Alcoholism: Clinical and Experimental Research

Vol. 40, No. 1
January 2016

Critical Review

Worldwide Prevalence of Fetal Alcohol Spectrum Disorders: A Systematic Literature Review Including Meta-Analysis

Sylvia Roozen, Gjalt-Jorn Y. Peters, Gerjo Kok, David Townend, Jan Nijhuis, and Leopold Curfs

Background: Although fetal alcohol spectrum disorders (FASD) affect communities worldwide, little is known about its prevalence. The objective of this study was to provide an overview of the global FASD prevalence.

Methods: We performed a search in multiple electronic bibliographic databases up to August 2015, supplemented with the ascendancy and descendancy approach. Studies were considered when published in English, included human participants, and reported empirical data on prevalence or incidence estimates of FASD. Raw prevalence estimates were transformed using the Freeman–Tukey double arcsine transformation so that the data followed an approximately normal distribution. Once the pooled prevalence estimates, 95% confidence intervals and prediction intervals were calculated based on multiple meta-analyses with transformed proportions using random effects models, these estimates were transformed back to regular prevalence rates. Heterogeneity was tested using Cochran's Q and described using the I^2 statistic.

Results: Among studies that estimated prevalence in general population samples, considerable differences in prevalence rates between countries were found and therefore separate meta-analyses for country were conducted. Particularly high-prevalence rates were observed in South Africa for fetal alcohol syndrome (55.42 per 1,000), for alcohol-related neurodevelopmental disorder (20.25 per 1,000), and FASD (113.22 per 1,000), For partial fetal alcohol syndrome high rates were found in Croatia (43.01 per 1,000), Italy (36.89 per 1,000), and South Africa (28.29 per 1,000). In the case of alcohol-related birth defects, a prevalence of 10.82 per 1,000 was found in Australia. However, studies into FASD exhibited substantial heterogeneity, which could only partly be explained by moderators, most notably geography and descent, in meta-regressions. In addition, the moderators were confounded, making conclusions as to each moderator's relevance tentative at best.

Conclusions: The worldwide pooled prevalence estimates are higher than assumed so far, but this was largely explained by geography and descent. Furthermore, prevalence studies varied considerably in terms of used methodology and methodological quality. The pooled estimates must therefore be interpreted with caution and for future research it is highly recommended to report methodology in a more comprehensive way. Finally, clear guidelines on assessing FASD prevalence are urgently needed, and a first step toward these guidelines is presented.

Key Words: Fetal Alcohol Spectrum Disorder(s), Epidemiology, Prevalence, Systematic Literature Review, Meta-Analysis.

From the Governor Kremers Centre (SR, GK, DT, JN, LC), Maastricht University Medical Centre, Maastricht, the Netherlands; Department of Work and Social Psychology (SR, GJYP, GK), Maastricht University, Maastricht, the Netherlands; Faculty of Psychology and Education Science (GJYP), Open University of the Netherlands, Heerlen, the Netherlands; Department of Health, Ethics & Society (DT), Maastricht University, Maastricht, the Netherlands; Department of Obstretrics & Gynaecology (JN), GROW School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht, the Netherlands; and Department of Genetics (LC), Maastricht University Medical Centre, Maastricht, the Netherlands.

Received for publication August 11, 2015; accepted October 14, 2015.

Reprint requests: Sylvia Roozen, Governor Kremers Centre, Maastricht University, PO Box 5800, 6202 AZ Maastricht, the Netherlands; Tel.: +31 (0)43 3884108; E-mail: sylvia.roozen@maastrichtuniversity.nl

DOI: 10.1111/acer.12939

THE PURPOSE OF this article was to identify the prevalence rates of the fetal alcohol spectrum Disorders (FASD) worldwide. FASD is the spectrum of disorders caused by maternal alcohol consumption during pregnancy (Hoyme et al., 2005). The lifelong consequences can range from minor to severe disabilities and therefore FASD has frequently been reported to be an important preventable cause of mental retardation (Stratton et al., 1996). The syndrome may contribute to poor academic achievement, inadequate social relationships, and inability to live independently (Abel and Sokol, 1987, 1991; Koren et al., 2003; Popova et al., 2011b; Thanh and Jonsson, 2009). Therefore, FASD is likely to be a social and economic burden in every society where women drink during pregnancy.

