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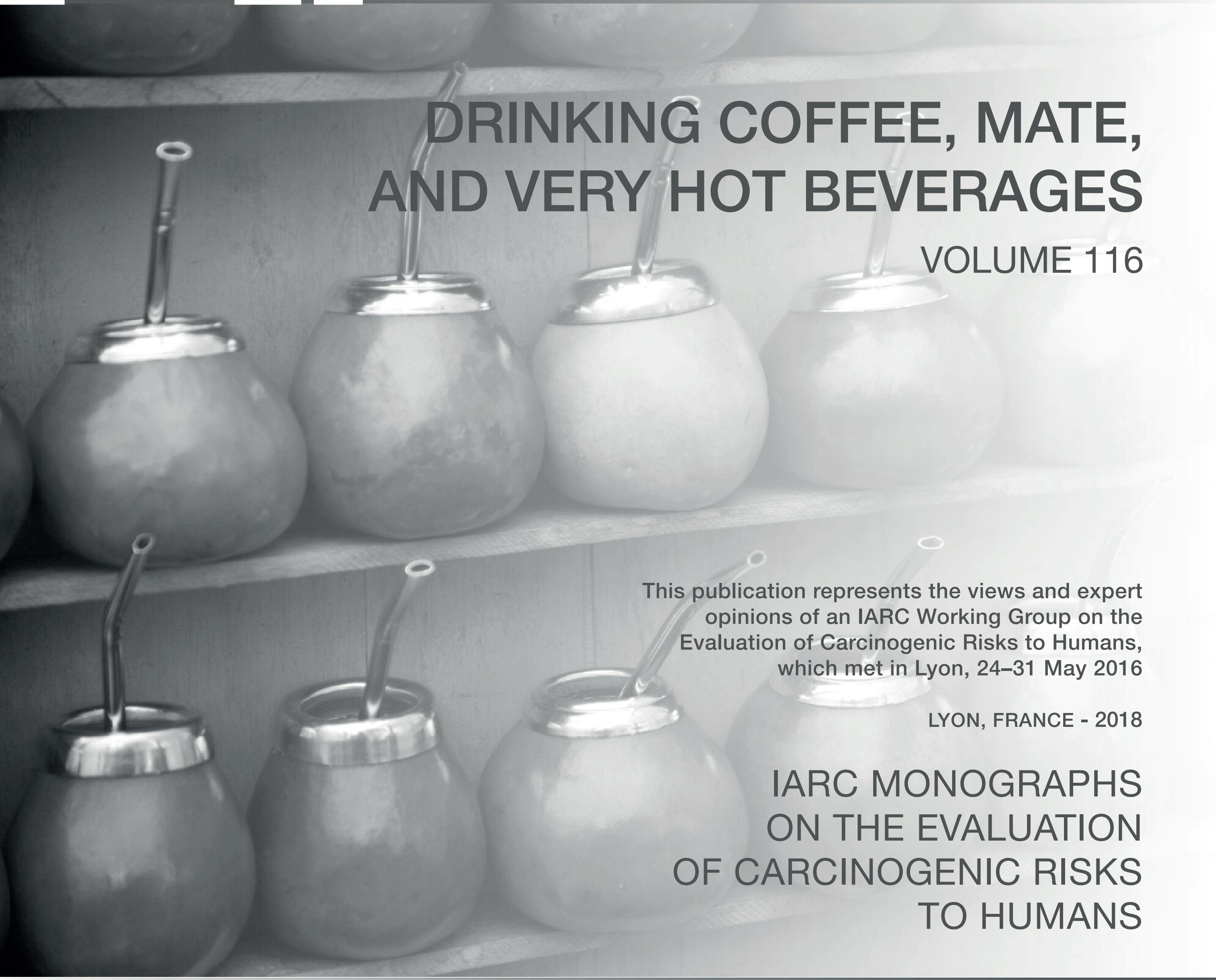

DRINKING COFFEE, MATE, AND VERY HOT BEVERAGES

VOLUME 116

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IARC MONOGRAPHS ON THE EVALUATION OF CARCINOGENIC RISKS TO HUMANS

International Agency for Research on Cancer

World Health Organization

1. EXPOSURE DATA

Coffee seeds (known as beans) are contained in fruits from trees and shrubs grown naturally in the shade of eastern African forests encompassing Ethiopia and the islands of Madagascar and Mauritius, among other countries. Coffee has attracted the attention of explorers and botanists from all over the world from the 16th century, when the first coffee trees were reported in the literature (Charrier & Berthaud, 1987); in particular, many new species were discovered in the second half of the 19th century. The interest may have been partly due to its stimulating effects in animals and humans, compounded with its enchanting aroma after roasting. Today, it is known that different coffee species originated in different parts of Africa and that there are still species being discovered, some in Ethiopia (Farah & Ferreira dos Santos, 2015).

The year 575 AD is often cited as the date of the arrival of coffee on the Arabian peninsula from Ethiopia. Commercial and political links were at that time strengthening across the Red Sea (Wellman, 1961; IARC, 1991). Coffee cherries (*bun* or *bon*) were then probably only dried and chewed as a stimulant against fatigue. It was only by the middle of the 15th century that coffee as a beverage (*kahwah* in Arabic), an infusion of roasted and ground coffee beans cultivated in Yemen, near the harbour of Mocha, came into general use throughout the Ottoman empire. By the end of the 16th century it had crossed the Mediterranean Sea, and in less than a century it had spread throughout Europe and to the British colonies in North America (Wellman, 1961; IARC, 1991).

During the 17th century the cultivation of coffee spread to the Malabar coast of India and to Ceylon. From the beginning of the 18th century, seedlings of *Coffea arabica* L. cultivated in European glasshouses, as first described by Linnaeus in 1737 (Debry, 1989), were introduced to the Dutch West Indies and to the French, Portuguese, and Spanish colonies of America and Asia (Wellman, 1961; IARC, 1991; Davis et al., 2007; Farah & Ferreira dos Santos, 2015).

1.1 Identification of the agent

1.1.1 Botanical data

(a) Nomenclature

Botanical name: *Coffea arabica* L., *Coffea canephora* Pierre ex A. Froehner, and various other species in the genus *Coffea*

Family: Rubiaceae

Subfamily: Ixoroideae

Tribe: Coffeeae

Genus: *Coffea*

Subgenus: Coffea

Common names: coffee, Arabica coffee, Robusta coffee

GRIN (2016)

The coffee tree belongs to the botanical family Rubiaceae, with the genus *Coffea* being

Fig. 1.1 The coffee plant, *Coffea arabica* L.

The figure shows the leaves, fruits, and berries.
From Spohn (2015) with permission from Dr Roland Spohn, www.spohns.de

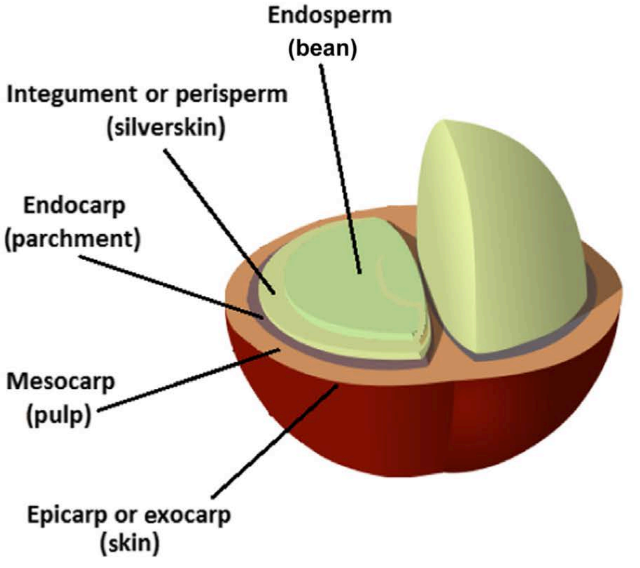
the most economically important member of this family (Murthy & Naidu, 2012). Because of the great variation in the types of coffee plants and seeds, botanists have failed to agree on a precise single system to classify them or even to designate some plants as true members of the *Coffea* genus. Although it is said that hundreds of species have been described, the National Center for Biotechnology Information (NCBI) in the USA and Davis et al. (2006; 2007) have described over 90 species within the *Coffea* genus, from which 25 have been more extensively studied (Davis et al., 2006; 2007; NCBI, 2014; Farah & Ferreira dos Santos, 2015). From these 25 species, only two have major commercial importance: *Coffea arabica* and *Coffea canephora*. It has been suggested that *C. arabica*, a tetraploid species ($2n = 4x = 44$), originated from natural hybridization between *C. canephora* and *C. eugenioides*, or ecotypes related to these two diploid ($2n = 2x = 22$) species (Charrier & Berthaud 1987; Lashermes et al., 1999; Anthony et al., 2002; Farah & Ferreira dos Santos, 2015).

(b) Description of the coffee plant

Coffee is an evergreen perennial plant. The shapes of the coffee tree and roots vary depending on the species and, in some cases, variety (Murthy & Naidu, 2012; FAO, 2014). In general, the coffee tree consists of an upright main shoot (trunk) with primary, secondary, and tertiary lateral branches. Naturally grown trees may be 4–6 m tall for *C. arabica* and 8–12 m for *C. canephora* (Illy & Viani, 2005).

Each leaf pair is opposite to the next leaf pair. Leaves appear shiny, wavy, and dark green in colour with conspicuous veins. In the axil of each leaf are four to six serial buds, which can develop into an inflorescence or secondary branches (Farah & Ferreira dos Santos, 2015; Fig. 1.1). The mature fruit, or “cherry” (Fig. 1.2), comprises: (1) skin (epicarp or exocarp), which is a red, dark

Fig. 1.2 Diagram of the coffee cherry fruit



Reproduced from Farah & Ferreira dos Santos (2015). The coffee plant and beans: introduction. In: Preedy V, editor. Coffee in health and disease prevention, 1st ed. San Diego (CA), USA: Academic Press; 5–10

pink or yellow monocellular layer covered with a waxy substance protecting the fruit; (2) pulp (mesocarp); (3) parchment or parch (endocarp); (4) silverskin, which is the seed coat composed mainly of polysaccharides (especially cellulose, hemicelluloses, and mannans); (5) two elliptical seeds (beans) containing the endosperm and embryo (CAC, 2009; Murthy & Naidu, 2012; Sánchez & Anzola, 2012; FAO, 2014; Farah & Ferreira dos Santos, 2015).

Arabica coffee grows optimally at altitudes of 550–1100 m in subtropical regions of latitudes 16–24° with well-defined rainy and dry seasons. The Brazilian regions of Minas Gerais and São Paulo, and Jamaica, Mexico, and Zimbabwe are examples of areas with these climate conditions (Illy & Viani, 2005). In the equatorial regions at latitudes below 10° coffee grows well at the higher altitudes of 1100–1900 m. Frequent rainfall causes almost continuous flowering, which results in two coffee harvesting seasons per year. Examples of countries that have this climate are Colombia, Costa Rica, Ethiopia, and Kenya (Illy & Viani, 2005).

C. canephora trees also grow at low elevations (from sea level to 900 m) in warmer climates in the equatorial regions at latitudes below 10°, and demonstrate higher resistance to diseases, but yield a beverage of inferior quality and lower market value compared to Arabica species. The species *Coffea liberica*, commanding less than 1% of the market, grows in warm climates and at low elevations; it is however susceptible to diseases and yields a beverage of poor quality (Illy & Illy, 1989; Hendre et al., 2008; FAO, 2014; Farah & Ferreira dos Santos, 2015; ICO, 2016).

