and the time spent near the kitchen while cooking were thus the most important determinants of exposure across these households in southern India among the other parameters examined that included stove type, cooking duration and smoke from neighbourhood cooking.

A few measurements of particulate size fractions have also been made in households that use biomass and coal (Aggarwal *et al*., 1982; Raiyani *et al*., 1993a). In these studies, which were carried out in households of peri-urban Gujarat (in western India) and measured TSPs (using a cascade impactor) during cooking, the proportion of particles less than 9 μm in aerodynamic diameter was estimated to be 96% (dung), 86% (wood) and 92% (coal). Dung use also gave the highest proportion of particles less than 2 μm in aerodynamic diameter (80%), followed by coal (70%) and wood (47%).

Finally, a few studies have measured emissions, area concentrations and size distributions of volatile and semi-volatile particle-bound PAHs released during solid fuel combustion. Personal exposure concentrations of benzo[*a*]pyrene measured over 15–30-min average sampling periods (in 15 urban households in western India) during wood and dung-cake combustion ranged from 1.30 to 9.30 μg/m^3 (Aggarwal *et al*., 1982). In another study in northern India (Bhargava *et al*., 2004), personal exposure and area measurements for PAHs were made during the cooking period in 20 households over two seasons. Concentrations of total PAHs in the respirable particulate fraction ranged from 4.5 to 33.5 μg/m^3. Personal exposure concentrations for cooks who used biofuels were significantly higher than corresponding area concentrations. Personal exposure concentrations during cooking were nearly an order of magnitude higher than those during other periods. Both concentrations were also higher in winter than in summer.

Area concentrations of 16 particulate PAHs measured over a cooking period of 45–60 min (five for each category of fuel; in households from a peri-urban cluster in western India) were 2.01, 3.46 and 3.56 μg/m^3, respectively, from wood, wood/dung-cake and dung-cake combustion (Raiyani *et al*., 1993b). Particulate PAH size distributions measured in these same indoor environments showed that houses that used cattle dung, wood and coal had 96%, 80% and 76% of the PAH mass, respectively, contained in particulates of ~ <2 μm aerodynamic diameter (Raiyani *et al*., 1993a). There was a predominance of benzo[*a*]pyrene (20%) and dibenz[*a*,*h*]anthracene (25%) and of chrysene (10%) and benzo[*a*]pyrene (13%), respectively, in particles from wood and dung-cake combustion. Laboratory emission studies for PAHs (Venkataraman *et al*., 2002) that used wood, dung cakes and biofuel briquettes in traditional and improved stoves have shown that dung-cake and briquette fuels are significantly more polluting than wood in terms of total emissions. The PAH profiles showed a predominance of fluoranthene, pyrene and benz[*a*]anthracene from all biofuels. The PAH size distributions from all stove–fuel systems were unimodal with mass median aerodynamic diameters in the 0.40–1.01 μm range for both semivolatile and nonvolatile PAHs.

(iv) *Measurement studies in Nepal*

While most studies within the region have been conducted in India and give a reasonably representative picture of pollution levels experienced in the area, a few studies conducted in Nepal illustrate the exposure situation in cold, hilly regions where solid fuels are used for cooking as well as heating. Ecological and climatic conditions play a central role in fuel choices and quantities, with associated implications for exposure. Earlier studies conducted in the 1980s (Davidson *et al*., 1986) reported stove use for cooking and heating in Nepali households to average 11.6 h per day, with additional use of a fireplace or nearly all-day operation of stoves for heating in many instances (in comparison, the average duration of stove use in the region without heating needs is estimated at 2.9 h per day). Correspondingly, fuel quantities used and time spent for fuel collection were higher (8.2 kg per day at high elevations and 2.8 kg per day in the lower elevations for 7.7 h per day, compared with an average of 1.9 kg per day for 0.5 h per day in Indian households at lower elevations during the same period). Levels of TSPs were in the range of 3–42 mg/m^3, with respirable suspended particles in the range 1–14 mg/m^3 in the houses sampled. Concentrations of potassium and methyl chloride (indicators for biomass sources) in outdoor air indicated significant contributions from indoor sources to outdoor air pollution in the area as well.

More recently, results from measurements of TSP matter, $PM_{2.5}$ and carbon monoxide have been reported (Reid *et al*., 1986; Pandey *et al*., 1990) in homes that used solid fuels in traditional and improved stoves. Use of improved stoves resulted in a two- to threefold reduction in cooking period concentrations of total TSP matter, $PM_{2.5}$ and carbon monoxide. Values for TSP matter in traditional stoves ranged from 1750 to 3170 μg/m^3 compared with 870 to 1370 μg/m^3 for improved stoves; mean values for $PM_{2.5}$ were 8200 μg/m^3 compared with 3000 μg/m^3 for improved stoves; and mean values for carbon

monoxide ranged from 64 to 310 μg/m^3 compared with 41 to 80 μg/m^3 for improved stoves. This finding is similar to that reported in other regions with improved stoves (e.g. in Guatemala, Kenya), where, despite being substantially lowered, the concentrations remain considerably higher than levels in households that used gaseous fuels as well as common health-based guideline values.

(v) *Measurements in Bangladesh*

Until recently, few measurement results had been reported from Bangladesh. A recent study conducted by the World Bank (Dasgupta *et al*., 2004a,b) now provides a substantial amount of information on the levels and distribution of pollutants across a very large number of exposure configurations. Using methods similar in nature to recent large-scale assessments in southern India, a stratified sample of 236 households was monitored using direct read-out and traditional gravimetric methods for particulates for periods of 22–24 h. Households were stratified on the basis of fuel, kitchen location and housing materials. Across households, 24-h average PM_{10} concentrations varied from 84 to 1165 μg/m^3 for firewood, 60 to 755 μg/m^3 for dung and 72 to 727 μg/m^3 for jute. Many houses reported fairly low levels during parts of the night and afternoon, when indoor readings resembled ambient readings. However, differences in cooking practices, structural arrangements and ventilation made a significant impact on overall concentrations. While most houses that used biomass reported high PM_{10} levels, a few were similar to households that used cleaner fuels such as LPG or natural gas, which suggests that ventilation is an important factor in reducing pollution levels. Improved stove use was found to be minimal which is similar to the situation found in the Indian studies. Exposure reconstructions using time–activity records in conjunction with area measurements confirmed observations from other studies of the region. Women in all age groups and children under the age of 5 years of both sexes in homes that used biomass faced the highest exposures compared with men in the working age group (24-h exposure concentrations of PM_{10} for women ranged from 209 to 264 μg/m^3 and for children from 156 to 209 μg/m^3 compared with 118 μg/m^3 for men in the age group of 20–60 years). Time spent outdoors was a major contributor to reduced exposures, as reflected by much lower exposures for adult men who spend a considerable fraction of the day outdoors. The study developed regression models that used the measurement results in conjunction with survey information on household level determinants and socioeconomic variables to create a basis for extrapolation to six regions within the country. Significant geographical differences were found, based: directly—on differential distribution of determinants including fuel choice, household ventilation and materials used for construction; and indirectly—on income, education and demographic variables through their effects on choice of fuel and prevalent household conditions.

(b) Conclusions and recommendations for further research

Exposure to indoor air pollutants associated with the combustion of solid fuels for cooking and heating is extensive in South Asia. Multiple determinants affect individual

exposures but it is clear that all users of solid fuel experience very high air pollution leading to exposure to a mixture of pollutants for extended periods during their lifetime.

Exposures are widespread and prevalent in half to three-quarters of the population in most countries of the region. Although evidence of extreme exposures has been available in the published literature for the last three decades, only recently have countries in the region undertaken efforts to collect information systematically on the extent of solid fuel use and estimated exposures. Despite limitations of being outside regulatory purviews and hence not being within a framework for consistent and routine data collection, the region has a robust series of research studies to document evidence of exposures. While quantitative assessments have been performed in many countries, a great majority focused on a few pollutants (such as PM and carbon monoxide) and showed limited evidence of their correlation to other toxic emissions; it would therefore be important for future research studies to undertake measurements of multiple pollutants. Additional measurements of carcinogenic compounds in biomass smoke are especially needed as very little is currently available in the region. Models that validate the choice of indicator pollutants and monitoring schemes that adequately describe the temporal and spatial variations are also urgently needed. Since most countries in the region have not yet developed specific standards, such models would facilitate guidance on what, when, where and how to monitor issues that duly take into account the technical and financial feasibilities of individual countries.

Women and children probably bear the largest burden of health risks from these exposures. Poverty, income and education are likely to aggravate further exposure potentials for vulnerable groups. Within the context of the Millennium Development Goals, it would be pertinent and almost necessary to identify and include indoor air pollution issues as an integral part of addressing the health problems of women and children in all countries. Indeed, if the region is to progress towards achieving even moderate human development indices within the next decades, indoor air pollution will probably be an important category of environmental risk factors in need of solutions.

1.3.4 *Latin America*

(a) Use of fuels

In Latin America, biomass fuels are mostly used in rural areas. Nearly 25% of the population of Latin America lives in rural areas where biomass fuels are most frequently used for cooking and heating. This rural population represents nearly 127 million people who are potentially exposed to biomass-related air pollution (Cordeu & Cerda, 2000). The percentage of the rural population varies from country to country and can be as high as 60%, for example in Guatemala. In Mexico, nearly 25 million people use biomass, particularly wood, as a primary source of energy for daily cooking. This number will probably remain similar or increase in the near future, since most rural families do not have the possibility of using a fuel that would be higher in the 'energy ladder' such as gas or electricity. A study conducted in Central America that included Guatemala, Honduras

and El Salvador concluded that 95% of the rural households used wood burning as a source of energy for cooking (Organización Latinoamerica de Energía, 2000). Using data from local estimates, surveys and some demographic and development indicators, Smith *et al*. (2004) built a model to predict the national use of solid fuels. For Latin America, those estimates were 24.6% (18.8–30.8%) for Mexico and Brazil and 52.9% (42.6–63.2%) for Ecuador.

In general, there is an inverse correlation between the size of the locality and the use of biomass; the smaller and most disperse communities are those that use biomass fuel most extensively (Riojas, 2003). In rural communities in Mexico, it has been estimated that the mean quantity of wood used per person per day is approximately 3 kg. For a typical family, consumption per year is equivalent to 4 tonnes of wood (Riojas, 2003).

(b) Exposure data

Several factors affect the concentration of pollutants within the household during the burning of open fires, in particular the volume and ventilation of the room, and the intensity of the fire. Climatic conditions are major determinants of exposure and are particularly important in some Latin American countries (e.g. Bolivia, Ecuador or Peru) where a large proportion of the rural population lives at high altitude. In addition, the type of cooking will also have an impact on exposure. Data from Mexico show that women can spend nearly 6–7 h per day close to biomass open-fire cooking (Brauer *et al*., 1996).

Most of the studies that measured pollutant concentrations were conducted in rural settings and attempted to characterize the distribution of levels in the kitchen. Cooking times for meals varied from study to study and ranged from 30 min to 3 h. However, time spent close to a burning fire can reach up to 12 h. The highest exposure occurs among women and their young children; however, other members of the households are also exposed because, in many cases, the kitchen is not a separate room or meals are eaten near the stove (Naeher *et al*., 2005).

(i) *Qualitative data*

In a study conducted in Guatemala, PM_{10} levels close to 1000 $\mu g/m^3$ or higher were observed in homes that used open fires and those of carbon monoxide were about 5–10 ppm and reached 25–50 ppm during use of the fire (Boy *et al*., 2002).

(ii) *Quantitative studies*

Table 1.25 presents results from studies conducted in Latin America, mostly in Guatemala and Mexico, on pollutant concentrations in households that use biomass fuel.

Studies in Guatemala

Several studies have compared different types of indoor cookstove conditions to determine the potential impact of intervention. Naeher *et al*. (2000a,b) determined particulate and carbon monoxide concentrations in highland Guatemala and compared different cookstove conditions: background (no stove use), traditional open stove, improved stove (plancha) and bottled gas (LPG) stove. Measurements were taken for

Table 1.25. Concentrations of pollutants in selected studies on the use of biomass fuel conducted in Latin America

Reference, location	No. of households	Season	Fuel	Stove type	Pollutant	Area	Average time	Method	Range of levels reported (μg/m^3 for PM, mg/m^3 [ppm] for gases)
Naeher *et al.* (2000a), indoor air, western highland of Guatemala, Quetzaltenango, 2500–2800 m	9	Fall Rainy season	Wood	Open fire Plancha LPG/open fire	Average CO	Kitchen	22 h	Drager CO	5.9 ppm 1.3 ppm 1.3 ppm
				Open fire Plancha LPG/open fire	Average $PM_{2.5}$	Kitchen		Gravimetry (SKC Universal Flow sample pump)	527.9 96.5 56.8
				Open fire Plancha LPG/open fire	Average PM_{10}	Kitchen		Gravimetry	717.1 186.3 210.2
				Open fire Plancha LPG/open fire	Average CO	Personal monitoring mother	10–12 h	Drager CO passive difusion	6.7 2.4 1.5
				Open fire Plancha LPG/open fire	Average $PM_{2.5}$	Personal monitoring mother		Gravimetry	481.2 257.2 135.6
				Open fire Plancha LPG/open fire	Average CO	Personal monitoring child		Drager CO passive difusion	2.7 1.9 2.0
					Average $PM_{2.5}$	Personal monitoring child		Gravimetry	279.1 169.7 148.5

Table 1.25 (contd)

Reference, location	No. of households	Season	Fuel	Stove type	Pollutant	Area	Average time	Method	Range of levels reported (μg/m^3 for PM, mg/m^3 [ppm] for gases)
Albalak *et al*. (2001), western highland of Guatemala, La Victoria rural community in San Juan Ostuncalco, 2000–2300 m	30	Dry season Part of rainy season	Wood	Open fire Plancha LPG/open fire	$PM_{3.5}$	Kitchen	24 h average (women spent 5 h/day)	SKC Aircheck samplers Gravimetry	1560 (GM) 280 (GM) 850 (GM)
Naeher *et al*. (2001), western highland of Guatemala, Quetzaltenango, 2500–2800 m[a]	15 open fire 25 improved stove	Summer (rainy season)	Wood	Open fire Plancha Open fire Plancha	CO $PM_{2.5}$	Kitchen Kitchen	24 h 24-h	Stain tube Gravimetric	4.0–22.7 0.0–7.1 324–2198 33–409
Bruce *et al*. (2004), Guatemala, western highland, La Victoria	29	Dry winter season	50% open fire 30% chimney stoves (plancha) 20% combination gas/open fires Wood, agricultural residues	Open fire Plancha Open fire (11) Plancha (5) Gas/other (8)	CO $PM_{3.5}$	Kitchen	24-h	Gas diffusion tubes Gravimetry	12.4 (10.2–14.5) 3.09 (1.87–4.30) 1019 (SD, 547) 351 (SD, 333) 579 (SD, 205)

Table 1.25 (contd)

Reference, location	No. of households	Season	Fuel	Stove type	Pollutant	Area	Average time	Method	Range of levels reported (μg/m^3 for PM, mg/m^3 [ppm] for gases)
Brauer *et al*. (1996), Mexico, San Jose Solis, 2450 m	22 homes	April–May Dry season	Biomass (corn stalks and husks) Wood and LPG	Open fire	Average $PM_{2.5}$	Kitchen Biomass Biomass+LPG LPG	9 h	Gravimetry	 554.7 (SD,492.9) 203.6 (SD, 180.6) 69.4 (SD, 54.2)
				LPG	PM_{10}	Biomass Biomass+LPG LPG			767.9 (SD, 540.5) 311.2 (SD, 247.8) 225.5 (SD, 260.8)
Riojas-Rodriguez *et al*. (2001), Mexico	38	Dry season	Wood	Ceta stove and open fire	Average PM_{10}	Kitchen Cooking area Stove Open fire Children area Stove Open fire	16 h	Gravimetry	 230 265 233 202
		Rainy season				Cooking area Stove Open fire Children area Stove Open fire			 206 287 158 305
Regalado *et al*. (2006), Mexico	*n*=778 samples		Biomass cooking fuel	Wood stove 12% with chimney	PM_{10} $PM_{2.5}$	Kitchen while cooking	1 h during cooking	Nephelometer	690 average 1390 peak 490 average 1040 peak

Table 1.25 (contd)

Reference, location	No. of households	Season	Fuel	Stove type	Pollutant	Area	Average time	Method	Range of levels reported (μg/m^3 for PM, mg/m^3 [ppm] for gases)
Zuk *et al*. (2007), Mexico, rural Michoàcan, 2600 m	53	Winter Nov to January	Wood	Open stove	$PM_{2.5}$	Near stove In kitchen On patio	48 h	Gravimetric	693 (246–1338) 658 (67–1448) 94 (36–236)
				Patsari (improved stove)		Near stove In kitchen On patio			246 (63–614) 255 (59–864) 92 (51–295)
Hamada *et al*. (1991), Brazil, rural southern Brazil, 930 m	28 wood stoves	Winter	Wood	Closed stove with flues	DBA BaP SPM	Kitchen	24 h	HPLC/spectro-fluorometer Gravimetry	9.79 [ng/m^3] 36.2 [ng/m^3] 108 μg/m^3
					NO_2	Kitchen Personal	24 h		14.6 [ppb] 9.0 [ppb]
Caceres *et al*. (2001), Chile, urban Santiago	24	Winter	Coal		PM_{10} CO SO_2	Kitchen	24 h	Gravimetric Real-time portable monitor	250 42 192 ppb
			Firewood		PM_{10} CO SO_2				489 57 295 ppb

Table 1.25 (contd)

Reference, location	No. of households	Season	Fuel	Stove type	Pollutant	Area	Average time	Method	Range of levels reported (μg/m^3 for PM, mg/m^3 [ppm] for gases)
Albalak *et al*. (1999), Bolivia, Altiplano, 4100 m	24 *n*=621 samples	January to October	Biomass fuel	Open fire	PM_{10}	*Kitchen* Indoor cooking Outdoor cooking *Home* Indoor cooking Outdoor cooking	6 h during cooking period in the morning	Gravimetry	 1830 (SD, 2990) 430 (SD, 140) 280 (SD, 330) 840 (SD, 400)

[a] This study also reports results presented in Naeher *et al.* (2000a).

BaP, benzo[*a*]pyrene; CO, carbon monoxide; DBA, dibenzanthracene; GM, geometric mean; HPLC, high-pressure liquid chromatography; LPG, liquid petroleum gas; NO_2, nitrogen dioxide; PM, particulate matter; SD, standard deviation; SO_2, sulfur dioxide; SPM, suspended particulate matter

22 hour during the rainy season in nine houses. Background kitchen $PM_{2.5}$ levels were 56 μg/m^3; levels were 528 μg/m^3 for open fires, 97 μg/m^3 for planchas and 57 μg/m^3 for gas stoves. Similar trends were observed for personal exposures of mothers and children. However, the authors mentioned that improved stoves (planchas) deteriorate over time and that maintenance is important to control indoor pollutant levels. In a similar study, the same authors collected samples from 15 homes that used open fires and 25 homes that had improved stoves and reported concentrations similar to those of the first study (Naeher *et al*., 2001). In another study conducted in the western highlands of Guatemala, 24-h $PM_{3.5}$ concentrations were monitored over 8 months for three fuel/cookstove combinations (10 in each category): a traditional open-fire cookstove, an improved cookstove called 'plancha mejorada' and LPG stove/open-fire combination for which mean levels were reported to be 1560 μg/m^3, 280 μg/m^3 and 850 μg/m^3, respectively (Albalak *et al*., 2001). Similar orders of magnitude of $PM_{3.5}$ levels were observed in the study of Bruce *et al*. (2004).

Studies in Mexico

A follow-up study in two rural communities of the state of Chiapas, Mexico, compared families who used an improved stove for cooking with those who used traditional open fires. Measurements (16-h) of PM_{10} showed that the concentration of particles was significantly lower in the kitchen area (158 μg/m^3 versus 233 μg/m^3) during the rainy season compared with the dry season (Riojas-Rodríguez *et al*., 2001). Two studies conducted in Mexico evaluated the impact of the use of biomass on the respiratory health of women. In a case–control study, 127 cases with chronic bronchitis or chronic airway obstruction and 280 controls were recruited at the National Institute of Respiratory Disease in Mexico (Pérez-Padilla *et al*., 1996). Cases reported a mean of 3 h of cooking with a wood stove per day and a range from none to 12 h. The mean duration of cooking with a wood stove was 28 years and ranged from none to 71 years. It was calculated that the h•year value of exposure (years of exposure multiplied by the average number of hours of exposure per day) was 80 (mean) and values ranged from 0 to 552 h•years. No objective measurement of particle levels was carried out; however, measurements taken in rural Mexico showed average levels of $PM_{2.5}$ of 555 μg/m^3 (range, 30–1492 μg/m^3) when biomass was burned in open fires (Brauer *et al*., 1996). Using an integrated nephelometer during 1 h of cooking time, levels of exposure to $PM_{2.5}$ measured in homes with stoves with (and without) a chimney averaged 490 (SD, 610) μg/m^3 with a peak of 1040 (SD, 1010) μg/m^3 (Regalado *et al*., 2006).

As part of a large health intervention study, Zuk *et al*. (2007) evaluated the impact of improved wood burning stoves on indoor air pollution in 52 homes in the rural town of Michoacan, Mexico, and monitored levels before and after the improved wood-burning stoves were received. Mean $PM_{2.5}$ concentrations (48-h) in homes that burned wood in open fires were 693 μg/m^3 near the stove and 658 μg/m^3 in the kitchen away from the stove. Paired measurements taken before and after installation of the patsari (improved

stove) indicated a median 71% reduction in $PM_{2.5}$ concentrations near the stove and a 58% reduction in the kitchen concentration.

Studies in other Latin American countries

In a study conducted in a rural community of southern Brazil during the winter, concentrations of PAHs and suspended particulate matter were assessed in homes that used wood and gas stoves. Higher levels of PAHs and suspended particulate matter were observed in homes that used wood stoves (Hamada *et al*., 1991).

Indoor air pollution was also measured in 24 houses in an area of low socioeconomic status in Santiago, Chile. The highest concentrations of PM_{10}, carbon monoxide and sulfur dioxide were measured during the time of heating with higher levels observed for firewood burning than coal. Coal, firewood and cigarette smoke were all sources of carcinogenic PAHs (Cáceres *et al*., 2001).

In a study conducted in a rural village of the Bolivian altiplano located at 4100 m above sea level, PM_{10} levels were measured in a total of 621 samples. In homes in which cooking was carried out indoors, the mean PM_{10} concentration in kitchens was 1830 $\mu g/m^3$ and ranged from 580 to 15 040 $\mu g/m^3$ over a 6-h cooking period. Daily exposure for women involved in indoor cooking was 11 280 $\mu g \cdot h/m^3$ during the working season (harvesting and planting season) and 15 120 $\mu g \cdot h/m^3$ during the non-work season (Albalak *et al*., 1999).

(iii) *Intervention studies*

Several intervention studies have shown the impact of improved stoves or installation of hoods or chimneys on exposure levels. Studies conducted in Guatemala showed that, compared with open fires alone, the LPG/open fire combination showed a 45% reduction in $PM_{3.5}$ ($p<0.07$) while the plancha mejorada showed a 85% reduction in $PM_{3.5}$ concentration compared with open fires ($p<0.0001$). Season did not affect pollutant concentration and the reduction of $PM_{3.5}$ was maintained throughout the 8 months of the study (Albalak *et al*., 2001). Bruce *et al*. (2004) reported an almost 65% reduction in indoor $PM_{3.5}$ levels with improved stoves. Similarly, a study conducted in Mexico showed that improved stoves could provide a median 71% reduction in $PM_{2.5}$ concentration near the stove and a 58% reduction in the kitchen (Zuk *et al*., 2007).

1.3.5 *Africa* (Table 1.26)

(a) Indoor air and personal exposure data

The percentage of households that use solid fuel in African has been estimated to be approximately 73% (68–78%) in Saharan Africa and 86% (81–89%) in sub-Saharan Africa (Smith *et al*., 2004*).* Studies from Africa have mainly been carried out in Kenya, The Gambia and South Africa. Daily measurements of PM_{10} usually exceeded 1500 $\mu g/m^3$ (Saksena & Smith, 2003). Recent data from Zimbabwe showed that women spend on average 5 h per day in the kitchen area and that the levels of PM_{10} were in the

Table 1.26. Concentrations of pollutants in selected studies on the use of biomass fuel conducted in Africa

Reference, location	No. of households	Season	Fuel	Stove type	Pollutant	Area	Average time	Method	Range of levels reported (μg/m^3 for PM, mg/m^3 [ppm] for gases)
Cleary & Blackburn (1968), New Guinea	9	Not reported	Wood	Not reported	Smoke density, aldehydes, CO	Native huts, new Guinea highlands	Different times for each hut described	Brass filter holder, hand pumps	666 (average) 1.08 ppm (average) 3.8 ppm (peak)
					CO				21.3 ppm (average) 150 ppm (peak)
WHO/UNEP (1988), The Gambia		Dry and rainy seasons	Wood		24-h SPM		14 h		2000 (GM) dry 2100 (GM) rainy
Boleij *et al*. (1989), Kenya	36 randomly selected from 250 in area	Rainy season (April, May)	Mostly wood sometimes biomass fuels (agricultural waste)	Traditional 3-stone open fire within house (58%), or in separate kitchen (42%)	Respirable particles NO_2	Rural area of Maragua, Kenya; kitchens	7 h/day (fire burning) Measure-ments 24 h average	Pump (Dupont P2500) and PAS-6 filter holder with glass fibre filters	1400 (mean) 180 (mean)
Collings *et al*. (1990), Zimbabwe	40	Spring	Wood, paraffin, gas, electricity	Mostly open fires in thatched huts.	PM	Kitchen	2 h	Casella 3131 TT personal sampler with Whatman 42 filter paper. EEL Densitometer No. 19	546 and 1998

Table 1.26 (contd)

Reference, location	No. of households	Season	Fuel	Stove type	Pollutant	Area	Average time	Method	Range of levels reported (μg/m^3 for PM, mg/m^3 [ppm] for gases)
Terblanche *et al*. (1992), South Africa			Biomass, tobacco, outdoor pollution		Median TSP		12.1 h		310 (school day) 298 (holiday)
Ellegard & Egneus (1993), Lusaka, Zambia	268 housewives	Not reported	Wood, charcoal, electricity	Wood Charcoal Electricity	Mean respirable particles <7.1 μm	Personal sample	2.5 h cooking time; 4-5 h monitoring time	Air pumps (Gil-Air) with cyclone, Millipore SCWP 03700 filter, Drager colorimetric diffusion tubes	890 380 240
Gachanja & Worsfold (1993), Kenya	9		Biomass fuels, wood, charcoal, dung, crop residues	Compared 2 charcoal burning stoves – traditional 3-stone and ceramic-lined	Total PAH Chrysene, benzo[*a*]-anthracene, benzo[*a*]-pyrene, benzo[*ghi*]-perylene, 3-methylchol-anthrene	Kenya highlands; kitchens	2–4 h	Glass microfibre filter and XAD-2 resin cartridge	2.6 (max.) 1–540 [ng/m^3] (range)

Table 1.26 (contd)

Reference, location	No. of households	Season	Fuel	Stove type	Pollutant	Area	Average time	Method	Range of levels reported (μg/m^3 for PM, mg/m^3 [ppm] for gases)
Ellegard (1994), Zambia	Not reported	March	Wood, charcoal, electricity	Wood Charcoal Electricity Charcoal producer	Mean TSP (respirable suspended particulates)	Kamaila, Chisamba, Zambia	4.7 h 4.8 h 4.5 h 2.3 h	Air pumps (Gil-Air SC) fitted with filter & cyclone	890 380 240 1400
Campbell (1997), The Gambia	18 (6 in each of 3 villages)	Over 12 months, dry and wet season	Biomass fuels (wood, dung, crop residues)	Not reported	TSP Benzo[*ghi*]-perylene Pyrene Benzo[*a*]-anthracene (particulates, NO_2, PAH)	2 Mandika villages, 1 Fula hamlet; kitchens	24 h	Boleij *et al.* (1988a,b)	2000 (mean) 246 [μg/g] (AM) 160 [μg/g] (AM) 147 [μg/g] (AM)
Ellegard (1997), Maputo	1000	Not reported	Mainly wood and charcoal; less common: electricity, LPG, kerosene, coal	Wood Charcoal Electricity LPG Kerosene Coal	Mean respirable particulates	10 suburban bairros around Maputo; cooking place varied.	2.84 h per day; monitoring period equal to actual cooking time (av 1.5h)	Air pumps (Gil-Air SC) with cyclone. Diffusion tube (Drager 6733191)	1200 540 380 200 760 940

Table 1.26 (contd)

Reference, location	No. of households	Season	Fuel	Stove type	Pollutant	Area	Average time	Method	Range of levels reported (μg/m^3 for PM, mg/m^3 [ppm] for gases)
Bailie *et al*. (1999)	75	Winter	Paraffin and electricity most common; gas and wood less common	Not reported	TSP	Poor urban environment	Includes peak fuel use periods	Electrochemical Exotox Model 75 continous monitors, Gil-Air model 224-XR pumps	7.15–432 continuous daily monitoring
Ezzati *et al*. (2000), Kenya	55	–	Wood, dung, charcoal	Wood Charcoal	Average daily PM_{10}		14 h/day, >200 days	Personal data RAM nephelometer	2795–4898
Sanyal & Madunaa (2000), South Africa	115	3 times: June-Sept, Oct-Dec, Mar-May	Wood, dung, coal	Very low income Low income Middle income	CO	Residential area of Victoria East; cooking and living areas	6 h (morning and afternoon)	EXOTOX Model 75 continuous gas monitors	180 118 67

Table 1.26 (contd)

Reference, location	No. of households	Season	Fuel	Stove type	Pollutant	Area	Average time	Method	Range of levels reported (μg/m^3 for PM, mg/m^3 [ppm] for gases)
ITDG (2002), West Kenya and Kajiado	50	2 rounds – wet and dry season	Wood, residues, biomass, kerosene	Before intervention	PM and CO	West Kenya Kajiado	3.8 2.5	Air sampler, stain tubes	1713 (PM), 10.1 (CO) 5526 (PM), 74.7 (CO)
	50	2 rounds – wet and dry season		After intervention	PM and CO	West Kenya Kajiado	3.14 1.52	Air sampler, stain tubes	628.9 (PM), 4.7 (CO) 3522.4 (PM), 51.4 (CO)
				Wood Charcoal Electricity	Mean CO				8.5 13 2.1
Mishra *et al*. (2004), Zimbabwe	150	15 August – 30 Nov	Wood, dung, charcoal, electricity, LPG, kerosene	Unvented cook stoves	CO PM_{10}	Zimbabwe, 10 provinces; kitchen	5 h	–	300–1000 (range) 1000–4000 (range)
Röllin *et al*. (2004), South Africa	105	Summer	Wood, paraffin (kerosene), electricity	With/without chimney	PM	South African rural villages, North-West Province; kitchen and on-person	24 h	Pumps with cyclones, Drager passive diffusion tubes	Unelectrified areas: median, 107; electrified areas: median, 37.5

CO, carbon monoxide; GM, geometric mean; LPG, liquid petroleum gas; NO_2, nitrogen dioxide; PAH, polycyclic aromatic hydrocarbons; PM, particulate matter; SO_2, sulfur dioxide; SPM, suspended particulate matter; TSP, total suspended particulates

range of 1000–4000 μg/m^3 and those of carbon monoxide were in the range of 300–1000 ppm (Mishra *et al*., 2004).

A study conducted in The Gambia, where combustion of biofuels is predominantly related to cooking fires, reported a mean level of suspended particulate matter (24-h average) of 2000 μg/m^3 with a range of 675–3444 μg/m^3. High concentrations of PAHs were also seen, with a mean level of benzo[*a*]pyrene of 102 ng/m^3 that ranged from 69 to 351 ng/m^3 and a mean level of dibenzo[*a*,*h*]anthracene of 149 ng/m^3 that ranged from 101 to 513 ng/m^3 (Campbell, 1997). Data from Kenya also reported high particulate levels during home cooking on three traditional stone open fires (using mostly wood). Fires were burning for almost 7 h per day. Average levels of suspended particulate (24-h) were approximately 1400 μg/m^3 (SD, 1000). PAHs were also measured; average levels of benzo[*a*]pyrene on filters were 60 μg/m^3 (SD, 50) and those of dibenz[*a*,*h*]anthracene were 100 μg/m^3 (SD, 90) (Boleij *et al*., 1989).

Indoor concentrations of 12 PAHs were measured in Burundi in 16 rural houses that used traditional wood stoves. In addition, 32 residents of these homes provided data on urinary excretion of 1-hydroxypyrene. Mean airborne concentrations of four volatile PAHs (naphthalene, fluorene, phenanthrene and acenaphthene) exceeded 1 μg/m^3 and that of benzo[*a*]pyrene was 0.07 μg/m^3. Naphthalene was the main PAH contaminant. Mean urinary 1-hydroxypyrene excretion of residents of traditional houses was 1.50 μmol/mol creatinine (range, 0.26–15.62 μmol/mol), a value that was 30 times higher than that of people who lived in the capital city of Burundi (Viau *et al*., 2000).

In a study conducted in Kenya, personal exposure from biomass burning in a rural population was determined using data on type of activity, emission concentrations, time spent in different microenvironments and proximity to the fire during the burning period. Because exposure to biomass burning varies from day to day (depending on the moisture content or density of the fuel, the type of food cooked, the choice of stove and fuel) and from season to season (different activity pattern, ventilation of the home), a detailed exposure measurement was made over several days (200 days) and seasons. Exposure was higher for women than men, but was similar in children of either sex under 5 years of age. The highest exposure was observed in women aged 15–49 years and reached 4.9 mg/m^3 per day (Ezzati & Kammen, 2001).

In a study conducted in Zambia, personal exposure to respirable particles (<7.1 μm) was measured in housewives exposed to different types of fuel during cooking time. Women exposed to emissions from wood burning had the highest level (890 μg/m^3) compared with those who used charcoal (380 μg/m^3) or electricity (240 μg/m^3) (Ellegard & Egneus, 1993).

(b) Impact of intervention studies

Using data from a study conducted in Kenya, Ezzati and Kammen (2002) estimated that various energy- or behaviour-based interventions can result in a 35–95% reduction in exposure to PM_{10}. It is clear that acceptance of the intervention is a crucial component for

its success and that, in each case, social, economic and environmental components need to be considered.

1.3.6 *Exposure in developed countries*

The previous sections have dealt with exposure from solid fuel combustion in developing countries; this section provides comparable figures on exposure from solid fuel combustion in developed countries. The two main sources of exposure to particles from biomass burning are wildfires and residential wood burning.

[Exposures due to agricultural burning also exist in developed countries but are localized in both space and time and do not affect a significant portion of the population. For example, in the early 1990s, agricultural burning in California contributed about 3.5 million tonnes per year to atmospheric particles, but that corresponded to only 1% of all emissions (Jenkins *et al.,* 1992). As an indication of the maximum PM concentrations that might be achieved, agricultural burning in Brazil is now carried out on a huge industrial scale, but is limited to 2 weeks per year; a 1-week monitoring programme during the burning season showed $PM_{3.5}$ levels of 191 $\mu g/m^3$, but this would correspond to a contribution to annual average concentrations of only 8 $\mu g/m^3$ (Reinhardt *et al*., 2001). Exposures elsewhere would in general be much smaller and therefore are not discussed further here.]

Wildfires are not dealt with here as they relate to outdoor exposure.

(a) Indoor air pollution

A study on a Navajo reservation in Arizona showed higher levels of respirable particles in homes that used wood for heating or cooking than in homes that used electricity or gas (Robin *et al*., 1996).

(b) Residential wood burning

All of the following studies relate to ambient (outdoor) air pollution due to wood burning for heating or to recreational use of fireplaces.

Source apportionment studies indicate that wood smoke is a major source of ambient PM during the winter months in several parts of the USA and Canada, particularly the western areas (Table 1.27). For example, 42% of the PM_{10} during winter months in San Jose, CA, was attributed to wood burning (Fairley, 1990). Chemical mass balance receptor-modelling of fine particles in Fresno and Bakersfield (CA) during wintertime identified both hardwood and softwood as sources of PM and organic compounds (Schauer & Cass, 2000), which were probably due to residential wood burning.

Outdoor PM levels in Seattle (WA) are also heavily influenced by residential woodstoves. Data from 3 years of sampling in Seattle were analysed for sources using positive matrix factorization (Maykut *et al*., 2003). The analysis found that vegetative burning contributed 34% to the total sources of PM in Seattle over 3 years.

Table 1.27. Wood smoke in developed countries: a sample of studies

Location	Wood smoke concentration	Reference
Indoor/personal		
Seattle personal	35% of total $PM_{2.5}$ mass	Larson *et al.* (2004)
Seattle indoor	49% of total $PM_{2.5}$ mass	Larson *et al.* (2004)
Fort Defiance, AZ	Indoor PM_{10} dominated by woodstove smoke	Robin *et al*. (1996)
Outdoor		
Santa Clara Co., CA	42% of chemical mass balance	Fairley (1990)
Seattle	62% of total $PM_{2.5}$ mass	Larson *et al*. (2004)
Atascadero, CA	Levoglucosan	Manchester-Neesvig *et al*. (2003)
Atlanta	11% of total $PM_{2.5}$ mass	Polissar *et al*. (2001)
Vermont	10–18% of $PM_{2.5}$	Polissar *et al*. (2001)
Christchurch, New Zealand	90% of $PM_{2.5}$ in winter	McGowan *et al*. (2002)

PM, particulate matter

Another study used a large data set from a 2-year exposure assessment and health effects panel study in Seattle during September 2000–May 2001. Data on indoor, outdoor, personal and fixed-site PM monitoring were available (Larson *et al*., 2004). Five sources contributed to indoor and outdoor samples: vegetative burning, mobile emissions, secondary sulfate, a chlorine source and a crustal-derived source. Vegetative burning contributed the largest fraction of PM mass in all the samples (49%, 62% and 35% in indoor, outdoor and personal mass, respectively).

The distribution of particle-phase organic compounds was measured in communities that had children who participated in the Southern California Children's Health Study (Manchester-Neesvig *et al*., 2003). Concentrations of levoglucosan, an efficient tracer for wood smoke aerosol, were seen in all 12 communities in the study. The average concentration increased in the winter, as would be expected for wood smoke emissions. The concentrations of levoglucosan were highest at the Atascadero site, which is about 15 miles inland. Earlier, these investigators identified two additional sugar anhydride tracers of wood smoke (galactosan and mannosan) in a study of urban sites in the San Joaquin Valley, CA (Nolte *et al*., 2001).

In Canada, where the winters are cold and the forests are abundant, wood smoke is a major source of particle emissions.

Christchurch, New Zealand, is another city that is impacted by wood smoke. It is estimated that more than 90% of wintertime ambient PM comes from heating stoves and open fires burning wood (McGowan *et al*., 2002). Frequent periods of air stagnation compound the problem by trapping PM near the ground and local meteorologists estimate that the relatively even mixing results in fairly homogeneous population exposure to PM.

Emissions inventories in Launceston, Australia, indicated that household wood burning accounted for 85% of annual PM_{10} emissions in 2000 (Jordan & Seen, 2005).

Source apportionment studies in Denmark showed that household wood burning was responsible for 47% of national $PM_{2.5}$ emissions in 2002 (Naeher *et al*., 2007). In addition, household wood burning increased by about 50% during the 1990s, compared with only a 7% increase for total energy use.

Earlier studies of the contribution of wood smoke to ambient PM were summarized by Larson and Koenig (1994). Eighteen studies in 40 locations in the Pacific Northwest (Alaska, Washington, Oregon, Idaho, Montana) were included. The ranges of concentrations for $PM_{2.5}$ and PM_{10} were 12–68 μg/m^3 and 7–205 μg/m^3, respectively. The interquartile range for the fractional contributions of wood smoke to these concentrations was about 20–70% with a median value of 54%.

1.4 Interventions and policies to reduce exposure

(a) Encouragement of the adoption of efficient biomass stoves

One major solution that could provide a bridge between biomass energy and the switch to commercial fuels but is unfortunately overlooked is the improvement of stoves that burn biomass. This is generally less expensive for households that are dependent on biomass and these stoves are often designed with chimneys to vent smoke out of the home. It is generally accepted that improved biomass stoves reduce smoke in households that use them, but the reduction is not as significant as that for households that switch completely to LPG.

International programmes for improved stoves can provide some insights into both the successes and problems that are involved in the promotion of efficient biomass stoves (Sinton *et al*., 2004a,c; Barnes *et al*., 2007). In addition, energy efficiency and increasingly improved health are recognized to be important selling points for improved stoves.

During the last 30–40 years, diverse programmes have been initiated on household energy, from small-scale initiatives led by non-governmental organizations and communities to very ambitious national programmes, the largest of which has seen the installation of some 200 million improved stoves in rural China. Although few have been subjected to rigorous evaluation, the Indian national programme of improved cookstoves (Table 1.28), the Chinese national improved stoves programme (Table 1.29) (Smith *et al*., 1993; Sinton *et al*., 2004a) and the promotion of LPG (UNDP, 2004) have been assessed. Several smaller initiatives have also been reported: for example, the ceramic and metal stoves in East Africa which have proved popular and provided local employment (Njenga, 2001) and improved stove interventions in Guatemala (UNDP/ESMAP, 2003). Current projects also include the evaluation of several household energy programmes in India, Mexico and Guatemala, which seek to promote effective and sustainable markets for improved biomass stoves.

Table 1.28. Key features and lessons from the Indian national stove programme

The Indian National Programme of Improved Cookstoves was established in 1983 with goals common to many initiatives such as:

- conserving fuel,
- reducing smoke emissions in the cooking area and improving health conditions,
- reducing deforestation,
- limiting the drudgery of women and children and reducing cooking time, and
- improving employment opportunities for the rural poor.

While the Ministry of Non-Conventional Energy Sources was responsible for planning, setting targets and approving stove designs, state-level agencies relayed this information to local government agencies or non-governmental organizations. A Technical Backup Unit in each state trained rural women or unemployed youths to become self-employed workers to construct and install the stoves.

Between 1983 and 2000, the Programme distributed more than 33 million improved *chulhas*, but despite extensive government promotion efforts, improved *chulhas* now account for less than 7% of all stoves. Among those that have been adopted, poor quality and lack of maintenance have resulted in a lifespan of 2 years at most and typically much less. Evaluation of the Programme identified four main problems:

- Most states placed inadequate emphasis on commercialization, now seen as crucial for effective and sustainable uptake.
- Overall, there was insufficient interaction with users, self-employed workers and non-governmental organizations, so that designs did not meet the needs of households, and there was very poor uptake of user training.
- Quality control for installation and maintenance of the stove and its appropriate use was lacking.
- High levels of subsidy (about 50% of the stove cost) were found to reduce household motivation to use and maintain the stove.

The more successfully managed areas of the Programme focused resources on technical assistance, research and development, marketing and dissemination of information. Recently, the government of India decentralized the programme and transferred all responsibility for implementation to the state level. Since 2000, the Programme promotes only durable cement stoves with chimneys that have a minimum lifespan of 5 years. The introduction of these stoves will make adhesion to technical specifications and quality control much easier.

Table 1.29. Household impacts of China's National Improved Stove Programme

In 2002, an independent multidisciplinary evaluation was undertaken by a team of US and Chinese researchers to evaluate (i) implementation methods used to promote improved stoves, (ii) commercial stove production and marketing organizations that were created, and (iii) household impacts of the programmes, including health, stove performance, socioeconomic factors and monitoring of indoor air quality. The first two objectives were assessed through a facility survey of 108 institutions at all levels. The third objective was assessed through a survey of nearly 4000 households in three provinces: Zheijang, Hubei and Shaanxi. Key findings were:

- The household survey revealed highly diverse fuel usage patterns: 28 and 34 different fuel combinations were used in kitchens in winter and summer, respectively. Most households owned at least one or more coal and one or more biomass stoves; 77% of the biomass stoves but only 38% of the coal stoves were classified as improved. On average, improved stoves had a mean efficiency of 14%, which is well below the Programme target of between 20% and 30%, but above the mean efficiency of 9% for traditional stoves.

Table 1.29. (contd)

- With respect to air quality (measured by PM_4, the 'thoracic fraction' of particulate matter and carbon dioxide, coal stoves showed significantly higher concentrations than biomass stoves during the summer but not during the winter. Among households that used biomass fuels (but not among those that used combinations of fuels that included coal or LPG), improved stoves showed significantly lower PM_4 and carbon dioxide concentrations than traditional stoves.
- In both children and adults, coal use was associated with higher levels of exposure as measured by carbon dioxide in exhaled breath, and improved biomass stoves had lower levels. Reported childhood asthma and adult respiratory disease were negatively associated with use of improved stoves and good stove maintenance. These results should, however, be treated as indicative due to the limited sample size.

Overall, several important conclusions emerge with relevance to future improved stove programmes:

- A wide range of combinations of different fuel and stove types may limit the impact of an improved stoves programme.
- Given the importance of space heating, providing an improved biomass stove for cooking may not be a sufficient strategy to reduce indoor air pollution. There is a need to promote improved coal stoves among rural Chinese households.
- Even among households that used improved stoves, PM_4 and carbon dioxide levels were higher than Chinese national indoor air standards, implying that a large fraction of China's rural population is still chronically exposed to pollution levels substantially above those determined by the Chinese government to harm human health.

Implementation of the Chinese national programme differed substantially from that in India, and offers an interesting comparison. Although the rural populations concerned are poor, they have greater effective purchasing power than those in many developing countries, which allowed the development of a programme in which the majority of consumers purchased the stoves at almost full price (Smith *et al.*, 1993). Among the key features of the Chinese programme that are reported to have contributed to its success are decentralization of administration, a commercialization strategy that provided subsidies for the development of rural energy enterprises and quality control through the central production of critical components, such as parts of the combustion chamber, and engaging local technical institutions to modify national stove designs to meet local needs. National-level stove competitions generated contests among counties for contracts, to ensure local interest and allow the best-placed counties to proceed first; financial payments were only provided to counties after completion of an independent review of their achievements. No large flow of funds came from central government (in contrast, for example, with India, Table 1.30) and the major financial contributions were provided by local governments. As a result, delays and other problems associated with transferring large amounts of money were avoided. The Chinese programme succeeded in shifting norms: most biomass stoves now available on the market have flues and other technical features that classify them as improved.

Table 1.30. Characteristics of the national programme on improved *chulhas* in India compared with international experience

International practices in stove dissemination	Practices of the national programme on improved *chulhas*
Focus on need-based users	Targeted approach, stress on number of villages to be covered rather than households; demand for stoves not taken into consideration
Minimal subsidy for the stove from government or donors	Subsidy on stove accounted for the largest share (50%) of government support. Users in periurban areas were willing to pay greater amounts subject to guarantee on stove quality.
Maximum support for research and development, production and distribution of stoves, credit, capacity building and public awareness	Programme funded technical back-up units, but inadequate support given for research and development, with no such support extended to non-governmental organizations. Support for capacity and awareness generation not adequate
Close interaction among the designers, producers and users of stoves	Adequate interaction between producer and user, but interaction negligible between designer, and producer and user
Dependence on centralized production of stove and stove parts to enable availability to larger number of people due to lower cost of supply	For fixed stoves, there was no scope for centralized production as these are built at user's homes. Mass production of stove parts (chimney, cowl) undertaken by private manufacturer. No mass production of the firebox.
Onus on producers and designers to meet needs of consumers	Consumer needs met by self-employed workers/non-governmental organizations through changes in stove design with low inputs from designers.
Long-term funding	Long-term target-based funding by government routed through nodal agencies and disbursed through non-governmental organizations for implementation.

The lessons from international programmes have been compared with a programme in India that was recently cancelled due to poor performance. The most successful international programmes target subsidies for the commercialization of the stoves rather than providing the user with extensive subsidies. The idea is to stimulate entrepreneurs to build the stoves and to create a real market for them. The role of subsidies in India's programme is mixed. In the successful programmes, subsidies have encouraged possible stove owners to purchase them. However, once purchased, there are no follow-up subsidies for spare parts or maintenance. Subsidies can be used to support the development of the technical back-up units, quality control facilities for testing stoves, monitoring surveys to discern stove functionality and the opinions of users on the stoves, and training or education regarding subjects such as stove design, indoor air pollution and

energy efficiency. However, this should be done in a way that integrates the design, construction and convenience of the stoves for users.

The best international programmes have developed stove programmes in the regions that have the greatest needs to conserve energy, such as those that have significant biomass shortages and emerging markets in the sale of fuelwood. The lack of availability of components and component parts appears to be a weakness in most of the programmes. Both producers and users complained about their availability and quality.

(b) Importance of electrification and other fuels

Electrification has an important role in development (International Energy Agency, 2002). There is some evidence from South Africa that communities with grid access experience lower pollutant exposure (Röllin *et al*., 2004). Electricity is not expected to bring about large reductions in exposure to indoor air pollution in most low-income countries, however, since most poor households can only afford to use it for lighting and entertainment appliances but not for the much more energy-intensive and polluting requirements of cooking and space heating. The International Energy Agency (2002) has recently carried out a detailed review of electrification, including the issues involved in supply and cost recovery among poor (and especially rural) communities.

Experience in the promotion of LPG has also been reported, for example from the Indian Deepam Scheme (UNDP/ESMAP, 2002; World Bank, 2004b), and from the LPG rural energy challenge (UNDP, 2004). This latter initiative, developed by UNDP and the World LPG Association in 2002, promotes the development of new, viable markets for LPG in developing countries. Key elements include the development of partnerships in countries, enabling regulatory environments which facilitate LPG business development and product delivery, taking steps that reduce barriers to adoption: for example, the introduction of smaller (more affordable) gas bottles, and greater government and consumer awareness of costs and benefits. McDade (2004) has recently identified several key lessons that emerged from experience with the promotion of LPG markets.

(c) Key lessons

Too often, intervention technologies have been developed without adequate reference to users' needs, and as a result have been poorly used and maintained, or abandoned. Consequently, it is important to involve users, particularly women, in assessing needs and developing suitable interventions. Sustainable uptake should also be promoted through greater availability of a choice of appropriately priced interventions in local markets.

A wide variety of interventions are already available, and new technologies and approaches are emerging. However, the greatest challenge is in securing widespread uptake of effective interventions among those most at risk (in effect, the rural and urban poor), in ways that are sustainable. Enabling policy across sectors, and at different levels in societies, is required.

Although levels of indoor air pollution associated with biomass and other solid fuel use can be reduced substantially, particularly by stoves with flues, experience shows that exposure levels are not reduced as much due to the fact that emissions remain high and people are exposed in the vicinity of their homes and from neighbours' homes. Biomass stoves using secondary combustion may offer advantages due to much reduced emissions.

Cleaner fuels, in particular LPG and natural gas, offer the largest reductions in indoor air pollution and exposure, but cost and practical issues—in particular whether these fuels meet the needs of poor households—may result in lesser reductions being achieved in practice. Electricity is important for development, but is unlikely to contribute to substantial reductions in exposure to indoor air pollution as it is rarely used for cooking (and space heating where needed) in poor communities due to the high cost of supply infrastructure and use. Finally, behavioural changes can complement technical interventions, but appear to have limited potential alone.

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2. Studies of Cancer in Humans

The studies described below focus predominantly on the risk of lung cancer following exposure to fumes from cooking and heating with fuels. The studies are organized by fuel type (coal, biomass, mixed coal/biomass) and region (inside China, outside China).

2.1 Coal

2.1.1 *Lung cancer*

(a) Case–control studies in China (organized from North to South) (see Table 2.1)

The text below summarizes the individual studies from China that assess indoor air pollution resulting from the burning of coal for cooking or heating. Selected results are highlighted in the text below but more detailed information can be found in Table 2.1.

(i) *Northern China*

Xu *et al*. (1989) conducted a case–control study in Shenyang that included 1249 lung cancer cases (729 men, 520 women) and 1345 population-based controls (788 men, 557 women); 86% of male and 55% of female cases and 70% of male and 35% of female controls were tobacco smokers. Pathological or cytological confirmation was obtained for 85.1% and 75.0% of lung cancers in men and women, respectively; 31% of these were adenocarcinoma of the lung. The risk for lung cancer was generally positively associated with exposure metrics reflecting coal use for heating, and, to a more limited degree, with coal use for cooking. After adjustment for age, education and active smoking, lung cancer risk increased in a dose–response fashion with increasing duration of using coal-heated 'burning *kangs'* (beds heated by stoves). Risk also increased with increasing duration of use of a coal stove with pipes to other rooms. Risk was higher when cooking took place in the bedroom or entry corridor to the bedroom than in a separate kitchen or elsewhere in the house. In men, the adjusted odds ratios were 1.0, 1.2 and 2.1 in relation to cooking in the bedroom for 0, 1–29 and ≥30 years, respectively (p for trend <0.05); the corresponding adjusted odds ratios in women were 1.0, 1.5 and 1.8 (p for trend <0.05). [This study overlaps with Sun *et al*. (1991).]

Wu-Williams *et al*. (1990) conducted a case–control study of 965 female lung cancer cases in northern China (445 in Harbin, 520 in Shenyang) and 959 female controls (404 in Harbin, 555 in Shenyang); 417 cases and 602 controls were nonsmokers. Seventy-four per cent (714) of the lung cancers were histologically/cytologically confirmed, of which 44% were adenocarcinoma. Cases and controls were compared with respect to indoor coal use (largely use of coal-heated *kangs*, cooking practices) and other risk factors. In multivariable logistic regression models, risk for lung cancer was generally positively and

Table 2.1. Case–control studies of lung cancer and use of coal in China

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios[a] (95% CI)	Adjustment for potential confounders	Comments
Northern China							
Xu *et al*. (1989), Shenyang, 1985–87	1249 cases (729 men, 520 women) in Shenyang aged 30–69 yrs; cell type histologically confirmed in 83% of men and 73% of women 1345 population-based controls (788 men, 557 women) selected by 3-stage procedure from urban Shenyang; frequency-matched on gender and age	In-person interview using a structured questionnaire; developed continuous index of indoor exposure to coal smoke from heating and cooking	**Coal stove with pipes to other rooms** *Men* 1–19 >20 *Women* 1–19 >20 **Cooking place in bedroom** *Men* 1–29 >30 *Women* 1–29 >30	 119 48 81 35 75 84 34 51	 1.1 (p>0.05) 2.3 (p<0.05) 1.4 (p>0.05) 1.5 (p>0.05) 1.2 (p>0.05) 2.1 (p<0.05) 1.5 (p>0.05) 1.8 (p<0.05)	Age, education, tobacco smoking	Population overlapped with the study by Wu-Williams *et al*. (1990)

Table 2.1 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios[a] (95% CI)	Adjustment for potential confounders	Comments
Wu-Williams *et al*. (1990), Shenyang and Harbin, 1985–87	965 incident female cases from local registries; age <70 yrs; cytologically verified 959 control women selected by multistage random sampling from general populations of Shenyang and Harbin; frequency-matched by 5-year age group	In-person interview using structured questionnaire	**Duration of heating device use (yrs) versus no exposure** *Coal stoves* 21–40 ≥41 *Non-coal stove* 1–20 21–20 >31 *Heated walls/floors* 1–20 >21 *Coal heaters* 1–20 >21 *Central heat* 1–20 >21	 511 253 367 259 118 127 243 258 173 258 173	 1.2 (1.0–1.6) 1.3 (1.0–1.7) 0.8 (0.6–1.1) 0.7 (0.5–0.9) 0.8 (0.5–1.1) 1.5 (1.1–2.1) 1.4 (1.1–1.9) 1.2 (1.0–1.6) 1.1 (0.8–1.4) 1.0 (0.8–1.3) 0.8 (0.6–1.0)	Age, education, smoking, study area	Experiencing eye irritation during cooking (sometimes or frequently) due to exposure to burning coal significantly increased the risk for lung cancer; population overlapped with the study by Xu *et al*. (1989)

Table 2.1 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios[a] (95% CI)	Adjustment for potential confounders	Comments
Sun *et al*. (1991), Harbin, 1985–87	418 women in whom 266 (63.6%) histologically or cytologically confirmed 398 community controls: women randomly selected from Harbin (sampling method not specified)	Questionnaire	Using smoky (soft) coal Time-trend effect Using brazier (presumably unvented)	NG NG	2.26 (1.53–3.33) $p<0.001$ 1.36 (1.01–1.83)	Pneumonia, pulmonary emphysema, smoky (soft) coal, tuberculosis, non-smoky coal (possibly anthracite), smoking, bronchitis, family cancer history, open fire basin, heating by open fire basin before 16 yrs old	Overlaps with Xu *et al*. (1989)
Dai *et al*. (1996), Harbin, 1992–93	120 nonsmoking women; 30–69 yrs old; lived in Harbin >10 yrs; 100% pathologically confirmed 120 randomly selected community controls matched on gender, 5-year age group and nonsmoking status	In-person interview using a questionnaire	*Coal stove in bedroom* 1–19 yrs ≥20 yrs * *Coal heating* 1–24 yrs 25–34 yrs Exposure to coal dust ≥10 yrs	 NG NG NG NG NG	 4.46 (1.61–12.33) 18.75 (3.94–29.32) 5.81 (1.67–20.22) 4.70 (1.28–17.18) 2.66 (1.09–6.52)	Not specified	Fried and deep fried cooking >5 times per month significantly increased the risk for lung cancer * Article erroneously reports ≥30

Table 2.1 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios[a] (95% CI)	Adjustment for potential confounders	Comments
Wang *et al*. (1996), Shenyang City, Liaoning Province, 1992–94	135 incident nonsmoking female cases from 18 hospitals; aged 35–69 yrs; 54.5% ADC, 16.4% SCC, 20.4% small- or oat-cell 135 nonsmoking controls matched by gender and age; randomly chosen from urban areas of Shenyang	In-person interview using a structured questionnaire	*Bivariate analysis* Cooking fume exposure Coal smoke exposure during cooking *Multivariate analysis* Cooking fume exposure Coal smoke exposure during cooking	 NG NG NG NG	 3.79 (2.29–6.27) 2.37 (1.44–3.91) 4.02 (2.38–6.78) Not statistically significant [NG]	Not specified	Modelled results may have been conservative; coal use not associated with lung cancer, but 100/135 cases and 107/135 controls used coal; no association of '*kang*' use for heating and lung cancer
Zhou *et al*. (2000), Shenyang City, Liaoning Province, 1991–95	72 female incident cases of adenocarcinoma; aged 35–69 yrs; from 18 major hospitals 72 women randomly selected from the Shenyang general population; age-matched (±5 yrs) to Liaoning lung cancer cases in 1988–89	In-person interview using standardized questionnaire	Coal burning	NG	0.97 (0.64–1.48)	Not specified	Both cases and controls had 'high level' of exposure to coal smoke

Table 2.1 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios[a] (95% CI)	Adjustment for potential confounders	Comments
Kleinerman *et al*. (2002), 2 prefectures (Pingliang and Qingyang) of Gansu Province, 1994–98	846 patients (626 men, 220 women) diagnosed by an expert review panel of physicians; aged 35–70 yrs 1740 randomly selected controls from the 1968 and 1990 population census lists of the 2 prefectures; frequency-matched on gender, age and prefecture	Interview using structured questionnaire ascertained 30-year history of main cooking and heating fuels and annual average coal use	**Men**	220	1.41 (1.09–1.82)	Gender, age, prefecture, television and cattle ownership (for socioeconomic status), tobacco use	Indoor levels of PM_{10}, PAH and gaseous pollutants were measured in 25 homes that burned coal and biomass. No significant differences in pollutant levels or ventilation rates were observed.
			Main fuel coal versus biomass				
			Amount of coal used, tertile versus 0				
			1	95	1.04 (0.77–1.39)		
			2	148	1.00 (0.76–1.34)		
			3	108	1.44 (1.02–2.04)		
			p for trend		0.04		
			Percentage of time using coal versus 0				
			0.7–56	62	1.69 (1.15–2.47)		
			>56	207	1.60 (1.22–2.10)		
			p for trend		0.013		
			Women				
			Main fuel coal versus biomass	58	1.03 (0.66–1.63)		
			Amount of coal used, tertile versus 0				
			1	51	1.48 (0.94–2.32)		
			2	59	1.18 (0.75–1.88)		
			3	26	0.93 (0.52–1.67)		
			p for trend		0.53		
			Percentage of time using coal versus 0				
			0.7–56	62	2.83 (1.60–5.00)		
			>56	207	1.33 (0.83–2.14)		
			p for trend		0.63		

Table 2.1 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios[a] (95% CI)	Adjustment for potential confounders	Comments
Xuan Wei County, Yunnan							
Lan *et al.* (1993), 1988–90	139 nonsmoking women (55 confirmed by pathology or cytology, 84 by X-rays and clinical history) 139 age-matched (± 2 yrs) female population controls	Interview using standardized, field-tested questionnaire that queried fuel type, history of smoky (bituminous) coal use, specifically from Laibin coal mine	**Smoky coal from Laibin Mine** Use versus no use *Tons/year used versus 0* <3 ≥3 *p* for trend *Period started use versus never* After age 20 Before age 20 Lifelong *p* for trend	74 23 51 12 10 57	7.53 (3.31–17.17) 8.24 (2.33–29.17) 7.53 (3.03–18.72) <0.001 1.84 (0.56–6.05) 5.10 (0.97–26.81) 9.89 (3.95–24.75) <0.001	Age, length of menstrual cycle, age at menopause, family history of lung cancer and chronic bronchitis	Methods unclear: all study subjects were former smokers but amount of past smoking was not specified nor was it considered as a potential confounder in the analysis.
Lan *et al.* (2000), 1995–96	122 incident cases; 100% confirmed by different methods 122 population controls taken randomly from the list of household registrations; individually matched by sex, age, village and type of fuel currently used for cooking and heating	In-person interviews using a standardized questionnaire	Smoky coal use without ventilation 130 tonnes vs ≥130 tonnes	71	2.4 (1.3–4.4)	Total smoky coal use without ventilation, pack-yrs, COPD and family history of lung cancer	

Table 2.1 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios[a] (95% CI)	Adjustment for potential confounders	Comments
Central China, excluding Xuan Wei							
Huang *et al*. (1992), Chengdu, Sichuan, 1990–91	135 'pre-invasive' lung cancer patients at three provincial hospitals 135 healthy subjects without respiratory illness from the same hospitals; matched on gender and age	In-person interview using a questionnaire	Indoor coal burning	NG	1.59 (1.01–2.07)	Unclear	The primary goal was to assess diet. [It is unclear what the reference group was, but it was possibly biomass.]
Shen *et al*. (1996), Nanjing, 1986–93	263 cases (83 SCC, 180 ADC) who were Nanjing residents for ≥20 yrs 263 population controls who were Nanjing residents; matched 1:1 for gender, age, ethnicity and 'street address'	Standardized questionnaire	Coal heating stove		3.72 (0.88–15.71)	Unclear	Results are presented for SCC. Fuel types within 'solid fuel' category were not specified. [Statistical tests were reported as one-sided, but implications are not clear.]

Table 2.1 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios[a] (95% CI)	Adjustment for potential confounders	Comments
Shen *et al*. (1998), Nanjing, 1993	70 never-smoking women diagnosed with primary lung ADC; all were Nanjing residents for ≥20 yrs 70 healthy community controls, matched 1:1 for gender, age, neighbourhood and occupation	In-person interview using a standardized questionnaire	Coal stove for heating		1.78 (0.79–4.02)	Unclear	The main purpose of the study was to assess lung cancer risk associated with passive smoking. This study may overlap with Shen *et al*. (1996).
Zhong *et al*. (1999), Shanghai, 1992–1994	504 never-smoking female incident cases; 35–69 yrs old; identified from the Shanghai Cancer Registry 601 never-smoking women; frequency-matched on age distribution of female lung cancer cases during 1987–89; randomly selected from the Shanghai Residential Registry	In-person interview using a structured questionnaire	Coal and gas vs. coal only	96	0.92 (0.63–1.35)	Age, education, income, vitamin C intake, respondent status, exposure to environmental tobacco smoke, occupation, family history of lung cancer	

Table 2.1 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios[a] (95% CI)	Adjustment for potential confounders	Comments
Southern China (Guangzhou and Hong Kong)							
Koo *et al.* (1983), Hong Kong, 1981–83	200 female lung cancer patients; mean age 61.8 yrs; 44% never smokers; 90% histologically confirmed (28% SCC, 18.5% small-cell, 34.5% ADC) 200 female community controls, matched on age (±5 yrs), residential district and housing type; mean age 60.6 yrs; 69% never smokers	Interviews with semi-structured questionnaire, using a life history approach; assessed use and duration of using coal, biomass fuels, kerosene, LPG and gas	Ever used coal for cooking	3	0.32 (p=0.15)	Unclear	The reference category is unclear for ever coal use.