Given this burden, it is unfortunate that little is known about the prevalence of FASD. One review has been published concerning prevalence characteristics of FASD (May et al., 2009) and 2 more systematic literature reviews have been published concerning the prevalence of FASD in child-care settings and correctional systems (Lange et al., 2013; Popova et al., 2011a). However, none of these reviews provides a general overview of FASD epidemiology worldwide. Achieving such an overview is further complicated by the difficulty of diagnosing FASD and the multiple definitions of the spectrum.

Specifically, FASD is an umbrella term used to categorize various diagnostic outcomes caused by prenatal alcohol exposure. The term fetal alcohol syndrome (FAS) is used when the diagnosis is based on different birth defects (craniofacial abnormalities, growth deficiencies, central nervous system [CNS] problems). When there is no growth deficiency present, the term partial fetal alcohol syndrome (pFAS) is used (also known as atypical FAS [aFAS]) (Jones and Smith, 1973; Stratton et al., 1996). In the earlier days of FASD research, a general term of fetal alcohol effects (FAE) was used to indicate a range of deficits related to prenatal alcohol exposure if the criteria of FAS could not be met (Clarren and Smith, 1978). Eventually, because FAE caused too broad an interpretation of the problem for clinicians, more specific diagnostic criteria have been commonly used (Aase, 1994; Aase et al., 1995; Hoyme et al., 2005; Stratton et al., 1996). The spectrum also includes less specific forms where prenatal alcohol exposure causes substantial damage to the body and brain. This can result in a possible diagnosis of alcohol-related birth defects (ARBD; used when there are alcohol-related congenital structural deficits) or alcohol-related neurodevelopmental disorder (ARND; Hoyme et al., 2005).

This variety in diagnostic outcomes necessitates distinguishing the prevalence rates of each outcome separately as well as aggregated. This means that although there are clear indications that FASD forms a considerable burden to society, no clear overview of the problem exists, and obtaining such an overview is complicated by the diagnostic complexity of FASD. Yet, formulating adequate policies and directing practice and prevention efforts requires such an overview. The purpose of the present study is to conduct a comprehensive systematic literature review and meta-analysis to present an overview of the FASD prevalence rates worldwide.

MATERIALS AND METHODS

The PRISMA and MOOSE guidelines were followed (Moher et al., 2009; Stroup et al., 2000). A more detailed description, including decision-making processes, can be found in the review protocol Supporting Information at the Open Science Framework (https://osf.io/cguji).

Ethics Statement

The current study extracted data from online databases where no participation of participants was involved; therefore, it was not necessary to obtain ethical permission.

Search Strategy

A search was conducted in PubMed, PsycINFO, PsycARTICLES, ERIC, CINAHL, EMBASE, and MEDLINE databases up to November 10, 2014 using an extensive query consisting of keywords related to FASD and prevalence (e.g., FASD, pFAS, burden, estimate and epidemiology; for the complete query including wildcards and logical operators, see https://osf.io/cguji). The query was iteratively updated as screeners identified new relevant keywords. This database search was complemented with the ascendancy and descendancy approaches (scanning cited and citing articles for the included publications). We also inspected the publications included in 2 prior review articles (May et al., 2009; Ospina and Dennett, 2013), the latter of which was an unpublished systematic review on the prevalence of FASD, to obtain possible missing articles for the present study. We re-ran the query just before submitting the manuscript in August 2015 (see Fig. 1). Finally, although we attempted to obtain gray literature when it was encountered, eventually, only peer-reviewed articles were included.

Study Selection

The resulting hits were exported and screened by 2 independent screeners in 3 rounds. The first screening round was based on titles only; the second on titles and abstracts; and the third on full-text articles. Three inclusion criteria were used: articles had to be written in English, include human participants, and empirically examine data of FASD prevalence. In each round, screeners tried to eliminate each entry using a system of progressive exclusion criteria, excluding entries using codes described in the screeners' guideline (see https://osf.io/cguji). In the first and second screening rounds, the screeners excluded duplicate entries; animal studies; studies not published in English; or studies that did not involve FASD. In the third screening round, the screeners also excluded articles that were an opinion piece or not a full text article (e.g., conference abstracts) and that did not report empirically acquired prevalence data. All remaining hits were selected for data extraction.