1.2 Methods of production, uses, and preparation

1.2.1 Green coffee production

(a) Harvesting

Harvesting begins when about 80% of the fruits are ripe. Coffee cherries (ripe fruits) tend to yield better-quality beverages, whereas immature and overripe fruits yield defective low-quality beans (Toci & Farah, 2008). Harvesting may be undertaken manually or mechanically. Manual picking tends to yield better-quality beans (Farah, 2009; Filho et al., 2015).

(b) Post-harvest processing

Fig. 1.3 summarizes the steps involved in dry, semi-dry (or semi-wet/semi-washed), and wet methods used for coffee primary processing.

After being harvested, the fruits are either sorted manually or washed and separated in flotation tanks, followed by processing for the separation of the seeds from the rest of the fruit.

In the original dry processing method, harvested seeds are parched by sun exposure outdoors and/or by air dryers until the moisture content is about 10–12% (Trugo, 2003; Farah, 2009). Unless air dryers are available, protection from rain during the harvesting period is required to avoid the growth of microorganisms and to produce good-quality coffee (CAC, 2009; Farah, 2009). Once the fruits are dried, they are cleaned and the dried pericarp (endocarp, mesocarp, and epicarp) is removed mechanically (Fig. 1.2), leaving the mucilaginous material that envelops the seeds (silverskin) still adhering to their surface (Geromel et al., 2006; CAC, 2009; Farah, 2009). The product of dry processed fruits is called "natural" green coffee (CAC, 2009; Farah, 2009). The dry method is commonly used in Brazil and Africa (Farah & Ferreira dos Santos, 2015). Seeds produced by the dry method keep the silverskin adhered to their surface and have been valued in the market for the preparation of blends, as the silverskin confers more "body" or thickness to the brew (Borrelli et al., 2004).

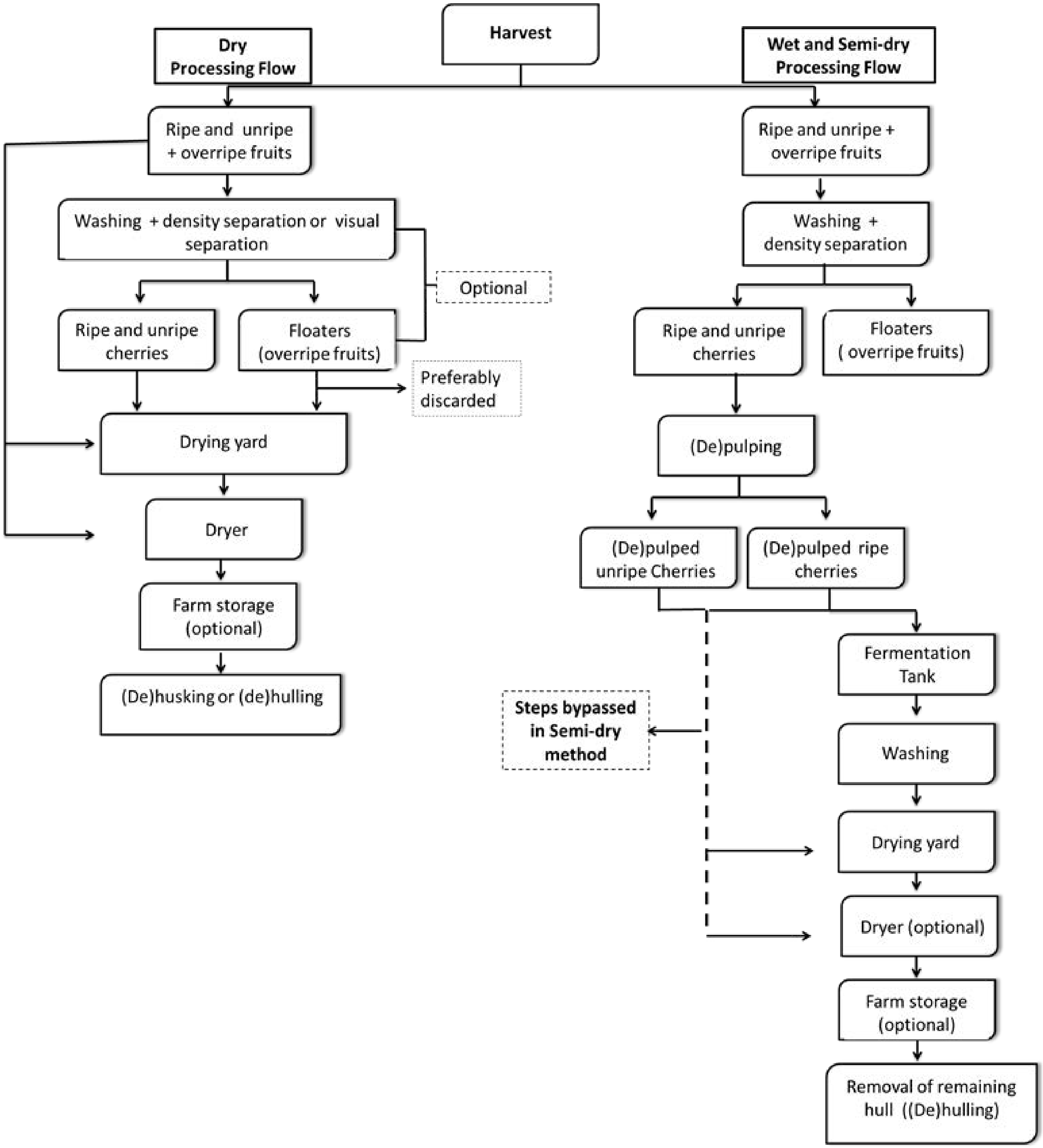
The wet process is more sophisticated and tends to generate a higher-quality beverage; generally only ripe cherries are processed this way. They can be selectively hand-picked or separated mechanically or in flotation tanks. Sorting is followed by mechanical (de)pulping, soaking, and fermenting in tanks, where the remaining pulp and silverskin are removed; acidity increases during this process and the pH may reduce to 4.5. The naked beans are washed and then dried in yards or in ventilated tables, possibly combined with hot air drying. After drying, the remaining part of the hull is often mechanically removed. Wet processing is frequently used in places where coffee is harvested by manual picking such as Asia, Central America, and Colombia; due to the higher market value, however, various farms in larger coffee-producing countries such as Brazil have also adopted this processing method. Wet-processed beans are called pulped coffees (Flament, 2002, Bee et al., 2005; Knopp et al., 2006; CAC 2009; Farah, 2009; Farah & Ferreira dos Santos, 2015).

At all steps of coffee processing, gram-negative and gram-positive bacteria, yeasts, and filamentous fungi are present at high levels. There has been a concern about the potential production of ochratoxin A and other mycotoxins by microorganisms during the fermentation in wet processing, when the natural growth of microorganisms can occur (see Section 1.4.2).

After the beans are treated by the dry or wet method, they are either stored or mechanically, manually, and/or electronically sized and sorted for quality control and commercialization. This process may be followed by an additional sorting with UV excitation.

Sorting yields coffee beans with extrinsic defects, such as stones, twigs, or other foreign matter, and intrinsic defects, such as immature,

Fig. 1.3 Coffee post-harvest processing: flow of dry, wet, and semi-dry/semi-washed methods



Reproduced from Farah & Ferreira dos Santos (2015). The coffee plant and beans: introduction. In: Preedy V, editor. Coffee in health and disease prevention, 1st ed. San Diego (CA), USA: Academic Press; 5–10 sour, or insect-damaged beans (Toci & Farah, 2008; Farah, 2009; Farah & Ferreira dos Santos, 2015). Avoiding undesirable contamination and the growth of microorganisms (especially mould) during harvesting, drying, and storage of the seeds is also critical. Defective beans are sold at a low price, roasted, blended with better-quality beans, and sold in the market as popular blends. The major concern here is the presence of moulded and oxidized defects, and therefore the potential presence of contaminants.

After marketing, green coffee beans are ready to undergo roasting. Optionally, they may be decaffeinated, steam-treated, or stored before roasting. If stored, this is another critical stage where the growth of microorganisms is common.

1.2.2 Decaffeination

Decaffeination is traditionally performed before roasting. For decaffeinated coffee, most countries require that the content of caffeine be reduced to less than 0.1% on a dry weight basis; however, decaffeinated coffees with up to 0.3% of caffeine can be found on the market. In addition to extracting caffeine, other substances are also extracted during the process including aroma precursors and bioactive compounds (Farah et al., 2006; Toci et al., 2006). As a result, decaffeinated products can taste very different from regular coffee.

Different solvents and adsorbent substances can be used for decaffeination, among which dichloromethane (see IARC, 1986, 1987, 2017), ethyl acetate (see IARC, 1979, 1987), edible fats and oils, supercritical carbon dioxide, and acid-activated carbon (used in extract decaffeination) are well known (IARC, 1991). The selectivity of solvents and adsorbent materials varies, along with the sensory result. Processes that do not employ an organic solvent are known as "water decaffeination". Currently, the industry in Europe and in the USA uses mostly water and supercritical carbon dioxide; the latter is employed at temperatures and pressures of 40–80 °C and 200–300 bar (i.e. above its critical point of 31.06 °C and 73.8 bar) for 5–30 hours (IARC, 1991). Dichloromethane or ethyl acetate are used in Central and South America, depending on the country.

1.2.3 Roasting, grinding, and packing

It is only during roasting that coffee acquires its characteristic aroma, a consequence of a dramatic change in chemical composition of the beans. The two main systems used for heat transfer in coffee roasters are conduction and convection. In roasters that use conduction, heat is transferred by direct contact with a hot surface and/or fire. In convection roasters heat is transferred by hot air circulation in the roasting chamber, distributing heat evenly. Most modern roasters work this way, and some use both convection and conduction. Convection roasters roast faster than conduction roasters, and this will have an influence on the chemical reactions that occur during the process (IARC, 1991; Holman, 2009; Soares et al., 2009; Fernandes, 2017). In addition to the different types of roasters, there are several variables that can be applied to the process such as time and temperature control.

During the roasting process the beans increase in volume, develop a brittle structure, and acquire a light to dark brown colour, while their composition changes dramatically as a consequence of pyrolysis, caramelization, and Maillard reactions. The roasting intensity will vary for different cultures and types of coffee. Roasting chamber temperatures generally vary over 190–270 °C, although the use of temperatures of 210–230 °C is more common in industry.

After cooling, which can be accelerated by quenching with vaporized water or a cool air stream, residual carbon dioxide trapped in the bean is slowly released over a period of days or up to 48 hours after grinding (IARC, 1991; Farah, 2012).

Coffee can be sold pre-ground and packaged after short degassing (2–4 hours) or under an initial slight vacuum in flexible bags (Viani, 1986). Unlike green beans, roasted coffee spoils relatively quickly if unprotected from oxygen and moisture; at ambient temperature, whole beans stale 4–6 weeks and ground coffee 2 weeks after roasting (Toci et al., 2013).

