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Global Prevalence of Fetal Alcohol Spectrum Disorder Among Children and Youth
A Systematic Review and Meta-analysis

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Editorial

Supplemental content

IMPORTANCE Prevalence estimates are essential to effectively prioritize, plan, and deliver health care to high-needs populations such as children and youth with fetal alcohol spectrum disorder (FASD). However, most countries do not have population-level prevalence data for FASD.

OBJECTIVE To obtain prevalence estimates of FASD among children and youth in the general population by country, by World Health Organization (WHO) region, and globally.

DATA SOURCES MEDLINE, MEDLINE in process, EMBASE, Education Resource Information Center, Cumulative Index to Nursing and Allied Health Literature, Web of Science, PsychINFO, and Scopus were systematically searched for studies published from November 1, 1973, through June 30, 2015, without geographic or language restrictions.

STUDY SELECTION Original quantitative studies that reported the prevalence of FASD among children and youth in the general population, used active case ascertainment or clinic-based methods, and specified the diagnostic guideline or case definition used were included.

DATA EXTRACTION AND SYNTHESIS Individual study characteristics and prevalence of FASD were extracted. Country-specific random-effects meta-analyses were conducted. For countries with 1 or no empirical study on the prevalence of FASD, this indicator was estimated based on the proportion of women who consumed alcohol during pregnancy per 1 case of FASD. Finally, WHO regional and global mean prevalence of FASD weighted by the number of live births in each country was estimated.

MAIN OUTCOMES AND MEASURES Prevalence of FASD.

RESULTS A total of 24 unique studies including 1416 unique children and youth diagnosed with FASD (age range, 0-16.4 years) were retained for data extraction. The global prevalence of FASD among children and youth in the general population was estimated to be 7.7 per 1000 population (95% CI, 4.9-11.7 per 1000 population). The WHO European Region had the highest prevalence (19.8 per 1000 population; 95% CI, 14.1-28.0 per 1000 population), and the WHO Eastern Mediterranean Region had the lowest (0.1 per 1000 population; 95% CI, 0.1-0.5 per 1000 population). Of 187 countries, South Africa was estimated to have the highest prevalence of FASD at 111.1 per 1000 population (95% CI, 71.1-158.4 per 1000 population), followed by Croatia at 53.3 per 1000 population (95% CI, 30.9-81.2 per 1000 population) and Ireland at 47.5 per 1000 population (95% CI, 28.0-73.6 per 1000 population).

CONCLUSIONS AND RELEVANCE Globally, FASD is a prevalent alcohol-related developmental disability that is largely preventable. The findings highlight the need to establish a universal public health message about the potential harm of prenatal alcohol exposure and a routine screening protocol. Brief interventions should be provided, where appropriate.

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Alcohol consumption during pregnancy may cause a wide range of adverse health effects to the developing fetus, including but not limited to cognitive, behavioral, emotional, and adaptive functioning deficits, as well as congenital anomalies. The health effects of prenatal exposure to ethyl alcohol have been subsumed under the umbrella term *fetal alcohol spectrum disorder* (FASD), which consists of as many as 4 diagnostic entities, including fetal alcohol syndrome (FAS), partial FAS, alcohol-related neurodevelopmental disorder, and depending on the diagnostic guideline, alcohol-related birth defects.[1-3] Alcohol can affect any organ or system in the developing fetus, and as such, individuals with FASD may experience a broad array of comorbid conditions. A recent study identified 428 comorbid conditions in individuals with FASD, with diagnoses from 18 of 22 chapters of the *International Statistical Classification of Diseases and Related Health Problems, 10th Revision* (*ICD-10*).[4] Thus, clinicians from all specialties and other health service professionals will likely encounter cases of FASD. The effects of prenatal alcohol exposure have lifelong implications, and thus, FASD is costly for society.[5,6] For example, the lifetime cost for a person with FASD in North America is estimated at more than $1 million.[7,8]