Table 2.1 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios[a] (95% CI)	Adjustment for potential confounders	Comments
Liu *et al*. (1993), Guangzhou, 1983–84	316 incident cases (224 men, 92 women); 55% diagnosed by X-ray/clinical history, 13% by bronchoscopy, 32% by cytology or histology 316 hospital controls matched on gender, age, residential district and date of diagnosis; respiratory and coronary heart disease excluded	In-person interview using structured questionnaire on smoking habits, cooking fuel use and other variables	*Coal use for cooking* Men Women	200 81	1.0 (reference) 1.0 (reference)		Not having a separate kitchen, poor air circulation, small size of ventilation openings in living area and kitchen and smaller room height increased the risk for lung cancer.
Du *et al*. (1996), Guangzhou, 2 case–control studies with cases who died in 1985	849 deceased lung cancer patients (566 men, 283 women); smokers and non-smokers 849 subjects who died of causes unrelated to lung cancer, matched on gender, age and residence	Standard questionnaire administered to next of kin of lung cancer patient	*Exposure to coal fumes* Men Women	 NG NG	 0.90 (p>0.05) 2.21 (1.16–4.21)	None	Mantel-Haenszel analysis tested for effects of coal smoke; data collection methods not specified; results on 120 nonsmokers were presented but the exposure was unclear.

Table 2.1 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios[a] (95% CI)	Adjustment for potential confounders	Comments
Lei *et al*. (1996), Guangzhou, 1986	792 cases deceased from primary lung cancer (563 men, 229 women) identified from 1986 death certificates 792 controls (563 men, 229 women) matched on street of residence, year of death, gender and age; no history of respiratory diseases or tumours	In person interviews with next of kin using a standardized questionnaire	**Exposure to coal smoke (versus infrequent)** *Regular* Men Women **Living conditions index (versus good)** *Men* Fair Poor *Women* Fair Poor	 126 288 64 111	 [1.08 (0.85–1.39)] [0.90 (0.57–1.42)] 1.17 (0.89–1.54) 0.99 (0.97–1.01) 2.56 (1.39–4.70) 1.89 (1.25– 2.85)	None	91.9% of families used coal in the last 20 yrs (46.2% used wood simultaneously). There was an increased risk for lung cancer in women with a fair/poor living condition index which may indirectly point to coal smoke exposure or cooking practices as risk factors. Living condition index = living area per person/room ventilation
Luo *et al*. (1996), Fuzhou	102 cases (78 men, 24 women); 57 ADC, 39 SCC 306 community controls matched on gender, age and ethnicity	In-person interview using a standardized questionnaire	*Indoor air pollution due to coal burning* SCC ADC	NG NG NG	7.6 (3.7–15.7) 14.1 [11.8–16.4] 6.0 [4.9–7.1]	Personal and passive smoking, deep inhalation of smoke, income, history of chronic bronchitis	

Table 2.1 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios[a] (95% CI)	Adjustment for potential confounders	Comments
Taiwan, Province of China							
Ger *et al*. (1993), Taipei, 1990–91	131 lung cancer patients (72 ADC, 30 SCC, 29 small-cell); 100% histopathologically confirmed 262 hospital controls (ophthalmology) matched on gender, age (±5 yrs), interview date and insurance status; 262 neighbourhood controls matched on gender, age and residence location	In-person interview using a structured questionnaire on the use of coal and other fuels for cooking	**Coal for cooking** *ADC* vs.hospital controls vs. neighbourhood controls *SCC/small-cell* vs.hospital controls vs. neighbourhood controls *SCC/small-cell* vs.hospital controls vs. neighbourhood controls	7 10 10 	 1.44 (0.44–4.69) 0.56 (0.20–1.54) 3.73 (1.27–11.02) 10.00 (2.19–45.61) 4.41 (1.20–16.20) 24.34 (2.97–199.49)	 Matching factors Matching factors Matching factors Matching factors Unclear Unclear	A higher percentage of proxy interviews were conducted for cases (21%) than controls from the neighbourhood (17%) or hospitals (12%) [matching on location of residence may have influenced effect estimates for fuel type due to overmatching.]

Table 2.1 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios[a] (95% CI)	Adjustment for potential confounders	Comments
Ko *et al*. (1997) Kaohsiung, 1992–93	105 nonsmoking female lung cancer patients 105 (presumably nonsmoking) women from same hospital's ophthalmic service or coming to hospital for routine check-up; matched on age (± 2 yrs) and interview date	In-person interview using a structured questionnaire	**By age of exposure** *Coal vs. gas or none* <20 yrs 20–40 yrs >40 yrs		 0.5 (0.2–1.6) 1.1 (0.4–3.0) 1.1 (0.1–8.0)	Socioeconomic status, education, residential area	[Selection of cases and controls from same hospital may have caused overmatching on exposures. The near-significant positive association of lung cancer risk with wood/charcoal use is unusual, conceivably related to the matching strategy.] Further adjusting for other covariates (not specified) did not affect the statistical significance nor magnitude of effects. Risk for lung cancer was significantly increased if the kitchen did not have a fume extractor.

Table 2.1 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios[a] (95% CI)	Adjustment for potential confounders	Comments
Le *et al*. (2001), Kaohsiung, 1993–99	527 histologically confirmed cases (236 men, 291 women); 18–83 yrs old; 28.2% SCC and small-cell carcinoma and 47.7% ADC 805 controls from same hospital without tobacco-related illness; matched on gender and age (± 2 yrs)	In-person interview using a structured questionnaire	**Women** *Coal vs. gas or none* SCC or small-cell carcinoma Coal or anthracite ADC Coal or anthracite	 14 49	 1.2 (0.5–3.0) 2.1 (1.2–3.7)	Smoking, residential area (urban, suburban, rural), education, socioeconomic status	Only 7% of men reported cooking for the family and thus data were not shown. In women, stir-frying, frying and deep-frying fumes emitted were statistically significantly associated with risk for ADC but not SCC or small-cell carcinoma. Long-term residence near industrial district was associated with lung cancer risk, especially in women. Risk for lung cancer was significantly increased if the kitchen did not have a fume extractor.

ADC, adenocarcinoma; COPD, chronic obstructive pulmonary disease; LPG, liquid petroleum gas; NG, not given; PAH, polycyclic aromatic hydrocarbons; PM_{10}, particulate matter ≤10 μm; SCC, squamous-cell carcinoma; yrs, years

[a] *p*-value reported if confidence interval was not specified

statistically significantly associated with duration of use of the following: *kangs* (especially directly-heated ones), coal stoves or floor/wall heating by pipes from the cooking stove.

[The Working Group noted that female lung cancer cases and controls included in the study by Xu *et al*. (1989) were also included in the study by Wu-Williams *et al*. (1990). Assessment of cooking practices was relatively limited in these two studies. It was also noted that both studies were large and well-conducted, but assessment of coal-related exposure may have been hampered by lack of exposure contrasts, i.e. coal exposures were mainly compared with exposure to biomass fuels possibly leading to an underestimation of the effect. This comment also applies to Wang *et al*. (1996) and Zhou *et al*. (2000).]

Dai *et al*. (1996) conducted a study of 120 nonsmoking women with adenocarcinoma of the lung and an equal number of nonsmoking population controls; all were long-term residents of Harbin. After adjustment, risk for adenocarcinoma was positively and significantly associated with several metrics of domestic coal use, including having a coal stove in the bedroom, having coal heating and long-term residential 'exposure to coal dust'. [The Working Group noted that confidence intervals in this report were wide, reflecting the relatively small number of subjects.]

In Shenyang, Wang *et al*. (1996) compared the experiences of 135 female lifetime nonsmokers diagnosed with primary lung cancer with those of an equal number of nonsmoking population control women. Of the lung cancers included, 57.2% were diagnosed pathologically or cytologically, 54.5% of which were adenocarcinoma. In bivariate analysis, but not multivariable analysis, exposure to coal smoke during cooking was positively and 'significantly' associated with lung cancer risk. Other metrics of coal use were not associated with risk. [The Working Group noted that this study was small and the exposure was limited to dichotomized (no/yes) assessment. The specific variables included in the multivariable analysis were not described. The validity of a diagnosis of adenocarcinoma is questionable because the authors stated that determining the histological cell type was based on relevant medical records, chest X-rays, CT films, and cytological and histological slides.]

Two studies in the Kaohsiung area, Taiwan, were reported by Ko *et al*. (1997) and Le *et al*. (2001) (described in detail in the monograph on high-temperature frying). Compared with those who did not cook or cooked with gas, the odds ratio for lung cancer was near unity for those who cooked with coal (odds ratio, 1.1; 95% confidence interval [CI], 0.4–3.6) (Ko *et al.*, 1997).

In a subsequent report (Le *et al*., 2001), the relationship between cooking fuel and risk for lung cancer was examined separately by lung cancer cell type. In the analysis which included 82 squamous-cell and small-cell lung cancers and 129 controls, the odds ratio was 1.2 for use of coal and/or anthracite (95% CI, 0.5–3.0) when compared with women who did not cook or used gas for cooking. In contrast, the risk for adenocarcinoma of the lung (158 cases, 262 controls) increased in relation to use of coal (odds ratio, 2.1; 95% CI, 1.2–3.7). Tobacco smoking, residential area, education and social class were adjusted for

in the analysis. [The Working Group noted that information on duration of wood and coal use was not reported in these two studies.]

Zhou *et al*. (2000) published another report using a subset of women from Wang *et al*. (1996) in Shenyang. Specifically, 72 women (52 nonsmokers) who had been diagnosed with adenocarcinoma of the lung between 1991 and 1995 were compared with an equal number of control women (49 of whom were nonsmokers). There was no association between coal burning and risk for lung cancer. [The Working Group noted that most of the lung cancer cases and controls included in the analysis by Zhou *et al*. (2000) were already in the report by Wang *et al*. (1996). Unadjusted odds ratios were reported. This study was small and the confidence intervals were very wide.]

Kleinerman *et al*. (2002) conducted a case–control study of lung cancer in relation to household use of coal and biomass fuel in two rural prefectures of Gansu Province, China; about 25% of subjects used coal and most coal users reported using bituminous coal. Of the patients, 846 were deemed to have lung cancer by an expert review panel, and 1740 controls were frequency-matched to patients on gender, age and prefecture of residence. Multivariable logistic regression analyses were conducted separately for men and women. In men, the risk for lung cancer was associated positively and significantly with use of coal (versus use of biomass), the amount of coal used and the percentage of time that coal was most frequently used as fuel in the past 30 years. None of these metrics for coal versus biomass exposure were significantly associated with the risk for lung cancer in women.

(ii) *Xuan Wei County, Yunnan Province*

Rural Xuan Wei County, Yunnan Province, is impacted by indoor air pollution due to traditionally used fuel types: 'smoky coal' (bituminous coal), 'smokeless coal' (anthracite) and wood. The great majority of residents were farmers, and residential stability was very high. There have been few stationary or mobile sources of outdoor air pollution.

Liu *et al*. (1991) and He *et al*. (1991) reported a case–control study in Xuan Wei that included 110 incident cases of lung cancer (56 men, 54 women) identified in regional hospitals/clinics in 1985–86, and 426 population controls (224 men, 202 women). Cases and controls were matched on gender, age, occupation (all were farmers) and village of residence. [Matching on village of residence overmatched on type of indoor fuel and type of home.] 'Smoky' coal was used at least four times more often than wood in this population. While duration and frequency of cooking food were significantly associated with risk for lung cancer in an exposure–response manner after adjustment for other risk factors, this precluded assessment of risk for lung cancer in relation to specific fuel types. [Although the analyses were duplicated in both studies, the Working Group noted discrepancies in the results. The instability of the risk estimates is demonstrated with the different choice of category cut-points in both studies. The Working Group also noted that inferences from these two studies are limited by the relatively small sample size and the uncertainty of the significance of the reference group.]

Another case–control study conducted among female farmers in Xuan Wei (Lan *et al*., 1993) was based on 139 incident female lung cancers that were diagnosed between 1988 and 1990 and 139 age-matched controls. Of the lung cancer cases, 55 (39.6%) were diagnosed cytologically/ pathologically. All cases and controls were current nonsmokers but all were former smokers. Use of smoky coal from the Laibin mine was significantly associated with risk for lung cancer by frequency and duration of use. [Although all participants were former smokers, the amount of past smoking was not specified nor was it considered as a potential confounder in the analysis.]

Lan *et al*. (2000) carried out a population-based case–control study of 122 cases and 122 controls. This study was designed to evaluate the relationship between genetic susceptibility and lung cancer. Controls were individually matched to cases by sex, age, village and type of fuel currently used for cooking and heating. Compared with subjects whose cumulative smoky coal use was less than 130 tonnes, subjects who used more than 130 tonnes of smoky coal had a 2.4-fold increased risk for lung cancer (95% CI, 1.3–4.4; 71 exposed cases; adjusted for total smoky coal use without ventilation, pack–years of smoking, chronic obstructive pulmonary disease and family history of lung cancer). [The Working Group noted that even with matching on fuel type, the study observed a cumulative effect of smoky coal.]

(iii) *Central China excluding Xuan Wei*

In Chengdu, Sichuan Province, Huang *et al*. (1992) performed a case–control study of 135 'pre-invasive' lung cancer patients drawn from three provincial hospitals and 135 healthy controls individually matched to cases on gender and age. Controls were enlisted from persons coming to the same three hospitals for routine health check-ups and matched on residential area. The primary goal of this study was to assess dietary risk factors for lung cancer. Burning coal indoors was associated with a statistically significantly higher risk for lung cancer than not burning coal indoors (Odds ratio, 1.59; 95% CI, 1.01–2.07). [It is unclear what the exposure of the reference group was, but it may have been biomass.]

Shen *et al*. (1998) conducted a case–control study in women in Nanjing that included 70 never-smoking lung cancer patients and 70 healthy community controls, matched 1:1 with cases on gender, age, neighbourhood and occupation. Subjects appear to have been a subset of those in Shen *et al*. (1996). Use of solid fuel (versus non-solid fuel) and of coal stoves was assessed, together with cooking-related metrics and other covariates. Use of a coal stove for heating was marginally significantly associated with lung cancer risk (odds ratio, 1.78; 95% CI, 0.79–4.02, p=0.08). [The Working Group noted several limitations in this study. The report lacked details regarding the study design (e.g. response rate), characteristics of the study population (e.g. gender distribution, active smoking history) and covariates included in the statistical models.]

Zhong *et al*. (1999) conducted a case–control study in Shanghai that included a total of 649 women who had been diagnosed with incident lung cancer during 1992–94 and 675 population controls. Subjects who had smoked at least one cigarette a day for at least

6 months (145 cases, 74 controls) were excluded from the analyses. Thus, results were based on 504 cases and 601 controls who were lifetime nonsmokers. Seventy-seven per cent of the lung cancers were diagnosed histologically or cytologically and 76.5% (*n*=296) of these were adenocarcinoma. The analysis explored cooking-related associations in more detail than those related to fuel. In multivariable logistic regression models, coal and gas use versus coal only was not associated with risk for lung cancer (odds ratio, 0.92; 95% CI, 0.63–1.35) but kitchen smokiness during cooking was positively and significantly associated with risk for lung cancer in a dose–response manner. [The Working Group noted that the contrast was between coal and gas versus coal only and therefore does not address the risk associated with exposure to coal.]

(iv) *Southern China*

Koo *et al*. (1983) reported a case–control study in Hong Kong Special Administrative Region that included 200 women hospitalized with lung cancer and 200 community controls matched on gender, age (±5 years), residential district and type of housing. Data were obtained by in-person interview using a semi-structured questionnaire and taking a life-history approach. The investigators assessed use and duration of use of biomass fuels, coal, kerosene, LPG and gas. Only 12 of 400 subjects (3%) used coal as cooking fuel—this proportion was 1.5% in cases and 4.5% in controls. The few subjects who had ever used coal had used it only when they had lived in mainland China but discontinued its use when they moved to Hong Kong Special Administrative Region. Unadjusted relative risks were calculated for matched and unmatched data. Use of coal was inversely and non-significantly associated with the risk for lung cancer (odds ratio, 0.32; p=0.15). [The Working Group noted that, in view of the few subjects using coal (three cases, nine controls), this study probably did not allow a very informative test of lung cancer risk in relation to coal use.]

Liu *et al*. (1993) conducted a case–control study in Guangzhou during 1983–1984 that included 316 incident lung cancer cases (224 men, 92 women) and 316 hospital controls individually matched by gender, age (±2 years), residential district and date of diagnosis. Controls were not chosen from the Tumor Hospital or Chest Hospital and those with respiratory and coronary heart disease were further excluded. Analyses using multivariable conditional logistic regression models adjusted for education, occupation, occupational exposure, history of tuberculosis, chronic bronchitis, family history of cancer, smoking, living area and passive smoke (in women only) were stratified by gender. Use of coal for cooking was the reference category (odds ratio, 1.0) for examining the risk for lung cancer associated with other cooking fuels (gas, wood); 89% (200/224) of men and 88% (81/92) of women had ever used coal for cooking.

Du *et al*. (1996) reported another case–control study in Ghangzhou. Cases were 849 deceased lung cancer patients (566 men, 283 women) who died in 1985 and controls were persons who died of causes unrelated to lung cancer, matched with cases on gender, age (±2 years) and residence. A standardized questionnaire was used to interview next of kin of the lung cancer patients [and presumably the controls]. Lung cancer risk in women

was positively and significantly associated with smoking and 'exposure to coal fumes'. Risk in men was significantly associated only with smoking.

Luo *et al*. (1996) reported a case–control study in Fuzhou that included 102 lung cancer cases (78 men, 24 women) and 306 community controls, matched with cases on gender, age and ethnicity. Data were analysed using conditional logistic regression, and separate analyses were conducted for squamous-cell carcinoma and adenocarcinoma. The presence of smoke in the living room during cooking with coal was positively and statistically significantly associated with risk for lung cancer (odds ratio, 7.6; 95% CI, 3.7–15.7 for all lung cancers; odds ratio, 14.1 [95% CI, 11.8–16.4]; p=0.026 for squamous-cell carcinoma; odds ratio, 6.0 [95% CI, 4.9–7.1]; p=0.002 for adenocarcinoma). [The Working Group noted that smoking was significantly associated with the risk for squamous-cell carcinoma, but only moderately for adenocarcinoma (not statistically significant).]

(v) *Taiwan*

Ger *et al*. (1993) conducted a case–control study in Taipei that included 131 primary lung cancers (92 men, 39 women) identified between 1990 and 1991. All were histologically confirmed (59 squamous-cell/small-cell carcinoma, 72 adenocarcinoma). Two control groups were interviewed: 262 hospital controls were matched to cases on sex, date of birth (±5 years), date of interview and insurance status whereas 262 neighbourhood controls were matched to cases on age, sex and residence of the case at the time of diagnosis. When lung cancer cases were compared with neighbourhood controls, use of coal for cooking was unrelated to risk for adenocarcinoma (odds ratio, 0.56; 95% CI, 0.20–1.54; adjusted for matching factors; seven exposed cases), but was strongly associated with risk for squamous-cell/small-cell carcinoma (odds ratio, 10.00; 95% CI, 2.19–45.61; adjusted for matching factors; 10 exposed cases). In multivariable analysis, use of coal as a cooking fuel remained a significant risk factor for squamous-cell/small-cell carcinomas. The magnitude of effect was smaller but also statistically significant when cases were compared with hospital controls. [The Working Group noted that this study included few female nonsmoking lung cancer patients: 48 cases compared with 229 controls (111 hospital controls, 118 neighbourhood controls) were nonsmokers. It is not clear whether the results for coal burning related to usual, past or current practices. The prevalence of coal burning differed substantially between the neighbourhood controls who were matched to the adenocarcinoma (14.6%) or the squamous-cell lung cancer cases (1.7%). The corresponding figures for the hospital controls selected for adenocarcinoma and squamous-cell lung cancer patients were 7.6% and 5.1%, respectively. Thus, the significantly increased risk for squamous-cell/small-cell cancers associated with coal burning may be related to differences among the control subjects. Furthermore, the Working Group also noted that a higher percentage of proxy interviews was conducted for cases (21%) than controls from the neighbourhood (17%) or hospitals (12%), and that matching on location of residence may have influenced effect estimates for fuel type due to overmatching.]

The study by Le *et al*. (2001) included lung cancer patients who had been diagnosed between 1993 and 1999. Women diagnosed with squamous-cell or small-cell carcinoma (*n*=84) or adenocarcinoma of the lung (*n*=162) and corresponding controls (*n*=407) were included in the analysis. Women with other lung cancer cell types (*n*=45 cases) were excluded. Risk for lung cancer was associated with type of cooking fuel: women who used coal or anthracite as a cooking fuel versus those who used gas or no fuel had a significantly increased risk for adenocarcinoma (odds ratio, 2.1; 95% CI, 1.2–3.7; 49 exposed cases) but not for squamous- or small-cell carcinoma (odds ratio, 1.2; 95% CI, 0.5–3.0; 14 exposed cases).

A third study by this research group (Ko *et al*., 2000) addressed lung cancer and cooking in some detail, but did not specifically address fuel or fuel smoke. This study is described in the monograph on high-temperature frying.

(b) Case–control studies outside China (see Table 2.2)

Wu *et al*. (1985) conducted a case–control study among white women in Los Angeles County, CA, USA. One hundred and forty-nine cases of adenocarcinoma and 71 cases of squamous-cell carcinoma of the lung identified from population-based tumour registry and a group of age-matched neighbourhood controls were interviewed by telephone. No information on the number of years that coal was used was available. Exposure to burning coal (used for heating or cooking) during the majority of childhood and teenage years increased the risk for lung cancer: the odds ratio for adenocarcinoma was 2.3 (95% CI, 1.0–5.5) and that for squamous-cell carcinoma was 1.9 (95% CI, 0.5–6.5) after adjusting for tobacco smoking. An increased risk for lung adenocarcinoma was seen when stratified by smoking status (odds ratio for nonsmokers, 3.2; 95% CI, 0.9–11.8; odds ratio for former smokers, 4.3; 95% CI, 1.0–17.8; odds ratio for current smokers, 9.5; 95% CI, 2.1–41.9). Multivariable logistic regression that adjusted for personal smoking, childhood pneumonia and β-carotene intake produced similar results.

Sharpe *et al*. (1989) conducted a case–control study of renal-cell carcinoma in Montreal, Canada. One hundred and sixty-four histologically confirmed cases of renal-cell carcinoma, diagnosed between 1982 and 1987 in four hospitals in the Montreal area, who responded to a mailed questionnaire were included in this analysis. One hundred and sixty-one controls without urinary tract tumours who were identified from urology files and who were matched to cases on sex, date of birth and urologist were also included in the analysis. Those who had been exposed indoors to burning coal had a non-statistically significantly increased risk for lung cancer compared with subjects who were not exposed. For those who lived in a house where coal was used as a fuel but did not handle it, the odds ratio was 1.07 (95% CI, 0.58–1.96; 53 exposed cases). The odds ratio for subjects who had handled coal only domestically was 1.41 (95% CI, 0.76–2.62; 56 exposed cases). [The covariates included in the multivariable logistic regression models were not specified. Four hundred and three cases were identified but only 168 cases

Table 2.2. Case–control studies of lung cancer and use of coal outside China

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios (95% CI)	Adjustment for potential confounders	Comments
Wu *et al*. (1985), Los Angeles, USA, 1981–82	220 white women diagnosed with lung cancer (149 ADC, 71 SCC) were identified from the tumour registry 220 healthy white women matched by age (±5 yrs) and neighbourhood	Telephone interview using a structured questionnaire	*Use of coal for heating/cooking in majority of childhood and teenage yrs* SCC ADC Nonsmoker and unexposed to coal Nonsmoker Former smoker Smoker	 NG NG NG NG NG NG	 1.9 (0.5–6.5) 2.3 (1.0–5.5) 1.0 (reference) 3.2 (0.9–11.8) 4.3 (1.0–17.8) 9.5 (2.1–41.9)	Tobacco smoking	The results did not change after adjusting for personal smoking, childhood pneumonia and β-carotene.
Malats *et al*. (2000), Brazil, France, Germany, Italy, Poland, Romania, Russia, Sweden, [period not specified]	122 nonsmoking cases (17 men, 105 women) diagnosed with histologically or cytologically confirmed lung cancer 121 nonsmoking controls (34 men, 87 women) identified from the Swedish population registry or the same hospitals as cases (admitted for non-tobacco related diseases)	In-person interview using a standard questionnaire	Indoor pollution from coal (>17 yrs)	NG	0.4 (0.1–1.1)	Age, gender, centre	Study period not specified

Table 2.2 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios (95% CI)	Adjustment for potential confounders	Comments
Gupta *et al.* (2001), Chandigarh, India, 1995–97	265 histologically confirmed lung cancer paitents (235 men, 30 women) 525 hospital controls (435 men, 90 women) matched by age and sex	In-person interview using a questionnaire	**Yrs of exposure to coal vs none** *For cooking* Men 1–45 yrs >45 yrs Women 1–45 yrs >45 yrs *For heating* Men 1–45 yrs >45 yrs Women 1–45 yrs >45 yrs	 14 23 2 6 14 42 2 5	 0.72 (0.36–1.46) 0.88 (0.49–1.57) 0.63 (0.11–3.63) 1.52 (0.33–6.98) 1.06 (0.51–2.17) 1.20 (0.75–1.91) 0.96 (0.15–6.26) 1.12 (0.26–4.84)	Age, smoking, education, cumulative tobacco consumption	

Table 2.2 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios (95% CI)	Adjustment for potential confounders	Comments
Lissowska *et al*. (2005), Central and Eastern Europe and United Kingdom, 1998-2002	2861 cases (2205 men, 656 women) from 15 hospitals 3118 hospital and population-based controls (2305 men, 813 women) matched by age, sex and area; persons with cancer or tobacco-related diseases were excluded	In-person interview using a structured questionnaire	Ever used coal only for cooking Ever used coal only for heating	872 772	1.13 (0.94–1.38) 1.08 (0.89–1.31)	Age, sex, education, tobacco pack-yrs, centre	Coal was the most common type of fuel used for heating (50%) or cooking. (44%); controls were hospital-based except in Warsaw, Poland and Liverpool, United Kingdom, where they were population-based. The authors could not rule out that the associations were due to some mixed (wood and coal) exposures, because subjects provided their principal fuel (if they used mainly coal but some wood, they would have indicated coal).

ADC, adenocarcinoma; CI, confidence interval; NG, not given; SCC, squamous-cell carcinoma; yrs, years

and matched controls agreed by telephone to receive a mailed questionnaire. Of those who received a mailed questionnaire, 164 cases and 161 controls responded.]

Malats *et al*. (2000) conducted a multicentre case–control study in eight countries (Brazil, France, Germany, Italy, Poland, Romania, the Russian Federation, Sweden) that primarily investigated the interaction between glutathione *S*-transferase (GST) M1 and T1 genotypes and environmental risk factors in 122 lung cancer cases (14% male) and 121 controls (58 population-based, 63 hospital-based). All cases were confirmed by histology or cytology. Information on exposure was obtained through personal interview using a standardized questionnaire. Indoor air pollution from the use of wood or coal for cooking or heating was dichotomized according to the median number of years of exposure to both sources of combustion among controls. Using coal for more than 17 years (versus less than 17 years) was not associated with an increased risk for lung cancer (odds ratio, 0.4; 95% CI, 0.1–1.1). [The Working Group noted that there could be possible confounding by smoking because nonsmokers were defined as occasional smokers (up to 400 cigarettes in a lifetime) and never smokers. The Working Group also noted the heterogeneous background of the study subjects and the fact that controls were not matched by age and sex may present difficulties in the interpretation of the results. Furthermore, the crude exposure indices used (i.e. <20 years of fuel use) did not enable a good assessment of the exposure–response relationship.]

Two hundred and sixty-five histologically confirmed, incident cases of lung cancer (235 men, 30 women) who were seen at the Department of Pulmonary Medicine, Chandigarh, India, and 525 age- and sex-matched controls (435 men, 90 women) who were selected among visitors and attendants of the patients were recruited in a case–control study conducted between January 1995 and June 1997 (Gupta *et al*., 2001). Trained interviewers collected information on demographic factors, lifetime tobacco smoking history, detailed occupational history and residence. Exposure to indoor air pollution was assessed on the basis of the type of fuel used for cooking or heating and the number of years spent in that household. Unconditional logistic regression models stratified by gender were adjusted for age, cumulative tobacco consumption and education. The odds ratio for exposure to indoor air pollution as measured by 45 or more years of exposure to coal for heating was 1.20 (95% CI, 0.75–1.91; 42 exposed cases) for men and 1.12 (95% CI, 0.26–4.84; 5 exposed cases) for women. The odds ratio for the use of coal for cooking for 45 or more years was 0.88 (95% CI, 0.49–1.57; 23 exposed cases) for men and 1.52 (95% CI, 0.33–6.98; six exposed cases) for women.

Lissowska *et al*. (2005) conducted a multicentre case–control study during 1998–2002 in six eastern and central European countries (Czech Republic, Hungary, Poland, Romania, the Russian Federation and Slovakia) and the United Kingdom to examine the association between burning coal and unprocessed biomass and the incidence of lung cancer in men and women. Cases included 2861 histologically or cytologically confirmed incident lung cancer patients (2205 men, 656 women) who were identified through the main hospitals in the 15 participating centres. A total of 3118 (2305 men, 813 women) hospital-based (13 centres) and population-based controls (two centres), who were

frequency-matched to cases by geographic area, 5-year age group and gender, were studied. A common structured questionnaire was used to collect information on risk factors for lung cancer such as active and passive tobacco smoking, occupational history, lifetime residential history and fuel use at every residence of at least 1 year. The study examined risk patterns in relation to modern non-solid fuels (gas, kerosene and electricity) versus traditional solid fuels (coal and biomass, mainly wood) used for cooking and heating after adjusting for centre, age, gender, education and tobacco pack–years. The odds ratios for exposure to coal were 1.13 (95% CI, 0.94–1.38; 872 exposed cases) for cooking and 1.08 (95% CI, 0.89–1.31; 772 exposed cases) for heating. [The Working Group noted many strengths in this large multicentre case–control study which used a common, standardized study protocol and questionnaire and collected information on lifetime fuel use and relevant covariates from in-person interviews with the study participants. The response rate was high in both cases and controls (>90%). Although the analysis was very thorough, exposure–response analyses by type of solid fuels (separately for coal and wood) were not provided.]

(c) Cohort studies (see Table 2.3)

Lan *et al*. (2002) followed a cohort of 21 232 farmers (11 168 men, 10 064 women) in China retrospectively from 1976 to 1992. The farmers were born between 1917 and 1951 into homes in which smoky coal and unvented stoves were used; however, 17 184 of these subjects (80.9%) later changed permanently to the use of vented stoves with chimneys. (The Chinese Government offered a small subsidy for the purchase of stoves with chimneys in 1976). Nearly all subjects were born in Xuan Wei (about 1% of men and 13% of women were born outside the immediate study area). In multivariable Cox proportional hazard models stratified by gender, in which stove improvement, duration of cooking (for women only) and duration of smoking (for men only; only 0.9% of women had ever smoked) were treated as time-dependent covariates, stove improvement was associated with a statistically significant reduction in the incidence rate of lung cancer (hazard ratio for men, 0.59; 95% CI, 0.49–0.71; hazard ratio for women, 0.54; 95% CI, 0.44–0.65). In both men and women, duration of cooking food was also positively and significantly associated with an increased risk for lung cancer, as was the daily average number of hours spent indoors through to the age of 20 years. [The Working Group noted that although fewer men than women cooked food, the significantly protective effect of stove improvement was of similar magnitude in both genders, which suggests that the protective effect of stove improvement related largely to the reduction of cooking fuel smoke.]

(d) Ecological studies

Rural Xuan Wei County, Yunnan Province, China, is impacted by indoor air pollution due to traditionally used fuel types: ‘smoky coal’ (bituminous coal), ‘smokeless coal’ (anthracite) and wood. The great majority of residents were farmers, and residential stability

Table 2.3. Cohort studies of use of coal and cancer in China

Reference, study location, study period	Cohort description	Exposure assessment	Exposure categories	No of exposed cases/deaths	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Lan *et al*. (2002) Xuan Wei, Yunnan, 1976–92	21 232 farmers, born 1917–51 into homes with unvented smoky coal stoves; 11 168 men, 10 068 women; total 313 579 person–yrs; all subjects were lifelong smoky coal users.	Did or did not install chimneys on previously unvented stoves, as ascertained by structured questionnaire. In 15 homes, indoor PM_{10} and benzo[*a*]pyrene levels were compared during coal burning with chimneys blocked and open.	*Men and women with and without chimney installation (stove improvement)* Before chimney installation After installation *After chimney installation versus before* Men Women **Cooking duration (yrs) vs ≤20 yrs** *Men* >20 *Women* 20–29 30–39 ≥40 *Born outside study area* Men Women	 NG NG NG NG NG NG NG NG	Age-adjusted lung cancer incidence per 100 000 person–yrs 554 383 0.59 (0.49–0.71) 0.54 (0.44–0.65) 1.42 (1.05–1.93) 1.38 (0.87–2.20) 1.79 (1.09–2.93) 3.08 (1.80–5.26) 0.34 (0.11–1.05) 0.49 (0.35–0.67)	All subjects: lung cancer in spouse and first-degree relatives, house and family size, COPD and tuberculosis history, time indoors in early life, annual coal consumption, birthplace, education, birth cohort, cooking history; men only: smoking, occupation	Analysed with Cox models, time axis = age, time-dependent covariates for stove improvement, smoking and cooking; mean indoor levels of PM_{10} and benzo[*a*]pyrene ($\mu g/m^3$) in 15 homes: chimney blocked, 2080 and 1.66; chimney open, 710 and 0.25

Table 2.3 (contd)

Reference, study location, study period	Cohort description	Exposure assessment	Exposure categories	No of exposed cases/deaths	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Wu *et al.* (2004), Chia-Yi city, Taiwan, 1999–2000	Subjects for the nested case–control study were selected from 32 466 women who underwent Pap smear screening in Chai-Yi City; ≥19 yrs of age. 100 women with biopsy confirmed lesions ≥CIN2 who completed a questionnaire. 197 population controls were randomly selected from women who lived in the same area as cases and had negative Pap smear results.	In-person interview using structured questionnaire	**Fuel used for cooking vs. gas** *While 20–40 yrs of age* Coal and gas Coal *While >40 yrs of age* Coal/coal and gas	 3 21 1	 0.65 (0.14–3.05) 2.09 (0.86–5.10) 1.53 (0.17–14.19)	Age, educational levels, cigarette smoking, number of prior Pap smears, age at first intercourse, work as a professional chef	

CI, confidence interval; CIN, cervical intraepithelial neoplasia; COPD, chronic obstructive pulmonary disease; Pap, Papanicolaou; PM_{10}, particulate matter ≤10 μm; yrs, years

was very high. There have been few stationary or mobile sources of outdoor air pollution. In a 1982 survey of all households in 11 of 20 Xuan Wei communes, the proportion of households that used smoky coal before 1958 was highly correlated with commune-specific mortality from lung cancer from 1973 to 1975 (r=0.82; p=0.002; Mumford *et al*., 1987; Chapman *et al*., 1988). Also during 1973–75, average annual lung cancer mortality was 34.7 per 100 000 in 14 communes that had smoky coal mines and 4.1 per 100 000 in six communes that did not [p=0.015] (Mumford *et al*., 1987).

Tao *et al*. (1991), in an ecological study from Shanghai, China, showed that men in a group that used coal indoors had 1.44 times higher mortality from lung cancer than a group that used coal-gas indoors and 30.4% of total lung cancer deaths in the former group could possibly be attributed to coal use indoors. The authors noted that this was a preliminary exploration.

(e) Aggregate analyses of studies of indoor air pollution and lung cancer in China

Gao (1996) reviewed risk factors for lung cancer in nonsmoking Chinese women using evidence from published case–control and cohort studies. The major conclusions were as follows: (i) the proportion of lung cancer cases that cannot be attributed to smoking varies by region in China; (ii) coal burning in poorly ventilated houses may contribute to 10–20% of the reported lung cancer cases; (iii) the volatile emissions generated by heating rapeseed and soya bean oil may contribute to an increased risk for lung cancer, especially among Chinese women who heat these oils to high temperatures during cooking; (iv) there is a consistent positive association between personal history of non-malignant lung disease and risk for lung cancer; this may be especially important in view of the heavy burden of such respiratory diseases in China; (v) infrequent consumption of fresh vegetables and fruit, especially those rich in carotene and vitamin C, increases the risk for lung cancer; (vi) although occupational factors increase the risk for lung cancer in highly industrialized cities, their contribution to the population-attributable risk for lung cancer is relatively small; (vii) observed effects of environmental tobacco smoke on lung cancer are ambiguous and inconsistent in case–control studies; (viii) outdoor air pollution is not unequivocally associated with lung cancer risk, as observed among a cohort of nonsmokers in Shanghai; and (ix) the menstrual histories of women warrant further study as a potential risk factor for lung cancer.

Zhao *et al*. (2006) conducted a meta-analysis of case–control studies in China that evaluated aggregate associations of lung cancer with indoor air pollution from coal consumption for heating and cooking, exposure to coal dust, exposure to cooking oil fumes and exposure to environmental tobacco smoke. Although the authors could not rule out the possibility of publication bias, they concluded that their meta-analysis confirmed the association of indoor air pollution with lung cancer in the Chinese population. Using a random-effects model, coal consumption through heating and cooking was associated with an increased risk for lung cancer (odds ratio for both sexes; 2.66; 95% CI, 1.39–5.07; odds ratio for women only, 1.83; 95% CI, 0.62–5.41). [The Working Group noted that

this analysis, together with previous publications, indicates joint contributions of coal smoke and cooking smoke to indoor air pollution but does not quantify their relative contributions. It is unclear whether exposure to coal dust represents an occupational exposure or serves as a proxy measure for coal smoke.]

2.1.2 *Cancer of the salivary glands*

All residents of urban Shanghai aged 20–75 years who were newly diagnosed with cancer of the salivary glands (International Classification of Diseases [ICD]-9, 142) during the period from 1 January 1988 to 28 February 1990 were eligible to participate in a case–control study (Zheng *et al*., 1996). A total of 44 eligible cases (19 men, 25 women) were identified from the Shanghai population-based cancer registry during the period in question. Of all identified cases, 41 (93.2%) were interviewed and three other cases could not be located or were too ill to be interviewed. Adenocarcinoma and adenoid cystic carcinoma were the two major cancers diagnosed and accounted for 46.3% and 24.4% of total cases, respectively. Controls were randomly selected from the general population of urban Shanghai by use of a frequency-matching method in accordance with the sex–age distribution of cases of all head and neck cancers reported to the Shanghai cancer registry during 1985–86. A total of 462 controls were selected, among whom 414 (89.6%) were interviewed. Information on demographic factors, tobacco and alcohol consumption, dietary habits, lifetime job history, occupational and household exposures and previous disease history was collected from each study subject. After adjusting for gender, age and income, the odds ratio was 1.6 for the use of coal for cooking (95% CI, 0.5–5.6; 38 exposed cases). [The Working Group noted that the sample size was relatively small.]

2.1.3 *Cancer of the oesophagus*

A nested case–control study within a cohort of workers of an iron–steel complex was carried out in Anshan, China, to evaluate the relationship of oesophageal cancer with occupational exposure to silica and other dusts, taking lifestyle exposure factors into consideration (Pan *et al*., 1999). A total of 141 men who were confirmed as having died from oesophageal cancer during 1980–88 were selected as cases. Two male controls were randomly selected and matched on age (within 5-year age groups) for each case from the death registry file of the company over the same period. The first control group consisted of workers who had died of diseases other than cancer or respiratory or digestive diseases (non-cancer controls) and the second control group consisted of workers who had died of cancers other than of the stomach or respiratory system (cancer controls). The number of cases whose relatives could be interviewed was 125 (88.7%). Each of the two groups of controls consisted of the same number of subjects (125) as the cases. Either the wife or a first-degree relative was interviewed for 95.2% of cases and 96.0% of controls. Information was obtained for smoking, drinking, diet, method of cooking and heating in the household and lifetime occupational history. A job-exposure matrix was applied to

lifetime job histories and dust exposures were categorized into no exposure, refractory silica dust, other silica dust, iron dust, founding dust, coal dust, wood dust, welding dust and other dusts. The results were presented for both controls combined since the results of the analysis using two control groups were very similar. In a univariate analysis, occupational exposure to silica dust, "other silica dust" and "any dust", domestic exposure to coal heating, cooking with coal, heavy smoking, alcohol drinking and consumption of salted vegetables were shown to be risk factors. Central heating, cooking with gas and consumption of fish, meat, eggs and fruit were found to be protective factors. In multivariate analysis, the odds ratio was 2.01 for cooking with coal (95% CI, 1.09–3.70). Exposure to silica dust for 25 years and more and cooking with coal for 20 years and more gave the highest risk: the odds ratio for the former was 8.87 (95% CI, 1.67–47.08) and that for the latter was 2.48 (95% CI, 1.29–4.78). [The Working Group noted that the findings were among long-term male steelworkers and not the general population, thus making extrapolations to other groups difficult. Comparison of deceased cases with deceased controls and the use of information obtained from relatives, not from subjects themselves, are the weakness of the study.]

2.1.4 *Cancer of the nasal cavity, paranasal sinuses and middle ear*

Cases of cancer of the nasal cavity, paranasal sinuses and middle ear (ICD-9, 160), aged 20–75 years, who had been newly diagnosed during the period from 1 January 1988 to 28 February 1990 were eligible to participate in a case–control study (Zheng *et al*., 1992). A total of 63 cases were identified from the Shanghai population-based cancer registry during the study period. Of these, 60 cases (39 men and 21 women) were interviewed and three cases (4.8%) could not be located; 51 cases (85%) were pathologically diagnosed. Controls were randomly selected from the general population of the Shanghai urban area by use of frequency-matching in accordance with the sex–age distribution of incident cases of oral, pharyngeal, laryngeal and nasal cancers reported to the Shanghai cancer registry in 1985–86. A total of 462 controls were identified and 414 (89.6%) were interviewed. Information on demographic factors, tobacco and alcohol consumption, dietary habits, occupational and household exposures and previous disease history was collected. Unconditional logistic regression was used to adjust for confounders and to calculate adjusted odds ratios. After adjusting for age, the odds ratio for coal used as cooking fuel was 1.1 (95% CI, 0.5–2.6; 53 exposed cases).

2.1.5 *Cancer of the cervix* (see Table 2.3)

Wu *et al*. (2004) conducted a nested case–control study of 100 women with cervical cancer and 197 population controls selected from a cohort of 32 466 women who underwent Papanicolaou (Pap) smear screening in Chai-Yi City, Taiwan, China. Use of coal compared to gas was positively, although not significantly, associated with the risk for cervical cancer (odds ratio, 2.09; 95% CI, 0.86–5.10; 21 exposed cases).

2.1.6 *Cancer of the kidney (renal-cell carcinoma)* (see Table 2.4)

Sharpe *et al*. (1989) conducted a hospital based case–control study in Montreal, Canada, that included 164 cases of renal-cell carcinoma (62% men) identified retrospectively from medical records and 161 age- and sex-matched controls who attended the same urologists; all were given mailed questionnaire with telephone follow-up. Cases were survivors and had less advanced disease. Occupational exposure to burning coal showed a dose–response relationship with renal- cell carcinoma by duration in months ($p<0.05$) Intensity of exposure, assessed by combining domestic and occupational exposures in a hierarchical ordinal manner, also showed a dose–response trend ($p<0.025$). Multivariable analysis adjusting for sex and age (smoking was not a statistically significant confounder and was removed from final model) showed that handling coal in a setting where it was being burned between the ages of 10 and 24 years was a risk factor. [Results on the duration of occupational exposure or the intensity of exposure (combining domestic and occupational) were not reported. In general, the results were not presented in a clear or understandable manner.]

2.2 Biomass fuel (wood, dung, *kang* use other than with coal)

2.2.1 *Cancer of the lung* (see Table 2.5)

Koo *et al*. (1983) (described in detail in Section 2.1.1) reported a case–control study in Hong Kong Special Administrative Region, China. Use of wood/grass did not have any appreciable effect on the risk for lung cancer (odds ratio, 0.74; $p=0.50$).

Sobue (1990) conducted a hospital-based case–control study of lung cancer in Osaka, Japan, that included 144 nonsmoking female lung cancer patients and 731 nonsmoking female controls. Newly admitted patients were asked to complete a questionnaire that asked about tobacco smoking habits, exposure to environmental tobacco smoke and other sources of indoor air pollution (i.e. use of straw or wood for cooking, use of heating appliances fueled with kerosene, gas, coal and charcoal and wood stoves without chimneys, and use of charcoal footwarmers). The odds ratio for lung cancer in nonsmoking Japanese women who used wood or straw compared with those who did not at age 30 years was 1.77 (95% CI, 1.08–2.91; 32 exposed cases; adjusted for age, exposure to passive smoke in adulthood and mother smoked during childhood). Current and previous (at ages 15 and 30 years) use of charcoal footwarmers for sleeping was not associated with risk. [The Working Group noted that the exposure variables were not well defined and were limited to dichotomized categorization. The reference category was not clearly defined and may have included the use of coal.]

In the study of Wu-Williams *et al.* (1990) (described in detail in Section 2.1.1) duration of use of non-coal, generally biomass-fueled stoves was not associated with risk, and there was no discernible association of risk with central heating (in which the heating fuel source was outside the home).

Table 2.4. Case–control study of renal cancer and coal use

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratios (95% CI)	Adjustment for potential confounders	Comments
Sharpe *et al*. (1989), Montreal, Canada, 1982–87	164 histologically confirmed cases diagnosed in 4 hospitals 161 controls without urinary tract tumors identified from urologist files; matched by age, sex, urologist	Mailed questionnaire with telephone follow-up	Renal (ICD-8, 189.0)	Lived in a house with coal used as a fuel but did not handle coal	53	1.07 (0.58–1.96)	Not clear	Subjects who mined or delivered coal were excluded. Occupationally exposed cases included janitors, foundry workers, locomotive engineers, cooks, prisoners of war doing forced labour, sailors and those involved in heating buildings.
				Domestic coal handling only	56	1.41 (0.76–2.62)		
				Occupational handing with or without domestic handling	14	2.42 (0.81–7.46)		
				Concurrent occupational and domestic handling	3	8.45 (0.42–168.68)		

CI, confidence interval; ICD, International Classification of Diseases

Table 2.5. Case–control studies of lung cancer and use of biomass fuel

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios (95% CI)	Adjustment for potential confounders	Comments
Koo *et al.* (1983), Hong Kong, China, 1981–83	200 female lung cancer patients; mean age 61.8 yrs; 44% never smokers; 90% histologically confirmed (28% SCC, 18.5% small-cell, 34.5% ADC) 200 female community controls, matched on age (±5 yrs), residential district and housing type; mean age 60.6 yrs; 69% never smokers	Interviews with semi-structured questionnaire, using a life history approach, assessed use and duration of using coal, biomass fuels, kerosene, LPG and gas	*Ever fuel use* Wood/grass Charcoal	 179 32	 0.74 (p=0.50) 0.96 (p=1.00)	Unclear	The reference category is unclear for ever fuel use.
Xu *et al.* (1989), Shenyang, China, 1985–87	1249 cases (729 men, 520 women) in Shenyang aged 30–69 yrs; cell type histologically confirmed in 83% of men and 73% of women. 1345 population-based controls (788 men, 557 women), selected by 3-stage procedure from urban Shenyang; frequency-matched on gender and age	In-person interview using a structured questionnaire; developed continuous index of indoor exposure to coal smoke from heating and cooking	No use (referent) **Burning *kang (yrs)*** *Men* 1–19 >20 *Women* 1–19 >20	 91 82 40 65	 1.7 (p<0.05) 2.1 (p<0.05) 1.3 (p>0.05) 2.3 (p<0.05)	Age, education, smoking	Population overlapped with the study by Wu-Williams *et al.* (1990)

Table 2.5 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios (95% CI)	Adjustment for potential confounders	Comments
Sobue (1990), Osaka, Japan, 1986–88	144 nonsmoking women enrolled from multiple hospitals; 40–79 yrs old; 100% microscopically confirmed (78% ADC, 8% SCC, 5% small-cell carcinoma; 5% large-cell carcinoma; 4% other) 731 unmatched nonsmoking women without lung cancer enrolled from multiple hospitals; 40–79 yrs old	Self-administered questionnaire	Used straw or wood for cooking at age 30	32	1.77 (1.08–2.91)	Age at admission, other household members smoked in adulthood, mother smoked in childhood	5% used wood for heating; no increased risk for use of charcoal footwarmers or fuel in heating stoves; no significantly increased risks seen for exposure to straw, wood or charcoal at age 15; controls (cancers of the breast, stomach or other sites; benign neoplasms; circulatory, respiratory, infectious or digestive diseases) were younger with higher education; excluding breast cancer controls (46%) did not change results

Table 2.5 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios (95% CI)	Adjustment for potential confounders	Comments
Wu-Williams *et al*. (1990), Shenyang and Harbin, northern China, 1985–87	965 incident female cases from local registries; age <70 yrs; cytologically verified 959 women selected by multistage random sampling from general populations of Shenyang and Harbin frequency-matched by 5-year age group	In-person interview using structured questionnaire	Kang (yrs) 1–39 40–49 ≥50 *Burning* kangs (yrs) 1–20 >21	 384 135 415 106 173	 1.4 (0.8–2.4) 1.1 (0.6–2.8) 1.6 (0.9–2.8) 1.2 (0.9–1.7) 1.5 (1.1–2.0)	Age, education, smoking, study area	Deep frying at least once a month significantly increased the risk for lung cancer.
Liu *et al.* (1993), Guangzhou, China, 1983–84	316 incident cases (224 men, 92 women); 55% diagnosed by X-ray/clinical history, 13% by bronchoscopy, 32% by cytology or histology 316 hospital controls matched on gender, age, residential district and date of diagnosis; respiratory and coronary heart disease excluded	In-person interview using structured questionnaire on smoking habits, cooking fuel use and other variables	*Wood used for cooking fuel vs. coal* Men Women	 8 3	 0.57 (0.11–3.0) 0.67 (0.04–11.7)	Education, occupation, occupational exposure, history of tuberculosis, chronic bronchitis, family history of cancer, smoking, living area, passive smoking	

Table 2.5 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios (95% CI)	Adjustment for potential confounders	Comments
Shen *et al.* (1996), Nanjing, China, 1986–93	263 cases (83 SCC, 180 ADC) who were Nanjing residents for ≥20 yrs 263 population controls who were Nanjing residents; matched 1:1 for gender, age, ethnicity and 'street address'	Standardized questionnaire	*SCC* Solid fuel vs. non-solid fuel		4.97 (0.80–30.88)	Unclear	Fuel types within 'solid fuel' category were not specified. Statistical tests were reported as one-sided, but implications are not clear.

Table 2.5 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios (95% CI)	Adjustment for potential confounders	Comments
Ko *et al*. (1997), Kaohsiung, Taiwan, Province of China, 1992–93	105 nonsmoking female lung cancer patients 105 (presumably nonsmoking) women from same hospital ophthalmic service or coming to hospital for routine check-up; matched on age (±2 yrs) and interview date	In-person interview using a structured questionnaire	**By age of exposure** *Cooking fuel vs. gas or none* Wood or charcoal <20 yrs 20–40 yrs >40 yrs	 56 53 4	 2.5 (1.3–5.1) 2.5 (1.1–5.7) 1.0 (0.2–3.9)	Socioeconomic status, education, residential area	[Selection of cases and controls from same hospital may have caused overmatching on exposures. The near-significant positive association of lung cancer risk with wood/charcoal use is unusual, conceivably related to the matching strategy.] Further adjusting for other covariates [not specified] did not affect the statistical significance or magnitude of effects. Risk for lung cancer was significantly increased if the kitchen did not have a fume extractor.

Table 2.5 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios (95% CI)	Adjustment for potential confounders	Comments
Malats *et al.* (2000) Brazil, France, Germany, Italy, Poland, Romania, Russia, Sweden, [period not specified]	122 nonsmoking cases (17 men, 105 women) diagnosed with histologically or cytologically confirmed lung cancer 121 nonsmoking controls (34 men, 87 women) identified from the Swedish population registry or the same hospitals as cases (admitted for non-tobacco related diseases)	In-person interview using a standard questionnaire	Indoor pollution from wood (>20 yrs) vs. no use	NG	2.5 (1.0–6.2)	Age, gender, centre	Not adjusted for smoking history although there was a difference in smoking history between cases and controls.

Table 2.5 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios (95% CI)	Adjustment for potential confounders	Comments
Gupta *et al.* (2001), Chandigarh, India, 1995–97	265 histologically confirmed lung cancer paitents (235 men, 30 women) 525 hospital controls (435 men, 90 women) matched by age and sex	In-person interview using a questionnaire	Yrs of exposure to wood			Age, education, smoking, sex	The selection of controls may have resulted in overadjustment.
			For cooking				
			Men				
			1–45	51	0.94 (0.58–1.54)		
			>45	105	0.87 (0.58–1.30)		
			Women				
			1–45	6	0.74 (0.20–2.65)		
			>45	12	1.11 (0.34–3.60)		
			For heating				
			Men				
			1–45	4	2.62 (0.47–14.5)		
			>45	67	0.97 (0.65–1.43)		
			Women				
			1–45	0	NG		
			>45	13	2.78 (0.97–7.98)		

Table 2.5 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios (95% CI)	Adjustment for potential confounders	Comments
Lee *et al*. (2001), Kaohsiung, Taiwan, Province of China, 1993–99	527 histologically confirmed cases (236 men, 291 women), 18–83 yrs old; cases SCC and small-cell carcinoma (28.2%) and ADC (47.7%) 805 controls from same hospital without tobacco-related illness; matched on gender, age (±2 yrs)	In person interview using a structured questionnaire	**Women** *Wood or charcoal vs. gas or none* SCC or small-cell carcinoma ADC	 22 40	 3.1 (1.0–9.2) 3.0 (1.4–6.4)	Smoking, residential area (urban, suburban, rural), education, socioeconomic status	Only 7% of men reported cooking for the family and thus data were not shown. In women, stir frying, frying and deep frying after fumes emitted were statistically significantly associated with risk for ADC but not SCC or small-cell carcinoma. Long-term residence near industrial district was associated with lung cancer risk, especially in women. Risk for lung cancer was significantly increased if the kitchen did not have a fume extractor.

Table 2.5 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios (95% CI)	Adjustment for potential confounders	Comments
Hernández-Garduño *et al*. (2004), Mexico City, Mexico, 1986–1994	113 histologically confirmed never smoking women identified from medical records at the National Institute for Respiratory Disease (INER); ≥44 yrs of age 273 nonsmoking women, ≥44 yrs of age; identified by medical records, hospitalized at INER (99 pulmonary tuberculosis, 110 interstitial lung disease, 64 miscellaneous pulmonary conditions) during the same time period as cases	Medical records	*Yrs of cooking with wood vs. none* 1–20 21–50 >50	 15 15 47	 0.6 (0.3–1.2) 0.6 (0.3–1.3) 1.9 (1.1–3.5)	Age, education, environmental tobacco smoke, socioeconomic status	Use of patient records may lead to error. Difficult to interpret as different control groups used. Although diseases in which wood smoke could be a risk factor were excluded (i.e. COPD, cancer or asthma), use of controls with respiratory diseases may underestimate the relative risk because these diseases may also be indirectly related to exposure to wood smoke. Confounding by the use of coal is not a concern in this study since coal is not used in Mexico.

Table 2.5 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratios (95% CI)	Adjustment for potential confounders	Comments
Lissowska *et al.* (2005), Central and eastern Europe and United Kingdom, 1998–2002	2861 cases (2205 men, 656 women) from 15 hospitals 3118 hospital and population-based controls (2305 men, 813 women) matched by age, sex and area; persons with cancer or tobacco-related diseases were excluded	In-person interview using a structured questionnaire	*Ever used wood only* For cooking For heating	 1065 1105	 1.23 (1.00–1.52) 1.31 (1.06–1.61)	Age, sex, education, tobacco, centrre	Coal was the most common type of fuel used for heating (50%)or cooking.(44%); Controls were hospital based except in Warsaw, Poland and Liverpool, United Kingdom where they were population-based; Authors could not rule out that the associations were due to some mixed (wood and coal) exposures, because subjects provided their principal fuel (if they used mainly coal but some wood, they would have indicated coal). [Although the analysis was very thorough, dose–response analyses by type of solid fuels (separately for coal and wood) were not provided.]

ADC, adenocarcinoma; CI, confidence interval; COPD, chronic obstructive pulmonary disease; LPG, Liquid petroleum gas; SCC, squamous cell carcinoma; yrs, years

In a hospital-based case–control study conducted in Guangzhou, China, Liu *et al*. (1993) studied the risk for lung cancer associated with the use of different cooking fuels (described in Section 2.1.1). Analyses using multivariable conditional logistic regression models adjusted for education, occupation, occupational exposure, history of tuberculosis, chronic bronchitis, family history of cancer, smoking, living area and passive smoke (in women only) were stratified by gender. Compared with use of coal for cooking, use of wood was inversely associated (although not statistically significant) with the risk for lung cancer in both men (odds ratio, 0.57; 95% CI, 0.11–3.0; eight exposed cases) and women (odds ratio: 0.67; 95% CI, 0.04–11.7; three exposed cases).

Two hospital-based case–control studies were conducted in Kaohsiung, a heavily industrialized city in Taiwan, China (Ko *et al*., 1997; Le *et al*., 2001). The first study included 117 female lung cancer cases identified between 1992 and 1993 who were compared with 117 female hospital controls admitted for a health check-up (n=55) or for eye diseases (n=62) (Ko *et al*., 1997). Information on histological type was not provided. Active smokers (11 cases, three controls) were excluded so that the analysis was based on 105 case–control pairs who were nonsmokers. Use of wood or charcoal before the age of 40, as opposed to other fuels including coal, was associated with an increased risk for lung cancer, after adjusting for socioeconomic status, education and residential area.

The case–control study by Le *et al*. (2001) included women diagnosed with squamous-cell or small-cell carcinoma (n=84) or adenocarcinoma of the lung (n=162) and corresponding controls (n=407) (described in detail in Section 2.1.1). Risk for lung cancer was associated with type of cooking fuel: women who used wood or charcoal as a cooking fuel compared with those who cooked with gas or did not cook showed a 3.1-fold (95% CI, 1.0–9.2; 22 exposed cases) increased risk for squamous-cell and small-cell cancer and a 3.0-fold (95% CI, 1.4–6.4; 40 exposed cases) increased risk for adenocarcinoma. Risk was also significantly higher for those who cooked in a kitchen without a fume extractor: the odds ratio was 3.0 (95% CI, 1.3–7.1; 31 exposed cases) for squamous-/small-cell cancer and 3.9 (95% CI, 2.3–6.6; 74 exposed cases) for adenocarcinoma. Only 7% of men reported cooking for the family and thus these data were not reported.

In a hospital-based case–control study among nonsmokers (including occasional smokers of up to 400 cigarettes in a lifetime), Malats *et al*. (2000) (described in detail in Section 2.1.1) presented an overall odds ratio for lung cancer for >20 years of use of wood of 2.5 (95% CI, 1.0–6.2). [The Working Group noted that there could be possible confounding by smoking because nonsmokers were defined as never smokers and occasional smokers (up to 400 cigarettes in a lifetime). The Working Group also noted the heterogeneous background of the study subjects and the fact that controls were not matched by age and sex may present difficulties in the interpretation of the results. Furthermore, the crude exposure indices used (i.e. <20 years of fuel use) did not enable a good assessment of the exposure–response relationship.]

In a case–control study of lung cancer in Chandigarh, India, Gupta *et al*. (2001) (described in detail in Section 2.1.1) reported that the odds ratio for the use of wood for

heating for 45 or more years was 0.97 (95% CI, 0.65–1.43; 67 exposed cases) for men and 2.78 (95% CI, 0.97–7.98; 13 exposed cases) for women. The odds ratio for the use of wood for cooking for 45 or more years was 0.87 (95% CI, 0.58–1.30; 105 exposed cases) for men and 1.11 (95% CI, 0.34–3.60; 12 exposed cases) for women. [The Working Group noted that the selection of controls may have resulted in overadjustment.]

In a study conducted in Mexico, Hernández-Garduño *et al*. (2004) determined the association between long-term exposure to wood smoke from cooking and lung cancer in nonsmoking Mexican women. Cases and controls, aged 44 years or more, were identified through a review of patient records (discharged between 1986 and 1994) at the Instituto Nacional de Enfermedades Respiratorias, a specialized hospital for respiratory diseases in Mexico City. All cases (*n*=113) were nonsmoking women with a histological confirmation of lung adenocarcinoma. Controls (*n*=273) were hospitalized at the same institute during the same period of time for pulmonary tuberculosis (*n*=99), interstitial lung disease (*n*=110) and other miscellaneous pulmonary conditions (*n*=64), of which 55 were pneumonia. Information on environmental exposures including wood smoke (ever used wood for cooking in their household, years of exposure) was obtained by personal interview at admission and abstracted from medical records for this study. Potential cases and controls with no information on cooking fuel exposure or socioeconomic status were excluded [numbers not given]. Of the patients, 75% were currently living in Mexico City or in the state of Mexico while the remainder lived in other states of Mexico. Cases were slightly older and more likely to come from rural areas and had lower socioeconomic status than controls, although the difference was not significant. The majority of women reported some use of wood for cooking during their lifetime (68.1% of cases; control groups: 67.7% with tuberculosis, 67.0% with interstitial lung disease, 62.5% with miscellaneous pulmonary conditions and 66.1% of the combined control group). For those who had ever used wood for cooking, the duration of exposure to wood smoke was significantly higher in the cases (median, 56 years) than in each of the control groups (median for the combined controls, 38 years). The percentage of women exposed for 1–20 and 20–50 years to wood smoke was higher in the control groups; however, the percentage of exposure over 50 years was higher in the cases. In a multivariate analysis adjusting for age, exposure to environmental tobacco smoke, education and socioeconomic status, the odds ratio for lung cancer for more than 50 years of exposure to wood smoke was 1.9 (95% CI, 1.1–3.5) compared with all control groups combined. This risk was higher when compared with the control group of miscellaneous pulmonary conditions (odds ratio, 2.6; 95% CI, 1.0–6.3). However, for the duration of exposure of 1–20 and 21–50 years, the odds ratios were less than 1 and not statistically significant. [The Working Group noted that the use of controls whose disease might be related to wood exposure could underestimate the relative risk but may also reduce interviewer bias. No information was provided on the cases and controls that were excluded due to lack of information on exposure to wood smoke. Since coal is not used in Mexico, confounding by the use of coal is not a concern in this study. The dose–response results are difficult to interpret with the use of multiple control groups.]

In a multicentre case–control study of lung cancer, Lissowska *et al*. (2005) (described in detail in Section 2.1.1) reported odds ratios for principal exposure to wood for cooking (odds ratio, 1.23; 95% CI, 1.00–1.52; 1065 exposed cases) and heating (odds ratio, 1.31; 95% CI, 1.06–1.61; 1105 exposed cases) after adjusting for centre, age, gender, education and tobacco pack–years. [The Working Group noted many strengths in this large multicentre case–control study which used a common, standardized study protocol and questionnaire and collected information on lifetime fuel use and relevant covariates from in-person interviews with the study participants. The response rate was high in both cases and controls (>90%). Although the analysis was very thorough, dose–response analyses by type of solid fuels (separately for coal and wood) were not provided.]