1.2.4 Brewing techniques

Brewing can be defined as the preparation of a beverage by "mixing, steeping, soaking, or boiling a solid in water" (Thesaurus, 2016). Coffee brewing is the process by which coffee soluble solids are extracted by water. Brewing techniques encompass a wide range of procedures used in different parts of the world, which are based on the types of coffee and roasting degrees traditionally used. Local cultural practices and the cup size used, associated with the variety of preparation methods, result in large differences in the chemical composition of the brew and a range of individual consumption patterns. Globalization has reduced cultural distances however, and a diversity of techniques and methods is available both for home preparation and in coffeehouses. An overview of the variety of coffee preparation methods is provided in Hatzold (2012).

In addition to the type of coffee and roasting degree, the particle size and the ratio of ground coffee to water vary considerably with techniques. Generally speaking, water temperature may vary from about 7–10 °C in cold brewing to 100 °C in boiling methods (see the monograph on Drinking Mate and Very Hot Beverages in the present volume for more information). After the extraction of coffee components, some techniques use filter paper to separate grounds from brew while others use a strainer, plunger, or no device at all. If no filter paper is used, the coffee will contain the diterpenes cafestol and kahweol (Urgert et al., 1995). The most common brewing techniques are described below.

(a) Decoction

(i) Boiled coffee

To prepare a boiled brew (most commonly consumed in northern Scandinavian countries), boiling water is poured onto coarsely ground roasted Arabica coffee and the decoction is boiled for up to 10 minutes. The decoction may also be allowed to sit without boiling. The brew is made at about 5% (weight/volume) [50 g coffee grounds in 1 L of water]. The ground coffee settles at the bottom and the brew is consumed. Cup volume is about 150 mL (IARC, 1991; van Dusseldorp et al., 1991; [expert knowledge of the Working Group]).

(ii) "Turkish" coffee

For coffee consumed in Greece, Turkey, parts of the Balkans, and parts of the Middle East, very finely ground coffee is brewed with sugar in a copper pot (*ibrik*) at about 8% w/v by gentle boiling. The ingredients are heated until a large bubble or foam is formed in the centre of the *ibrik*. The heat is interrupted and the process can be repeated up to three times. Cup volume is generally 60 mL (IARC, 1991).

(iii) Kopi tubruk

Another variation of boiled coffee is *kopi tubruk*, also called mud coffee. This is a common brewing method brought to Indonesia by Middle Eastern traders. The concentration is similar to "Turkish" coffee, but a medium to coarse grind is used instead of a fine grind. Coffee and sugar are placed in a cup or mug, boiling water is added, and the coffee is "cooked" until the grounds settle at the bottom. A variation is to heat water, coffee grounds, and sugar together and let them boil until the grounds settle. Cup/mug volume varies over 150–190 mL [expert knowledge of the Working Group].

(b) Infusion

In this technique roasted coarse coffee grounds are infused, usually followed by the use of a device to separate the grounds from the brew.

(i) Plunger pot

In this system, also called a "French press" or piston system, hot water is a poured over coarsely ground coffee with a concentration of about 4–10% (w/v), and a metal strainer is pushed down the coffee pot to separate the grounds from the brew after infusion. This system is used in Australia, Europe, and North America. A variation of this system uses a paper filter instead of a metal plunger. Cup/mug size varies over 150–190 mL (IARC, 1991) [expert knowledge of the Working Group].

(ii) Cold brewing

In this system, very coarsely ground coffee is placed in a receptacle with a lid. Cold to room-temperature water is poured over the ground coffee (about 12.5% w/v). The mixture is well stirred and the jar is covered and left for 12–24 hours. When brewed, the mixture is strained to remove solid residue. The resulting brew can be served cold or mixed with boiling water to serve hot. The main sensory characteristics of this brew are low acidity, gentleness, and sweetness [expert knowledge of the Working Group].

(c) Percolation

(i) Filtration

Filtered coffee is one of the most common brewing methods around the world; it is made by percolating pre-boiling water (95–98 °C) through medium-ground roasted coffee in a filter (usually paper but may be metal, nylon, or ceramic) set in a funnel. The brew drips into a warmed pot within about 2–5 minutes. The strength of the brew will vary with cultural habits, which includes roasting degree and coffee to water ratio of 7–14% w/v, which increases as the roasting degree becomes lighter. Light to medium roasts predominate in the USA, medium to dark roasts prevail in South America, and dark roasts are favoured in France and Italy. Cup size varies over 40–150 mL. Automatic coffee makers are available worldwide and have also been widely adopted by the food-services industry (IARC, 1991; [expert knowledge of the Working Group]).

(ii) Vaporization under pressure (moka pot)

In this technique water is heated to just above boiling point and forced by slight excess pressure through coarse medium-/dark-roasted coffee. Continuous recirculation over the coffee grounds occurs until the desired brew strength is reached. Ground coffee concentrations normally range over 8–12%. This method is traditional in Italian and Spanish households, and is becoming popular all over the world [expert knowledge of the Working Group].

(iii) Vaporization under pressure (espresso)

This method, which originated in Italy and is now popular worldwide, allows rapid extraction. In espresso machines, water at 92–95 °C is driven through a medium-/dark-roasted ground coffee packed bed by a pressure pump (8–12 bar) to extract soluble material over a period of 15–35 seconds. About 5–8 g of roasted coffee is used for each 25–60 mL cup. The extraction yield of coffee soluble solids from the roasted coffee is 18–26% with a soluble solids concentration in the cup of 20–60 g/L brew; 70–85% caffeine is recovered (Illy & Viani, 2005; Petracco, 2005; Corrochano et al., 2015). Automated methods for coffee preparation have gained popularity during the last decades, including fully automatic espresso-type machines that use coffee pods or capsules (Gloess et al., 2013).

1.2.5 Instant coffee production

Instant coffee is a dried water extract of roasted and ground coffee which readily dissolves in both cold and hot water, eliminating the need for brewing equipment. The unit operations performed during the manufacture of instant coffee are the same as for roasted coffee, followed by extraction, concentration, and drying of the extract (to a maximum of 5% moisture by spray-drying or freeze-drying), followed by agglomeration, aromatization, and packaging of the powder. Packaging is performed under vacuum or in an inert atmosphere in jars or flexible bags, and the packaged product can be stable for more than two years if unopened (Viani, 1986; IARC, 1991).

1.2.6 Other beverages containing coffee

Coffee may also be sold as a "convenience" product in a ready-to-drink form in cans or aseptic carton packaging, typically premixed with milk or other ingredients (Waizenegger et al., 2011).

1.2.7 Other uses of coffee and coffee byproducts

Numerous other products containing coffee are available on the market. Coffee and all forms of coffee extracts or instant coffee may be used as an ingredient in various foods, such as the flavouring of chocolate or in various bakery products. Infusions may be prepared with coffee byproducts from post-harvesting processing (dry cherry pulp) or from coffee leaves. Coffee can also be consumed as chocolate-coated roasted coffee beans.

Non-traditional uses of coffee or coffee extracts include the use in food supplements. The US Dietary Supplements Label Database, for example, lists more than 100 products that contain the word "coffee" in the product name (NLM, 2016). Specifically, green coffee extract and roasted and green blends have been marketed for purported effects such as weight loss and intake of antioxidants. The methods of encapsulated green coffee extract production can be similar to those applied to instant coffee production. Decaffeinated hydroalcoholic extracts and alternative technologies are also available. Coffee silverskin is another byproduct of coffee production; its use for human consumption can be an alternative to its environmental disposal. The high fibre and antioxidant compound content means that use of coffee silverskin (as well as its extract) as a supplement for different purported purposes such as weight control or for antioxidant intake has been proposed (Borrelli et al., 2004; Narita & Inouye, 2012).

1.3 Exposure assessment and biological markers

This section reviews the methods used to assess coffee consumption and exposure to coffee components. Food consumption data, which are typically obtained by questionnaire, provide estimates of external exposures to coffee and related substances, while biological markers may be used to assess internal exposures.

1.3.1 Questionnaires

Dietary assessment methodologies are under continuous development in an attempt to improve the validity of dietary exposure data, while also profiting from rapid evolution in innovative technologies such as mobile applications, scan- and sensor-based technologies, and many other upcoming technologies (Illner et al., 2012). A comprehensive review of dietary assessment methodologies and technologies used in epidemiological studies is beyond the scope of this report, but can be found in Thompson & Subar (2013) and Slimani et al. (2015).

(a) Concepts, design, and applications

The majority of epidemiological studies investigating associations between coffee consumption and cancer risk have used a food frequency questionnaire (FFQ) to assess individual usual coffee intake and/or particular coffee components (e.g. caffeine). The food frequency approach asks respondents to report their usual frequency of consumption of specific food items from a list covering a specific period of time. FFQs are typically used in epidemiological studies to assess "usual" dietary intake in individuals for several reasons. First, FFQs are the only feasible approach in case–control studies where usual diet (often in the distant past) must be ascertained retrospectively. Second, in large prospective cohort studies FFQs are often the instrument of choice because of their time- and cost-efficient characteristics, including low investigator burden and cost. The FFQ can be distributed by mail or online to a large number of participants, can be self-administered, may be optically scanned, computer assisted, or web-based, and is often pre-coded to facilitate data handling. Third, the FFQ has the advantage that it does not affect the respondent's eating behaviour and that usual individual intake is being requested (over a long timeframe), avoiding the need for repeated measurements.

Nevertheless, the completion of an FFQ may be a challenge for respondents as usual consumptions, and particularly portion sizes, are difficult to estimate precisely. The ability to quantify total dietary intake depends on the number of food items listed in the FFQ and on the level of detail collected within the questionnaire, whether or not portion sizes are included, what timeframe of intake or reference period is used, and, for caffeine intake specifically, the differentiation between caffeinated and decaffeinated coffee in the food list (Block et al., 1986; Rimm et al., 1992).

FFQs generally include 50–150 (mostly generic) food items, with the number of frequency categories varying according to the study objectives and designs. The appropriateness of the food list is crucial as the full variability of an individual's diet, which includes many foods and mixed dishes, cannot be captured by a finite food list.

Whether portion size information is also required depends on the study aims. Three different types of FFQ can be distinguished depending on the portion size information required in the questionnaire. If no portion size information is included then the questionnaire is called a qualitative or non-quantitative FFQ, while a questionnaire including detailed portion size information (e.g. in grams or number of units) is called a quantitative FFQ. Some questionnaires include several portion size categories (e.g. ≤ 1 cup; 2–3 cups; ≥ 4 cups) which the subject can choose from, and is called a semi-quantitative FFQ. Researchers have used methods to improve assessment of portion size (e.g. picture booklets to estimate cup size) in the studies included in this report (see Tables 1.1 and 1.2).

Some FFQs also include extra questions regarding food preparation methods (e.g. brewing method for coffee), and identification of the type (e.g. caffeinated versus decaffeinated) and brand of certain types of foods.

FFQs are used widely in case–control and cohort studies to assess associations between dietary intake and disease risk but, importantly, they are generally used for ranking subjects according to food or nutrient intake rather than for estimating absolute levels of intake (Beaton, 1994; Kushi, 1994).

The FFQs used in the epidemiological studies included in this report were developed with a broader aim than only coffee assessment; details regarding the type of coffee and/or preparation method were therefore often lacking. This limitation should be considered when comparing results from different regions/countries as quantities of coffee powder/beans used to brew a coffee may differ between countries and cultures, although this information is lacking in most studies.

