Estimation of national, regional, and global prevalence of alcohol use during pregnancy and fetal alcohol syndrome: a systematic review and meta-analysis

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Summary

Background Alcohol use during pregnancy is the direct cause of fetal alcohol syndrome (FAS). We aimed to estimate the prevalence of alcohol use during pregnancy and FAS in the general population and, by linking these two indicators, estimate the number of pregnant women that consumed alcohol during pregnancy per one case of FAS.

Methods We began by doing two independent comprehensive systematic literature searches using multiple electronic databases for original quantitative studies that reported the prevalence in the general population of the respective country of alcohol use during pregnancy published from Jan 1, 1984, to June 30, 2014, or the prevalence of FAS published from Nov 1, 1973, to June 30, 2015, in a peer-reviewed journal or scholarly report. Each study on the prevalence of alcohol use during pregnancy was critically appraised using a checklist for observational studies, and each study on the prevalence of FAS was critically appraised by use of a method specifically designed for systematic reviews addressing questions of prevalence. Studies on the prevalence of alcohol use during pregnancy and/or FAS were omitted if they used a sample population not generalisable to the general population of the respective country, reported a pooled estimate by combining several studies, or were published in iteration. Studies that excluded abstainers were also omitted for the prevalence of alcohol use during pregnancy. We then did country-specific random-effects meta-analyses to estimate the pooled prevalence of these indicators. For countries with one or no empirical studies, we predicted prevalence of alcohol use during pregnancy using fractional response regression modelling and prevalence of FAS using a quotient of the average number of women who consumed alcohol during pregnancy per one case of FAS. We used Monte Carlo simulations to derive confidence intervals for the country-specific point estimates of the prevalence of FAS. We estimated WHO regional and global averages of the prevalence of alcohol use during pregnancy and FAS, weighted by the number of livebirths per country. The review protocols for the prevalence of alcohol use during pregnancy (CRD42016033835) and FAS (CRD42016033837) are available on PROSPERO.

Findings Of 23 470 studies identified for the prevalence of alcohol use, 328 studies were retained for systematic review and meta-analysis; the search strategy for the prevalence of FAS yielded 11 110 studies, of which 62 were used in our analysis. The global prevalence of alcohol use during pregnancy was estimated to be 9·8% (95% CI 8·9–11·1) and the estimated prevalence of FAS in the general population was 14·6 per 10 000 people (95% CI 9·4–23·3). We also estimated that one in every 67 women who consumed alcohol during pregnancy would deliver a child with FAS, which translates to about 119 000 children born with FAS in the world every year.

Interpretation Alcohol use during pregnancy is common in many countries and as such, FAS is a relatively prevalent alcohol-related birth defect. More effective prevention strategies targeting alcohol use during pregnancy and surveillance of FAS are urgently needed.

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Introduction

Alcohol use can result in harm not only to the drinker, but also to other individuals associated with the drinker.[1] A classic example of this harm to others is the harm caused by consuming alcohol during pregnancy. Alcohol is a teratogen that can readily cross the placenta, resulting in damage to the brain and other organs of the developing embryo and fetus. Alcohol use during pregnancy has been established as a risk factor for adverse pregnancy outcomes including stillbirth,[2] spontaneous abortion,[3] premature birth,[4–6] intrauterine growth retardation,[6,7] and low birthweight.[6,8] One of the most disabling potential outcomes of drinking during pregnancy is the risk of developing fetal alcohol syndrome (FAS), the most severe and visibly identifiable form of fetal alcohol spectrum disorder (FASD).[9–12]

FAS, first described in 1973,[13] is associated with a wide range of effects including permanent brain damage, congenital anomalies, prenatal or postnatal growth restriction, and characteristic dysmorphic facial features, along with cognitive, behavioural, emotional, and

Research in context

Evidence before this study

Alcohol use during pregnancy is an established cause of fetal alcohol syndrome (FAS). To date, most countries do not have population-level prevalence data for alcohol use during pregnancy or FAS. To fill these knowledge gaps, we have completed the first comprehensive epidemiological study to estimate the actual (based on existing empirical studies) and predicted (for countries with one or no empirical studies) prevalence of these indicators. It was also unknown what proportion of women who drink during pregnancy will deliver a child with FAS.

Added value of this study

This study has estimated that globally, about 10% of women in the general population consume alcohol during pregnancy and one in 67 women delivered a child with FAS. This finding means that, on average, about 15 of every 10 000 livebirths worldwide will have FAS, translating to about 119 000 children born with FAS globally every year. In some regions (most notably in the WHO European Region) a high proportion (about a quarter) of pregnant women in the general population consume alcohol during pregnancy, which is mirrored by also having the highest FAS prevalence that is 2·6 times higher than the global average (14·6 per 10 000; 95% CI 9·4–23·3). In countries of the WHO Eastern Mediterranean Region and South-East Asia Region, where the rates of abstinence are very high, the prevalence of alcohol use during pregnancy and FAS was estimated to be the lowest.