Although human research has not been able to delineate the pattern, amount, and/or critical period of prenatal alcohol exposure necessary for structural and/or functional teratogenesis, animal models have demonstrated that all stages of embryonic development are vulnerable to the teratogenic effects of alcohol.[9] Furthermore, the type and severity of birth defects induced by prenatal alcohol exposure are largely dependent on the pattern of exposure, the dose, and the developmental stage of the embryo at the time of exposure.[9-13] Multiple animal models have also shown that even low levels of prenatal alcohol exposure can lead to brain dysfunction, which can lead to behavioral abnormalities.[14] However, beyond the amount of alcohol consumed and the gestational timing of consumption, multiple factors (eg, variability in the metabolism and genetic background of the mother and fetus, environmental influences, maternal age, smoking, nutritional status, stress levels, and possibly paternal lifestyle) modify fetal susceptibility to the teratogenic effects of ethanol.[15-17]

Updated prevalence estimates are essential to effectively prioritize, plan, and deliver health care to high-needs populations, such as children and youth with FASD. These estimates are also vital for assessing the population burden of disease and allocation of resources for health care and prevention. In much of the world, no prevalence estimates of FASD exist, which may influence prioritization of health care expenditures for care related to FASD. Until recently, a meaningful estimate of FASD prevalence was not possible. However, the publication of more representative rates of prenatal alcohol exposure and improved data on the prevalence of FASD in some settings now allows for estimates of the prevalence of FASD globally. Therefore, in the present study, we aimed to estimate the prevalence of FASD among children and youth in the general population globally, by World Health Organization (WHO) region, and by country. We then compared the global prevalence estimate of FASD among children and youth in the general population with the prevalence of FASD among special populations, such as aboriginal, correctional, and low socioeconomic status populations; those undergoing psychiatric care; and children in care (eg, in foster care, residing in orphanages, and adopted), obtained from select studies.

Key Points

Question What is the prevalence of fetal alcohol spectrum disorder among children and youth in the general population?

Findings In this meta-analysis of 24 unique studies and 1416 unique children and youth with fetal alcohol spectrum disorder, approximately 8 of 1000 in the general population had fetal alcohol spectrum disorder, and 1 of every 13 pregnant women who consumed alcohol during pregnancy delivered a child with fetal alcohol spectrum disorder. The prevalence of fetal alcohol spectrum disorder was found to be notably higher among special populations.

Meaning The prevalence of fetal alcohol spectrum disorder among children and youth in the general population exceeds 1% in 76 countries, which underscores the need for universal prevention initiatives targeting maternal alcohol consumption, screening protocols, and improved access to diagnostic services, especially in special populations.

Methods

The comprehensive systematic literature search and meta-analyses were conducted and reported according to the standards of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guidelines.[18,19] The full review protocol is available in the PROSPERO database.[20]

Comprehensive Systematic Search Strategy

We performed a systematic literature search of MEDLINE, MEDLINE in process, EMBASE, Education Resource Information Center, Cumulative Index to Nursing and Allied Health Literature, Web of Science, PsychINFO, and Scopus to identify all studies that have reported the prevalence of FASD among the general population (keywords are given in eTable 1 in the Supplement). The search was not limited geographically or by language of publication and included studies published from November 1, 1973 (when FAS was first described[21]), through June 30, 2015. Non–English-language studies deemed to be potentially relevant were translated by colleagues fluent in the respective language or using Google Translate (and subsequently cross-checked by a native speaker). In addition to the electronic search, we manually reviewed the content pages of the major epidemiologic journals and the citations in the relevant articles. Effort was also made to contact the leading international FASD experts and researchers to identify any pending publications on the prevalence of FASD.

Inclusion and Exclusion Criteria

Articles were included in the meta-analysis if they (1) consisted of original, quantitative research published in a peer-reviewed journal or scholarly report; (2) involved a measurement of FASD (or a combination of any of the diagnoses within the spectrum); (3) provided the prevalence of FASD with a measure of uncertainty (CI or SE) or the necessary information to calculate uncertainty (ie, sample size or number of cases); (4) specified the diagnostic guideline or case definition used to ascertain cases; and (5) used active case ascertainment (when researchers actively seek, assess, and identify cases; ie, the criterion standard) or clinic-based methods (prospectively conducted studies in prenatal clinics or hospitals). We excluded articles from the meta-analysis if they (1) reported a pooled estimate by combining several studies; (2) used passive surveillance (the use of existing record collections) to obtain the prevalence of FASD; or (3) were published in iteration. We placed no restriction on the age of participants (ie, articles were not excluded if they reported the prevalence of FASD among adults).