(b) Validation and calibration

Assessments of the relative validity of a FFQ provide information about how well the instrument is measuring what it is intended to measure. This is evaluated by comparing dietary intake

Table 1.1 Summary of methods used in cohort studies investigating the relationship between coffee consumption and cancer risk

Study, country, reference	Information-collection method	Period of information collection	Respondents	Distinction between caffeinated/ decaffeinated	Exposure metrics
Melbourne Collaborative Cohort Study (MCCS), Australia (Ireland et al., 1994)	General: FFQ Coffee-specific questions: frequency of coffee consumption, consumption of milk with coffee	At baseline	24 500 women and 17 000 men aged 40–69 yr	No	1–3 cups/mo, 1 cup/wk, 2–4 cups/wk, 5–6 cups/wk, 1 cup/day, 2–3 cups/day, 4–5 cups/day, > 6 cups/day
The Singapore Chinese Health Study, Singapore (Ainslie-Waldman et al., 2014)	General: 165-item FFQ, in conjunction with the Singapore Food Composition Database for the ascertainment of 96 items including caffeine Coffee-specific questions: frequency of caffeinated coffee consumption Questionnaire not available	At baseline	63 257 Chinese men and women aged 45–74 yr	No	Never or hardly ever, 1–3 times/mo, once/wk, 2–3 times/wk, 4–6 times/wk, once/day, 2–3 times/day, 4–5 times/day, ≥ 6 times/day
Life Span Study, Japan (Sauvaget et al., 2002)	General: 22-item FFQ Coffee-specific questions: frequency of coffee consumption Questionnaire not available	At baseline	40 349 Japanese men and women	No	1 cup/wk, 2–4 cups/wk, Almost daily, Do not eat/drink

Table 1.1 (continued)

Study, country, reference	Information-collection method	Period of information collection	Respondents	Distinction between caffeinated/ decaffeinated	Exposure metrics
Japan Public Health Center-based Prospective (JPHC) study, Japan (Makiuchi et al., 2016)	General: self-administered questionnaire including questions on beverage consumption Coffee-specific questions: circle the frequency of your average consumption of coffee; how many teaspoons of sugar do you use per cup of coffee?	At baseline	140 420 male and female Japanese subjects aged 40–69 yr at baseline	No	Studies using baseline questionnaire: Almost never 1–2 days/wk, 3–4 days/wk, 1–2 cups/day, 3–4 cups/day, > 5 cups/day Study using 5-year follow-up questionnaire: 0 cups/wk, 1–2 cups/wk, 3–4 cups/wk, 5–6 cups/wk, 1 cup/day 2–3 cups/day, 4–6 cups/day, 7–9 cups/day, 10 cups/day
Miyagi Cohort, Japan (Naganuma et al., 2008)	General: self-administered questionnaire with 36 food items and 4 beverages including coffee Coffee-specific questions: frequency of coffee consumption Questionnaire not available	At baseline	25 279 men and 26 642 women 40–64 yr at baseline	No	Never, < 1 cup/day 1–2 cups/day, 3–4 cups/day, 5 cups/day
Japan Collaborative Cohort (JACC) study, Japan (Yamada et al., 2014)	General: self-administered questionnaire including questions on beverage consumption Coffee-specific questions: frequency of coffee consumption; addition of sugar and milk in coffee Questionnaire not available	At baseline	110 792 Japanese men and women aged 40–79 yr at baseline	No	Seldom or never, 1–2 cups/mo, 1–4 cups/wk, 1 cup/day, 2–3 cups/day, > 4 cups/day
Takayama city cohort, Japan (Oba et al., 2008)	General: 169- item FFQ Coffee-specific questions: frequency of coffee consumption Questionnaire not available	At baseline	13 392 men and 15 695 women aged ≥ 35 yr	No	Never, > 1 cup mo to 4–6 cups/wk, > 1 cup/day

Table 1.1 (continued)

Study, country, reference	Information-collection method	Period of information collection	Respondents	Distinction between caffeinated/ decaffeinated	Exposure metrics
National Breast Screening Study (NBSS), Canada (Silvera et al., 2007)	General: 86-item FFQ Coffee-specific questions: frequency of coffee consumption Questionnaire not available	At baseline	89 835 women, aged 40–59 yr	No	None, 0–1 cup/day, 2–3 cups/day, ≥ 4 cups/day
Health Professionals Follow-up study, USA (Wilson et al., 2011)	General: 130-item FFQ Coffee-specific questions: how frequently did you drink a cup of caffeinated coffee? How frequently did you drink a cup of decaffeinated coffee?	At baseline in 1986 and every 4 yr thereafter	47 911 male health professionals aged 40–75 yr at baseline	Yes	None, < 1 cup/day, 1–3 cups/day, 4–5 cups/day, 6 cups/day
Iowa Womens' Health Study, Iowa (Lueth et al., 2008)	General: 127-item FFQ Coffee-specific questions: number of cups per day for normal or decaffeinated coffee Questionnaire not available	At baseline	98 826 women in Iowa aged 55–69 yr at baseline	Yes	< 1/mo, 1–3 cups/mo, 1 cup/wk, 2–4 cups/wk, 5–6 cups/wk, 1 cup/day, 2–3 cups/day, 4–5 cups/day, 6 cups/day
NIH-AARP Diet and Health Study, USA (Dubrow et al., 2012)	General: 124-item FFQ Coffee-specific questions: how many cups of coffee caffeinated or decaffeinated did you drink? When you drank coffee, mark whether you usually drank caffeine-free or caffeine-containing types (didn't drink this beverage, more than half the time I drank caffeine-free, more than half the time I drank caffeine containing)	At baseline	3.5 million men and women from American Association of Retired Persons	Yes	10 frequency categories ranging from never to > 6 times/day
Black Women's Health study, USA (Boggs et al., 2010)	General: 68-item modified version of the National Cancer Institute Block FFQ, 85-item version in 2001 Coffee-specific questions: how often did you drink coffee with caffeine? How often did you drink decaffeinated coffee? Milk or cream in coffee	At baseline and after 6 yr	59 000 African-American women	Yes	Nine frequency categories ranging from never or 1 time/mo to 6 times/day

Table 1.1 (continued)

Study, country, reference	Information-collection method	Period of information collection	Respondents	Distinction between caffeinated/ decaffeinated	Exposure metrics
Nurses' Health Study and Nurses' Health Study 2, USA (Holick et al., 2010)	General: NHS1: 61-item semi-quantitative FFQ at baseline, after 130-item FFQ NHS2: 131-FFQ Coffee-specific questions: how often did you use coffee not decaffeinated (cups) in the precedent year?	At baseline and every 3 yr	121 700 female nurses 30–55 yr old at baseline (NHS1), 116 686 female nurses 25–42 yr old at baseline (NHS2)	Yes	0–1 cups/day, 2 cups/day, 3 cups/day, 4 cups/day, 5 cups/day
Prostate, Lung Colorectal and Ovarian (PLCO) cohort, USA (Dominianni et al., 2013)	General: 77-item FFQ, NIH Health Diet History Questionnaire (DHQ) in addition for coffee intake Coffee-specific questions: how many cups of coffee caffeinated or decaffeinated did you drink? How often was the coffee you drank decaffeinated? How often did you add sugar or honey to your coffee? Each time sugar or honey was added to your coffee how much was usually added? How often did you add artificial sweetener to your coffee? What kind of artificial sweetener do you usually use? How often was non-dairy creamer added to your coffee?	At baseline	154 901 men and women, aged 55–74 yr at baseline	Yes	None, < 1 cup/day, 1 cup/day, 2–3 cups/day, > 4 cups/day
Women's Health Initiative, USA (Giri et al., 2011)	General: questionnaires on demographic characteristics, medical history, family history, reproductive history, lifestyle/ behavioural factors, and quality of life Coffee-specific questions: do you usually drink coffee each day? Number of cups of coffee	At baseline and after 3 yr	93 676 women aged 50–79 yr at baseline	Yes	0 or 1 cup/day, 1 cup/day, 2–3 cups/day, 4 cups/day 4–5 cups/day > 6 cups/day
7th Day Adventists, USA (Phillips & Snowdon, 1983; Butler et al., 2008)	General: Lifestyle questionnaire, 51-item FFQ Coffee-specific questions: frequency of coffee consumption	At baseline	34 192 members of 7th Day Adventist church in California, > 25 yr old; non-Hispanic whites	No	< 1 cup 1–2 cups/day 3–4 cups/ day 5+ cups/day

Table 1.1 (continued)

Study, country, reference	Information-collection method	Period of information collection	Respondents	Distinction between caffeinated/ decaffeinated	Exposure metrics
Lutheran Brotherhood Insurance Study, USA (Murray et al., 1981)	General: FFQ Coffee-specific questions: frequency of coffee consumption Questionnaire not available	At baseline	17 818 male, white policy holders, aged ≥ 35 yr, of the Lutheran Brotherhood Insurance Society	No	None < 1 cup/day 1–2 cups/day < 3 cups/day 3–4 cups/day, 5–6 cups/day, ≥ 7 cups/day
Leisure World Cohort, USA (Paganini-Hill et al., 2007)	General: FFQ Coffee-specific questions: frequency of coffee consumption Questionnaire not available	At baseline	13 978 residents of Leisure World, California; men and women. The mean of age at entry was 75.0 yr for men and 73.8 yr for women	Yes	None < 1 cup/day 1 cup/day, 2–3 cups/day, ≥ 4 cups/day
Kaiser Permanente Medical Care Program Study, USA (Efird et al., 2004)	General: lifestyle questionnaire Coffee-specific questions: frequency of coffee consumption Questionnaire not available	At baseline	182 357 Kaiser Foundation Health Plan members	No	≤ 6 cups/day, > 6 cups/day
Cancer Prevention Study II, USA (Hildebrand et al., 2013)	General: 66-item FFQ Coffee-specific questions: frequency of coffee consumption (currently and in the previous year)	At baseline	968 432; men and women (average age 57 yr)	Yes	< 1 cup/day, 1–2 cups/day, 3–4 cups/day, > 4 cups/day
Lutheran Brotherhood Insurance Study, USA (Murray et al., 1981)	General: FFQ Coffee-specific questions: frequency of coffee consumption Questionnaire not available	At baseline	17 633 male white policy holders, aged ≥ 35 yr, of the Lutheran Brotherhood Insurance Society	No	< 3 cups/day 3–4 cups/day, 5–6 cups/day, ≥ 7 cups/day
The Glostrup Population Studies, Denmark (Sjøl et al., 1991)	General: standardized questionnaire for coffee consumption Coffee-specific questions: number of cups of coffee Questionnaire not available	At baseline	5207 Danish women	No	0–2 cups/day, 3–6 cups/day, > 7 cups/day
The ATBC study, Finland (Lai et al., 2013)	General: FFQ in conjunction with a validated comprehensive nutrient database Coffee-specific questions: how many cups did you drink per week or per day? Sugar, whipping cream, coffee cream, light cream, milk	At baseline	29 133 Finnish male smokers	No	Participants indicated the average number of cups of coffee consumed per day or per week in the previous year

Table 1.1 (continued)

