Supplemental Table S1. Information on study methodologies for styrene cohort and nested case–control studies

Reference	Location	Follow-up/enrolment period	Study design	Population size	Description	Exposure assessment method
Bertke et al. (2018)	Washington State, USA	Enrolment from 1959 to 1978 Follow-up from 1960 to 2016	Cohort (SMR and internal analysis)	5201 workers (4522 men, 679 women) 203 404 person-years of follow-up (mean follow-up = 39 years) Loss to follow-up: not reported	Two reinforced plastics (boat-building) plants Exposed for at least 1 day Alive and living in Washington State in 1991 Probable high exposure: • 43 ppm (Plant A – fibrous glass department) • 72 ppm (Plant B – lamination department Probable low exposure – all other departments) Exposure measures: • ever/never worked in highly exposed job (40% of cohort) • employment duration in highly exposed job (median = 0.3 years)	Work history information was used to construct an exposure index based on exposure duration and exposure potential (from industrial hygiene surveys conducted at each plant)
Christensen et al. (2017)	Denmark	Enrolment from 1964 to 2007 Follow-up from 1968 to 2012	Cohort (SIR analysis)	72 292 workers (60 478 men, 11 774 women) 1 686 342 person-years of follow-up (mean follow-up = 23 years) Loss to follow-up: minimal	443 small and medium-sized companies producing reinforced plastics	Exposure estimates based on survey of workers producing an estimate of the probability of exposure
Christensen et al. (2018)	Denmark	Enrolment from 1964 to 2007 Follow-up from 1968 to 2011	Cohort (internal analysis)	73 306 workers (men and women, but gender mix not stated) 1 581 976 person-years of follow-up (mean follow-up = 22 years) Loss to follow-up: minimal	456 small and medium-sized companies producing reinforced plastic Exposure measures of cumulative exposure, mean exposure, mean exposure probability, duration of employment	Exposure estimates based on employment history, survey data and historical styrene exposure measurements Semiquantitative exposure scores modelled using job title, exposure probability, exposure measurements from 1970s onwards and duration of employment

Supplemental Table S1. Information on study methodologies for styrene cohort and nested case–control studies

Reference	Location	Follow-up/enrolment period	Study design	Population size	Description	Exposure assessment method
Coggon et al. (2015)	England	Enrolment from 1947 to 1984 (depending on company) Follow-up from 1947 to 2012 Cases diagnosed between 1970 and 1991, identified using underlying and contributing causes of death and cancer registrations Controls randomly selected (up to 10 controls per case) from non-cases at the date of diagnosis of the case, matched to each case using sex, factory of work, and age within 2 years	Cohort (SMR analysis) plus nested case–control study of lymphopoietic cancer	7970 workers (6650 men, 1320 women) Loss to follow-up: 11% Case–control study had 122 cases of lymphopoietic cancer and 1138 controls	Eight companies that used styrene in the manufacture of glass-reinforced plastics 44% of workers had worked in high exposure jobs at some time (18% for 1 year or longer) High exposure estimated to correspond to 8-hour time-weighted average exposure of 40–100 ppm	Exposure estimates based on job categories; no hygiene data were available for the early years of styrene use – these were estimated based on measurements at five of the factories after 1975
Collins et al. (2013)	USA	Enrolment from 1948 to 1977 Follow-up from 1948 to 2008 (average follow-up: 35 years)	Cohort (SMR analysis)	15 826 workers (11 958 men, 3868 women) 561 530 person-years of follow-up (mean follow-up = 35 years) Loss to follow-up: < 1%	Workers from 30 US reinforced plastic facilities; exposed for at least 6 months Four measures of dose: • cumulative exposure (mean time-weighted average = 28 ppm) • peak exposure (mean days above 100 ppm = 113) • duration of exposure (mean = 4.3 years) • average exposure (mean = 27 ppm)	Exposure estimates based on hygiene monitoring results and expert judgement after inspection of plants and consideration of historical information on plant functions and changes

Supplemental Table S1. Information on study methodologies for styrene cohort and nested case–control studies