Critical Appraisal of Identified Studies

We critically appraised each study by using a tool recently developed specifically for use in systematic reviews addressing questions of prevalence.[22] The following 7 criteria were used: (1) representative sample of the target population; (2) appropriate recruitment of participants; (3) adequate sample size (≥300); (4) detailed description of participants and setting; (5) sufficient coverage of the identified sample (ie, nonresponders were described and compared with those in the study); (6) use of objective, standard criteria for ascertaining FASD; and (7) appropriateness of statistical analysis.

Data Extraction

After the data were extracted from the identified articles, one of us (S.L.) checked extracted data for accuracy against the original articles. All discrepancies were reconciled by team discussion. We extracted the following variables from the identified articles: country, study year(s), sample size, number of cases, prevalence, 95% CI, age range, percentage of male participants in the sample, method of ascertainment, and the diagnostic guideline or case definition used.

Meta-analyses

To estimate the pooled prevalence of FASD, we performed a meta-analysis assuming a random-effects model[23] for each country with 2 or more existing studies on the prevalence of FASD. As recommended for meta-analyses of prevalence and to prevent the overweighting of studies reporting extremely low prevalence (ie, a prevalence approaching zero),[24,25] we transformed the data using the Freeman-Tukey double arcsine transformation.[26] We assessed heterogeneity between prevalence estimates using the Cochrane Q test and the I^2 statistic.[27,28] We assessed publication bias by (1) visually inspecting the funnel plot (SE plotted against the point estimate) for a skewed distribution; (2) by using a ranked correlation test[29]; and (3) a weighted regression test.[30] However, we deemed publication bias to be unlikely because an observed prevalence of FASD that was substantially different than had previously been estimated would likely have been published. Therefore, if found to be present, we did not adjust for publication bias. All meta-analyses were performed using R software (version 3.2.2).[31]

Prevalence Estimation

For countries with 1 or no empirical study, we estimated the prevalence of FASD by using country-specific data on the prevalence of alcohol use during pregnancy (obtained from Popova et al[32]). First, we estimated a quotient of the mean number of women who consumed alcohol during pregnancy per 1 case of FASD by using the pooled estimates of the prevalence of FASD available from countries with a WHO drinking pattern score of 3 or less.[32] A country's drinking pattern score reflects how people in the respective country drink instead of how much they drink and is measured on a scale from 1 (least risky pattern of drinking) to 5 (most risky pattern of drinking); the higher the score, the greater the alcohol-attributable burden of disease. To produce the most conservative estimations, we excluded the estimates of the prevalence of FASD available from countries with a drinking pattern score of 4 or more, because it would have led to an unrealistically high ratio. These data were then linked to the prevalence of alcohol use during pregnancy for each respective country. Second, we applied this quotient to the country-specific prevalence of alcohol use during pregnancy to estimate the prevalence of FASD. To derive the CI for the FASD prevalence point estimate, we conducted Monte Carlo simulations,[33] generating 1 million samples per country. We used the 2.5th and 97.5th percentiles of the resulting distribution as the CI. The Monte Carlo simulations were performed using Python software (version 2.7).[34] Additional methodological details can be found in the eMethods in the Supplement and in the study by Popova and colleagues.[32]

Global and Regional Estimates of the Prevalence of FASD Among Children and Youth in the General Population

To estimate the prevalence of FASD by WHO region and globally, we calculated a weighted mean prevalence of FASD, weighted by the number of live births in each country for the latest available year (2000-2014).[35] We conducted Monte Carlo simulations to estimate the CI (as described above).

Comparison of the Global Prevalence of FASD Among Children and Youth in the General Population With the Prevalence in Special Populations

We compared the global prevalence estimate of FASD among children and youth in the general population with the prevalence of FASD in special populations of various countries, using select studies in the current literature. The associated CI was estimated based on an exact binomial distribution.