Implications of all the available evidence

More effective prevention strategies targeting alcohol use during pregnancy and surveillance of FAS are urgently needed. Future efforts should be made to obtain countries' own prevalence data on alcohol use during pregnancy and FAS, which will provide a basis for public health policy, health-care planning, and resource allocation for FAS prevention initiatives.

adaptive functioning deficits.[9–12,14] We have shown[14] that individuals with FAS experience many comorbid conditions, with the most prevalent conditions occurring within the congenital malformations, deformities, and chromosomal abnormalities (43%) and mental and behavioural disorders (18%) chapters of the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10).[15] Some of these comorbid conditions (eg, language, auditory, visual, developmental, cognitive, mental, and behavioural problems) are highly prevalent in individuals with FAS, ranging from 50% to 91%.[14] The neurodevelopmental impairments associated with FAS can, later in life, lead to substantial secondary disabilities (eg, academic failure, substance abuse, mental health problems, contact with law enforcement, and an inability to live independently and obtain and maintain employment) and thus, have lifelong implications.[16] Moreover, FAS is an intergenerational issue, with younger siblings of a diagnosed child being at an increased risk of FAS. The complexity and chronicity of FAS affects both the individual and their family, and in many cases, people with FAS require lifelong assistance from a wide range of services including health, community, remedial education, and many others. Accordingly, FAS is recognised to impart a substantial economic burden on society.[17–19]

To set priorities for public health policy, funding for public health initiatives, and health-care planning, it is necessary to know the prevalence of FAS and its main causal risk factor—alcohol use during pregnancy. However, to date, most countries do not have prevalence data at a population level for alcohol use during pregnancy or for FAS. Furthermore, to the best of our knowledge, the number of pregnant women in the general population who consume alcohol during pregnancy per case of FAS has not been previously estimated.

Although human research has not been able to delineate the pattern, amount, or critical period of prenatal alcohol exposure necessary for structural or functional teratogenesis, we do know that not every woman who drinks during pregnancy will deliver a child with FAS. This uncertainty is especially true given that there are some other factors at play that might influence a fetus's vulnerability to the teratogenic effects of alcohol, such as variability in the metabolism and genetic background of both the mother and fetus, environmental influences, maternal smoking behaviour, nutritional status, stress levels,[20,21] and possibly paternal lifestyle.[22]

To fill these knowledge gaps, we aimed to estimate the prevalence of alcohol use during pregnancy and of FAS among the general population, by country, WHO region (ie, African region [AFR], Eastern Mediterranean region [EMR], European region [EUR], region of the Americas [AMR], South-East Asia region [SEAR], and Western Pacific region [WPR]), and globally. We also aimed to estimate the number of pregnant women in the general population who consumed alcohol per one case of FAS by linking data on the prevalence of alcohol use during pregnancy with data on the prevalence of FAS. With the growing body of literature, increased recognition of prenatal alcohol exposure and FAS as serious and costly public health problems, and advancements in statistical techniques, this study is not only now feasible, but also urgently needed and timely.

In line with the International Charter on Prevention of FASD, published in *The Lancet Global Health* in 2014,[23] the current study provides the best understanding of the scope of the problem at this time and is intended to both inform and draw the attention of health-care practitioners,

public health authorities, policy makers, and government officials.

Methods

Search strategy and selection criteria

We began by systematically reviewing the literature on the prevalence of alcohol use (of any amount) during pregnancy. The search terms were: alcohol, binge, OR ethanol; AND behavi*, consum*, OR drink*; AND maternal, mother, primigravida, OR wom*n; AND pregnant, pregnanc*, OR prenatal; AND epidemiology, frequenc*, occurrence, OR prevalence. We searched multiple electronic bibliographic databases to identify studies published between Jan 1, 1984, and June 30, 2014 (ie, in the past 30 years), without language and geographic restriction, including: Canadian Centre on Substance Abuse Library Collection Database, Campbell Collaboration, CINAHL, Cochrane Database of Systematic Reviews, CSA Sociological Abstracts, Embase, ERIC, Google Scholar, MEDLINE, National Institute on Alcohol Abuse and Alcoholism's Alcohol and Alcohol Problems Science Database, PsycINFO, Scopus, Social Work Abstracts, and Web of Science (including Science Citation Index, Social Sciences Citation Index, and Arts and Humanities Citation Index). Subsequently, we searched the content pages of major epidemiology journals (ie, *International Journal of Epidemiology*, *European Journal of Epidemiology*, and *American Journal of Epidemiology*) and screened citations in any of the relevant articles in order to identify additional studies. We included articles if they consisted of original quantitative research published in a peer-reviewed journal or scholarly report, and reported the prevalence of alcohol use during pregnancy among the general population of the respective country. We omitted articles if they excluded abstainers from the sample or estimate, used a sample population not generalisable to the general population of the respective country (ie, on a sample drawn from a special population—for example, Indigenous women, adolescents, women of a low socioeconomic status, women with HIV, and women with an alcohol use disorder), reported a pooled estimate of alcohol use during pregnancy by combining several studies, or were published in iteration. In cases where a study reported more than one prevalence estimate of alcohol use during pregnancy, we gave preference to the estimate obtained after pregnancy recognition (rather than before recognition), during the entire pregnancy (instead of just one trimester), within 6 weeks post partum, or using a validated method for identification of alcohol use.