2.2.2 *Cancers of the oral cavity, pharynx and larynx* (see Table 2.6)

Two partially overlapping hospital-based case–control studies conducted in Brazil (São Paulo, Curitiba and Loiania) examined the risk for cancers of the larynx, pharynx (excluding nasopharynx) and mouth (excluding salivary glands) in relation to the use of wood stoves for cooking and/or heating (Franco *et al*., 1989; Pintos *et al*., 1998). Franco *et al*. (1989) compared 232 oral cancer cases with 464 non-cancer control patients matched by age, sex, study site and trimester of admission and reported an odds ratio for ever/never use of wood stove adjusted for alcohol and tobacco use of 2.5 (95% CI, 1.6–3.9; 134 exposed cases). Pintos *et al*. (1998) identified 784 incident cases of cancer of the larynx, pharynx and mouth and 1568 controls from hospital inpatients (patients with cancer or mental disorders were excluded), matched to cases on age, sex, study site and trimester of hospital admission. Ever/never use of wood stoves, adjusted for tobacco and alcohol consumption, was associated with an increased risk for cancer at all sites (odds ratios: for all sites, 2.39; 95% CI, 1.88–3.05; mouth, 2.34; 95% CI, 1.67–3.29; pharynx, 2.78; 95% CI, 1.70–4.53; larynx, 2.37; 95% CI, 1.40–4.02). Presenting results of wood stove exposure by levels of tobacco and alcohol consumption resulted in statistically significant odds ratios above 2.0. [The increased risk seen in the groups that consumed the least alcohol and tobacco suggested that residual confounding was unlikely.] Stratifying by gender and subsite while also adjusting for race, income, rural residence and schooling resulted in statistically significant odds ratios above 2.0 for men while the point estimates varied considerably with wide confidence intervals for women because the data for women were sparse (adjusted odds ratio for laryngeal cancer: in men 2.03; 95% CI, 1.12–3.67; in women, 16.24; 95% CI, 2.66–99.1). [The Working Group noted that exposure assessment was crude; use of wood stoves for cooking or heating was ascertained only via a single yes/no question. No attempt was made to determine duration of use and the reference group was not described.]

Table 2.6. Case–control studies of cancer of the upper aerodigestive tract

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratios (95% CI)	Adjustment for potential confounders	Comments
Biomass								
Franco *et al.* (1989), Brazil, 1986–88	232 incident cases from 3 Brazilian hospitals; 100% histopathologically confirmed; 87% men		Tongue, gum, mouth floor, oral cavity (141, 143–145)	Use of woodstove for cooking and heating	134	2.5 (1.6–3.9)	Smoking, alcohol	Interviewers were blinded to etiological hypotheses being tested. There is probably considerable overlap of the two oral cancer case groups with Pintos *et al.* (1998).
	464 hospital-based controls excluding neoplastic diseases and mental disorders; matched by age, sex, study site and trimester of admission		Tongue Other oral cavity		NG NG	6.5 (2.8–15.0) 1.4 (0.8–2.4)		

Table 2.6 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratios (95% CI)	Adjustment for potential confounders	Comments
Pintos *et al.* (1998), Brazil, 1987–89	784 cases (salivary glands and nasopharynx excluded) with SCC from 3 Brazilian hospitals; 100% histopathologically confirmed; 87% men. 1568 hospital-based controls excluding neoplastic diseases and mental disorders; matched by age, sex, study site and trimester of admission	In-person interview using questionnaire	UADT Mouth (140–145) Pharynx (146–149) Larynx (161)	Use of woodstove for cooking or heating	397 NG NG NG	2.39 (1.88–3.05) 2.34 (1.67–3.29) 2.78 (1.70–4.53) 2.37 (1.40–4.02)	Tobacco, alcohol, matching factors (by conditional logistic regression)	Presenting results of wood stove exposure by levels of tobacco and alcohol consumption resulted in statistically significant odds ratios above 2.0. The increased risk seen in the groups that consumed the least alcohol and tobacco suggested that residual confounding was improbable. Stratifying by gender and UADT subsite while also adjusting for race, income, rural residence and schooling resulted in statistically significant odds ratios above 2.0 for men while the point estimates varied considerably with wide confidence intervals for women. Exposure assessment was crude: only yes/no use of wood stoves for cooking or heating was ascertained and duration was not recorded. The reference group was not described.

Table 2.6 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Odds ratios (95% CI)	Adjustment for potential confounders	Comments
Dandara *et al.* (2006), South Africa, 1997–2003	245 patients admitted for dysphagia with histologically confirmed SCC; 59% men 288 healthy, age-matched, population based controls recruited from the same geographical area as cases; 57% men	In-person interview using a questionnaire	Oesophagus	*Use of wood and charcoal for cooking and heating in the last 20 yrs compared with electricity* Blacks Mixed ancestry	 63 28	 15.2 (8.2–28.2) 1.2 (0.6–2.3)	Alcohol, tobacco	Difference in risk by ethnicity not explained
Mixed coal/biomass								
Dietz *et al.* (1995), Heidelberg, Germany, 1989–92	Patients with cancers of the larynx (*n*=164), oral cavity (*n*=100), and oropharynx and hypopharynx (*n*=105) 4 controls selected from medical clinics and general outpatient departments matched to cases (656 for larynx, 400 for oral cavity, 420 oropharynx and hypopharynx) by age, sex, size of residence	Interview	Larynx Pharynx Oral cavity Larynx Pharynx Oral cavity	>40 yrs use of single stove heating units with fossil fuels vs. 0–20 yrs use >40 yrs use of single stoves with fossil fuels for cooking vs. 0–20 yrs use	NG NG NG NG NG NG	2.0 (1.10–3.46 3.3 (1.43–7.55) 2.4 (1.26–4.4) 1.4 (0.76–2.41) 2.5 (1.03–6.30) 1.6 (0.90–2.97)	Tobacco, alcohol consumption	Percentage use of separate fuels provided but no statistical tests; fossil fuels were considered to be coal, briquettes, coke, peat, gas and oil.

ADC, adenocarcinoma; NG, not given; SCC, squamous cell carcinoma; UADT, upper aerodigestive tract; yrs, years

2.2.3 *Cancer of the salivary glands*

In a case–control study of cancer of the salivary glands, Zheng *et al*. (1996) (described in detail in Section 2.1.2), the odds ratio was 1.6 for use of wood/straw for cooking (95% CI, 0.6–4.4; six exposed cases) after adjusting for gender, age and income.

2.2.4 *Cancer of the nasopharynx* (see Table 2.7)

The earliest publication on cancer and indoor pollution from biomass fuel focused on nasopharyngeal cancer using an ecological comparison of rates by elevation in rural Kenya (Clifford, 1972). A small (eight-household) indoor air pollution survey during evening cooking was undertaken to indicate that concentrations of total PM, total organic matter, benzo[*a*]pyrene and benz[*a*]anthracene from wood burning varied by elevation, presumably because of lower ventilation and more fuel use due to the need for more space heating at higher elevations. The incidence of nasopharyngeal cancer varied by region.

Shanmugaratnam *et al*. (1978) conducted a case–control study of nasopharyngeal carcinoma (NPC) among persons of Chinese origin who were permanent residents of Singapore. A total of 379 histologically confirmed NPC patients (266 men, 113 women) were recruited from the Ear, Nose and Throat (ENT) Department of Singapore General Hospital. Two control groups were enrolled: 595 (311 men, 284 women) ENT patients without NPC and 1044 (738 men, 306 women) other hospital controls. Trained interviewers conducted in-person interviews between March 1966 and August 1968 using a standardized questionnaire that included the main type of fuel used over a period of more than 10 years. Charcoal use was not significantly associated with the risk for NPC (odds ratio, <1.0; $p>0.05$) using either control group as a comparison. Firewood use was significantly associated with NPC compared with ENT controls (odds ratio, 1.71; $p<0.01$) but not when compared with other hospital controls (odds ratio, 0.87; $p>0.05$). [The Working Group noted that a greater proportion of the ENT controls may have used gas instead of firewood since this group had a higher socioeconomic status.]

In a case–control study (Zheng *et al*., 1992) of cancer of the nasal cavity, paranasal sinuses and middle ear (ICD-9, 160) (described in detail in Section 2.1.4) after adjusting for age, ever-use of wood or straw as cooking fuels was associated with a significantly increased risk for nasal cancer (ICD-9, 160) (odds ratio, 3.3; 95% CI, 1.7–6.7). In multivariate analysis after adjusting for related variables such as age, intake of oranges/tangerines, consumption of salted fish/meat/vegetables, ever exposure to wood/silica/petroleum products and ever diagnosed with chronic nasal diseases, ever use of wood/straw as cooking fuels was associated with a risk for nasal cancer and yielded an odds ratio of 3.3 (95% CI, 1.5–7.3). Consistent associations in both men and women were found for use of wood/straw as cooking fuels (odds ratio for men, 2.2; 95% CI, 0.9–5.4; odds ratio for women, 8.5; 95% CI, 2.3–31.8). [The Working Group noted that the sample size was relatively small. The variable use of wood/straw as cooking fuels was only classified

Table 2.7 Case–control studies of nasopharyngeal cancer

Reference, study location and period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds Ratio (95% CI)	Adjustment for potential confounders	Comments
Biomass							
Shanmugaratnam *et al*. (1978), Singapore, 1966–68	379 (266 men, 113 women) Chinese patients from ENT department of Singapore General hospital; age 10–>70 yrs, histologically confirmed Two sets of Chinese controls: 595 (311 men, 284 women) ENT patients without NPC; 1044 (738 men, 306 women) other hospital controls	Trained interviewer-administered standardized questionnaire in the local dialect of interviewees	**Main type of fuel used over the past 10 yrs** *Charcoal* ENT controls Other controls *Firewood* ENT controls Other controls	 NG NG NG NG	 0.69 (p>0.05) 0.75 (p>0.05) 1.71 (p<0.01) 0.87 (p>0.05)	Age, sex, interviewer	Greater proportion of the ENT controls may have used gas instead of firewood since this group had higher socioeconomic status; participants were all permanent residents of Singapore

Table 2.7 (contd)

Reference, study location and period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds Ratio (95% CI)	Adjustment for potential confounders	Comments
Hubert *et al*. (1993); Zheng *et al*. (1994), Guangxi, China, January 1986–unspecified	88 cases of histologically confirmed undifferentiated NPC enrolled from regional cancer institutes (29 in Wuzhou, 59 in Zangwu); 73% men; 15.9% aged ≤30, 32.9% between 31 and 40; 34.2% between 41 and 50 and 17% older than 50 176 population controls matched on age (±4 year), sex and neighbourhood; interviewed the same week as the case	Interviewer-administered standardized questionnaire	*Wood fuel use vs. none in the year before diagnosis* Yes Yes	 80 80	 6.4 (p=0.003) 5.4 (1.5–19.8)	 Socioeconomic score Socioeconomic score, consumption of herbal tea in year before diagnosis and consumption of salted fish in porridge before the age of 2 yrs Matching variables adjusted for in conditional logistic regression analyses	Socioeconomic score based on type of housing in childhood, presence of windows in house and monthly income the year before diagnosis; this study completely overlaps with Hubert *et al.* (1993)

Table 2.7 (contd)

Reference, study location and period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds Ratio (95% CI)	Adjustment for potential confounders	Comments
Chelleng *et al.* (2000) Nagaland, India, 1996–97	47 histologically confirmed cases who were permanent residents of Nagaland; 72% men 94 neighbourhood controls; matched by age, sex and ethnicity	In-person interview using standard questionnaire	Soot in house Wood vs. gas for cooking fuel	20 42	1.4 (0.6–3.3) 1.6 (0.4–6.6)	Yes but unclear	This study was not well powered; significant association with smoked meat: 11.5 (3.4–38.5)
Mixed coal/biomass							
Cai & Ye (1996), Fujian, China, 1991	115 primary NPC patients, pathology confirmed and lived in Fujian more than 10 yrs; 86 men 230 (115 non-tumour, 115 tumour) controls, who lived in Fujian more than 10 yrs; matched on age, gender, diagnosis date	In-person interview using a questionnaire	Use of coal or firewood/straw as fuels		Non-tumour control in 1978, 6.52 (1.90–22.32) Tumour control in 1968, 3.14 (1.18–8.36) Tumour and non-tumour control in 1968, 3.35 (1.36–8.27)		Coal and firewood/straw were not reported separately. In 1978 and 1968 means fuel use under conditions in different eras.

into two groups (never, ever) which resulted in a lack of information on dose–response relationship.]

Eighty-eight incident cases of NPC diagnosed after 1 January 1 1986 in Zanhwu and Wuzhou, an area in China that is endemic for NPC, were enrolled in a case–control study (Hubert *et al*., 1993; Zheng *et al*., 1994). One hundred and seventy-six controls were selected in the immediate neighbourhood, matched on sex, age (±4 years) and place of residence. The controls were interviewed within the same week as the patients and under the same conditions. Information was collected on past and present conditions including educational level, marital status, place of birth, residential history, personal or family income, housing, types of fuel used, kitchen and toilet equipment and sleeping conditions, as well as diet (including methods of preparation and preservation). A sociodemographic score was established to describe living conditions according to three variables: monthly income, lack of house windows during the preceding year and type of housing in childhood. Odds ratios and 95% CIs were calculated using conditional logistic regression. Use of wood as fuel in the year before diagnosis was positively associated with the risk for NPC after adjusting for sociodemographic score (odds ratio, 6.4; p=0.003; 80 exposed cases) and after additional adjustment for consumption of herbal tea in year before diagnosis and consumption of salted fish in porridge before the age of 2 years (odds ratio, 5.4; 95% CI, 1.5–19.8; 80 exposed cases). Exposure to wood as a fuel in early childhood was not significantly associated with NPC. The risk for NPC from the use of wood fire was also studied in conjunction with other environmental factors that may affect the level of exposure. [The Working Group noted that exposure to wood fuel was assessed crudely, in that it was classified as a dichotomous variable, and no information on a dose–response relationship was presented. The Working Group noted that almost all subjects were exposed to wood combustion in early childhood and therefore 'current use' may be a better surrogate for cumulative exposure.]

A case–control study was designed in Nagaland, India, to evaluate the determinants of nasopharyngeal cancer (Chelleng *et al*., 2000). The study included 47 histologically confirmed cases recruited at the Bhobaneswar Boruah Cancer Institute between 1996 and 1997 and 94 neighbourhood controls matched on age, sex and ethnicity. Information on risk factors including dietary, environmental and sociodemographic factors was obtained from an in-person interview using a standard questionnaire. Of the cases, 72.3% were men and a large majority (68.1%) were over 40 years of age at the time of diagnosis. Questions on biomass exposure included presence of soot in the house, cooking fuel used, location of the kitchen, and type of house and the number of windows. None of these variables was significantly associated with the risk for nasopharyngeal cancer. In the multivariate logistic regression that accounted for tobacco smoking and socioeconomic status among other factors, the presence of soot in the house gave an odds ratio of 1.4 (95% CI, 0.6–3.3; 20 exposed cases) and use of wood for cooking (versus gas) gave an odds ratio of 1.6 (95% CI, 0.4–6.6; 42 exposed cases). [The Working Group noted that the consumption of smoked meat and a previous history of nasal drop use were significantly related to cancer. The Working Group further noted that this study had a

poor characterization of exposure to wood burning (dichotomous wood versus gas) and no specification on current or past exposure. In addition, the power was low due to the small number of cases.]

2.2.5 *Cancer of the oesophagus and its precursors*

Chronic oesophagitis is considered to be a precusor condition for oesophageal cancer. A study was carried out to collect information on the prevalence of chronic oesophagitis at early ages in a high-risk area for oesophageal cancer and to identify risk factors associated with the prevalence of this disease (Chang-Claude *et al*., 1990). Study subjects were young adults aged 15–25 years from all households where cases of oesophageal cancer had been diagnosed after 1981 until October 1987 and twice the number of randomly selected households where no oesophageal cancer was diagnosed (with neither a diagnosis nor a family history of oesophageal cancer or dysplasia). A total of 227 and 660 young adults from these two types of household were eligible for inclusion in the study. In May 1988, 545 (62%) subjects participated in the study. They were interviewed and information was collected on dietary habits in the early 1970s and in the past 5 years, methods of food preparation, types of oil used, alcohol consumption, tobacco smoking, use of coal and other fuels, cooking fumes, ventilation, family history of oesophageal cancer, occupation and dental hygiene. A physical examination with collection of a 10-ml blood sample and early morning urine was conducted for each subject. Endoscopic examination of the oesophagus and stomach was also performed. Variables identified in univariate analysis were then evaluated in multivariate logistic regression models. A total of 538 subjects (354 men, 184 women) underwent an oesophagoscopy with biopsy. Of these, 166 came from cancer households and 372 from non-cancer households. Since the distributions of variables of interest among subjects with very mild oesophagitis were similar to those with a normal oesophagus, very mild oesophagitis was classified as normal in the analysis of risk factors for chronic oesophagitis. In univariate analysis (the household was controlled for as a confounder), in addition to other significant risk factors, cottonseed oil used for cooking most frequently (odds ratio for men, 2.3; 95% CI, 1.2–4.5; odds ratio for women, 1.6; 95% CI, 0.5–5.9), use of wood as fuel in the early 1970s (odds ratio for men, 2.5; 95% CI, 1.2–5.2; odds ratio for women, 2.6; 95% CI, 0.7–9.2) and use of wood as fuel in the past 5 years (odds ratio for men, 1.4; 95% CI, 0.3–7.0; odds ratio for women, 9.9; 95% CI, 2.3–43.2) were statistically significant variables for the risk for chronic oesophagitis in this rural area. In multivariate analysis, there was no statistically significant association of these variables, adjusted for other risk factors including age and sex (adjusted odds ratio for use of wood as fuel in the past 5 years, 1.72; p=0.19). The authors stated that the unexpected finding of an association of the use of wood as fuel with disease occurrence could be a chance association, since the relationship virtually disappeared in multivariate analysis. [The Working Group noted that the participation rate (62%) in this study was relatively low, and selection bias might exist.]

A study was conducted to determine whether functional polymorphisms in xenobiotic metabolizing genes could affect the risk for oesophageal cancer in different population groups (Dandara *et al*., 2006, in Table 2.6). A total of 245 patients with histologically confirmed squamous-cell carcincinoma and admitted for dysphagia were recruited from a hospital in Cape Town, South Africa. A total of 288 age-matched, healthy population controls were recruited from the same geographical location as the patients; 145 cases and 194 controls were black and 100 cases and 94 controls were of mixed ancestry. As part of the questionnaire, information on cooking and heating fuels used during the past 20 years was recorded and smokers were classified as individuals who had smoked at least one cigarette per day for at least 1 year. Subjects were also classified as alcohol consumers if they consumed alcohol regularly (at least once at week). Among black subjects, the burning of wood or charcoal for cooking and heating (compared with electricity) was significantly associated with an increased risk for oesophageal cancer (odds ratio, 15.2; 95% CI, 8.15–28.2; p=0.001; 63 exposed cases), as were smoking pipes and consumption of home brewed beer. In the subjects of mixed ancestry, wood or charcoal use was not associated with oesophageal cancer (odds ratio, 1.19; 95% CI, 0.60–2.34; p=0.62; 28 exposed cases); however, alcohol consumption and tobacco smoking were strong risk factors for oesophageal cancer. [The Working Group noted that the exposure variable used was dichotomous and that no dose–response information was available. There was concern for residual confounding because the risk estimates were adjusted for overall consumption of alcohol and tobacco (not associated in the data set with oesophageal cancer in blacks) but not for pipe smoking or home brewed beer consumption (which were strong risk factors oesophageal cancer in the black population).]

2.2.6 *Cancer of the cervix* (see Table 2.8)

A case–control study was conducted in Honduras to determine whether exposure to wood smoke increases the risk for invasive cervical cancer (Velema *et al*., 2002). One hundred and twenty-five women aged 20–64 years who had different grades of cervical intraepithelial neoplasia (CIN) (44 CIN I, 36 CIN II, 45 CIN III) were recruited from a screening programme. Each case was matched by age, clinic and calendar time to two controls (241 controls in total) without cervical abnormalities. All women were from low socioeconomic backgrounds. Cervical scrapes were tested for the presence of human papilloma virus (HPV) and HPV genotyping was performed. An interview was conducted in the clinic for case and control women to determine whether they had ever cooked with wood and, if so, the duration of use and the number of years since stopping use of wood for cooking. Exposure to wood during childhood was also determined. HPV DNA was detected in 48% of women with CIN I, 67% with CIN II and 89% with CIN III. Exposure to wood smoke for 35 or more years increased the risk for CIN III (odds ratio, 4.89; 95% CI, 0.51–47.1; p=0.017; nine exposed cases) compared with women with no exposure. Restriction of the analysis to women who reported exposure yielded a positive association with development of CIN III for women exposed for more than 35 years versus those

Table 2.8. Case–control study of cervical cancer

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment for potential confounders	Comments
Velema *et al.* (2002), Tegucigalpa City, Honduras, 1993–95	125 women with CIN (44 CIN I, 36 CIN II, 45 CIN III) from 14 hospitals; aged 20–64 yrs 241 women without cervical abnormalities from the same screening clinic as cases; matched by age, clinic, calendar time	In-person interview	In CIN III women, yrs of exposure to wood smoke vs. none 1–14 15–24 25–34 35+	 11 8 8 9	 0.36 (0.11–1.18) 0.35 (0.09–1.39) 1.34 (0.20–9.18) 4.89 (0.51–47.1)	Adjusted for matching factors by conditional logistic regression	When stratified by HPV status (positive, negative), the authors concluded that there was a significant dose–response effect among HPV- positive patients; however, the Working Group thought the analytical approach was questionable.

CI, confidence interval; CIN, cervical intraepithelial neoplasia; HPV, human papillomas virus; yrs, years

exposed for 1–14 years (odds ratio, 9.5; 95% CI, 1.16–77.4; p=0.017; nine exposed cases). There was no significant association with CIN I or II. [The Working Group noted that this significant association was observed only when unexposed women were excluded from the analysis and unstable point estimates resulted after stratification by CIN stages and duration of exposure.] Among HPV-positive women, more than 35 years of exposure to wood smoke increased the risk for CIN compared with 1–14 years of exposure to wood smoke (odds ratio, 5.69; 95% CI, 1.00–32.70). [The Working Group also noted that these results are difficult to interpret because women who reported not having used wood in the kitchen had a risk higher than those with low or intermediate exposure and the analytical approach was questionable.]

2.3 Mixed coal/biomass (coal and/or wood/dung/*kang* use)

2.3.1 *Cancer of the lung* (see Table 2.9)

Chen *et al*. (1990) conducted a case–control study in Taipei, Taiwan, China that included 323 serial lung cancer cases from four teaching hospitals (133 epidermoid, 47 small-cell and 134 adenocarcinomas) and 617 healthy controls who were ophthalmic patients in the study hospitals that were frequency-matched to cases on hospital, gender and age. Logistic regression models adjusted for sex and age showed no significant effect of burning coal or wood compared to other fuels (charcoal, gas) and electricity.

Mzileni *et al*. (1999) conducted a hospital-based case–control study that included 288 men and 60 women who had been diagnosed with incident lung cancer between 1993 and 1995 in the main tertiary referral hospital in the northern Province of South Africa. Controls were 183 men and 197 women who had been diagnosed with other incident cancers (predominantly of the prostate, liver and breast, colorectal and haematological cancers) in the same hospital as cases during the same study period. Cases and controls were interviewed regarding their tobacco smoking habits, residence, main occupation and fuel use (wood and coal) at home. The risk for lung cancer was increased in relation to the use of wood or coal in the house in men (odds ratio, 1.9; 95% CI, 0.9–3.3; 260 exposed cases) and women (odds ratio, 1.4; 95% CI, 0.6–3.2; 51 exposed cases) after adjusting for smoking, dusty occupation and residential exposure to asbestos. The positive association between the risk for lung cancer and the use of wood or coal in the house was statistically significant in men and women combined (adjusted odds ratio, 2.0; 95% CI, 1.1–3.6). Active tobacco smoking and living in asbestos-polluted areas were also significantly associated with risk for lung cancer in men and women combined after adjusting for age, sex, dust and use of wood for fuel. [The Working Group noted that results were presented for wood and coal use combined and as a dichotomous variable (no/yes). The independent effects of coal and wood could not be examined because the information on these two types of fuel were not presented separately. Because of the strong significantly positive associations between risk for lung cancer, smoking and residence in asbestos-

Table 2.9. Case–control studies of lung cancer and use of mixed coal/biomass fuel

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment for potential confounders	Comments
Chen *et al*. (1990), Taipei, Taiwan, Province of China [period not specified]	323 serial cases from 4 teaching hospitals in Taipei, all pathologically confirmed: 133 epidermoid, 47 small-cell and 134 ADC 617 ophthalmic patients from study hospitals; frequency-matched on hospital, gender, age	In-person interview using a structured questionnaire	Burning coal or wood versus other fuels (charcoal, gas) and electricity *Epidermoid* *Small-cell* *ADC*	 NG NG NG	 0.85 (p>0.05) 1.08 (p>0.05) 1.02 (p>0.05)	Age, sex	
Mzileni *et al*. (1999), northern Province, South Africa, 1993–95	348 cases (288 men, 60 women) enrolled from a referral hospital 380 patients (183 men, 197 women) with cancers 'not thought to be related to smoking'	In-person interview	*Wood or coal use at home* Men Women	311 260 51	2.0 (1.1–3.6) 1.9 (0.9–3.3) 1.4 (0.6–3.2)	Smoking, dusty job, household asbestos	Coal and wood were not reported separately. The northern Province is one of the poorest provinces in South Africa and also an important source for exposure to asbestos.

Table 2.9 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment for potential confounders	Comments
Behera & Balamugesh (2005), Chandigarh, India, 1999–02	67 women enrolled from a lung cancer clinic; 75% nonsmokers; 100% confirmed by histology or cytology 46 women with non-cancer respiratory disease; 93% nonsmokers	Questionnaire	*Biomass use for cooking compared with LPG users* In nonsmokers	NG NG	3.6 (1.1–12.0) 5.3 (1.7–16.7)	Smoking, environmental tobacco smoke	Exposure and duration were not clearly defined; biomass fuel was considered as coal, wood, cow dung cake, agricultural waste, although about 95% of the Indian rural population still relies primarily on biomass fuels (dung, crop residues and wood); no age adjustment; selection of controls with respiratory diseases could underestimate the relative risk.

Table 2.9 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment for potential confounders	Comments
Pisani *et al.* (2006), Lampang Province, Thailand, 1993–95	211 cases (66% men) enrolled from the provincial hospital; confirmed by histology or cytology Age and sex matched population (*n*=202) and hospital controls (*n*=211; also matched to cases by residence); tobacco-related diseases excluded	In-person interview using a standard questionnaire	**Cumulative index of years of exposure to domestic fumes** <9 9–14 15–20 >21 *In nonsmokers* <15 >15	 51 67 43 50 11 5	 1.0 1.3 (0.7–2.2) 0.8 (0.4–1.4) 0.8 (0.5–1.5) 1.0 0.4 (0.1–2.0)	Age, sex, cumulative cigarettes smoked	Both coal and wood exposure contributed to domestic fumes and were not assessed separately. Tests for trend were not presented. No trend versus index level. Index = years cooking with coal/wood indoors +0.5 of the time spent cooking outdoors

Table 2.9 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratio (95% CI)	Adjustment for potential confounders	Comments
Ramanakumar, *et al.* (2007), Montreal, Canada, 1996–2001	1205 cases from 18 hospitals (61% male); 100% histologically confirmed; 37% proxy respondents 1541 population controls; matched by age, sex; 8% proxy respondents	In-person interview using a structured questionnaire	**Women only** *Wood or coal stove for heating the living space vs. no exposure* Any exposure Age <20 yrs Age ≥20 yrs Smoking status Medium/heavy None/light Respondent type Self Proxy *Wood or gas stove for cooking vs. no exposure* Any exposure Age <20 yrs Age ≥20 yrs Smoking status Medium/heavy None/light Respondent type Self Proxy *Exposed for* Heating only Cooking only Heating and cooking	 289 239 185 219 70 192 97 358 315 176 264 94 247 111 32 102 253	 2.0 (1.4–2.8) 2.0 (1.4–2.9) 2.4 (1.5–3.7) 2.1 (1.4–3.3) 1.7 (1.0–2.9) 2.0 (1.4–2.9) 1.2 (0.3–4.3) 1.6 (1.1–2.3) 1.7 (1.2–2.6) 1.3 (1.1–2.0) 2.0 (1.2–3.2) 1.3 (0.7–2.3) 1.8 (1.2–2.7) 0.3 (0.1–1.5) 1.8 (1.0–3.2) 1.2 (0.7–1.9) 2.5 (1.5–3.6)	Age, ethnic groups, family income, smoking, place of birth, surrogate or not, education, occupational hazard	No significantly increased risks were observed in men. Most cases were ever smokers. Coal, wood and gas exposures were not defined separately. Risks were the most increased for small-cell carcinoma (in women) and squamous-cell carcinoma (men and women)

ADC, adenocarcinoma; CI, confidence interval; LPG, liquefied petroleum gas; NG, not given; yrs, years

polluted areas, it is difficult to rule out the role potential confounding effects of these exposures in the association between wood/coal use and lung cancer.]

Two studies in the Kaohsiung area, Taiwan, were reported by Ko *et al*. (1997) and Le *et al*. (2001) (described in detail in the monograph on high-temperature frying). Risk patterns associated with cooking fuels were reported. The first report included 106 nonsmoking lung cancer cases and an equal number of hospital controls (Ko *et al*., 1997). Compared with women who did not cook or cooked with gas at age 20 years or younger, those who cooked with coal experienced no increased risk for lung cancer (odds ratio, 0.5; 95% CI, 0.2–1.6) whereas those who cooked with wood and/or charcoal had more than a twofold increased risk (odds ratio, 2.5; 95% CI, 1.3–5.1). Results were similar when they examined cooking practices between the ages of 20–40 years. Compared with those who did not cook or cooked with gas, the risk for lung cancer was increased among those who cooked with wood/charcoal (odds ratio, 2.5; 95% CI, 1.1–5.7). Few subjects cooked with wood or coal after 40 years of age and thus meaningful analyses could not be conducted.

In a subsequent report (Le *et al*., 2001) (described in detail in Section 2.1.1), the relationship between cooking fuel and risk for lung cancer was examined separately by lung cancer cell type. The use of wood was associated with a threefold increased risk for lung cancer (odds ratio, 3.1; 95% CI, 1.0–9.2) compared with women who did not cook or used gas for cooking. In contrast, the risk for adenocarcinoma of the lung (158 cases, 262 controls) increased in relation to the use of wood (odds ratio, 3.0; 95% CI, 1.4–6.4). Tobacco smoking, residential area, education and social class were adjusted for in the analysis. [The Working Group noted that information on duration of wood and coal use was not reported in these two studies.]

Sixty-seven women who had histologically or cytologically confirmed lung cancer seen at the Department of Pulmonary Medicine, Chandigarh, India, and 46 controls with non-malignant respiratory disease were recruited in a case–control study between January 1999 and December 2002 (Behera & Balamugesh, 2005). A questionnaire was used to collect information on demographic factors, lifetime exposure to smoking, detailed occupational history, residence and exposure to indoor air pollution due to burning of organic fuels. [The Working Group noted that 'organic fuels' were not clearly defined but probably included coal, wood, cow dung cake and agricultural waste.] Unconditional logistic regression models were used for analyses. Among the lung cancer cases, 50 (74.6%) were nonsmokers among whom adenocarcinoma was the predominant histology (50%). In women who smoked, squamous- and small-cell carcinoma were the most common histological types. When adjusted for active and passive smoking [not stated if adjusted for age] and compared with the use LPG as the reference category, the odds ratio for use of biomass fuel was 3.6 (95% CI, 1.1–12.0). Among nonsmokers, the corresponding odds ratio was 5.3 (95% CI, 1.7–16.7). [These results were presented in a table and in the text and it was unclear if the analyses were stratified or unstratified univariate. The Working Group also noted that the selection of controls with respiratory diseases could underestimate the relative risk.]

Pisani *et al*. (2006) carried out a case–control study of lung cancer with 211 hospital cases (66% men; including smokers and nonsmokers), 202 population controls and 211 hospital controls without tobacco-related diseases matched by age and sex (and also residence for the hospital controls). This study primarily investigated the interactions between smoking and genetic polymorphisms in northern rural Thailand. Information was obtained through in-person interviews. The exposure index of solid fuel use was calculated by combining years of cooking with coal/wood indoors (weight=1) and outdoors (weight=0.5). The majority of cases (99%) were microscopically verified; 45% were squamous-cell carcinomas and 21% were adenocarcinomas. Only 7% of men and 33% of women in the overall study group were never smokers. No significant effects or trends were found for the cumulative index of exposure to domestic fumes for the whole group after adjusting for age and sex (and also cumulative smoking in smokers). [The Working Group noted that the coal and wood exposures were not separated and therefore made the study results uninformative for either type of fuel. The use of fuel for cooking and heating was also not separated.]

Ramanakumar *et al*. (2007) conducted a hospital-based case–control study in Montreal, Canada, which was originally designed to examine occupational risk factors. This analysis included 1205 (739 men, 466 women) histologically confirmed lung cancer patients who were diagnosed between 1996 and 1997 at the 18 largest hospitals in the study area. A total of 1541 (925 men, 616 women) population controls were selected from electoral lists and were interviewed. Structured interviews were conducted to collect information on smoking history, occupational history, sources of traditional heating (defined as wood or coal stove in living space) and cooking (defined as a wood or gas stove) and other risk factors. To assess exposure to traditional cooking sources, subjects were asked if they had ever lived full-time in a house/apartment where the cooking was carried out on a gas or wood stove. Similarly, to assess exposure to traditional heating sources, subjects were asked if they had ever lived in a house/apartment that was mainly heated by a stove or fireplace located in the living quarters. No significant associations with exposure to traditional heating or cooking were found for men, with most of the odds ratios below 1.0. For women, however, most of the odds ratios associated with traditional heating or cooking were above 1.0 and were statistically significant. In women, elevated risks associated with traditional heating were found in subjects who were older (≥60 years) at the age of onset, self-respondent, and in smokers. An increased risk for lung cancer was also observed in women classified as nonsmokers and light smokers. [The Working Group noted that the assessment of 'traditional cooking' combined cooking with gas and wood whereas the assessment of 'traditional heating' may have included exposure to wood/coal. In addition, there was incomplete specification of fuel use; for example, no mention was made of the use of electricity for cooking or oil and electricity for heating which further complicated the interpretation of this study.]

2.3.2 *Cancer of the oral cavity, pharynx and larynx* (see Table 2.6)

Three concurrent case–control studies were conducted in Heidelberg, Germany, to examine the association between fossil fuel stoves and the risk for laryngeal, pharyngeal and oral cavity cancer (Dietz *et al*., 1995; Maier & Tisch, 1997). A total of 164, 100 and 105 cases of laryngeal, oral cavity and pharyngeal cancer, respectively, were ascertained between 1989 and 1992 from all patients seeking treatment at the Otorhinolaryngology Department within 3 years from first diagnosis. Almost all cases were current or former smokers. Controls were recruited from the same medical centre and general outpatient department at the University of Heidelberg from among non-cancer patients and matched to cases on sex, age and size of the place of residence. Fossil fuel emissions from stoves and cooking and the type of burning materials used (coal, briquette, coke, peat, gas and oil) were ascertained. Use of fossil fuel stoves or cookers were associated with all three types of cancer: adjusting for tobacco and alcohol use, the odds ratio for >40 versus 0–20 years was 2.0 for fossil fuel heating (95% CI, 1.10–3.46) and 1.4 for cooking (95% CI, 0.76–2.41) for laryngeal cancer, 3.3 for fossil fuel heating (95% CI, 1.43–7.55) and 2.5 for cooking (95% CI, 1.03–6.30) for pharyngeal cancer and 2.4 for fossil fuel heating (95% CI, 1.26–4.40) and 1.6 for cooking (95% CI, 0.90–2.97) for oral cavity cancer. [The Working Group noted that no dose–response trend with duration of use and no association for the 20–40-year exposure category for any of the cancer sites were observed; also, the specific type of fuel responsible for the increase in risk at the highest duration of stove use could not be determined.]

2.3.3 *Cancer of the nasopharynx* (see Table 2.7)

A case–control study of 115 cases of NPC (86 men, 29 women) newly diagnosed pathologically in the hospitals of Fujian Province during the period from March to May 1991, who had lived in Fujian at least for 10 years, was conducted (Cai & Ye, 1996). Controls (115 cancer controls and 115 non-cancer controls) were randomly selected from the patients and matched on sex, age (within 5-year age group) and date of hospitalization (same month) to the cases. The controls had also lived in Fujian at least for 10 years. The cancer controls were patients with cancers other than of the respiratory system, while the non-cancer controls were patients without cancer or respiratory diseases. Information in 1968 and 1978 on demographic factors, residential, dietary and occupational history, smoking and alcohol drinking, family history of cancer and chronic diseases of ear, nose, pharynx and larynx was collected. In multivariate analysis using non-cancer controls, the odds ratio for use of straw as domestic fuel was 6.52 in 1978 (95% CI, 1.90–22.32). Use of coal and firewood/straw in 1968 was positively associated with NPC for cancer controls (odds ratio, 3.14; 95% CI, 1.18–8.36) and for the combined control groups (odds ratio, 3.35; 95% CI, 1.36–8.26). [The Working Group noted that the odds ratio for straw was estimated using coal fuel as a reference group. Consumption of salted fish was only assessed in 1978, but not in childhood, and because both salted fish consumption and

straw use may be associated with socioeconomic status, the odds ratio for straw may be confounded.]

A hospital-based case–control study of NPC (Huang *et al*., 2002) was carried out in Guangxi to search for risk factors of NPC other than Epstein-Barr virus (EBV) infection; 175 cases of NPC (132 men, 43 women) pathologically diagnosed and treated at First Hospital and Cancer Hospital affiliated to Guangxi Medical University during the period from March 2000 to May 2001 were involved in the study. The cases had lived in Guangxi for at least 10 years and had originated from Guangxi. A total of 350 controls (264 men, 86 women) were selected from patients without cancer or respiratory diseases treated at the same hospital and same period, and matched on sex, age (±4 years), occupation, at least 10 years of living in Guangxi and same place of origin as the cases. Information on demographic factors, occupational history, residential environment, life and dietary habits, previous diseases, family history of NPC and psychological factors was collected by use of a structured questionnaire. Use of coal or firewood as fuel was associated with a significantly increased risk for NPC (odds ratio, 3.68; 95% CI, 2.15–6.29).

2.4 Proxies for indoor air pollution

2.4.1 *Cancer of the lung* (see Table 2.10)

The studies that are included in this section of mixed exposures did not examine specific exposures such as type of cooking oil or frequency of high-temperature cooking but rather examined measures related to general cooking practices (e.g. age started or years of cooking) or ventilation.

The first study that included data on cooking practices and lung cancer was a hospital-based case–control study conducted in Singapore (MacLennan *et al*., 1977) which included 233 lung cancer cases (147 men, 39 Cantonese women, 47 non-Cantonese women) and 300 hospital control subjects (134 men, 80 Cantonese women, 86 non-Cantonese women) who were identified from three main hospitals. In total, 46 lung cancer cases (20%) and 124 controls (41%) were nonsmokers. Thirty-six per cent (84/233) of the lung cancer cases were histologically confirmed. The risk for lung cancer in relation to domestic cooking was 1.55 [95% CI, 0.75–3.22] in men, 1.74 [95% CI, 0.67–4.47] in Cantonese-speaking women and 0.40 [95% CI, 0.21–0.92] in non-Cantonese-speaking women. [The Working Group noted that no adjustment for active smoking or use of gas/kerosene was made in the analysis. No description of the questions asked on cooking was given: the frequency, duration and intensity of cooking were not included.]

In a case–control study in Shenyang, China, Xu *et al*. (1989) (described in Section 2.1.1) developed a continuous index of average long-term indoor air pollution intensity, based on duration of living at each residence, presence of coal heating, cooking fuel and location of cooking place (e.g. separate or not). This index was positively associated with

Table 2.10. Case-control studies of lung cancer and proxies of indoor air pollution

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratio (95% CI)[a]	Adjustment for potential confounders	Comments (covariates considered)
MacLennan *et al*. (1977), Singapore, 1972–74	233 cases (147 men, 86 women) from 3 hospitals; 36% confirmed histologically; 80% smokers 300 (134 men, 166 women) controls who did not have smoking-related disease; matched on sex, age, dialect; 59% smokers	In-person interview	**Ever cooked** Men Cantonese Women Non-Cantonese women	 80 21 32 27	 1.01 (p>0.05) 1.55 [0.75–3.22] 1.74 [0.67–4.47] 0.40 [0.21–0.92]	None	Exposure index not well defined; gas/kerosene use was not a risk factor. The Working Group calculated the confidence intervals assuming an unmatched analysis. It was not clear how the authors calculated the odds ratio for the 'ever cooked' category.
Xu *et al*. (1989), Shenyang, China, 1985–87	1249 cases (729 men, 520 women) in Shenyang aged 30–69 yrs; cell type histologically confirmed in 83% of men and 73% of women 1345 population-based controls (788 men, 557 women), selected by 3-stage procedure from urban Shenyang; frequency-matched on gender, age	In-person interview using a structured questionnaire; continuous index of indoor exposure to coal smoke from heating and cooking	**Indoor air index versus <1** *Men* 1.0–1.4 1.5–1.9 >2.0 *Women* 1.0–1.4 1.5–1.9 >2.0 **Perceived indoor smokiness during heating versus none** *Men* Somewhat smoky Smoky *Women* Somewhat smoky Smoky	 258 168 94 183 110 56 249 198 146 116	 1.1 (0.8–1.4) 1.2 (0.9–1.6) 1.6 (1.1–2.3) 1.2 (0.9–1.6) 1.3 (0.9–1.9) 1.5 (1.0–2.4) 1.2 (1.0–1.5) 1.3 (1.0–1.7) 1.2 (0.9–1.6) 2.0 (1.4–2.8)		The indoor air index ranged from 0 to 3, with values below 1 indicating potential for relatively low lifetime exposure to indoor air pollution from burning coal. [This study overlaps with Sun *et al*. (1991)]

Table 2.10 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratio (95% CI)[a]	Adjustment for potential confounders	Comments (covariates considered)
He *et al*. (1991); Liu *et al*. (1991), Xuan Wei, China, 1985–86	110 diagnosed lung cancer patients (56 men, 54 women) 426 controls (224 men, 202 women); matched on gender, age (±2 yrs) occupation (all farmers), village of residence; 1–5 controls per case (mean, 3.87)	In-person interview using a structured, field-tested questionnaire	**Men** *Often cooks food* **Women** *Age started cooking versus >15 yrs* 11–15 ≥10 *p* for trend *Yrs of cooking versus ≥30* 31–44 ≥45 *p* for trend *≥45 yrs using unventilated fire pit (versus <45 yrs)* Men Women	 12 30 11 28 19 34 33	 3.36 (1.27–8.88) 2.37 (1.09–5.15) 1.25 (0.45–3.49) >0.05 9.18 (1.76–47.49) 14.70 (1.61–134.03) >0.05 1.78 (0.46–6.93) 0.73 (0.20–2.60)	Unclear	Although the analyses were duplicated in both studies, the Working Group noted discrepancies in the results. The instability of the risk estimates is demonstrated with the different choice of category cut-points in both studies. Matching by village provided matching on indoor fuel type and home type, allowing more incisive analysis of other factors such as smoking and duration and frequency of cooking food. Male and female subjects burned more smoky coal (range; 4.0–4.2 tonnes/yr than wood (range; 0.8–1.0 tonnes/yr)

Table 2.10 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratio (95% CI)[a]	Adjustment for potential confounders	Comments (covariates considered)
Liu *et al*. (1991) Xuan Wei, China 1985–86	110 cases (56 men, 54 women); 17% histologically confirmed; 52 men and 0 women smoked	In-person interview	**Men**			Smoking index (yrs×amount of smoking)	Conditional logistic regression was used to adjust for matching factors.
			Often cooked food				
			No	44	1.0		
			Yes	12	3.36 (1.27–8.88)		
			Women			Unspecified	
			Age started to cook				
	426 controls (224 men, 202 women); matched by age (± 2 yrs), sex, village of residence; 205 men, 1 woman smoked		>15 yrs	13	1.0		
			11–15 yrs	30	2.37 (1.09–5.15)		
			≤10 yrs	11	1.25 (0.45–3.49)		
			p for trend		>0.05		
			Yrs of cooking				
			≤30	7	1.0		
			31–44	28	5.18 (1.76–47.49)		
			≥45	19	14.70 (1.61–134.0)		
			p for trend		>0.05		

Table 2.10 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratio (95% CI)[a]	Adjustment for potential confounders	Comments (covariates considered)
Koo & Ho (1996), Hong Kong, 1981–83	200 female lung cancer patients, mean age 61.8 yrs; 44% never smokers; 90% histologically confirmed (28% SCC, 18.5% small-cell, 34.5% ADC) 200 female community controls; matched on age (±5 yrs), residential district, housing type; mean age 60.6 yrs; 69% never smokers	Interviews with semi-structured questionnaire, using a life history approach; assessed use and duration of using biomass fuels, coal, kerosene, LPG and gas.	*Yrs of cooking among never smokers* 0–25 26–40 ≥41 *p* for trend	 NG NG NG	 1.00 0.38 (0.17–0.88) 0.37 (0.14–0.96) <0.001	Age, number of live births, education	Risk associated with cooking fumes was evaluated.
Shen *et al*. (1996), Nanjing, China 1986–93	263 cases (83 SCC, 180 ADC) who were Nanjing residents for ≥20 yrs 263 population controls who were Nanjing residents; matched 1:1 for gender, age, ethnicity, 'street address'	Standardized questionnaire	*Cooking fumes* SCC ADC	 NG NG	 3.81 (1.06–13.73) 2.99 (1.68–5.34)	Unclear	Fuel types within 'solid fuel' category were not specified. Statistical tests were reported as one-sided, but implications are not clear.

Table 2.10 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratio (95% CI)[a]	Adjustment for potential confounders	Comments (covariates considered)
Shen *et al*. (1998), Nanjing, China, 1993	70 never-smoking women diagnosed with primary lung ADC; all were Nanjing residents for ≥20 yrs 70 healthy community controls; matched 1:1 for gender, age, neighbourhood, occupation	In-person interview using a standardized questionnaire	Cooking fumes		2.45 (1.06–5.66)	Unclear	The main purpose of the study was to assess lung cancer risk associated with passive smoking. This study may overlap with Shen *et al*. (1996).
Zhong *et al*. (1999), Shanghai, China, 1992–94	504 never-smoking female incident cases, 35–69 yrs old, identified from the Shanghai Cancer Registry 601 never-smoking women; frequency-matched on age distribution of female lung cancer cases during 1987–89; randomly selected from the Shanghai Residential Registry	In-person interview using a structured questionnaire	Not cooking in separate kitchen Cooking hot with visible fumes *Kitchen smokiness during cooking* Somewhat Considerable *Eye irritation during cooking* Rarely Sometimes Frequently	248 165 241 86 49 74 43	1.28 (0.98–1.68) 1.64 (1.24–2.17) 1.67 (1.25–2.21) 2.38 (1.58–3.57) 1.49 (0.91–2.43) 1.75 (1.16–2.62) 1.68 (1.02–2.78)	Age, education, income, vitamin C intake, respondent status, exposure to environmental tobacco smoke, occupation, family history of lung cancer	

Table 2.10 (contd)

Reference, study location, study period	Characteristics of cases and controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds ratio (95% CI)[a]	Adjustment for potential confounders	Comments (covariates considered)
Zhou *et al*. (2000), Shenyang City, Liaoning Province, China, 1991–95	72 female incident cases of adeno-carcinoma, aged 35–69 yrs, from 18 major hospitals 72 women randomly selected from the Shenyang general population, age-matched (±5 yrs) to Liaoning lung cancer cases in 1988–89	In-person interview using standardized questionnaire	*Kitchen location versus separate kitchen* In living room In bedroom *Eye irritation from smoke versus none* Infrequent Sometimes Frequent *p* for trend *Smokiness during cooking versus none* Slight Medium Heavy *p* for trend	 63 3 35 22 3 15 35 3 	 1.40 (0.41–4.88) 1.00 (0.11–8.93) 1.33 (0.53–3.35) 7.33 (1.92–29.76) 1.67 (0.22–12.93) 0.006 0.73 (0.28–1.90) 2.71 (1.09–6.80) 1.32 (0.18–9.50) 0.027	Not specified	Fuel type not specified for exposure to cooking fumes

ADC, adenocarcinoma; CI, confidence interval; LPG, liquefied petroleum gas; NG, not given; SCC, squamous-cell carcinoma; yrs, years
[a] *p*-value is specified if no confidence interval is indicated

lung cancer risk in a dose–response fashion in both men and women. [This study overlaps with Sun *et al*. (1991).]

One study in Xuan Wei County, China (Liu *et al*., 1991), was based on 110 incident lung cases (56 men, 54 women) identified in regional hospitals and clinics between 1985 and 1986 and 426 population controls (224 men, 202 women) matched on age, sex, occupation and village of residence. Almost all of the men (52 cases, 205 controls) but few of the women (no cases, one control) were smokers. Only 17% of the lung cancers were pathologically or cytologically confirmed. Men who reported that they often cooked food had a significantly increased risk for lung cancer (odds ratio, 3.36; 95% CI, 1.27–8.88; 12 exposed cases) after adjusting for smoking and other unspecified covariates. Women who started cooking at a young age showed an increased risk but there was no significant trend of increasing risk with decreasing age when starting to cook. Compared with women who started cooking at age 15 years or older, the adjusted odds ratio for lung cancer was 2.37 (95% CI, 1.09–5.15; 30 exposed cases) for starting cooking at age 11–15 years and 1.25 (95% CI, 0.45–3.49; 11 exposed cases) for starting cooking at age 10 years or younger (p for trend >0.05). However, the risk increased with increasing years of cooking (adjusted odds ratios, 1.00, 9.18 and 14.70 for ≤30, 31–44 and ≥45 years of cooking, respectively; p for trend >0.05), but the confidence intervals were very wide. [The Working Group noted that this small study had only indirect measures of cooking practices, based on age when started cooking and duration of cooking. The study was limited because only 83% of the lung cancers were diagnosed clinically or radiologically. Potential confounding was not adequately addressed in the statistical analysis.]

Liu *et al*. (1993) presented the results of a hospital-based case–control study of indoor air pollution and lung cancer in Guangzhou, China (described in detail in Section 2.1.1). After the in-person interview, the interviewer measured the size of the windows and doors that opened onto the outside of the building, thereby providing an estimation of ventilation capacity. If the subject had lived in his or her present home for less than 20 years, the interviewer asked similar questions regarding the preceding residences and their ventilation conditions. Data on up to three residences were collected. Not having a separate kitchen and poor air circulation were significantly associated with the risk for lung cancer in men and women. There was a significant dose–response relationship (p for trend <0.05) and a significant inverse association with risk for lung cancer seen with size of ventilation openings in the kitchen and living area and room height. Increased risks for lung cancer were found for men (adjusted odds ratio, 2.4; 95% CI, 1.4–4.2) and women (adjusted odds ratio, 5.9; 95% CI, 2.1–16.0) who lived in homes that did not have a separate kitchen. Similarly, living in a house with poor air circulation was associated with an increased risk in men (adjusted odds ratio, 2.1; 95% CI, 1.2–3.6) and women (adjusted odds ratio, 3.6; 95% CI, 1.4–9.3). In contrast, significant trends of decreasing risk were observed in association with better ventilation, based on variables that measured size of ventilation openings in living areas and in kitchens (see Table 2.10). However, no differences were observed between cases and controls in the number of meals they cooked per day or the presence of chimneys in their homes. [The Working Group noted

that this study did not include direct measures of cooking fumes/practices. However, this was one of the few studies that attempted to obtain a more objective measure of ventilation. As part of the study, the interviewers measured the size of the windows and doors that opened onto the outside of the building in each participant's home. In addition, information on ventilation in up to three previous residences was obtained. A limitation is that a high percentage of the lung cancers were not cytologically/histologically confirmed].

Du *et al*. (1996) also reported a case–control study in which cases were 120 nonsmokers drawn from 849 decedent cases. In conditional logistic regression models, risk for lung cancer in women was significantly associated with increasing indoor air pollution and decreasing kitchen size. These factors were not associated with risk in men. [The Working Group noted that these studies are limited by use of proxy respondents and overall exposure assessment.]

Lei *et al*. (1996) conducted a case–control study in Guangzhou, China, among 792 cases who had died from primary lung cancer (563 men, 229 women), identified from 1986 death certificates, and 792 controls matched on gender, age, street of residence and year of death. Controls had no history of respiratory diseases or tumours. Women with a fair or poor living conditions index (living area per person/room ventilation) had a significantly increased risk for lung cancer while this association was much weaker and only of borderline statistical significance in men.

Koo and Ho (1996) examined the role of cooking fumes and lung cancer risk in a case–control study that included 200 female lung cancer cases and 200 neighbourhood controls. Histology was determined in 90.5% of the cases of which 34% were adenocarcinoma. Forty-four per cent of cases (88/200) and 68.5% of controls (137/200) were never smokers (Koo *et al*., 1983). A significant inverse association was observed between the duration of cooking and risk for lung cancer among never smokers. After adjusting for age, number of live births and education, the risk for lung cancer declined with increasing years of cooking; the adjusted odds ratios were 1.0, 0.38 (95% CI, 0.17–0.88) and 0.37 (95% CI, 0.14–0.96) for 0–25, 26–40 and ≥41 years of cooking (p for trend <0.001). [The Working Group noted that this study only presented results on indirect measures of cooking and that results in smokers were not reported. From an earlier report by Koo *et al*. (1983), kerosene was the main fuel that was used and thus confounding by coal use is unlikely to be a main issue in this analysis.]

In Shen *et al*. (1996, 1998) (described in detail in Section 2.1.1), multivariable analysis showed that exposure to fumes or pollution from cooking was significantly associated with risk for lung cancer (odds ratio, 2.45; 95% CI, 1.06–5.66; p=0.02). [The Working Group noted several limitations in this study. The report lacked details regarding the study design (e.g. response rate), characteristics of the study population (e.g. gender distribution, active smoking history) and covariates included in the statistical models.]

In two hospital-based case–control studies conducted in Kaohsiung, a heavily industrialized city in Taiwan (China) (Ko *et al*., 1997; Le *et al*., 2001) (in detail in Section

2.1.1), the use of a fume extractor in the kitchen was also significantly associated with a reduced risk for lung cancer.

Zhou *et al*. (2000) (described in detail in Section 2.1.1) showed that, compared with women who had a separate kitchen for cooking, the risk for lung cancer was not increased for cooking in the living room (crude odds ratio, 1.40; 95% CI, 0.41–4.88) or bedroom (crude odds ratio, 1.00, 95% CI, 0.11–8.93). However, in multivariable regression analysis, frequent eye irritation from smoke had an independent impact on risk. Compared with women who reported no eye irritation from smoke, those who reported slight, medium and heavy eye irritation had elevated risks; the respective adjusted odds ratios were 1.58, 11.45 and 3.41 (p for trend=0.002). [The Working Group noted that most of the lung cancer cases and controls included in the analysis by Zhou *et al*. (2000) were already in the report by Wang *et al*. (1996). Unadjusted odds ratios were reported. This study was small and the confidence intervals were very wide.]

In the case–control study of lung cancer by Le *et al*. (2001) (described in detail in Section 2.1.1), risk was significantly higher for those who cooked in a kitchen without a fume extractor: the odds ratio was 3.0 (95% CI, 1.3–7.1; 31 exposed cases) for squamous-/small-cell cancer and 3.9 (95% CI, 2.3–6.6; 74 exposed cases) for adenocarcinoma. Only 7% of men reported cooking for the family and thus these data were not reported.

2.4.2 *Cancer of the nasopharynx*

A hospital-based case–control study of NPC was conducted in Minan Prefecture, Fujian Province, China (Ye *et al*., 1995), on 135 cases of NPC that were pathologically diagnosed and treated at Second Hospital affiliated to Fujian Medical University in Quanzhou. Controls were patients of surgical and osteological departments of the same hospital without cancer or respiratory diseases, were matched on sex, age (within 5-year group) and date of hospitalization and had lived in Minan Prefecture for at least for 10 years with the same place of origin. Information on demographic factors, residence, family cancer history, dietary history, smoking, alcohol drinking, tea drinking, occupational history and chronic diseases of the ear, nose, pharynx and larynx was collected. In a multivariable conditional logistic regression analysis, smokiness during cooking was associated with an elevated risk for NPC with an odds ratio of 2.30 (P=0.012). The other significant factors associated with risk were intake of green melon (protective factor), index of passive smoking during adulthood, consumption of salted preserved vegetables and cooking (risk factors).

In a case–control study (Hubert *et al*., 1993; Zheng *et al*., 1994) (described in detail in Section 2.2.4), absence of windows, poor ventilation, cooking outside the house in a shack and the presence of a fireplace in the kitchen during childhood significantly increased the excess of risk for NPC associated with using wood as a fuel.

Two hospital-based case–control studies on NPC that used a similar study design and questionnaire were conducted in Guangzhou and Heilungjiang Province (Huang *et al*., 1997). A total of 104 cases of NPC who were pathologically diagnosed at each of two

hospitals (cancer hospitals affiliated to Sun Yat-Sen Medical University in Guangzhou and Harbin Medical University in Harbin) during the period from 1 October 1992 to 1 March 1994 and who had lived in Guangzhou or Heilungjiang for more than 80% of their life were involved in the study. The cases were recruited sequentially in accordance with the order of entrance to each hospital until 104 cases had been obtained. One control per case was matched on sex, age (±5 years) and some place of origin as the case and was selected from residents without cancer in the next residential community to the cases. Information on demographic factors, residence, occupation, dietary history, previous diseases and family cancer history was collected from cases and controls by use of a unified questionnaire. In multivariate analysis, cooking inside the house and use of a stove without a chimney were two significant variables associated with the risk for NPC. Taking the odds ratio for cooking inside the house for 35 or less than 35 years as 1.0, the odds ratio for more than 35 years was 1.96 (95% CI, 1.23–3.71). Taking the odds ratio for use of a stove without a chimney for 10 or less than 10 years as 1.0, the odds ratio for more than 10 years was 2.69 (95% CI, 1.54–4.68). In Harbin, in comparison with the use of coal or wood, the use of gas as fuel decreased the risk for NPC, with an odds ratio of 0.93 (95% CI, 0.90–0.97; p=0.027). [The Working Group noted the discrepancy between the relatively small number of subjects and the narrow confidence intervals.]

Sihui City, Guangdong Province, is one of the endemic areas of NPC in China with an incidence rate of about $20/10^5$. A case–control study on NPC was conducted that included 57 cases who were alive and pathologically diagnosed in Sihui City between January 1998 and June 1999 (Cao *et al*., 2000). The control group consisted of spouses and relatives of spouses of these 57 cases. In multivariate analysis, family cancer history, connection of the bedroom with the kitchen during childhood and tobacco smoking were significant risk factors for NPC. The odds ratio for separation of the bedroom from the kitchen was 0.48 (95% CI, 0.30–0.78).

2.4.3 *Cancer of the cervix*

A nested case–control study to investigate the association of exposure to cooking oil fumes with the risk for cervical neoplasm was carried out between October 1999 and December 2000 on 32 466 women aged over 19 years who underwent Pap smear screening in Chi-Yi City of Taiwan, China (Wu *et al*., 2004). Among 420 women newly diagnosed as having CIN lesions ≥CIN1, 349 were followed-up by biopsy. Among the 349 subjects with biopsy follow-up, 116 women had lesions ≥CIN2 confirmed by biopsy. These 116 women were eligible as cases for the study. The controls were randomly selected from women whose Pap smear results were negative in the first screening of the study period. The case–control ratio was 1:2 with matches for age (±2 years), residence and the time that the Pap smear was performed (within 6 months of the cases). The findings of previous Pap smears taken before this study were found to be normal in both cases and controls. The subjects were interviewed in their homes between October 2000 and March 2001. Information on demographical characteristics, education, smoking,

exposure to environmental tobacco smoke, exposure to X-ray examinations or hair dye, occupation (especially professional chef), sexual and reproductive history and times of prior cervical smears, as well as cooking and kitchen ventilation status, was collected. A multivariable logistic regression model was used to assess the association between case–control status and different cooking and ventilation conditions, after adjusting for age, education, smoking, age at first intercourse, number of prior Pap smears and profession as a chef. Of the 116 cases with ≥CIN2, 16 women who had no questionnaire information were excluded from the study. Among the 100 cases with a completed questionnaire, 39, 12, 46 and three cases had CIN2, CIN3, carcinoma *in situ* and invasive cancer, respectively. The results of the age at which one started cooking, years of cooking and hours spent on cooking were insignificant. Subjects who cooked in a kitchen without a fume extractor at 20–40 years of age had a 2.29-fold higher risk (95% CI, 1.08–4.87) for developing CIN than those who used a fume extractor, after adjusting for corresponding factors. The odds ratio was 3.16 (95% CI, 1.19–8.43) for women who cooked in kitchens without fume extractors at >40 years of age. The use of coal as cooking fuel had a higher risk for CIN than that of gas for the women in the group who cooked at 20–40 years of age (adjusted odds ratio, 2.09; 95% CI, 0.86–5.10) and at >40 years of age (adjusted odds ratio, 1.53; 95% CI, 0.17–14.19), but the difference in risk was insignificant. Among the women over 40 years of age, those who did not have kitchen fume extractors at home at both 20–40 years and >40 years of age had a 3.46-fold greater risk of developing CIN than those who did have fume extractors during the same two periods, after adjusting for corresponding factors. The odds ratio for having a fume extractor only during one period but not the other was 2.05 (95% CI, 0.86–4.86). It was also found that women who had been professional cooks had a 3.97-fold greater risk (95% CI, 1.02–15.41) than those who had not. [The Working Group noted that the results were not stratified by or adjusted for HPV.]

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3. Studies of Cancer in Experimental Animals

A series of animal and human studies of cancer were begun in China in the 1980s due to the generally high concentrations of air pollution from burning coal for fuel. Coal was widely used in China; in fact, in Xuan Wei County, Yunnan Province, mortality from lung cancer is among the highest in China and could not be accounted for by tobacco or occupational exposures. The emissions from smoky coal that were collected indoors in homes where it was used for cooking and heating without chimney ventilation contained a large proportion of submicron particles with a high concentration of PAHs. These studies evaluated the carcinogenicity of emissions from several types of coal (e.g. smoky coal and smokeless coal), wood smoke and, in several studies, particles from different cities in China were compared (e.g. Xuan Wei, Beijing and Tai Yuan) (Mumford *et al.*, 1987).

3.1 Coal smoke and soots from household combustion of coal

3.1.1 *Whole-body and inhalation exposure*

(a) Mouse

Two studies of whole-body exposure to coal soot that were reported in the 1930s were reviewed by a previous IARC Working Group that was convened to evaluate soots (IARC, 1985). These included an early study that used soot from a coal furnace as bedding in the cages that housed 3-month-old Buffalo strain mice. The exposure was maintained by shaking the cages two to three times per day. Eight lung adenocarcinomas were reported in the 100 exposed mice and one in controls (Seeling & Benignus, 1936). [At that time, the Working Group noted the unusually high mortality in controls and lack of reporting on skin tumours.] The second study used an inhalation chamber to expose mice, 3 months of age [strain unknown] for 1 year to a 'moderate' cloud of soot, once an hour, for 6 h on 5 days per week. No increase in the incidence of lung tumours was found at the end of 2 years and no skin tumours were found (Campbell, 1939). [At that time, the Working Group noted the short duration of treatment.]

Groups of 113–160 male and 50–58 female randomly bred Kunming mice, weighing ~21 g, [age unspecified] were exposed to indoor air pollution or control air for 15 months. The two exposure rooms had a round shallow pit dug in the centre and bituminous coal was incompletely burned to simulate the normal indoor air conditions under which human exposures occur in Xuan Wei County, China. The control room air moved freely between indoors and outdoors and no coal was burned where the control mice were housed. Pollutants were monitored several times a day and included TSP (0.91 mg/m^3 for the controls and 14.38 mg/m^3 for coal smoke), sulfuric acid fume and carbon monoxide. The

concentrations of benzo[*a*]pyrene were: control group, 1.47 μg/10 m^3; and coal smoke, 506.44 μg/10 m^3. The total incidence of lung cancer was 17% of 171 mice in the control group (adenocarcinomas only) and 89.5% of 210 mice in the coal smoke-exposed group. The coal smoke-treated group also had the highest incidence of all three types of lung cancer identified including squamous-cell carcinomas (11.4%), adenosquamous carcinomas (21.4%) and adenocarcinomas (56.6%). The total incidence of pulmonary tumours (including adenomas) in the coal smoke-exposed group was 196/210 (93.3%) (Liang *et al.*, 1988).