Results

Comprehensive Systematic Literature Search

A total of 24 unique studies including 1416 unique children and youth diagnosed with FASD (age range, 0-16.4 years) were retained and selected for data extraction. We identified no studies conducted among adults. Data on the prevalence of FASD among children and youth in the general population were available from the following 8 countries: Australia (2 studies),[36,37] Canada (1 study),[38] Croatia (2 studies),[39,40] France (4 studies),[41-44] Italy (2 studies),[45,46] Norway (1 study),[47] South

Africa (6 studies),[48-53] and the United States (6 studies)[54-59] (eFigure 1 in the Supplement). Eighteen studies[36-40,48-53,55,57,59] (75.0%) used active case ascertainment, 5 studies[41,42,44,54,56] (20.8%) used a clinic-based method, and 1 study[37] (4.2%) used a mixed-methods approach. Most of the studies (45.8%) used the clarification of the Institute of Medicine criteria[60] for the diagnosis of FASD. Study characteristics and prevalence of FASD reported in the identified studies are given in **Table 1**; the diagnostic breakdown of FASD in the identified studies is provided in eTable 2 in the Supplement; and the critical appraisal of the identified studies is presented in eTable 3 in the Supplement.

Prevalence of FASD Among Children and Youth in the General Population

The 5 countries with the highest prevalence of FASD were South Africa at 111.1 per 1000 population (95% CI, 71.1-158.4 per 1000 population), obtained via meta-analysis; Croatia at 53.3 per 1000 population (95% CI, 30.9-81.2 per 1000 population), obtained via meta-analysis; Ireland at 47.5 per 1000 population (95% CI, 28.0-73.6 per 1000 population), obtained via prediction model; Italy at 45.0 per 1000 population (95% CI, 35.1-56.1 per 1000 population), obtained via meta-analysis; and Belarus at 36.6 per 1000 population (95% CI, 23.7-53.2 per 1000 population), obtained via prediction model. Seventy-six countries (of 187 for which observed or predicted estimates were available) had a prevalence of FASD of greater than 1%. The global prevalence of FASD was estimated to be 7.7 per 1000 population (95% CI, 4.9-11.7 per 1000 population), with the European Region having the highest overall prevalence at 19.8 per 1000 population (95% CI, 14.1-28.0 per 1000 population) and the Eastern Mediterranean Region having the lowest overall prevalence at 0.1 per 1000 population (95% CI, 0.1-0.5 per 1000 population). Furthermore, 1 of 13 pregnant women who consumed alcohol while pregnant was estimated to deliver a child with FASD. This estimation would result in a cohort of 630 000 children born with FASD globally every year. **Figure 1** and eTable 4 in the Supplement provide the prevalence of FASD by country based on actual and estimated data, and **Table 2** provides the global and regional prevalence. A forest plot of the country-specific meta-analyses is presented in eFigure 2 in the Supplement. The results of the tests of heterogeneity and publication bias for the meta-analyses on the prevalence of FASD among children and youth in the general population by country and region are presented in eTable 5 in the Supplement.

Comparison of the Global Prevalence of FASD Among Children and Youth in the General Population With the Prevalence in Special Populations

The prevalence of FASD in special populations, based on select studies, was found to be notably higher than the estimated global prevalence among children and youth in the general population (eTable 6 in the Supplement). Specifically, the prevalence of FASD among special populations was 15.6 to 24.6 times higher among aboriginal populations,[66,67] 5.2 to 67.7 times higher among children in care,[68-71] 30.3 times higher in a correctional population,[72] 23.7 times higher in a population with low socioeconomic status,[73] and 18.5 times higher among a population in psychiatric care[74] compared with the global prevalence among children and youth in the general population (**Figure 2**).