Data Management and Quality Assessment

Different diagnostic guidelines and tools for FASD have been reported. The most commonly reported guidelines are the Institute of Medicine (IOM) diagnostic criteria 1996 (Stratton et al., 1996) and the revised IOM (Hoyme et al., 2005). In order to assess the quality of diagnosis, all studies were scored using IOM 1996 and 2005 criteria checklists (https://osf.io/cguji). Each criterion on the checklist received a score from 1 (low quality) to 4 (high quality) by 1 researcher (SR): (1) if the study did not investigate or report this criterion; (2) if the study investigated this criterion but did not specify how this was done nor which cutoff scores were used; (3) if the study investigated this criterion but used deviant cutoff scores; and (4) if the study investigated this criterion and used the advised cutoff scores. A second researcher (LC) verified these ratings for a randomly selected sample of publications. An interrater reliability for independent measures (Cohen's Kappa) showed an almost perfect agreement of 0.91.

Data Extraction

Extraction forms, source code files for R (R Development Core Team, 2014), were completed using Notepad++. Information was entered by SR through specifying variable values in a template file. Specifically, prevalence, syndrome category (e.g., FAS, ARBD, etc.), geography, descent (native and nonnative, where nonnative populations are descendants of colonizers), year of data collection, sample size, case identification method (active case ascertainment, where researchers collect data in the field, e.g., at schools; passive surveillance, where researchers inspect existing records; or clinic-