We then did a systematic literature review to identify all studies that reported the prevalence of FAS. A comprehensive systematic literature search was done to identify all studies that have reported the prevalence of FAS among the general population of the respective country. The search terms were: epidemiolog*, frequenc*, incidence*, morbidit*, occurren*, prevalence*, probability, rate*, OR statistic*; AND alcohol* embryopath*, fas, fetal alcohol syndrome*, foetal* alcohol syndrome*, prenatal* alcohol expos*, OR pre-natal* alcohol expos*; AND cohort stud*, cross* sectional stud*, prospective cohort stud* OR retrospective cohort stud*. We searched multiple electronic bibliographic databases, including: CINAHL, Embase, ERIC, MEDLINE, PsycINFO, Scopus, and Web of Science (including Science Citation Index, Social Sciences Citation Index, and Arts and Humanities Citation Index). The search was not limited geographically or by language of publication, and identified all studies published from Nov 1, 1973 (when FAS was first described)[13] to June 30, 2015. The search was limited to human studies in all databases that allow for this restriction to be specified. We manually reviewed the content pages of the major epidemiological journals in paediatrics (ie, *Paediatric and Perinatal Epidemiology*, *Pediatrics*, and *JAMA Pediatrics*), and the citations in any of the relevant articles in order to identify additional studies. Articles were retained if they consisted of original, quantitative research published in a peer-reviewed journal or scholarly report, and reported the prevalence of FAS with either a measure of uncertainty (CI or SE), or the sample size, or number of cases. We excluded articles if they used a sample not generalisable to the general population of the respective country (ie, on a sample drawn from a special population—for example, Indigenous and correctional populations, children in care, and children born to women with an alcohol use disorder), reported a pooled estimate by combining several studies, or were published in iteration.

We began the study selection for both systematic reviews by screening titles and abstracts for inclusion. Then, we considered full-text articles of all studies screened as potentially relevant. Two investigators, SP and SL, did each study selection step independently; any disagreements were reconciled by team discussion. In cases where multiple studies used the same dataset or cohort, we included the study with the larger sample size. SL extracted data and then a second investigator, SP, independently crosschecked these data for accuracy against the original studies. All discrepancies were reconciled by team discussion. Non-English-language studies deemed to be potentially relevant were translated either by colleagues fluent in the respective language or using the Google Translate (and subsequently crosschecked by a native speaker). A protocol is available on PROSPERO for the systematic review and meta-analysis on alcohol prevalence in pregnancy (CRD42016033835) and for the prevalence of FAS (CRD42016033837).

Meta-analyses

SP and SL independently appraised the quality of each study using a checklist for observational studies developed on the criteria described and validated by Wong and colleagues.[24] Investigators assessed the representativeness of the sample (probability *vs* non-probability sampling), adequate sample size (n≥300), method used to ascertain alcohol use during pregnancy

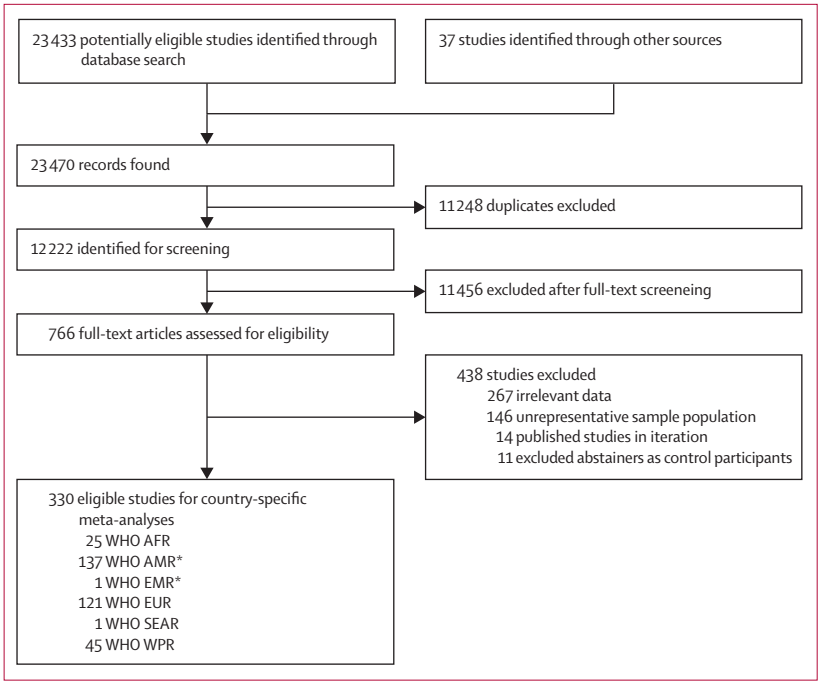

Figure 1: **Study selection for the prevalence of alcohol use (any amount) during pregnancy in the general population**
AFR=African region. AMR=Region of the Americas. EMR=Eastern Mediterranean region. EUR=European region. SEAR=Southeast Asia region. WPR=Western Pacific region. *Some studies report the prevalence of alcohol use during pregnancy for more than one country or year.

See Online for appendix

(validated method *vs* questionnaire), and adequate response or participation rate (≥70%; appendix pp 21–26). All discrepancies in quality ratings were reconciled by team discussion.

For countries with two or more empirical studies, we did country-specific random-effects meta-analyses[25] to estimate the pooled prevalence of alcohol use during pregnancy. Before doing the meta-analyses, prevalence estimates were transformed using a double arcsine transformation (appendix p 1).[26] Heterogeneity between estimates was assessed using the Cochrane Q test[27] and the I^2 statistic.[28] Publication and selection bias was tested by: visually inspecting the funnel plot (the SE plotted against the point estimate) for a skewed distribution, using a rank correlation test, evaluating the correlation between observed point estimates and corresponding sampling variances,[29] and employing a weighted regression test for disproportionate small-study influence.[30] For countries with one or no empirical studies (or where the meta-analysis resulted in a CI of 0–100%), we predicted the country's prevalence of alcohol use during pregnancy by using a fractional response regression modelling (ie, a generalised linear model with a binomial family and a logit link) to restrict predictions to values between zero and one.[31] Country-specific predictor variables were gross domestic product (GDP) adjusted for purchasing power parity per capita (obtained from the World Bank),[32] mean total consumption of alcohol among women (obtained from WHO Global Information System on Alcohol and Health),[33] and the WHO region within which the country is located. In regard to WHO regions, we split WHO EUR and WHO AMR into high-income and low-income regions (ie, European Union [EU] member states *vs* non-EU-member, and Canada and USA *vs* all remaining countries in the Americas, respectively). Other explanatory variables that we considered for inclusion are presented in the appendix (p 1).