Discussion

This study identified several important public health issues. First, based on the existing data, 1 of every 13 pregnant women who consumed alcohol during pregnancy is estimated to have had a child with FASD. Second, this finding leads to an estimate that more than 1700 infants with FASD are born every day (630 000 every year) globally. Third, FASD is notably more frequent among special populations (eg, aboriginal populations, children in care, incarcerated populations, and those in psychiatric care). The higher prevalence emphasizes that these high-risk populations deserve special attention for the planning and organization of targeted screening strategies, improved access to diagnostic services, and prevention of maternal alcohol consumption. Fourth, the burden of FASD is elevated in 76 of the 187 countries included in this study, as demonstrated by having a prevalence of FASD that exceeds 1%. In these countries, the prevalence of FASD among children and youth in the general population is higher than the prevalence of some common birth defects in the United States, such as anencephaly, Down syndrome, spina bifida, and trisomy 18.[75]

Most affected children and youth will require lifelong care for the ever-changing phenotype of FASD. The demands for this care will affect virtually every specialty in medicine. The present findings suggest that prenatal alcohol exposure should be a public health priority. With the current level of awareness and extremely limited access to diagnostic services,[76] very few of these alcohol-affected children and youth will ever be diagnosed with FASD. As a result, the focus of their care will often be on a comorbid condition (eg, attention-deficit/hyperactivity disorder or conduct disorder).[69] This focus diminishes the likelihood of care organized around their developmental course, prevention of exposure in their younger siblings, and anticipation of the long-term impairments likely to occur in children and youth with FASD.[77]

A diagnosis of FASD has several potentially important benefits for affected children and youth, namely, early access to developmental interventions, improved quality of life, and ultimately a more prosperous developmental trajectory in terms of social functioning. Currently, several clinical guidelines are available for diagnosing FASD, and although the current criteria overlap with one another, they lack diagnostic reliability owing to low convergent validity.[78] Furthermore, the specificity, sensitivity, and accuracy of the various diagnostic criteria are unknown because, at present, no external standard against which a diagnostic systems classification function can be measured exists.[78,79]

The absence of widely accepted standardized criteria can ultimately lead to diagnostic misclassification.[80] Thus, a need exists for a common diagnostic approach to be developed. Ideally, novel and reliable biomarkers for detecting fetal effects of alcohol and low and moderate levels of alcohol consumption during pregnancy will be identified. Accurate diagnosis is complicated by the fact that children and youth with FASD have increased rates of comorbidities. Recently, Popova and colleagues[4] reported that more than 9 in 10 of those with FAS had co-occurring problems with conduct, approximately 8 in 10 had communication disorders related to understanding or expressing language, and more than half had attention-deficit/

Table 1. Study Characteristics and Prevalence of FASD Among Children and Youth in the General Population Reported in the Identified Studies by Country and WHO Region

Source	Country (State, Province, or Territory)	Study Period	Sample Size	No. of FASD Cases	Prevalence of FASD per 1000 Population	Diagnostic Guidelines or Case Definition	Male Participants, %	Age Range, y	Method
African Region									
Chersich et al,[48] 2012	South Africa (Northern Cape, De Aar, and Upington)	2003-2010	809	72	89.0	Clarification of the IOM criteria[60]	49.5	9.5-11.0	ACA
May et al,[49] 2007	South Africa (Western Cape)	2002-2003	818	73	89.2	Clarification of the IOM criteria[60]	51.5	6-7	ACA
May et al,[50] 2013	South Africa (Western Cape)	2008-2009	747	155	207.5	Clarification of the IOM criteria[60]	49.0	6-7	ACA
Olivier et al,[51] 2013	South Africa (rural Western Cape)	2008	160	28	175.0	Clarification of the IOM criteria[60]	50.0	4.8-16.4	ACA
Urban et al,[52] 2008	South Africa (Northern Cape, De Aar, and Upington)	2001-2004	1830	161	88.0	IOM criteria[3]	49.7	6-7	ACA
Urban et al,[53] 2015	South Africa (Northern Cape)	2012-2013	1503	96	63.9	Clarification of the IOM criteria[60]	52.6	6-7	ACA
European Region									
Petković and Barišić,[39] 2010	Croatia (urban)	NA	466	19	40.8	Clarification of the IOM criteria[60]	46.1	6.6-11.1	ACA
Petković and Barišić,[40] 2013	Croatia (rural)	NA	824	55	66.8	Clarification of the IOM criteria[60]	NA	7.0-11.9	ACA
Bloch et al,[41] 2008	France (Alsace, Isère, Paris, Puy de Dôme, and Rhône)	2008	45 919	18	0.4	Case definition provided	NA	0-1 (Newborns)	Clinic based
Dehaene et al,[42] 1981	France (Roubaix)	1977-1979	8284	45	5.4	Case definition provided	NA	0-1 (Newborns)	Clinic based
Serreau et al,[43] 2002	France (Saint-Pierre, Reunion Island)	1996	1320	75	66.0	IOM criteria[3]	NA	NA	ACA
Toutain and Lejeune,[44] 2008	France	1995-2003	5000	28	5.6	Guidelines established by the Fetal Alcohol Study Group of the RSA[61]	NA	0-1 (Newborns)	Clinic based
May et al,[45] 2006	Italy (Lazio)	2004	543	22	40.5	Clarification of the IOM criteria[60]	51.0	6-7	ACA
May et al,[46] 2011	Italy (Lazio)	2005-2007	976	46	47.1	Clarification of the IOM criteria[60]	50.6	6-7	ACA
Elgen et al,[47] 2007	Norway (Hordaland)	1999-2004	29 091	32	1.1	CDC diagnostic guidelines[62]	NA	NA	ACA
Region of the Americas									
Asante and Nelms-Matzke,[38] 1985	Canada (Northwest British Columbia and Yukon)	1983-1984	33 485	176	5.3	Guidelines established by the Fetal Alcohol Study Group of the RSA[61]	63.0	0-16	ACA
Barr and Streissguth,[54] 2001	United States (Washington State)	1974-1975	1439	36	25.0	Case definitions provided	NA	0-7	Clinic based
Clarren et al,[55] 2001	United States (Washington State)	NA	3740	26	7.0	4-Digit diagnostic code[63]	NA	6-7	ACA