Study, country, reference	Information-collection method	Period of information collection	Respondents	Distinction between caffeinated/ decaffeinated	Exposure metrics
Hu et al. (2008), Finland	General: lifestyle questionnaire Coffee-specific questions: frequency of coffee consumption Questionnaire not available	At baseline (seven independent cross-sectional population surveys were carried out in six geographical areas of Finland in 1972, 1977, 1982, 1987, 1992, 1997 and 2002)	62 015 Finish participants for seven surveys, aged 25–74 yr	No	0–1cups/day, 2–3 cups/day, 4–5 cups/day, 6–7 cups/day, ≥ 8 cups/day
Bidel et al. (2013), Finland	General: lifestyle questionnaire Coffee-specific questions: frequency of coffee consumption Questionnaire not available	At baseline	60 041 Finnish men and women aged 26–74 yr	No	1–2 cups/day, 3–4 cups/day, 5–6 cups/day, 7–9 cups/day, ≥ 10 cups/day
Norwegian National Health Screening Service for CVD, Norway (Veierød et al., 1997)	General: semi-quantitative questionnaire with 54 questions obtained information on general meal pattern, amounts, frequencies and types of specified foods and beverages Coffee-specific questions: number of cups of coffee Questionnaire not available	At baseline	25 708 men and 25 049 women aged 16–56 yr at baseline attending a Norwegian health screening in 1977–1983	No	< 2 cups/day, 3–4 cups/day, 5–6 cups/day, > 7 cups/day
Norwegian Women and Cancer (NOWAC) study, Norway (Gavrilyuk et al., 2014)	General: questionnaire on health, lifestyle, and reproductive factors Coffee-specific questions: how many cups of each kind of coffee/tea do you usually drink? (filtered, boiled, instant) Do you use sugar, milk, or cream in coffee?	At baseline	97 926 women resident in Norway, aged 30–70 yr at baseline	No	≤ 1cup/day, 2–3 cups/day, 4–7 cups/day, ≥ 8 cups/day Almost never

Table 1.1 (continued)

Study, country, reference	Information-collection method	Period of information collection	Respondents	Distinction between caffeinated/ decaffeinated	Exposure metrics
Swedish Women's Lifestyle and Health cohort study, Sweden (Weiderpass et al., 2014)	General: self-administered FFQ Coffee-specific questions: how many cups per day or per week during the preceding year	At baseline	48 249 women residing in the Uppsala Health Care Region in Sweden between 1991 and 1992	No	No
Swedish Mammography Cohort, Sweden (Friberg et al., 2009)	General: 67-item FFQ Coffee-specific questions: how often do you drink coffee?	At baseline and after 7 yr	60 634 women born between 1914–1948 living in Uppsala County of Central Sweden, women born during 1917–1948 living in Västmanland county	No	1 cup/day, 2–3 cups/day, 4 cups/day
Västerbotten Intervention Project (VIP), Sweden (Norberg et al., 2010)	General: 84-item VIP FFQ (1992–1996), 64 items VIP FFQ (1997–2007) Coffee-specific questions: two questions on coffee, one for filtered and one for boiled coffee Questionnaire not available	At baseline	64 603 residents of the county of Västerbotten turning 40, 50, and 60 yr of age	No	Never, A few times/yr, 1–3 times/mo, 1 time/wk, 2–3 times/wk, 4–6 times/wk, 1 occasion/day, 2–3 occasions/day, 4 occasions/day
Swedish Twin Registry Study, Sweden (Isaksson et al., 2002)	General: lifestyle questionnaire Coffee-specific questions: frequency of coffee consumption Questionnaire not available	At baseline	1884 men and women recruited in 1961, aged 36–75 yr	No	0–2 cups/day, 3–6 cups/day, ≥ 7 cups/day
Discacciati et al. (2013), Sweden	General: 96-item FFQ Coffee-specific questions: frequency of coffee consumption Questionnaire not available	At baseline	48 645 men aged 45–79 yr residing in Västmanland and Örebro counties in central Sweden	No	None, < 1 cup/day, 1–3 cups/day, 4–5 cups/day, ≥ 6 cups/day
Netherlands Cohort Study, Netherlands (Steevens et al., 2007)	General: FFQ including question about coffee intake (yes/no, how many cups per day) Coffee-specific questions: number of cups of coffee of coffee Questionnaire not available	At baseline	120 852 men and women aged 55–69 yr at baseline	No	0 – < 1 cups/day 1 – < 3 cups/day 3 to < 5 cups/day > 5 cups/day

Table 1.1 (continued)

Study, country, reference	Information-collection method	Period of information collection	Respondents	Distinction between caffeinated/ decaffeinated	Exposure metrics
Million Women Study, UK (Yang et al., 2015)	General: questionnaire on health, lifestyle, and reproductive factors Coffee-specific questions: How many teaspoons of sugar do you add to coffee? Do you add milk to your coffee?	At baseline and approximately after 3 yr	1.3 million middle-aged women	No	< 1 cup/day, 1–2 cups/day, 3–4 cups/day, ≥ 5 cups/day
Supplementation en Vitamines et Mineraux Antioxydants Study (SUVIMAX), France (Mennen et al., 2007; Hercberg et al., 2004)	General: 24 hours dietary recall Coffee-specific questions: indication of the portion size	At baseline and every 2 mo	7876 women aged 35–60 yr and 5141 men aged 45–60 yr	No	No
Fagherazzi et al. (2011), France	General: 208-item FFQ Coffee-specific questions: frequency of coffee consumption Questionnaire not available	At baseline and after 3 yr	67 703 women	Yes	≤ 1 cup/day, 1–3 cups/day, > 3 cups/day
EPIC, 10 European countries (Bhoo-Pathy et al., 2015)	General: Country-specific questionnaires: self-administered semi-quantitative FFQ (± 260 food items), dietary history questionnaires (> 600 food items), semi-quantitative food-frequency questionnaires combined with a food record Coffee-specific questions: number of cups of coffee Questionnaires not available	At baseline	521 448 men and women	Yes, except for Denmark and France	Different exposure metrics depending on the country
Multiethnic Cohort Study of Diet and Cancer (MEC) (Kolonel et al., 2000)	General: lifestyle questionnaire including diet history Coffee-specific questions: frequency of coffee consumption Do you add any of the following to coffee: cream or half and half; milk; non-diary cream; sugar or honey; sugar substitute	At baseline	215 000 men and women primarily of African-American, Japanese, Latino, native Hawaiian and Caucasian origin	Yes	Never or hardly never, Once a month, 2–3 times/mo, Once a week, 2–3 times/wk, 4–6 times/wk Once a day, 2–3 times/day, > 4 times/day

FFQ, food frequency questionnaire; mo, month(s); wk, week(s); yr, year(s)

Table 1.2 Summary description of methods used in cohort studies investigating the relationship between coffee consumption and cancer risk

Study, country, reference	Portion size	Specific components measured	Method validated for coffee consumption
Melbourne Collaborative Cohort Study (MCCS), Australia (Ireland et al., 1994)	No	No	No
Singapore Chinese Health Study, Singapore (Ainslie-Waldman et al., 2014)	Yes, three possible portion sizes	Daily caffeine intake	No
Life Span Study, Japan (Sauvaget et al., 2002)	No	No	Yes, correlation with 24 h diary: 0.51
Japan Public Health Center-based Prospective (JPHC) study, Japan[a] (Makiuchi et al., 2016)	No	No	Yes, Spearman correlation coefficient with diet record data: Baseline Q: 0.42 for men and 0.38 for women 5 yr follow-up Q: 0.75 in men and 0.80 in women
Miyagi Cohort, Japan (Naganuma et al., 2008)	No	No	Yes, Spearman rank correlation with 3-day diet records: 0.70
Japan Collaborative Cohort (JACC) study, Japan (Yamada et al., 2014)	No	No	Yes, Spearman rank correlation 12-day dietary record: 0.81
Takayama City Cohort, Japan (Oba et al., 2008)	No	No	No
National Breast Screening Study (NBSS), Canada (Silvera et al., 2007)	Yes	No	No
Health Professionals Follow-up study, USA (Wilson et al., 2011)	No	Daily caffeine intake	Yes, correlation with two week-long diet records: 0.93
Iowa Womens' Health Study, Iowa (Lueth et al., 2008)	No	Daily caffeine intake	Yes, correlation between caffeine intake estimates from dietary recalls and FFQ: 0.95
NIH-AARP Diet and Health Study, USA (Dubrow et al., 2012)	No	Daily caffeine intake	No
Black Women's Health study, USA (Boggs et al., 2010)	Yes (small, medium, or large)	Daily caffeine intake	Yes
Nurses' Health Study and Nurses' Health Study 2, USA (Holick et al., 2010)	No	Daily caffeine intake	Yes, Pearson correlation with 1 wk diet record: 0.93
Prostate, Lung Colorectal and Ovarian (PLCO) cohort, USA (Dominianni et al., 2013)	No	Daily caffeine intake	No
Women's Health Initiative, USA (Giri et al., 2011)	No	No	No
7th Day Adventists, USA (Phillips and Snowdon, 1983)	No	No	No
Leisure World Cohort, USA (Paganini-Hill et al., 2007)	No	No	No

Table 1.2 (continued)

Study, country, reference	Portion size	Specific components measured	Method validated for coffee consumption
Kaiser Permanente Medical Care Program Study, USA (Efird et al., 2004)	No	No	No
Cancer Prevention Study II, USA (Hildebrand et al., 2013)	No	No	No
Lutheran Brotherhood Insurance Study, USA (Murray et al., 1981)	No	No	No
Glostrup Population Studies, Denmark (Sjøl et al., 1991)	No	No	No
ATBC study, Finland[b] (Lai et al., 2013)	Yes, using a colour picture booklet (four possible portion sizes)	No	Yes, correlation with diet records: 0.72–0.79
Hu et al. (2008), Bidel et al. (2013) Finland	No	No	Yes, Spearman correlation with food records: 0.89 in men, 0.85 in women
Norwegian National Health Screening Service for CVD, Norway (Veierød et al., 1997)	No	No	No
Norwegian Women and Cancer (NOWAC) study, Norway (Gavrilyuk et al., 2014)	No	No	Yes, Spearman correlation with 24 h recall: 0.82
Swedish Women's Lifestyle and Health cohort study, Sweden (Weiderpass et al., 2014)	Yes (small, medium, or large)	Daily caffeine intake	Yes, Spearman correlation with weighted record: 0.60
Swedish Mammography Cohort, Sweden (Friberg et al., 2009)	No	No	Yes, Spearman correlation with weighted record: 0.60
Västerbotten Intervention Project (VIP)[b], Sweden (Norberg et al., 2010)	No	No	Yes, correlation with 24 h recall: 0.72–0.84
Swedish Twin Registry Study, Sweden (Isaksson et al., 2002)	No	No	No
Discacciati et al. (2013), Sweden	No	No	Yes, Spearman correlation with 24 h recall: 0.71
Netherlands Cohort Study, Netherlands (Steevens et al., 2007)	No	No	Yes, validated against a 9-day diet record
Million Women Study, UK (Yang et al., 2015)	No	No	No
Supplementation en Vitamines et Mineraux Antioxydants Study (SUVIMAX), France (Mennen et al., 2007)	Yes	No	Yes
Fagherazzi et al. (2011), France	Yes	Daily caffeine intake	No

Table 1.2 (continued)

Study, country, reference	Portion size	Specific components measured	Method validated for coffee consumption
EPIC, 10 European countries (Bhoo-Pathy et al., 2015)	Yes, except for Denmark, Italy, Norway, and Umeå (Sweden)	No	No
Multiethnic Cohort Study of Diet and Cancer (MEC), Hawai (Kolonel et al., 2000)	No	Daily caffeine intake	Yes, Spearman correlation with 24 h recall: 0.72

All studies in the table used retrospective dietary assessment methods to assess coffee exposure
Temperature at which the coffee was consumed was not assessed in any of these studies
[a] In the Japan Public Health Center-based Prospective (JPHC) study, canned coffee was also assessed as specific coffee type
[b] In the ATBC study, Norwegian Women and Cancer (NOWAC) study and the Västerbotten Intervention Project (VIP), the preparation method was specified as filtered or boiled
h, hour(s); wk, week(s); yr, year(s)

assessed using an FFQ to intake assessed in the same individuals using a reference method that is deemed to be superior, but that may be prohibitive to use in large epidemiological studies due to participant burden or cost.