Predictions of the prevalence of alcohol use during pregnancy were made for the year 2012. The standard error for each country estimate was based on the variation between studies of the meta-analysis. All meta-analyses and the fractional response regression modelling were performed using R version 3.2.2.[34]

For the meta-analysis of FAS prevalence, we critically appraised each study using a method specifically used in systematic reviews addressing questions of prevalence.[35] The studies were assessed by use of the following ten criteria: studies needed to show representativeness of the sample to the general population; appropriate recruitment of participants; adequate sample size (n≥300); well described participants and setting; sufficient coverage of the identified sample; use of an objective, standard criterion for measuring FAS; reliability of condition measurement; the use of appropriate statistical analysis; identification and consideration of confounders, subgroups, and differences; and the use of objective criteria for the identification of subpopulations (appendix pp 37–38). SP and SL independently appraised the quality of each study, and all discrepancies in quality ratings were reconciled by team discussion.

To estimate the pooled prevalence of FAS for countries with two or more observational studies, we did country-specific random-effects meta-analyses, as described for the prevalence of drinking during pregnancy. For the pooled prevalence of FAS, we did primary and secondary analyses. For the primary analysis we included studies that used active case ascertainment (ACA; in which cases are actively sought and diagnosed) or clinic-based methods (prospectively done in prenatal clinics or hospitals) and specified the diagnostic guideline or case definition used to ascertain cases. We did a secondary analysis using less restrictive inclusion criteria and, in addition to those studies included in the primary analysis, also included studies that made use of passive surveillance methods (the use of existing record collections—eg, birth certificates, registries, medical charts, adoption records) and did not provide the diagnostic guideline or case definition used.

For countries with one or no empirical studies (or where the meta-analysis resulted in a CI of 0–100%), we predicted the prevalence of FAS using data on the prevalence of alcohol use during pregnancy. This method included the following steps: first, we estimated a quotient for the average number of pregnant women who consumed alcohol per one case of FAS for countries with available data and then we predicted prevalence of FAS by applying