(continued)

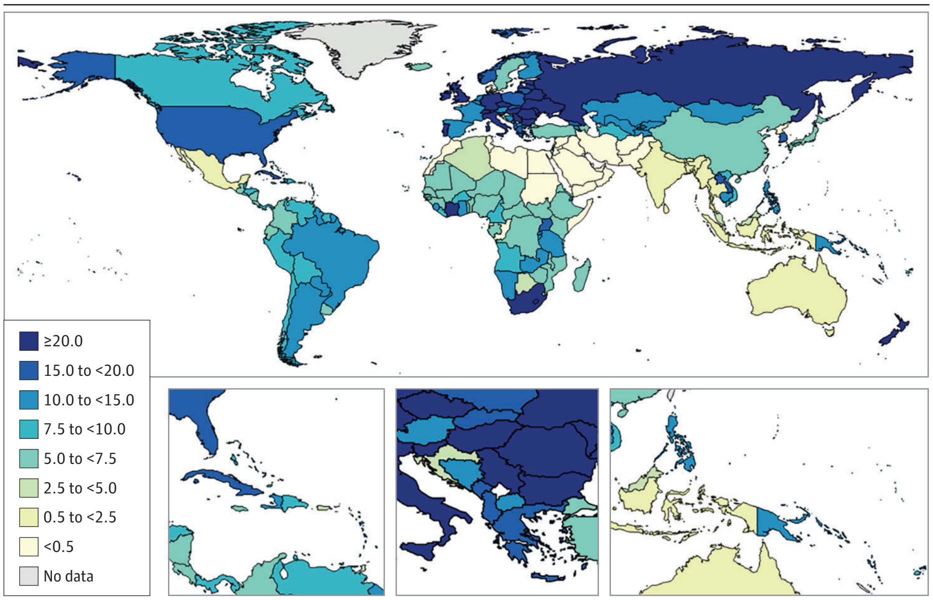
hyperactivity disorder. In addition, more than 50% had hearing loss, more than 60% had problems with vision, and approximately 5 in 10 had congenital malformations of the spine. However, most comorbid conditions found to occur among chil-

Table 1. Study Characteristics and Prevalence of FASD Among Children and Youth in the General Population Reported in the Identified Studies by Country and WHO Region (continued)