Reference	Location	Follow-up/enrolment period	Study design	Population size	Description	Exposure assessment method
Kogevinas et al. (1994)	Denmark Finland, Italy, Norway, Sweden, United Kingdom	Follow-up: earliest start was 1945 and latest finish was 1991 (average follow-up: 13 years). Denmark (1970–1990), Finland (1958–1989) Italy (Liguria: 1969–1991) Italy (Emilia-Romagna: 1956–1989) Norway (1956–1991), Sweden (1955–1987) United Kingdom (1: 1945–1990) United Kingdom (2: 1961–1988)	Cohort (SMR and internal analysis)	40 688 workers (34 560 men, 6128 women) 539 479 person-years of follow-up (214 965 person-years > = 10 years since first exposure; mean follow-up = 13 years) Loss to follow-up and emigration: 3%	Workers from 660 reinforced plastics facilities About 60% employed in the industry for < 2 years Proportion of short-term workers varied from 9% (Finland) to 81% (Denmark); about 50% employed before 1975	Exposure estimates based on employment history, personal environmental measurements conducted during the period 1955–1990 and measurements of styrene metabolites in urine, conducted in the late 1980s; earlier exposures were based on measurements for Denmark and modelling for other countries (two models – linear extrapolation; assumption that earliest measures reflected levels before that)
Kolstad et al. (1994)	Denmark	Enrolment from 1964 to 1988 Follow-up from 1970 (or 1 January of the year of first employment if later) to 1989	Cohort (SIR and internal analysis)	53 720 male workers: • 36 525 exposed • 14 254 unexposed • 2941 unknown exposure 584 556 person-years of follow-up (mean follow-up = 11 years) Loss to follow-up: < 2%	552 companies (386 made reinforced plastics; 84 did not; for 82 there was no information) Mean levels for the subset of 128 companies with exposure estimates: • 1964–1970 = 180 ppm • 1971–1975 = 88 ppm • 1976–1988 = 43 ppm	Exposure probability based on employers reports of the proportion of work hours involved in reinforced plastics production. Information from measurements taken by Government inspection service used for subanalysis of workers from 128 companies with such measurements

Supplemental Table S1. Information on study methodologies for styrene cohort and nested case–control studies

Reference	Location	Follow-up/enrolment period	Study design	Population size	Description	Exposure assessment method
Kolstad et al. (1996)	Denmark	Cases diagnosed between 1970 and 1991 identified from national cancer registry Controls (3 per case) randomly selected from non-cases at the time each case was diagnosed, matched for age	Nested case–control study of myeloid leukaemia	50 779 male workers: • 36 525 exposed • 14 254 unexposed 25 AML cases – chromosome data available for 12 9 CML cases – chromosome data available for 7 12 cases had chromosomal aberrations Loss to follow-up: chromosomal data not available for 44%	470 companies (386 made reinforced plastics; 84 did not) Study was primarily of styrene exposure and the risk of myeloid leukaemia with clonal chromosomal aberrations	Exposure probability based on employers reports of the proportion of work hours involved in reinforced plastics production
Loomis et al. (2019)	Denmark Finland, Italy, Sweden, United Kingdom	Follow-up: earliest start was 1945 and latest finish was 1991 (average follow-up: 13 years) Denmark (1970–1990), Finland (1958–1989) Italy (Liguria: 1969–1991) Italy (Emilia-Romagna: 1956–1989) Sweden (1955–1987) United Kingdom (1: 1945–1990) United Kingdom (2: 1961–1988)	Cohort (internal analysis)	37 021 workers (31 692 men, 5692 women) 506 459 person-years of follow-up (mean follow-up = 14 years) Loss to follow-up and emigration: ~3%	Workers from 634 reinforced plastics facilities Mean duration of employment: 3.1 years Exposure measures: • employment in exposed jobs • employment as a laminator • duration in exposed jobs: mean = 2.2 years • cumulative styrene exposure (ppm-years): mean = 158 ppm-years • mean styrene concentration (ppm) in exposed jobs: mean = 63 ppm	Exposure estimates based on employment history, personal environmental measurements conducted during the period 1955–1990 and measurements of styrene metabolites in urine, conducted in the late 1980s; earlier exposures were based on measurements for Denmark and modelling for other countries (two models – linear extrapolation; assumption that earliest measures reflected levels before that)

Supplemental Table S1. Information on study methodologies for styrene cohort and nested case–control studies