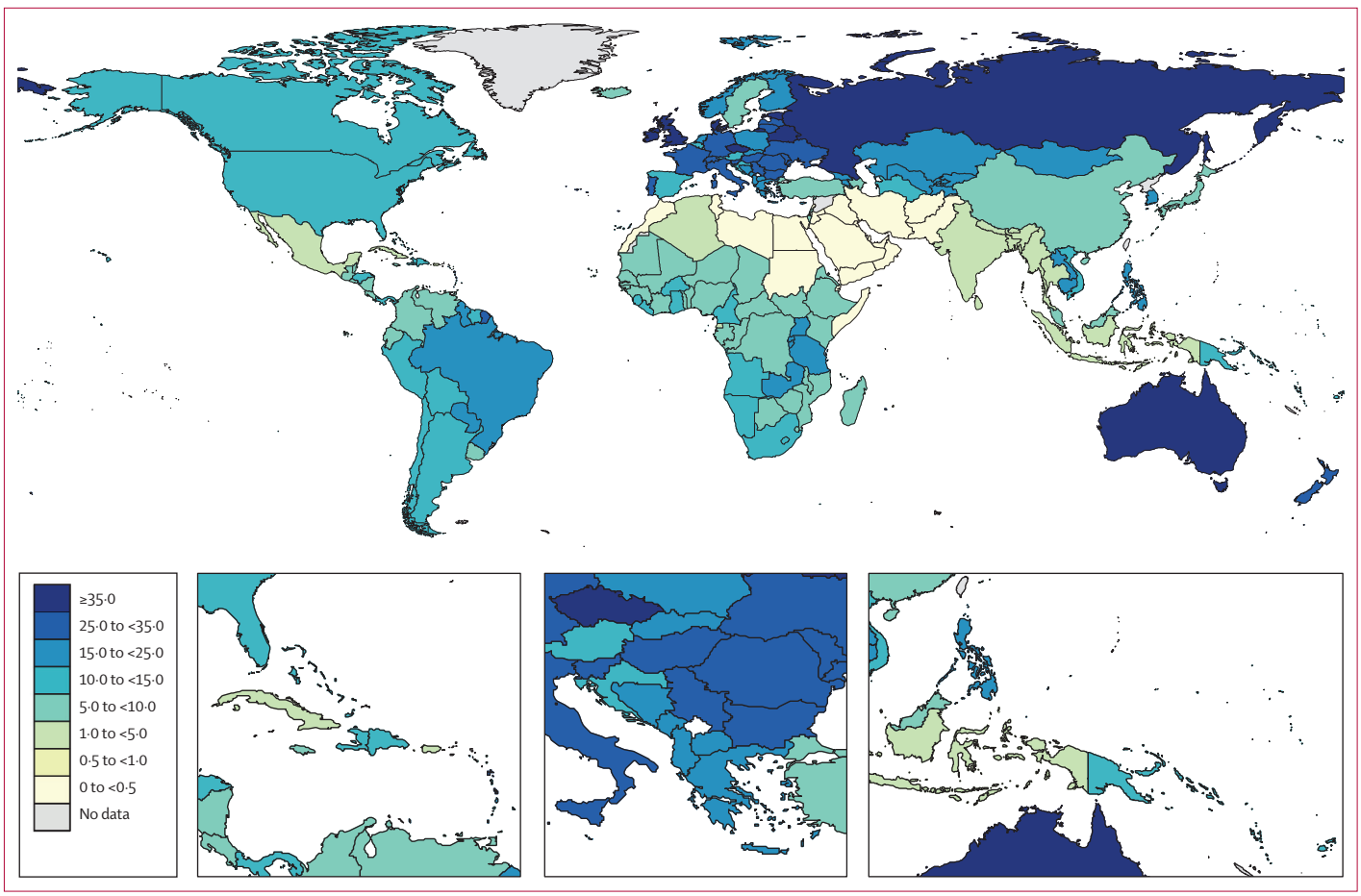

Figure 2: **Global prevalence (%) of alcohol use (any amount) during pregnancy among the general population in 2012**

this quotient to the country-specific prevalence of alcohol use during pregnancy. To derive the CI for the point estimate of the prevalence of FAS, we applied the Monte Carlo method,[36] generating 1000000 samples per country and using the 2·5th and 97·5th percentiles of the resulting distribution as the CI (appendix pp 2–3). The Monte Carlo simulations were done using Python version 2.7.12.[37]

To estimate the prevalence of alcohol use during pregnancy and FAS by the six WHO regions and globally, we calculated a weighted average of the prevalence of alcohol use during pregnancy and FAS weighting by the number of livebirths in each country for the latest available year (2000–14).[38] To determine the uncertainty around these point estimates, we drew 1000000 samples from each country's specific distribution and we calculated the corresponding 1000000 weighted averages. The 2·5th and the 97·5th percentiles of the resulting distribution of averages were used as the CI.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

For the prevalence of alcohol use during pregnancy in the general population, of 23470 studies, we found 328 studies contained relevant data and were retained for data extraction (figure 1). Data on the prevalence of alcohol use during pregnancy in the general population were available from 50 countries, representing all six WHO regions. The study characteristics and the prevalence of alcohol use during pregnancy among the general population reported in the identified studies are presented in the appendix (pp 4–16).

We estimated the prevalence of alcohol use during pregnancy among the general population via random-effects meta-analyses for 29 countries and via fractional response modelling for 158 countries (ie, countries with one or no empirical studies; figure 2; appendix pp 17–19). The five countries with the highest estimated prevalence of alcohol use during pregnancy were Russia (36·5%, 95% CI

	Alcohol use during pregnancy (%)	FAS (per 10 000)
AFR	10·0% (8·5–11·8)	14·8 (8·9–21·5)
AMR	11·2% (9·4–12·6)	16·6 (11·0–24·0)
EMR	0·2% (0·1–0·9)	0·2 (0·2–0·9)
EUR	25·2% (21·6–29·6)	37·4 (24·7–54·2)
SEAR	1·8% (0·9–5·1)	2·7 (1·3–8·1)
WPR	8·6% (4·5–11·6)	12·7 (7·7–19·4)
Worldwide	9·8% (8·9–11·1)	14·6 (9·4–23·3)

Data are prevalence estimates (95% CI). AFR=African region. AMR=Region of the Americas. EMR=Eastern-Mediterranean region. EUR=European region. FAS=Fetal alcohol syndrome. SEAR=South-East Asia region. WPR=Western Pacific region.

***Table*: Global prevalence of alcohol use (any amount) during pregnancy and fetal alcohol syndrome (FAS) in the general population in 2012, by WHO region**

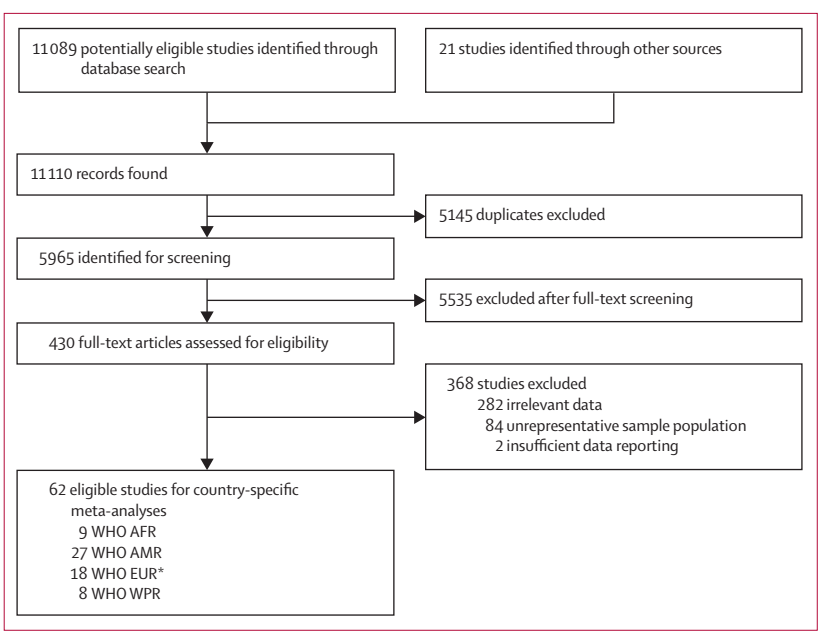

***Figure 3*: Study selection for the prevalence of FAS in the general population**
AFR=African region. AMR=Region of the Americas. EMR=Eastern Mediterranean region. EUR=European region. *Some studies report the prevalence of FAS for more than one country.