Source	Country (State, Province, or Territory)	Study Period	Sample Size	No. of FASD Cases	Prevalence of FASD per 1000 Population	Diagnostic Guidelines or Case Definition	Male Participants, %	Age Range, y	Method
Hingson et al,[56] 1982	United States (Boston, Massachusetts)	1977-1979	1690	37	21.9	Guidelines established by the Fetal Alcohol Study Group of the RSA[61]	NA	0 (Live births)	Clinic based
May et al,[57] 2014	United States (Midwestern)	2010-2011	1433	48	33.5	Clarification of the IOM criteria[60]	51.8	6-7	ACA
May et al,[58] 2015	United States (Northern Plains)	2007-2009	2334	26	11.1	Clarification of the IOM criteria[60]	54.5	6-7	ACA
Poitra et al,[59] 2003	United States	1992-2000	1384	7	5.1	Criteria by Sokol and Clarren[64]	NA	5-6	ACA
Western Pacific Region									
Elliott et al,[36] 2008	Australia	2001-2004	1 533 333	92	0.1	IOM criteria[3]	NA	0-15	ACA
Harris and Bucens,[37] 2003	Australia (Northern Territory)	1990-2000	25 209	43	1.7	Adapted 4-digit diagnostic code[63] and the criteria by the AAP[65]	NA	0-10	Mixed methods (passive surveillance and clinic based)

Abbreviations: ACA, active case ascertainment; AAP, American Academy of Pediatrics; CDC, Centers for Disease Control and Prevention; FASD, fetal alcohol spectrum disorder; IOM, Institute of Medicine; NA, not available; RSA, Research Society on Alcoholism; WHO, World Health Organization.

Figure 1. Global Prevalence of Fetal Alcohol Spectrum Disorder Among Children and Youth in the General Population in 2012



Data are expressed as number per 1000 population.

dren and youth with FASD were in those chapters of the *ICD-10* pertaining to congenital malformations and mental disorders.[4] This finding highlights the need for expanded attention to FASD and prenatal alcohol exposure in medical education generally and especially for clinicians who provide prenatal care, pediatricians, and psychiatric and mental health care professionals. The finding also stresses the need for improved prevention programs and access to early interventions to minimize the severity of FASD in affected children and youth.

Strengths and Limitations

The strengths of this study include the comprehensive search strategy, strict inclusion and exclusion criteria, critical appraisal of identified studies, rigorous identification of dual publications (thereby avoiding any potential of double counting cases), analytic strategy, use of country-specific indicators to predict the prevalence of alcohol use during pregnancy, and innovative evidence-based statistical analysis. Although the present study used the best available data and provides, to our knowledge, the first estimates of FASD globally, by WHO region, and for 187 countries, several limitations support the need for further research in this area. First, the prevalence of FASD in those countries with 1 or no empirical study was estimated using self-report data on the prevalence of alcohol use during pregnancy, which is vulnerable to reporting and recall biases. As such, the prevalence of alcohol use during pregnancy may be an underestimate. Second, the identified studies used different diagnostic guidelines and case definitions to ascertain cases of FASD, which may have affected the estimated pooled prevalence of FASD in the present study (the direction of this effect depends on the sensitivity and specificity of the diagnostic system[79]). Third, not all studies included in the meta-analyses were conducted on nationally representative population-based samples (eg, clinic-based studies); therefore, some regionally confined studies may have been conducted where FASD was more prevalent. Fourth, the estimated predicted prevalence may differ from the true prevalence owing to the fact that the data from which the values were estimated carry measurement error and uncertainty. Fifth, examination of the effect of timing, dose, and frequency of prenatal alcohol exposure on the risk of FASD was not possible.[81]

In addition, not many countries have actual data on the prevalence of FASD. Thus, the results of the present study highlight the need for countries to conduct their own cross-sectional active case ascertainment studies to obtain their own prevalence data on FASD. When such data become available, the present estimates can be refined. For example, 2 recent studies from South Africa[82,83] (not included in the current analysis, because they were published outside the time frame covered) reported a prevalence of FASD that ranged from 170 to 259 per 1000 population, which is higher than previously reported.