To illustrate, in the National Institutes of Health–American Association of Retired Persons (NIH-AARP) cohort study, the FFQ used was validated against two non-consecutive 24-hour dietary recalls (Thompson et al., 2008). In a validation set of participants, Spearman correlations between 24-hour dietary recalls and the food frequency questionnaire were 0.80 for coffee, 0.64 for caffeinated coffee, and 0.48 for decaffeinated coffee (Thompson et al., 2008; Sinha et al., 2012). Further, data obtained through a semi-quantitative FFQ in the Health Professionals Follow-Up Study (HPFS) and the FFQs used in the different waves of the Nurses' Health Study have been tested for reproducibility in a subgroup of participants who completed two FFQs 1 year apart and two 1-week diet records 6 months apart during the intervening year. Pearson correlations between the average coffee intake, assessed by two 1-week diet records completed 6 months apart, and the baseline FFQ was 0.93 in the HPFS and 0.78 in the Nurses' Health Study (Holick et al., 2010).

In the European Prospective Investigation into Cancer and Nutrition (EPIC), dietary intakes over the previous year were assessed at enrolment through validated study centre specific questionnaires which also enquired about coffee intake. This method was reported to yield very good reliability of coffee consumption compared with repeated 24-hour recalls ($r = 0.70$) (Aleksandrova et al., 2015).

Calibration studies are used to calibrate a FFQ to a reference method using a regression model (e.g. an interviewer-led diet history or multiple 24-hour recalls). For example, the EPIC study used a computerized 24-hour diet recall method to calibrate dietary measurements across countries and to correct for systematic over- or underestimation of dietary intakes (Slimani et al., 2002).

Each epidemiological study included in Section 2 of this monograph has been examined to determine whether the FFQ used to assess coffee exposure has been validated.

(c) Cohort studies

A major strength of cohort studies in nutritional epidemiology is the ability to demonstrate a temporal relationship between dietary exposure and cancer risk, as all dietary assessments are completed before diagnosis. This mitigates concerns related to recall bias and reverse causation. However, a limitation of many cohort studies is that exposures are often measured only once, usually during enrolment, whereas cancer cases develop over a long period of time. In the case of coffee consumption, however, there is a high correlation between successive measurements taken over time.

In the Nurses' Health Study (Willett et al., 1985; 1988), data were obtained at baseline in 1980 through a validated, self-administered, 61-item, semi-quantitative FFQ which was later expanded and applied every 4 years thereafter (Michels et al., 2005). Essentially the same validated, self-administered, semi-quantitative FFQ questionnaire with 131 items was used in the HPFS (Rimm et al., 1992). For each item, participants were asked to report their average use of each food and beverage over the preceding year. Consumption of caffeinated and decaffeinated coffee was measured in cups per day. Most analyses from the Nurses' Health Study and HPFS of coffee intake have used the cumulative average intake of coffee over time, incorporating information from the repeated questionnaires (Michels et al., 2005). [A strength of these studies was that the FFQs used were extensively validated and tested for reproducibility, demonstrating good validity for coffee intake estimations. A limitation was the lack of an assessment of preparation methods, which likely affects the concentration of different compounds in coffee.]

Sinha et al. (2012) used data from the NIH-AARP Diet and Health Study in which the National Cancer Institute's Diet History Questionnaire, a 124-item FFQ with information on the frequency of intake and portion sizes over the past year, was used. Coffee intake was assessed from 0 to 6 cups/day and participants were dichotomized according to whether they reported drinking caffeinated or decaffeinated coffee more than half the time. [A strength of this study was that the FFQs used were extensively validated against 24-hour dietary recalls, showing good validity of coffee estimates (Thompson et al., 2008). Limitations were the lack of an assessment of preparation methods, which likely affect the concentration of different compounds in coffee, and the fact that decaffeinated coffee drinkers were also defined on the basis of drinking either beverage more than half of the time, which could have led to misclassification.]

In the EPIC cohort study (Riboli et al., 2002; Aleksandrova et al., 2015), dietary intake over the 12 months before enrolment was measured by country-specific validated dietary questionnaires (88–266 food items, depending on the country), self-administered in most countries. A second dietary measurement was taken from an 8% random sample of the cohort (36 900 participants) using a computerized 24-hour diet recall method to calibrate dietary measurements across countries and to correct for systematic over- or underestimation of dietary intakes. [A major strength of this study was the large variability in dietary intake across populations and the use of a computerized 24-hour diet recall method to calibrate dietary measurements across countries. A limitation was the use of different dietary questionnaires in each participating country, requiring post-harmonization and calibration of the dietary data.]

In the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) study (Lai et al., 2014), researchers used a self-administered, modified dietary history method to capture usual dietary intake 12 months before recruitment. The dietary history method included 276 food items and a picture booklet of photographs illustrating different portion sizes (Pietinen et al., 1988). To assess coffee consumption, participants were also asked to indicate their typical cup size. [A strength of this study was that the assessment of coffee intake was shown to be valid after comparison with food records. Another important advantage of this study was that information on coffee preparation methods was collected, allowing exploration of whether the associations between coffee intake and disease risk differed by brewing method. A limitation was that no information was collected on whether intake of coffee was caffeinated or not, and coffee intake was only assessed a single time.]

In the Iowa Women's Health Study cohort, usual dietary intake during the previous year was assessed by a 127-item, validated, semi-quantitative, self-administered FFQ, virtually identical to that used in the 1984 survey of the Nurses' Health Study (Lueth et al., 2008). For decaffeinated coffee and regular coffee, the specified daily portion size was one cup (8 fluid ounces). The validity of the FFQ was evaluated by comparing nutrient values from the FFQ to those from the average of five 24-hour dietary recall surveys for 44 study participants. Reliability was assessed by repeating the FFQ after 3–6 months. [This study had several strengths, including the assessment of reliability and accuracy of the FFQ in the Iowa cohort and the possibility of allowing for multivariable adjustment due to the extensive FFQ. A limitation was the lack of an assessment of preparation methods, which likely affects the concentration of different compounds in coffee.]

In the Singapore Chinese Health Study, cohort members completed an in-person interview that included a validated 165-item FFQ that assessed coffee intake at nine predefined levels (Johnson et al., 2011). Decaffeinated coffee consumption was not assessed. [A strength of this study was that the FFQ was shown to be valid, while the fact that only a baseline assessment of self-reported coffee intake was available should be considered a limitation because of the potential for non-differential misclassification.]

In the Norwegian Women and Cancer (NOWAC) study the questions assessing coffee consumption varied according to the year of enrolment; women were asked about either their total coffee consumption or their consumption of filtered, boiled, and instant coffee (Gavrilyuk et al., 2014). The categories of coffee consumption in cups per day or week were also different in two versions of the questionnaire. Post-harmonization of the dietary data was therefore needed to create a common version of frequencies. Based on a 24-hour recall investigation in the NOWAC cohort, a standard cup size of 2.1 dL (7.1 oz) was assumed. [An advantage of this study was the broad range of exposures in the cohort and information on several coffee brewing methods. Limitations were the lack of information about decaffeinated coffee and preparation methods, which can also influence the level and properties of some coffee compounds.]

In the multiethnic, prospective, population-based Northern Manhattan Study (NOMAS), participants were administered a modified Block National Cancer Institute FFQ at baseline. Questions assessed the average consumption of decaffeinated and regular (caffeinated) coffee in units of medium cups according to nine different frequency categories (Gardener et al., 2013). [Despite the use of a validated and reliable Block FFQ, there were some limitations to the coffee exposure data. The analysis focuses on frequency of consumption and is not standardized for cup size. Although the FFQ was designed to measure average consumption over the previous year, dietary information was collected at one time (baseline) and information on duration of coffee consumption as well as changes during follow-up was lacking. Further, the questionnaire did not determine whether individuals were drinking boiled unfiltered or filtered coffee.]

In the Japan Collaborative Cohort Study (Yamada et al., 2014), information about coffee consumption and other lifestyle factors was obtained using a self-administered questionnaire. The question regarding coffee consumption was previously assessed by a validation study, which reported a strong agreement with 12-day weighted dietary records. [A limitation of this study was that only baseline data were collected; no details of coffee consumption, such as the use of caffeinated or decaffeinated coffee and the method of coffee preparation (e.g. filtered or boiled), were collected.]

(d) Case–control studies

A description of the case–control studies included in this report is provided in Section 2. Case–control studies investigating the association between coffee intake and cancer risk are limited as they assess dietary intake after cancer has been diagnosed, which can lead to recall bias if intakes of the distant or recent past are assessed. In addition, for some cancer types, notably cancers of the digestive tract, patients may change their dietary intake with the potential to bias assessment of the usual coffee intake in the past. As a result, investigators usually ask cases included in their studies to recall dietary intake in a period before the diagnosis of cancer in an attempt to capture usual diet before diagnosis.

For these reasons, the approach used to assess dietary intake in the distant past is often conceptualized differently from the typical FFQs used in cohort studies by including extra questions to help the respondent remember details of past consumption. For example, in the Yale Study of Skin Health in Young People, Ferrucci et al. (2014) participants were first asked whether they drunk at least one cup of caffeinated coffee per week for at least 6 months. Those who responded affirmatively were then asked the age at which they began drinking caffeinated coffee at this frequency, as well as whether they were currently drinking it at least weekly or, if not, the age at which they had stopped. Thereafter, participants reported the average number of cups of coffee they drank per day and the number of years of consumption. [Even though the possibility of recall bias was still a limitation in this case–control study, this cognitive approach is considered an important strength in avoiding such bias.]

In the Western Australian Bowel Health Study (WABOHS), data on coffee consumption 10 years previously were collected by self-administered questionnaire (Green et al., 2014). The questions were adapted from the Arizona Tea Questionnaire, which was shown to have high test–retest reliability and high relative validity relative to 4-day food records. Data were collected on the frequency of consumption of hot caffeinated coffee, hot decaffeinated coffee, and iced coffee. [A limitation of this study was that asking participants to recall their dietary intake 10 years before may have affected the quality of recall, leading to increased likelihood of exposure misclassification which could bias the risk estimates towards the null.]

(e) Covariates of coffee consumption

The estimation of cancer risk associated with coffee intake may be influenced by other dietary and/or lifestyle factors that are correlated with coffee consumption. However, few studies investigated associations between coffee consumption and other lifestyle factors, which can vary depending on the population under study.

Freedman et al. (2012) investigated associations of coffee consumption with other dietary and lifestyle factors in the NIH-AARP Diet and Health Study in the USA. Coffee drinkers were more likely than non-drinkers of coffee to smoke cigarettes and also consume more alcoholic drinks and more red meat; coffee drinkers also tended to have lower levels of education, vigorous physical activity, and intake of fruits and vegetables (Freedman et al., 2012).

In a Japanese study, Yamada et al. (2014) reported that subjects who consumed high quantities of coffee were also more likely to be smokers, alcohol drinkers, and to regularly eat beef or pork, but were younger and better educated.