Groups of 30 male and 30 female Kunming mice, 40 days of age and weighing 13±1 g, were exposed by inhalation for 2 years to coal smoke from burning 60, 105 and 160 g coal per day to simulate the normal indoor air conditions under which human exposures occur in Harbin City, Hei Long Jang Province, China. Controls had no exposure to smoke [no exposure metric was used to provide exposure concentration]. The incidence of lung tumours (all adenocarcinomas) was 3.6% in the control group, 9.4% at the lowest (60 g) dose, 12.8% at the mid (105 g) dose and 24.3% at the high (160 g) dose. The cancer incidence in the two highest doses was significantly higher than that in the control group ($p<0.05$) (Lin *et al.*, 1995).

(b) Rat

Groups of 55–62 male and 51–63 female randomly bred Wistar rats, weighing ~105 g, [age unspecified] were exposed to indoor air pollution or control air for 19 months. The two exposure rooms had a round shallow pit dug in the centre and bituminous coal and wood were incompletely burned to simulate the normal indoor air conditions under which human exposures occur in Xuan Wei County, China. The control room air moved freely between indoors and outdoors and no coal was burned where the control rats were housed. Pollutants were monitored several times a day and included TSP (0.91 mg/m^3 for the controls and 14.38 mg/m^3 for coal smoke), sulfuric acid fume and carbon monoxide. The concentrations of benzo[*a*]pyrene were: controls, 1.47 μg/10 m^3; and coal smoke-exposed, 506.44 μg/10 m^3. The total incidence of lung cancer was 0.9% of 110 rats in the control group and 67.2% of 125 rats in the coal smoke-exposed group. All cancers in the coal smoke-exposed group were squamous-cell carcinomas. No squamous-cell carcinomas were observed in control animals. The only adenocarcinoma occurred in the control group and none was observed in the coal smoke-exposed rats. The total incidence of pulmonary tumours (including adenomas) was 84/125 (67%) in the coal smoke-exposed group and 1/110 (0.9%) in the control group (Liang *et al.*, 1988).

3.1.2 *Intratracheal administration*

(a) Mouse

Coal-fume extracts were generated from collections of coal smoke from an area of high cancer incidence in Xuan Wei County, China. Soot was extracted with an aqueous solution of Tween-80 and 0.1 mL vehicle solution. Vehicle solution containing

12.5 mg/mL soot was instilled intratracheally into 43 and 72 male Kunming mice, respectively, once every 10 days for an average period of 100 days; the animals were then held until 18 months, at which time they were killed. Overall lung tumour incidence (adenomas and adenocarcinomas combined) was 25.6 and 52.8% in the vehicle and soot instilled mice, respectively. The incidence of lung adenocarcinomas was 16.3 and 40.3% ($p<0.01$) in the vehicle and treated groups, respectively (Yi *et al.*, 1984).

(b) Rat

One intratracheal instillation study in rats (Võsamäe, 1979) was reviewed by an IARC Working Group that was convened to evaluate coal soot (IARC, 1985). [The Working Group noted that the experimental details were unclear and felt that the study did not contribute to the evaluation of coal soot in experimental animals.]

3.1.3 *Dermal application*

(a) Mouse

Carcinogenicity studies of coal-derived soot extracts and fractions, and also of shale oil-derived soot, woodsoot, fuel-oil soot extracts, applied to mouse skin were reported between 1922 and 1979 and were reviewed by an IARC Working Group that was convened to evaluate soots (IARC, 1985). The studies on dermal application that were reviewed included studies of mice treated with various types of coal-derived soot extracts and fractions. The sources of these soots included bituminous coal-derived household soot, domestic chimney coal-derived soot, oil-derived soots and solid shale oil-derived soot. It was concluded that coal-soot extracts applied to the skin of mice produced skin tumours in three studies (Passey, 1922; Passey & Carter-Braine, 1925; Campbell, 1939). Studies of shale oil-derived soot applied to mouse skin also produced skin tumours in mice (Bogovski, 1961; Võsamäe, 1963, 1979). The wood-derived and fuel oil-derived soot extracts were inadequately tested by skin application (Sulman & Sulman, 1946; Mittler & Nicholson, 1957).

Indoor coal smoke particles (<10 μm) were collected from Xuan Wei County, China, for a study of tumour initiation–promotion. Groups of 40 female Kunming mice [age unspecified] received skin applications of 1, 5, 10 or 20 mg acetone extracts of each smoke type. Control groups included a group that received 50 mg benzo[*a*]pyrene in 0.2 mL and groups treated with the tumour promoter 12-*O*-tetradecanoylphorbol-13-acetate (TPA) or acetone. One week after initiation, the animals in the treatment group and TPA group received twice-weekly skin applications of 2 μg TPA (dissolved in 0.2 mL acetone) for 26 weeks and were then held for an additional 6 weeks of observation. A dose–response in skin tumour incidence was observed in the coal smoke-treated group at weeks 20, 26 and 32, respectively. At week 26, the skin tumour incidence was 25–60% in the coal smoke-treated groups, 50% in the benzo[*a*]pyrene-treated group, 10% in the TPA-treated group and 0% in the acetone control group. The tumour incidence in the coal smoke-treated groups and benzo[*a*]pyrene-treated group were

significantly higher than those in TPA-treated group and control group ($p<0.01$). The first tumour was observed during weeks 9–12 in coal smoke-treated groups and at week 11 in the benzo[*a*]pyrene-treated group. The higher dose of the coal smoke extract resulted in a shorter time to the incidence of the first tumour. The largest number of tumours (11 skin tumours/mouse) was observed in the group treated with 10 mg coal-smoke extract (Liang & Wang, 1987).

Indoor air particles (<10 μm) were collected during cooking periods in Xuan Wei homes without chimneys and in different communes that had access to one of the following fuels: smoky coal, smokeless coal and wood (pine). The smoky coal was low-sulfur (0.9%) coal with high heating value (27.1 MJ/kg) and 20% ash content (comparable with US medium-volatile bituminous coal). The smokeless coal was a low-grade coal with 14.5 MJ/kg heating value, 1.9% sulfur and 49% ash. The PAH content per milligram of organic matter was high for both the smoky coal and smokeless coal compared with the wood; however, the concentrations of PAH per microgram per cubic metre were at least 10-fold higher in the homes that used smoky coal compared with those that used smokeless coal and wood. Groups of 40 female SENCAR mice, 7–9 weeks of age, received dermal applications of 0, 1, 2, 5, 10 or 20 mg dichloromethane extracts of coal particles, benzo[*a*]pyrene (positive control) or solvent alone (control). One week after tumour initiation with the particle extracts, 2 μg TPA in 0.2 mL acetone were applied twice weekly to each mouse for 26 weeks and, beginning at 6 weeks, animals were scored for skin papillomas weekly until the study was terminated. The survival rate was over 95% and all three samples showed a dose-related response in both incidence and multiplicity of the papillomas. The tumour-initiating activity of the extracts at 1 mg was 2.7 papillomas/mouse for the smoky-coal extracts and 1.3 papillomas/mouse for the smokeless-coal extracts (Mumford *et al.*, 1990).

In the same study, groups of 40 female SENCAR mice, 7–9 weeks of age, received dermal applications of 1 mg/mouse dichloromethane extracts of smoky coal from Xuan Wei County twice a week for 52 weeks and were then held for an additional 25 weeks. Smokeless coal was not tested. The negative and positive control groups were treated with acetone (0.2 mL/mouse) and benzo[*a*]pyrene (50 μg/mouse) twice a week, respectively. A high percentage (88%) of the mice treated with smoky-coal extract developed carcinomas (1.1 carcinoma/tumour-bearing mouse on average) at the end of the study at 77 weeks. No carcinomas were observed in the acetone-treated controls (Mumford *et al.*, 1990).

3.1.4 *Subcutaneous injection*

(a) Mouse

A group of 30 hybrid F1 (C57Bl×CBA) male mice, 1.5–2 months of age, received five subcutaneous injections of 3.5 mL olive oil containing coal extracts collected from individual houses that were heated by brown coal [type of coal and burning conditions not specified] over an 8-week period (total amount of benzo[*a*]pyrene, 0.2 mg/animal).

Vehicle (olive oil) and positive (0.2 mg benzo[*a*]pyrene) control groups were included in the experiment. The experiment was terminated after 55 weeks. Tumours appeared in benzo[*a*]pyrene-treated mice at 15 weeks with almost 80% mortality by week 39. In the coal soot-treated animals, five (17%) mice developed subcutaneous tumours [tumour type not specified] at approximately the same time. No tumours or mortality occurred in control mice (Khesina *et al.*, 1977).

Groups of 38–57 male Kunming mice [age unspecified], weighing 18–26 g, received weekly 0.1-mL subcutaneous injections of 0, 500 or 1000 mg cyclohexane extracts of coal soot collected from Xuan Wei County or 2 mg benzo[*a*]pyrene dissolved in Tween 80 and saline solution into the back of the neck week for 10 weeks. The experiment was terminated after 10 months. The total incidence of lung cancer (squamous-cell carcinoma, adenosquamous carcinoma and adenocarcinoma) was: 1/38 (2.6%) control, 44/57 (77.2%) low-dose, 36/56 (64.3%) high-dose and 6/38 (15.8%) benzo[*a*]pyrene-treated animals. The total incidence of lung cancer in the soot extract-treated groups was significantly higher than that in control or benzo[*a*]pyrene-treated groups. The incidence of squamous-cell carcinoma was 8/57 (14.0%) and 12/56 (21.4%) in low- and high-dose animals, respectively. The incidence of adenosquamous carcinoma was 10/57 (17.5%) and 6/56 (10.7%) in low- and high-dose animals, respectively. Lung squamous-cell carcinoma and adenosquamous carcinoma were not observed in the control or benzo[*a*]pyrene-treated group. The incidence of adenocarcinoma was 26/57 (45.6%) low-dose animals, 18/56 (32.1%) high-dose animals, 6/38 (15.8%) benzo[*a*]pyrene-treated animals and 1/38 (2.6%) controls, and that of fibrosarcoma was 1/57 (1.7%) and 4/38 (10.5%) in low-dose and benzo[*a*]pyrene-treated animals, respectively. In addition, the incidence of adenoma was 5/38 (13.2%) control, 2/57 (3.5%) low-dose, 5/56 (8.9%) high-dose and 3/38 (7.9%) benzo[*a*]pyrene-treated animals. At the injection site, the incidence of tumours *in situ* was 5/57 (8.8%) dermal squamous-cell carcinomas, 1/57 (1.8%) fibrosarcoma and 2/57 (3.5%) adenomas in the low-dose group; and 2/56 (3.6%) dermal squamous-cell carcinomas, 1/56 (1.8%) fibrosarcoma and 0/57 adenomas in the high-dose group. No dermal squamous-cell carcinoma was found in the benzo[*a*]pyrene-treated group, while the incidence of fibrosarcoma was 32/38 (84.2%). No tumour was found in other tissues except for a few thymus tumours (Liang *et al.*, 1983).

Groups of about 60 male Kunming mice (weighing 18–22 g) [age unspecified] received weekly 0.1-mL subcutaneous injections of extracts of coal soot collected from Xuan Wei County dissolved in Tween 80 and saline solution in the back of the neck for 10 weeks (total doses, 119 mg (0.15 μg benzo[*a*]pyrene) and 400 mg (0.52 μg benzo[*a*]pyrene)). Sixty control animals were injected with Tween 80/saline only. The experiment was terminated at 311 days. The total incidence of lung cancer was 52/58 (89.5%) [$p<0.001$] and 39/59 (66.1%) [$p<0.001$] in low- and high-dose animals, respectively. The incidence of squamous-cell carcinoma was: 1/58 (1.7%) and 8/59 (13.6%) in low- and high-dose animals, respectively; that of adenosquamous carcinoma was: 3/58 (5.2%) and 7/59 (11.9%) in low- and high-dose animals, respectively; and that of adenocarcinomas was: 48/58 (82.8%) and 24/59 (40.7%) in low- and high-dose

animals, respectively. One fibrosarcoma of the lung was also found in a low-dose animal. Control animals developed 6/60 (10%) lung cancers which were all adenocarcinomas. Some adenomas were also found in all groups (Liang *et al.*, 1984).

3.1.5 *Veterinary epidemiology*

(a) Dog

A case–control study of the influence of environmental exposures on sinonasal cancers was conducted in pet dogs. All cases of canine intranasal or sinus cancer (diagnosed between 1989 and 1993) in the histopathology database at the University of Pennsylvania School of Veterinary Medicine were included. The controls (unmatched) included other non-respiratory related cancers (e.g. stomach, bowel and liver) from the same database and diagnosed during the same 5-year period. The study included 129 dogs with sinonasal cancers and 176 controls. Indoor use of coal was a strong risk factor with a significant adjusted odds ratio of 4.24 (95% CI, 1.30–16.52). Exposure to environmental tobacco smoke was not significant (odds ratio, 0.70, 95% CI, 0.41–1.19) (Bukowski *et al.*, 1998).

3.2 Wood smoke

3.2.1 *Whole-body and inhalation exposure*

(a) Mouse

Groups of 58 male and 59 female Kunming and 60 male Beijing mice (Kunming strain), weighing ~21 g, [age unspecified] were exposed for 12 h per day for 15 months to incompletely combusted wood smoke [burn rates not specified] generated from a fire pit located in the centre of a room [size unspecified] to mimic that of peasants in the Xuan Wei County of southwestern China. Similar numbers and strains of mice were exposed to ambient air in a similar open-air room. As measured by PM, exposures to wood smoke averaged 14.99 mg/m^3 over the course of the study (control, 0.91 mg/m^3). The concentrations of benzo[*a*]pyrene were: control, 1.47 μg/10 m^3; and wood smoke-treated, 43.1 μg/10 m^3. At the end of the exposure period, lung tumour incidence was calculated and tumours were classified. The overall incidence of lung tumours in mice (combined sexes and strains) was 45.8% (81/177) in exposed groups and 17.0% (29/171) in the control groups. Female Kunming mice had the highest tumour incidence in both the exposed and control groups (49.3% and 26.9%, respectively), followed by male Kunming mice (37.9% of exposed and 13.2% of controls) and male Beijing mice (30% of exposed and 10% of controls). Tumours were generally classified as adenocarcinoma. The induction time of tumours in all mice was similar to that of controls (Liang *et al.*, 1988).

Groups of 20 male and 20 female Strain A/J mice, ~6 weeks of age, were exposed by whole-body inhalation to clean air (control) or to 30, 100, 300 and 1000 μg/m^3 whole hardwood-smoke emissions (as measured by PM) for 6 h per day on 7 days per week for

6 months. The hardwood smoke was generated from an uncertified wood stove (Pineridge Model 27000) that burnt wood of mixed oak species (from Missouri, USA). The fire was started (i.e. initiation of animal exposures) with unprinted/unbleached newspaper (newspaper end-rolls) and split hardwood kindling (the same wood type was used for the entire test). Daily exposures included three burn phases: kindling (~15–20 min with newspaper and kindling wood), a high burn rate (~90 min with ~4–6 kg wood) and a low burn rate (remainder of exposure period with an additional ~4–6 kg wood) that were controlled by the air intake damper. The sliding damper position ranged from open (maximum air intake) during the kindling and high-burn phases to an aperture of approximately 0.3×6.5 cm during the low-burn cycle. Transition through each phase of the burn cycle was indicated by ~75% of the fuel mass being burned. The atmosphere was extensively characterized for over 1000 individual physical and chemical species (McDonald *et al.*, 2006). Mice were held for 6 months after exposures, at which time they were killed and tumours were classified and enumerated under gross examination. No exposure-related mortality was observed. No significant difference in lung tumorigenesis measured as either the percentage of mice with tumours or the number of tumours per tumour-bearing mouse was observed between exposed groups and controls, and no evidence of a progressive exposure-related trend was observed. The percentage of mice (both sexes combined) that had tumours ranged from 47 to 58%; the mean number of tumours per mouse ranged from 0.67 to 0.75; and the mean number of tumours per tumour-bearing mouse ranged from 1.24 to 1.43 among all exposure groups and controls. Representative lung tumours from both control and exposed mice were characterized histologically as bronchioalveolar adenomas (Reed *et al.*, 2006).

(b) Rat

Groups of 55 male and 55 female Wistar rats (weighing ~105 g) [age unspecified] were exposed for 12 h per day for 19 months to incompletely combusted wood smoke [burn rates not specified] generated from a fire pit located in the centre of a room [size unspecified] to mimic that of peasants in the Xuan Wei County of southwestern China. Similar numbers of rats were exposed to ambient air in a similar open-air room. As measured by PM, exposures to wood smoke averaged 14.99 mg/m^3 over the course of the study (controls, 0.91 mg/m^3). The concentrations of benzo[*a*]pyrene were: control, 1.47 μg/10 m^3; and wood smoke-treated, 43.1 μg/10 m^3. At the end of the exposure period, lung tumours were enumerated (incidence) and classified. Only one (0.9%) pulmonary cancer was reported in control rats and none in rats exposed to wood smoke (Liang *et al.*, 1988).

3.2.2 *Subcutaneous injection*

(a) Mouse

A group of 30 hybrid F1 (C57Bl×CBA) male mice, 1.5–2 months of age, received five subcutaneous injections of 2.5 mL olive oil containing soot extracts collected from a

wood-fired wood-working atelier [type of wood and burn conditions not specified] over an 8-week period (total amount of benzo[*a*]pyrene, 0.2 mg/animal). Vehicle (olive oil) and positive (0.2 mg benzo[*a*]pyrene) control groups were included in the experiment. The experiment was terminated after 55 weeks. Tumours appeared in benzo[*a*]pyrene-treated mice at 15 weeks with almost 80% mortality by week 39. In the wood-soot treated animals, five (17%) mice developed subcutaneous tumours [tumour type not specified] approximately at the same time. No tumours or mortality occurred in 30 control mice (Khesina *et al.*, 1977).

Two groups of about 60 Kunming male mice (weighing 18–22 g) [age unspecified] received weekly 0.1-mL subcutaneous injections of extracts of wood smoke collected from Xuan Wei County dissolved in Tween 80 and saline solution in the back of the neck for 10 weeks (total dose, 148 mg (0.074 μg benzo[*a*]pyrene) and 296 mg (0.15 μg benzo[*a*]pyrene)). Sixty control animals were injected with Tween 80/saline only. The experiment was terminated at 311 days. The total incidence of lung cancer was 6/60 (10%) controls, 31/60 (51.7%) [$p<0.001$] low-dose animals and 36/58 (62.1%) [$p<0.001$] high-dose animals. All lung cancers were adenocarcinomas. Some adenomas were also found in all groups (Liang *et al.*, 1984).

3.2.3 *Subcutaneous implantation*

(a) Rat

Groups of 18 female and 18 male rats, weighing 120 and ~150 g respectively, [strain and age unspecified] received subcutaneous implants of fragments (5–20 mg) of wood (eucalyptus) soot, from the smoking chamber of a sausage factory, near the right axilla and in the scrotal sac, respectively. No tumour was found in male rats after 2.5 years of observation. Three female rats developed sarcomas at the site of implantation with latent periods of 12, 17 and 24 months, respectively. No tumour was observed in 18 male and 18 female untreated controls observed during the same interval (Sulman & Sulman 1946). [The Working Group noted that survival data were not provided.]

3.2.4 *Dermal application*

(a) Mouse

A group of 10 adult female mice [strain and age unspecified] received daily dermal applications on the neck skin of an ethanol extract of wood (eucalyptus) soot from the smoking chamber of a sausage factory for 2 years. No skin tumour was observed. Two mice developed para-urinary bladder sarcomas after 5 and 12 months, respectively, and one mouse developed a bladder carcinoma 21 months after the beginning of the experiment. No tumour was reported in 20 control mice after 2 years of observation (Sulman & Sulman, 1946). [The Working Group noted the small group size and the inadequate reporting of the treatment of the control group.]

In a tumour initiation–promotion study, eight groups of 40 female Kunming mice (average weight, 28.7 g) [age unspecified] received a dermal application of 1, 5, 10 or 20 mg/kg extracts of inhalable particles (<10 μm) of indoor wood smoke collected from Xuan Wei County. The study also included a positive-control group that received an application of 50 mg/kg benzo[*a*]pyrene, and control groups that received applications of TPA or the solvent acetone. One week after initiation, the animals in the extract-treated group and TPA-treated group received twice weekly applications of 2 μg TPA dissolved in 0.2 mL acetone for 26 weeks and were then held for an additional 6 weeks of observation. A clear dose–response in skin tumour incidence was observed in the wood smoke-treated group at weeks 20, 26 and 32, respectively. At week 26, the tumour incidence was 12.5–41% for wood smoke-treated groups, 50% for the benzo[*a*]pyrene-treated group, 10% for the TPA-treated group and 0% for acetone control group. The skin tumour incidence in the wood smoke-treated and benzo[*a*]pyrene-treated groups was significantly higher than that in TPA-treated and control groups ($p<0.01$). The first tumour was observed at weeks 10–13 in the wood smoke-treated group and at week 11 in the benzo[*a*]pyrene-treated group. Moreover, the time to first tumour incidence was decreased with increasing dose of the smoke extract. The results indicated that wood smoke was carcinogenic through tumour initiation (Liang & Wang, 1987).

In a tumour initiation study, groups of 40 female SENCAR mice, 7–9 weeks of age, received two dermal applications of 1, 2, 5, 10 and 20 mg/kg body weight (bw) wood-smoke extract in 0.2 mL acetone over a 1–5-day period. PM (<10 μm) from the combustion of pine was collected from homes during cooking periods in the Rhu Shui commune, Xuan Wei County, by high-volume sampling onto glassfibre filters. Dichloromethane extracts obtained form Soxhelet extraction of filter samples were evaporated under nitrogen and transferred to acetone. One week after initiation, mice received twice-weekly applications of 2 μg TPA for 26 weeks. In a complete carcinogenesis study, groups of 40 female SENCAR mice, 7–9 weeks of age, received twice weekly skin applications of 1 mg/kg bw extract for 52 weeks and were held for an additional 25 weeks. All mice were observed daily and skin papillomas were scored on a weekly basis. Dose-related responses to initiation by wood-smoke extract were observed and tumour incidence levelled at 23 weeks of treatment. Incidence was ~40, 45, 70, 80 and 90% for each respective dose level versus ~10% in control animals. Tumour multiplicity ranged from 0.4 to 1.0 tumours per mouse with doses of 1, 2 and 5 mg/kg to 2.0 and 2.8 tumours per mouse with doses of 10 and 20 mg/kg, respectively. Approximately 0.2 tumours per mouse were observed in control animals. In the complete carcinogenesis study, only two mice (5%) treated with the wood-smoke sample developed carcinomas versus no animals [not significant] in an acetone-control group and 100% of mice treated with benzo[*a*]pyrene as a positive control (Mumford *et al.*, 1990).

A series of tumour initiation–promotion studies in female SENCAR mice using the same protocol described by Mumford *et al.* (1990) was summarized in Lewtas (1993). One study was reported on the tumour-initiating potency of extracts of particle emissions of a mixture of softwoods (e.g. pine) and a mixture of hardwoods (e.g. oak) burned in a

wood stove, using the same doses (1, 2, 5, 10 and 20 mg) of extracts (dichloromethane extracts administered in 0.2 mL acetone after removal of dichloromethane). The extracts of wood-stove particle emissions from softwoods were more tumorigenic (0.046 papillomas/mouse/mg; 40 mice) than the hardwood mixtures (0.0087 papillomas/mouse/mg; 40 mice). In another study, two ambient air samples of particle extracts were collected in Boise, Idaho (USA), and apportioned into wood-smoke and mobile source contributions to the organic mass (Lewtas, 1993; Cupitt *et al.*, 1994). One of these composite ambient air samples with 78% wood smoke (and 11% mobile sources and 11% residual unidentified mass) was positive in the tumour initiation–promotion protocol in female SENCAR mice using the same doses (1, 2, 5, 10 and 20 mg) applied dermally. The tumour-initiation potency was 0.095 papillomas/mouse/mg (40 mice) (Lewtas, 1993; Cupitt *et al.*, 1994).

3.2.5 *Veterinary epidemiology*

Dog

A case–control study investigated the utility of using canine sinonasal cancers as an indicator of risk for human cancer from residential exposures. Primary cases of sinonasal cancers that occurred between 1989 and 1993 were obtained from the histopathology database at the University of Pennsylvania and were included and compared with a set of unmatched controls. Data on exposures, confounders and behaviour were obtained by questionnaire and telephone from veterinarians and owners. A total of 129 cases were compared with 176 controls. Overall exposure to wood fires within a residence was weakly associated with the risk for cancer (odds ratio, 1.58 [95% CI, 0.81–3.09]) even with more than 220 cumulative occurrences of exposure to wood fire (Bukowski *et al.*, 1998).

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4. Mechanistic and Other Relevant Data

4.1 Toxicokinetics

4.1.1 *General considerations*

The toxicokinetics of inhaled compounds is defined by exposure, absorption of the material and its local metabolites, the tissue–plasma concentration–time curve, distribution within the body, and overall metabolism and excretion. Under controlled conditions of animal studies and human clinical trials, total exposures and estimated doses of individual compounds or simple mixtures of aerosols, gases and PM can readily be defined.

However, methods for defining the toxicokinetic and toxicodynamic properties of mixtures at this time are ill equipped to deal with exposures to atmospheres that contain thousands of individual components at varying concentrations. In general, attempts have been made to model and define empirically the disposition of only very simple mixtures. For example, the most complex of toxicokinetic data and models generated have been with refined gasoline and seven to eight primary chemical components (Dennison *et al.*, 2003, 2004). The caveat to these studies is that, unlike the variety of chemical components that are contained within combustion-derived materials, many liquid- and vapour-phase gasoline components have similar structure and generally similar pathways of absorption, metabolism, distribution and excretion.

The definition of the toxicokinetics of anthropogenic indoor air pollutants such as those from wood smoke and coal combustion emissions are complicated by two main factors: (*a*) the diversity and concentration of components and (*b*) the phase distribution of components.

(a) Diversity and concentration of components

Combustion emissions are composed of hundreds to thousands of individual components that can overlap in many cases yet be discrete in others, depending on the material burned (coal versus wood versus dung), its subtype (species of wood, type of coal), its application (open fire, stove, pit, cooking, heating) and the burn rate (hot fire/smoldering fire). The sheer number of components, many in very small quantities, makes an empirical definition of the toxicokinetics of individual compounds or classes of compounds extremely challenging. In addition, up to 85% of the PM within some complex mixtures remains ill-defined which makes assessments of these species impossible (McDonald *et al.*, 2006).

PAHs in hardwood-smoke emissions may be used to highlight this issue. Combined PAHs (58 individual compounds) from the vapour-phase semivolatile organic compounds of diluted whole hardwood smoke generated from a wood stove operated over a three-phase burn cycle and delivered to an animal exposure chamber system totalled ~11 μg/m^3

on average. In the same atmosphere, particle-phase PAH mass totalled only 465 ng/m^3 (of ~1000 μg/m^3 total PM mass). This value was minuscule compared with the 85% of the PM mass that remained unidentified in these experiments. Overall, total PAHs equaled only ~0.06% of the total mass of material within the exposure atmosphere (total mass, ~20.4 mg/m^3) (McDonald *et al.*, 2006; Reed *et al.*, 2006). The impact of these hundreds of other organic, inorganic and elemental species probably plays a profound role in the toxicokinetics of PAHs (see also Section 4.1.2).

(b) Phase distribution of components

Combustion emissions are composed of gaseous, semivolatile and particulate physical phases. Each phase has independent physical and chemical characteristics that determine the relative dose of the chemical components contained therein to the lung. As described in Section 4.1.2, aerodynamic physical traits determine the deposition of PM, but the chemical make-up and physical state (liquid or carbonaceous) may determine the dose distribution and toxicokinetics subsequent to deposition. At the opposite end of the spectrum, simple diffusion generally dictates gaseous transport and effective dose of gas-phase components. Gas-phase furans for example, present in relatively small quantities in wood smoke and other combustion emissions (McDonald *et al.*, 2006), have been evaluated as 'reasonably anticipated to be human carcinogens' (National Toxicology Program, 1999) or *possibly carcinogenic to humans* (IARC, 1995).

Semivolatile organic compounds that undergo a phase transition among the gaseous and PM phases of combustion mixtures complicate the situation. A definition of dose (gas/diffusion/particle/deposition) and ultimately the toxicokinetics of such compounds remains challenging. PAHs were present in the PM and gas phases within the example of a hardwood-smoke atmosphere noted above. The PM contribution of PAHs was minor (0.05%) compared with the remainder of the PAH mass contained in the gaseous phase (McDonald *et al.*, 2006). In this case, the overall dose and toxicokinetics of PAHs were probably influenced heavily by the gaseous components and the inherent diffusive processes that determine the overall final disposition and kinetics.

The physical solid/liquid state of PM may also play a role in this process. In the hardwood smoke generated above, the PM phase was mostly liquid in origin, while in other atmospheres such as diesel emissions, coal emissions and wood smoke generated under higher burn conditions, PM may be more carbonaceous/elemental in nature (e.g. coal ash) (Liang *et al.*, 1988; McCrillis & Burnet, 1990; Tesfaigzi *et al.*, 2002; Reed *et al.*, 2004). In the latter case, particle clearance and the leach rate of associated chemicals would play a more important role in the toxicokinetics of specific chemical species. With particles that form in the liquid state, dissolution of chemicals within the liquid droplet into airway lining fluid and the hydrophobicity or hydrophilicity of the individual chemical or chemical class determine the toxicokinetics.

(c) Other parameters of toxicokinetics

The concentration of combustion-derived chemical components deposited in the lung combined with time and clearance parameters define overall exposure (area under the curve [AUC]). As mentioned above, the daily exposure to individual chemicals or classes of compounds of interest can be minimal. Chemical methods developed for tissue analyses are generally specific to an individual chemical or class, are not trivial to develop and validate and in many cases lack the sensitivity required to measure trace amounts of compounds within the biological milieu. When one combines the limitations of assay methodology with the limited quantities of many components deposited within the lung, a definition of the collective or individual AUC of the multiple components with combustion-derived material remains a challenge.

Transport and excretion of lung-deposited components of mixtures to and from other compartments, organs or cell types may be of less relative importance for lung cancer than some other pollutant-associated disease types (e.g. cardiovascular disease). Because the lung is the affected organ, it is unlikely (although unproven) that transport, metabolic activation or sequestration at distant sites around the body lead to a sustained or transient re-exposure of lung tissue to chemical species associated with the mixture. It is unclear how processes such as these might lead to initiation or promotion events that are relevant to lung carcinogenesis. Assuming this is the case, any processes associated with exposure to the mixture and subsequent carcinogenic events would be expected to take place in the local environment of the lung.

The lung is fully capable of metabolizing multiple chemical species. It is difficult to imagine how the plethora of chemical compounds within combustion mixtures might affect the metabolic processes. However, it is important to note that elimination of metabolites of gas-phase or PM-phase components from the lung is probably processed through pathways similar to those described for the parent compounds.

4.1.2 *PAHs and inhalable particles*

As indicated above, combustion products associated with most chemical mixtures, including those evaluated in this monograph, typically comprise many chemical classes, such as PAHs and aromatic amines. Although the Working Group recognized that toxicokinetic information is available for many of these chemical classes, the evidence for the role of PAHs in some of the combustion emissions evaluated in this monograph has been well documented. In addition, the particulate fraction in these emissions also contributes to the development of adverse respiratory effects. Therefore, the toxicokinetics of PAHs and of inhalable particles are discussed below.

A detailed overview of the toxicokinetics of selected PAHs is available in a previous volume of *IARC Monographs* (IARC, 2010a); some of this information is summarized here. Although some data on this topic have been determined in humans, including analyses of urinary PAH metabolites and PAH–DNA adducts in lymphocytes, most of the

available data on the toxicokinetics of PAHs derive from studies of PAHs in experimental animals, much of which involve studies of a single PAH, benzo[*a*]pyrene.

The biological properties of PAHs, as they pertain to combustion sources, are influenced by four main factors: phase distribution (vapour pressure, adsorption onto surfaces of solid carrier particles), absorption into liquid carriers, lipid/aqueous partition coefficient in tissues, and limits of solubility in the lipid and aqueous phases of tissues.

(a) Absorption through the respiratory tract, gastrointestinal tract and skin

The phase distribution of PAHs is dependent on their vapour pressure, which decreases with increasing molecular weight: two-ringed compounds are largely in the gas phase, whereas five-ringed compounds are mostly in the solid phase (generally adsorbed on airborne particles at room temperature) (IARC, 2010a).

Exposure comes from virtually all media: air, soil, water and food. PAHs are generally transported by diffusion across lipid/lipoprotein membranes, which facilitates their absorption by the respiratory tract, gastrointestinal tract and skin. PAHs that have two or three rings are absorbed more rapidly and extensively than those that have five or six rings (IARC, 2010a).

The rate and extent of absorption by the respiratory tract of PAHs from particles that contain them are generally dependent on particle size, i.e. aerodynamic diameter, which influences regional deposition in the respiratory tract and the rate of release of PAHs from the particle. Highly lipophilic PAHs that are released from particles deposited in the conducting and bronchial airways are largely retained for several hours and absorbed slowly by a diffusion-limited process. In contrast, PAHs that are released from particles in alveolar airways are generally absorbed within minutes (Gerde & Scott, 2001; IARC, 2010a). The metabolism of PAHs in the epithelium probably accelerates transport of lipophilic PAHs into the circulation. However, the low mobility of the highly lipophilic PAHs in tissues complicates the toxicokinetics of PAHs. Thus, the delayed equilibration between blood and tissue needs to be taken into account. The relatively longer retention of PAHs released in the conducting airways (compared with the air-exchange region) may allow substantial metabolism within this region of deposition (IARC, 2010a).

PAHs can be absorbed by the gastrointestinal tract via diffusion across cellular membranes based on the lipophilicity of the PAH and via the normal absorption of dietary lipids (O'Neill *et al.*, 1991). Results from animal studies indicate that absorption is rapid, that fractional absorption of lower-molecular-weight PAHs may be more complete than that of higher-molecular-weight PAHs and that the presence of other materials, such as bile salts or components of the diet, can influence the rate or extent of absorption of PAHs from the intestine (IARC, 2010a).

Dermal absorption of PAHs in humans has been confirmed by the detection of elevated levels of PAH metabolites in the urine after exposure to complex PAH mixtures. Studies in animals indicate that dermal absorption of PAHs can be rapid and extensive (IARC, 2010a).

(b) Distribution

In rats, adsorbed PAHs are distributed widely to most organs and tissues. PAHs tend to accumulate in fatty tissues, which can serve as storage sites from which they may be released. The gastrointestinal tract can contain high levels of PAHs and their metabolites after exposure by any route due to mucociliary clearance from the respiratory tract and hepatobiliary excretion of metabolites (IARC, 2010a). For example, in rats exposed to benzo[*a*]pyrene aerosols, this PAH is eliminated rapidly from the lung, and higher levels are found in the stomach and small intestine than in any other tissue, although significant amounts are detected in the liver and kidneys. Similar results have been obtained in rats exposed by inhalation to benzo[*a*]pyrene absorbed onto ultrafine particles. Thus, PAHs are generally cleared rapidly from the site of initial deposition in the respiratory tract and are then distributed to a significant extent in the gastrointestinal tract, liver and kidney (IARC, 2010a).

Transporter proteins may play a role in the biological activity of PAHs. For example, ATP binding cassette (ABC) transporters transport specific molecules across lipid membranes, including hydrophobic compounds (Schinkel & Jonker, 2003). Among these ABC transporters, multidrug resistance 1 P-glycoprotein transports mainly non-metabolized compounds and multidrug resistance protein-1 and -2 transport conjugates of xenobiotic compounds (Haimeur *et al.*, 2004). In addition, some ABC transporters are polymorphic (Sakaeda *et al.*, 2004).

(c) Metabolism

PAHs are metabolized rapidly to more soluble metabolites (quinones, epoxides, phenols, dihydrodiols, phenol dihydrodiols, dihydrodiol epoxides and tetrols) through a series of enzymatic reactions (IARC, 2010a; see also Section 4.2.1). PAH oxidation by cytochrome P450 (CYP) mono-oxygenase is complex and involves a one electron abstraction rebound mechanism as well as a one-electron radical cation mechanism (Cavalieri & Rogan, 2002; Mulder *et al.*, 2003). CYP1A1, CYP1A2 and members of the CYP1B, CYP2B, CYP2C and CYP3A families of enzyme can catalyse the initial oxidation of benzo[*a*]pyrene and other PAHs to varying extents (WHO, 1998; Xue & Warshawsky, 2005). PAHs can induce CYP enzymes and, thus, can influence the balance of phase I and phase II enzymes that may be associated with a decreased or increased tumorigenic response (WHO, 1998).

Epoxides may rearrange spontaneously to phenols, be hydrated via epoxide hydrolase catalysis to dihydrodiols or be conjugated with glutathione (GSH), either spontaneously or via glutathione-*S*-transferase (GST) catalysis (WHO, 1998; IARC, 2010a). Cavalieri *et al.* (1988) proposed that CYP isoforms convert PAHs to hydroxyl-PAHs and then to quinones, which then can be converted to hydroquinone derivatives by quinone reductase or else conjugated with GSH, sulfate or glucuronic acid (WHO, 1998; IARC, 2010a).

Dihydrodiol derivatives can be oxidized further by CYPs to form phenol dihydrodiols or dihydrodiol epoxides. Dihydrodiol epoxides may also be formed from dihydrodiols by

reaction with peroxyl radicals generated from the oxidative biosynthesis of prostaglandins from fatty acids via prostaglandin H synthase (IARC, 2010a).

Dihydrodiol epoxides may be conjugated with GSH or bind covalently to macromolecules, such as DNA, resulting in DNA damage that might be processed into a mutation (IARC, 2010a). Dihydrodiols may also be metabolized to *ortho*-quinones by aldo-keto reductases (AKR) 1C1–1C4 and AKR1A1. The resulting *ortho*-quinone derivatives may produce reactive oxygen species, via redox cycling with the reduced form of nicotinamide adenine dinucleotide phosphate (NADPH) and copper (Penning *et al.*, 1999). PAH *ortho*-quinones, are also ligands for the aryl hydrocarbon receptor (AhR), which may play a role in the mutagenicity and carcinogenicity of PAHs (Burczynski & Penning, 2000). The stereochemistry of dihydrodiol epoxide derivatives also plays a critical role in the mutagenicity and carcinogenicity of the resulting PAH metabolite (WHO, 1998).

In addition to the phase I enzymes such as the CYPs, AKRs and epoxide hydrolase, phase II enzymes, such as GSTs, uridine diphosphate-*N*-acetylglucosamine transferase and sulfotransferases also play a role in the metabolism of PAHs. Many of these phase I and phase II enzymes are polymorphic in humans, and this genetic variability can modify the activity of the enzymes. Studies in humans indicate that genetic variants of these enzymes modify cancer risk due to exposure to PAHs, adding an additional level of complexity to assessments of health risks involving PAHs (IARC, 1999).

(d) Elimination

Animal studies show that PAH metabolites can form conjugates with sulfate, GSH or glucuronic acid. PAHs are eliminated from the body principally as conjugated metabolites in the faeces via biliary excretion and in the urine. If not conjugated, these metabolites may bind covalently with macromolecules, such as DNA, to form DNA adducts (WHO, 1998; IARC, 2010a).

4.1.3 *Insoluble particles*

In this section, the toxicokinetics, including deposition, clearance and retention, of insoluble particles are discussed for both humans and laboratory animals.

(a) Particle deposition, clearance and retention in the human respiratory tract

The deposition of a particle within a region of the respiratory tract depends on the particle characteristics and the physical factors that influence the transport of particles in the airways (e.g. air velocity and airway structure). The primary mechanisms for deposition of particles in the respiratory tract are sedimentation, impaction and diffusion. Deposition by sedimentation and impaction depends on the aerodynamic diameter of the particle, while deposition by diffusion depends on its thermodynamic diameter (ICRP, 1994).

Following inhalation, particles may either deposit in the extrathoracic, tracheobronchial or pulmonary airways or remain in the air stream and be eliminated through exhalation. The deposition of particles in the respiratory tract depends primarily on the size of the inhaled particle, the route of breathing (i.e. through the nose and/or mouth) and the breathing pattern (e.g. volume and frequency). Particles near 0.3 μm in diameter have minimal mobility in air, i.e. they are large enough that their diffusive mobility is minimal but are small enough that their sedimentation and impaction are also minimal. As a consequence, particles in this size range also have minimal deposition in the lung. In general, the deposition fraction for humans for most particle sizes less than 3–4 μm (aerodynamic diameter) is greater for the alveolar region than for the tracheobronchial airways. The deposition fraction decreases in the alveolar region for particles above 3–4 μm and below 0.01 μm due to their removal in the extrathoracic (particularly during nasal breathing) and tracheobronchial airways (NCRP, 1997; Maynard & Kuempel, 2005).

Several terms have been adopted to refer to the characterization of airborne particles and their deposition in the respiratory tract. The term 'respirable' refers to particles that are capable of penetrating into the alveolar or gas-exchange region of the lungs (≤2.5 μm). Particle size fractions include ultrafine or nanoparticle (<0.1 μm diameter of primary particle), fine (0.1–2.5 μm) and coarse (>2.5–10 μm). The term 'thoracic' refers to particles that are capable of depositing in the tracheobronchial region (≤10 μm) (ISO, 1995).

Particles are frequently aggregates of smaller primary particles. The aerodynamic and thermodynamic properties of these aggregates (rather than the primary particles) affect their behaviour in the air and their probability of deposition in the respiratory tract. Once deposited, properties such as the size and surface area of both the aggregate and primary particle can potentially affect the kinetics of clearance (ICRP, 1994; Oberdörster, 1996).

Few experimental studies are available in humans on the kinetics of clearance and retention of inhaled particles in the respiratory tract. Retention is determined by the balance between the rate of deposition and the rate of clearance. Particles that deposit in the tracheobronchial region are cleared by mucociliary clearance, which is relatively rapid (retention half-times of approximately 24–48 h) (Oberdörster, 1988; ICRP, 1994), although some fraction of the particles that deposit in the airways is cleared more slowly than expected (Stahlhofen *et al.*, 1995). For particles that deposit in the alveolar region, the primary mechanism of clearance is phagocytosis by alveolar macrophages followed by migration of the macrophages to the terminal bronchioles and subsequent mucociliary clearance; the particles are eventually swallowed or expectorated (Oberdörster, 1988; ICRP, 1994). Particles that deposit in the alveolar region are associated with a slow clearance phase (retention half-times from months to years in humans) (Bailey *et al.*, 1985; Freedman & Robinson, 1988; ICRP, 1994). Translocation of particles to the interstitial region (interstitium) further increases the retention time of particles in the lungs (Oberdörster, 1988; Freedman & Robinson, 1988; ICRP, 1994). Some fractions of particles that deposit in the alveolar region may also be translocated to the lung-associated

lymph nodes. Translocation may occur by transepithelial migration of alveolar macrophages following phagocytosis of the particle or by translocation of free particles to the interstitium, where they may be phagocytosed by interstitial macrophages. Inflammation may alter mucociliary clearance, phagocytosis by alveolar macrophages and the uptake and transport of particles to and through the respiratory epithelium (Oberdörster, 1988; ICRP, 1994).

The deposition and clearance of particles vary among individuals for a number of reasons, including age, gender, tobacco smoking status and health status. Pre-existing lung diseases or conditions such as asthma or chronic obstructive pulmonary disease can influence the efficiency and pattern of deposition within the respiratory tract. Deposition also depends on the level of activity and breathing patterns. Deposition and retention determine the initial and retained dose of particles in each region and may therefore influence the risk for developing diseases specific to those respiratory tract regions (Oberdörster, 1988; ICRP, 1994).

(b) Particle deposition, clearance and retention in the rodent respiratory tract

As in humans and other species, the deposition of particles in the rodent respiratory tract depends on the aerodynamic characteristics of the particles, the airflow properties and the airway structure. The rat is the most frequently used animal in experimental studies of inhaled particles. Significant differences in the respiratory physiology of rats and humans must be considered when assessing hazards for humans based on studies in rats (Miller, 2000). Rats are obligatory nose breathers. In contrast, humans breathe through both the nose and mouth, with the proportion varying among individuals and with activity level (the proportion of mouth breathing generally increases with exertion). Rats have more extensive airways in the nasal region, and particle deposition in this region is greater for rats than humans. The size of particles that are inhalable (capable of entering respiratory tract) differs in rats and humans (Ménache *et al.*, 1995; Miller, 2000). The airway branching system is symmetric (bi- or tripodal) in humans and asymmetric (monopodal) in rats. The type of branching system influences the site of deposition (airway impaction tends to be greater in the human tracheobronchial region). Rats do not have respiratory bronchioles, while humans do. All of these factors influence the kinetics of particle deposition in the respiratory tract and thus potential differences between rats and humans (Ménache *et al.*, 1996; Miller, 2000).

Once insoluble particles are deposited, their removal or retention is based on mechanisms of biological clearance. In rats, like humans, particles in the tracheobronchial region are cleared by the mucociliary pathway and by alveolar macrophages in the alveolar region. Particles that enter the interstitium may also enter the lymph and blood circulation. Although the mechanisms are similar, the rates at which they occur may differ between rats and humans. While tracheobronchial clearance is relatively rapid in both rats and humans (half-times of the order of hours or days), the normal alveolar clearance rate in rats is approximately 10 times faster than that in humans (Snipes, 1989).

Studies in rodents (primarily rats) have shown that, depending on the concentrations and durations of exposure, the long-term retention of particles can be greater than that predicted from studies that used lower concentrations or shorter durations. This increase in particle retention has been attributed to the overloading or impairment of alveolar macrophage-mediated clearance (Morrow, 1988, 1992; ILSI Risk Science Institute Workshop Participants, 2000). The mechanisms of particle overload, the lung responses to overload and the implications for carcinogenic hazard are discussed in Section 4.2.

4.2 Mechanisms of carcinogenesis

4.2.1 *Polycyclic aromatic hydrocarbons (PAHs)*

Ample evidence (summarized in IARC, 2004, 2010a) supports a role for PAHs in lung cancer due to exposure to indoor emissions from smoky coal or from cigarette smoking. A general genotoxic mechanism has emerged in which PAHs such as benzo[*a*]pyrene are metabolized to electrophilic forms that adduct to DNA. If these adducts are not repaired, then misreplication converts them to G→T transversion mutations in the *TP53* gene in the lung. An overrepresentation of G→T transversions has been found on the non-transcribed strand, of DNA, which is consistent with the lack of transcription-coupled DNA repair on that strand and results in mutations. A preference for G→T transversions in the methylated CpG dinucleotides in human lung tumours also has been found, in agreement with in-vitro studies that show the same dinucleotide as a target of benzo[*a*]pyrene diol epoxide. Accumulation of additional mutations in key genes within stem cells, together with epigenetic and/or non-genetic changes, such as disruption of cell–cell communication, apoptosis and cell-cycle regulation, can result in tumour formation (IARC, 2010a).

Based on several lines of evidence (IARC, 2010a), PAHs may be activated via two main pathways: (*i*) mono-oxygenation to yield diol epoxides and (*ii*) one-electron oxidation to form radical cations. The two reactive intermediates, diol epoxides and radical cations, can bind to DNA to form adducts, with the potential to be processed into mutations, resulting presumably in tumour formation. Some PAHs are activated exclusively to diol epoxides, such as 5-methylchrysene, and benzo[*c*]phenanthrene, whereas several other PAHs, such as benzo[*a*]pyrene, dibenzo[*a,l*]pyrene, 7,12-dimethylbenz[*a*]anthracene (DMBA) and 3-methylcholanthrene, are activated by formation of diol epoxides and radical cations.

Adenine and guanine are the two DNA bases most susceptible to the nucleophilic attack of PAHs. The adducted nucleotides can be processed into mutations by two general mechanisms: (*i*) error-prone DNA repair and (*ii*) erroneous replication through any unrepaired lesions. Apurinic sites generated by depurinating DNA adducts appear to be mutated by error-prone repair (Chakravarti *et al.*, 2000, 2001), whereas the repair of stable DNA adducts is largely error-free (Choi *et al.*, 1996). However, replication through unrepaired adducted bases can sometimes cause mutations (Moriya *et al.*, 1996). In

conclusion, the induction of specific mutations by PAHs is determined by mechanisms that determine (*i*) adduct formation at specific DNA sequences and (*ii*) the incorporation of mispaired bases (either by error-prone repair or by erroneous replication) at lesions in specific DNA sequence contexts.

(a) Bay- and fjord-region PAH diol epoxides

The bay-region theory of PAH metabolism emphasizes that angular benzo ring fusions on PAHs create a topological indentation on the polycyclic ring structure, which is called the bay region. For example, the bay region of benzo[*a*]pyrene encompasses four carbons (carbons 10, 10a, 10b and 11) and three carbon–carbon bonds. Metabolism by CYPs at the C7–C8 aromatic double bond creates an arene oxide (i.e. benzo[*a*]pyrene-7,8-oxide) that disrupts the aromatic nucleus by saturating that carbon–carbon bond. The arene oxide is hydrated by epoxide hydrolase to form a dihydrodiol (diol), which is further epoxidized by CYPs at the C9–C10 double bond to give the bay-region diol epoxide, benzo[*a*]pyrene-7,8-diol-9,10-oxide. This diol epoxide possesses an inherent activity to undergo carbon–oxygen bond scission or ring opening to form a carbocation (or carbonium, i.e. a positively charged carbon atom) on carbon 10. Carbocations are highly reactive species that react with nucleophiles such as DNA and proteins to form covalent adducts. The more reactive the carbocation, the greater is the tumorigenic activity of the PAH (Jerina *et al.*, 1976).

PAHs such as dibenzo[*a,l*]pyrene contain a fjord region, which encompasses five carbons and four carbon–carbon bonds. In some cases, the steric interactions between atoms within the fjord region forces the PAH ring system out of planarity (Katz *et al.*, 1998). Some PAH fjord-region diol epoxides are non-planar and these non-planar PAH diol epoxides possess high reactivities (Lewis-Bevan *et al.*, 1995). The formation and degradation of stereochemically specific diol epoxides are dependent on species, strain, sex, organ, tissue, type of CYPs and phase II enzymes (IARC, 2010a).

One of the original tenets of the mechanism for bay-region or fjord-region diol epoxides is that, as the PAH is metabolically activated in sequence through the diol to the diol epoxide, this process creates intermediates that generally possess greater biological activities than their precursors. This is true for some (Wislocki *et al.*, 1979) but not all PAHs (Buening *et al.*, 1979).

Bay-region and fjord-region diol epoxides possess many biological activities, and one of the most important of these is their ability to form stable covalent adducts with DNA. The nature of these adducts is influenced by the absolute configuration, molecular conformation and stereochemistry of the diol epoxide, the specific purine or pyrimidine base that is adducted, the site of adduction within the base and the sequence of the DNA that is adducted (Jerina *et al.*, 1986). When diol epoxides react with DNA, each can form both *cis* and *trans* adducts, to give a total of 16 possible DNA adducts. These DNA adducts can then either be repaired, or they can be misrepaired or not repaired at all, in which case translesion DNA synthesis can result in mutation—i.e. a change in DNA

sequence (Rodriguez & Loechler, 1995; Frank et al, 2002). PAH diol epoxide–DNA adducts are generally repaired by nucleotide excision repair (Geacintov *et al.*, 2002).

Bay- and fjord-region diol epoxides of PAHs induce DNA damage and mutations in a wide variety of biological organisms and systems, and they induce mutations in critical genes associated with chemical carcinogenesis, such as proto-oncogenes (e.g. *ras*; Prahalad *et al.*, 1997; Chakravarti *et al.*, 1998) and tumour-suppressor genes (e.g. *p53*; Ruggeri *et al.*, 1993; Rämet *et al.*, 1995). In general, DNA adducts induced by PAHs at deoxyguanosine result in mutations in the *ras* gene at codons 12 or 13, whereas adducts formed by PAHs at deoxyadenosine result in mutations in the *ras* gene at codon 61. Adducts induced by PAHs at both purine bases result in both types of mutations (Ross & Nesnow, 1999). Diol epoxide–DNA adducts of PAHs also have been found in populations exposed to complex mixtures containing PAHs, such as foundry workers, coke-oven workers, cigarette smokers, chimney sweeps and people exposed to emissions from smoky coal (IARC, 2010a). In addition to their genotoxic effects, some bay- or fjord-region diol epoxides can induce apoptosis and cell-cycle arrest (Chramostová *et al.*, 2004).

(b) Radical cations

Removal of one electron from the π system (the system of six delocalized electrons) by CYPs or peroxidases generates a radical cation in which the positive charge is localized mainly at an unsubstituted carbon atom or adjacent to a methyl group. Nucleophilic attack at the position of highest charge density in the first case produces an intermediate radical that is then further oxidized to an arenium ion to complete the substitution reaction. When the charge is localized adjacent to the methyl group, the latter becomes electrophilic and can react with a nucleophile (Cavalieri & Rogan, 1985, 1992).

The notion that radical cations play an important role in the metabolic activation of some PAHs derives from certain features that are common to several carcinogenic PAHs. These characteristics are (*i*) a relatively low ionization potential, which allows the removal of one electron and the formation of a relatively stable radical cation, (*ii*) a charge localization in the radical cation that renders this intermediate specifically and efficiently reactive toward nucleophile and (*iii*) an optimal geometric configuration that allows the formation of appropriate intercalating radical cation complexes with DNA and favours the formation of covalent adducts with DNA (IARC, 2010a).

(c) Formation of ortho-quinones and generation of reactive oxygen species

PAHs with a terminal benzo-ring in a bay region can be metabolically activated or form arene oxides, which can then be hydrated by epoxide hydratase to form non-K region *R,R-trans*-dihydrodiols (Shimada *et al.*, 1996; IARC, 2010a). These *trans*-dihydrodiols can undergo further mono-oxygenation by CYPs to form predominantly

bay-region *anti*-diol epoxides. The formation of *trans*-dihydrodiols represents a branch point in PAH metabolism (IARC, 2010a).

Non-K region *trans*-dihydrodiols also undergo NADP-dependent dehydrogenation that is catalysed by monomeric cytosolic oxidoreductases of the AKR superfamily to yield ketols, which rearrange spontaneously to yield catechols. The catechols are extremely air-sensitive and undergo two sequential one-electron auto-oxidation events to yield the corresponding reactive and redox-active PAH *ortho*-quinones (Smithgall *et al.*, 1988; IARC, 2010a). An intermediate in this auto-oxidation is the corresponding *ortho*-semiquinone anion radical. Each one-electron oxidation event (either catechol to *ortho*-semiquinone anion radical or *ortho*-semiquinone anion radical to *ortho*-quinone) yields reactive oxygen species (superoxide anion, hydrogen peroxide and hydroxyl radical) (Penning *et al.*, 1996, 1999; IARC, 2010a).

The resulting PAH *ortho*-quinone is a highly reactive Michael acceptor and can undergo 1,4- or 1,6- Michael addition reactions with cellular nucleophiles to yield conjugates (Sridhar *et al.*, 2001; IARC, 2010a) or with macromolecules to yield adducts (Balu *et al.*, 2004; IARC, 2010a). PAH *ortho*-quinones also can be reduced back to the catechol, either non-enzymatically by the addition of $2H^+ + 2e^-$ by cellular reducing equivalents (e.g. NADPH) or in two sequential one-electron steps catalysed by NADPH:CYP reductases (Flowers-Geary *et al.*, 1993, 1995). Once re-formed, the catechol can undergo further auto-oxidation to create a futile redox cycle in which each round of auto-oxidation forms reactive oxygen species, generating a reactive oxygen species amplification system. Generation of reactive oxygen species continues until the reducing equivalent is exhausted, which leads to oxidative stress and a pro-oxidant state. The PAH *ortho*-quinones and the reactive oxygen species that they generate have the capacity to form either mutagenic lesions in DNA or to act as electrophilic and pro-oxidant signals that may have consequences on cell growth (promotion). In this manner, the pathway may contribute to the complete carcinogenicity of the parent PAH. In humans, five AKR isoforms catalyse the oxidation of non-K region *trans*-dihydrodiols to *ortho*-quinones (Palackal *et al.*, 2002a,b; IARC, 2010a).

Much remains to be understood regarding the possible role of the PAH *ortho*-quinone pathway and reactive oxygen species in carcinogenesis: (i) only a few relevant PAHs have been examined for their metabolism via this pathway; (ii) human AKRs, other than AKR1A1 and AKR1C1–AKR1C4, may be involved in the activation of PAH *trans*-dihydrodiols; (iii) there is little information regarding the competing roles of CYP- versus AKR-mediated activation of PAHs; (iv) covalent DNA adducts or oxidative lesions produced by PAHs through the AKR pathway have yet to be detected; (v) the mutagenicity of PAH *ortho*-quinones in mammalian cells has not been completely demonstrated; (vi) the transforming potential of the PAH *ortho*-quinones has not yet been determined; and (vii) the tumorigenicity of PAH *ortho*-quinones as initiators, promoters or both has not been examined systematically (IARC, 2010a).

(d) Cyclopenta-ring oxidation

The mechanism of cyclopenta-ring oxidation involves the formation of the arene oxide at a highly electron-rich isolated double bond that is located at a five-membered ring within a PAH. The cyclopenta ring is an external five-membered carbocyclic ring that is situated on a carbocyclic hexameric fused-ring system. In general, cyclopenta-ring derivatives of PAHs are more mutagenic (Kohan *et al.*, 1985) and more carcinogenic (Nesnow *et al.*, 1998) than their unsubstituted counterparts. CYPs (e.g. 1A1, 1A2, 3A4) metabolize cyclopenta-fused PAHs at the cyclopenta ring double bond to give cyclopenta-ring oxides and diols (IARC, 2010a). The cyclopenta-ring oxides are reactive intermediates that form DNA adducts (Hsu *et al.*, 1999), that result in mutations and cell transformation (Bartczak *et al.*, 1987; Nesnow *et al.*, 1991). They are hydrated by epoxide hydrolase to diols, and some are conjugated to sulfate esters, which are also highly reactive intermediates (Surh *et al.*, 1993).

(e) Meso-region biomethylation and benzylic oxidation

The role of the mechanisms of meso-region biomethylation and benzylic oxidation in the carcinogenesis of PAHs is based on the formation of methylated PAHs from unsubstituted PAHs and the subsequent metabolic activation of the methyl group to electrophilic forms. The meso region of PAHs (also known at the L-region) has been reported to be a region of high reactivity either in an aromatic nucleus or on a side chain (Flesher *et al.*, 2002, 2004). Accordingly, the chemical and biochemical pathways of the activation of both unsubstituted and meso-substituted PAHs are essentially the same because unsubstituted PAHs are converted to generally more carcinogenic meso-methyl-substituted PAHs in the process of metabolic activation (IARC, 2010a).

The first step in a series of three transformation reactions is the aralkylation (methylation) of unsubstituted PAHs at a meso centre of high reactivity. This conversion is mediated by the methyl donor, *S*-adenosyl methionine. The second step is the hydroxylation of a meso-region methyl group by CYPs, and a chemical one-electron oxidation process has also been proposed. The third step is the formation of a reactive ester (e.g. sulfuric acid ester) catalysed by 3′-phosphoadenosine-5′-phosphosulfate sulfotransferase (PAPS SULT). Sulfoxymethyl esters generate a highly reactive benzylic carbonium ion and react with DNA to form DNA adducts; some of the latter are mutagenic (Flesher *et al.*, 2004; Ravi Kumar *et al.*, 2005; IARC, 2010a).

(f) Receptor-mediated mechanism

Several of the biological effects of PAHs, such as enzyme induction, immunosuppression, teratogenicity and carcinogenicity, may be mediated by activating the arylhydrocarbon receptor (AhR). This receptor is widely distributed and has been detected in most cells and tissues. There is also evidence that AhR signals through a variety of pathways and with other nuclear receptors to enable cell type- and tissue-specific control of gene expression (IARC, 2010a).

Responses of AhR signalling involve a variety of cellular responses. AhR induces phase I and II enzymes; additional responses include lipid peroxidation and production of arachidonic acid-reactive metabolites, decreased levels of serum thyroxine and vitamin A, persistent activation of thyroid hormone receptor and communication with steroid hormone receptors. Responses to altered AhR signalling may, therefore, be designated as adaptive or toxic and/or as perturbations of endogenous pathways (IARC, 2010a).

(g) Immunological and haematological mechanisms

A significant number of studies have demonstrated that PAHs are immunosuppressive in animal models and also in human leukocytes exposed *in vitro*. In animals, the concentrations of PAHs that are required to produce immunosuppression are generally quite high compared with those that produce cancer. There are limited human epidemiological data that show that PAHs are immunosuppressive following environmental exposures (IARC, 2010a).

The biological and toxicological actions of PAHs on the immune and haematopoietic systems represent a complicated interplay between the ability of a specific PAH to bind to endogenous AhR and induce CYPs in central and peripheral organs, which results in the formation of oxidative and electrophilic metabolites and the removal of reactive molecules via secondary metabolic processes. Thus, the toxicity of PAHs to the immune system is dependent upon the exposure of cells and tissues to circulating parent compounds and metabolites, their ability to activate AhR and their propensity to form bioactive versus detoxified metabolites. The dose and route of exposure to PAHs are important determinants of immunotoxicity in animals and humans. In general, the total cumulative dose of exposure to PAHs correlates with immunoxicity in mice. It should be noted that PAHs have been observed to produce biphasic dose–response curves in which low doses stimulate immune responses and high doses produce inhibition (Burchiel & Luster, 2001; Booker & White, 2005; IARC, 2010a).

The overall effects of PAHs on the immune and haematopoietic systems result from activation of both genotoxic and epigenetic pathways. Because of the heterogeneity of lymphoid and myeloid cell populations and the complex interplay between different types of cells and secreted products, the mechanisms of action of PAHs have been difficult to assess. Many PAHs clearly exert effects on the developing as well as the mature immune system, and some correlation exists between the carcinogenicity of PAHs and their ability to produce immunosuppression (IARC, 2010a).

As reported previously, the AhR plays a critical role in the activation of immunotoxic PAHs such as benzo[*a*]pyrene, via diol epoxide mechanisms, which lead to DNA interactions that cause genotoxicity and suppress immunity by P53-dependent pathways. Benzo[*a*]pyrene diol epoxide may also affect protein targets and modulate lymphocyte signalling pathways via epigenetic mechanisms. Certain oxidative PAHs may be formed via CYP-dependent and -independent (peroxidase) pathways. Redox-cycling PAH-quinones may exert oxidative stress in lymphoid cells. Human exposures to PAHs are usually in the form of complex mixtures, and it is difficult to attribute the relative

contributions of individual PAHs to the overall immunotoxic effects. Although there is some evidence that environmental exposures to PAHs may produce immunotoxicity, further epidemiological studies are needed (IARC, 2010a).

(h) Phototoxicity

Early studies indicated that ultraviolet (UV) radiation could enhance the carcinogenicity of PAHs on mouse skin (Santamaria *et al.*, 1966), and two pathways can result in phototoxicity. The first is dynamic phototoxicity or damage to cells during photo-transformation of chemical species. This includes excited-state energy transfer to biological macromolecules resulting in electron transfer that may convert both the PAH and the biological molecule into free radicals, and the production of short-lived reactive intermediates such as reactive oxygen species (Yu, 2002). The second is the formation of toxic photoproducts during photolysis. They consist of some relatively light-stable compounds that may be toxic both in the presence or absence of metabolic or light-induced activation (Sinha & Chignell, 1983).

Upon absorption of light energy, PAHs are excited to upper energy states (singlet or triplet) that undergo electron or energy transfer to molecular oxygen, solvents or biological molecules in the cell to generate reactive species. These reactive species or intermediates damage cellular constituents such as the cell membrane, nucleic acids or proteins. Thus PAHs are activated by light irradiation to cause cellular damage and exert toxicity, including carcinogenicity. This activation pathway is usually similar to the enzymatic activation pathway in that it converts relatively inert PAHs to reactive species (IARC, 2010a).