Table 2. Global Prevalence of FASD Among Children and Youth in the General Population by WHO Region in 2012

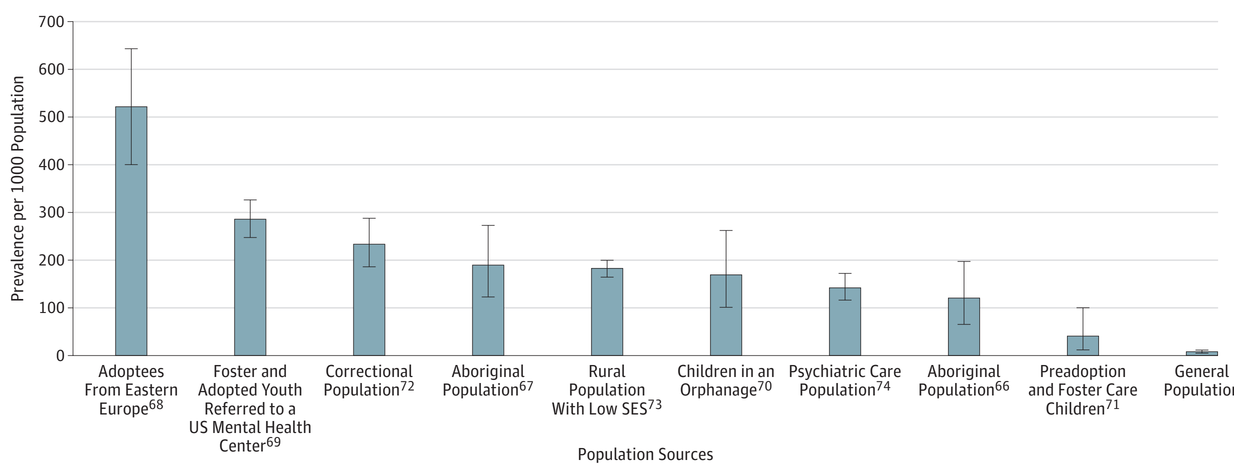
WHO Region	Prevalence Estimate (95% CI) per 1000 Population
African Region	7.8 (5.4-10.7)
Eastern Mediterranean Region	0.1 (0.1-0.5)
European Region	19.8 (14.1-28.0)
Region of the Americas	8.8 (6.4-13.2)
Southeast Asia Region	1.4 (0.6-5.3)
Western Pacific Region	6.7 (4.5-11.7)
Globally	7.7 (4.9-11.7)

Abbreviations: FASD, fetal alcohol spectrum disorder; WHO, World Health Organization.

Conclusions

Our data indicate that FASD is a relatively prevalent alcohol-related developmental disability. However, FASD is a largely preventable condition. Because the present study was restricted to the general population, the current findings emphasize that FASD is not restricted to disadvantaged groups but rather occurs throughout society, regardless of socioeconomic status, educational attainment, or ethnicity. Given the current trend in unplanned pregnancies in developing and developed countries (39% and 47%, respectively[84]), efforts should be made to educate all women of childbearing age about the potential detrimental effects of prenatal alcohol exposure on the developing fetus. Health care professionals are in the best position to do this. Development of a universal screening protocol to detect problematic drinking before and during pregnancy is a potentially inexpensive strat-

Figure 2. Comparison of the Prevalence of Fetal Alcohol Spectrum Disorder in Special Populations With the Global Prevalence Among Children and Youth in the General Population



Data in special populations are obtained from select studies. Special populations include adoptees from Eastern Europe in Sweden (521.1 per 1000 population; Landgren et al[68]), foster and adopted youth referred to a US children's mental health center (285.2 per 1000 population; Chasnoff et al[69]), a correctional population in Canada (233.5 per 1000 population; Fast et al[72]), an aboriginal population in Canada (189.7 per 1000 population; Robinson et al[67]), a rural population with low socioeconomic status (SES) in South Africa (182.4 per 1000 population; de Vries et al[73]), children in an orphanage in Brazil (170.2 per 1000 population; Strömland et al[70]), a US population in psychiatric care (142.4 per 1000 population; Bell and Chimata[74]), an aboriginal population in Australia (120.4 per 1000 population; Fitzpatrick et al[66]), and children before adoption or in foster care in Israel (40.0 per 1000 population; Tenenbaum et al[71]). Prevalence in the general population is described in Table 2. Error bars indicate 95% CI.

egy that can be widely implemented.[85,86] Last, detection of drinking during pregnancy and successful intervention can eliminate alcohol exposure in subsequent pregnancies, which eliminates risk for FASD in younger siblings.

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