18·7–56·4), UK (41·3%, 32·9–49·%), Denmark (45·8%, 30·9–61·2), Belarus (46·6%, 42·4–50·7; based on prediction), and Ireland (60·4%, 42·8–76·8); all of which belong to WHO EUR. The five countries with the lowest prevalence of alcohol use during pregnancy (ie, 0%) were Oman, United Arab Emirates, Saudi Arabia, Qatar, and Kuwait (all of which belong to WHO EMR, and are based on prediction). The average prevalence of alcohol use during pregnancy was the highest in the WHO EUR at 25·2% (95% CI 21·6–29·6) and the lowest in the WHO EMR at 0·2% (0·1–0·9; table). The global prevalence of consuming any amount of alcohol during pregnancy in the general population was estimated to be 9·8% (8·9–11·1). The results of the tests of heterogeneity and publication bias for meta-analyses on the prevalence of alcohol use during pregnancy are presented in the appendix (p 20).

With regard to the prevalence of FAS in the general population, the search strategy initially yielded 11 110 studies, 62 of which contained relevant data and were retained for data extraction (figure 3). Data on the prevalence of FAS among the general population were available from 19 countries, representing four WHO regions (AFR, AMR, EUR, and WPR). 22 studies used ACA, 20 used passive surveillance, 14 studies were clinic-based, and six studies used a mixed-methods approach. In total, 40 studies used an established FAS diagnostic guideline or provided the case definition used to ascertain cases. The study characteristics and prevalence of FAS among the general population reported in the identified studies are presented in the appendix (pp 28–31).

We estimated the pooled prevalence of FAS among the general population via random-effects meta-analyses for seven countries and via applying a quotient of the average number of women who consumed alcohol during pregnancy per one case of FAS for 180 countries (figure 4). The five countries with the highest prevalence of FAS per 10 000 people were Belarus (69·1, 95% CI 42·1–103·5; based on prediction), Italy (82·1, 42·1–134·6), Ireland (89·7, 50·4–142·8; based on prediction), Croatia (115·2, 34·8–236·0), and South Africa (585·3, 430·7–761·7). The five countries with the lowest prevalence of FAS (ie, <0·05 per 10 000 people; based on prediction) were Oman, United Arab Emirates, Saudi Arabia, Qatar, and Kuwait (WHO EMR). In line with the prevalence of alcohol use during pregnancy, the prevalence of FAS was the highest in WHO EUR (37·4 per 10 000 people, 95% CI 24·7–54·2) and the lowest in the WHO EMR (0·2 per 10 000 people, 0·2–0·9; table). The global prevalence of FAS among the general population was estimated to be 14·6 per 10 000 people (95% CI 9·4–23·3; appendix pp 32–34). The results of the tests of heterogeneity and publication bias for meta-analyses on the prevalence of FAS are presented in the appendix (p 35). On the basis of data for the seven countries (Australia, Canada, Croatia, France, Italy, South Korea, and USA) with the prevalence of both alcohol use during pregnancy and FAS available, we estimated that one in every 67 mothers who consumed alcohol during pregnancy delivered a child with FAS, which translates to approximately 119 000 children born with FAS in the world each year (based on a total of 81 536 534 livebirths worldwide; the sum of the number of livebirths for each country for the latest available year [2000–14]).[38] The results of the secondary analysis described in the methods are presented in the appendix (p 36).

Overall, the secondary analysis resulted in lower point estimates of the prevalence of FAS for those countries with available studies that made use of passive surveillance or did not specify the diagnostic guideline or case definition used (ie, Australia, France, Italy, and USA). This finding was expected since it has been shown that ACA is the most effective approach to estimating the prevalence of FAS.[39]