DNA damage resulting from the interaction of light with a PAH includes PAH–DNA adducts, single- and double-strand DNA breaks, DNA–DNA and DNA–protein cross-links, depurination/depyrimidiation and the formation of the oxidative product 8-hydroxyguanine (IARC, 2010a). Yan *et al.* (2004) showed that 11 of 16 PAHs were photomutagenic in the Ames mutagenicity assay, and a close association was observed between the photomutagenicity and reported carcinogenicity.

Phototoxicity, including photomutagenicity, is closely related to the photochemical reactions that generate reactive PAH intermediates and reactive oxygen species during photolysis (Yu, 2002). Certain PAHs with extended aromatic ring systems can absorb light in the UVA (320–400 nm) and visible (> 400 nm) region. Usually, PAHs with three or four aromatic rings can absorb UVA light and those with five or more aromatic rings as well as the hydroxyl-, amino- and nitro-substituted PAHs with three or four aromatic rings can absorb visible light (Dabestani & Ivanov, 1999).

(i) Non-genetic effects

PAHs, such as benzo[*a*]pyrene, can increase cell proliferation (Tannheimer *et al.*, 1998) and can cause an influx of extracellular Ca^{2+} into the cell (perhaps by perturbing the physical organization of phosphatidylcholine membranes) (Jiménez *et al.*, 2002). This

may be important for the activation of protein kinase C pathways, which are associated with tumour promotion (Tannheimer *et al.*, 1999). PAH quinones may also increase the epidermal growth factor receptor pathway, the serine-threonine kinase Akt and the extracellular signal-regulated kinase activity (Burdick *et al.*, 2003). Benzo[*a*]pyrene can induce P53 accumulation and a partial S-phase arrest (Plísková *et al.*, 2005). Benzo[*a*]pyrene diol epoxide increases the level of Cdc25B (which regulates cell-cycle progression and genetic stability), mRNA and protein levels in terminal squamous differentiated human bronchial epithelial cells and lung cancer cells but not in undifferentiated bronchial cells (Oguri *et al.*, 2003).

Benzo[*a*]pyrene also has been shown to induce apoptosis in murine and human cells (Chen *et al.*, 2003; Raychoudhury & Kubinski, 2003; Ko *et al.*, 2004). There are many ways by which compounds can induce apoptosis, and PAHs may affect different pathways in different cell types.

Gap-junctional communication is important in cell proliferation, differentiation and apoptosis, and it has been suggested to be important for the promotion of carcinogenesis. Of 35 PAHs tested for inhibition of gap-junctional communication in rat liver epithelial cells, 12, including benzo[*a*]pyrene, were found to be strong but transient inhibitors (Bláha *et al.*, 2002).

4.2.2 *Particles*

This section addresses the mechanisms of carcinogenesis of particles and is based on an extensive database for poorly soluble, respirable particles of low toxicity that can be found in a previous volume of the *Monographs* (IARC, 2010b). The extent to which these mechanisms are fully relevant for particles generated from combustion is not known.

(a) Lung overload

The concept of 'overload' is central to the relevance of using rodent studies for the evaluation of human health hazards from inhaled particles. Overload is a biological mechanism that involves the dose-dependent impairment of alveolar macrophage-mediated clearance of respirable particles. In the alveolar region of the respiratory tract, the primary mechanism for particle clearance is phagocytosis by alveolar macrophages with subsequent removal of particle-containing macrophages by mucociliary clearance. High particle burdens in the lungs can result in overload because alveolar macrophage-mediated clearance is overwhelmed, which results in a decreased rate of clearance and an increased retention of particles. Overloading of lung clearance has been observed in rats, mice and hamsters exposed to different insoluble respirable particles (e.g. carbon black, titanium dioxide, talc, toner and diesel exhaust particulates) (Strom *et al.*, 1989; Muhle *et al.*, 1990; Bellmann *et al.*, 1991; National Toxicology Program, 1993; Warheit *et al.*, 1997; Bermudez *et al.*, 2002, 2004; Elder *et al.*, 2005) and asbestos fibres (Davis *et al.*, 1978; Bolton *et al.*, 1983).

(i) *Mechanisms that underlie lung overload*

Experimentally, overloading of lung clearance has been inferred from the observation of a greater lung burden of particles or fibres than that expected on the basis of results from lower concentrations or shorter durations of exposure (Davis *et al.*, 1978). A steady-state lung burden should be achieved when the rate of deposition equals the rate of clearance, and overloading represents a deficit in that clearance. Impaired clearance attributed to overloading has been expressed as a reduction in the clearance rate coefficient (Muhle *et al.*, 1990; Bellmann *et al.*, 1991) or an increase in the amount of particles retained in the lungs following exposure (Strom *et al.*, 1989; Bermudez *et al.*, 2002, 2004; Elder *et al.*, 2005). Increased translocation of particles to the lung-associated lymph nodes has also been observed at doses at which overload occurs (Strom *et al.*, 1989; Bellmann *et al.*, 1991).

Morrow (1988) hypothesized that overload was a consequence of macrophages that become progressively immobilized and aggregated. When the dose of particles reaches a critical particle volume, clearance by macrophages is suppressed and particles accumulate in the lungs. Based on the lung burden of particle mass associated with increased retention in rat lungs (approximately 1 mg/g of lung tissue for unit density particles) and data on the volume and number of alveolar macrophages in rat lungs, it was hypothesized that impairment of clearance would be initiated when the particle volume exceeded an average of 6% of the macrophage volume, and clearance would be completely impaired when particle volume exceeded an average of 60% of the macrophage volume. The upper particle volume estimate (60%) was supported by Oberdörster *et al*. (1994), who showed that clearance was no longer detectable 200 days after instillation of 10-μm diameter polystyrene particles in rat lungs. The overload mechanism pertains specifically to poorly soluble respirable (<10 μm) particles of low toxicity. Factors other than the volumetric overload can lead to impaired alveolar clearance. For example, particles that are toxic to macrophages (e.g. crystalline silica) can cause impaired clearance at doses lower than those of low-toxicity particles (Bellmann *et al.*, 1991). Ultrafine particles have been recognized as differing from fine particles with regard to overloading. Morrow (1992) noted that ultrafine particles impair clearance at lower mass or volume concentrations than those expected for larger respirable particles. Oberdörster (1996) confirmed this observation and showed that increased particle retention and inflammation were related to particle surface area.

One mechanism for the impaired clearance of ultrafine particles may be their ineffective phagocytosis (Churg *et al.*, 1998; Renwick *et al.*, 2001, 2004; Geiser *et al.*, 2005), which leaves the particles free in the alveolar region and more readily able to translocate to the lung interstitium (Ferin *et al.*, 1992, 1994). The surface properties of particles may also influence phagocytosis. For example, Castranova (2000) found that chronic inhalation exposure to 2 mg/m^3 coal dust activated alveolar macrophages, while the same exposure to diesel exhaust depressed phagocytic activity. Wolff *et al.* (1986) noted that additional factors other than non-specific particle effects must be important because the exposure level that resulted in overloading and lung tumours was higher for

some particles than others (e.g. 250 mg/m^3 fine-sized titanium dioxide versus ~7 mg/m^3 diesel exhaust).

(ii) *Mechanisms that underlie lung response to overload*

An increase in neutrophilic inflammation has been defined as the critical biological response to lung overload (ILSI Risk Science Institute Workshop Participants, 2000). An increase in polymorphonuclear leukocytes (granulocytes) in bronchioalveolar lavage (BAL) fluid in rats has been associated with increased retention of particles in the lungs (Tran *et al.*, 1999). Mice also appear to be susceptible to overloading doses and adverse pulmonary responses, but they regain normal clearance more readily when exposure ceases. Hamsters clear particles much faster than rats or mice, experience overloading at higher doses and recover more easily. Lung responses follow the clearance kinetics for inhaled particles—rats show a more severe, sustained response to inhaled particles than mice, while hamsters have only a temporary inflammatory response (Bermudez *et al.*, 2002, 2004; Elder *et al.*, 2005). In rats, lung responses to overloading include increased lung weight, chronic inflammation, fibrosis and lung cancer (Muhle *et al.*, 1991).

The cascade of events that describes the biological process that starts from particle deposition at critical target cells or tissues within the rat lung and results in tumours includes: sustained inflammation, production of reactive oxygen species, depletion of antioxidants and/or impairment of other defence mechanisms, cell proliferation and gene mutations. These individual steps comprise an overall mode of action that can be used to compare responses of rats with those of other species including humans (IARC, 2010b).

At a lung burden of particle mass at which overload is observed in rats (estimated to begin at ~0.5 mg/g of lung tissue and to be fully developed at ~10 mg/g), a sustained and widespread cellular inflammatory response occurs. The cell population is dominated by activated and probably (under these conditions) persistent neutrophil granulocytes and secretes a collection of mediators (pro- and anti-inflammatory cytokines, proteases, cytotoxins, fibrogenic mediators and other growth factors) that act through the pulmonary milieu on surrounding cells or tissues and surrounding structures (Castranova, 2000; IARC, 2010b).

The degree of sustained inflammation experienced by rodents (most notably rats) at high lung burdens is not observed in humans. However, humans may experience sustained inflammation in certain disease states. One such human condition (which may be particle-stimulated, e.g. by silica, or may be cryptogenic) is late-stage interstitial pulmonary fibrosis. Patients who have interstitial pulmonary fibrosis and chronic inflammation have been reported to experience a higher incidence of lung tumours (Daniels & Jett, 2005). Rom (1991) found a statistically significant increase in the percentage of neutrophil granulocytes in BAL fluid of workers with respiratory impairment who had been exposed to asbestos, coal or silica (4.5% in cases versus 1.5% in controls). Elevated levels (sevenfold increase over controls) of neutrophil granulocytes have been observed in the BAL fluid of miners who had simple coal workers'

pneumoconiosis (Vallyathan *et al.*, 2000) and in patients with acute silicosis (a 10-fold increase over controls) (Goodman *et al.*, 1992; Lapp & Castranova, 1993).

The precise role of chronic inflammation in the development of cancer is uncertain, but considerable evidence shows that chronic inflammation may have a multi-faceted role in this process. Activated cells in the lung are known to release various reactive intermediates, most notably those derived from oxygen. Sustained excess of oxidant activity is known to deplete antioxidant defences gradually. Clear differences among these defence mechanisms in the lungs exist between humans and rats, and evidence shows that humans overall are relatively deficient in some of these mechanisms relative to rats (Hatch *et al.*, 1985). Reactive oxygen species within cells may damage DNA directly and potentially induce mutations. Moreover, cell damage and promitotic stimuli initiated by reactive oxygen species promote cell turnover and proliferation, both of which may enhance the risk for DNA replication error and/or expand a mutated or transformed cell to initiate the tumorigenic process (see Section 4.2.1).

(iii) *Dosimetric correlation between lung particle burden and response*

Because particle overload is the critical determinant that underlies the adverse biological response to inhaled particles, an understanding of the appropriate dosimetric expression for overload is essential for hazard evaluation. A number of studies have shown that, for particles of different sizes but with the same chemical composition, the dose expressed as particle surface area is a better predictor of adverse pulmonary inflammation than particle mass (Oberdörster *et al.*, 1992; Tran *et al.*, 1999; Bermudez *et al.*, 2002, 2004). Particle surface area is also related to pulmonary inflammation in mice (Lison *et al.*, 1997). Oberdörster and Yu (1990) and Driscoll *et al.* (1996) showed that particle surface area is also a better predictor of lung tumours than particle mass in rats exposed to various poorly soluble particles of fine or ultrafine size.

The particle characteristics and method used to estimate particle surface area may influence the magnitude of the observed response. For example, carbon black that has a high specific surface area (220 m^2/g) was shown to cause a lower inflammatory response than that expected based on the total particle surface area dose (Driscoll *et al.*, 1996). This could be due to less disaggregation of deposited carbon black into smaller units compared with ultrafine titanium dioxide for instance (Oberdörster, 1996). It may also be due to a more porous carbon black surface (carbon black has a higher internal surface than titanium dioxide), which may increase the surface area measured by nitrogen absorption but does not accurately measure the effective surface area in contact with the epithelial cell surface (Tran *et al.*, 1999).

(b) Interspecies comparison of particle retention in the lung

Impairment of clearance leads to an increased retention of particles, which is the hallmark of lung overload. Thus, an understanding of interspecies differences in the mechanisms of particle retention can aid hazard evaluation and risk assessment.

Differences in the patterns of particle retention of coal dust or diesel exhaust were observed in rats and monkeys; a higher volume percentage of coal dust was retained in the alveolar lumen in rats and in the interstitium in monkeys that were exposed by inhalation to 2 mg/m^3 coal dust and/or diesel exhaust particulate for 2 years (Nikula *et al.*, 1997a,b). A greater proportion of particles were also retained in the interstitium in humans compared with rats. In humans, as the duration of exposure and assumed concentration of coal dust increased, the pattern of retention changed so that the proportion of particles in the interstitium increased. In contrast, the pattern of retention in rats did not vary with increasing concentrations of diesel exhaust particulate from 0.35 to 7.0 mg/m^3 (Nikula *et al.*, 2001).

One class of insoluble particles—carbon black—has been identified in human lungs, although no quantitative data are available on its retention in humans. However, based on studies with other poorly soluble particulate materials, it can be assumed that the normal retention half-times of particles such as carbon black in humans is longer than that measured in rats and mice. For example, Bailey *et al.* (1985) found that the retention time of inhaled monodisperse 1- and 4-μm diameter fused aluminosilicate particles in humans followed a two-component exponential function with phases having half-times of the order of tens of days and several hundred days, respectively. At 350 days after inhalation, retention of the remaining material averaged 46±11% for the 1-μm particles and 55±11% for the 4-μm particles. In contrast, data in rats (Oberdörster, 1995) and mice (Kreyling, 1990) demonstrate retention half-times of ~70 days and ~55 days, respectively.

Heavy exposure to particles in occupational settings may lead to high particle burdens in the human lung. By analogy to the rat, if the human lung burden exceeds ~0.5–1 mg/g lung, it would be expected that the normal retention half-time may be prolonged. Indeed, there is some evidence that workers in occupations that are associated with high particle burden in the lungs (e.g. coal mining) show increased long-term retention of particles (Stöber *et al.*, 1965; Freedman & Robinson, 1988). Retention half-times of the order of years have been measured in a number of human studies that involved accidental exposure to radionuclides (ICRP, 1994).

Little is known about overloading in non-rodent species including humans. Perhaps the most often cited human data are in coal miners, which is one of the best studied occupational cohorts regarding quantitative exposure–response relationships (Attfield & Kuempel, 2003). Coal miners have historically experienced high rates of occupational lung diseases including increased morbidity and mortality from pneumoconiosis and chronic obstructive lung diseases (National Institute for Occupational Safety and Health, 1995). Excess mortality from lung cancer has generally not been observed in coal miners (National Institute for Occupational Safety and Health, 1995), although in a more recent study of German coal miners, elevated lung cancer mortality was detected in miners who had developed pneumoconiosis (standardized mortality ratio, 1.57), which was independent of the effect of tobacco smoking (Morfeld *et al.*, 2002).

Retained lung burdens have also been relatively high; an average of ~14 mg/g lung has been observed historically in coal miners in the USA (Kuempel *et al.*, 2001) and the

United Kingdom (Tran & Buchanan, 2000). This mean lung burden is comparable with retained mass lung burdens in rats that had overload. Because an elevated incidence of lung cancer has generally not been observed in coal miners, it has been suggested that the rat may not be a good model to predict lung cancer in humans. However, although the mean lung burden is relatively high in coal miners, it is actually lower than the mean lung burdens associated with the excess incidence of lung tumours in rats. For example, in rats chronically exposed to coal dust, mass lung burdens of 24 mg/g lung tissue were associated with an 11% incidence of lung tumours (versus 0% in unexposed controls) (Martin *et al.*, 1977). In rats exposed to fine-sized titanium dioxide, lung burdens up to ~35 mg/g were not associated with lung tumours, and increased incidences of lung tumours were observed only in rats with lung burdens greater than ~100 mg/g (approximately 16% in male and female rats, excluding keratinizing cystic squamous-cell carcinomas) (Lee *et al*., 1985a,b, 1986). In female rats that chronically inhaled talc for two years, 9 mg talc/g lung tissue was not associated with an elevated incidence of lung tumours (0/48, 0%), while an average retained burden of 29 mg/g lung was associated with a 26% (13/50) incidence of alveolar/bronchiolar tumours (National Toxicology Program, 1993).

Based on these chronic inhalation studies in rats exposed to various fine-sized, poorly soluble particles of relatively low toxicity, lung tumours were not observed in rats that had lung burdens similar to those of coal miners. Rats that developed lung tumours following chronic inhalation of these particles had retained mean mass lung burdens that were at least twice as high as those in coal miners. Thus, the observed lung tumour response in rats and the absence of reported tumours in coal miners when both are exposed chronically to fine-sized, poorly soluble particles such as coal dust are somewhat consistent.

The surface area of particles may be a more appropriate dose metric for predicting response; therefore, it is useful to evaluate rat and human responses to particle surface area dose in addition to particle mass dose. In rat lungs, fine and ultrafine particles of similar composition have shown consistent dose–response relationships when dose is expressed as particle surface area rather than as particle mass. The mean surface area dose of coal dust in miners' lungs from studies in the USA and United Kingdom can be calculated as 0.1 m^2 coal dust/g lung tissue (assuming 7.4 m^2/g coal dust; Vallyathan *et al.*, 1988; Tran & Buchanan, 2000; Kuempel *et al.*, 2001). In rats, the lowest observed surface area doses associated with elevated incidences of lung tumours (excluding keratinising cystic squamous-cell tumours) following chronic inhalation were: 0.18 m^2 coal dust/g lung tissue in female rats, (assuming 7.4 m^2/g coal dust), with an 11% tumour incidence versus 0% in controls (Martin *et al.*, 1977); 0.58 m^2 carbon black/g lung tissue for female rats, with a 7.5% tumour incidence versus 0% in controls (Nikula *et al.*, 1995); 6.9 m^2 carbon black/g lung tissue in female rats, with a 28% tumour incidence versus 0.46% in controls (Heinrich *et al.*, 1995); 1.3 m^2 ultrafine titanium dioxide/g lung tissue in female rats, with a 19% tumour incidence versus 0.46% in controls (Heinrich *et al.*, 1995); 1.2 m^2 fine titanium dioxide/g lung tissue, with a 16 or 17% tumour incidence in

male and female rats versus 2 or 0% in male and female controls, respectively (Lee *et al.*, 1985a); and 0.27 m^2 talc/g lung tissue in female rats, with a 26% tumour incidence versus 2% in controls (National Toxicology Program, 1993). These comparisons show that the retained particle surface area dose in coal miners was lower—by a factor of approximately 2–70—than that associated with elevated incidences of lung tumours in rats exposed to either fine or ultrafine poorly soluble particles. Thus, using particle surface area as the dose metric, excess lung cancer would not necessarily be expected to be observed in coal miners given the relatively low particle surface area dose compared with that associated with lung tumours in rats.

These comparisons illustrate the importance of using normalized doses to compare responses across species. Furthermore, due to the faster clearance rate, rats do not attain lung burdens comparable with those observed in humans who work in dusty jobs (e.g. coal miners) unless they experience overloading of lung clearance.

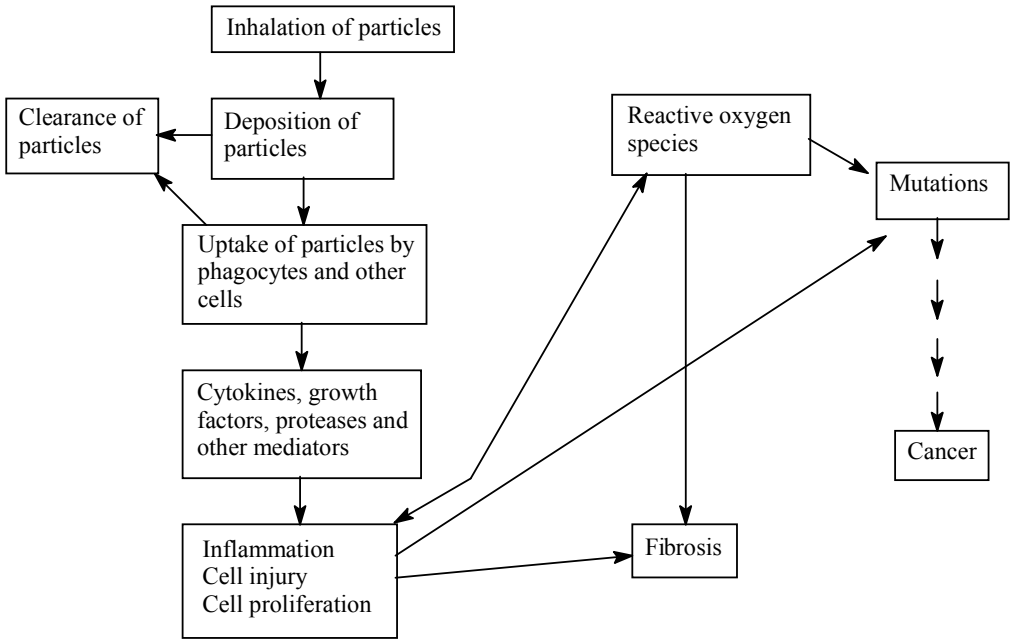
(c) Relevance of mechanistic data for assessing carcinogenic hazard in humans

To evaluate the appropriateness of the rat as an experimental model to assess the carcinogenic hazard of poorly soluble particles in the lungs of humans, it is useful to evaluate the scientific evidence that allows for comparisons among species regarding exposure, dose–response and mode of action. A conceptual framework is presented in Figure 4.1.

(i) *Exposure–dose*

Inhaled particles may present a hazard when they deposit in sufficient quantities (dose) and interact with cells/tissues at responsive target sites along the respiratory tract. The relationship between particle exposure and inhaled dose is described by the kinetics of particle deposition and clearance, and that retained at or within respiratory tract tissues (Section 4.1.2). Inhaled and deposited particles clear from the normal lungs of healthy rats at a faster rate than those from humans. However, at high lung burdens, normal clearance from the rat lung can be impaired and overwhelmed, such that in time clearance effectively ceases. This phenomenon (termed ‘overload’) is observed with particles that are poorly soluble and are generally considered to be of low toxicity (Morrow, 1988). Particle lung burdens observed in humans in some dusty jobs (e.g. coal miners) have sometimes approximated the overload dose in rats. At sufficient concentrations and durations of inhalation, rats may accumulate particles to a greater extent than the lung burdens seen in most workers. For ultrafine particles, the attained mass doses associated with impaired clearance in rodents approximate those that could occur in workers. For any experimental model used for hazard assessment in humans or to evaluate dose–response relationships, it is widely appreciated that it is important to evaluate doses in experimental animals that are comparable with those that may occur in humans.

Figure 4.1. Conceptual framework of carcinogenesis induced by poorly soluble particles in rats



The scheme represents the sequence of events and modes of action that are considered to be involved in the formation of tumours that are observed in the lungs of rats after high exposure to poorly soluble particles (from IARC, 2010b)

Lung clearance can be impaired in humans and experimental animals for many reasons. In humans, toxic gases and particles have been shown to impair clearance by affecting normal cilia function, mucus rheology and phagocytosis. Ultrafine particles may be cleared less effectively due to impaired phagocytosis compared with larger particles (Renwick *et al.*, 2001, 2004; Geiser *et al.*, 2005).

Much more is known about overload in rats than in humans. Overwhelmed or impaired clearance in rats has been postulated as a pivotal factor in the development of lung overload (Morrow, 1988). It is clear that the same factors that can interfere with clearance in rats may contribute to mass dose accumulation in humans (e.g. the cytotoxicity of the material and/or ineffective phagocytosis). Overload was originally described in terms of mass- or volume-based dose. For fine and ultrafine carbon black and titanium dioxide, surface area dose has been shown to be a better predictor of impaired clearance (Oberdörster & Yu, 1990; Oberdörster *et al.*, 1992; Oberdörster, 1996; Tran *et al.*, 1999).

Impaired clearance and overload are not unique to the rat, but can also occur in other species although to different degrees. For example, overload has not been observed in hamsters at concentrations at which it readily appears in rats and mice (Bermudez *et al.*,

2002, 2004; Elder *et al.*, 2005). How human lung clearance would behave under similar circumstances is unclear but, by analogy to coal workers, impairment of clearance does occur with chronic exposure and often persists long after exposure ceases (Freedman & Robinson, 1988).

Rats chronically exposed to sufficiently high concentrations of poorly soluble particles experience a steady reduction in their alveolar clearance rates and an accumulation of particles in the alveolar lumen and interstitium (Ferin *et al.*, 1992, 1994; Warheit *et al.*, 1997; Bermudez *et al.*, 2002, 2004). In rodents, ultrafine particles translocate to the interstitium to a greater extent than fine particles (Ferin *et al.*, 1992; Oberdörster, 1996). In studies that compare the patterns of particle retention in the lungs of rats, monkeys and humans exposed to coal dust and/or diesel exhaust, the largest volume percentage of dust was observed in the alveolar lumen in rats and in the interstitium of monkeys and humans (Nikula *et al.*, 1997a,b, 2001); however, no data were available to compare the actual retained doses in the specific lung regions of each species. The biological significance of the interstitial/lumenal distribution in the development of overload and the toxic sequelae is not clear, either within a given species or among species.

(ii) *Dose–response and mode of action*

With continued inhalation of high concentrations of particles, rats that achieve overload may develop pulmonary fibrosis and both benign and malignant tumours (Lee *et al.*, 1985a,b, 1986; Warheit *et al.*, 1997). Oberdörster (1996, 2002) has proposed that high-dose effects observed in rats may be associated with two thresholds: (i) a pulmonary dose that results in a reduced macrophage-mediated clearance leading to overload and (ii) a higher dose associated with overload at which normal antioxidant defences within the lung are overwhelmed and pulmonary tumours may be induced.

As discussed above, a cascade of events proposed to describe the biological process that starts with some particle deposition at critical target cells or tissues within the rat lung and results in rat lung tumours includes: sustained inflammation, production of reactive oxygen species, depletion of antioxidants and/or impairment of other defence mechanisms, cell proliferation and gene mutations. These individual steps comprise an overall mode of action that can be used to compare rat responses with those of other species including humans (see Figure 4.1).

At a particle mass lung burden at which overload is observed in the rat (estimated to begin at ~0.5 mg/g lung and to be fully developed at ~10 mg/g lung; Muhle *et al.*, 1990), a sustained and widespread cellular inflammatory response occurs. The degree of sustained inflammation experienced by rodents (most notably the rat) at high lung burdens is not observed in humans, although humans may experience sustained inflammation in certain disease states.

(iii) *Interspecies extrapolation*

Several studies have shown that rats, but not mice or hamsters, develop an excess incidence of lung cancer at chronic 'overloading' doses of inhaled poorly soluble particles. A number of studies have discussed this phenomenon and the challenges it poses for the extrapolation of chronic effects in rats to the human situation (Morrow, 1994; Levy, 1995; Oberdörster, 1995; Watson & Valberg, 1996; ILSI Risk Science Institute Workshop Participants, 2000; Miller, 2000; Oberdörster, 2002; Hext *et al.*, 2005).

Uncertainty remains with regard to the identification in detail of the cascade of events that lead to lung cancer in rats following inhalation of poorly soluble particles (i.e. talc, carbon black, titanium dioxide). However, as shown in Figure 4.1, a number of important steps can be identified that are supported by a substantial rodent database. An important question that needs to be addressed is the extent to which the steps outlined in Figure 4.1 for rat lung cancer are also operative in other animal species including humans. The majority of animal studies that have evaluated the effects of poorly soluble particles on the respiratory tract have been conducted in rats. It is necessary to consider species differences such as particle inhalability, breathing conditions, respiratory tract structure and pulmonary defences when extrapolating toxicological findings from rodents to humans (Brown *et al.*, 2005).

All animals species that are routinely used in particle toxicology, as well as humans, are susceptible to impairment of clearance of poorly soluble particles from the lungs. Impaired clearance is probably one of the first steps necessary to initiate a sequence of events that may lead to lung cancer in rats (see Figure 4.1). Importantly, however, different animal species exhibit differences in particle-induced impairment of clearance, which can result in different lung burdens (expressed as mass or surface area) following exposures to the same particle concentrations.

Similarly, pulmonary inflammation has been reported as a consequence of exposures to poorly soluble particles in both experimental animals and humans. The patho-physiology of particle-induced fibrosis in humans and fibrosis and lung cancer in rats from lung overload involves chronic inflammation, hyperplasia and cell proliferation, and altered collagen deposition and architecture.

Rats and mice, in contrast to hamsters, exhibit sustained inflammation associated with particle lung burden, but lung tumours induced by poorly soluble particles have been observed only in rats. It has been shown that the rat is uniquely susceptible to particle-induced lung cancer relative to the mouse and hamster. Although some of the steps indicated in Figure 4.1 have been demonstrated in humans exposed to poorly-soluble particles, it is not known to what extent humans are susceptible to particle-induced lung cancers.

4.2.3 *Genetic and related effects*

(a) Humans

(i) *Biomarkers of exposure (DNA adducts, cytogenetic effects and mutagenic activity)*

Biomarkers of exposure to mutagens

The presence of mutagenic PAH metabolites in urine, that of PAH–DNA adducts and the mutagenic activity of urine extracts or concentrates have been employed as biomarkers of human exposure to mutagenic substances in indoor air.

Significantly increased levels of urinary 1-hydroxypyrene were observed in Polish children who were exposed to emissions from indoor heating and cooking with coal-burning stoves in comparison with those exposed to emissions from other heating or cooking facilities (Siwińska *et al.*, 1999). Mumford *et al.* (1995) studied PAHs, hydroxy-PAHs and methylated PAHs in urine samples from smoking men and nonsmoking women in the Xuan Wei region of China who were exposed to unvented emissions from smoky coal. Controls were nonsmoking men and women from Kunming (China) and nonsmoking Chinese American women who used gas/electricity. The results indicated that the concentrations of 9-hydroxybenzo[*a*]pyrene were significantly ($p<0.05$) higher in Xuan Wei residents than in controls. The mean levels of methylated phenanthrene, pyrene and benz[*a*]anthracene in the urine of Xuan Wei men and women were 5.8- and 9.8-fold higher than those of the parent PAHs, respectively. The high urinary level of methylated PAHs is consistent with the high concentrations of methylated PAHs measured in smoky coal emissions.

Casale *et al.* (2001) used liquid chromatography/quadrupole ion-trap MS (LC/QMS) to detect the presence of the depurinated benzo[*a*]pyrene-adducted DNA bases, 7-(benzo[*a*]pyren-6-yl)guanine and 7-(benzo[*a*]pyren-6-yl)adenine, in urine samples from three of seven women exposed to smoky coal emissions in the Xuan Wei region. These adducts were not detected in 13 control subjects. Depurinating benzo[*a*]pyrene adducts profile were correlated with the profile of G→T transversions observed in the *P53* gene of human lung tumours.

A supportive occupational study by Kato *et al.* (2004) monitored urinary mutagenicity and excretion of urinary metabolites (i.e. 2-naphthol and 1-pyrenol) in Brazilian charcoal workers exposed to high levels of eucalyptus wood smoke. The results showed markedly enhanced levels of urinary mutagenicity (odds ratio, 5.31; 95% CI, 1.85–15.27) and metabolite excretion (odds ratio, 17.13; 95% CI, 6.91–42.44) in the highly exposed kiln tenders in comparison with unexposed tree cutters.

Cytogenetic effects (sister chromatid exchange, micronucleus formation and chromosomal aberrations)

Cytogenetic effects such as sister chromatid exchange, micronuclei and chromosomal aberrations have been documented in studies that examined the genotoxic effects of human exposure to indoor combustion emissions.

Biomass combustion (including wood)

Öztürk *et al.* (2002) investigated the frequency of sister chromatid exchange in peripheral blood lymphocytes from 20 patients who experienced acute carbon monoxide intoxication from exposure to indoor wood or coal combustion emissions. They found significantly higher levels of sister chromatid exchange frequency (p=0.008) in the exposed group (8.1±2.4 per metaphase) compared with 20 healthy controls (6.3±1.6 per metaphase). Musthapa *et al.* (2004) investigated cytogenetic effects in 179 Indian women exposed to cooking emissions generated using various biofuels, including cow dung, cow dung/wood combinations, wood and kerosene. Because it was difficult to find suitable controls with no exposure to cooking fuel smoke, users of LPG were used as a control group because LPG generates comparatively low levels of smoke and respirable airborne particulates. Micronucleus formation in human blood lymphocytes in women burning cow dung (30.0±3.6 micronucleated cells/1000 binucleates), cow dung/wood (26.2±3.1) or wood (22.9±4.0) was significantly higher (p<0.05) than that in LPG users (10.3±2.7). Analyses of the frequency of chromosomal aberrations showed a similar trend (i.e. cow dung [10.8%] > cow dung/wood [8.2%] > wood [7.0%] > LPG [3.1%]; p<0.05 versus LPG users).

Coal combustion

Analyses of the peripheral blood lymphocytes of 184 villagers from Guizhou province, China (Zhang *et al.* 2007), where arsenism linked to indoor exposure to coal combustion emissions is endemic, showed significantly higher levels of sister chromatid exchange, chromosomal aberrations and micronucleus formation compared with those of 53 villagers who did not use coal containing high levels of arsenic.

DNA adducts and DNA–protein cross-links

Coal combustion

Levels of DNA adducts have been employed as a sensitive biomarker of internal dose and DNA damage in tissues from Xuan Wei women exposed to emissions from the indoor combustion of smoky coal.

A study of DNA adduct levels and profile (by ^{32}P-postlabelling) in placenta, blood and lung cells of Xuan Wei residents exposed to unvented indoor emissions from smoky coal failed to show significant increases in either placental or white blood cell DNA adducts, compared with controls from Kunming who used electricity/gas. However, levels of DNA adducts in lung BAL cells from coal smoke-exposed individuals (n=24) were fourfold higher (25.5 adducts/10^8 bases) than in those from unexposed individuals

(5.9 adducts/10^8 bases; n=8) (Gallagher *et al.*, 1993). Similarly, much higher levels of PAH–DNA adducts were found in brush cells from fibrobronchoscopies of 30 lung cancer patients from Xuan Wei exposed to coal smoke compared with those of 10 controls from Kunming with no exposure to coal smoke. The authors suggest that the relatively high levels of DNA adducts in lung cells indicates that the respiratory tract is the target tissue for exposure to emissions from smoky coal (Xu *et al.*, 1997). Moreover, enzyme-linked immunosorbent assay (ELISA) measurements in placentas and peripheral and cord white blood cells from Xuan Wei women exposed to emissions from smoky coal showed higher levels of DNA adducts in placentas and peripheral white blood cells in comparison with Beijing residents exposed to natural gas combustion emissions (Mumford *et al.*, 1993).

Sensitive analytical techniques such as LCQ/MS and capillary electrophoresis with laser-induced fluorescence detection have also been applied to assess the levels of benzo[*a*]pyrene-adducted DNA bases in urine samples from women in Xuan Wei exposed to coal smoke. The results showed high levels of the benzo[*a*]pyrene-adducted DNA base 7-(benzo[*a*]pyren-6-yl)guanine, which were about 20–300-fold greater than those of 7-(benzo[*a*]pyren-6-yl)adenine. The authors suggested that the presence of benzo[*a*]pyrene-adducted DNA bases in urine could be a promising biomarker for enhanced cancer risk linked to chronic indoor exposures to PAHs (Casale *et al.*, 2001). In addition, Zhang *et al.* (2000, 2007) reported that exposure to coal combustion emissions is associated with increased levels of DNA–protein cross-links and unscheduled DNA synthesis in peripheral blood lymphocytes. However, the authors concluded that the observed DNA damage was probably due to exposure to arsenic in coal emissions.

Wood combustion

Reddy *et al.* (1990) reported that residential wood combustion in the USA did not increase the level of aromatic DNA adducts (measured by ^{32}P-postlabelling) in 12 DNA samples of white blood cells or placentas from nonsmoking women, but tissue-specific endogenous adducts were observed. [The Working Group noted that this lack of enhanced DNA adduct levels in human blood cells may suggest that the exposure dose was low and/or duration was short.] A similar Dutch study failed to show increased levels of aromatic DNA adducts in white blood cells in five individuals from homes where residential wood combustion occurred, despite the fact that indoor air monitoring showed that wood combustion in an open fireplace increased the mutagenicity of indoor air samples in the *Salmonella* TA98 strain, as well as the benzo[*a*]pyrene and pyrene concentrations (Heussen *et al.*, 1994). However, competitive fluorescence ELISA did reveal enhanced levels of DNA adducts in 56% (9/16) of the placental samples from Xuan Wei women who used wood as cooking fuel compared with 25% (4/16) of the samples from Beijing women who used natural gas (Mumford *et al.*, 1993).

(ii) Mutations in TP53 and KRAS, and P53 protein accumulation

Mutation spectrum analyses

Coal combustion

DeMarini *et al.* (2001) investigated the spectrum of *P53* and *KRAS* mutations in lung tumours associated with smoky coal combustion among Xuan Wei residents. The results clearly showed that GC→TA transversions were the predominant mutation for both *KRAS* (86%) and *P53* (76%), which is consistent with the mutation spectrum induced by exposures to PAHs. Moreover, Keohavong *et al.* (2003) compared the *KRAS* mutations in lung carcinomas from 41 nonsmoking women and 61 smoking men exposed to smoky coal in Xuan Wei and found that 67 and 86% of the *KRAS* mutations were GC→TA transversions, respectively. When analysed by Granville *et al.* (2003) using the *Salmonella* mutagenicity assay, PAH-rich extracts of smoky coal combustion emissions from Xuan Wei showed enhanced potency (more than threefold) in the base-pair mutation strain TA100 in comparison with the frameshift mutation strain TA98. In addition, the mutagenic activity in strain TA100 was enhanced (8.7-fold) in the presence of an Aroclor 1254-induced postmitochondrial supernatant from male rat liver. Furthermore, investigations of the mutation spectra of smoky coal combustion emissions in strain TA100 also showed that the mutations were primarily (78–86%) GC→TA transversions. Because of the similarity between the mutation spectrum observed in lung tumours linked epidemiologically with exposures to smoky coal emissions (i.e. GC→TA transversions) and that observed in strain TA100 following exposure to PAH-rich extracts of smoky coal emissions, the authors suggested that the high concentration of PAHs in smoky coal emissions plays a critical role in the induction of mutations and lung tumours.

In a later study of 15 Xuan Wei women who had lung cancer, Keohavong *et al.* (2004) used a laser capture micro-dissection method to isolate epithelial cells from sputum samples and to score *P53* and *KRAS* mutations. The results confirmed *P53* and/or *KRAS* mutations in sputum cells from seven patients (five patients with *KRAS* mutation, one with *P53* mutation, one with *KRAS* and *P53* mutations). This method proved to be more sensitive than earlier, more conventional methods that detected mutations in only two of the 15 samples. This sensitive method has also been applied by Keohavong *et al.* (2005) to screen for *P53* and *KRAS* mutations in sputum samples from 92 Xuan Wei individuals with no evidence of lung cancer. Cells from 13 individuals (14.1%) showed mutations in *P53*, cells from one individual showed a mutation in *KRAS* and one individual showed mutations in both. Mutation spectrum analyses again showed that GC→TA transversions (71%) were the predominant type of mutation in the epithelial cells collected. The high frequency of *P53* mutations and, in particular, the high proportion GC→TA transversions in cells from sputum are consistent with exposure to PAH-rich emissions from smoky coal. Moreover, the authors suggested that the prevalence of *P53* mutations in sputum cells might be a useful biomarker of risk for lung cancer.

P53 protein accumulation

Coal and wood combustion

Using an immunofluorescent assay, accumulation of P53 protein was observed in nine of 16 tumour cell samples obtained from the sputum of Xuan Wei lung cancer patients (nine smoking men and seven nonsmoking women) who had a history of exposure to emissions from smoky coal combustion. In contrast, none of the sputum samples from 17 healthy Xuan Wei residents also exposed to smoky coal emissions showed P53 accumulation (Feng *et al.*, 1999). A population-based case–control study in Xuan Wei County confirmed that more frequent use of smoky coal is associated with a higher incidence of lung cancer. Moreover, the associations were stronger when the analyses were restricted to female Xuan Wei residents (almost all of whom were nonsmokers) who were exposed to high levels of smoky coal emissions and who showed overexpression and accumulation of P53 protein in exfoliated tumour cells isolated from sputum samples (Lan *et al.*, 2001).

Other epidemiological studies showed elevated levels of several proteins, including P53, RAS, NEU [HER2] and murine double minute 2 (MDM2), in cancer patients exposed to emissions from wood or coal combustion. For example, Li *et al.* (1997) found significantly higher serum concentrations of RAS, P53 and NEU proteins in 19 lung cancer patients who were exposed to emissions from coal burning, relative to 19 unexposed cases without lung cancer. Delgado *et al.* (2005) studied lung cancer associated with exposure to wood smoke and used western blot analyses to demonstrate a significant increase in P53, phosphorylated-P53 and MDM2 proteins in plasma samples from 24 lung cancer patients with a history of exposure to domestic wood smoke in comparison with nine smokers who had chronic obstructive pulmonary disorder and nine healthy control volunteers with no exposure to wood smoke. Hu *et al.* (2001) used immunohistochemical techniques to show significantly elevated ($p<0.01$) levels of mutated P53 protein in 18 skin carcinoma patients with arseniasis caused by coal burning in comparison with 11 patients who presented precancerous lesions or 39 controls.

(b) Experimental systems

(i) *In-vivo systems*

Coal combustion

An inhalation study in Kunming mice (Lin *et al.*, 1995) showed that all 13 lung tumours induced by samples of coal smoke showed overexpression of *p53*, and nine of the 13 tumours showed c-*myc* over-expression whereas no *p53* or c-*myc* expression was detected in control animals.

(ii) *In-vitro systems*

Coal combustion

Several types of mammalian cell have been employed to assess the genotoxicity of combustion emissions in the indoor environment. Qin *et al.* (1985) reported a concentration-dependent increase in sister chromatid exchange frequency in Chinese hamster ovary (CHO) cells exposed, in both the presence and absence of metabolic activation, to organic extracts of respirable indoor particulates (<10 μm) from homes where coal or wood were burned. The results showed significant induction of sister chromatid exchange but no significant difference in genotoxic potency between particles from homes where coal or wood were burned (Qin *et al.*, 1985). Significant morphological transformation, including random or criss-cross orientations and dense piling of cells, have been observed in diploid Syrian hamster embryo cells exposed to extracts of coal smoke (Zhang *et al.*, 1989). Yu *et al.* (1993) studied the indoor air particle size distribution and size-associated mutagenic and carcinogenic activity of samples collected in Xuan Wei homes that used smoky coal. Particles were divided into five fractions (>7.0 μm, 3.3–7.0 μm, 2.0–<3.3 μm, 1.1–<2 μm and <1.1 μm), and the finest fraction accounted for 61% of the total mass and 73% of the total extractable organic compounds. The finest particles (<1.1 μm) had the greatest mutagenic potency in *Salmonella* (3248 revertants/m^3 with and 1085 revertants/m^3 without metabolic activation, which accounted for 62 and 77%, respectively, of the total mutagenic activity). Analyses of CHO cells showed a dose-related increase in sister chromatid exchange frequency, with similar responses observed for all size fractions. Nevertheless, the finest particles yielded the highest frequency of sister chromatid exchange when expressed per cubic metre of sampled air. The authors suggested that the mutagenic potency of particles in coal smoke are inversely related to particle size.

Biomass combustion (including wood)

Hytönen *et al.* (1983) reported that the emissions from an airtight residential wood stove induced a dose-related increase in sister chromatid exchange frequency in CHO cells exposed both in the presence and absence of exogenous metabolic activation. The response was highest without metabolic activation. Wood smoke samples generated under air-starved conditions were an order of magnitude more potent than those generated under standard conditions. Salomaa *et al.* (1985) investigated the genotoxicity of smoke emissions collected from a residential wood stove and showed that organic extracts of both the particle (i.e. collected on a filter) and vapour phases (i.e. adsorbed on to XAD-2 resin) significantly increased sister chromatid exchange frequency in CHO cells in a concentration-related manner. A significant positive response was obtained in the absence of exogenous metabolic activation, and the response increased in the presence of exogenous metabolic activation. Chemical fractionation of the organic extracts demonstrated that the most potent genotoxic activity was present in the non-polar, PAH-containing fraction. Moreover, the authors noted that the potency of the extracts of wood

combustion emissions, in terms of their ability to induce sister chromatid exchange in CHO cells, was comparable with that of cigarette-smoke condensate. A similar study by Alfheim *et al.* (1984a) noted that organic extracts of both the particle and vapour phases significantly increased the frequency of sister chromatid exchange in CHO cells. The polar fraction, which would be expected to contain compounds such as aza-arenes and aromatic ketones, and the non-polar fraction were the most active. The authors also noted the same pattern of activity in the Syrian hamster embryo cell transformation assay. Leonard *et al.* (2000) have shown that wood smoke is able to generate stable carbon-centred radicals as well as reactive hydroxyl radicals in the presence of hydrogen peroxide. These reactive species are known to induce cellular toxicity via lipid peroxidation and DNA damage, and the authors also showed that these wood smoke emissions induced DNA damage (as measured by the comet assay) and lipid peroxidation in RAW 264.7 mouse macrophage cells.

Karlsson *et al.* (2006) showed induction of DNA damage (comet assay) in cultured human lung carcinoma AS49 cells after exposure to wood combustion particles.

(iii) Salmonella *reverse-mutation assay*

Numerous studies have used the *Salmonella* reverse mutation assay to assess the mutagenic activity of indoor air samples and/or source-specific samples of emissions from the combustion of coal or biomass-derived fuels. Moreover, enhanced levels of indoor air mutagenicity have been associated with an enhanced risk for lung cancer, particularly in indoor environments contaminated by unvented coal combustion emissions, such as in Xuan Wei County (Mumford *et al.*, 1987a,b). Early studies, such as that by Lioy *et al.* (1985), showed that, although the organic extracts of indoor air particulates elicit a significant positive response in the *Salmonella* mutagenicity assay, the exact source(s) of the mutagenic activity could not be identified. Subsequently, a wide range of source-specific studies has confirmed the *Salmonella* mutagenic activity of emissions from smoky coal combustion (e.g. Mumford *et al.*, 1987a,b) and wood/biomass combustion (e.g. Alfheim *et al.*, 1984a; van Houdt *et al.*, 1986, 1989; Bell *et al.*, 1990; Asita *et al.*, 1991; Heussen *et al.*, 1994), and highlighted that these sources are significant contributors to the mutagenic activity of indoor air. Moreover, several studies have noted a positive empirical relationship between the *Salmonella* mutagenic activity of indoor air (in revertants/m^3) and the concentration of airborne PM (Mumford *et al.*, 1987b). This relationship is logical because combustion emissions are composed of PM, and several researchers (e.g. Maertens *et al.*, 2004, 2008) have commented on the tendency for mutagens in combustion emissions, such as PAHs, to adsorb onto particulate material and solid surfaces (e.g. upholstery, carpets). Analyses of indoor areas contaminated with coal combustion emissions have noted PM concentrations as high as 39 mg/m^3 (Mumford *et al.*, 1987b). Much lower particle concentrations have been recorded in indoor environments contaminated with emissions from wood combustion (Sexton *et al.*, 1984).

Table 4.1 provides a summary of some studies that have used the *Salmonella* mutagenicity assay to investigate the mutagenic activity of indoor air particulates from

biomass, coal and wood combustion. The data indicate that organic extracts of indoor air particulate material collected from areas with no obvious source of combustion have *Salmonella* mutagenic potency values in the range of 1–10 TA98 revertants/m^3 (e.g. Heussen *et al.*, 1994; Nardini *et al.*, 1994). Table 4.2 provides a summary of some studies that investigated the mutagenic potency of organic extracts of source-specific particulate emissions from wood/biomass and coal combustion.

The highest reported mutagenic potency values (5.9×10^4 TA98 revertants/m^3 and 3120 TA98 revertants/mg of particle with metabolic activation) correspond to indoor environments contaminated with emissions from unvented smoky coal combustion (Mumford *et al.*, 1987a; Nakanishi *et al.*, 1997). The enhanced mutagenic activity in the presence of exogenous metabolic activation is consistent with the supposition that PAHs from unvented smoky coal combustion are responsible for much of the mutagenic activity. The most mutagenic sources, in terms of TA98 potency with metabolic activation, also included emissions from wood combustion. The highest reported mutagenic potency in the presence of exogenous metabolic activation was 1.1×10^4 TA98 revertants/m^3 and 4700 revertants/mg of particle (Mumford *et al.*, 1987a; Ramdahl *et al.*, 1982).

[On average, smoky coal emissions are five times or 10 times more mutagenic than those from wood in terms of activity per miligram of particle or activity per cubic metre of air, respectively.]

Bioassay-directed fractionation studies have frequently been employed to determine the identity and/or physicochemical properties of the putative mutagens in complex extracts of indoor air PM and emissions from the combustion of selected solid fuels. Numerous studies in the Xuan Wei region of China have revealed that PAHs and alkylated PAHs are the major *Salmonella* mutagens in smoky coal emissions and smoky coal-contaminated indoor air, which again suggests that these compounds probably play a critical role in the enhanced frequency of lung cancer observed in Xuan Wei women (Chuang *et al.*, 1992a,b). However, substantial levels of direct-acting mutagenic activity support the hypothesis that the mutagenic activity of smoky coal emissions cannot be accounted for by PAHs alone. Bioassay-directed fractionation analyses of emissions from wood combustion indicate that there are several sources of mutagenic activity. Several studies have noted that a substantial, albeit variable, portion of the metabolically activated mutagenic activity (approximately 10–50%) can be attributed to PAHs, or PAH-containing non-polar neutral fractions (Alfheim *et al.*, 1984a,b; Kamens *et al.*, 1985; Bell *et al.*, 1990). Variability in the fraction of metabolically activated mutagenic activity that can be attributed to PAHs and PAH derivatives is consistent with studies that have noted a relationship between wood types or burning conditions and the emission rate of genotoxic PAHs (Zou *et al.*, 2003). In addition, several studies have highlighted the involvement of polar compounds in the determination of the level of direct-acting mutagenic activity of extracts of wood combustion particulates. Kamens *et al.* (1985) noted that chemical fractions containing compounds with the polarity of aromatic ketones could explain 4% of the total direct-acting mutagenic activity of wood smoke emission

Table 4.1. *Salmonella* mutagenicity of organic extracts of indoor air particulate matter from biomass, coal and wood combustion

Indoor activity	Source	Country	Particle concentration ($\mu g/m^3$)	Mutagenic potency (revertants/m^3)		Reference
				Without metabolic activation	With metabolic activation	
TA98						
Coal combustion	Charcoal	Italy	1300	1601	1155	Nardini *et al.* (1994)
Coal combustion	Smoky coal	China	24 400	ND	58 900	Mumford *et al.* (1987a)
Coal combustion	Smoky coal	China	9500	ND	17 000	Mumford *et al.* (1987a)
Coal combustion	Smokeless coal	China	1100	ND	1300	Mumford *et al.* (1987a)
Wood combustion	Wood	Italy	2800	736	667	Nardini *et al.* (1994)
Open fireplace	Wood	Norway	US	53	100	Alfheim & Ramdahl (1984)
Open fireplace	Wood	Norway	US	48	150	Alfheim & Ramdahl (1984)
Wood combustion	Wood	Netherlands	39.3	4	16	Heussen *et al.* (1994)
Wood combustion	Wood	Netherlands	38.8	5	12	Heussen *et al.* (1994)
Wood combustion	Wood	Netherlands	47.6	6	13	Heussen *et al.* (1994)
Wood combustion	Wood	Netherlands	38.9	7	12	Heussen *et al.* (1994)
Wood combustion	Wood	Netherlands	US	13	21	van Houdt *et al.* (1986)
Wood combustion	Wood	Netherlands	US	6	14	van Houdt *et al.* (1986)
Wood combustion	Wood	Netherlands	US	7	23	van Houdt *et al.* (1986)
Wood combustion	Wood	Netherlands	US	71	96	van Houdt *et al.* (1986)
Wood combustion	Wood	China	22 300	ND	11 000	Mumford *et al.* (1987a)
TA100						
Open fireplace	Wood	Norway	US	200	50	Alfheim & Ramdahl (1984)
Open fireplace	Wood	Norway	US	200	60	Alfheim & Ramdahl (1984)

ND, no data; US, unspecified

Table 4.2. *Salmonella* mutagenicity of organic extracts of particulate emissions from biomass, coal and wood combustion

Indoor activity	Source	Country	Particle concentration ($\mu g/m^3$)	Mutagenic potency (revertants/mg)		Reference
				Without metabolic activation	With metabolic activation	
TA98						
Biomass combustion	Dried cow dung	USA, Hawaii	~30	40	630	Bell & Kamens (1990)
Biomass combustion	Coconut shell	USA, Hawaii	~30	1560	1580	Bell & Kamens (1990)
Biomass combustion	Dried cow dung	India	~30	280	1000	Bell & Kamens (1990)
Biomass combustion	Crop residue	India	~30	40	280	Bell & Kamens (1990)
Biomass combustion	Peat	US	~30	250	380	Bell & Kamens (1990)
Wood combustion	Pine	US	~30	480	1200	Bell & Kamens (1990)
Wood combustion	Red oak	US	~30	90	810	Bell & Kamens (1990)
Wood combustion	Wood	Italy	2800	254	215	Nardini *et al.* (1994)
Wood combustion	White mangrove	Japan	US	ND	150	Asita *et al.* (1991)
Wood combustion	Red mangrove	Japan	US	ND	300	Asita *et al.* (1991)
Wood combustion	Mahogany	Japan	US	ND	100	Asita *et al.* (1991)
Wood combustion	Abura	Japan	US	ND	140	Asita *et al.* (1991)
Wood combustion	Alstonia	Japan	US	ND	250	Asita *et al.* (1991)
Wood combustion	Black afara	Japan	US	ND	140	Asita *et al.* (1991)
Wood combustion	Ponderosa Pine	USA	US	140	380	Dasch (1982)
Wood combustion	Willow	USA	US	67	1500	Dasch (1982)
Wood combustion	Hickory	USA	US	100	1100	Dasch (1982)
Wood combustion	Hickory (impinger)	USA	US	160	56	Dasch (1982)
Wood combustion	Synthetic log	USA	US	670	240	Dasch (1982)
Wood combustion	Pine	USA	US	290	1300	Lewtas (1982)
Wood combustion	Oak	USA	US	150	900	Lewtas (1982)
Wood combustion	Birch	Norway	US	4700	4700	Ramdahl *et al.* (1982)
Wood combustion	Spruce	Norway	US	900	1800	Ramdahl *et al.* (1982)
Coal combustion	Charcoal	Norway	US	14	6	Ramdahl *et al.* (1982)
Coal combustion	Charcoal	Italy	1300	982	795	Nardini *et al.* (1994)
Coal combustion	Coke	USA	US	ND	1200	Lewtas (1982)
Coal combustion	Coal	China	US	635	1810	Yu *et al.* (1993)
Coal combustion	Smoky coal	China	US	1280	3120	Nakanishi *et al.* (1997)

Table 4.2 (Contd)

Indoor activity	Source	Country	Particle concentration ($\mu g/m^3$)	Mutagenic potency (revertants/mg)		Reference
				Without metabolic activation	With metabolic activation	
TA98 (contd)						
Coal combustion	Smoky coal	China	US	240	390	Nakanishi *et al.* (1997)
Coal combustion	Smoky coal	China	US	240	410	Nakanishi *et al.* (1997)
Coal combustion	Coalite	China	US	120	210	Nakanishi *et al.* (1997)
Coal combustion	Smokeless coal	China	US	150	270	Nakanishi *et al.* (1997)
TA98NR						
Wood combustion	Wood	Italy	2800	227	ND	Nardini *et al.* (1994)
Coal combustion	Charcoal	Italy	1300	1024	ND	Nardini *et al.* (1994)
YG1024						
Coal combustion	Coal	China	US	6200	ND	Taga *et al.* (2005)
TA100						
Biomass combustion	Dried cow dung	USA	~30	20	150	Bell & Kamens (1990)
Biomass combustion	Coconut shell	USA	~30	2610	830	Bell & Kamens (1990)
Biomass combustion	Dried cow dung	India	~30	630	910	Bell & Kamens (1990)
Biomass combustion	Crop residue	India	~30	120	420	Bell & Kamens (1990)
Wood combustion	White mangrove	Japan	US	ND	300	Asita *et al.* (1991)
Wood combustion	Red mangrove	Japan	US	ND	560	Asita *et al.* (1991)
Wood combustion	Abura	Japan	US	240	250	Asita *et al.* (1991)
Wood combustion	Alstonia	Japan	US	ND	900	Asita *et al.* (1991)
Wood combustion	Black Afara	Japan	US	ND	310	Asita *et al.* (1991)
Wood combustion	Red oak	USA	~30	210	310	Bell & Kamens (1990)

ND, no data; US, unspecified

extracts. Bell *et al.* (1990) noted that the polar acidic fractions of organic wood-smoke extracts (phenolic compounds) could account for 28% of the direct-acting mutagenic activity. Alfheim *et al.* (1984a,b) noted that the direct-acting mutagenic activity of an organic extract of particulate material collected from the combustion of a spruce/birch mixture was predominantly contained in the most polar chemical fractions. The authors suggested that the putative mutagens include aza-arenes (aromatic amines) and/or nitroarenes, and the involvement of nitroarenes was confirmed by assays performed with the nitroreductase-deficient strains of *Salmonella* which showed a clear mutagenicity reduction.

4.3 Genetic susceptibility

4.3.1 *Polymorphisms in carcinogen-metabolizing genes*

Carcinogenic PAHs are formed during incomplete combustion of carbon-based fuels such as coal, wood and biomass. Numerous phase I and phase II enzymes are involved in the metabolic activation and detoxification of PAHs. Genetic variation in the enzymes responsible for activating and detoxifying PAHs or other carcinogens present in these environments may confer susceptibility to individuals exposed to coal, wood and biomass smoke, as well as to cooking oil fumes, and could result in significant interindividual differences in risk at the same level of exposure (Table 4.3).

Most studies of cancer and the above-mentioned exposures have focused on lung cancer, whereas a few have studied cervical and oesophageal cancer. Of these, only a few have evaluated genetic variants and performed a quantitative or semi-quantitative exposure assessment. The main focus of genetic studies has been on analysis of variants in phase I and phase II genes that play a key role in metabolizing PAHs, although other chemicals can serve as substrates for these enzymes. Studies are included in this review if indoor air pollution was shown previously to play an important role in the etiology of cancer in the study population, if subgroups of the population were identified who were exposed to indoor air pollution or if genetic risk factors were studied among nonsmokers in a population thought to have potential exposure to indoor air pollution, even if exposure assessment was not carried out in the reported study. Studies in which tobacco smoke was thought to be the primary cause of lung cancer in the study population were excluded if no analyses were presented among subgroups exposed to some measure of indoor air pollution, or if no analyses were presented among nonsmokers with some potential for exposure to indoor air pollution.

The association between *CYP1A1* and *GSTM1* polymorphisms and lung cancer was evaluated in urban Shenyang, China, in a population-based case–control study of 200 female cases and 144 female age-matched controls (Yang *et al.*, 2004). An excess incidence of lung cancer had been found in this region previously and was linked to indoor

Table 4.3. Polymorphisms of genes involved in metabolism and exposure to indoor cooking and heating with coal, wood and biomass in relation to risk for lung cancer

Reference	Gene	Mutation/allele	Country	No. of cases/ controls	Odds ratio (95% CI)	Comments
Yang *et al.* (2004)	*CYP1A1*	Exon 7 Ile462Val	China	200/144	S: Ile/Val vs Ile/Ile, 2.7 (1.7–4.3) NS: Val/Val vs Ile/Ile, 1.7 (0.6–4.6)	All cases and controls were women, 55% of cases and 37% of controls were ever smokers
	GSTM1	Gene deletion			NS: *GSTM1* null	S: Combination of *CYP1A1* variant heterozygous or homozygous carrier (Val) and *GSTM1* null
Lan *et al.* (2000)	*GSTM1*	Gene deletion	Xuan Wei County, China	122/122	S: *GSTM1* null, 2.3 (1.3–4.2)	S: Interaction between smoky coal use and *GSTM1* null genotype (p=0.05), study subjects were farmers
	GSTT1	Gene deletion			NS: *GSTT1* null	
Malats *et al.* (2000)	*GSTM1*	Gene deletion	Brazil, France, Germany, Italy, Poland, Romania, Russia and Sweden	122/121	NS: *GSTM1* null, 1.5 (0.9–2.7)	All study subjects were nonsmokers; 86% of cases and 72% of controls were women
	GSTT1	Gene deletion			NS: *GSTT1* null	

Table 4.3 (contd)

Reference	Gene	Mutation/allele	Country	No. of cases/ controls	Odds ratio (95% CI)	Comments
Chan-Yeung *et al.* (2004)	*GSTM1*	Gene deletion	China, Hong Kong SAR		NS: *GSTM1* null	Study subjects were potentially exposed to indoor pollution due to cooking and heating; 57% of cases and 40% of controls were smokers
	GSTT1	Gene deletion			S: *GSTT1* null, 1.7 (1.1–2.6)	
Chen *et al.* (2006)	*GSTM1*	Gene deletion	Hunan Province, China	97/197	S: *GSTT1* null, 2.0 (1.2–3.2)	All study subjects were nonsmokers, with potential indoor air pollution exposure; no exposure assessment performed
	GSTT1	Gene deletion			S: *GSTT1* null, 2.1 (1.3–3.4)	
	GSTP1	Wild-type Ile			NS: Variant GSTP1 Val vs wild-type Ile	
	NAT2	Rapid acetylator			NS: rapid vs slow acetylators	S: Any two or three 'at risk' genotype combination of *GSTM1* null, *GSTT1* null, *GSTP1* (Val); all four 'at risk' genotypes combined (all three *GST*s, *NAT2* rapid acetylator)

Table 4.3 (contd)

Reference	Gene	Mutation/allele	Country	No. of cases/ controls	Odds ratio (95% CI)	Comments
Lan *et al.* (2004)	*AKR1C3*	Gln5Gln	Xuan Wei County, China	119/113	NS: Gln5Gln vs His/His+His/Gln, 1.8 (1.0–3.5); S: female HSCU, 13.0 (2.2–107.8); NS: male HSCU	Only 4 or 5 subjects in some of the cells in stratified analysis; test for interaction with smoky coal use was not significant
	MnSOD	Val/Ala or Ala/Ala			NS: Val/Ala or Ala/Ala vs Val/Val	
	NQO1	Pro/Ser or Ser/Ser			NS: Pro/Ser or Ser/Ser vs Pro/Pro	
Pisani *et al.* (2006)	*CYP1A1*	Exon 7 Ile462Val or *2C; MspI RFLP or *2A	Thailand	211/211	NS: *CYP1A1**2A and *2C	93% cases and 81% controls were smokers; no indoor air pollution exposure assessment
	GSTM1	Gene deletion			NS: *GSTM1* null	

Table 4.3 (contd)

Reference	Gene	Mutation/allele	Country	No. of cases/ controls	Odds ratio (95% CI)	Comments
Shen *et al.* (2005a)	*CBS*	Ex12+41 CC, IVS3-1489AA, Ex8+33CT	Xuan Wei County, China	119/113	S: Ex12+41, TC vs TT, 4.3 (1.7–10.9), CC vs TT, 2.0 (1.1–3.6); NS: IVS3-1489AA or Ex8+33CT	S: Smoky coal use <130 tons, CC vs TT, 7.9 (2.1–29.2); only 5 controls carried CC genotype for subjects that used < 130 tonnes of smoky coal, test for interaction was not significant
	MTHFR	Ala222Val, Ala429Glu			S: Ala/Val vs Ala/Ala, 2.6 (1.4–4.8), Ala/Val+Val/Val, 2.5 (1.4–4.4); NS: Ala429Glu	
	SLC19A1	Ex4-254CC, Ex7-233TT			S: Ex4-254, CC vs TT, 2.1 (1.0–4.5); NS: Ex7-233TT	S: Coal use <130 tonnes, TC vs TT, 4.6 (1.7–12.6), CC vs TT, 3.3 (1.1–9.8); test for interaction with smoky coal use, p=0.03

CI, confidence interval; HSCU, heavy smoky coal user; NS, not significant; S, significant

coal use (Xu *et al.*, 1991). Genotyping was performed via the Taqman® assay, and the *CYP1A1* genotype was in Hardy-Weinberg equilibrium for controls. The frequencies of *CYP1A1* Val 462Val were 5.6% and 4.8% for cases and controls, respectively. There was a significant increased risk for lung cancer for the variant *CYP1A1* 462Val genotypes (odds ratio, 2.5; 95% CI, 1.6–4.0) compared with *CYP1A1* Ile462Ile, when adjusted for age, ever-smoking status, family history of cancer and eye irritation when cooking (an indication of indoor air pollution). Stratification by smoking status yielded significant results only among the nonsmokers (odds ratio, 3.7; 95% CI, 1.9–7.3), although a test of multiplicative interaction was not significant (p=0.13). This study did not find any association with the *GSTM1* null genotype (58% in cases and 54% in controls) (odds ratio, 1.2; 95% CI, 0.8–1.8) and risk for lung cancer or a significant interaction between *CYP1A1* Ile462Val and *GSTM1* null genotypes. No interaction was demonstrated between the indoor air pollution index and genotype.