In the Singapore Chinese Health Study, Ainslie-Waldman et al. (2014) investigated differences in lifestyle and sociodemographic factors by the amount of coffee consumption. Among both men and women, a higher level of coffee consumption was associated with a higher prevalence of current smoking and alcohol consumption, as well as lower proportions with a higher education or a history of diabetes. Those who drank more coffee also consumed more total energy but less fruit and vegetables. However, men who drank more than 4 cups of coffee per day had lower levels of BMI compared to those consuming < 1 cup per day.

The effect of coffee consumption on the risk of cancer may therefore be confounded by intake of other foods and lifestyle factors, in particular smoking status, but also drinking, BMI, meat consumption, and age. Adequate adjustment for these potential confounders is therefore essential, but only possible if researchers have included robust measures of exposure to these potential confounders and have used analytical methods that adequately adjust for these variables. Each study reviewed in this monograph, considered by cancer site in Section 2, has been examined in terms of ability to adequately adjust for potential confounders.

(f) Limitations

There was substantial heterogeneity across the studies reviewed by the Working Group due to a variety of factors, such as methods of dietary assessment and/or measurement, variable definitions (e.g. food groups, serving sizes), levels of detail (e.g. caffeinated versus decaffeinated), analytical categorizations (e.g. servings per week, grams per day), exposure contrasts (analytical cut-points and comparisons of intake levels), and degree of adjustment for potential confounding factors.

An important limitation in almost all epidemiological studies investigating the relationship between coffee consumption and cancer risk is the lack of details in the description of the coffee consumed. Descriptors such as the preparation method (e.g. filtered or not), the coffee concentration, and drinking temperature (see the monograph on Drinking Mate and Very Hot Beverages in the present volume) are almost always missing, although some of these factors could be important to consider in the relationship between coffee consumption and cancer risk. Another limitation is the reporting of the exposure assessment, which is sometimes insufficiently detailed to allow a critical and correct evaluation of the results reported (Lachat et al., 2016). These limitations in exposure assessment should be considered when interpreting the results reported in epidemiological studies.

(g) Biological markers

To date, very few studies have used biomarkers to estimate coffee intake in cancer epidemiological studies. However, the use of mass spectrometry techniques and metabolomic approaches has recently allowed the identification of several promising coffee biomarkers. A metabolomic analysis of baseline serum samples from participants in the Prostate, Lung, Colorectal, and Ovarian (PLCO) trial in the USA identified trigonelline, quinate, 1-methylxanthine and paraxanthine, along with *N*-2-furoylglycine and catechol sulfate, as potential biomarkers of coffee intake (Guertin et al., 2014). In a nested case–control study of colorectal cancer risk in the same cohort, plasma trigonelline and quinate concentrations were best correlated with coffee intake as assessed by FFQ (Guertin et al., 2015). Negative associations of these metabolites and several others with diagnosis of cancer of the colorectum were observed.

Biomarkers of coffee consumption have also been investigated through comparisons of coffee consumers and non-consumers in studies of free-living subjects. Dihydrocaffeic acid and its 3-glucuronide measured in 24-hour pooled urine were found to discriminate between high and low levels of coffee consumption with high sensitivity and specificity in a dietary intervention study in the UK, suggesting potential as markers of habitual coffee consumption (Lloyd et al., 2013). In the EPIC cohort, concentrations of 16 conjugated metabolites of phenolic acids, mostly glucuronide or sulfate esters, were measured in 24-hour urine samples, and their levels were found to be correlated with both acute and regular coffee intake (Edmands et al., 2015). Dihydroferulic acid sulfate, feruloylquinic acid glucuronide, ferulic acid sulfate, and guaiacol glucuronide were the metabolites whose measured intensities best predicted the highest or lowest quintile of coffee intake. Coffee intake markers including non-phenolic metabolites were searched for in morning spot urine of 39 French coffee consumers from the Supplémentation en Vitamines et Minéraux Anti-oxydants (SUVIMAX) cohort (Rothwell et al., 2014). The intensities of several coffee-derived metabolites accurately classified consumers into high- and low-intake groups. The most effective of these were the diterpene atractyligenin glucuronide, the cyclic amino acid cyclo(isoleucyl-prolyl), and trignolline.

Several small, short-term intervention studies provided detailed information of coffee compounds found in blood or urine after coffee consumption. For example, urinary concentrations of trigonelline and the product of the coffee roasting process *N*-methylpyridinium best distinguished subjects given coffee from controls (Lang et al., 2011). Both compounds remained elevated in the urine of coffee consumers for at least two days after coffee consumption. Another coffee roasting product, *N*-2-furoylglycine, was identified as a promising biomarker of coffee intake in a metabolomic study based on spot urine profiles of five volunteers administered one cup of espresso coffee (Heinzmann et al., 2015). Trigonelline, caffeine, dimethylxanthine, methylxanthine, and ferulic acid in urine were also found to discriminate subjects administered a standardized dose of coffee from controls (Lang et al., 2013). [Dimethylxanthine and methylxanthine are metabolites of caffeine, so intake of other beverages containing caffeine (e.g. soft drinks, energy drinks, or tea) limit the specificity of caffeine and its metabolites as biomarkers of coffee intake.] Several other metabolites of chlorogenic acids were found to discriminate coffee consumers from controls. Dihydroferulic acid 4-*O*-sulfate and dihydrocaffeic acid 3-*O*-sulfate attained the highest plasma concentrations after coffee intake, while the latter compound and feruloylglycine were reported as the most effective urinary biomarkers of intake (Stalmach et al., 2009). Most of these coffee metabolites are eliminated within one day (Stalmach et al., 2009; Lang et al., 2013). [The rapid elimination of these metabolites should not be a limitation to using them as coffee biomarkers, due to the regular intake of coffee by most coffee consumers.]

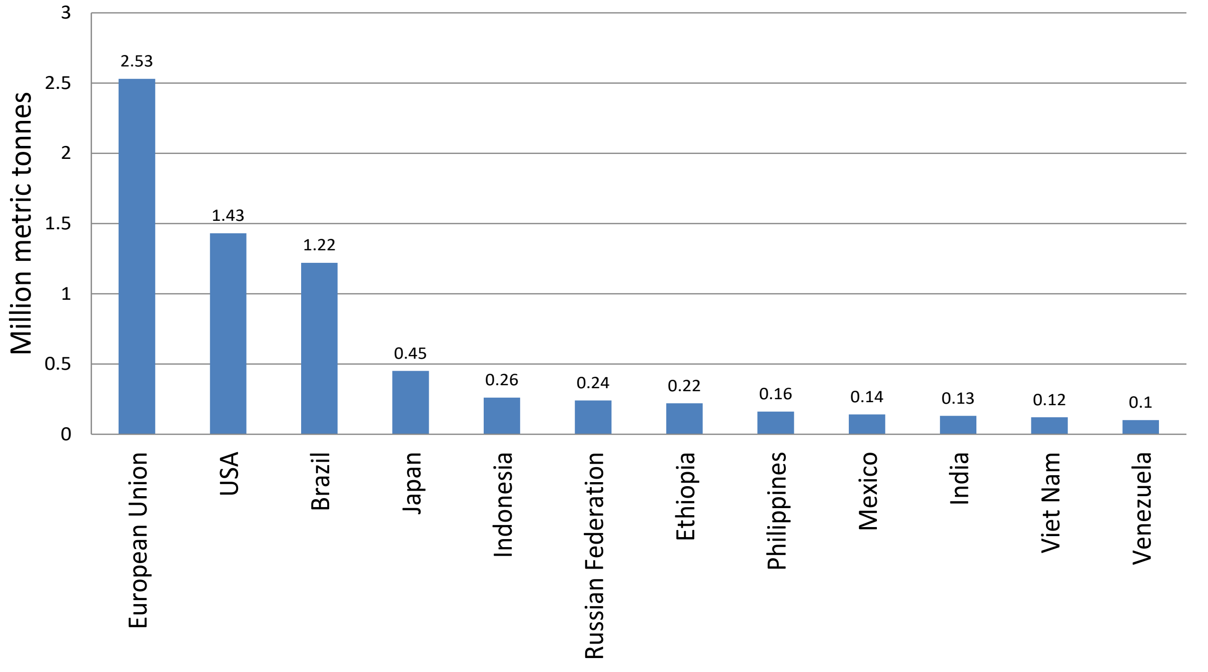
[The Working Group noted that the specificity of biomarkers for coffee drinking has not always been assessed as it relies on the known presence or absence of such compounds in other foods or beverages, and this information is not always available. In addition, some biomarkers might be specific to particular coffee brews, roasts, or varieties. The combinations of several biomarkers may provide clues regarding the type of coffee consumed (e.g. caffeinated vs decaffeinated coffee, varying degrees of roasting). The validity of biomarkers identified in clinical trials should be treated with caution and cannot necessarily be generalized to diverse free-living populations.]

1.3.2 Production and consumption volumes

Coffee production in 2015 was estimated to be about 9 million tonnes (ICO, 2016). In recent years, about two thirds of the world production has typically been Arabica coffee and one third Robusta. Brazilian production (mainly Arabica) accounted for 30%, followed by Viet Nam (19%, mainly Robusta), Colombia (9%, mainly Arabica), Indonesia (8%), and Ethiopia (4%), among others (ICO, 2016; USDA, 2016).

World coffee consumption in 2014 and 2015 was estimated to be about 9 million tonnes (ICO, 2016; USDA, 2016). Together, the European

Fig. 1.4 Total annual coffee consumption in 2014, in selected countries or regions with high consumption



From International Coffee Organization (ICO, 2016)

Union countries are responsible for 28% of the world coffee consumption. Because of their large territorial extension and populations associated with high consumptions, the USA and Brazil are the individual countries with the highest consumption, accounting for about 16% and 13% of total world consumption, respectively. Japan (5.6%) and the Russian Federation (2.2%) follow (ICO, 2016; Fig. 1.4).

The consumption of decaffeinated coffee as a percentage of total consumption in 2009 was estimated as being highest in Spain (17%), USA (16%), UK (13%), Netherlands (12%), and Belgium/Luxembourg (10%). In all other countries the percentage was below 10% (ITC, 2012).

Coffee consumption at the population level can be measured in several ways. Data on the amounts of coffee in international trade are typically expressed in terms of disappearance, defined as net imports into a country, estimated by the difference between gross imports and re-exports (ICO, 2016). An estimate of per capita coffee consumption can be obtained by dividing disappearance (typically reported in kilograms per year) by population. This indicator is primarily useful for ranking countries with respect to relative levels of consumption. Disappearance data for trade in green coffee beans indicate that the Nordic countries Finland, Norway, Denmark, and Iceland and Austria are leading consumers of coffee by this measure (Table 1.3). Other important consumers are Switzerland, Montenegro, Sweden, Lebanon and Germany (ICO, 2016). Historical consumption data from 2011 to 2014 (ICO, 2016) show a modest increase in worldwide consumption, with stagnation in countries with a high per capita consumption, mainly in Europe. A few countries in Central America, Mexico, and South America also showed this trend. Increasing consumption is observed in countries that are

Table 1.3 Annual coffee consumption per person from disappearance data for green coffee beans (10 highest consuming countries, 2013)

Country	Arithmetic mean consumption (kg/person per year)
Finland	12.07
Norway	9.01
Denmark	8.75
Austria	8.74
Iceland	8.43
Switzerland	8.29
Montenegro	7.61
Sweden	7.33
Lebanon	6.97
Germany	6.92

With permission from the International Coffee Organization (unpublished work)

currently lower per capita consumers, situated mainly in Asia, Oceania and Africa. Examples are Egypt, India, Indonesia, Philippines, Saudi Arabia, Thailand, Turkey, and Viet Nam.