Reference	Location	Follow-up/enrolment period	Study design	Population size	Description	Exposure assessment method
Nissen et al. (2018)	Denmark	Cases diagnosed between 1968 and 2011 identified from national cancer registry. Controls (10 per case) randomly selected from non-cases in cohort at the time each case was diagnosed, matched on age (within 2 years), sex, and employment in a reinforced plastics company producing boats or employment in wood industry since 1964	Nested case–control study of sinonasal cancer, focusing on adenocarcinoma	73 092 workers (men and women, but gender mix not stated) 1 585 772 person-years of follow-up (mean follow-up = 22 years) 37 cases of sinonasal cancer • 9 adenocarcinomas • 15 squamous cell carcinomas • 13 other histological subtypes 370 controls Loss to follow-up: minimal	456 small and medium-sized companies producing reinforced plastic Measures of cumulative exposure, mean exposure, mean exposure probability, duration of employment	Exposure estimates based on employment history, survey data and historical styrene exposure measurements. Semiquantitative exposure scores modelled using job title, exposure probability, exposure measurements from 1970s onwards and duration of employment
Ruder & Bertke (2017)	Washington State, USA	Enrolment from 1959 to 1978 Follow-up from 1991 to 2007	Cohort (SIR and SRR analysis)	3704 workers (3165 men, 539 women) 63 117 person-years of risk (mean follow-up = 17 years) Mean years of employment: 1.7 years Loss to follow-up: not reported	Two reinforced plastics (boat-building) plants Exposed for at least 1 day Alive and living in Washington State in 1991 Probable high exposure: • 43 ppm (Plant A – fibrous glass department) • 72 ppm (Plant B – lamination department Probable low exposure – all other departments) Exposure measures: • ever/never worked in highly exposed job (40% of cohort) • employment duration in highly exposed job (median = 0.3 years)	Work history information was used to construct an exposure index based on exposure duration and exposure potential (from industrial hygiene surveys conducted at each plant)

Supplemental Table S1. Information on study methodologies for styrene cohort and nested case–control studies

Reference	Location	Follow-up/enrolment period	Study design	Population size	Description	Exposure assessment method
Wong (1990)	USA	Cases deceased between 1948 and 1977, identified using company records, social security administration records and supplemented by local follow-up Controls selected (up to 3 controls per case) from deceased non-cases in the cohort, matched to each case using sex, age at death (within 5 years), year of death (within 5 years), race, and plant	Nested case–control study of lung cancer	15 908 workers (12 028 men, 3880 women) Loss to follow-up: 16% Case–control study had 44 cases (40 used in analysis) of lung cancer and 102 matched controls	30 manufacturing plants in the reinforced plastics and composites industry Exposed for at least 6 months About 46% employed at the plants for < 2 years 6545 workers: > 12 ppm 8694 workers: < 12 ppm 669 workers: ill-defined exposure levels	Exposure estimates based on job title and area measurements, with supplementation from additional sources
Graff et al. (2005)	USA (Texas, Louisiana and Kentucky) and Canada	Enrolment from 1943 to 1990 Follow-up from 1944 to 1998 (start date of follow-up depended on plant)	Cohort (internal analysis)	16 579 male workers 500 174 person-years of follow-up (mean follow-up = 30 years) Loss to follow-up: probably < 3%	Six synthetic rubber industry plants Worked for at least 1 year Actively working during a particular calendar year (that varied by plant) between 1943 and 1950 Exposure measure was styrene total ppm-years	Exposure estimates based on work histories, linked to a JEM. Expert judgement was used to estimate relevant exposure levels (ppm) to styrene, butadiene and dimethyldithiocarbamate. Mathematical models were used to estimate job and time period-specific exposure estimates to use in the JEM
Sathiakumar & Delzell (2009)	USA (Texas, Louisiana and Kentucky) and Canada	Enrolment from 1943 to 1991 Follow-up from 1943 to 2002 (start date of follow-up depended on plant)	Cohort (SMR and internal analysis)	4863 female workers 181 831 person-years of follow-up (mean follow-up = 37 years) Loss to follow-up: probably < 3%	Six synthetic rubber industry plants Worked for at least 1 day (median years worked = 1.6) Actively working during a particular calendar year (that varied by plant) between 1943 and 1950 Exposure measure was styrene total ppm-years	Exposure estimates based on work histories, linked to a JEM. Expert judgement was used to estimate relevant exposure levels (ppm) to styrene, butadiene and dimethyldithiocarbamate. Mathematical models were used to estimate job and time period-specific exposure estimates to use in the JEM
Sathiakumar et al. (2005)	USA (Texas, Louisiana and Kentucky) and Canada	Enrolment from 1943 to 1990 Follow-up from 1944 to 1998 (start date of follow-up depended on plant)	Cohort (SMR analysis)	17 924 male workers 540 568 person-years of follow-up (mean follow-up = 30 years) Loss to follow-up: < 3%	Eight synthetic rubber industry plants Worked for at least 1 year (median years worked = 11)	Exposure estimates based on work histories, allowing subjects to be allocated to different work areas