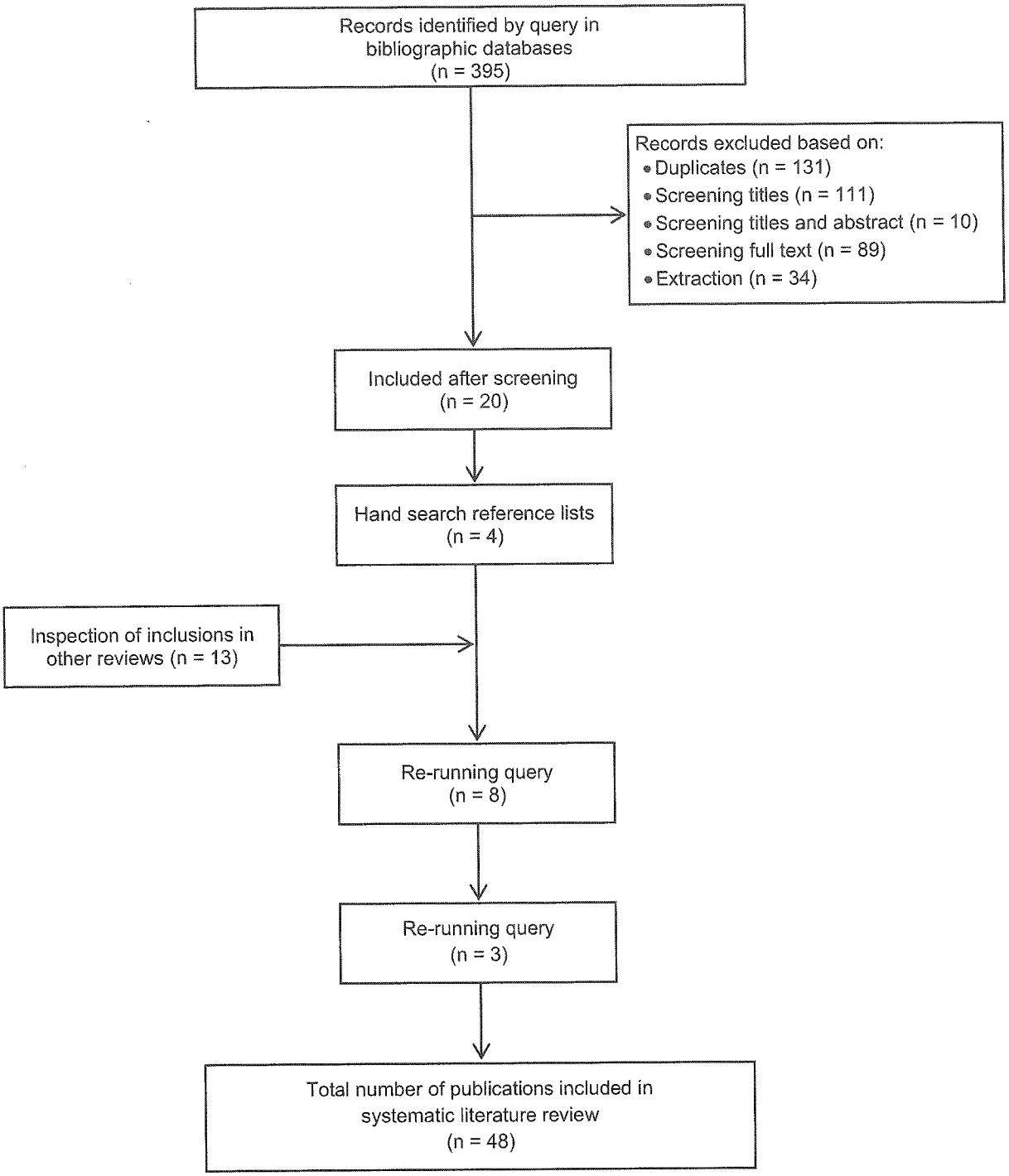

Fig. 1. Flow chart of the selection of studies on prevalence and fetal alcohol spectrum disorder included in the review. Forty-eight articles were retained, representing 166 samples.

based, where researchers examine consenting mother-newborn dyads following childbirth), diagnosis method (e.g., IOM 2005 or 4-digit diagnostic code), and who diagnosed the participants (e.g., a pediatrician or physician) were extracted. Regarding syndrome category, prevalence rates were only considered pertaining to FASD if the original authors labeled it as such, and syndrome categories were reassigned based on IOM 2005 criteria, such that only 5 categories remained (FAS, pFAS, ARND, ARBD, FASD). In addition, the ages of the youngest and oldest participants in each study were extracted, and the range between this start and end age was computed. When the start and end year of the study was not reported, the year of publication was extracted. Moreover, Excel spreadsheets were used to create checklists and overview tables to secure integrity of the extracted data (available at https://osf.io/cguji). The extraction was randomly sampled and verified by a second researcher (GJYP).

All authors of included studies were requested by email to confirm the data used from their publication(s). In case of ambiguity, authors were asked to provide more details. Cases where authors did not respond or could not be contacted, and therefore data interpretation was not straightforward, were resolved through discussion among the research team. Out of 46 contacted authors, 36 responded, of whom 29 could provide the requested information (78%).

Definitions. Because FASD is a birth defect, using the term "incidence" is not appropriate, and "prevalence" is preferred instead (Mason et al., 2005). However, some publications (e.g., Elliott et al., 2008; Habbick et al., 1995; Williams et al., 1998) report incidence nonetheless. In the current review, for all included articles, we have computed the prevalence rather than incidence using equation 3 from Mason and colleagues (2005): prevalence = 10^3 multiplied by the number of cases divided by the total number of live births. We extracted the total number of live births as pertaining to the relevant cohort (e.g., same age range), and verified these computations with the authors.

Statistical Analysis

All completed R source code files ("extraction forms") were then processed by an R script (available at https://osf.io/cguji). This made it easy to perform computations, generate overviews, and, in the case of sufficient homogeneity, conduct meta-analyses and meta-regressions using Metafor, a free R package (Viechtbauer, 2010).

Meta-Analysis. The Freeman–Tukey double arcsine transformation was used to enable meta-analysis. Raw prevalence estimates were transformed so that the data followed an approximately normal distribution (Freeman and Tukey, 1950). Then, multiple meta-analyses were conducted with the transformed proportions using random effects models. These were then back-transformed to prevalence rates to facilitate interpretation of the outcomes and confidence interval (CI) and prediction interval (PI) bounds (Barendregt et al., 2013; note that all reported CIs and PIs are 95% intervals). Heterogeneity was tested using Cochran's Q (Cochran, 1954), and described using the I^2 statistic (Higgins and Thompson, 2002). Although unlikely in the case of prevalence studies, publication bias was assessed by the inspection of Funnel plots. Forest plots were also generated and are available in the Supporting Information (https://osf.io/cguji).