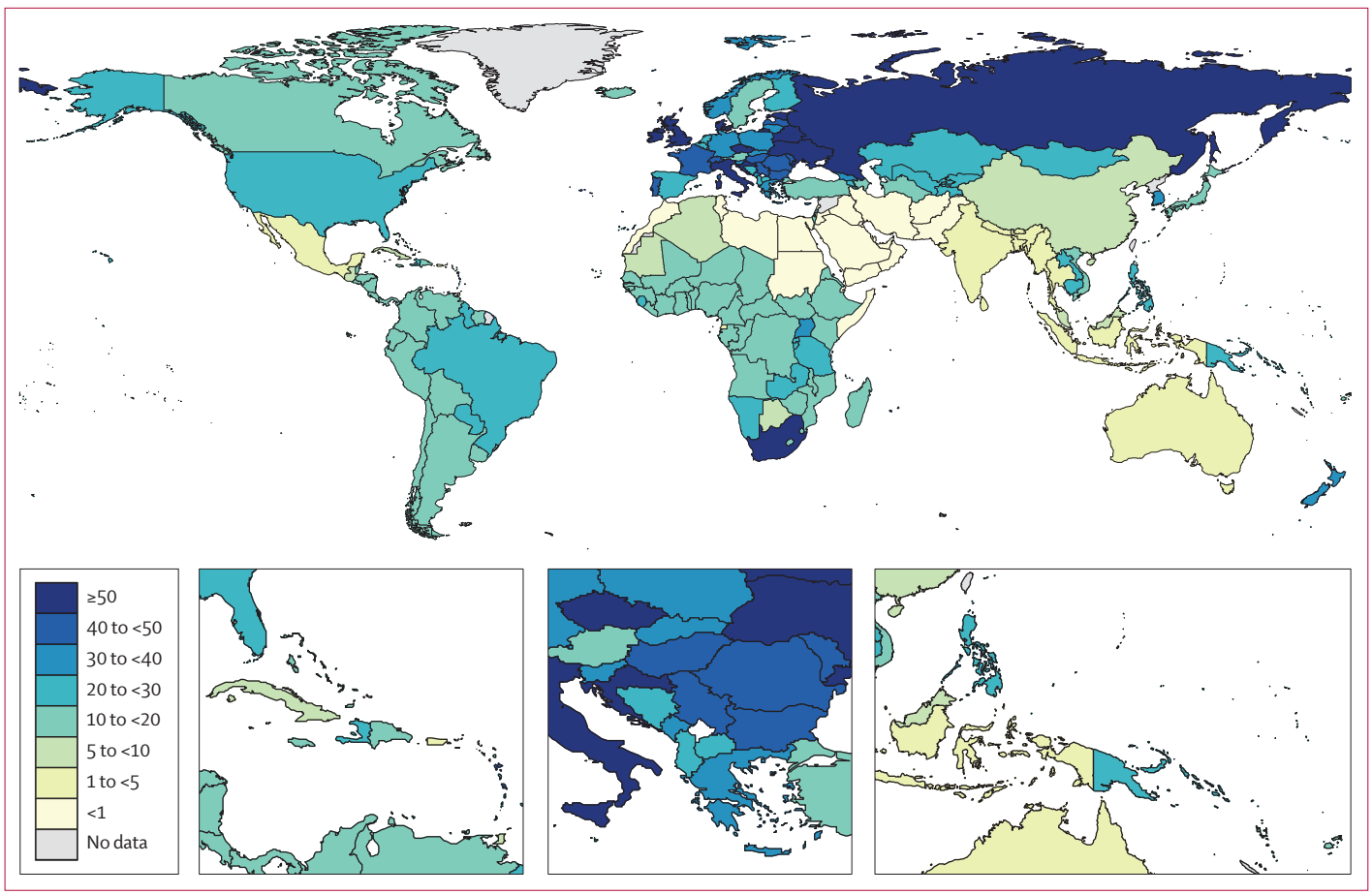

Figure 4: **Global prevalence (per 10 000 people) of FAS among the general population in 2012**

Discussion

This study estimated that on average about 15 of every 10 000 people worldwide will have FAS. For the USA, the prevalence of FAS exceeds that of other birth defects such as anencephaly, spina bifida, and trisomy 18, and is similar to trisomy 21 (Down's syndrome).[40] Furthermore, globally, about 10% of women in the general population consume alcohol during pregnancy, and one of every 67 of these women delivered a child with FAS. This finding is corroborated by previous research, which estimated that 4·3% of children born among heavy-drinking pregnant women (defined as an average of two or more drinks per day, or five to six drinks per occasion) will have FAS[41]—ie, one of every 23 heavy-drinking pregnant women will deliver a child with FAS, which is about three times greater than the quotient estimated among women in the general population who consumed any amount of alcohol during pregnancy.

Despite public health efforts to eliminate or reduce the consumption of alcohol during pregnancy in many countries (see, for example, clinical guidelines advising women to abstain during pregnancy in Australia,[42] Canada,[43] Denmark,[44] France,[45] and USA[46] as well as WHO guidelines for identification and management of substance use in pregnancy),[47] the results of the current study indicate that in some regions (most notably, WHO EUR), a high number of pregnant women continue to consume alcohol. Alarmingly, about a quarter of women in the general population of Europe drink alcohol during pregnancy, which, as one would expect, is mirrored by also having the highest FAS prevalence—a prevalence that is 2·6 times higher than the global average. The lowest prevalence of alcohol use during pregnancy and FAS was found in the WHO EMR (50 times lower than the global average) and WHO SEAR (five times lower than the global average). This is unsurprising given the cultural factors in these regions, which prescribe female abstinence (eg, for WHO EMR most of the population is of Muslim faith, a religion associated with very high rates of abstention from alcohol). Furthermore, the prevalence of FAS in South Africa is notably high in relation to the prevalence of alcohol use during pregnancy. This can be explained that in general, the WHO AFR has a low prevalence of heavy episodic drinking of 16·4%,[48] but alcohol consumption per capita

among drinkers aged 15 years or older is extremely high (ie, 19·5 litres). Therefore, those women who consume alcohol during pregnancy are most likely to practise the most detrimental pattern of drinking (ie, binge drinking), which is a direct cause of FAS.

We would like to highlight two important aspects of this study. First, this study estimated the prevalence of only one alcohol-related diagnosis (ie, FAS) that falls under the FASD umbrella (which includes partial FAS and alcohol-related neurodevelopmental disorder, in addition to FAS).[9] It is believed that the prevalence ratio of FAS to FASD is about one to nine or ten, indicating that FAS is only the tip of the iceberg.[49] Second, the estimates presented in this report are for the general population of the respective countries. However, the prevalence of alcohol use during pregnancy has been reported to be much higher among some at-risk populations. For example, the prevalence of alcohol use during pregnancy among Inuit women in northern Quebec (QC, Canada) was reported to be 60·5%, which is over ten times higher than the estimate for the general population of Canada.[50] Similar to alcohol use during pregnancy, the prevalence of FAS is also much higher among some populations. For example, Fitzpatrick and colleagues[51] have reported the prevalence of FAS in an Indigenous population in Australia to be 92·6 per 10 000 (approximately 39 times higher than in the general population), and Strömland and colleagues[52] have reported a prevalence of 3191 per 10 000 people for FAS in children residing in an orphanage in Brazil (>14 times higher than in the general population).