The *CYP1A1* and *GSTM1* genotypes were also studied in a case–control study of 211 lung cancer cases and two sets of controls, one that was recruited from the resident population (n=197) and a second group of patients who were admitted to the hospital for diseases predominantly unrelated to tobacco smoking (n=211) in Lampang, Thailand (Pisani *et al.*, 2006). Controls were frequency-matched to cases by gender and age. Genotyping was performed by polymerase chain reaction (PCR) methodology. The two *CYP1A1* single nucleotide polymorphisms rs1048943 (also called *CYP1A1**2C or *CYP1A1*-Ile462Val) and rs4646903 (also called *CYP1A1**2A or *CYP1A1* MspI) studied were in Hardy-Weinberg equilibrium for controls. An index of exposure to domestic fumes (total years spent using coal or wood) was derived from the type of fuel used (coal or wood versus none, gas or electricity), indoor or outdoor cooking and the number of years lived in the particular exposure environments. Exposure to domestic fumes was not associated with an increased risk for lung cancer. This study found no association between lung cancer and the *CYP1A1**2C (odds ratio for variant homozygous, 0.8; 95% CI, 0.3–1.7) or *CYP1A1**2A (odds ratio for variant homozygous, 1.5; 95% CI, 0.8–2.7), or the *GSTM1* null (odds ratio, 0.8; 95% CI, 0.5–1.2) genotypes when adjusting for gender, age and lifetime total tobacco smoke. No interaction was tested between exposure to domestic fumes and genotypes.

A population-based case–control study in Xuan Wei, China, assessed the risk for lung cancer caused by indoor coal combustion in relation to *GSTM1* and *GSTT1* genotypes (Lan *et al.*, 2000). Previous studies have shown an etiological link between lung cancer mortality and domestic smoky coal use (Mumford *et al.*, 1987a). Using a PCR-based method, 122 cases and 122 controls, matched on age (±2 years), gender, village and type of fuel currently used for cooking and heating at home were genotyped. Genotyping results were adjusted for total smoky coal use without ventilation, pack–years of smoking, chronic obstructive pulmonary disease and family history of lung cancer. The frequency of the *GSTM1* null genotype was 67% among cases and 51% among controls. Subjects with the *GSTM1* null genotype were 2.3 times more likely to have lung cancer than subjects with a positive *GSTM1* genotype (odds ratio, 2.3; 95% CI, 1.3–4.2). A potential

gene–environment interaction between the *GSTM1* null genotype and smoky coal was evaluated. For all subjects, the risk for lung cancer increased 1.7 fold per 100 tonnes of lifetime coal use (95% CI, 1.3–2.4). When stratified by *GSTM1* genotype, risk was non-significantly increased by 1.2-fold per 100 tonnes (95% CI, 0.8–1.9) for *GSTM1*-positive subjects and increased by 2.4-fold per 100 tonnes for those with the *GSTM1* null genotype (95% CI, 1.6–3.9) (test for multiplicative interaction, p=0.05). The *GSTT1* null genotype yielded non-significant results (odds ratio, 1.3; 95% CI, 0.7–2.3).

A case–control study of nonsmokers in eight countries (Brazil, France, Germany, Italy, Poland, Romania, Russia and Sweden) evaluated the association between *GSTM1* and *GSTT1* and risk for lung cancer (Malats *et al.*, 2000). Cases were histologically or cytologically confirmed in the same hospitals where the majority of controls were recruited among patients with non-tobacco-related diseases. The remaining controls were from population registries from two countries (Germany and Sweden). Using a multiplex PCR, genotypes for the 122 nonsmoking lung cancer cases and 121 nonsmoking controls were determined. Among them, 86% of cases and 72% of controls were women. Although subjects in this study population were suspected to have relatively low levels of environmental exposures to indoor fuel combustion and cooking oil fumes, data were analysed regarding exposure to indoor wood combustion. In general, more cases resided in rural than in urban settings (p=0.004), were exposed to more indoor air pollution from wood combustion (p=0.001), were exposed to more environmental tobacco smoke (p=0.04) and were more likely to be occasional smokers [p=0.01] than the controls. The frequency of the *GSTM1* null genotype was 54% among cases and 44% among controls. Subjects with the *GSTM1* null genotype had a non-significant increased risk for lung cancer (odds ratio, 1.5; 95% CI, 0.9–2.7) compared with *GSTM1*-positive subjects when adjusted for gender, age and centre. The *GSTT1* null genotype was not associated with lung cancer (odds ratio, 0.6; 95% CI, 0.3–1.2). The effect of exposure to emissions from wood combustion was also evaluated after stratification by *GSTM1* and *GSTT1* genotypes. Compared with subjects with less than 20 years of wood-smoke exposure, subjects with more than 20 years of exposure had a higher risk for lung cancer among those with the *GSTM1* null genotype (odds ratio, 6.2; 95% CI, 1.5–25). In contrast, long-term exposure to emissions from wood combustion was associated with a lower risk (odds ratio, 1.8; 95% CI, 0.5–7.1) among those with the *GSTM1*-positive genotype, although the test for interaction was not significant. No gene–environment interactions were observed for the *GSTT1* null genotype.

The effect of genetic variants of the *GSTM1* and *GSTT1* genotypes on modifying the risk for lung cancer was also evaluated in a population-based case–control study in Hong Kong of 229 consecutive incident cases and 197 healthy controls (Chan-Yeung *et al.*, 2004). Based on a previous study that evaluated the risk for lung cancer in Hong Kong, the study subjects were suspected of having been exposed to cooking oil fumes without an exposure assessment (Chan-Yeung *et al.*, 2003). Genotyping was carried out using a multiplex PCR methodology. Only the *GSTT1* null genotype was associated with lung cancer when adjusting for age, gender, education and tobacco smoking (odds ratio,

1.7; 95% CI, 1.1–2.6). The frequency of the *GSTT1* null genotype was 62% among cases and 52% among controls. Repeated analysis stratified by smoking status yielded only significant results for nonsmokers (odds ratio, 2.2; 95% CI, 1.2–3.9). No associations were found with the *GSTM1* null genotype (odds ratio, 0.8; 95% CI, 0.6–1.3).

Another case–control study consisting of 97 nonsmoking lung cancer patients (55 women and 42 men) and 197 healthy nonsmoking controls (101 women and 96 men) from a screening survey in Hunan Province, China, evaluated the phase II metabolic genotypes, *GSTM1, GSTT1, GSTP1* and *NAT2* (Chen *et al.*, 2006). The study population was believed to have indoor air exposure to cooking and heating fuels, as well as cooking oil fumes; however, no exposure assessment was performed. Genotyping was carried out by PCR, Hardy-Weinberg equilibrium results were not presented and only crude odds ratios were provided. Both the *GSTM1* null (odds ratio, 2.0; 95% CI, 1.2–3.2) and *GSTT1* null (odds ratio, 2.1; 95% CI, 1.3–3.4) genotypes were associated with an increased risk for lung cancer, whereas the *GSTP1* Ile/Val genotype was not (odds ratio, 1.2; 95% CI, 0.7–2.1). The *GSTM1* null genotype was found in 62% of cases and 45% of controls; the *GSTT1* null genotype was found in 61% of cases and 43% of controls. Combined effects of the various genotypes were evaluated. Subjects who had any two of these three *GST* 'at risk' genotypes (odds ratio, 2.3; 95% CI, 1.1–4.9) or who had all three genotypes (odds ratio, 4.7; 95% CI, 1.7–13.2) had an increased risk for lung cancer compared with subjects who were positive for the *GSTM1, GSTT1* and *GSTP1* Ile/Ile genotypes. Only 14 cases and 10 controls possessed all three *GST* 'at risk' genotypes. *NAT2* genotypes were not associated with risk for lung cancer. However, an increased risk for lung cancer was seen in subjects who had the *NAT2* rapid-acetylating genotype, were null for *GSTM1* and *GSTT1* and were wild-type for *GSTP1* (odds ratio, 5.5; 95% CI, 1.2–24.8) compared with subjects who were positive for *GSTM1* and *GSTT1* and had *GSTP Ile/Ile* and *NAT2* slow-acetylating genotypes; however, these results are based on only 12 cases and six controls.

Polymorphisms in other genes, such as oxidative stress-related genes (*AKR1C3*, *NQO1* and *MnSOD*; Lan *et al.*, 2004), one-carbon metabolism-related genes (*BHMT, CBS, FPGS, FTHFD, GGH, MTHFD2, MTHFR, MTHFS, MTRR, SHMT1, SLC19A* and *TYMS*; Shen *et al.*, 2005a) and DNA repair-related genes (*ERCC1, ERCC2/XPD, ERCC4/XPF, ERCC5/XPG, RAD32B*, *XPC, OGG1*, *APEX1, LIG3, XRCC1*, *ADPRT* and *NBS1*; Shen *et al.*, 2005b,c; Lan *et al.*, 2004, 2005), have been studied for their association with lung cancer. No firm conclusion can be drawn from these analyses due to small sample sizes (Tables 4.3 and 4.4).

A limited number of studies have evaluated populations exposed to indoor air pollution from the combustion of coal, wood, biomass or cooking oil fumes for associations between polymorphisms in genes that are involved in xenobiotic metabolism and risk for lung cancer. However, sample sizes were small for almost all studies, which can result in both false-negative and false-positive findings. There is some evidence that the *GSTM1* null genotype was associated with increased risk for lung cancer in some studies in which at least part of the study population was definitely or probably exposed to

Table 4.4. Polymorphisms of DNA repair genes and associations with exposure to indoor cooking and heating with coal, wood and biomass in relation to risk for lung cancer

Reference	Gene	Mutation/allele	Country/ ethnicity	No. of cases/ controls	Odds ratio (95% CI)	Comments
Shen *et al.* (2005b)	*ERCC2*	Ex23+61A>C (Lys751Gln), IVS19-70 C>T, Ex6-10A>C (Arg156Arg)	Xuan Wei County, China	119/113	S: Ex23+61A>C, CC+AC vs AA, 0.4 (0.2–0.9), IVS19-70 C>T, CT+TT vs CC 0.4 (0.2–0.9); BS: Ex6-10A>C, CC vs AA, 0.5 (0.2–1.0)	Haplotype analysis of *ERCC2* genes yield similar results to the single SNP analysis; no gene-environment interaction was found
	RAD23B	Ala249Val			S: Ala/Val+Val/Val vs Ala/Ala, 1.8 (1.0–3.1)	*RAD23B* and *XPC* work collectively to recognize DNA damage. Subjects with both the *XPC* 939Gln/Gln genotype and either the *RAD23B* 249Ala/Val or 249Val/Val genotype had a 6-fold increased risk for lung cancer
	XPC	Lys939Gln, Ala499Val, Ex16+315C>G			NS: all variant genotypes	
Lan *et al.* (2004)	*OGG1*	Ser326Cys	Xuan Wei County, China	119/113	S: Ser/Cys vs Ser/Ser, 2.0 (1.1–3.6); NS: Cys/Cys vs Ser/Ser, 1.9 (0.8–4.1)	S: Increased risk for lung cancer for Ser/Cys women who used more than 130 tonnes of smoky coal compared with Cys/Cys women who used less than 130 tonnes

Table 4.4 (contd)

Reference	Gene	Mutation/allele	Country/ ethnicity	No. of cases/ controls	Odds ratio (95% CI)	Comments
Shen *et al.* (2005c)	*XRCC1*	Arg399Gln, Arg280His, Arg194Trp	Xuan Wei County, China	119/113	S: Arg/Gln vs Arg/Arg, 0.6 (0.3–1.0); NS: Gln/Gln vs Arg/Arg	Effect of *XRCC1* on lung cancer was not modified by age, gender or lifetime smoky coal use.
Lan *et al.* (2005)	*NSB1*	Exon 2 Leu34Leu	Xuan Wei County, China	119/113	S: AA vs. GG, 2.15 (0.9–5.1); NS: GA vs GG, 1.4 (0.8–2.4)	No significant interaction between smoky coal use and genotypes. All women were nonsmokers. Two SNPs highly correlated
		Exon 5 Gln185Glu			BS: Glu/Glu vs Gln/Gln, 2.5 (1.1–6.1); NS: Gln/Glu vs Gln/Gln, 1.4 (0.8–2.5)	

BS, borderline significant; CI, confidence interval; NS, not significant; S, significant; SNP, single nucleotide polymorphisms

indoor air pollution, particularly when exposure to PAHs was suspected to be a contributing agent. However, results for polymorphisms in other genes are inconsistent or have been analysed in only one study. Therefore, no firm conclusion can be made regarding the effect of polymorphisms of genes other than *GSTM1* on the risk for lung cancer in these populations.

4.4 Mechanistic considerations

The most extensive exposure, animal and other experimental data for the combustion emissions considered in this monograph have been generated for coal compared with wood and other biomass fuel. Human, animal and other experimental data from coal combustion emissions, and especially those from poorly ventilated homes using smoky coal in Xuan Wei County, Yunnan Province, China, are consistent with the following carcinogenic mechanism.

At least six major pathways must be disrupted by a mixture of genetic and epigenetic changes for a normal cell to be transformed to a tumour cell (Hanahan & Weinberg, 2000). Molecular analyses show that exposure to smoky coal emissions disrupts many of these pathways. For example, lung tumours from nonsmokers who had been exposed to smoky coal emissions in poorly vented homes and whose lung tumours were linked epidemiologically to such exposures had mutations in the *KRAS* gene, which affects cell growth and signalling, and in the *P53* gene, which effects cell growth and replication, among other pathways.

Chemical analyses and bioassay-directed fractionation of smoky coal emissions have identified PAHs as an important chemical class that accounts for much of the mutagenicity and carcinogenicity of such emissions. The epidemiological link between exposure to smoky coal emissions and an increased risk for lung cancer is strengthened mechanistically by the fact that the mutation spectra of the *P53* tumour-suppressor gene and the *KRAS* oncogene in lung tumours from nonsmokers exposed to the emissions from smoky coal reflect an exposure to PAHs and is distinct from the mutation spectra found in these genes in lung tumours from cigarette smokers. Thus, the mutation spectra in lung tumours from nonsmokers whose cancers are linked epidemiologically to exposure to emissions from smoky coal reflect the primary DNA damage induced by the most prominent class of mutagens/carcinogens in these emissions.

The available data support a multistep model of carcinogenesis in which components of the emissions from smoky coal are the direct cause of the cellular changes that accumulate to initiate the carcinogenic process. There are many varieties of coal, and these may produce emissions with a range of carcinogenic potencies and chemical compositions. Nevertheless, the carcinogenesis model described here may be generally applicable to the risk for lung cancer associated with exposure to combustion emissions from coal other than smoky coal.

Compared with smoky coal, less extensive molecular epidemiological evidence exists for lung cancer risk and exposure to emissions from wood and other biomass fuel.

However, the available data suggest that the mechanism described above for emissions from smoky coal may be plausible for the lung cancer risk associated with these other emissions. In contrast to smoky coal, the indoor emissions from wood combustion comprise relatively low levels of PAHs, and the mutagenicity of these emissions are due to a combination of chemical classes, including PAHs and acidic/polar compounds such as aza-arenes, aromatic ketones, nitroarenes and phenolic compounds. Molecular evidence, including changes in P53 protein phosphorylation in lung cancer patients whose cancers are associated with exposure to combustion emissions from wood, as well as systemic genotoxicity among charcoal workers, is consistent with the mechanism described above.

The relevance of mechanisms for particle-induced lung cancer to particles generated from combustion of the agents evaluated in this monograph has not been thoroughly investigated. For particle-induced lung cancer, the cascade of events that starts with particle deposition at critical target cells and results in lung tumours includes sustained inflammation, production of reactive oxygen species, depletion of antioxidants, impairment of other defence mechanisms, cell proliferation and gene mutations. These events are well documented in experimental animals but, for humans, information is incomplete. However, some of these events have been observed in experimental animals, humans exposed to the combustion products of coal and wood, or coal miners exposed to coal dust.

Although the emissions described in this monograph have some similarities in chemical composition and biological effects, they are also clearly distinctive. Thus, carcinogenic mechanisms unique to each of the types of emission may also underlie the general carcinogenic mechanisms described here.

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5. Summary of Data Reported

5.1 Exposure data

The use of solid matter as household fuel is widespread and affects approximately half of the human population, almost exclusively in countries with low and medium resources, and the use of biomass is much more frequent than that of coal in most parts of the world. Exposure to emissions from the combustion of these fuels occurs as a result of cooking or heating, usually in poorly ventilated spaces. Women and young children especially may be exposed to extremely high levels of these emissions.

The factors that determine the use of solid fuels involve a combination of issues related to economics, social status, convenience and physical availability. Income and education play a major role in the selection of fuel; the households that use solid fuels tend to have lower levels of education and income because biomass fuels are frequently collected from the local environment, whereas liquid fuels must be purchased at a local market or fuel retailer.

Access to both solid and liquid fuels also plays a major role in the selection of fuel for household use. The ready availability of biomass from the local environment or agricultural residues encourages its use as a cooking fuel, since cash expenditure is not required. When liquid fuels are not available in local markets or significant initial costs represent a barrier to their adoption, the probability that solid fuels will be used is greater.

Energy policies in specific countries that involve issues of access and energy prices, taxes or subsidies also play a role in the selection of the type of fuel used. Taxes on liquid fuels reduce the probability that people will use them for cooking, whereas subsidies encourage their use. Additional factors that influence exposure to indoor air pollution from solid fuels include the type and quality of the fuel, the type and condition of stoves, the presence of a flue, the type of ventilation and housing, the task, the skill of the stove operator and weather conditions, all of which play a role in determining the level of pollutants. These factors vary by day, season and year, and generalization of the levels of exposure that can occur from individual monitoring studies that are conducted under widely differing conditions is difficult.

Typical household combustion of biomass and coal diverts 10–30% of fuel carbon into products of incomplete combustion. Total emissions of these products from coal and biomass overlap, largely depending on the species of fuel and the type of stove. Thousands of chemical species have been identified in the gas-phase and particle-phase of products of incomplete combustion. The mixture contains fine and ultrafine particles and a large number of semi-volatile and non-volatile organic compounds, including known carcinogens such as benzene, formaldehyde and benzo[*a*]pyrene. On the basis of results

from a limited number of studies that measured emission factors, combustion of the same amount of coal and wood in household stoves generates relatively comparable amounts of benzene and benzo[*a*]pyrene. However, combustion of wood appears to generate larger amounts of formaldehyde and acetaldehyde than combustion of the same amount of coal.

Virtually all of the rural population of China (about 740 million) uses solid fuels, and most rely on coal or a variety of biomass fuels for most of their energy needs. A considerable portion of the urban population (560 million) uses coal, which is increasingly in the form of briquettes. Improved biomass fuel stoves are very common, as are unvented portable coal stoves. Typical average indoor exposure levels of particulate matter <10 μm in size range from several tens to several hundred micrograms per cubic metre and those for benzo[*a*]pyrene range from low single digits to more than 40 ng/m^3. In some households, average exposure levels can be an order of magnitude higher. While gas fuels and electricity are progressively replacing solid fuels, the latter remain prevalent, even in wealthier rural households.

Exposure to indoor air pollutants that are associated with the combustion of solid fuels for cooking and heating is extensive in South Asia. Exposures are widespread and prevalent in half to three-quarters of the population in most countries of the region. In Latin America, nearly 25% of the population live in rural areas where biomass fuels are most frequently used for cooking and heating. In Africa, biomass fuel is used almost exclusively in rural areas and is still widely used in most urban areas.

Although there is some variability in exposure levels as a result of a differential distribution of determinants, levels of pollutants that range from several hundreds of micrograms per cubic metre of particulate matter of varying size during the day to several thousands of micrograms per cubic metre during cooking have consistently been reported in many countries in these regions.

A variety of interventions are already available, and new technologies and approaches are emerging. A small body of evidence shows that interventions can substantially reduce exposure and the incidence of lung cancer (chimney stoves, switching to cleaner fuels) and chronic obstructive pulmonary disease (chimney stoves). Levels of indoor air pollutants associated with the use of biomass and other solid fuels can be substantially reduced, particularly by stoves with flues, but experience shows that exposure levels remain high and people are exposed in the vicinity of their homes and from neighbours' homes. Biomass stoves that use secondary combustion may offer advantages due to greatly reduced emissions. Cleaner fuels, in particular liquefied petroleum gas and natural gas, offer the largest reductions in exposure, but cost and practical issues may result in lesser reductions being achieved in practice. Electricity is important for development, but is unlikely to contribute to substantive reductions in exposure as it is rarely used for cooking and heating in poor communities due to the high cost of supply, infrastructure and use. Behavioural changes can complement technical interventions, but appear to have limited potential alone.

5.2 Human carcinogenicity data

5.2.1 *Lung cancer*

(a) Combustion of coal

More than 20 case–control studies and one cohort intervention study reported on the association between exposure to coal smoke and the risk for lung cancer. The majority of them were conducted in China; in addition, a few studies were available from North America and Europe. Several studies that used different epidemiological designs originated from Xuan Wei County, China. Initially, an ecological study from this area showed a strong correlation between communities that used several different types of smoky coal and mortality from lung cancer. Two population-based case–control studies reported a positive association between the use of smoky coal and an increased risk for lung cancer. A statistically significant exposure–response relationship between the amount of smoky coal used and risk for lung cancer was observed in both of these studies. In one of these, in which controls were matched to cases on village and fuel type, the amount of smoky coal used was still significantly associated with risk for lung cancer in an exposure–response manner. A cohort study carried out in Xuan Wei County that included more than 20 000 farmers who used smoky coal throughout their lifetimes and approximately 1300 lung cancer cases showed that transition to the use of a stove with a chimney was associated with a reduced risk for lung cancer in both men and women that became evident 10 years and more after the intervention.

Two case–control studies from northern China that used general population controls provided evidence for an association between exposure to indoor air pollution from coal smoke and the risk for lung cancer. The first, a large, well-conducted study in Shenyang, reported internally consistent, positive exposure–response associations for different metrics of exposure to coal smoke, including a cumulative index of indoor exposure to coal smoke from heating and cooking, that were adjusted for tobacco smoking and education. The second study, from Harbin, reported a strong exposure–response relationship among nonsmoking women for years of use of a coal stove in the bedroom and risk for lung cancer after adjustment for several potential confounders.

One hospital-based case–control study from Taiwan, China, observed a statistically significant twofold increase in risk for adenocarcinoma of the lung with use of ‘coal or anthracite’ as cooking fuel that was adjusted for smoking and socioeconomic status; no exposure–response results were provided. A population-based case–control study on lung cancer among women in Los Angeles (CA, USA) reported a twofold increased risk for adenocarcinoma of the lung with the use of coal for heating or cooking in childhood and adolescence; results were adjusted for potential confounders, but exposure–response analyses were not provided.

(b) Combustion of biomass

To examine the role of biomass in the risk for lung cancer, the Working Group considered that four studies that collected information on the use of this fuel type for cooking and/or heating were the more informative, and that, among these, a case–control study conducted in Taiwan, China, and a large well-conducted European multicentre case–control study were the most informative. In the study in Taiwan, compared with people who did not use wood, nonsmoking women who used wood for cooking showed a significant twofold increased risk for lung cancer. In a subsequent expanded study, use of wood was also associated with a significant threefold increased risk for squamous–cell carcinoma and adenocarcinoma of the lung. In the large European case–control study, compared with men and women who never used coal and/or wood for cooking or heating, a significant 20–30% increased risk for lung cancer was found among those who cooked or heated with wood but never with coal after adjustment for active tobacco smoking and other potential confounders. However, neither the Taiwanese nor the European studies provided information on duration of exposure to wood smoke and thus exposure–response relationships could not be examined.

The other two informative studies were in nonsmoking women, one in Japan and one in Mexico, and found an increased risk for lung cancer in relation to exposure to smoke from wood or wood and straw. No information on duration of exposure was available in the Japanese study and the significantly increased risk was restricted to women who had been exposed to wood smoke at the age of 30 years. In the Mexican study, an approximate twofold increased risk was restricted to women who had used wood for >50 years whereas the risks were not increased for those who had used wood for 1–20 or 21–50 years. Thus, the accumulated evidence suggests that exposure to smoke from wood that was used for heating and/or cooking may be associated with an increased risk for lung cancer but information on the effect of duration and intensity of exposure was lacking.

5.2.2 *Aerodigestive tract cancers and combustion of coal or biomass*

Several studies investigated the relationship between the use of coal or biomass and the risk for nasopharyngeal carcinoma (the majority of which were conducted in Chinese populations and one in India). One study of nasopharyngeal carcinoma among Chinese reported a statistically significant fivefold increased risk associated with current use of wood as fuel after adjustment for consumption of salted fish during weaning; however, no information on an exposure–response relationship was presented, except for some assessment of ventilation conditions. In other studies of nasopharyngeal carcinoma, assessment of exposure was also crude, the baseline comparison group was not clearly specified or included people who used coal or fuels other than coal and wood and no adjustment was made for consumption of salted fish.

A few studies by cancer site investigated the relationship of exposure to emissions from the combustion of coal or biomass and other cancers of the aerodigestive tract,

including the oral cavity, pharynx, larynx, nasal cavities and oesophagus. These studies were not very informative because they were very small, the baseline comparison group was not clearly specified and mixed exposures were investigated or the exposure was based on a dichotomized variable with no information on exposure–response relationships.

5.3 Animal carcinogenicity data

5.3.1 *Coal*

In one study, inhalation exposure to a high concentration of emissions generated from coal burned under conditions similar to those of human exposure in Xuan Wei County, China, increased the incidence of various types of malignant lung tumour (squamous-cell carcinomas, adenosquamous carcinomas and adenocarcinomas) in male and female Kunming mice and that of squamous-cell carcinomas in male and female Wistar rats. In another study in Kunming mice exposed by inhalation to an unspecified concentration of coal emissions from an unspecified source in Harbin City, China, the incidence of adenocarcinoma was increased.

Intratracheal administration of extracts of coal-derived soot from Xuan Wei County induced an increase in the incidence of lung adenocarcinomas. In two studies, subcutaneously administered extracts of coal emissions from Xuan Wei County increased the incidence of various types of malignant pulmonary tumours (squamous-cell carcinomas, adenosquamous carcinomas and adenocarcinomas) in Kunming mice. These extracts were used in a complete carcinogenesis study by dermal application and induced an increase in the incidence of skin carcinomas in SENCAR mice. Extracts of coal emissions from the same region increased the incidence of benign skin papillomas in two tumour initiation–promotion studies by dermal application in Kunming and SENCAR mice.

A veterinary epidemiological study of dogs also showed an association between exposure to coal emissions and sinonasal cancer.

5.3.2 *Wood smoke*

In one study, inhalation exposure to a high concentration of emissions generated from wood burned under conditions similar to those of human exposure in Xuan Wei County increased the incidence of lung adenocarcinomas in male and female Kunming mice. The same inhalation exposure failed to increase the incidence of lung tumours in either sex of Wistar rats. Wood smoke generated from oak of mixed species that was burned in an uncertified wood stove over a simulated cycle induced no increase in tumour formation in Strain A mice exposed for 6 months and held for a 6-month period with no exposure.

Subcutaneously administered extracts of wood smoke from Xuan Wei County increased the incidence of pulmonary adenocarcinomas in male Kunming mice. Extracts

of wood smoke from the same region increased the incidence of benign skin papillomas in two tumour initiation–promotion studies by dermal application in female Kunming and SENCAR mice. Similar regional extracts used in a complete carcinogenesis study by dermal application induced a non-statistically significant increase in the incidence of skin carcinomas in female SENCAR mice. Extracts of relevant particulate matter from wood smoke generated from a wood stove in which hardwood and softwood were burned increased the incidence of benign skin papillomas in tumour initiation–promotion studies in female SENCAR mice following multiple topical applications to the skin.

5.4 Mechanistic and other relevant data

Emissions from the combustion of organic materials, such as coal or wood, are complex mixtures that contain numerous different gases, aerosols and chemical compounds admixed with and/or adsorbed onto particulate matter.

The primary mechanisms for deposition of airborne particles in the respiratory tract are sedimentation, impaction and diffusion. Deposition by sedimentation and impaction depends on the aerodynamic diameter of the particle, whereas deposition by diffusion depends on its thermodynamic diameter. Following inhalation, particles may either deposit in the extrathoracic, tracheobronchial or pulmonary airways or remain in the air stream and be eliminated upon exhalation. The deposition of particles in the respiratory tract depends primarily on the size of the inhaled particle, the route of breathing (i.e. through the nose and/or mouth) and the breathing pattern (e.g. volume and frequency).

Particles are frequently aggregates or agglomerates of smaller primary particles. The aerodynamic and thermodynamic properties of these aggregates (rather than the primary particles) affect their behaviour in the air and their probability of deposition in the respiratory tract. Once deposited, properties such as the size and surface area of both the aggregate and primary particle can potentially affect the kinetics of clearance.

The deposition and clearance of particles vary among individuals for a number of reasons, including age, gender, tobacco smoking status and health status. Pre-existing lung diseases or conditions such as asthma or chronic obstructive pulmonary disease can influence the efficiency and pattern of deposition within the respiratory tract. Deposition also depends on the level of activity and breathing patterns. Deposition and retention determine the initial and retained dose of particles in each region and may, therefore, influence the risk for developing diseases specific to those regions of the respiratory tract.

Studies in rodents (primarily rats) have shown that, depending on the concentrations and durations of exposure, the long-term retention of particles in humans can be greater than that predicted from rodent studies that used lower concentrations or shorter durations of exposure.

A cascade of events proposed to describe the biological process that starts from some particle deposition on critical target cells or tissues within the rat lung and results in rat lung tumours includes sustained inflammation, production of reactive oxygen species, depletion of antioxidants and/or impairment of other defence mechanisms, cell

proliferation and gene mutations. These individual steps comprise an overall mode of action that can be used to compare responses of rats with those of other species, including humans. Particle surface area is a better predictor of lung tumours than particle mass in rats exposed to various poorly soluble particles of fine or ultrafine size.

Among other compounds, polycyclic aromatic hydrocarbons are important chemical components of combustion emissions. These compounds are absorbed through the respiratory tract, gastrointestinal tract and skin, and smaller molecules (two to three rings) are absorbed more rapidly than larger ones. Active transport and passive diffusion are both involved, and, once absorbed, polycyclic aromatic hydrocarbons are distributed widely to most organs and tissues and tend to accumulate in fatty tissue. They are metabolized rapidly to more soluble (and in some cases more reactive) metabolites, such as epoxides, phenols, dihydrodiols, phenol dihydrodiols, dihydrodiol epoxides, quinones and tetrols. At least three pathways of metabolism are involved: the cytochrome P450 pathway, the cytochrome P450/aldo-keto reductase (oxidative) pathway and a cytochrome P450/peroxidase (radical cation) pathway. In addition to these phase I metabolic pathways, polycyclic aromatic hydrocarbon metabolites may bind with macromolecules, which can lead to toxic, mutagenic or carcinogenic effects, or they may be eliminated in a conjugated form via phase II metabolism.

Polycyclic aromatic hydrocarbons may be metabolized to their bay- and fjord-region diol epoxides or undergo cyclopenta-ring oxidation. These can be electrophilic and bind to DNA and proteins, which results in genotoxic effects—primarily through the formation of DNA adducts. Polycyclic aromatic hydrocarbons also have non-genotoxic effects that may include the interruption of gap-junctional communication and changes in gene expression; radical cations, *ortho*-quinones and reactive oxygen species may also be formed by their metabolism. They may also operate through receptor-mediated mechanisms that involve the aryl hydrocarbon receptor. These compounds can have immunological and haematological effects and can also be phototoxic.

Several studies evaluated populations who are exposed to indoor air pollution from coal, wood or other biomass fumes for associations between polymorphisms in genes that are involved in xenobiotic metabolism and risk for lung cancer. However, multiple comparisons and generally small sample sizes could have resulted in both false-positive and false-negative findings. Some evidence indicated that the *GSTM1* null genotype was associated with increased risk for lung cancer in studies in which at least part of the study population was definitely or probably exposed to indoor air pollution, particularly when exposure to polycyclic aromatic hydrocarbons was suspected to be a contributing agent. However, results for polymorphisms in other genes are inconsistent or have been analysed in only one study. Therefore, no firm conclusion can be made regarding the effect of polymorphisms of genes other than *GSTM1* on risk for lung cancer in these populations.

The available information on the mutagenicity and genotoxicity of smoky coal emissions from Xuan Wei County includes a wide range of end-points that encompasses mutations in *KRAS* and *TP53* genes in lung tumours from nonsmokers who were exposed to smoky coal emissions and whose tumours were linked epidemiologically to exposure

to the emissions. In addition, studies show that such an exposure results in the excretion of several polycyclic aromatic hydrocarbon metabolites, and that exposed individuals exhibit elevated levels of PAH–DNA adducts and accumulation of TP53 protein. Two studies also showed that emissions from other types of coal induced sister chromatid exchange in exposed individuals.

The available information on the genotoxicity and mutagenicity of emissions from wood combustion includes a number of human studies that showed the induction of cytogenetic damage in exposed individuals, including micronuclei, sister chromatid exchange and chromosomal aberrations. Also, exposed individuals had an elevated level of DNA adducts, DNA damage and accumulation of TP53 protein. In cultured cells, extracts of the emissions (mostly from wood) induced DNA strand breaks and sister chromatid exchange.

In many experiments, extracts or condensates of emissions from coal and wood were mutagenic in *Salmonella*. In strain TA98 in the presence of a metabolic activation system, the potency in terms of revertants per milligram of particle can reach 3000 for smoky coal and 4700 for wood. However, on average, smoky coal emissions were five times more mutagenic than those from wood in terms of activity per milligram of particle. In contrast, the mutagenic potencies of these emissions expressed as revertants per cubic metre of air reached 60 000 for smoky coal and 11 000 for wood. On average, smoky coal emissions were 10 times more mutagenic than those from wood. This larger range of potencies reflects the range of the amount of organic compounds (together with the potency of the organic compounds) emitted under the test conditions by the two combustion processes.

Bioassay-directed fractionation studies with *Salmonella* have identified that, for smoky coal, most of the mutagenic activity is due to polycyclic aromatic hydrocarbons and methylated polycyclic aromatic hydrocarbons. For wood, these compounds contribute 10–50% of the activity and polar aromatic compounds (aromatic amines and ketones) and nitropolycyclic aromatic hydrocarbons contribute to some of the remaining activity.

6. Evaluation and Rationale

6.1 Combustion of coal

There is *sufficient evidence* in humans for the carcinogenicity of household combustion of coal. Household combustion of coal causes cancer of the lung.

There is *sufficient evidence* in experimental animals for the carcinogenicity of emissions from combustion of coal.

There is *sufficient evidence* in experimental animals for the carcinogenicity of extracts from coal-derived soot.

Overall evaluation

Indoor emissions from household combustion of coal are *carcinogenic to humans (Group 1)*.

6.2 Combustion of biomass

There is *limited evidence* in humans for the carcinogenicity of household combustion of biomass fuel (primarily wood). Household combustion of biomass fuel (primarily wood) causes cancer of the lung.

There is *limited evidence* in experimental animals for the carcinogenicity of emissions from combustion of wood.

There is *sufficient evidence* in experimental animals for the carcinogenicity of wood-smoke extracts.

Overall evaluation

Indoor emissions from household combustion of biomass fuel (primarily wood) are *probably carcinogenic to humans (Group 2A*).

In reaching this evaluation, the Working Group considered mechanistic and other relevant data. These data include (*i*) the presence of polycyclic aromatic hydrocarbons and other carcinogenic compounds in wood smoke, (*ii*) evidence of mutagenicity of wood smoke and (*iii*) multiple studies that show cytogenetic damage in humans who are exposed to wood smoke.

HIGH-TEMPERATURE FRYING

HIGH-TEMPERATURE FRYING

1. Exposure Data

1.1 Definition

'Cooking fumes' or 'cooking oil fumes' is the term commonly used to describe the visible emissions generated during cooking by frying with oil. However, these emissions are not technically 'fumes'. In occupational and environmental hygiene, 'fumes' are defined as submicron-sized solid particles (particulate matter) created by the cooling of hot vapour. During cooking, such vapour is formed when the cooking oil is heated above its boiling point. In addition to this ultrafine particulate matter, cooking, especially frying and grilling, generates aerosol oil droplets, combustion products, organic gaseous pollutants, and steam from the water contents of the food being cooked.

1.2 Constituents of cooking fumes

Cooking, in particular frying, generates substantial amounts of airborne particulate matter (PM), which includes ultrafine particles (UFP) and fine PM ($PM_{2.5}$), and is a major contributor to their indoor levels. In addition, particles created during cooking have organic substances adsorbed on their surface. These include polycyclic aromatic hydrocarbons (PAHs) and heterocyclic amines. Certain gaseous pollutants such as formaldehyde (IARC, 2006), acetaldehyde (IARC, 1999), acrylamide (IARC, 1994) and acrolein (IARC, 1995) are also produced during cooking.

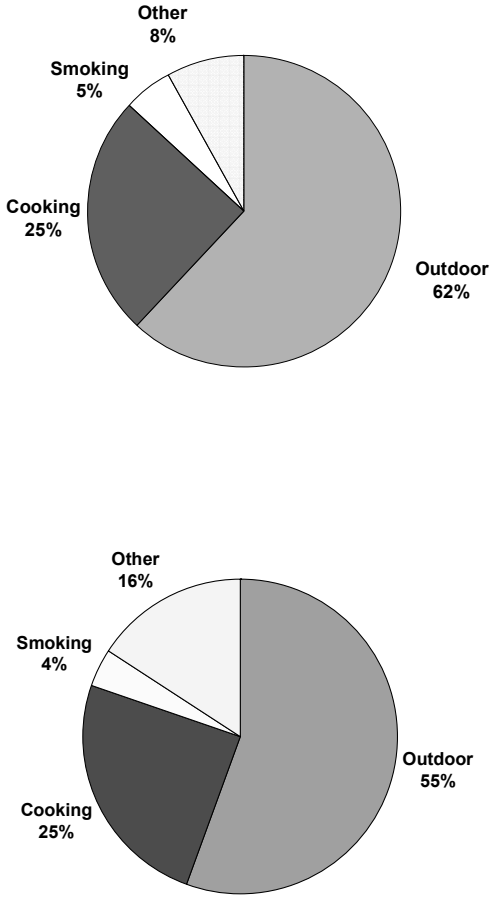
The concentrations of these constituents measured in cooking fumes in field and controlled studies are presented below.

1.2.1 *Ultrafine and fine particulate matter*

The Particle Total Exposure Assessment Methodology (PTEAM) study was carried out by the Research Triangle Institute and the Harvard University School of Public Health in the USA in 1989–90 (Clayton *et al.*, 1993). Particle concentrations were measured for a probability-based sample of 178 nonsmokers who represented the non-institutionalized population of Riverside, CA (~139 000 persons). Personal samples of PM_{10} were taken;

the indoor and outdoor samples included both PM_{10} and $PM_{2.5}$. Cooking produced both fine and coarse particles. Homes where cooking took place during monitoring (about 55%) had average PM_{10} concentrations ~20 μg/m^3 higher than those where no cooking took place (Özkaynak *et al.*, 1996a,b). The proportion of $PM_{2.5}$ and PM_{10} due to cooking was 25% for both particle sizes (Figure 1.1). However, when considered as a fraction of particles due to indoor sources alone, the proportion was 65% and 55%, respectively (Özkaynak *et al.*, 1996b).

Figure 1.1 Fraction of $PM_{2.5}$ due to cooking (top); fraction of PM_{10} due to cooking (bottom).



A large-scale study of personal, indoor and outdoor exposures was undertaken for more than 100 persons living in Seattle, WA, USA (Seattle Study; Liu *et al.*, 2003). Based on 195 cooking events, the average $PM_{2.5}$ concentration due to cooking was estimated to be 5.5 (standard error [SE], 2.3) μg/m^3 (Allen *et al.*, 2004).

A study of personal, indoor and outdoor exposure to $PM_{2.5}$ and associated elements was carried out on 37 residents of the Research Triangle Park area in North Carolina, USA (Research Triangle Park Study; Wallace *et al.*, 2006a,b). Burned food added an average of 11–12 μg/m^3 to the indoor concentration (Wallace *et al.*, 2006b). In continuous measurements, the mean estimated $PM_{2.5}$ personal exposures during more than 1000 h of cooking were found to be 56 μg/m^3 higher than background (Wallace *et al.* 2006b). The 24-h average increase due to cooking was about 2.5 μg/m^3. A different analysis of the results from this study concluded that cooking contributed 52% of personal exposure to $PM_{2.5}$ and more than 40% of the indoor concentration of $PM_{2.5}$ (Zhao *et al.*, 2006).

A long-term study of indoor and outdoor particle concentrations was carried out between 1997 and 2001 in an occupied townhouse in Reston, VA, USA (Reston, VA Townhouse Study). Cooking produced about an order of magnitude higher number of the smallest UFP (10–50 nm) and from 1.2- to 9.4-fold higher levels of the larger particles compared with identical times when no cooking occurred (Table 1.1; Wallace *et al.*, 2004). The mean mass concentration increased at dinner (4-h averages) from 3.7 μg/m^3 to 11.8 μg/m^3 assuming a density of combustion particles of 1 g/cm^3. About 70% of the particles emitted during dinnertime were <0.05 μm.

Table 1.1. Number and concentration of $PM_{2.5}$ during dinnertime cooking compared with no cooking

Size (μm)	Dinnertime cooking		No cooking	
	Mean	SE	Mean	SE
Number[a]				
0.010–0.018	6472	165	465	10
0.018–0.05	13363	342	1507	22
0.05–0.1	7085	221	1701	29
0.1–0.2	2226	77	807	11
0.2–0.3	277	10	128	1.4
0.3–0.5	76	3	16	0.15
0.5–1	5	0.086	1.3	0.015
1–2.5	1	0.016	0.15	0.0016
Concentration (μg/m^3)				
0.010–0.018	0.0085	0.0002	0.0006	0.00001
0.018–0.05	0.3	0.01	0.039	0.0006
0.05–0.1	1.4	0.04	0.4	0.006
0.1–0.2	2.9	0.10	1.1	0.014
0.2–0.3	2.6	0.12	1.2	0.013
0.3–0.5	2.4	0.05	0.5	0.005

Table 1.1. (contd)

Size (μm)	Dinnertime cooking		No cooking	
	Mean	SE	Mean	SE
Concentration (μg/m^3) (contd)				
0.5–1	0.8	0.01	0.2	0.003
1–2.5	1.4	0.04	0.3	0.003
Sum ($PM_{2.5}$)	11.8		3.7	

From Wallace *et al*. (2004)
PM, particulate matter; SE, standard error
[a] No. of samples between 2400 and 12 800

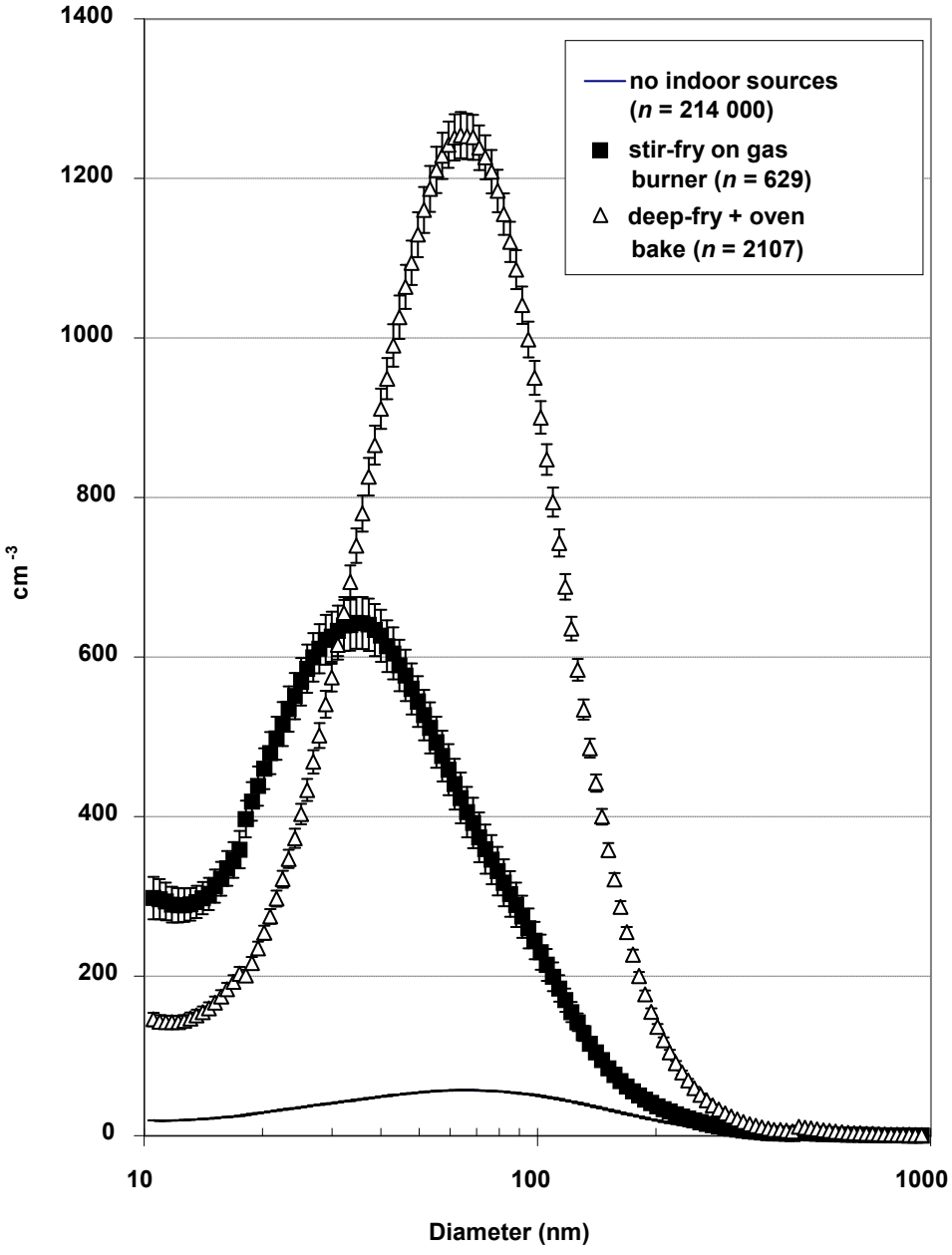
In a more detailed analysis, 44 high-particle-production (frying, baking, deep-frying) cooking episodes on a gas stove were assessed (Wallace *et al.*, 2004). Most of the particles were in the ultrafine range, but the largest volume was contributed by particles between 0.1 μm and 0.3 μm in diameter. The total particle volume concentration created by the 44 high-particle-production cooking events averaged a little more than 50 (μm/cm)^3, corresponding to an average concentration of about 50 μg/m^3, about an order of magnitude higher than average values for all types of cooking combined.

The size distribution of ultrafine particles during cooking was studied by Wallace (2006) and Ogulei *et al.* (2006). Stir-frying using one gas burner produced a peak of PM ~35 nm, whereas deep-frying using one gas burner followed by baking in the oven produced a peak about twice as high and at a diameter of 64 nm (Figure 1.2).

Brauer *et al.* (2000) reported $PM_{2.5}$ concentrations in the range of 24–201 g/m^3 in residential kitchens during frying, with peak $PM_{2.5}$ concentrations above 400 μg/m^3. Kamens *et al.* (1991) estimated that 5–18% of an 8-h personal particle exposure could be attributed to cooking one meal in one of three homes that they studied.

Abt *et al*. (2000) studied 17 selected cooking events in three homes that provided mean peak volume concentrations of particles between 20 and 500 nm ranging between 29 and 57 (μm/cm)^3. Long *et al.* (2001) studied nine homes for 6–12 days each and found mean peak volume concentrations for UFP (20–100 nm) of 2.2–18.2 (μm/cm)^3. He *et al*. (2004a) studied 15 homes for 48 h during cooking under good and poor ventilation conditions and found a range of peak submicrometer number concentrations for cooking events between 16 000 and 180 000 particles/cm^3. Estimates of the emission rate ranged between 0.2–4 × 10^{12} particles/min. Finally, 24 cooking events with high concentrations and well-shaped decay curves, including concurrent air exchange rate measurements, were analysed more accurately, taking into account losses due to deposition during the lag time required to reach the peak, for their source strengths (Wallace *et al.*, 2004). A value of 3×10^{12} UFP/min was obtained.

Figure 1.2. Size distribution of ultrafine particles from cooking. *n* = number of 5-min measurements. Error bars are standard errors. Stir-frying on one gas burner produced a peak at ~35 nm; deep-frying on one gas burner followed by baking in the oven produced a peak at 64 nm that was twice as high.



A study in Amsterdam and Helsinki found that cooking increased $PM_{2.5}$ concentrations by 1.9–3.4 μg/m^3 (14–24%) among two groups of 47 and 37 elderly residents in the two cities, respectively (Brunekreef *et al.*, 2005; the ULTRA Study).

Kleeman *et al.* (1999) used an industrial charbroiling facility to cook >100 hamburgers. The particle mass consisted mainly of organic compounds, with a very small amount of elemental carbon, and a large unknown component. Most of the particle mass came from particles between 0.1 and 0.4 μm in diameter.

Emission rates during cooking with commercial institutional-scale deep-fryers have been reported (Schauer *et al.*, 1998). Professional chefs prepared vegetables by stir-frying in soya bean or canola oil and deep-frying potatoes in oil. Fine particle emission rates were 21.5±1.2, 29.5±1.3 and 13.1±1.2 mg/kg for stir-frying vegetables in the two oils and deep-frying potatoes, respectively. [Emissions during food preparation by a professional chef using large commercial cookers may differ substantially from emissions in a residence.]

In a recent study in a residential setting in Canada (Evans *et al.* 2008), real-time measurements were taken during frying to estimate the time-integrated exposure to PM associated with frying food. The production rates and concentrations of UFP and $PM_{2.5}$ during and at the end of frying a variety of breakfast foods typical of the Canadian diet at medium temperatures were assessed (Table 1.2).

Table 1.2. The production rates and concentrations of UFP and $PM_{2.5}$ during and at the end of frying of various types of foods

Food	Food temperature (°C)[a]	Production rate during frying		Concentration at the end of frying	
		UFP (particles/cm^3 s)	$PM_{2.5}$ (μg/m^3 s)	UFP (particles/cm^3)	$PM_{2.5}$ (μg/m^3)
Bacon	314	45	0.092	$2.2*10^4$	38
Pancakes	297	25	0.17	$2.5*10^4$	55
Peppers and onions	336	78	0.12	$2.0*10^4$	60
Vegetable stir-fry	280	31	ND	$2.0*10^4$	ND
Vegetable mix	249	59	ND	$4.5*10^4$	ND
Fried egg	271	60	ND	$2.5*10^4$	ND
Fried rice	274	6	ND	$1.0*10^4$	ND
Breaded eggplant	280	88	1.1	$8.0*10^4$	1000
Overall		44	0.13		

From Evans *et al*. (2008)
ND, not determined because no elevated $PM_{2.5}$ concentration was observed; PM, particulate matter; UFP, ultrafine particles
[a] Refers to maximum temperature

1.2.2 *Volatile organic compounds*

A large proportion of the vapours generated during cooking is steam from the water contents of the food or from the water used to cook the food. However, during frying (with oil), fatty acid esters that are constituents of edible oils and fat can decompose and produce volatile organic compounds, as well as semi-volatile compounds that can condense to form particles. A wide variety of organic compounds have been identified in cooking emissions, including alkanes, alkenes, alkanoic acids, carbonyls, PAHs and aromatic amines. Felton (1995) reported that the main volatile compounds generated during frying were aldehydes, alcohols, ketones, alkanes, phenols and acids. Of particular concern in relation to carcinogenicity are PAHs, heterocyclic amines and aldehydes.

(a) PAHs

Dubowsky *et al.* (1999) reported peak total particle-bound PAH concentrations in a range from undetectable to 670 ng/m^3 during cooking when measured with a Gossen PAS monitor.

A study in Taiwan found several PAHs in the fumes of three cooking oils (safflower, vegetable and corn oil) (Chiang *et al.*, 1999a).

By contrast, Wallace (2000) did not measure increased concentrations of total PAHs during cooking.

(b) Aldehydes

Schauer *et al.* (1998) reported emissions of 20 100 µg formaldehyde/g of food during stir-frying of vegetables on an institutional-size cooker. They reported emissions of 12 400 µg/g formaldehyde and 20 900 µg/g acetaldehyde during deep-frying of potatoes.

(c) Aromatic amines

One study found the aromatic amines 2-naphthylamine and 4-aminobiphenyl in the fumes of three different cooking oils (sunflower oil, vegetable oil and refined lard) (Chiang *et al.*, 1999b).

(d) Other volatile compounds

Rogge *et al*. (1991) measured the fine aerosol emission rates for single organic compounds from charbroiling and frying hamburger meat. The compounds detected were *n*-alkanes, *n*-alkanoic acids, *n*-alkenoic acids, dicarboxylic acids, *n*-alkanals and *n*-alkenals, *n*-alkanones, alkanols and furans.

Ho *et al.* (2006) studied emissions of 13 carbonyl compounds in cooking exhaust fumes from 15 restaurants in Hong Kong Special Administrative Region, China, and developed a new method of analysis using Tenax coated with a hydrazine compound followed by thermal desorption and mass spectrometry. This allowed them to separate three similar compounds: acetone, acrolein and propanal. The most prevalent compounds were formaldehyde (in all but four of the restaurants), acrolein, acetaldehyde and nonanal,

which accounted for 72% of all carbonyl emissions. Based on a small sample of restaurants, the authors estimated total annual emissions for acrolein, formaldehyde and acetaldehyde of 7.7, 6.6 and 3.0 tonnes per year from cooking compared with 1.8, 10 and 33 tonnes per year, respectively, from vehicles.

1.3 Effect of different parameters of cooking on emissions

The chemical composition of cooking emissions varies widely depending on the cooking oils used, the temperature, the kind of food cooked, as well as the method and style of cooking adopted.

1.3.1 *Effect of the type of oil and temperature*

(a) Mixture of volatile components

Studies were undertaken to identify qualitatively the volatile components emitted during the heating of cooking oils to 265–275°C (Li, *et al.* 1994; Pellizzari *et al.* 1995; Shields *et al.* 1995; Chiang *et al.*, 1999a; Wu *et al.* 1999). The oils tested were rapeseed, canola, soya bean and peanut. The major constituents identified in the oil vapours were saturated, unsaturated and oxygenated hydrocarbons. These studies detected a variety of agents in emissions from heated cooking oils including 1,3-butadiene, benzene, benzo[*a*]pyrene, dibenz[*a,h*]anthracene, acrolein, formaldehyde and acetaldehyde. Emissions were highest for rapeseed oil and lowest for peanut oil. In one study, the emission levels of 1,3-butadiene and benzene were approximately 22-fold and 12-fold higher, respectively, for rapeseed oil than for peanut oil (Shields *et al.*, 1995). Compared with rapeseed oil heated to 275°C, fourfold and 14-fold lower levels of 1,3-butadiene were detected when the oils were heated to 240°C and 185°C, respectively.

(b) PAHs and nitro-PAHs

In a study performed in a controlled environment (Air Resources Board of the State of California Study; Fortmann *et al.*, 2001), five untreated cooking oils were extracted and analysed for PAHs (Table 1.3). All were found to contain some PAHs; olive oil and peanut oil contained generally higher concentrations than rapeseed, corn or vegetable oils.

In a similar study, PAHs levels in samples of five raw cooking oils (canola, olive, corn, soya bean and vegetable oil) were not increased compared with the blank (Kelly, 2001).

Fume samples from three different commercial cooking oils commonly used in Taiwan, China (lard oil, soya bean oil and peanut oil), were collected and tested for PAHs. All samples contained dibenz[*a,h*]anthracene and benz[*a*]anthracene; extracts of fume samples from the latter two also contained benzo[*a*]pyrene (Chiang *et al.*, 1997). In a later study, fume samples from safflower, olive, coconut, mustard, vegetable and corn oil were similarly tested (Chiang *et al.*, 1999a). Extracts of fumes from safflower oil,

vegetable oil and corn oil contained benzo[*a*]pyrene, dibenz[*a,h*]anthracene, benzo-[*b*]fluoranthene, and benz[*a*]anthracene. Concentrations are shown in Table 1.4.

Table 1.3. Concentrations (ng/g) of polycyclic aromatic hydrocarbons in untreated cooking oils

Compound	Olive	Peanut	Rapeseed	Corn	Vegetable
Acenaphthylene	ND	ND	ND	ND	ND
Acenaphthene	19.9	ND	ND	ND	ND
Phenanthrene	10.7	ND	ND	ND	ND
Anthracene	1.12	2.60	1.12	1.54	0.56
Fluoranthene	4.07	1.28	0.71	0.65	1.64
Pyrene	7.10	10.2	1.79	ND	ND
Benz[*a*]anthracene	4.49	13.6	6.51	ND	2.22
Chrysene	3.29	14.7	ND	ND	2.22
Benzo[*b+j+k*]fluoranthene	77.3	72.8	ND	4.68	5.28
Benzo[*e*]pyrene	0.26	19.4	ND	2.70	3.66
Benzo[*a*]pyrene	8.32	24.5	ND	11.0	4.22
Indeno[1,2,3-*cd*]pyrene	16.2	30.3	2.67	2.03	9.84
Benzo[*ghi*]perylene	5.31	26.6	18.7	3.20	8.40
Fluorene	1.73	ND	0.21	0.28	0.30
1-Methylphenanthrene	4.25	0.74	3.56	3.59	4.38
Perylene	1.50	15.5	ND	1.90	3.06
Dibenzo[*a,h+a,c*]anthracene	9.26	27.1	ND	0.59	9.20
Naphthalene	31.7	13.9	15.5	13.3	17.6
1-Methylnaphthalene	10.1	ND	ND	ND	0.66
Biphenyl	2.99	0.12	0.72	0.26	ND
2,6+2,7-Dimethyl naphthalene	8.63	ND	ND	ND	ND
2,3,5+i-Trimethyl naphthalene	4.63	0.16	0.63	ND	0.32

From Fortmann *et al*. (2001)
ND, not detected

Table 1.4. The polycyclic aromatic hydrocarbon contents (μg/m^3) of fumes from various oils heated to 250±10°C for 30 min

Carcinogens	Cooking oil		
	Safflower	Vegetable	Corn
Benzo[*a*]pyrene	22.7±1.5	21.6±1.3	18.7±0.9
Dibenz[*a,h*]anthracene	2.8±0.2	3.2±0.1	2.4±0.2
Benzo[*b*]fluoranthene	1.8±0.3	2.6±0.2	2.0±0.1
Benz[*a*]anthracene	2.5±0.1	2.1±0.4	1.9±0.1

From Chiang *et al.* (1999a)

Wei See *et al.* (2006) studied three ethnic food stalls in a food court for levels of $PM_{2.5}$ and PAHs. PAHs varied from 38 to 141 to 609 ng/m^3 at the Indian, Chinese and Malay stalls, respectively. The trend was considered to be related to the cooking temperature and amount of oil used (simmering, stir-frying and deep-frying). Frying provided relatively more high-molecular-weight PAHs compared with simmering, which produced relatively more low-molecular-weight PAHs.

In addition to PAHs, fumes from three different commercial cooking oils frequently used in Chinese cooking (lard oil, soya bean oil and peanut oil) also contained nitro-PAHs such as 1-nitropyrene and 1,3-dinitropyrene (Table 1.5) (Wu *et al.*, 1998).

Table 1.5. Concentrations of PAHs and nitro-PAHs (μg/m^3) in fumes from various oils heated to 250±10°C for 30 min

Carcinogens	Type of cooking oil		
	Lard	Soya bean	Peanut
PAHs			
Benzo[*a*]pyrene	ND	21.1±0.8	19.6±0.5
Benz[*a*]anthracene	2.3±0.2	2.1±0.5	1.5±0.2
Dibenz[*a,h*]anthracene	2.0±0.3	2.4±0.4	1.9±0.1
Nitro-PAHs			
1-Nitropyrene	1.1±0.1	2.9±0.3	1.5±0.1
1,3-Dinitropyrene	0.9±0.1	3.4±0.2	0.4±0.1

From Wu *et al.* (1998)
ND, not detected

Zhu and Wang (2003) studied 12 PAHs in the air of six domestic and four commercial kitchens. Mean concentrations of benzo[*a*]pyrene were 6–24 ng/m^3 in the domestic kitchens and 150–440 ng/m^3 in the commercial kitchens. Cooking oils were ranked lard>soya bean oil>rapeseed oil. Increases in cooking temperature produced increased PAH concentrations.

Various samples of cooking oil fumes were analysed in an effort to study the relationship between the high incidence of pulmonary adenocarcinoma in Chinese women and cooking oil fumes in the kitchen (Li *et al.*, 1994). The samples included oil fumes from three commercial cooking oils. All samples contained benzo[*a*]pyrene and dibenz[*a,h*]anthracene. The concentration of dibenz[*a,h*]anthracene in the fume samples was 5.7–22.8 times higher than that of benzo[*a*]pyrene. Concentrations of benzo[*a*]pyrene and dibenz[*a,h*]anthracene were, respectively, 0.463 and 5.736 μg/g in refined vegetable oil, 0.341 and 3.725 μg/g in soya bean oil and 0.305 and 4.565 μg/g in vegetable oil.

(c) Heterocyclic amines

Hsu *et al.* (2006) studied the formation of heterocyclic amines in the fumes from frying French fries in soya bean oil or lard. Lard was more susceptible to form these compounds than soya bean oil heated alone (Hsu *et al.*, 2006). Fumes from soya bean oil heated alone were found to contain three heterocyclic amines, namely, 2-amino-3-methylimidazo[4,5-*f*]quinoxaline (IQx), 2-amino-3-methylimidazo[4,5-*f*]quinoline (IQ) and 1-methyl-9*H*-pyrido[4,3-*b*]indole (Harman), whereas two additional amines, 2-amino-3,4-dimethylimidazo[4,5-*f*]quinoline (MeIQ) and 3-amino-1,4-dimethyl-5*H*-pyrido[4,3-*b*]indole (Trp-P-1), were generated with lard.

(d) Aldehydes and other volatile organic compounds

Higher aldehydes [C>7] have been detected in emissions from pan-frying beefsteak using four different types of oil (Table 1.6) (Sjaastad & Svendsen 2008). The aldehyde *trans*,*trans*-2,4-decadienal (*t,t*-2,4-DDE) has been found and quantified in both frying oils and fumes generated during frying. The quantity of *t,t*-2,4-DDE in fried potatoes was considered to be dependent on the oil used, on the frying process and, to a lesser extent, on oil deterioration. The degree of unsaturation of the frying oil was also considered to promote the formation of *t,t*-2,4-DDE.