Supplemental Table S1. Information on study methodologies for styrene cohort and nested case–control studies

Reference	Location	Follow-up/enrolment period	Study design	Population size	Description	Exposure assessment method
Sathiakumar et al. (2009)	USA (Texas, Louisiana and Kentucky) and Canada	Enrolment from 1943 to 1990 (1991 for women) Follow-up from 1944 to 1998 (2002 for women) (start date of follow-up depended on plant)	Cohort (internal analysis)	19 999 workers (15 598 men, 4101 women) • exclusions from previous cohorts due to working at the two plants excluded because of inadequate exposure records, and dropping out at an age less than the youngest identified lung cancer decedent Loss to follow-up: 3%	Six synthetic rubber industry plants Worked for at least 1 year (men) or at least 1 day (women) Actively working during a particular calendar year (that varied by plant) between 1943 and 1950 Exposure measure was styrene total ppm-years	Exposure estimates based on work histories, linked to a JEM. Expert judgement was used to estimate relevant exposure levels (ppm) to styrene, butadiene and dimethyldithiocarbamate. Mathematical models were used to estimate job and time period-specific exposure estimates to use in the JEM
Sathiakumar et al. (2015)	USA (Texas, Louisiana and Kentucky) and Canada	Enrolment from 1943 to 1990 Follow-up from 1944 to 2009 (start date of follow-up depended on plant)	Cohort (internal analysis)	16 579 male workers (slightly less for specific analyses) 595 013 to 611 880 person-years of follow-up, depending on the specific analysis Loss to follow-up: < 1%	Six synthetic rubber industry plants Worked for at least 1 year Actively working during a particular calendar year (that varied by plant) between 1943 and 1950 Exposure measure was styrene total ppm-years	Exposure estimates based on work histories, linked to a JEM. Expert judgement was used to estimate relevant exposure levels (ppm) to styrene, butadiene and dimethyldithiocarbamate. Mathematical models were used to estimate job and time period-specific exposure estimates to use in the JEM
Bond et al. (1992)	USA (Michigan, Texas, Connecticut, California)	Enrolment from 1937 to 1970 Follow-up from 1940 to 1986	Cohort (SMR and internal analysis)	2904 male workers Nearly 90 000 person-years of follow-up (mean follow-up = approximately 31 years) Loss to follow-up: 0.4%	Chemical plant (development or production of styrene-based products) Worked for at least 1 year	Exposure estimates based on employment history and expert assessment of exposure intensity
Frentzel-Beyme et al. (1978)	Germany	Enrolment from 1931 to 1976 Follow-up from 1956 to 1976	Cohort (SMR analysis)	1960 workers (gender mix not stated) 20 138 person-years of follow-up (mean follow-up = 10 years) Loss to follow-up: 7% for German workers; 71% for other nationalities	Chemical plant (production and polymerization of styrene) Worked for at least 1 month	Exposure estimates based on employment records

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Reference	Location	Follow-up/enrolment period	Study design	Population size	Description	Exposure assessment method
Hodgson & Jones (1985)	United Kingdom	Enrolment from 1945 to 1974 Follow-up (deaths) from 1946 to 1978 Follow-up (cancers) from 1962 to 1981	Cohort (SMR and internal analysis)	3694 male workers • 622 chemical workers (131 potentially exposed to styrene among other chemicals in laboratory work and 491 manual workers potentially exposed to styrene during production or polymerization of styrene or the manufacture of products) • 3072 unexposed manual workers 45 621 person-years of follow-up Loss to follow-up: 5%	Chemical plant (production, polymerization and processing of styrene) Chemical workers exposed for at least 1 year Classified as exposed or not exposed	Exposure estimates based on company records of job title
Nicholson et al. (1978)	USA	Enrolment in 1960 Follow-up from 1960 to 1975	Cohort (SMR analysis)	560 male workers Loss to follow-up: 0%	Chemical plant (styrene production and polymerization) Employed at the plant for at least 5 years (follow-up commenced after 10 years of work)	Exposure estimates based on air measurements in 1974 and urine metabolites in workers in a separate survey, applied to company records of job title

AML, acute myeloid leukaemia; CML, chronic myeloid leukaemia; JEM, job-exposure matrix; ppm, parts per million; SIR, standardized incidence ratio; SMR, standardized mortality ratio; SRR, standardized rate ratio

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