Regardless of the preventable nature of FAS, there is reason to believe that its prevalence could increase around the globe in the coming years. This speculation is primarily based on two factors: first, the rates of alcohol use, binge drinking, and drinking during pregnancy are increasing among young women in a number of countries,[53,54] and second, a large percentage of pregnancies in developing and developed countries are unplanned.[55–58] Unplanned pregnancies can put embryos at risk of being unintentionally exposed to alcohol in the earliest stage of pregnancy, when brain and facial development are particularly vulnerable to its effects.[59,60]

The current study has several notable strengths, namely the comprehensive search strategies, strict inclusion and exclusion criteria, critical appraisals, rigorous identification of dual publications (thereby avoiding any potential of double counting cases), analytical strategy, and innovative evidence-based statistical analysis. However, this study is not without its limitations. First, some studies included in meta-analyses of the prevalence of alcohol use during pregnancy used non-representative sampling strategies, or did not use validated tools to ascertain alcohol use. Yet it has been shown that non-probability sampling strategies can be an acceptable sampling technique when exploring exposures during pregnancy[61] and that a single question can detect as many (if not more) women who drink as can other commonly used prenatal screens.[62] Second, data on alcohol use during pregnancy were obtained through self-reported measures and as such, are vulnerable to reporting and recall biases. Therefore, the prevalence of alcohol use during pregnancy and, as a consequence, the prevalence of FAS, might be underestimated in the current study. Third, drinking patterns (frequency and quantity) were not included in the current analysis because these data were either not reported or reported inconsistently across the included studies. However, such information would be important in advising future clinical and research practice and for developing appropriate FAS prevention strategies. Fourth, with regard to the FAS prevalence studies, many studies did not use or specify the diagnostic guideline or case definition to ascertain cases and those that used different diagnostic guidelines or case definitions. One study[63] showed that the FAS diagnosis unreliable because of the inconsistency in existing FASD diagnostic systems; therefore, the diagnostic guidelines used in the included studies are likely to have affected the reported prevalence (the direction of this effect depends on the sensitivity and specificity of the diagnostic system). Fifth, the predicted prevalence estimates might diverge from the true prevalence because the data from which the values are predicted have some measurement error. There could also be other relevant explanatory variables influencing the prevalence of alcohol use during pregnancy (eg, alcohol guidelines or policies) that were not taken into account in the predictions. Sixth, the studies on the prevalence of FAS were most often regionally confined and had been done in areas where a high prevalence was expected. Even so, the data indicate that FAS is a relatively prevalent alcohol-related birth defect in those countries where studies have been done. Finally, it should also be noted that this study was limited to WHO Member States.

Nonetheless, this study used the best available data and provides a working estimate of the prevalence of alcohol use during pregnancy and FAS in countries that do not currently have actual data. These data provide a useful indicator of the public health burden of the condition and a basis for health policy and resource allocation for FAS prevention initiatives. The results of this study should inspire countries to do their own research to obtain their own prevalence data on alcohol use during pregnancy and FAS, and when such data become available, further research can refine the current estimates over time.

The current findings show that every year more than 100 000 children are born with FAS worldwide—a lifelong disorder with a known and preventable cause. The harmful effects of alcohol on a fetus, representing many cases of preventable long-term disability, should be recognised globally as a public health problem. The data presented here show the urgent need to establish an FAS surveillance system to monitor its prevalence throughout

the world. Further efforts should be made to better educate women of childbearing age about the risks of alcohol use (especially binge and frequent drinking) during pregnancy. Moreover, prevention programmes aiming to change alcohol use behaviour during and before pregnancy—since it greatly affects the likelihood of prenatal drinking[64,65]—should be implemented around the world.

Appropriate screening for alcohol use in all women of childbearing age in combination with preconception health promotion, contraceptive counselling, and referral to substance abuse programmes for those women identified to have an alcohol use disorder should become a routine standard of care in all primary care settings. Referrals to substance abuse programmes, if necessary, are of the utmost importance as effective treatment of any identified cases of alcohol dependence or alcohol use disorders could reduce the risk of having a child with FAS. In patients in whom it is not possible to detect alcohol use before pregnancy, detection of prenatal alcohol use should be the focus, as decreasing or eliminating the use of alcohol during pregnancy could reduce the severity of the effects on the fetus. As the first point of contact, physicians and other health-care providers are in a position to fulfil a crucial role in the primary prevention of FAS and other alcohol-related birth defects.

Contributors

SP led the conception and design of the study, the development of the data collection instrument, data collection, quality assessment, data analysis, and data interpretation, and wrote and revised the manuscript; SL contributed to study design, the development of the data collection instrument and data analysis, performed data collection and quality assessment and extraction, assisted in data interpretation, and wrote and revised the manuscript; CP and GG performed the statistical analysis, assisted in data interpretation, and contributed to revising the manuscript; and JR contributed to the statistical analysis, data interpretation and reviewed and revised the manuscript.

Declaration of interests

We declare no competing interests.

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