Table 1.6. Levels[a] of total particles (mg/m^3) and higher aldehydes (µg/m^3) measured in the breathing zone of the cook during pan-frying of beefsteak using different oils or margarine

	Margarine	Rapeseed oil	Soya bean oil	Olive oil
Total particles	11.6 (0.7)	1.0 (0.3)	1.4 (0.7)	1.0 (1.1)
t,*t*-2,4-Decadienal	10.33 (2.52)	0.63 (1.32)	0.52 (0.80)	ND
2,4-Decadienal	25.33 (4.51)	ND	ND	ND
t-2-Decenal	25.33 (9.70)	3.60 (6.40)	0.50 (1.20)	0.50 (1.20)
s-2-Decenal	ND	0.82 (1.08)	2.20 (5.29)	3.67 (2.94)
2-Undecenal	20.67 (7.64)	3.81 (5.21)	2.02 (3.62)	3.33 (2.34)
Alkanals	426.00 (70.00)	107.00 (75.00)	128.00 (53.00)	121.00 (85.00)
Alkenals	55.70 (11.00)	1.80 (4.00)	4.00 (2.70)	0.90 (1.30)

From Sjaastad & Svendsen (2008)
ND, not detected; ; *s*, *cis*; *t*, *trans*
The results are given as arithmetic mean (standard deviation)

Emissions of low-molecular-weight aldehydes from deep-frying with extra virgin olive oil, olive oil and canola oil (control) were investigated at two temperatures, 180 and 240°C, for 15 and 7 h, respectively. Seven alkanals (C-2 to C-7 and C-9), eight 2-alkenals (C-3 to C-10) and 2,4-heptadienal were found in the fumes of all three cooking oils. The

generation rates of these aldehydes were found to be dependent on heating temperature, and showed significant increases with increases in temperature. The emissions of low-molecular-weight aldehydes from both kinds of olive oil were very similar and were lower than those observed from canola oil under similar conditions (Fullana *et al.*, 2004a,b).

The composition of the fumes was studied at different temperatures (190–200, 230–240 and 270–280°C). A strong peak was observed within the wavelength range of 260–270 nm in each condensate sample. From gas chromatography–mass spectrometry results, it was tentatively deduced that there were some 2,4-dialkylenaldehydes and other conjugated compounds in the condensates. Large amounts of hexanal and 2-heptenal were present in the cooking oil fumes. The total aldehyde peak areas of the condensates from four kinds of oil were around 30–50% of the total peak area at 270–280°C (Zhu *et al.*, 2001).

Concentrations of ethylene oxide and acetaldehyde were assessed during the simulated frying of soya bean oil without or with flavouring herbs and spices (garlic, onion, ginger, basil) under nitrogen or air at 1atm (Lin *et al*., 2007). The tests were performed at 130, 150, 180 and 200°C.

The concentration of both ethylene oxide and acetaldehyde in the oil and vapour phases increased with frying temperature within the range of 130 to 200°C. Under air, the amounts of ethylene oxide and acetaldehyde generated in either phase were several times higher when compared with amounts generated under nitrogen. In the oil phase, concentrations of ethylene oxide and acetaldehyde increased linearly from 7.6 ppm at 130°C to 26.2 ppm at 200°C, and from 6.0 ppm to 16.6 ppm, respectively. Similarly, ethylene oxide concentrations in the vapour phase increased from 7 ppm to 85 ppm.

The impact of the combination of flavouring sources and soya bean oil was assessed. Both ethylene oxide and acetaldehyde were distributed between the gas phase and the oil phase after cooking each herb or spice at 150°C for 5 minutes under either atmosphere. In each scenario, the amounts of ethylene oxide and acetaldehyde produced were different when compared with heating soya bean oil alone.

1.3.2 *Effect of the type of food, type of cooking or mode of frying*

(a) Studies in a controlled environment

In an experimental study, airborne cooking by-products from frying beef (hamburgers), pork (bacon strips) and soya bean-based food (tempeh burgers) were collected, extracted and chemically analysed. 2-Amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP) was the most abundant heterocyclic amine, followed by 2-amino-3,8-dimethylimidazo[4,5-*f*]quinoxaline (MeIQx) and 2-amino-3,4,8-trimethylimidazo[4,5-*f*]quinoxaline (DiMeIQx). No 2-amino-9*H*-pyrido[2,3-*b*]indole (AαC) was detected in the food samples fried at about 200°C, although it was present in the collected airborne products. The total amounts of heterocyclic amines in the smoke condensates were 3 ng/g

from fried bacon, 0.37 ng/g from fried beef and 0.177 ng/g from fried soya-based food (Table 1.7) (Thiébaud *et al.*, 1995).

Table 1.7. Concentration of heterocyclic amines from frying meat and soya-based patties (ng/g of cooked samples)

Food sample (average temperature)	In the fried food sample				In the bead-trap smoke condensate			
	MeIQx	DiMeIQx	PhIP	AαC	MeIQx	DiMeIQx	PhIP	AαC
Beef patties (198°C)	4.3	1.3	4.9	ND	0.14	0.006	0.14	0.084
Beef patties (277°C)	16	4.5	68	21	1.1	0.25	1.8	4.0
Bacon strip (208°C)	45	12	106	ND	ND	ND	1.0	2.0
Soya-based patties (226°C)	ND	ND	ND	ND	ND	ND	0.007	0.17

From Thiébaud *et al.* (1995)
AαC, 2-amino-9*H*-pyrido[2,3-*b*]indole; DiMeIQx, 2-amino-3,4,8-trimethylimidazo[4,5-*f*]quinoxaline; ND, not detected (<0.1ng/g); PhIP, 2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine; MeIQx, 2-amino-3,8-dimethylimidazo[4,5-*f*]quinoxaline

One study compared emissions of particles, nitrogen oxides, carbon monoxide, PAHs and formaldehyde in an experimental chamber during seven different types of cooking activity including pan-frying (Table 1.8; Kelly, 2001). Samples were integrated over periods of 1–4 h. [Temperatures were measured but not reported.]. Except for the hamburger cooked on gas, all tests showed an increase in total PAHs, with indoor levels averaging about twice or more the outdoor concentrations. Since the outdoor concentrations would be expected to be roughly half of those indoors in the absence of indoor sources, the increase over normal indoor levels is by a factor of about 3. For seven particle-bound PAHs that are considered to be probably carcinogenic, indoor:outdoor ratios averaged from 1–1.5. Emissions of nitrogen dioxide were found only when the gas stove was used, and were 10 mg/kg for pan-frying of hamburgers. Emissions of formaldehyde remained below 10 ppb (see footnote in Table 1.8).

Another major controlled study of cooking emissions was sponsored by the Air Resources Board of the State of California (Fortmann *et al.*, 2001). $PM_{2.5}$ and PM_{10} particles, carbon monoxide, nitrogen oxide, nitrogen dioxide, PAHs and aldehydes were measured. Cooking activities included wok stir-frying of chicken and vegetables, deep-frying of French fries and pan-frying of bacon, tortillas or hamburgers. The cooking activities were studied under standard conditions or worst-case scenarios. Wok stir-frying was performed with 65 g peanut oil for 1 or 3 min at high temperatures, using chicken and vegetables as food. The concentrations of $PM_{2.5}$ particles emitted during the cooking activities under different conditions are given in Table 1.9. Of the 13 PAHs targeted for analysis, pyrene, benzo[*e*]pyrene, benzo[*a*]pyrene and benzo(*b*+*j*+*k*)phenanthrenes were detected in more than 60% of the samples. Duplicate samples collected during the worst-case stir-fry test showed that the precision of the PAH sampling method was poor.

[Because of the short test, the mass of PAHs in the samples was low, and there was large analytical uncertainty associated with the measurement.]

Table 1.8. Concentrations[a] of $PM_{2.5}$, PAHs and formaldehyde in a research house during pan-frying

Type of stove Food cooked	$PM_{2.5}$ (μg/m^3)		Total PAHs (ng/m^3)		Seven PAHs[b] (ng/m^3)		Formaldehyde[c] (ppb)
	Stove	Kitchen	Indoor	Outdoor	Indoor	Outdoor	Indoor
Gas							
Hamburger	115	60	294	288	0.93	1.76	3
Steak	2270	2670	833	189	3.70	1.93	48
Electric							
Hamburger	252	160	425	251	3.59	1.68	<2
Steak	542	457	610	431	2.56	3.24	9

From Kelly (2001)
PAH, polycyclic aromatic hydrocarbon; PM, particulate matter
[a] Average of three replicate runs
[b] Benz[*a*]anthracene, chrysene, benzo[*b*+*k*]fluoranthene, benzo[*a*]pyrene, indeno[1,2,3-*cd*]pyrene, dibenzo[*a*,*h*]anthracene, benzo[*ghi*]perylene
[c] Values were confounded by background emissions from building materials and by variations due to purging air between tests.

(b) Field studies

Samples of cooking oil fumes from three catering shops were analysed (Li *et al.*, 1994). All samples contained benzo[*a*]pyrene and dibenz[*a*,*h*]anthracene. PAH concentrations at the three catering shops showed levels of benzo[*a*]pyrene of 41.8 ng/m^3 at a Youtiao (deep-fried twisted dough sticks) shop, 22.8 ng/m^3 at a Seqenma (candied fritters) workshop and 4.9 ng/m^3 at a kitchen of a restaurant; concentrations of dibenz[*a*,*h*]anthracene were 338, 144 and 30.3 ng/m^3, respectively.

Another study in China showed that the cooking method affected the concentration of benzo[*a*]pyrene in kitchen air (Du *et al.*, 1996). In the same kitchens, the level of benzo[*a*]pyrene was elevated in indoor air from the baseline value of 0.41 μg/100m^3 to 0.65 μg/100m^3 when meat was boiled, and was further increased to 2.64 μg/100m^3 when meat was stir-fried.

Li *et al.* (2003) measured PAHs emitted from the rooftop exhausts of four types of restaurant in Taiwan, China. Although gaseous PAHs outweighed particle-bound PAHs by about 4:1, when expressed in benzo[*a*]pyrene-equivalents, the ratio was reversed. Chinese food contributed the majority of the level of benzo[*a*]pyrene-equivalents, while western food contributed about seven times less and fast food and Japanese food contributed negligible amounts. Compared with traffic in the city, restaurants contributed somewhat less total PAHs but about 10 times the benzo[*a*]pyrene-equivalent amount.

Zhu and Wang (2003) studied 12 PAHs in the air of six domestic and four commercial kitchens. Mean concentrations of benzo[*a*]pyrene were 6–24 ng/m^3 in the

Table 1.9. $PM_{2.5}$ concentrations under different cooking conditions in a research house

Type of cooking	Food	Type of stove	Conditions	Temperature (°C)[a]		$PM_{2.5}$ concentration ($\mu g/m^3$)			
				Food	Burner	Kitchen	Living room	Bedroom	Outdoors
Stir-frying	Chicken and vegetables	Gas	Standard[d]	79.6	85[b]	241	191	185	7
			Replicate[d]	88.3–100	418–439	185	323	301	8.8
			Worst case[d]	119–124	284–398	1289	850	798	8.1
			Vegetable oil	95.3–104	295–513	392	294	303	8.1
		Electric	Standard	105	289	214	1124	364	5.6
Deep-frying	French fries	Gas	Standard	182[c]	729	195	71.9	83.3	4.2
			Replicate	186.9[c]	277	162	91.9	70.5	4.1
		Electric	Standard	171.4[c]	446	374	94.7	90.2	5.7
Pan-frying	Bacon	Gas	Standard	148–156	105–108[b]	482	142	286	7
			Worst case	143.6–184.1	268–337	484	711	771	8.8
		Electric	Standard	72.8–73.7	272–298	207	276	235	5.7
	Tortillas	Gas	Standard	172[c]	97[b]	566	260	77.4	4.2
		Electric	Standard	232.9[c]	ND	1269	1175	1173	5.7
	Hamburger	Gas	Cast iron pan	93.0–93.7	270–304	153	7.73	8.64	1.5
		Gas	Cast iron pan	95.3	ND	51.9	8.6	8.8	3.6
		Gas	Pan lid	NR	253–300	355	5.8	6.4	4

From Fortmann *et al.* (2001)
ND, not detected; NR, not reported; PM, particulate matter
[a] Peak temperature of the food during the test; average temperature for burner or oven during the test
[b] Thermocouple proble location for this test was inconsistent with later tests that yielded variable flame temperatures, but other parameters indicate similar cooking temperatures.
[c] Temperature of cooking oil
[d] Peanut oil

domestic kitchens and 150–440 ng/m^3 in the commercial kitchens. Cooking practices produced PAHs in the rank order broiling>frying>>boiling.

The influence of frying conditions (deep-frying, pan-frying) was studied (Boskou *et al.*, 2006). In all cases tested, the highest concentration of *trans*,*trans*-2,4-decadienal was detected during deep-frying.

Studies have shown that the total amount of organic compounds per milligram of particulate organic matter is much higher in western-style fast food cooking than in Chinese cooking; however, Chinese cooking has a much greater contribution of PAHs to particulate organic matter (Table 1.10) (Zhao *et al.*, 2007a,b).

Table 1.10. Concentrations of organic compounds from western-style fast food and from Chinese cooking (ng/mg of particulate organic matter)

Organic compounds	Western-style fast food cooking[a]	Chinese cooking[b]
n-Alkanes	3 863	1 883
Polycyclic aromatic hydrocarbons	40	2 855
n-Alkanals	29 172	3 444
n-Alkanones	22 702	2 443
Lactones	13 323	2 142
Amides	4 692	531
Saturated fatty acids	374 699	26 804
Unsaturated fatty acids	93 299	29 028
Dicarboxylic acids	57 877	2 051
Monosaccharide anhydrides	97	314
Sterols	487	1 684
Other compounds	63	208

From Zhao *et al*. (2007a,b)

[a] Average of six samples

[b] Average of four different styles of Chinese cooking

1.4 Human exposure

Neither occupational nor non-occupational exposure to emissions from cooking has been characterized systematically. Most of the available studies examined the nature and amount of emissions produced during different types of cooking in different settings, including the release of emissions from kitchens into the ambient environment. As the substances measured varied widely among studies, it is difficult to summarize quantitatively exposures in different settings. Furthermore, co-exposures were not specifically mentioned. Results from various field studies, carried out primarily in South-East Asia, are summarized in Tables 1.11 and 1.12.

Only one recent study provided information on biological monitoring of exposure and effect in the occupational setting (Table 1.11) (Pan *et al.*, 2008).

Table 1.11. Occupational exposures to emissions from high-temperature frying

Reference, location	Setting	Study design/ samples	Exposure(s) measured	Main results
Vainiotalo & Matveinen (1993), Finland	8 workplaces (2 bakeries, a food factory, 5 restaurant kitchens)	Field measurements, sampling during frying/grilling of meat or fish or during deep-frying	Fat aerosol Acrolein Formaldehyde Acetaldehyde Heterocyclic amines PAHs	Highest concentrations (9–16 mg/m^3) in kitchens using the ordinary frying method; lower concentrations at other workplaces (<0.01–3.2 mg/m^3) Range, 0.01–0.59 mg/m^3 Highest concentrations in grill kitchens (0.24 and 0.75 mg/m^3) Highest concentrations in bakeries (0.67 and 1.5 mg/m^3) Mutagenic heterocyclic amines below detection limits Low concentrations
Svendsen *et al.* (2002), Norway	4 hotels, 2 hamburger chain restaurants, 10 à la carte restaurants and 3 small local restaurants, serving mostly fried food	Personal sampling in kitchens	Fat aerosols Aldehydes	Highest concentration (6.6 mg/m^3) in a small local restaurant; arithmetic mean for all kitchens, 0.62 mg/m^3 Highest level of the sum of the aldehydes, 186 µg/m^3; arithmetic mean, 69 µg/m^3
He *et al*. (2004b), Shen Zhen, China	2 cooking styles of Chinese cuisine: Hunan cooking and Cantonese cooking	Sampling of cooking fumes during regular operation	PM, organic compounds	More than half of the $PM_{2.5}$ mass is due to organic compounds, and over 90 species of organic compound were identified and quantified, accounting for 26.1% of bulk organic particle mass and 20.7% of $PM_{2.5}$. Fatty acids, diacids and steroids were the major organic compounds emitted from both styles of cooking. Of the quantified organic mass, over 90% was fatty acids. The mass of organic species, and the molecular distribution of *n*-alkanes and PAHs indicated the dissimilarities between the two different cooking styles, but generally the major parts of the organic particulate emissions of the two restaurants were similar.

Table 1.11. (contd)

Reference, location	Setting	Study design/ samples	Exposure(s) measured	Main results
He *et al*. (2004b), Beijing, China	2 commercial restaurants, 1 with Chinese foods cooked over gas flame, 1 Uigur style (mutton charbroiled by charcoal)	Sampling during regular operation	$PM_{2.5}$, organic compounds including series of alkanes, *n*-alkanoic acids, *n*-alkanals, alkan-2-ones and PAHs	Mass concentrations of fine particles, alkanes, *n*-alkanoic acids and PAHs in air emitted from the Uigur [Chinese Islamic] style cooking were a hundred times higher than ambient $PM_{2.5}$ in Beijing.
Lee & Jeong (2008), South Korea	3 types of restaurants: Korean barbecue house, Chinese restaurant, Japanese restaurant	Personal exposure measurements in the breathing zone during eating periods	PM [PM_{10}, $PM_{2.5}$ and $PM_{1.0}$]	Highest concentrations at Korean barbecue house, with average concentrations of PM_{10}, $PM_{2.5}$ and $PM_{1.0}$ of 169, 124, and 63 μg/m^3, respectively; average exposure ratios for $PM_{1.0}/PM_{10}$, $PM_{2.5}/PM_{10}$ and $PM_{1.0}/PM_{2.5}$ at the barbecue house were 0.38, 0.73 and 0.52, respectively, which were much higher than those at other restaurants. Second highest $PM_{2.5}$ and PM_{10} concentrations at Chinese restaurant
			Formaldehyde	Range, 89.7–345.9 μg/m^3; highest concentrations in the Japanese restaurant
Pan *et al.* (2008), Taiwan, China	23 Chinese restaurants	Cross-sectional study; measurements in kitchens and dining areas	Airborne PM and PAHs	Airborne PM and PAH levels in kitchens significantly exceeded those in dining areas.
			Urinary 1-hydroxypyrene (1-OHP)	Geometric mean: kitchen staff, 4.5 μg/g creatinine; service staff, 2.7 μg/g creatinine (significantly higher)
			Urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG)	Geometric mean: kitchen staff, 7.9 μg/g creatinine; service staff , 5.4 μg/g creatinine (significantly higher)
				Urinary 1-OHP level, work in kitchens, gender and work hours per day were four significant predictors of urinary 8-OHdG levels after adjustments for covariates.

Table 1.11. (contd)

Reference, location	Setting	Study design/ samples	Exposure(s) measured	Main results
Yeung & To (2008), Hong Kong, China	Commercial cooking settings	Survey during commercial cooking processes	Size distributions of the aerosols	Log normal distribution; mode diameter of aerosols increased with increasing cooking temperature, especially in the size range between 0.1 and 1.0 μm.

PAH, polycyclic aromatic hydrocarbon; PM, particulate matter

Table 1.12. Environmental exposure to cooking emissions from commercial restaurants

Reference, location	Setting	Study design/ samples	Exposure(s) measured	Main results
To *et al.* (2007), Hong Kong, China	Commercial kitchens of Chinese restaurants, western restaurants and food servicing areas	Territorial-wide survey on the quantification of cooking fumes discharged from commercial kitchens	Organic compounds (*n*-alkanes, PAHs, fatty acids and aromatic amines)	Wide spectrum of organic compounds including *n*-alkanes, PAHs, fatty acids and aromatic amines PAHs: no statistically significant difference in the composition of fumes between restaurants; *n*-alkanes: mean concentrations in fumes from exotic food servicing areas significantly higher than those for Chinese or western restaurants ($p<0.05$)
Yang *et al.* (2007), Taiwan, China	16 restaurants with 3 types of cooking: Chinese, western and barbecue	Samples from kitchen exhausts	*trans*,*trans*-2,4-decadienal (*t*,*t*-2,4-DDE)	Emission factor (μg/customer): barbecue, 1990 > Chinese, 570 > Western, 63.8.

Table 1.12. (contd)

Reference, location	Setting	Study design/ samples	Exposure(s) measured	Main results
Zhao *et al.* (2007a), Guang Zhou, China	1 commercial western-style fast food restaurant	Sampling from exhaust	Chemical composition of particulate organic matter (POM)	The total amount of quantified compounds of per mg POM in western-style fast food cooking is much higher than that in Chinese cooking. The predominant homologue is fatty acids, accounting for 78% of total quantified POM, with the predominant one being palmitic acid. Dicarboxylic acids display the second highest concentration in the quantified homologues with hexanedioic acid being predominant, followed by nonanedioic acid. C-max of *n*-alkanes occurs at C25, but they still appear at relatively higher concentrations at C29 and C31. The relationship of concentrations of unsaturated fatty acids (C16 and C18) with a double bond at C9 position and C9 acids indicates the reduction of the unsaturated fatty acids in the emissions could form the C9 acids. Moreover, the non-linear fit indicates that other C9 species or other compounds are also produced, except for the C9 acids. The potential candidates of tracers for the emissions from western-style fast food cooking could be: tetradecanoic acid, hexadecanoic acid, octadecanoic acid, 9-octadecenoic acid, nonanal, lactones, levoglucosan, hexanedioic acid and nonanedioic acid.

Table 1.12. (contd)

Reference, location	Setting	Study design/ samples	Exposure(s) measured	Main results
Zhao *et al.* (2007b), Guang Zhou, China	4 Chinese restaurants: Cantonese style, Hunan style, Sichuan style and Dongbei style	Sampling from exhaust	Chemical composition of POM in $PM_{2.5}$	The quantified compounds account for 5–10% of total POM in $PM_{2.5}$. The dominant homologue is fatty acids, constituting 73–85% of the quantified compounds. The emissions of different compounds are impacted significantly by the cooking ingredients. The candidates of organic tracers used to describe and distinguish emissions from Chinese cooking in Guangzhou are tetradecanoic acid, hexadecanoic acid, octadecanoic acid, oleic acid, levoglucosan, mannosan, galactosan, nonanal and lactones.

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2. Studies of Cancer in Humans

2.1 Introduction

Since the 1970s, a total of 17 case–control studies have explored the relationship between exposure to cooking fumes and the risk for lung cancer. These studies were conducted in Chinese populations residing in China (including Taiwan and Hong Kong Special Administrative Region) and Singapore. While active tobacco smoking is a well-established major cause of lung cancer in Chinese men and women, a relatively high proportion of lung cancer in Chinese women, many of whom are nonsmokers, can not be explained by active smoking. Thus, one motivation for these studies was to investigate the role of other lifestyle factors, including indoor air pollution from cooking oil fumes, in the etiology of lung cancer in Chinese women.

Exposure assessment of cooking practices and cooking oil fumes varied substantially (Tables 2.1 and 2.2). Two aspects related to cooking oil fumes have been investigated: (i) the types of oil used and practices of high-temperature cooking, including frequency, stir-frying, deep-frying and pan-frying, and (ii) cooking practices, including the availability of a separate kitchen, ventilation in the kitchen based on the number and size of windows, the use of a fume extractor, personal assessment of ventilation, such as frequency of eye irritation during cooking and smokiness in the kitchen, duration of exposure (years of cooking) and susceptible time of exposure (age started to cook). In four studies (Lan *et al*., 1993; Dai *et al*., 1996; Shen *et al*., 1996; Wang *et al*., 1996), results were based on a single variable that represented some aspect of cooking practices. In contrast, exposure assessment was more comprehensive in seven studies (Gao *et al*., 1987; Ko *et al*., 1997; Zhong *et al*., 1999; Ko *et al*., 2000; Lee *et al*., 2001; Metayer *et al*., 2002; Yu *et al*., 2006). In several studies, the authors specified that past cooking practices or those experienced earlier in life (Seow *et al*., 2000) or at a particular age or time period in life (Ko *et al*., 1997, 2000; Lee *et al*., 2001) were investigated. Behaviours related to the type of cooking oil used most often and the frequency of high-temperature cooking (stir-frying, pan-frying, deep-frying) were also frequently examined. However, in most of the studies, no discussion was included regarding the timing of exposure or whether the information collected was related to current, usual or past cooking practices. Other factors included frequency of eye irritation during cooking, frequency of smokiness in the house, location of the kitchen, windows in the kitchen and the presence of fume extractors; these are viewed as indirect measures to assess the severity of exposure to cooking fumes and general household ventilation. Greater attention was paid to the measures of exposure that were considered to be more objective and whether duration, frequency and intensity of exposure to cooking oil fumes were assessed.

Of the 17 case–control studies that have investigated the relationship of exposure to cooking oil fumes and lung cancer, one was a study of lung cancer mortality (Lei *et al*.,

Table 2.1. Assessment of cooking practices/fumes included in the published case–control studies of lung cancer

Reference	Cooking in separate kitchen	Windows in kitchen/size	Fumes visible	Smokiness in kitchen	Eye irritation	No. of meals cooked/day	Age started cooking	Years of cooking
MacLennan *et al*. (1977)	–	–	–	–	–	–	No/yes (cooking)	–
Gao *et al*. (1987)	–	–	–	–	Never to frequent	–	–	–
Xu *et al*. (1989)	Cooking in bedroom (yrs)	–	–	–	–	–	–	–
Wu-Williams *et al*. (1990)	–	–	–	–	Never to frequent	–	–	–
Liu *et al*. (1991)	–	–	–	–	–	–	≤10 vs. >15 yrs	≤30, 31–44, ≥45
Ger *et al*. (1993)	–	–	–	–	–	–	–	–
Lan *et al*. (1993)	–	–	–	–	–	–	–	–
Liu *et al*. (1993)	No/yes	Size; chimneys	–	Ventilation (no/yes)	–	0–1, 2, 3	–	–
Dai *et al*. (1996)	–	–	–	–	–	–	–	–
Koo *et al*. (1996)	–	–	–	–	–	–	–	<25, 26–40, ≥41
Lei *et al*. (1996)	Size kitchen	–	–	–	–	–	–	Infrequent, ≤20, 20–40, >40
Shen *et al*. (1996)	–	–	–	No/yes	–	Times/week (no results)	–	–
Wang *et al*. (1996)	–	–	No/yes	–	–	–	–	–
Ko *et al*. (1997)	–	–	Fume extractor (no/yes)	–	–	–	7–20 vs. ≥ 21 yrs	–
Zhong *et al*. (1999)	No/yes	Area of window	No/yes	None to considerable	Never to frequent	–	–	–

Table 2.1. (contd)

Reference	Cooking in separate kitchen	Windows in kitchen/size	Fumes visible	Smokiness in kitchen	Eye irritation	No. of meals cooked/day	Age started cooking	Years of cooking
Ko *et al*. (2000)	–	<2 vs. ≥2, size of opening: small or medium, large	Fume extractor	Ventilation Poor/good	Rarely vs. frequently	Daily (no/yes) meals (1, 2, ≥3)	≤20 vs. 20 yrs	1–20, 21–40, ≥40
Seow *et al*. (2000)	–	–	<Daily/daily	–	–	–	–	–
Zhou *et al*. (2000)	(location) Separate Living room, Bedroom	–	Medium/heavy vs slight	None, slight, medium, heavy	Never to frequent	–	–	–
Lee *et al*. (2001)	–	–	Fume extractor	–	–	–	≤20 vs. 20 yrs	–
Metayer *et al*. (2002)	–	–	–	No to considerable by oil type	Ever to frequent by oil type	≤2 vs. ≥3	≤13, 14–16, ≥17 yrs	≤29, 30–39, 40–49, ≥50
Chan-Yeung *et al.* (2003)	–	–	–	–	–	–	–	
Shi *et al.* (2005)	–	–	Fuel smoke, cooking oil smoke	–	–	–	–	–
Yu *et al*. (2006)	–	–	Fume extractor/ exhaust fan	–	–	–	–	–

Table 2.2. Assessment of cooking practices/fumes by type of oil, type of frying and type of fuel included in the published case–control studies of lung cancer

Reference	Rapeseed oil	Other type of oil	Amount of oil	No. of times stir-frying	No. of times deep-frying	No. of times pan-frying	No. of times boiling	Fuel for cooking	Fuel for heating
MacLennan *et al.* (1977)	–	–	–	–	–	–	–	Gas	Kerosene
Gao *et al*. (1987)	Never to frequent	Never to frequent	–	≤20–≥30/wk	0–≥3/wk	–	≤3–≥12/wk	Coal/gas/ wood	
Xu *et al*. (1989)	–	–	–	–	–	–	–	Gas	Coal
Wu-Williams *et al.* (1990)	–	–	–	–	0–≥3/mo	–	–	Coal	Coal
Liu *et al*. (1991)	–	–	–	–	–	–	–	Coal	Wood
Ger *et al*. (1993)	–	–	–	No/yes	No/yes	No/yes	No/yes	Coal	–
Lan *et al*. (1993)	Never vs. often	–	–	–	–	–	–	Coal	–
Liu *et al*. (1993)	–	–	–	–	–	–	–	Coal/gas/ wood	–
Dai *et al*. (1996)	–	–	–	–	≤5 vs. ≥5/mo*	≤5 vs. ≥5/mo*	–	Coal	Kerosene
Koo & Ho (1996)	–	–	–	–	–	–	–	Gas	Kerosene
Lei *et al*. (1996)	–	–	–	–	–	Preferred/ average/not preferred	–	–	–
Shen *et al*. (1996)	–	–	Use per mo (no results)	–	–	–	–	Solid/non-solid fuel	Coal
Wang *et al*. (1996)	–	–	–	–	–	–	–	–	–

Table 2.2. (contd)

Reference	Rapeseed oil	Other type of oil	Amount of oil	No. of times stir-frying	No. of times deep-frying	No. of times pan-frying	No. of times boiling	Fuel for cooking	Fuel for heating
Ko *et al*. (1997)	–	No/lard/ vegetable oil	–	0–4 vs. ≥5/wk	0–4 vs. ≥5/wk	0–4 vs. ≥5/mo	–	Gas/coal/ wood	–
Zhong *et al*. (1999)	Used frequently	Soya bean used frequently	–	<7, 7, >7/wk	≤1 vs. >1/wk	≤1 vs. >1/wk	–	Coal/coal gas/gas	–
Ko *et al*. (2000)	–	–	–	No/yes after fumes, fume extractor	No/yes after fumes, fume extractor	No/yes after fumes, fume extractor	–	Coal	Gas
Seow *et al*. (2000)	–	Unsaturated vs. saturated oil	–	Not daily vs. daily	–	–	–	–	–
Zhou *et al*. (2000)	–	–	–	–	–	0–1 vs. ≥2/wk	–	–	–
Lee *et al*. (2001)	–	Lard/vegetable oil	–	No/yes after fumes, fume extractor	No/yes after fumes, fume extractor	No/yes after fumes, fume extractor	–	Gas/coal/ wood	–
Metayer *et al*. (2002)	No/yes	Linseed/ perilla/ hempseed oil	Catty/mo ≤3–≥6	≤15–≥3/mo	≤1–≥3/mo	–	–	Coal/wood	–
Chan-Yeung *et al*. (2003)	–	–	–	–	–	No exposure <3.5/wk 3.5–7/wk >7/wk	–	–	–
Yu *et al*. (2006)	Never/seldom, sometimes, always	Peanut/corn oil		≤50 dish-years 51–100 101–150 151–200 >200	≤50 51–100 101–150 151–200 >200	≤50 51–100 101–150 151–200 >200		–	–

* deep-frying and pan-frying combined

1996); the other studies included six population-based (Gao *et al*., 1987; Xu *et al*., 1989; Wu-Williams *et al*., 1990; Lan *et al*.., 1993; Zhong *et al*., 1999; Metayer *et al*., 2002) and 10 hospital-/clinic-based studies of incident lung cancers (Ger *et al*., 1993; Dai *et al*., 1996; Shen *et al*., 1996; Wang *et al*., 1996; Ko *et al*., 1997, 2000; Seow *et al*., 2000; Zhou *et al*., 2000; Lee *et al*., 2001; Yu *et al*., 2006). Twelve studies included only women (Gao *et al*., 1987, Wu-Williams *et al*., 1990; Lan *et al*., 1993; Dai *et al*., 1996; Wang *et al*., 1996; Ko *et al*., 1997; Zhong *et al*., 1999; Ko *et al*., 2000; Seow *et al*., 2000; Zhou *et al*., 2000; Metayer *et al*., 2002; Yu *et al*., 2006), seven of which studied only nonsmokers (Lan *et al*., 1993; Dai *et al*., 1996; Wang *et al*., 1996; Ko *et al*., 1997; Zhong *et al*., 1999; Ko *et al*., 2000; Yu *et al*., 2006). Men and women, smokers and nonsmokers were included in the other five studies (Xu *et al*., 1989; Ger *et al*., 1993; Lei *et al*., 1996; Shen *et al*., 1996, Lee *et al*., 2001).

These studies used heterogeneous methodologies and included different sources of cases, types of controls, methods of data collection and use of surrogate respondents; the degree of pathological confirmation of lung cancer diagnoses also differed. Relevant information regarding each of the case–control studies (i.e. study population, study period, sources of cases and controls, number of cases and controls, response rate, number of proxy interviews, percentage of pathologically/cytologically confirmed cases) and selected results are shown in Table 2.3.

2.2 Case–control studies

2.2.1 Northern China

Two large population-based case–control studies carried out in industrial areas in northern China during the late 1980s provided information on cooking practices and the risk for lung cancer. The main objectives of these two studies were to examine the role of active and passive smoking, and pollution from industrial and domestic sources. Xu *et al*. (1989) studied men and women who had lung cancer in Shenyang while Wu-Williams *et al*. (1990) examined the pattern of risk for lung cancer among women in Harbin and Shenyang.

The study in Shenyang included 1249 lung cancer cases (729 men, 520 women) and 1345 population-based controls (788 men, 557 women); 86% of male cases and 70% of male controls were smokers; the corresponding figures in women were 55% of cases and 35% of controls (Xu *et al*., 1989). Nearly 80% (85.1% in men, 75.0% in women) of the lung cancers were pathologically/cytologically confirmed; 31% of these were adenocarcinoma of the lung. After adjusting for age, education and active smoking, the risk for lung cancer was higher when cooking took place in the bedroom or entry corridor to the bedroom than in a separate kitchen or elsewhere in the house. In men, the adjusted odds ratios were 1.0, 1.2 and 2.1 in relation to cooking in the bedroom for 0, 1–29 and ≥30 years, respectively (p trend <0.05); the corresponding adjusted odds ratios in women were 1.0, 1.5 and 1.8 (p trend <0.05).

Table 2.3. Case–control studies of cooking practices/fumes and lung cancer in China

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Gao *et al.* (1987), Shanghai, 1984–86	672 women; 81% HC; 61% ADC; 22% SqCC; 6% SCLC; 11% other; 236 smokers; aged 35–69 years permanent residents of the area, Shanghai Cancer Registry ICD-9 (162)	735 frequency-matched by age and selected from the general population of Shanghai; 130 smokers	Response rate: cases, 672/765 (88.0%); controls, 735/802 (91.3%)	*Oil used*			Age, education, smoking	Study population and exposure indices defined clearly; use of coal/gas was unrelated to risk
				Soya bean	269	1.0		
				Rapeseed	322	1.4 (1.1–1.8)		
				Stir-frying (dishes/week)				
				≤20	336	1.0		
				20–24	198	1.2 (0.9–1.5)		
				25–29	48	1.2 (0.8–1.9)		
				≥30	34	2.6 (1.3–5.0)		
				Deep-frying (dishes/week)				
				0	502	1.0		
				1	85	1.5 (1.0–2.1)		
				2	21	1.6 (0.8–3.2)		
				≥3	8	1.9 (0.5–6.8)		
				Boiling (dishes/week)				
				≤3	96	1.0		
				4–7	390	1.0 (0.7–1.3)		
				8–11	63	1.8 (1.1–3.0)		
				≥12	67	2.2 (1.3–3.7)		
				Eye irritation/ smokiness				
				Never/none	244	1.0		
				Never/considerable	55	1.6 (1.0–2.5)		
				Frequent/none	212	1.6 (1.2–2.1)		
				Frequent/considerable	109	2.6 (1.8–3.7)		

Table 2.3. (contd)

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Xu *et al.* (1989), Shenyang, 1985–87	1249 (729 men, 520 women); 79% HC; 31% ADC; 43% SqCC; 16% SCLC; 10% other; 86% men and 55% women smoked; aged 30–69 yrs; newly diagnosed with primary lung cancer; Shenyang Cancer Registry ICD-9 (162)	1345 (788 men, 557 women) population controls, frequency-matched on age and sex; 70% men and 35% women smoked	Response rate: cases, 1249/1318 (94.8%); controls, 100%	*Cooking in bedroom* 0 year 1–29 yrs ≥30 yrs *p* for trend 0 year 1–29 yrs ≥30 yrs *p* for trend	*Men* 570 75 84 *Women* 503 25 29	 1.0 1.2 2.1 <0.05 1.0 1.5 1.8 <0.05	Age, education, smoking	CIs not reported; coal use was not adjusted for in the analysis
Wu-Williams *et al*. (1990), Shenyang, 1985–87	965 women (520 from Shenyang, 445 from Harbin); 74% HC; 44% ADC; 28% SqCC; 16% SCLC; 12% other; 545 smokers (56.7%); aged 30–69 years; Shenyang Cancer Registry; 729 men from Shenyang	959 female (555 from Shenyang, 404 from Harbin) population controls, frequency-matched by age; 357 smokers (37.2%); 788 male controls from Shenyang	Response rate: cases, 962/1049 (92.7%); controls, 100%	*Deep-frying (times/month)* 0 1 2 ≥3 *Eye irritation* Never/rarely Occasionally Frequently *Burning kangs* 0 1–20 21+	 324 326 170 121 647 218 89 677 106 173	 1.0 1.2 (1.0–1.5) 2.1 (1.5–2.8) 1.9 (1.4–2.7) 1.0 1.6 (1.2–1.8) 1.8 (1.3–2.6) 1.0 1.2 (0.9–1.7) 1.5 (1.1–2.0)	Age, education, smoking, study area	

Table 2.3. (contd)

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Ger *et al*. (1993), Taipei, Taiwan, 1990–91	131 hospital patients (92 men, 39 women); 100% HC; 50% ADC; 27% SqCC; 14% SCLC; 48 nonsmokers	524 (262 hospital, 262 neighbourhood) matched to cases on age, sex, insurance status/ residence; 229 nonsmokers (111 hospital controls, 118 neighbourhood controls)	In-person interview; response rate: cases, 131/143 (92%); hospital controls, 88%; neighbourhood controls, 83%	**ADC**				Results shown were based on neighbour-hood controls. Matched analysis: variables included were not specified. Definition of cooking practices was not presented.
				Frying				
				No	46	1.0		
				Yes	26	0.71 (0.36–1.39)		
				Stir-frying				
				No	28	1.0		
				Yes	44	1.19 (0.58–2.44)		
				Deep-frying				
				No	63	1.0		
				Yes	9	0.63 (0.26–1.55)		
				Boiling				
				No	38	1.0		
				Yes	34	1.75 (0.99–3.12)		
				SqCC-/SCLC				
				Frying				
				No	44	1.0		
				Yes	15	0.93 (0.37–2.32)		
				Stir-frying				
				No	33	1.0		
				Yes	26	1.00 (0.47–2.14)		
				Deep-frying				
				No	51	1.0		
				Yes	8	1.22 (0.42–3.52)		
				Boiling				
				No	36	1.00		
				Yes	23	1.26 (0.61–2.60)		

Table 2.3. (contd)

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Lan *et al.* (1993), Xuan Wei County, 1988–90	139 female farmers; 39.6% HC; 49.1% ADC; 36.4% SqCC; 14.6% NOS with primary lung cancer; all nonsmokers	139 female farmers from the general population matched ± 2 years; all nonsmokers	In-person interview; response rate not reported	*Rapeseed oil* Never Occasional Often	 24 106 9	 1.00 1.26 (0.68–2.63) 4.58 (0.56–37.08)	Age, length of menstrual cycle, menopause age, family history of lung cancer	Coal use was not adjusted for in the analysis. Definition of occasional use was not provided.
Dai *et al.* (1996), Harbin, 1992–93	120 women with primary lung cancer; 100% HC; 100% ADC; aged 30–69 years; Harbin resident at least 10 years; all nonsmokers	120 population 1:1 matched by age (±5 yrs); all nonsmokers	In-person interview in the hospital or at home; response rate not reported	*Pan-fried and deep-fried* ≤5 times/month >5 times/month	 	 1.0 9.20 (1.53–55.3) p=0.152	Income, area of resident, years of coal use in bedroom, years of coal heating, exposure to coal, intake of carrot, family history of cancer	

Table 2.3. (contd)

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Lei *et al*. (1996), Guangzhou, 1986	792 (563 men, 229 women) who died from lung cancer; 0% HC; no information on cell type; 566 smokers (443 men, 123 women)	792 (563 men, 229 women); 1:1 matched on sex, age (± 5 years), year of death, block of residence; no history of respiratory disease; 422 smokers (361 men, 61 women)	In-person interview with next of kin; response rate, 792/831 (95.3%); home interviews with spouses or relatives·	**Men**	Deaths			Crude analysis was presented; odds ratios were calculated based on the data presented. Definition of frying was not provided.
				Kitchen space				
				<1	18	1.0		
				1–2	66	[0.70]		
				≥2	431	[0.78]		
				Cooking activity				
				Infrequent	339	1.0		
				≤20 yrs	83	[0.92]		
				20–40 yrs	79	[1.10]		
				>40 yrs	30	[1.00]		
				Cooking frying				
				Preferred	192	1.0		
				Average	177	[0.72]		
				Not preferred	177	[0.89]		
				Women				
				Kitchen space				
				<1	6	1.0		
				1–2	28	[1.20]		
				≥2	179	[1.82]		
				Cooking activity				
				Infrequent	29	1.0		
				≤20 yrs	28	[0.72]		
				20–40 yrs	83	[0.88]		
				>40 yrs	62	[0.75]		
				Cooking frying				
				Preferred	55	1.0		
				Average	93	[0.88]		
				Not preferred	77	[1.06]		

Table 2.3. (contd)

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Lin *et al*. (1996), Harbin City	122 cases of adenocarcinoma; nonsmokers aged 30–69 years		122 matched controls by gender and age; non-smokers	>3 times per month frying	NR	3.00 (1.35–6.69)		Age adjusted
Shen *et al*. (1996), Nanjing, 1986–93	263 (men and women); 100% HC; ≥20 years old	263 general population; healthy residents of Nanjing, matched on age (±5 years), sex, neighbourhood	In-person interview; response rate not reported	**Cooking fumes** *SqCC* No Yes *ADC* No Yes		 1.0 3.81 (1.06–13.73) 1.0 2.99 (1.68–5.34)	Active smoking, chronic bronchitis, family history of cancer, coal stove for heating, fuel index.	Many limitations in the study methods—no information on gender, smoking or other factors
Wang *et al*. (1996), Shenyang, 1992–94	135 newly diagnosed cases of lung cancer; 57% HC; 100% HC; 54.5% ADC; 20% SCLC; 16.4% SqCC; 9.1% other; aged 35–69 years; all nonsmokers; ICD-9 (162)	135 general population matched on age (±5 years), sex, lifetime nonsmoking status	In person interview; response rate not reported	*Exposed to cooking fumes* No Yes Yes (adjusted)*	 77	 1.0 3.79 (2.29–6.27) 4.02 (2.38–6.78)*	* All study variables were considered in multivariate analysis, but results on cooking fumes were adjusted for coal smoke during cooking	

Table 2.3. (contd)

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Ko *et al*. (1997), Kaohsiung, Taiwan, 1992–93	117 female cases with primary lung cancer; 64.8% ADC; 17.1% SqCC; 15.2% SCLC; 2.9% LCC; 106 nonsmokers included in analysis ICD-9 (162)	117 hospital controls matched on age (±2 years), date of interview, nonsmoking-related disease	Personal interviews; response rate: cases, 117/128 (91.4%); controls, 117/125 (93.6%)	**Use of fume extractor** *Stir-frying* 0–4/week ≥5/week *Pan-frying* 0–4/week ≥5/week *Deep-frying* 0–4/month ≥5/month *Age when first cooking* ≥21 yrs 7–20 yrs *Before 20 yrs of age* Yes No *At 20–40 yrs of age* Yes No No (adjusted)* *After 40 yrs of age* Yes No	 14 91 29 76 82 23 36 67 7 60 25 78 76 22	 1.0 2.4 (1.1–5.2) 1.0 2.3 (1.2–4.6) 1.0 0.9 (0.5–1.9) 1.0 1.6 (0.8–3.0) 1.0 5.3 (1.1–25.6) 1.0 6.4 (2.9–14.1) 8.3 (3.1–22.7)* 1.0 2.3 (1.1–5.1)	Social class, residential area, and education were adjusted in all analysis. *Additional adjustment for tuberculosis, cooking fuels, living near industrial district	Coal use not significant Wood/charcoal use was significant ≤40 yrs Cooking fuel use was only adjusted for in selected analysis.

Table 2.3. (contd)

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Ko *et al.* (1997) (contd)				**Cooking oils**				
				Before 20 yrs of age				
				No cooking	38	1.0		
				Lard	51	1.6 (0.8–3.1)		
				Vegetable oil	16	2.0 (0.8–4.8)		
				At 20–40 yrs of age				
				No cooking	2	–		
				Lard	38	1.0		
				Vegetable oil	65	1.4 (0.8–2.6)		
				After 40 yrs of age				
				No cooking	2	–		
				Lard	7	1.0		
				Vegetable oil	91	0.5 (0.1–2.2)		

Table 2.3. (contd)

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Zhong *et al*. (1999), Shanghai, 1992–94	504 nonsmoking women ~77% HC; 76.5% ADC; 12.4% SqCC; 1.8% SCLC; 0.3% LCC; 9.0% mixed cells; aged 35–69 years; permanent residents of the area; Shanghai, China Cancer Registry; 145 smokers excluded from analysis	601 nonsmoking general population frequency-matched to age distribution by 5-year age intervals; 74 smokers excluded from analyses	In-person interview at hospital, home or work; response rate: cases, 649/706 (91.9%) (for smokers and nonsmokers); controls, 84%	*High-temperature cooking*			Age, education, income, intake of vitamin C, respondent status, exposure to passive smoking, family history of lung cancer, employment in high-risk occupation	
				No	339	1.0		
				Yes	165	1.64 (1.24–2.17)		
				Most frequently used oil				
				Soya bean oil	444	1.0		
				Rapeseed oil	49	1.84 (1.12–3.02)		
				Both oils	11	0.92 (0.37–2.28)		
				Stir-frying (no./week)				
				<7	40	1.0		
				7	434	0.38 (0.19–0.75)		
				>7	30	2.33 (0.68–7.95)		
				Pan-frying (no./week)				
				≤1	464	1.0		
				>1	40	2.09 (1.14–3.84)		
				Deep-frying (no./week)				
				≤1	469	1.0		
				>1	35	1.88 (1.06–3.32)		
				Smokiness in kitchen				
				None	177	1.0		
				Somewhat	241	1.67 (1.25–2.21)		
				Considerable	86	2.38 (1.58–3.57)		
				Eye irritation				
				Never	338	1.0		
				Rarely	49	1.49 (0.91–2.43)		
				Occasionally	74	1.75 (1.16–2.62)		
				Frequently	43	1.68 (1.02–2.78)		

Table 2.3. (contd)

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Ko *et al.* (2000), Kaohsiung, Taiwan, 1993–96	131 women with primary carcinoma of the lung; 100% HC; 19.8% SqCC; 62.6% ADC; 13.7% SCLC; 2.3% LCC; 1.5% NOS; >40 years of age; nonsmokers ICD-9 (162)	252 hospital eye or orthopaedic patients, or in for check-ups (diseases unrelated to smoking); 262 community, age-matched randomly selected from a computerized population database.; matched for age and date of interview; nonsmokers	Personal interviews; response rate: cases, 131/148 (88.5%); hospital controls, 252/281 (89.7%); community controls, 262/294 (89.1%)	*Daily cooking* No Yes *Age cooking started* >20 yrs ≤20 yrs *Yrs cooking at home* 1–20 21–40 ≥40 *Meals cooked/day* 1 2 ≥3 *Windows in kitchen* <2 ≥2 *Ventilation of kitchen* Poor Good	 1 130 47 83 36 74 20 13 71 46 62 69 71 60	 1.0 5.9 (0.7–53.6) 1.0 1.5 (0.9–2.4) 1.0 1.3 (0.6–2.6) 1.0 (0.4–2.9) 1.0 3.1 (1.6–6.2) 3.4 (1.6–7.0) 1.0 1.3 (0.8–2.1) 1.0 0.9 (0.6–1.4)	Socio-economic status, occupation, previous lung disease, passive smoking	Results shown are based on comparison with community controls. Role patterns were similar for hospital controls

Table 2.3. (contd)

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Ko *et al.* (2000) (contd)				*Eye irritation*				
				Rarely	84	1.0		
				Frequently	46	2.1 (1.3–3.5)		
				Stir-fry after fumes emitted				
				No	22	1.0		
				Yes	108	2.4 (1.4– 4.2)		
				Use of fume extractor				
				Before 20 yrs of age				
				Yes	40	1.0		
				No	43	0.9 (0.4–2.0)		
				Aged 20–40 yrs				
				Yes	85	1.0		
				No	45	2.2 (1.3–3.8)		
				Aged >40 yrs				
				Yes	114	1.0		
				No	12	1.3 (0.6–2.8)		

Table 2.3. (contd)

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Seow *et al*. (2000), Singapore, 1996–98	303 women; 100% HC; 54.8% ADC; 18.5% SqCC; 6.9% SCLC; 15.2% LCC; 4.6% NOS; aged <90 years; 127 smokers, 176 nonsmokers	765 hospital controls, frequency-matched for age, hospital, date of admission; no history of cancer, heart chronic disease or renal failure; 100 smokers, 663 nonsmokers	In-person interview within 3 months of diagnosis; response rate: cases, 361/380 (95.0%); controls, 765/789 (96.9%)	**Smokers** *Stir-frying* Less than daily Daily Less than daily with meat **Lifetime nonsmokers** *Stir-frying* Less than daily Daily Less than daily with meat **Smokers** *Stir-frying meat less than daily* Daily with meat Less than daily with meat with fume-filled kitchen Daily with meat with fume-filled kitchen **Lifetime nonsmokers** *Stir-frying meat less than daily* Daily with meat Less than daily with meat with fume-filled kitchen Daily with meat with fume-filled kitchen	 25 97 21 52 122 41 46 75 23 52 93 76 34 42	 1.0 ref 2.0 (1.0–3.8) 1.0 (0.5–2.4) 1.0 ref 1.0 (0.7–1.5) 0.9 (0.6–1.5) 1.0 ref 2.7 (1.3–5.5) 1.7 (0.7–3.9) 3.7 (1.8–7.5) 1.0 ref 0.9 (0.6–1.4) 1.1 (0.7–1.7) 1.0 (0.6–1.4)	Age , birthplace, family history of cancer, intake of fruits and vegetables. For smokers, odds ratios were additionally adjusted for duration of smoking (in years) and number of cigarettes smoked/day.	Current and ex-smokers grouped together

Table 2.3. (contd)

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Zhou *et al*. (2000), Shenyang, 1991–95	72 women with primary lung cancer; 100% HC; 100% ADC; aged 35–69 years; 20 smokers	72 general population, age 1:1 matched (±5 years) to cases; 23 smokers	In person interview; response rate not reported	*Eye irritation from smoke*		**Multivariate odds ratio**	Income, family history of lung cancer, number of live births	Fuel use for cooking/ heating was not considered in the analysis.
				Never		1.0		
				Slight		1.58 (0.62–4.03)		
				Medium		11.45 (3.10–42.4)		
				Heavy		3.41 (0.52–22.5)		
				p for trend		0.002		
				Location of kitchen		**Crude odds ratio**		
				Separate	6	1.00		
				In living room	63	1.40 (0.41–4.88)		
				In bedroom	3	1.00 (0.11–8.93)		
				p for trend		0.83		
				Cooking oil fumes				
				Slight	30	1.0		
				Medium/heavy	42	4.53 (2.09–9.94)		
				Deep-fried (no./week)				
				0–1		1.0		
				≥ 2	5	1.68 (0.45–6.84)		
				Extent of smoke when cooking	67			
				None	19	1.0		
				Slight	15	0.73 (0.28–1.90)		
				Medium	35	2.71 (1.09–6.80)		
				Heavy	3	1.32 (0.18–9.50)		
				p for trend		0.027		

Table 2.3. (contd)

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Lee *et al*. (2001), Kaohsiung, Taiwan, 1993–99	236 male, 291 female; only women with ADC, SqCC and SCLC retained for this analysis; 100% HC; 55.7% ADC; 20.3% SqCC; 8.6% SCLC; 2.1% LCC; 5.5% BA; 7.9% NOS; aged 18–83 years	407 hospital patients; matched to cases on sex, age (±2 years); ~2 controls per case; smoking in female controls not reported	In-person interview; response rate (presented for men and women combined): cases, 527/574 (91.8%); controls, 805/883 (91.2%)	*Kitchen with fume extractor*		***SqCC/SCLC***	Residence area (urban, suburban, rural), educational levels, socio-economic status (high, medium low), smoking (cumulative pack–years)	Wood/charcoal use was a significant risk factor; this was not adjusted for in the analysis.
				Yes	51	1.0		
				No	31	3.0 (1.3–7.1)		
				Cooking oils				
				Lard	28	1.0		
				Vegetable oil	54	0.7 (0.3–1.4)		
				Age first cooked (yrs)				
				>20	27	1.0		
				≤20	55	1.5 (0.7–3.1)		
				Stir-frying after fumes				
				No	23	1.0		
				Yes	59	0.9 (0.4–1.9)		
				Pan-frying after fumes				
				No	24	1.0		
				Yes	58	0.8 (0.4–1.5)		
				Deep-frying after fumes				
				No	44	1.0		
				Yes	38	1.0 (0.5–2.0)		

Table 2.3. (contd)

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Lee *et al*. (2001) (contd)				*Kitchen with fume extractor*		***ADC***		
				Yes	84	1.0		
				No	74	3.9 (2.3–6.6)		
				Cooking oils				
				Lard	50	1.0		
				Vegetable oil	108	1.2 (0.7–1.9)		
				Age first cooked (yrs)				
				>20	65	1.0		
				≤20	93	1.1 (0.7–1.7)		
				Stir-frying after fumes				
				No	29	1.0		
				Yes	29	2.0 (1.2–3.3)		
				Pan-frying after fumes				
				No	20	1.0		
				Yes	138	2.6 (1.5–4.5)		
				Deep-frying after fumes				
				No	68	1.0		
				Yes	90	1.6 (1.0–2.6)		
Metayer *et al*. (2002), Gansu Province, 1994–98	233 women; 37% HC; cell type distribution not presented; aged 30–75 years; 27 smokers	459 randomly selected from 1990 population census list of study areas; frequency-matched by age (± 5 years), Prefecture; 47 smokers	In-person interview; response rate: cases, 233/238 (98%); controls, 459/509 (90%)	*Type of oil (ever use)*			Age, Prefecture, socio-economic factors, respondent type.	
				Linseed	80	1.0		
				Rapeseed	53	1.65 (0.8–3.2)		
				Rapeseed + linseed	90	1.70 (1.0–2.8)		
				Perilla + hempseed	5	3.25 (0.8–14.0)		
				Stir-fying (times/month)				
				<15	71	1.0		
				15–29	60	1.96 (1.1–3.5)		
				30	52	1.73 (1.0–3.1)		
				≥31	45	2.24 (1.1–4.5)		
				p for trend		<0.05		

Table 2.3. (contd)

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Metayer *et al*. (2002) (contd)				*Deep-frying (times/month)*				
				Never/<1	70	1.0		
				1–2	86	0.82 (0.5–1.3)		
				≥3	38	0.83 (0.5–1.5)		
				Years of cooking				
				≤29	52	1.00		
				30–39	76	1.26 (0.6–2.8)		
				40–49	65	2.51 (0.9–6.8)		
				≥50	29	2.46 (0.8–7.9)		
				Age started cooking (yrs)				
				≤13	63	1.0		
				14–16	85	0.69 (0.4–1.1)		
				≥17	80	0.69 (0.4–1.2)		
				No. of meals cooked/day				
				≤2	193	1.0		
				≥3	36	1.36 (0.8–2.4)		
				Eye–throat irritation				
				Never	72	1.0		
				Occasionally/seldom	100	1.37 (0.8–2.2)		
				Frequently	54	2.82 (1.6–5.0)		
				p for trend		<0.01		
				Home smokiness				
				No	49	1.0		
				Some/little	155	0.90 (0.6–1.5)		
				Considerable	23	0.76 (0.4–1.6)		

Table 2.3. (contd)

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Chan-Yeung *et al.* (2003), Hong Kong, 1999–2001	331 histologically or cytologically proven cases of lung cancer	331 in- and out-patients without cancer; matched for age, sex	Personal interviews for cases and controls; response rates not given	**Frying foods** *Men* No or <2 yrs <3.5 yrs 3.5–7 yrs >7 yrs *Women* No or <2 yrs <3.5 yrs 3.5–7 yrs >7 yrs	 146 27 22 13 34 37 27 21	 1.0 0.69 (0.32–1.49) 0.83 (0.38–1.80) 1.22 (0.38–3.99) 1.0 1.08 (0.50–2.32) 1.05 (0.46–2.42) 1.54 (0.57–4.13)	Place of birth, educational status, family history of lung cancer, smoking (in men); educational status, smoking status (in women)	
Shi *et al* (2005), Shenyang, 2000–2002	618 newly diagnosed female patients with primary lung cancer	Randomly selected from the general population in urban districts	Face-to-face interviews	Cooking oil smoke		4.11 (2.14–7.89)		In multivariate analysis cooking oil smoke remained statistically significant but fuel smoke did not remain significant

Table 2.3. (contd)

Reference, study location, period	Characteristics of cases, histological confirmation (HC), cell type (%)	Characteristics of controls	Data collection, response rate	Exposure categories	No. of cases	Relative risk (95% CI)	Adjustment factors	Comments (covariates considered)
Yu *et al.* (2006) Hong Kong	291 women newly diagnosed with primary carcinomas; 96% participation rate; 68.5% ADC; aged 30–79 yrs; 67 smokers	661 randomly sampled residents from same districts as cases; frequency matched ±10 years; 322 (48.7% participation rate)	In-person interviews	*Total dish–years*			Age, education, employment status, previous lung diseases and history of lung cancer in first degree relatives (for model 1 regarding total dish-years); age, history of lung cancer in first degree relatives, intake of dark green vegetables, yellow orange vegetables, meat, coffee drinks, multivitamins, total dish–years	
				≤50		1.0		
				51–100		1.31 (0.81–2.11)		
				101–150		2.80 (1.52–5.18)		
				151–200		3.09 (1.41–6.79)		
				>200		8.09 (2.57–25.45)		
				Heating a wok to high temperatures				
				Never/seldom	25	1		
				Sometimes	37	1.02 (0.51–2.06)		
				Always	131	1.97 (1.06–3.65)		
				Use of fume extractor				
				Never	12	1		
				Ever	183	0.73 (0.29–1.87)		
				Use of peanut oil				
				Seldom/sometimes	70	1		
				Always	125	1.36 (0.87–2.15)		
				Use of corn oil				
				Seldom/sometimes	146	1		
				Always	49	1.27 (0.76–2.10)		
				Use of canola oil				
				Seldom/sometimes	181	1		
				Always	14	1.40 (0.59–3.30)		

ADC, adenocarcinoma; BA, basal-cell cancer; CI, confidence interval; ICD, International Classification of Diseases; LCC, large-cell carcinoma; NOS, not otherwise specified; SqCC, squamous-cell carcinoma; SCLC, small-cell cancer

The report by Wu-Williams *et al*. (1990) was based on 965 female lung cancer cases in northern China (445 in Harbin, 520 in Shenyang) and 959 female controls (404 in Harbin, 555 in Shenyang); 417 cases and 602 controls were nonsmokers. Seventy-four per cent (714/965) of the lung cancers were histologically/cytologically confirmed of which 44% were adenocarcinoma of the lung. Cases and controls were compared in terms of deep-frying practices. Compared with no deep-frying, the adjusted odds ratios were 1.2, 2.1 and 1.9 for deep frying once, twice and more than three times per month, respectively. Cases reported that their homes became smoky during cooking more often than controls and that they had irritated eyes more frequently during cooking. Compared with women who never or rarely experienced eye irritation during cooking, the risk was increased among those who occasionally (odds ratio, 1.6; 95% CI, 1.2–1.8) or frequently (odds ratio, 1.8; 95% CI, 1.3–2.6) reported such irritation. The authors noted that results were similar for squamous-/oat-cell cancers and adenocarcinomas and for smokers and nonsmokers. Pollution from coal burning for heating was a major risk factor in this area in northern China; in a multivariate analysis, deep-frying and eye irritation remained significant risk factors after adjusting for active smoking, previous lung diseases and coal burning (i.e. use of *kangs*). [The Working Group noted that, although coal heating was adjusted for in the multivariate analysis, the risk associated with frequent eye irritation may be due to fuel smoke and cooking smoke. The assessment of cooking practices was relatively limited in these two studies.]

Two small studies were conducted in Harbin (Dai *et al*., 1996) and Shenyang during the early 1990s (Wang *et al*., 1996; Zhou *et al*., 2000). The study by Dai *et al*. (1996) included 120 nonsmoking women who had adenocarcinoma of the lung and an equal number of nonsmoking controls; all were long-term (at least 10 years) residents of Harbin. The risk for adenocarcinoma of the lung was significantly influenced by frequency of frying food; women who pan-fried and deep-fried more than five times per month experienced a more than ninefold increased risk (adjusted odds ratio, 9.20; 95% CI, 1.53–55.28) after adjustment for various covariates including exposure to coal burning. [The Working Group noted that the prevalence of frying was not presented; the wide confidence interval is a concern. It is unclear whether these questions related to current or usual frying practices and whether other questions on cooking practices were asked. One Chinese study by Lin *et al.* (1996) evaluated the exposure to cooking oil fumes and the risk of lung adenocarcinoma among female nonsmokers. An age-adjusted increased risk of lung cancer (odds ratio, 3.0; 95% CI, 1.35–6.69) was observed for those who reported to fry food more than 3 times per month.

In a hospital-based study conducted in Shenyang, Wang *et al*. (1996) compared the experiences of 135 female lifetime nonsmokers who had been diagnosed with primary lung cancer and an equal number of nonsmoking female population controls. Of the lung cancers included, 57.2% were diagnosed pathologically or cytologically, 54.5% of which were adenocarcinoma. The risk for lung cancer increased significantly in association with some or frequent exposure to cooking fumes (odds ratio, 3.79; 95% CI, 2.29–6.27). In a multivariate analysis, exposure to cooking fumes remained a significant risk factor

(adjusted odds ratio, 4.02; 95% CI, 2.38–6.78) after adjusting for exposure to coal smoke and other factors. [The Working Group noted that this study was small and the exposure was limited to dichotomized (no/yes) assessment. The specific variables that were included in the multivariate analysis were not described. Coal use and exposure to coal smoke were reported in this study and may confound the findings related to cooking fumes. The validity of a diagnosis of adenocarcinoma is questionable because the authors stated that determination of the histological cell type was based on relevant medical record, chest X-rays, CT films and cytological and histological slides.]

Zhou *et al*. (2000) published another report on a subset of women from the hospital-based study in Shenyang (Wang *et al*., 1996). Specifically, 72 women (52 nonsmokers) who had been diagnosed with adenocarcinoma of the lung between 1991 and 1995 were compared with an equal number of control women (49 nonsmokers). A nonsignificant increased risk was observed in relation to deep-frying; the crude odds ratio was 1.68 (95% CI, 0.45–6.84) for deep-frying two or more times per week compared with none or once a week. The risk for adenocarcinoma increased significantly among women who reported that they experienced medium/heavy exposure to cooking fumes (crude odds ratio, 4.53; 95% CI, 2.09–9.94) or had frequent eye irritation and exposure to smoke during cooking. The risk for lung cancer was not significantly associated with whether cooking was carried out in a separate kitchen or in the living-room or bedroom. In a multivariate regression analysis, frequent eye irritation from smoke had an independent impact on risk. Compared with women who reported no eye irritation from smoke, those who reported slight, medium and heavy eye irritation showed elevated risks; the respective adjusted odds ratios were 1.58, 11.45 and 3.41 for (p for trend=0.002). [The Working Group noted that most of the lung cancer cases and controls included in the analysis by Zhou *et al*. (2000) represented a select subgroup of subjects reported by Wang *et al*. (1996) and the selection criteria were not described. This study was small and the confidence intervals were very wide.]