The preceding estimates of per capita consumption of traded coffee beans may not reflect the amounts of coffee beverage consumed by individuals, however. Individual-level consumption of coffee beverages is assessed by dietary surveys (see Section 1.3.1) or specialized surveys of coffee drinking. An important consideration in survey data is that the proportion of coffee drinkers in a given population is less than 100%, with that proportion varying between and within countries. Consequently, average consumption among all respondents tends to be less than the average among coffee drinkers only. The latter quantity corresponds most closely to dose and is comparable to the exposure indicators typically used in epidemiological studies. Table 1.4 presents survey data on the average coffee consumption of adult coffee drinkers in countries with available data. A limitation of such survey data is that they are not available for all countries and the details available within countries may not be comparable. Data in Table 1.4 were obtained from a FFQ for the USA (NCA, 2016), 24-hour recall for Europe (EFSA, 2011), and purchasing data for Brazil (ABIC, 2016). Consumption is organized by range of consumption and average amount consumed daily. Based on these assessments, the highest individual coffee consumption is in Denmark followed by the USA, Netherlands, and Germany. There is also a very large individual variation (23–1914 g/day). [The Working Group noted that the data from the different countries, including within Europe, were collected from different sources with differences in years and types of questionnaires, among others.]

1.4 Chemical constituents

1.4.1 Major constituents

An overview of compounds present in green, roasted, brewed, instant, and decaffeinated coffees was provided in the previous *IARC Monograph* on coffee (IARC, 1991). More recent updates have been published (Farah, 2012; Oestreich-Janzen, 2013).

The compounds in coffee are typically classified into non-volatile and volatile fractions. The non-volatile compounds include water, carbohydrates and fibre, proteins and free amino acids, lipids, minerals (40% potassium), organic acids,

Table 1.4 Mean daily coffee beverage consumption among coffee drinkers in selected countries

Country, year	Arithmetic mean[d] (mL/day)	Range[d] (mL/day)	Proportion of consumers within population (%)
Denmark, NR[a]	846	86–1914	83
USA, 2016[b]	740[e]	NR	57 consuming on previous day, 76 in previous year
Netherlands, 2007–2010[a]	573	100–1253	75
Germany, NR[a]	539	100–1199	82
Sweden, 2010–2011[a]	431	75–875	78
Latvia, 2004[a]	309	90–650	83
Ireland, NR[a]	259	23–783	54
Brazil, 2016[c]	222	NR	54
Italy, 2005–2006[a]	108	20–240	89
Romania, 2005–2006[a]	93	11–253	68
UK, NR[a]	147	9–552	34

[a] European Food Safety Association (EFSA, 2011)
[b] National Coffee Association (NCA, 2016)
[c] Brazilian Coffee Industry Association (ABIC, 2016)
[d] Converted to L/day with a density of 1.0
[e] Reported mean of 2.96 cups/day converted to g/day assuming 250 g/cup
NR, not reported

chlorogenic acids, trigonelline, and caffeine. The volatile fraction may contain more than 950 different compounds from chemical classes such as furans and pyrans, pyrazines, pyrroles, ketones, phenols, hydrocarbons, alcohols, aldehydes, pyridines, and other compounds (IARC, 1991; Farah, 2012). An overview of the composition of roasted coffee seeds is provided in Table 1.5. Minor compounds such as 16-*O*-methylcafestol and kahweol (Monakhova et al., 2015) or minor chlorogenic acid compounds (Farah & Donangelo, 2006) vary between Arabica and Robusta species.

As a natural product, the chemical composition of coffee may vary to a wide degree depending on the species and degree of maturation, as well as soil composition, climate, agricultural practices, and storage conditions (Farah, 2012). For example, the caffeine content in coffee beverages (including decaffeinated beverages) may range over 0.3–380 mg/100 mL (Farah, 2012; Lachenmeier et al., 2013); the niacin content may range over about 10–40 mg/100 mL (Adrian & Frangne, 1991); and cafestol may be present in quantities of 2–5 mg/100 mL (Zhang et al., 2012). Table 1.6 presents the typical composition of coffee brew from medium-roasted coffee beans.

Caffeine is thought to be one of the principal components with pharmacological effects in coffee, and its mild stimulating effect may be the reason for the popularity of this beverage (Lachenmeier et al., 2012). According to a review by the European Food Safety Authority (EFSA), a standard cup of coffee in Europe has a caffeine concentration of about 38–69 mg/100 mL; an average of 45 mg/100 mL was used for intake assessment (EFSA, 2015).

For further details on caffeine, see IARC (1991).

1.4.2 Other constituents and contaminants

Some compounds found in coffee have known toxic properties and, in some cases, carcinogenic effects. Coffee constituents and contaminants that have been evaluated by IARC and classified as *possibly carcinogenic to humans* (Group 2B) or higher are shown in Table 1.7. These include heating-induced compounds benzo[*a*]pyrene

Table 1.5 Chemical composition of roasted *Coffea arabica* and *Coffea canephora* seeds

Compounds	Concentration[a] (g/100 g)	
	Coffea arabica	*Coffea canephora*
Carbohydrates/fibre		
Sucrose	4.2–tr	1.6–tr
Reducing sugars	0.3	0.3
Polysaccharides (arabinogalactan, mannan, and glucan)	31–33	37
Lignin	3.0	3.0
Pectins	2.0	2.0
Nitrogenous compounds		
Protein	7.5–10	7.5–10
Free amino acids	ND	ND
Caffeine	1.1–1.3	2.4–2.5
Trigonelline	1.2–0.2	0.7–0.3
Nicotinic acid	0.016–0.026	0.014–0.025
Lipids		
Coffee oil (triglycerides with unsaponifiables)	17.0	11.0
Diterpene esters	0.9	0.2
Minerals	4.5	4.7
Acids and esters		
Chlorogenic acids	1.9–2.5	3.3–3.8
Aliphatic acids	1.6	1.6
Quinic acid	0.8	1.0
Melanoidins	25	25

[a] Content varies according to cultivar, agricultural practices, climate, soil composition, methods of analysis, and roasting degree
ND, not detected; tr, trace
Reproduced from Farah (2012). Coffee Constituents. Coffee: Wiley-Blackwell; 2012. p. 21–58

(Group 1), acrylamide (Group 2A), acetaldehyde and furan (both Group 2B), the mycotoxins aflatoxin (Group 1) and ochratoxin A (Group 2B), and pesticides DDT, captafol (both Group 2A), and dichlorvos (Group 2B).

The prevalence of mycotoxins, notably aflatoxins and ochratoxin A, in green coffee beans is high (Soliman, 2002; Paterson et al., 2014). In tropical and subtropical regions where coffee is grown, ochratoxin A and aflatoxin B_1 are produced by *Aspergillus* species. Contamination will vary not only with country but with individual farms, depending on manufacturing practices. It has been speculated that with climate change aflatoxin may gain importance as a hazard to coffee production (Paterson et al., 2014).

The high temperatures of coffee roasting significantly decrease aflatoxin and ochratoxin A levels in coffee; reductions of the concentration of ochratoxin A by more than 90% have been observed, depending on the degree of roasting (Soliman, 2002; Romani et al., 2003; Ferraz et al., 2010).

Few studies have assessed the levels of ochratoxin A in coffee beverages. Only trace levels of ochratoxin A (< 1 µg/L) were detected in ready-to-drink coffee (Noba et al., 2009), and ochratoxin A has been detected in instant coffee (IARC, 1991; Vecchio et al., 2012). Although aflatoxin has been detected in green and roasted coffee beans (Soliman, 2002), data on aflatoxin occurrence in brewed coffee are unavailable (Vieira et al., 2015).

Another group of coffee contaminants are biogenic amines, which may be produced by microorganisms in defective beans or during storage. Putrescine, spermidine, and spermine

Table 1.6 Typical chemical composition per 100 mL of coffee brew from medium roasted coffee

Constituent[a]	Concentration (mg/100 mL)
Caffeine	50–380
Chlorogenic acids	35–500
Trigonelline	40–50
Soluble fibre	200–800
Protein	100
Lipids	0.8
Minerals	250–700
Niacin	10
Melanoidins	500–1500

[a] Brew composition varies according to blend, roasting degree, grind, and method of preparation
From Farah (2012)

Table 1.7 Summary of IARC-evaluated compounds that may be present in coffee

Agent	*IARC Monographs* evaluation of carcinogenicity			*IARC Monographs* Volume (year of publication in print)
	In animals	In humans	IARC Group	
Acetaldehyde	Sufficient	Inadequate	2B	71 (1999)
Acrylamide	Sufficient	Inadequate	2A	60 (1994)
Aflatoxins	Sufficient	Sufficient	1	100F (2012)
Benzo[*a*]pyrene	Sufficient	No data	1	100F (2012)
Caffeic acid	Sufficient	No data	2B	56 (1993)
Captafol	Sufficient	No data	2A	53 (1991)
DDT and associated compounds	Sufficient	Limited	2A	113 (2018)
Dichlorvos	Sufficient	Inadequate	2B	53 (1991)
Dichloromethane	Sufficient	Limited	2A	110 (2017)
Furan	Sufficient	Inadequate	2B	63 (1995)
Methyl isobutyl ketone	Sufficient	No data	2B	101 (2013)
Ochratoxin A	Sufficient	Inadequate	2B	56 (1993)

are considered to be major amines in coffee. Tyramine (one of the most toxic amines), cadaverine, and others are considered to be minor amines in coffee (Farah, 2012).

While roasting largely destroys contaminants such as mycotoxins and thermolabile pesticide residues that may exist in the green coffee, several heat-induced contaminants may be formed during roasting. These include acetaldehyde (Uebelacker & Lachenmeier, 2011), furan (Wenzl et al., 2007; Petisca et al., 2013; Lachenmeier, 2015), acrylamide (Lantz et al., 2006; Guenther et al., 2007), and polycyclic aromatic hydrocarbons (PAHs) including benzo[*a*]pyrene (Houessou et al., 2007). It has been reported that lower roasting temperatures and shorter roasting times tend to reduce the formation of PAHs and acrylamide (Guenther et al., 2007; Houessou et al., 2007; Soares et al., 2009).

Among the heat-induced contaminants in coffee, only furan has been systematically studied; it occurs in every coffee brew at about 40–100 µg/L depending on the preparation method (Waizenegger et al., 2012). The average furan intake per cup of coffee was estimated as 0.12 µg/kg body weight (Lachenmeier, 2015). In an experimental study, Houessou et al. (2007) reported total PAH concentrations of < 1 µg/L in brewed coffee. [The Working Group noted the absence of systematic survey data on PAHs in coffee beans or coffee brews.]

Some cohort studies have reported coffee as one of the largest contributor to acrylamide intake (e.g. Larsson et al., 2009; Wilson et al., 2012). [Other data indicated that fried potatoes and bread products are the major contributors to the dietary exposures of acrylamide for most countries (JECFA, 2011). The Working Group noted that the populations in some cohort studies may therefore have been biased towards groups with a high consumption of coffee relative to fried foods.]

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