RESULTS

Systematic Literature Review Results

The systematic literature search results are shown in Fig. 1. In total, 48 articles, reporting data from 166 samples, were included (see Table 1). Where the same data were reported in multiple publications, the most complete publication was included for further analysis (see footnotes in Table 1).

Characteristics. The included publications manifested substantial heterogeneity in used methods of sampling and diagnosis. The study characteristics are described below and can be seen in Table 1. The results will be described qualitatively before a number of meta-analyses and meta-regressions are reported.

Sample Characteristics and Methodology. Of the 166 samples, 135 were sampled from the general population (81.3%) and 31 were sampled from suspected high-prevalence subpopulations, such as orphanages (18.7%). Most samples were collected in the United States (83 samples from 17 publications), Australia (23 samples from 7 publications), Canada (17 samples from 8 publications), and South Africa (20 samples from 9 publications). Five samples were collected each in Israel and Italy (described in 1 publication for each country), 4 in Brazil and Sweden each (again, described in 1 publication per country) and Croatia (described in 2 publications), and 1 in New Zealand. In most samples, cases were identified through passive surveillance (e.g., inspection of hospital records; 51.2%, $n = 85$), followed by active case ascertainment (e.g., diagnosing first graders; 41.5%, $n = 69$) and clinic-based studies (e.g., diagnosing 7.2%, $n = 12$) (details available at https://osf.io/cguji).

Many different syndrome categories associated with alcohol use by the mother were reported, sometimes several in 1 publication. The FAS diagnosis was most common (107 samples or 64.5%), followed by pFAS (24 samples or 14.5%), FASD (16 samples or 9.6%), ARND (12 samples or 7.2%), and ARBD (7 samples or 4.2%).

Diagnostic Tools—The included publications used a variety of diagnostic methods (i.e., tools and guidelines). The most commonly used methods were the 1996 IOM guideline, alone (Stratton et al., 1996) or in combination with other methods (Chudley et al., 2005) (48 samples or 28.9%; see the Supporting Information for more details at https://osf.io/cguji) and the revised IOM guidelines (Hoyme et al., 2005) (34 samples or 20.5%). The 4-Diagnostic Digital Code (Astley and Clarren, 2000) was reported in 5 samples (3.0%). Five samples (3.0%) reported the guidelines for describing the impact of prenatal alcohol on the offspring (Sokol and Clarren, 1989). Two samples (1.2%) reported the Canadian guidelines (Chudley et al., 2005). However, many of the publications did not report crucial information for establishing which methods they used (e.g., which cutoffs were employed, or whether maternal drinking was considered; 52 samples or 31.3%; see the Supporting Information at https://osf.io/cguji). A total of 7 samples (4.2%) did not report anything about which diagnostic methods were used.

Diagnostic Providers—Many publications did not specify or report the diagnosis provider (82 samples, 49.4%). When they did, professions were rarely specified sufficiently, and rarely defined. Using the original publication' terminology, physicians[1] were most commonly reported (32 samples, 19.3%), in 4 of these samples in combination with dysmorphologists[1] (2.4%). The second most frequently reported

[1]Please note that the terminology for disciplines can differ between articles. For instance, authors may distinguish disciplines that are not recognized as such in other countries (e.g., dysmorphologist and clinical geneticist).