2.2.2 *Other parts of China and Singapore*

One of the first studies of exposure to cooking oil fumes and the risk for lung cancer was a large population-based case–control study conducted in the mid-1980s in Shanghai that was designed to examine lifestyle factors and lung cancer (Gao *et al*., 1987). The study included 672 women who had lung cancer and 735 population controls, of whom 436 cases and 605 controls were nonsmokers. Eighty-one per cent (542/672) of the lung cancers were diagnosed histologically or cytologically. Questions on cooking practices included type of oil used most often, frequency of frying, smokiness in the kitchen during cooking and frequency of eye irritation during cooking. Several measures of cooking practices were associated with an increased risk for lung cancer after adjusting for age, education and tobacco smoking. Compared with women who most frequently used soya bean oil, those who used rapeseed oil had an increased risk for lung cancer (adjusted odds ratio, 1.4; 95% confidence interval [CI], 1.1–1.8). The increased risk associated with the

use of rapeseed oil existed at each level of reported frequency of eye irritation when cooking. However, the increased risk associated with frequent eye irritation when cooking was found among both women who used soya bean oil and those who used rapeseed oil, although the highest risk was found in women who used rapeseed oil and frequently experienced eye irritation (adjusted odds ratio, 2.8; 95% CI, 1.8–4.3). There was a stepwise increase in risk associated with smokiness in the house. Specifically, women who reported occasional/frequent eye irritation and a considerable amount of smokiness in the house showed a more than twofold increased risk (adjusted odds ratio, 2.6; 95% CI, 1.8–3.7). Risk increased with increasing number of dishes prepared by stir-frying (adjusted odds ratios, 1.0, 1.2, 1.2 and 2.6 for ≤20, 20–24, 25–29 and ≥30 times per week, respectively) and deep-frying (adjusted odds ratios, 1.0, 1.5, 1.6 and 1.9 for 0, 1, 2 and ≥3 times per week, respectively). The risk patterns were similar for adenocarcinoma and squamous-cell/oat-cell carcinoma of the lung. [The Working Group noted that this was one of the first well-conducted population-based studies on this topic and had many strengths. The Working Group also noted that the increased risk was found with increasing number of dishes prepared by boiling food. Since it should produce less oil vapour than stir-frying and deep-frying, the comparably high odds ratios associated with boiling food were unexpected, although the authors suggested that oil was also added during boiling.]

In the 1990s, Zhong *et al*. (1999) conducted another study in Shanghai that used study methods similar to those used by Gao *et al*. (1987) and included a total of 649 women who had been diagnosed with incident lung cancer during 1992–94 and 675 population controls. Subjects who had smoked at least one cigarette a day for at least 6 months (145 cases, 74 controls) were excluded from the analyses. Thus, results on cooking practices were based on 504 cases and 601 controls who were lifetime nonsmokers. Seventy-seven per cent (387/504) of the lung cancers were diagnosed histologically or cytologically; 76.5% (296/387) of these were adenocarcinoma. Women who did not cook in a separate kitchen experienced a small increased risk (adjusted odds ratio, 1.28; 95% CI, 0.98–1.68). Risk for lung cancer was higher among those who had used rapeseed oil most frequently compared with those who had used soya bean oil (adjusted odds ratio, 1.84; 95% CI, 1.12–3.02). However, the risk was not elevated when both types of oil had been used (adjusted odds ratio, 0.92; 95% CI, 0.37–2.28). Risk also increased with higher frequency of frying. Compared with women who deep-fried once a week or less often, those who deep-fried more than once a week had a nearly twofold increased risk (adjusted odds ratio, 1.88; 95% CI, 1.06–3.32). Similarly, compared with women who pan-fried food once a week or less often, those who pan-fried food more than once a week had a significantly increased risk (adjusted odds ratio, 2.09; 95% CI, 1.14–3.84). However, the risk pattern in relation to stir-frying was less consistent. Compared with stir-frying less than seven times a week, women who stir-fried seven times a week had a reduced risk (adjusted odds ratio, 0.38; 95% CI, 0.19–0.75), but those who stir-fried more than seven times a week showed an increased risk (adjusted odds ratio, 2.33; 95% CI, 0.68–7.95). Women exposed to visible fumes from high-temperature frying had an increased risk

(adjusted odds ratio, 1.64; 95% CI, 1.24–2.17). This risk more than doubled for women who reported considerable smokiness (i.e. smokiness affected vision during cooking) from 'cooking oil or fumes' (adjusted odds ratio, 2.38; 95% CI, 1.58–3.57) compared with those who reported no smokiness. There was also a trend of increasing risk with increasing frequency of self-reported eye irritation; the adjusted odds ratio was 1.68 (95% CI, 1.02–2.78) for women who reported frequent (≥5 times per week) eye irritation compared with those who reported no eye irritation. Risk patterns related to Chinese-style cooking were generally similar in analyses that were restricted to all self-respondents (400 cases, 581 controls) or to self-respondents with histologically confirmed lung cancer (308 cases, 581 controls). Results were also comparable for women who had adenocarcinomas (296 cases), non-adenocarcinomas (91 cases) or unknown cell type (i.e. diagnosed clinically/radiologically) of lung cancer (117 cases). In a multivariate regression analysis, cooking temperature, smokiness in the kitchen during cooking, type of cooking oil and the frequency of stir-frying and of pan-frying displayed independent effects on the risk for lung cancer after adjustment for variables on ventilation (e.g. area of windows, cooking in a separate kitchen). Frequency of eye irritation and frequency of deep-frying were correlated with the other variables and did not exhibit independent effects on risk. [The Working Group noted several strengths in this population-based study: it was conducted among lifetime nonsmokers, the assessment of cooking practices was comprehensive and the analyses were thorough. Results were generally consistent across various subgroup analyses by histological and respondent type. The type of fuel used for cooking (coal, gas) was not significantly associated with risk and was not adjusted for in the multivariate analysis. It should be noted that the distribution of stir-frying was skewed and the confidence intervals were wide for stir-frying. The prevalence of use of rapeseed oil was 7.2% among controls in this study compared with 47.2% in Shanghai in the mid-1980s. The reason for the large differences in the pattern of use of rapeseed oil was not discussed but may be due to differences in the questions asked in the two studies.]

Two other studies were conducted in urban areas of China to examine the relationship between exposure to cooking oil fumes and risk for lung cancer. Shen *et al*. (1996) investigated potential risk factors for lung cancer among long-term (at least 20 years) residents of Nanjing in a hospital-based, case–control study that included 263 cases of lung cancer and an equal number of population controls. Only histologically confirmed lung cancers were studied (83 squamous-cell carcinomas, 180 adenocarcinomas). Exposure to cooking fumes was associated with an increased risk for squamous-cell carcinoma (adjusted odds ratio, 3.81; 95% CI, 1.06–13.73) and adenocarcinoma (adjusted odds ratio, 2.99; 95% CI, 1.68–5.34) of the lung. [The Working Group noted that the study had serious limitations. The report lacked details regarding the study design (e.g. response rate) and characteristics of the study population (e.g. gender distribution, active smoking history). The source of information on exposures was not presented. Only significant results were presented; risk patterns in relation to the amount of oil used in cooking and frequency of cooking per week were not presented.]

Cooking practices and lung cancer mortality were investigated in a case–control study in Guangzhou (Lei *et al*., 1996). Using registered deaths that occurred in this city in 1986, the analysis was based on 792 (562 men, 229 women) lung cancer deaths reported in long-term (at least 10 years) Guangzhou residents. The comparison group included other registered decedents who were matched to cases on gender, age (±5 years) and residence and whose cause of death was unrelated to cancer or respiratory disease. A standardized interview administered to spouses or cohabiting relatives of the decedents collected information on active smoking, exposure to secondhand smoke, living conditions, cooking facilities, exposure to coal dust and dietary habits. In analyses conducted separately in men and women, cases and controls did not differ significantly in their preference of frying, years of cooking (infrequent, ≤20, 20–40, >40 years) or size the of kitchen (<1, 1–2, ≥2 m^2 per household). Similarly, living conditions (type of building, location of residence, interior dimensions of residence) and average size of the living area did not differ significantly between lung cancer cases and controls. [The Working Group noted that the study had several deficiencies. The quality of information on cooking practices obtained from next of kin is questionable; a considerable amount of information was missing; the data analysis was confined to crude analysis; and the accuracy of lung cancer diagnosis based on reviewed death records is not known for China.]

In addition to the above-mentioned studies that were conducted largely in urban areas of China, two studies were conducted in more rural parts of China: one in Xuan Wei County, Yunnan Province (Lan *et al*., 1993), an area where mortality rates for lung cancer are very high among women, and one in Gansu Province, a rural area in northwestern China (Metayer *et al*., 2002).

The study in Xuan Wei County, Yunnan Province, investigated the use of rapeseed oil in the study population and was based on 139 incident female lung cancers that were diagnosed between 1988 and 1990 and 139 age-matched controls (Lan *et al*., 1993). Of the lung cancer cases, 55 (39.6%) were diagnosed cytologically/pathologically. All cases and controls were nonsmokers. Compared with women who never used rapeseed oil, those who used it occasionally or frequently showed an increased risk; the respective adjusted odds ratios were 1.26 (95% CI, 0.68–2.63) and 4.58 (95% CI, 0.56–37.08) after adjusting for age, length of menstrual cycle, age at menopause and family history of lung cancer. [The Working Group noted that coal use was prevalent in this study population and was not considered in the analysis on cooking oil. In addition, the definition of occasional or frequent use of rapeseed oil was not provided. Few subjects (2.2% of controls) were frequent users of rapeseed oil and the confidence limits were wide. It is unclear whether other questions related to cooking practices were asked.]

Metayer *et al*. (2002) conducted a population-based case–control study that was designed to examine the association between cooking oil fumes and other sources of indoor air pollution and lung cancer in Gansu Province. The study included 233 female lung cancer cases and 459 control subjects; 206 cases and 411 controls were nonsmokers. Thirty-seven per cent of the cases were cytologically or histologically confirmed. Smokers (27 cases, 47 controls) were included in the analysis on cooking practices.

Compared with women who only used linseed oil, an elevated risk was associated with the use of rapeseed oil alone (adjusted odds ratio, 1.65; 95% CI, 0.8–3.2), rapeseed and linseed oil in combination (adjusted odds ratio, 1.70; 95% CI, 1.0–2.5) and perilla/hempseed oil (adjusted odds ratio, 3.25; 95% CI, 0.8–14.0). The risk for lung cancer was unrelated to the frequency of deep-frying (adjusted odds ratio, 1.0, 0.82 and 0.83 for never/less than once a month, 1–2 times per month and ≥3 times per month, respectively). However, there was a significant exposure–response of increased risk with increasing frequency of stir-frying (adjusted odds ratios, 1.00, 1.96, 1.73 and 2.24, for stir-frying <15, 15–29, 30 and ≥31 times per month; p for trend=0.03). Risk tended to increase with decreasing age when started to cook (adjusted odds ratio, 0.69 for started cooking at age ≥17 versus ≤13 years), with increasing number of meals cooked per day (adjusted odds ratio, 1.36 for ≥3 meals versus ≤2 meals) and with increasing years of cooking (adjusted odds ratio, 1.0, 1.26, 2.51 and 2.46 for ≤29, 30–39, 40–49 and ≥50 years) (p for trend <0.09). Although women who reported frequent eye–throat irritation showed a significantly increased risk (adjusted odds ratio, 2.82; 95% CI, 1.6–5.0) compared with those who never experienced such irritation (p trend <0.01), the general level of indoor smokiness was unrelated to risk. Risk for lung cancer was not elevated among women who reported considerable home smokiness (odds ratio, 0.76; 95% CI, 0.4–1.6) compared with those who reported no smokiness. The authors hypothesized that, as underground cave dwellings in Gansu Province reported high ventilation rates as measured by air exchanges per hour, this may explain the lack of any risk associated with general smokiness. The positive associations with stir-frying, years of cooking and eye irritation were found in women who cooked with linseed oil only (80 cases, 247 controls) and in those who cooked with rapeseed oil (148 cases, 205 controls). In addition, the authors reported that the results were generally similar when the analyses were restricted to self-respondents or to histologically confirmed lung cancer cases. [The Working Group noted that this study included a comprehensive assessment of cooking practices and conditions. Coal use for heating/cooking was not significantly associated with lung cancer risk in this population. Although coal use was not considered in the analysis on cooking practices, it is unlikely to confound the findings. The results suggest that fumes from all types of oil may have deleterious effect. This study is limited by a relatively large number of only clinically/radiologically diagnosed lung cancers and because interviews were conducted with next-of-kin respondents for 123 cases (53%) and 20 controls (4%).]

Shi *et al*. (2005) conducted a case–control study that included nonsmoking women who had been newly diagnosed with lung cancer between June 2000 and December 2002 in city hospitals of urban Shenyang. Eighty-four per cent of cases were diagnosed pathologically or cytologically. Controls were randomly selected from the general female population of urban areas and matched on age (within ±2 years). Information on demographic factors, exposure to cooking oil smoke, types of fuel used, exposure to coal smoke, use of heated *kangs*, passive smoking, history of lung disease and other factors was obtained. Risk for lung cancer increased significantly in association with exposure to

cooking oil smoke (odds ratio, 3.18; 95% CI, 2.55–3.97) and fuel smoke (odds ratio, 2.56; 95% CI, 1.83–4.55) after adjusting for education and social class. Risk was unrelated to the use of *kangs* (odds ratio, 1.12; 95% CI, 0.91–1.39). In a multivariate analysis, the increased risk associated with cooking oil smoke remained statistically significant (adjusted odds ratio, 4.11; 95% CI, 2.14–7.89) but the risk associated with fuel smoke was no longer statistically significant. [The Working Group noted that, although the finding on cooking oil smoke was adjusted for fuel smoke, it is difficult to rule out residual confounding in this study.]

Seven studies on cooking practices and the risk for lung cancer have been conducted in other parts of China, including one study in Hong Kong Special Administrative Region (Yu *et al*., 2006), four in Taiwan (Ger *et al*., 1993; Ko *et al*., 1997, 2000; Lee *et al*., 2001) and two in Singapore (MacLennan *et al*., 1977; Seow *et al*., 2000).

(a) Hong Kong Special Administrative Region

Chan-Yeung *et al*. (2003) conducted a case–control study in Hong Kong Special Administrative Region during the late 1990s which included 331 Chinese residents (212 men, 119 women) who had been diagnosed with a histologically confirmed primary lung cancer in a large teaching hospital. An equal number of age- and gender-matched residents identified from the same hospital who had non-malignant respiratory diseases were used as controls. Most of the women were nonsmokers (106 cases, 113 controls) while many of the men were smokers (160 cases, 116 controls). All cases and controls were interviewed by one interviewer and were asked about regular exposure to cooking fumes from frying in the house. Years of regular exposure to frying food was not significantly related to the risk for lung cancer in men or women. For women with no or less than 2 years of exposure, the respective odds ratios associated with <3.5 years, ≥3.5–≤7 and >7 years of exposure to frying food were 1.08 (95% CI, 0.50–2.32), 1.05 (95% CI, 0.46–2.42) and 1.54 (95% CI, 0.57–4.13) after adjustment for demographic factors and smoking habits. The corresponding risk estimates in men were 0.69 (95% CI, 0.32–1.49), 0.83 (95% CI, 0.38–1.80) and 1.22 (95% CI, 0.38–3.99). [The Working Group noted that this study included a single measure of exposure to frying in the house. Control subjects had non-malignant respiratory diseases and may have had risk factor profiles that are more similar to the lung cancer patients than control subjects selected from the general population. Thus, estimates of risk associated with exposure to frying may be underestimated.]

Yu *et al*. (2006) conducted a case–control study in Hong Kong Special Administrative Region during the early 2000s that included 200 nonsmoking Chinese women who had been diagnosed with a histologically confirmed primary lung cancer in a large oncology centre and 285 population controls. All but 12 participants (six cases, six controls) were interviewed in person using a standardized structured questionnaire that asked extensive questions about lifetime cooking habits since childhood and included number of years of cooking, the frequencies of stir-frying, pan-frying and deep-frying, the types of cooking oils used, the use of a fume extractor or exhaust fans and the habit of

heating up a wok to high temperatures. The risk for lung cancer increased significantly with increasing total cooking 'dish–years', a composite index that was constructed to account for both the frequency and the duration of cooking. The odds ratios were 1.00, 1.31, 2.80, 3.09 and 8.09, respectively, for ≤50, 51–100, 101–150, 151–200 and ≥200 'total frying dish–years' after adjusting for age, education, employment status, previous lung disease and family history of lung cancer. The results remained significant after further adjustment for factors that may contribute to indoor air pollution (e.g. radon, exposure to environmental tobacco smoke, use of kerosene, use of firewood, burning of incense and use of mosquito coils) and dietary factors. In addition, a trend of increasing risk with heating a wok to high temperature was observed; the odds ratio was 1.0, 1.02 and 1.97 in relation to never/seldom, occasionally and always engaging in such cooking habits. Risk (per 10 dish–years) was highest for deep-frying (odds ratio, 2.56; 95% CI, 1.31–5), intermediate for pan-frying (odds ratio, 1.47; 95% CI, 1.27–1.69) and lowest for stir-frying (odds ratio, 1.12; 95% CI, 1.07–1.18). However, risk was not significantly associated with the use of a particular type of oil (peanut oil, corn oil, canola oil) for cooking or with using a fume extractor. A pattern of risk associated with total cooking dish–years was observed for adenocarcinoma and for non-adenocarcinoma, although the results were stronger for adenocarcinoma of the lung, which represented 69% of the lung cancer cases included in this study. [The Working Group noted that this study included a comprehensive assessment of lifetime cooking habits. Duration and frequency of exposure was captured by a composite index, 'total cooking dish–years', which permitted a quantitative assessment of cumulative exposure. While the confidence interval for the highest exposure category (>200 dish–years) was wide, there was a monotonic increase in risk with increasing exposure. It should be noted that this index was computed based on the number of dishes cooked by the three cooking methods (stir-frying, pan-frying and deep-frying). Although the response rate among controls was modest (~50%), few differences between cases and controls were noted for demographic factors except for a higher rate of employment among controls (88%) compared with cases. Elevated risks associated with moderate to high levels of cooking (>100 dish–years) remained after further adjustment for employment status.]

(b) Taiwan (China)

Four hospital-based case–control studies of lung cancer from Taiwan investigated the role of cooking practices. The main type of oil used in Taiwan is vegetable oil (mainly peanut or soya bean oil).

Ger *et al*. (1993) conducted a hospital-based case–control study in Taipei, Taiwan, that included 131 primary lung cancers (92 men, 39 women) identified between 1990 and 1991. All were histologically confirmed. Two control groups were interviewed; 262 hospital controls were matched to cases on sex, date of birth (±5 years), date of interview (±4 weeks) and insurance status and 262 neighbourhood controls were matched to cases on age, sex and residence of case at the time of diagnosis. In total, 48 cases and 229 controls (111 hospital controls, 118 neighbourhood controls) were nonsmokers. Risk

for adenocarcinoma and squamous-/small-cell cancers in men and women combined was unrelated to cooking style; cases and controls did not differ in pan-frying, stir-frying, deep-frying or boiling practices after adjusting for active smoking and other covariates. Risk for adenocarcinoma increased significantly in persons who reported that they were professional cooks (adjusted odds ratio, 5.54; 95% CI, 1.49–20.65); no increased risk was found for squamous-cell cancer (adjusted odds ratio, 1.16; 95% CI, 0.32–422). [The Working Group noted that this study included few female lung cancer patients. Results were based on dichotomized cooking variables (e.g. no/yes frying) that were not defined.]

Three hospital-based case–control studies were conducted in Kaohsiung, a heavily industrialized city in Taiwan (Ko *et al*., 1997, 2000; Lee *et al*., 2001). The designs of these studies were similar. The first study included 117 female lung cancer cases identified between 1992 and 1993 who were compared with 117 hospital controls who were admitted for a health check-up (55 controls) or for eye diseases (62 controls) (Ko *et al*., 1997). Active smokers (11 cases, three controls) were excluded so that the analysis was based on 105 case–control pairs who were nonsmokers. In a univariate analysis, risk for lung cancer increased with increased frequency of stir-frying (odds ratio, 2.4; 95% CI, 1.1–5.2 for ≥5 versus 0–4 times per week), pan-frying (odds ratio, 2.3; 95% CI, 1.2–4.6 for ≥5 versus 0–4 times per week) but not with deep-frying (odds ratio, 0.9; 95% CI, 0.5–1.9 for ≥5 versus 0–4 times per month). Risk also increased with younger age when started to cook (odds ratio, 1.6; 95% CI, 0.8–3.0 for started at ages 7–20 versus after age 21 years). Risk for lung cancer was elevated in women who cooked in a kitchen without a fume extractor; this was found at different ages of cooking including before age 20 years (odds ratio, 5.3; 95% CI, 1.1–25.6), between the ages of 20 and 40 years (odds ratio, 6.4; 95% CI, 2.9–14.1) or after 40 years of age (odds ratio, 2.3; 95% CI, 1.1–5.1). The risk for lung cancer was not significantly related to types of cooking oil (lard versus vegetable oil). In a multivariate analysis, use of a fume extractor during cooking between the ages of 20 and 40 years remained statistically significant (adjusted odds ratio, 8.3; 95% CI, 3.1–22.7). [The Working Group noted that, while there was no increased risk associated with cooking with coal, the risk increased significantly in relation to cooking with wood or charcoal before 20 years of age and between the ages of 20 and 40 years. These investigators examined the combined effects of frying and use of fume extractors between the ages of 20 and 40 years. The increased risks associated with stir-frying and pan-frying remained regardless of use of fume extractors.]

A second study conducted by the same group of investigators was based on 131 lung cancer cases identified between 1993 and 1996, 252 hospital controls and 262 community controls; all participants were nonsmokers (Ko *et al*., 2000). All lung cancers were histologically confirmed; 63% were adenocarcinoma of the lung. Of the more than 10 variables related to cooking practices that were investigated, risk for lung cancer was associated with five. There was a significant trend of increasing risk with number of meals cooked per day (adjusted odds ratios, 1.0, 3.1 and 3.4 for cooking 1, 2 and 3 meals per day, respectively). Risk was also elevated for women who cooked between the ages of 20 and 40 years without a fume extractor (adjusted odds ratio, 2.2; 95% CI, 1.3–3.8). In

addition, women who reported frequent eye irritation (odds ratio, 2.1; 95% CI, 1.3–3.5) showed significantly elevated risks. Subjects who usually waited until fumes were emitted from the oil and then stir-fried, pan-fried or deep-fried also experienced about a twofold increased risk that was statistically significant. In contrast, years of cooking at home, general ventilation in the kitchen, number of windows in kitchen (<2 versus ≥2) and size of openings (windows) to the outside did not differ between cases and controls. The risk estimates presented above were obtained when cases were compared with community controls, and risk patterns were generally similar when lung cancer cases were compared with hospital controls. [The Working Group noted that use of coal and wood/charcoal was not reported. However, since this study overlapped with the earlier study (Ko *et al*., 1997), the same comments relating to cooking fuel are applicable.]

A further expansion of the previous two studies included lung cancer patients diagnosed between 1993 and 1999 (Lee *et al*., 2001). Women who had been diagnosed with squamous-/small-cell (84 cases) cancer or adenocarcinoma of the lung (162 cases) and 407 corresponding controls were included in the analysis. Women who had other lung cancer cell types (45 cases) and men who had lung cancer were excluded from the analysis of cooking practices. Prevalence of smoking in female controls was not presented but, among female cases, 96.9% of those with adenocarcinoma of the lung and 81.6% of those with squamous-/small-cell lung cancer were nonsmokers. Risk was significantly higher for those who cooked in a kitchen without a fume extractor; the adjusted odds ratio was 3.0 (95% CI, 1.3–7.1) for squamous-/small-cell cancer and 3.9 (95% CI, 2.3–6.6) for adenocarcinoma of the lung. Women who stir-fried, pan-fried or deep-fried only when fumes were emitted from the oil showed significantly higher risk for adenocarcinoma (respective odds ratios, 2.0, 2.6 and 1.6) but not for squamous-/small-cell cancer of the lung (respective odds ratios, 0.9, 0.8 and 1.0). Risk for either cell type of lung cancer was not significantly influenced by age when first started to cook (>20 versus ≤20 years) or type of cooking oils (lard versus vegetable oils). In a multivariate regression analysis, cooking in a kitchen that was not equipped with a fume extractor remained a significant risk factor for both squamous-/small-cell lung cancer and adenocarcinoma of the lung; the respective adjusted odds ratios were 3.3 (95% CI, 1.2–9.2) and 3.8 (95% CI, 2.1–6.8). In addition, waiting to fry until the cooking oil has reached a high temperature was associated with an increased risk for adenocarcinoma of the lung (adjusted odds ratio, 2.1; 95% CI, 1.1–3.0) but not for squamous-/small-cell lung cancer. [The Working Group noted that there was an overlap of cases and controls in the three reports by Ko and colleagues. An advantage of the second report (Ko *et al*., 2000) is that a group of population controls was also included and most of the risk patterns were similar compared with both control groups. It should be noted that use of wood/charcoal, a significant risk factor for both cell types of lung cancer, was not adjusted for in the analysis on cooking practices.]

(c) Singapore

Seow *et al*. (2000) conducted a hospital-based case–control study in Singapore during the late 1990s; 303 women who had been diagnosed with a pathologically confirmed primary lung cancer (56% were adenocarcinoma of the lung) and 765 hospital controls were compared. Analyses were conducted separately for smokers (former and current smokers combined; 127 cases, 100 controls) and lifetime nonsmokers (176 cases, 663 controls). All participants were interviewed in person using a standardized questionnaire that asked extensive questions on diet, reproductive history, exposure to secondhand smoke and cooking practices. Specifically, questions included the frequency of stir-frying, types of oil used and usual cooking practice 20–30 years before diagnosis. Subjects were also asked how often the air in their kitchen became filled with oily 'smoke' during frying. For each of these cooking exposures, there were six possible responses ranging from never/less than yearly, less than monthly, to daily and more than once a day. Among smokers, the risk for lung cancer doubled in association with daily stir-frying (adjusted odds ratio, 2.0; 95% CI, 1.0–3.8) after adjusting for a large number of potential confounders. This increase in risk was confined to those who stir-fried meat on a daily basis (adjusted odds ratio, 2.7; 95% CI, 1.3–5.5). Compared with smokers who stir-fried meat less frequently than daily, risk was intermediate for those who stir-fried meat less than daily in a fume-filled kitchen (adjusted odds ratio, 1.7; 95% CI, 0.7–3.9) and was highest for those who stir-fried daily and reported a smoke-filled kitchen (adjusted odds ratio, 3.5; 95% CI, 1.8–6.9). Women who stir-fried meat daily and primarily used unsaturated oils had the highest risk (adjusted odds ratio, 4.6; 95% CI, 1.6–13.0), while risk was intermediate for those who stir-fried daily but did not use unsaturated oils exclusively (adjusted odds ratio, 2.2; 95% CI, 1.2–4.2). In contrast, the risk for lung cancer in nonsmokers was unrelated to stir-frying (adjusted odds ratio, 1.0; 95% CI, 0.7–1.5) or stir-frying meat daily (adjusted odds ratio, 0.9; 95% CI, 0.6–1.4). Risk for lung cancer in nonsmokers was not affected by smokiness of kitchen or types of oil used. [The Working Group noted that this study presented no data on pan-frying or deep-frying. Although fuel use was not considered in this analysis, it is unlikely to be an important confounder because gas/kerosene is usually used (MacLennan *et al*., 1977). However, this was one of the few studies that described the questions that were asked regarding cooking practices and that specifically addressed cooking practices during the period 20–30 years before cancer diagnosis/interview. Reasons for the differences in findings by smoking status are not apparent but the sample size of smokers was modest. The risk estimates presented in the tables were slightly different from the numbers presented in the text; the numbers presented in the tables are those given in this Monograph.]

2.3 Meta-analysis

Feng & Ling (2003) carried out a meta-analysis on case–control studies among nonsmoking women that were published between 1992 and 2002 in the English and

Chinese literature and examined the relationship between exposure to cooking oil fumes and lung cancer. Six studies (two in English and four in Chinese) were conducted in mainland China and two (in English) in Taiwan. All studies reported significantly increased odds ratios ranging from 2.10 to 9.20. The combined odds ratio using a fixed effects model was 2.94 (95% CI, 2.43–3.56). [The Working Group noted that the two studies in Taiwan had some overlap in their study subjects. Two reports by the same group of authors in China (Wang *et al*., 1996), one in English and one in Chinese, essentially overlap one another. The exposure metrics were not uniform and the rationale for selecting certain odds ratios out of a range in each paper was not entirely clear.

2.4 References

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3. Studies of Cancer in Experimental Animals

3.1 Cooking oil fumes

Whole-body and inhalation exposure

(a) Mouse

Four groups of 30–32 male and 30–32 female Balb/c mice (weighing 15±3 g) [age unspecified] were exposed to air heated at 22–30°C (control) or ~9, 21 and 39 mg/m^3 cooking oil fumes for 30 min per day for 2 months, then every other day for a period of 6 months (150 times overall) after which time they were killed. Oil fumes were generated by heating an unspecified volume of unrefined rapeseed oil at a temperature of 270±5°C in a steel container with an electric heating element. Fumes were directed into a cylindrical 1-m^3 exposure chamber. The incidence of lung tumours in both sexes combined was 0.0 (0/61), 15.09 (8/53; p<0.05), 20.00 (10/50; p<0.05) and 22.00% (11/50; p<0.05) for the control, low-, mid- and high-dose groups, respectively. The incidence in females was 0.00 (0/31), 12.00 (3/25; p<0.05), 25.00 (5/20; p<0.05) and 25.92% (7/27; p<0.05), respectively, and that in males was 0.00 (0.30), 17.86 (5/28; p<0.05), 16.67 (5/30; p<0.05) and 17.39% (4/23; p<0.05), respectively. The lung tumours were mainly adenocarcinomas (Zhang *et al*., 2003; Chen *et al*., 2005).

(b) Rat

Four groups of 30–35 male and 30–35 female Sprague-Dawley rats (weighing ~127 g) [age unspecified] were exposed to air or ~7, 15 and 35 mg/m^3 cooking oil fumes for 30 min every other day for 12.5 months after which they were killed. Oil fumes were generated by heating 250 mL unrefined rapeseed oil to a temperature of 260°C in steel container with an electric heating element. Fumes were directed into a cylindrical 2.2-m^3 exposure chamber. The incidence of lung carcinoma in both sexes combined was 0.0 (0/70), 6.56 (4/61), 8.96 (6/67) [p<0.05] and 12.70% (8/63) [p<0.005] for the control, low-, mid- and high-dose groups, respectively. The incidence in females was 0.0 (0/35), 6.45 (2/31), 11.76 (4/34) and 19.35% (6/31) [p<0.01], respectively, and that in males was 0.0 (0/35), 6.67 (2/30), 6.06 (2/33) and 6.25% (2/32), respectively (Long *et al*., 2005).

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4. Mechanistic and Other Relevant Data

4.1 Toxicokinetics

See the monograph on Household use of solid fuels.

4.2 Mechanisms of carcinogenesis

4.2.1 *Polycyclic aromatic hydrocarbons (PAHs)*

See the monograph on Household use of solid fuels.

Siegmann and Sattler (1996) detected a variety of genotoxic PAHs (e.g. benzo[*a*]anthracene, chrysene, benzo[*a*]pyrene) in vegetable oils (rapeseed, corn and peanut) heated to above 260ºC (1.1–22.8 μg/m^3 PAHs). Wu *et al*. (1998) detected a variety of mutagenic PAHs (e.g. benzo[*a*]pyrene) and nitro-PAHs (e.g. 1,3-dinitropyrene) in fumes of lard, soya bean oil and peanut oil heated to above 250ºC; the emission of PAHs and nitro-PAHs were reduced upon addition of the antioxidant catechin.

4.2.2 *Particles*

See the monograph on Household use of solid fuels.

4.2.3 *Genetic and related effects*

(a) Humans

Cherng *et al*. (2002) used the reverse-transcription polymerase chain reaction to investigate expression of human 8-oxoguanine DNA glycosylase 1 (HOGG1), a repair enzyme that removes 8-hydroxydeoxyguanine (8-OHdG) from damaged DNA, in the peripheral blood lymphocytes of 94 professional cooks and 43 home cooks exposed to cooking oil emissions. The results showed that HOGG1 expression in cooking oil emissions-exposed cooks was significantly higher than that in 111 control subjects. Odds ratios, adjusted for age, sex and smoking and drinking status, for home cooks versus controls and professional cooks versus controls were 3.94 (95% CI, 0.95–16.62) and 10.12 (95% CI, 2.83–36.15), respectively. Furthermore, significant induction of HOGG1 expression was confirmed *in vitro* in human lung adenocarcinoma CL-3 cells after exposure to cooking oil emissions extracts.

(b) Experimental systems

(i) *Experimental animals*

Glaser *et al*. (1989) reported that flow cytometric analyses of lung cells from Wistar rats exposed to emissions (20 mg/m^3) from fish frying in fat for 28 days showed alterations in the structure and content of nuclear DNA. In comparison with the control group, samples from exposed animals showed a significant shift and broadening of the G_1 peak, which may be caused by loss of chromosomal fragments or by chromosomal aberration during cell division.

Several studies have documented clastogenic effects, genotoxic effects and oxidative stress in experimental animals exposed to cooking oil fumes.

Intraperitoneal injection of male Kunming mice with condensates of emissions from rapeseed oil heated to 270ºC (doses of 800, 1600, 2400 or 3200 mg/kg body weight [bw]) induced a significant dose-dependent increase in the frequency of micronucleated polychromatic erythrocytes in the bone marrow. The addition of the antioxidant butylated hydroxyanisole to the oil reduced the magnitude of the effect (Chen *et al*., 1988; Qu *et al*., 1992). Two studies have shown induction of bone-marrow cell micronuclei in mice exposed to cooking oil fumes. Chen *et al*. (1992) reported a time- and dose-dependent increase in bone-marrow micronuclei in male Swiss mice exposed by inhalation to rapeseed oil fumes for 3 h per day, 6 days per week for 4 weeks. Liu *et al*. (1987) showed an increase in the frequency of bone-marrow cell micronuclei in mice exposed by inhalation for 5 days to 1/16 of the LD_{50} of cooking oil fumes from soya bean oil heated at 250–270ºC. A subsequent study by Li *et al*. (1998) showed that intratracheal instillation of refined vegetable oil (heated to 270–280ºC)-fume condensate into Sprague-Dawley rats (doses of 225, 450 or 900 mg/kg bw) elicited a significant increase in bone-marrow cell micronuclei.

Chen *et al*. (1996) revealed significant induction of chromosomal aberrations in diploid male germ cells (diakenesis/meiosis I) of ICR mice exposed to rapeseed oil emissions condensate (270–280ºC) by daily intraperitoneal injections of 100, 400 or 1600 mg/kg bw for 5 days.

Zhang *et al*. (2001) observed significant increases in DNA damage in peripheral blood lymphocytes (comet assay) of Balb/c mice following inhalation exposure for 8 months to 9.1–39 mg/m^3 fumes of heated rapeseed oil.

Kawai *et al*. (2006) showed that 4-oxo-2-hexenal (4-OHE), a mutagenic substance formed by the peroxidation of ω-3 polyunsaturated fats such as linolenic acid, was present in a condensate of smoke released during fish frying. In an earlier study, Kasai *et al*. (2005) noted that oral administration of 4-OHE to mice induced an increase in the levels of DNA adducts (4-OHE-deoxycytosine, 4-OHE-deoxyguanosine, and 4-OHE-5-methyl-deoxycytosine) in the gastrointestinal tract (i.e. oesophagus, stomach and intestine). They also showed that 4-OHE, which was detected in the volatile emissions of heated perilla oil (from *Perilla frutescens,* a member of the mint family) and broiled fish, seems to be produced by the oxidation of ω-3 fats (e.g. linolenic acid). Xi *et al*. (2003) showed that

intratracheal instillation of heated cooking oil emissions condensate into Wistar rats induced a dose- and time-dependant increase in the frequency 8-OHdG–DNA adducts in lung tissue. Li *et al*. (1998) also noted a decrease in superoxide dismutase activity and an increase in malondialdehyde (an indicator of oxidative stress) in lung tissue. Similarly, significantly decreased superoxide dismutase activity and increased malondialdehyde content in lung tissue was reported in Sprague-Dawley rats exposed by inhalation to 43 mg/m^3 fumes from cooking oil heated to 270–280ºC for 20–60 days (Rang *et al.*, 2000).

Rang *et al.* (2000) showed in the study above that lung tissue samples showed high P53 protein content. Using immunohistochemical methods, Liu *et al*. (2005) also observed overproduction of P53 and a decrease in P16 protein in lung tissues of Sprague-Dawley rats exposed by inhalation to 43.9 mg/m^3 fumes from cooking siritch oil [i.e. Chinese *Hu-Ma* oil or linseed oil] (heated to 200–220ºC) for 20–60 days. Long *et al*. (2005) showed that Sprague Dawley rats exposed by inhalation to fumes from rapeseed oil heated to 260ºC (6.9–35 mg/m^3 for 30 min every other day for 12.5 months) developed pulmonary carcinoma in addition to enhanced production of P53 and a decrease in fragile histidine triad protein in lung (bronchial epithelia) tissue sections.

A study that used the *Drosophila melanogaster* sex-linked recessive lethal assay showed that exposure to a condensate of a cooking oil fume (110, 320 and 960 mg/L in food) induced heritable mutations (Li *et al*., 1999). Wang *et al*. (1995) revealed that tracheal epithelial cells removed from Wistar rats exposed to rapeseed oil condensate by three intratracheal instillations of 0.1 or 1.5 mg/kg bw displayed a high frequency of cell transformation *in vitro*. Finally, Zhang *et al*. (1999) showed that exposure of female Kunming mice to cooking oil emissions condensates from rapeseed oil, soya bean oil and salad oil by subcutaneous injection (1.1–2.3 g/kg) caused an inhibition of the delayed hypersensitivity response and of the activity of natural killer cells in comparison with controls.

(ii) *In-vitro exposure of human cells*

Several studies investigated the effect of cooking oil emissions condensates on cultured human lymphocytes. Jin and Cu (1997) noted significant induction of unscheduled DNA synthesis in cultured human lymphocytes exposed to cooking oil emissions condensate (200ºC) from rapeseed oil and soya bean oil. Similarly, Shen *et al*. (1998) reported that fume condensates from heated rapeseed oil collected in Nanjing, China, induced unscheduled DNA synthesis in human peripheral blood lymphocytes with and without metabolic activation. Hou *et al*. (2005) reported that cooking oil emissions condensate significantly increased chromosomal aberrations but not micronucleus frequency in human peripheral blood lymphocytes.

^{32}P-Postlabelling was used to show dose-dependent induction of DNA adducts in human lung adenocarcinoma CL-3 cells exposed to extracts of cooking oil fumes from fish fried in soya bean oil. Subsequent liquid chromatography/mass spectrometry confirmed that the DNA adduct in CL-3 cells induced by exposure to cooking oil

emissions extract was benzo-[*a*]pyrene-7,8-diol-9,10-epoxide-N^2-deoxyguanosine (Yang *et al*., 2000). In addition, the comet assay showed induction of DNA damage (DNA strand breaks) in human lung adenocarcinoma CL-3 cells following exposures to 100 µg/mL cooking oil emissions condensate from fried fish (Lin *et al*., 2002). Dose-dependent induction of DNA damage, measured using the comet assay, was also observed in human lung carcinoma A549 cells treated with extracts of fumes from heated peanut oil (Wu & Yen, 2004), sunflower oil, soya bean oil and lard (Dung *et al*., 2006).

Dung *et al*. (2006) determined in the study above that *trans-trans*-2,4-decanedial (*t,t*-2,4-DDE), which is a by-product of lipid peroxidation and is one of the most abundant and potent mutagens identified in cooking oil fumes to date (Wu *et al*. 2001), was present in all three condensate samples, and induced a significant increase in the level of 8-OHdG adducts. It is also thought to induce intracellular formation of reactive oxygen species and has been shown to induce a dose-dependent increase in 8-OHdG in CL-3 cells (Cherng *et al*., 2002). Chang *et al*. (2005) also studied oxidative stress in human bronchial epithelial BEAS-2B cells, and confirmed that *t,t*-2,4-DDE induced a concentration-dependent increase in the production of reactive oxygen species and a decrease in the reduced glutathione/oxidized glutathione ratio (glutathione status). The data also suggest that *t,t*-2,4-DDE leads to cell proliferation, significant increases in unscheduled DNA synthesis (measured by bromodeoxyuridine incorporation), as well as induction of tumour necrosis factor-α and interleukin-1β gene expression and release of the corresponding cytokines in cultured BEAS-2B cells. Co-treatment of BEAS-2B cells with the antioxidant *N*-acetylcysteine prevented *t,t*-2,4-DDE-induced release of cytokines and concomitant cell proliferation.

(iii) *Other in-vitro systems*

Several studies have shown that exposure of Chinese hamster V79 cells to rapeseed oil cooking fumes induced a marked increase in the frequency of sister chromatid exchange (Zhu *et al*., 1990; Chen *et al*., 1992) and, moreover, the magnitude of the genotoxic effect was inversely related to the degree of hydrogenation of the cooking oil (Zhu *et al*., 1990). Qu *et al*. (1992) noted that exposure of V79 cells to an extract of cooking fumes from heated unrefined rapeseed oil and heated refined rapeseed oil induced a significant increase in sister chromatid exchange frequency; however, fume condensate from unrefined rapeseed oil supplemented with the antioxidant butylated hydroxyanisole (0.02%) failed to induce a concentration-dependent significant increase in sister chromatid exchange frequency. Additional analyses of fumes from hydrogenated rapeseed oil samples also failed to induce a significant increase in sister chromatid exchange frequency. Wu *et al*. (1999) noted a concentration-related increase in sister chromatid exchange frequency, both with and without exogenous metabolic activation, in Chinese hamster ovary (CHO-K_1) cells exposed to condensates of fumes from lard or soya bean oil. The same condensates have also been shown to induce DNA damage (SOS Chromotest) in *Escherichia coli* PQ37.

Pu *et al*. (2002) noted a time-dependent increase in DNA cross-links and single-strand breaks in rat type II lung cells exposed to cooking oil emissions condensates. A reduction in cytotoxicity, DNA cross-links and strand breaks following pretreatment with the antioxidant *N*-acetylcysteine suggested that cooking oil fumes induced oxidative stress in exposed cells. Similarly, Zhang *et al*. (2002) noted a concentration-related increase in DNA damage, as measured by the comet assay, in rat type II pneumocytes exposed to a condensate of cooking fumes (obtained from a kitchen ventilator) at concentrations up to 10 µg/mL. Yin *et al*. (1998) also noted a significant increase when these cells were exposed to cooking oil emissions condensate from vegetable oil heated to 270±5ºC.

Finally, three studies demonstrated that cooking oil fumes induced DNA damage in calf thymus DNA. Wu *et al*. (1992) demonstrated that exposure to rapeseed oil (heated to 280ºC)-fume condensate can induce adducts in naked calf thymus DNA without metabolic activation, and Yin *et al*. (1997) demonstrated that exposure to rapeseed and soya bean oil (heated to 270ºC)-fume condensates can induce cross-links in calf thymus DNA. Xi *et al*. (2003) demonstrated that exposure to cooking oil emissions condensates can induce 8-OHdG formation in calf thymus DNA.

Cooking oil emissions emissions were also investigated in several cell transformation assays. A dose-dependent increase in the frequency of morphological transformation was observed in BALB/c3T3 cells exposed to condensates of cooking fumes (Shen *et al*., 1998). Zhao *et al*. (2000) observed dose-dependent malignant transformation in KMB-17 diploid human embryo lung cells exposed to a condensate of cooking oil fumes. The transformed cells showed a variety of distinct features, including loss of density inhibition, loss of contact inhibition, growth at low serum concentration, agglutination at low concentrations of concanavalin A, aneuploidy and deviation from diploid status and loss of anchorage dependence (Zhao *et al*. 2002).

(iv) Salmonella *reverse mutation assay*

Studies have related mutagenic activity in *Salmonella* to a host of indoor activities, including cooking (e.g. Sexton *et al*., 1986; Teschke *et al*., 1989). A wide range of source-specific studies has confirmed the mutagenic activity in *Salmonella* of emissions from heated cooking oil (e.g. Qu *et al*., 1992; Nardini *et al*., 1994; Shields *et al*., 1995; Chiang *et al*., 1997, 1998; Wu *et al*., 2001) and highlighted that these sources are significant contributors to the mutagenic activity of indoor air. Moreover, several studies have noted a positive empirical relationship between the mutagenic activity of indoor air (in revertents/m^3) in *Salmonella* and the concentration of airborne PM (Mumford *et al*., 1987; Chiang *et al*., 1999). This relationship is not unexpected because combustion emissions are composed of PM, and several researchers (e.g. Maertens *et al*., 2004, 2008) have commented on the tendency for mutagens in combustion emissions, such as PAHs, to adsorb to particulate material and solid surfaces (e.g. upholstery, carpets). Chiang *et al*. (1999) noted particle concentration levels as high as 28 mg/m^3 in dwellings that were filled with cooking oil fumes.

Table 4.1 provides a summary of studies that have used the *Salmonella* assay to investigate the mutagenic activity (in revertants/m^3) of indoor air particulates from high-temperature frying. The data indicate that organic extracts of indoor air particulate material collected from areas without any obvious source of contamination have mutagenic potency values in *Salmonella* in the 1 and 10 TA98 revertants/m^3 range. Table 4.2 provides a summary of studies that investigated the mutagenic potency (in revertants/mg) in *Salmonella* of source-specific particulate emissions from high-temperature frying.

The mutagenic potency values reached several hundreds of TA98 revertants/m^3 and several thousands of TA98 revertants/mg of particle with or without exogenous metabolic activation (Sexton *et al*., 1986; Löfroth *et al*., 1991; Wu *et al*., 2001). It is interesting to note that two studies (Qu *et al*., 1992; Xu *et al*., 1995) described a relationship between the mutagenicity of cooking oil emissions condensates and heating temperature. Qu *et al*. (1992) noted that condensates of fumes from unrefined rapeseed oil did not elicit a significant response unless the oil was heated to 270ºC (TA98 with metabolic activation). Similarly, Xu *et al*. (1995) only detected a significant mutagenic response (TA98 with metabolic activation) when the rapeseed oil was heated to 230ºC or 280ºC.

Several studies have used bioassay-directed fractionation methods to identify mutagenic agents in condensates of cooking oil fumes. Wu *et al*. (2001) determined that the mutagenic activity in *Salmonella* TA98 of methanolic extracts from heated peanut oil fumes without metabolic activation is contained within a neutral fraction. Detailed chemical analyses of the neutral fraction resulted in the identification of four direct-acting alkenals: *t*,*t*-2,4-DDE, *trans*-*trans*-2,4-nonadienal, *trans*-2-decenal and *trans*-2-undecenal. The most potent agent, *t*,*t*-2,4-DDE, elicited 385 revertants/µg in TA100 and 18 revertants/µg in TA98 (without metabolic activation). Qu *et al*. (1992) hypothesized that the mutagenic agents in condensates of heated rapeseed oil are the oxidized products of unsaturated fatty acids such as linoleic and linolenic acid, and noted contrasting levels of mutagenic activity between unsaturated oil samples and highly hydrogenated samples. Unsaturated rapeseed oil samples with 10 and 12% linolenic and linoleic acid, respectively, elicited significant positive responses, whereas highly hydrogenated samples without either acid failed to elicit a positive response. Moreover, complete elimination of mutagen formation by the addition of 0.1% butylated hydroxyanisole supported this hypothesis. In addition, Shields *et al*. (1995) showed that mutagenic activity in TA98 (with metabolic activation) was induced when unsaturated fatty acids such as linoleic acid and linolenic acid were heated to 240ºC. Moreover, the mutagenic activity (TA98 with metabolic activation) of condensates from heated Chinese rapeseed oil (275–280ºC), heated peanut oil (260–265ºC) and heated soya bean oil (260–265ºC) was positively related to the content of linolenic acid. The presence of several other mutagens in the condensates of heated oils was also confirmed. These included 1,3-butadiene, benzene, acetaldehyde and acrolein.

Table 4.1. Mutagenicity in *Salmonella* of organic extracts of indoor air particulate matter from high-temperature frying (in revertants/m^3)

Source	Country	Particle concentration (μg/m^3)	Mutagenic potency in revertants/m^3		Reference
			Without metabolic activation	With metabolic activation	
TA98					
Olive oil	Italy	31600	329	108	Nardini *et al*. (1994)
Deep fry[a]	Canada	US	618	ND	Teschke *et al*. (1989)
Wok[a]	Canada	US	617	ND	Teschke *et al*. (1989)
Frying hamburger[a]	USA	US	~50	~220	Sexton *et al*. (1986)
TA100					
Frying hamburger[a]	USA	US	~960	~1180	Sexton *et al*. (1986)

ND, no data; US, unspecified
[a] Type of cooking oil not specified

Table 4.2. Mutagenicity in *Salmonella* of organic extracts of particulate emissions from high-temperature frying (in revertants/mg)

Source	Country	Particle concentration ($\mu g/m^3$)	Mutagenic potency (revertants/mg)		Reference
			Without metabolic activation	With metabolic activation	
TA98					
Rapeseed oil 230ºC	China	US	ND	[46.1]	Xu *et al.* (1995)
Rapeseed oil (unrefined) 270ºC	China	US	neg.	[62.2]	Qu *et al.* (1992)
Rapeseed oil (refined) 270ºC	China	US	neg.	[123.9]	Qu *et al.* (1992)
Rapeseed oil 275ºC	China	US	ND	[282.5]	Shields *et al.* (1995)
Rapeseed oil 280ºC	China	US	ND	[109.7]	Xu *et al.* (1995)
Sunflower oil 300ºC	China	25.1	[19.6]	[62.4]	Chiang *et al.* (1999)
Refined lard 300ºC	China	26.8	[12.5]	neg.	Chiang *et al.* (1999)
Vegetable oil 300ºC	China	28.3	[8.1]	[21]	Chiang *et al.* (1999)
Olive oil	Italy	31600	10	3	Nardini *et al.* (1994)
Lard	China	26.2	neg.	[180]	Chiang *et al.* (1997)
Lard 100°C	China	US	neg.	54	Chiang *et al.* (1998)
Lard 200°C	China	US	35	101	Chiang *et al.* (1998)
Lard 200°C	China	US	61	180	Chiang *et al.* (1998)
Lard 300°C	China	US	82	236	Chiang *et al.* (1998)
Lard 300°C	China	US	43	122	Chiang *et al.* (1998)
Soya bean oil	China	28.5	neg	[80]	Chiang *et al.* (1997)
Soya bean oil 200°C	China	US	neg.	82	Chiang *et al.* (1998)
Soya bean oil 260ºC	China	US	ND	[45.6]	Shields *et al.* (1995)
Soya bean oil 270ºC	China	US	neg.	[101]	Qu *et al.* (1992)

Table 4.2. (contd)

Source	Country	Particle concentration ($\mu g/m^3$)	Mutagenic potency (revertants/mg)		Reference
			Without metabolic activation	With metabolic activation	
TA98 (contd)					
Soya bean oil 300°C	China	US	neg.	61	Chiang *et al.* (1998)
Soya bean oil 300°C	China	US	42	112	Chiang *et al.* (1998)
Peanut oil	China	27.1	neg.	[40]	Chiang *et al.* (1997)
Peanut oil 300°C	China	US	neg.	66	Chiang *et al.* (1998)
Peanut oil	China	US	[12600]	[11600]	Wu *et al.* (2001)
Lean pork, minced[a]	Sweden	US	ND	7400	Löfroth *et al.* (1991)
Commercial pork, minced[a]	Sweden	US	ND	800	Löfroth *et al* (1991)
Pork chops	Sweden	US	ND	15	Löfroth *et al* (1991)
Baltic herring[a]	Sweden	US	ND	25	Löfroth *et al* (1991)
TA98NR					
Olive oil[b]	Italy	31600	10	ND	Nardini *et al.* (1994)
TA100					
Peanut oil	China	US	[21000]	[18030]	Wu *et al.* (2001)

ND, no data; neg., negative; US, unspecified

[a] type of cooking oil not specified

[b] spilled on a hot plate

4.3 Genetic susceptibility

See the monograph on Household use of solid fuels.

4.4 Mechanistic considerations

The mutagenicity of emissions from high-temperature frying may be due to PAHs and lipid peroxidation products, among other compounds. Unlike emissions from the combustion of wood and coal, for which extensive, positive genotoxicity data have been generated almost exclusively in humans *in vivo*, nearly all of the mutagenicity data for emissions from high-temperature frying have been generated in experimental animals and in cells *in vitro*. The large number of genotoxic end-points and largely positive results, especially in experimental animals, provide plausible evidence that a carcinogenic mechanism similar to that described for coal emissions also applies to emissions from high-temperature frying.

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5. Summary of Data Reported

5.1 Exposure data

A large proportion of the emissions generated during cooking is steam from the water contents of the food. However, during frying (with oil), fatty acid esters that make up edible oils and fat can decompose and produce volatile organic compounds, as well as semi-volatile compounds that can condense to form particles. A wide variety of organic compounds have been identified in cooking emissions, including alkanes, alkenes, alkanoic acids, carbonyls, polycyclic aromatic hydrocarbons and aromatic amines. The main volatile compounds generated during frying were aldehydes, alcohols, ketones, alkanes, phenols and acids. Of particular concern in relation to carcinogenicity are polycyclic aromatic hydrocarbons, heterocyclic amines and aldehydes. The contribution of commercial cooking operations to outdoor levels of polycyclic aromatic hydrocarbons can be substantial.

Cooking also increases the concentrations of fine and ultrafine particles.

The chemical composition of cooking emissions varies widely depending on the cooking oils used, the temperature, the kind of food cooked, and the method and style of cooking adopted.

5.2 Human carcinogenicity data

To examine the potential association between emissions from cooking oil and the risk for lung cancer, the Working Group considered studies to be more informative when cooking-related effects were separated from fuel-related effects and when the studies reported results on the exposure–response relationships between high-temperature frying (i.e. stir-frying, deep-frying and pan-frying) and lung cancer. Studies that only collected information on cooking habits (e.g. age at starting to cook, years of cooking), ventilation in the kitchen or frequency of eye irritation due to cooking or smokiness in the kitchen were considered to be less informative because they did not allow the effects of emissions from cooking oil to be distinguished from those of combustion products of cooking fuels.

On this basis, four case–control studies were considered to be the most informative. The study conducted in Hong Kong Special Administrative Region used a composite index that accounted for both the frequency and the duration of all three types of high-temperature frying; it found a significant threefold increased risk for lung cancer associated with moderate to high categories of exposure (>150 total dish–years) and an eightfold increased risk associated with the highest category (>200 total dish–years).

In the other three informative studies in Shanghai (two studies) and Gansu, China, the risk for lung cancer increased generally with increasing frequency of stir-frying, deep-frying and pan-frying and a nearly twofold increased risk was associated with the highest

frequency of high-temperature frying. In the study conducted in Gansu, however, the risk for lung cancer increased significantly with increasing frequency of stir-frying but not of deep-frying. However, potential confounding by solid cooking fuel could not be ruled out with reasonable confidence in these three studies. In the study from Hong Kong that compared risk (per 10 dish–years) for the three types of high-temperature frying, the magnitude of risk was highest for deep-frying, intermediate for pan-frying and lowest for stir-frying, but all were associated with a significantly elevated risk for lung cancer. In the studies in Shanghai and Gansu, the effects of the different types of frying were not mutually adjusted for and, because of the substantial differences in the frequency of stir-frying and deep-frying, a direct comparison of the risk estimates associated with an individual type of frying could not be made.

These four studies also provided information on the specific type of cooking oil. There was no significant difference in risk estimates for lung cancer with use of any particular type of cooking oil (peanut oil, corn oil or canola oil — a type of rapeseed oil) in the study in Hong Kong. In the three other studies, risk was higher for women who cooked with canola oil most frequently. Some increased risk was associated with cooking with linseed oil in the population-based case–control study conducted in Gansu and with cooking with soya bean oil in the study in Shanghai.

In summary, results from the four most informative studies demonstrate an exposure–response relationship between increased frequency of or cumulative exposure (frequency and duration) to high-temperature frying and increased risk for lung cancer. These four studies were conducted in different populations in Hong Kong, urban Shanghai (two studies) and rural Gansu where study characteristics differed, and where cooking practices and other co-factors may also have differed. However, confounding by cooking fuel could not be ruled out with reasonable confidence in the latter three studies. Furthermore, all epidemiological evidence was based on case–control studies and recall bias may have contributed to the positive findings in some of these studies.

5.3 Animal carcinogenicity data

Inhalation of high concentrations of emissions from high-temperature frying of unrefined rapeseed oil caused an increase in the incidence of lung carcinomas (mainly adenocarcinomas) in male and female mice in one study and female rats in another study.

5.4 Mechanistic and other relevant data

See also Section 5.4 in the monograph on household use of solid fuels.

The available information on the genotoxic and mutagenic activity of cooking oil fumes includes data from professional and home cooks that show the induction of 8-oxoguanine DNA glycosylase 1, which is a DNA repair enzyme that removes 8-hydroxydeoxyguanine. In experimental animals, cooking oil-fume condensates from rapeseed and soya bean oils induced micronuclei in the bone marrow of both mice and

rats, oxidative DNA damage, enhanced transformation of tracheal epithelia and accumulation of TP53 protein. Cooking oil-fume condensate also induced chromosomal aberrations in the diploid male germ cells of mice. In cultured human or animal cells, cooking oil fumes from a variety of oils induced DNA adducts, DNA damage (comet assay), oxidative damage, sister chromatid exchange, chromosomal aberrations, unscheduled DNA synthesis and DNA cross-links. Cooking oil fumes induced DNA damage in naked calf thymus DNA.

Extracts or condensates of emissions from cooking oil fumes are mutagenic in *Salmonella*. In strain TA98, in the presence or absence of a metabolic activation system, the mutagenic potency in terms of revertants per milligram of particle reached several thousands or in terms of revertants per cubic metre of air reached several hundreds.

Several studies showed that the mutagenicity of cooking fumes in *Salmonella* was positively correlated with heating temperature, the extent of unsaturation and the concentration of unsaturated fatty acids. Polycyclic aromatic hydrocarbons and lipid peroxidation products also contribute to the mutagenic activity of cooking oil fumes.

6. Evaluation and Rationale

There is *limited evidence* in humans for the carcinogenicity of emissions from high-temperature frying.

There is *sufficient evidence* in experimental animals for the carcinogenicity of emissions from high-temperature unrefined rapeseed oil.

Overall evaluation

Emissions from high-temperature frying are *probably carcinogenic to humans (Group 2A)*.

Rationale

Among the studies of cancer in humans, four were considered most informative because they allowed the effects of cooking-oil emissions to be distinguished from those of the fuels used for heating the stove. These studies, in four different populations, consistently showed an increased risk for lung cancer and showed an exposure–response relationship between increased frequency or duration of high-temperature frying and increased risk for lung cancer. Confounding by the fuel used to heat the stove could be ruled out with reasonable confidence in only one of these studies.

These epidemiological results are supported by the evidence from studies in experimental animals. Although positive results in experimental animals were observed only for unrefined rapeseed oil heated to high temperatures, positive results for mutagenicity were observed in virtually every category of in-vivo test. These mutagenicity data would have been enough to support an evaluation of Group 2A if the evidence of carcinogenicity in experimental animals had been less than *sufficient* or the evidence of carcinogenicity in humans had been less than *limited*. The mechanistic data also show that lipid peroxidation is an important mechanism that leads to carcinogenesis by these mixtures, although there may also be a contribution from the mechanisms by which polycyclic aromatic hydrocarbons induce cancer (see Volume 92).

The evaluation was made for 'emissions from high-temperature frying'. This wording was determined after considering several aspects of the available data.

The available studies involved frying at high temperatures. Emissions from low-temperature cooking methods can be considerably different from those studied. Data indicate that cooking oil has little mutagenic potential when heated below 100°C and high mutagenic potential when heated above 230°C.

No differences were apparent between stir-frying, deep-frying and pan-frying when these methods were investigated separately. Other high-temperature cooking methods

(e.g. baking) were not included because the Working Group reasoned that their emissions could be considerably different from those of frying.

The epidemiological data are not detailed enough to distinguish between different cooking oils and fats and experimental animal data were available for unrefined rapeseed oil only, although data are available that indicate a higher mutagenic potency for unsaturated fats.

The epidemiological data do not permit the risk to be attributed to a specific chemical compound or to the cooking oil alone. Some risk could be attributable to the food being cooked, to emissions from the heated stove or cooking vessel itself or to the fuel used to heat the stove. Nevertheless, it might be reasonable to attribute some risk to cooking oils, because in-vivo and in-vitro data indicate that emissions from some oils heated to high temperatures are mutagenic.

LIST OF ABBREVIATIONS

ABC	adenosine triphosphate binding cassette
ADC	adenocarcinoma
AhR	aryl hydrocarbon receptor
AKR	aldo-keto reductase
Asymp. sig.	asymptote significance
ATP	adenosine triphosphate
AUC	area under the curve
avg.	average
BA	basal-cell cancer
BAL	bronchioalveolar lavage
B(a)P	benzo[*a*]pyrene
Bcm	billion cubic metres
BP	benzo[*a*]pyrene
bw	body weight
CI	confidence interval
CIN	cervical intraepithelial neoplasia
CO	carbon monoxide
COPD	chronic obstructive pulmonary disease
CV	coefficient of variation
CYP	cytochrome P450
DBA	dibenz[*a*]anthracene
DMBA	7,12-dimethylbenz[*a*]anthracene
DMSO	dimethyl sulfoxide
ELISA	enzyme-linked immunosorbent assay
ENT	ear, nose and throat
GC	gas chromatography
GM	geometric mean
GSH	glutathione
GST	glutathione *S*-transferase
HOGG1	human 8-oxyguanine DNA glycosylase 1
HPLC	high-performance liquid chromatography
HPV	human papilloma virus
HSCU	heavy smoky coal user
ICD	International Classification of Diseases
LC	liquid chromatography
LPG	liquefied petroleum gas

Max.	maximum
MDM2	murine double minute 2
MS	mass spectrometry
Mt	million tones
N	number
NADPH	nicotinamide adenine dinucleotide phosphate
ND	not detected
NG	not given
NOS	not otherwise specified
NO_x	nitrogen oxide
NPC	nasopharyngeal carcinoma
NS	not significant
8-OHdG	8-hydroxydeoxyguanine
4-OHE	4-oxo-2-hexenal
PAH	polychlorinated aromatic hydrocarbon
Pap	Papanicolaou
PARP	poly(ADP-ribose)polymerase
PCB	polychlorinated biphenyl
PCDD	polychlorinated dibenzo-*para*-dioxin
PCDF	polychlorinated dibenzofuran
PCR	polymerase chain reaction
PJ	peta joules
PM	particulate matter
QMS	quadruple ion-trap mass spectrometry
S	significant
SCC	squamous-cell carcinoma
SD	standard deviation
SD	standard deviation
SE	standard error
SM	small-cell cancer
SNP	single nucleotide polymorphisms
SO_2	sulfur dioxide
SPM	suspended particulate matter
SULT	sulfotransferase
t,*t*-2,4-DDE	*trans*,*trans*-2,4-decadienal
TLC	thin-layer chromatography
TPA	12-*O*-tetradecanoylphorbol-13-acetate
TSP	total suspended particles
TWA	time-weighted average
TWh	terawatt hours
UFP	ultrafine particles
US	unspecified

CUMULATIVE CROSS INDEX TO *IARC MONOGRAPHS ON THE EVALUATION OF CARCINOGENIC RISKS TO HUMANS*

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