Table 1. Summary All Included Samples in This Review

References	Study year	Age range (in years)	Country	Sample method	Case ascertainment[a]	Prevalence (*n*/*N* per 1,000 live births)
Fast and colleagues (1999)	1995 to 1996	12 to 18	Canada	Suspected high-prevalence subpopulation	Active case ascertainment	FAS 10.45 (3/287); FAE 223.00 (64/287)
Landgren and colleagues (2010)	1998 to 2002	4.8 to 10.5	Sweden	Suspected high-prevalence subpopulation	Active case ascertainment	FAS 295.77 (21/71); pFAS 140.85 (10/71); ARND 84.51 (6/71); ARBD 112.68 (8/71)
Olivier and colleagues (2013)	2013	4.8 to 16.4	South Africa	Suspected high-prevalence subpopulation	Active case ascertainment	FAS 100.00 (16/160); pFAS 75.00 (12/160)
Rojas and Gretton (2007)	1985 to 2004	12 to 18	Canada	Suspected high-prevalence subpopulation	Active case ascertainment	FASD Aboriginal 656.86 (67/102); FASD Nonaboriginal 634.24 (163/257)
Strömland and colleagues (2014)	2014	0.25 to 14	Brazil	Suspected high-prevalence subpopulation	Active case ascertainment	FAS 31.91 (3/94); pFAS 63.83 (6/94); ARND 74.47 (7/94); FASD 180.85 (17/94)
Tenenbaum and colleagues (2011)	2011	0.04 to 2	Israel	Suspected high-prevalence subpopulation	Active case ascertainment	FAS 0.00 (0/100); pFAS 20.00 (2/100); ARND 0.00 (0/100); ARBD 0.00 (0/100); FAS alcohol not confirmed 20.00 (2/100)
Astley and Clarren (1995)	1993 to 1995	0.2 to 10	United States	Suspected high-prevalence subpopulation	Clinic-based	FAS 139.18 (27/194); aFAS 61.86 (12/194); PFAE 582.47 (113/194)
Astley and colleagues (2002)	1999	0 to 12	United States	Suspected high-prevalence subpopulation	Clinic-based	FAS 10.00 (600/100)
Benoit and colleagues (2002)	1999 to 2001	≤7 to 18	Canada	Suspected high-prevalence subpopulation	Clinic-based	FAS 93.02 (36/387); pFAS 173.13 (67/387); ARND 237.73 (92/387)
Greenbaum and colleagues (2002)	1994 to 1999	4 to 18	Canada	Suspected high-prevalence subpopulation	Clinic-based	ARND 538.46 (28/52)
Habbick and colleagues (1995)	1973 to 1992	6 to 28	Canada	Suspected high-prevalence subpopulation	Clinic-based	FAS 1973 to 1977 = 0.515 (40/(40/(0.515/1,000))) FAS 1978 to 1982 = 0.620(53/(53/(0.620/1,000))) FAS 1983 to 1987 = 0.610 (54/(54/(0.610/1,000))) FAS 1988 to 1992 = 0.589(47/(47/(0.589/1,000)))
Bower and colleagues (2000)	1980 to 1997	*Not reported*	Australia	Suspected high-prevalence subpopulation	Passive surveillance	FAS 0.18 (77/436,148)
Burd and colleagues (1999)	1999	3 to 14	United States	General population	Active case ascertainment	FAS 5.92 (6/1,013)
CDC (2003)	2001	5 to 10	South Africa	General population	Active case ascertainment	FAS 19.28 (16/830)
Chersich and colleagues (2012)	2002 to 2005	0.79 to 0.92	South Africa	General population	Active case ascertainment	FAS 39.56 (32/809); pFAS 49.44 (40/809); FASD 89.00 (72/809)
Clarren and colleagues (2001)	2001	5 to 7	United States	General population	Active case ascertainment	County A: FAS other 4.91 (8/1,630); FAS-aFAS 3.03 (5/1,630); County B: FAS other 5.21 (11/2,110); FAS-aFAS 0.95 (2/2,110)
Elliott and colleagues (2008)	2001 to 2004	0 to 11.9	Australia	General population	Active case ascertainment	FAS 0.45 (25/55,392); pFAS 1.17 (65/55,392); FAS alcohol not confirmed 0.04 (2/55,392)
Fitzpatrick and colleagues (2015)	2010 to 2011	7.5 to 9.6	Australia	General population	Active case ascertainment	FAS 7.87 (1/127); pFAS 94.49 (12/127)
May and colleagues (1983)	1980 to 1982	0 to 14	United States	General population	Active case ascertainment	FAS 2.40 (55/22,963); FAE 1.31 (30/22,963)
May and colleagues (2000)	2000	5 to 7	South Africa	General population	Active case ascertainment	FAS 46.37 (46/992)

Continued.

Table 1. (Continued)

References	Study year	Age range (in years)	Country	Sample method	Case ascertainment[a]	Prevalence (*n*/*N* per 1,000 live births)
May and colleagues (2006)[b]	2006	First graders	Italy	General population	Active case ascertainment	FAS 7.37 (4/543); pFAS 31.31 (17/543); ARND 1.84 (1/543)
May and colleagues (2007)	2005 to 2006	First graders	South Africa	General population	Active case ascertainment	FAS 67.24 (55/818); pFAS 22.00 (18/818)
May and colleagues (2011)	2005 to 2007	First graders	Italy	General population	Active case ascertainment	FAS 8.20 (8/976); pFAS 36.89 (36/976); ARND 1.02 (1/976); ARBD 1.02 (1/976); FASD 47.13 (46/976)
May and colleagues (2013)	2013	First graders	South Africa	General population	Active case ascertainment	FAS 91.03 (68/747); pFAS 69.61 (52/747); ARND 46.85 (35/747); FASD 207.50 (155/747)
May and colleagues (2014)	2010 to 2011	6 to 7	United States	General population	Active case ascertainment	FAS 8.37 (12/1,433); pFAS 16.05 (23/1,433); ARND 9.07 (13/1,433); ARBD 0.00 (0/1,433); FASD 33.50 (48/1,433)
O'Leary and colleagues (2010)	1995 to 1997	<6	Australia	General population	Active case ascertainment	ARBD 10.82 (51/4,714)
Petković and Barišić (2010)	2010	6.6 to 11.1	Croatia	General population	Active case ascertainment	FAS 6.44 (3/466); pFAS 34.33 (16/466)
Petković and Barišić (2013)	2013	7 to 11.9	Croatia	General population	Active case ascertainment	FAS 16.99 (14/824); pFAS 49.76 (41/824)
Poitra and colleagues (2003)	2003	Kindergarten	United States	General population	Active case ascertainment	FAS 4.34 (6/1,384); pFAS 0.72 (1/1,384)
Robinson and colleagues (1987)	1984 to 1985	≤18	Canada	General population	Active case ascertainment	FAS–FAE 189.66 (22/116)
Urban and colleagues (2008)	2001 to 2004	First graders	South Africa	General population	Active case ascertainment	FAS 67.21 (123/1,830); pFAS 20.77 (38/1,830)
Urban and colleagues (2015)	2012 to 2013	First graders	South Africa	General population	Active case ascertainment	FAS 54.97 (83/1,510); pFAS 3.97 (6/1,510); ARND 4.64 (7/1,510); FASD 63.58 (96/1,510)
Viljoen and colleagues (2005)	2005	First graders	South Africa	General population	Active case ascertainment	FAS 74.16 (64/863)
Weiss and colleagues (2004)	1998 to 1999	1.75 to 3.42	United States	General population	Active case ascertainment	FAS 0.23 (13/56,247)
Allen and colleagues (2007)	1995 to 2002	Babies	Australia	General population	Passive surveillance	FAS 0.01 (7/498,016)
CDC (1993), Alaska	1978 to 1991	0 to 19	United States	General population	Passive surveillance	FAS 1978 to 1982 1.97 (19/9,642); FAS 1983 to 1987 2.92 (36/12,311); FAS 1988 to 1991 1.37 (15/10,979)
CDC (1995a), Georgia	1989 to 1992	*Not reported*	United States	General population	Passive surveillance	FAS 0.23 (35/(35/(2.3/10,000)))
CDC (1995c), Indian Health	1981 to 1993	0 to 31	United States	General population	Passive surveillance	FAS 2.74 (52/19,000)
CDC (1995b), US	1979 to 1993	0 to 0	United States	General population	Passive surveillance	FAS 0.22 (2,032/9,434,560)
CDC (1997), Georgia	1981 to 1989	3 to 10	United States	General population	Passive surveillance	FAS 0.10 (29/285,538); pFAS 0.14 (41/285,538)

Continued.

Table 1. (Continued)

References	Study year	Age range (in years)	Country	Sample method	Case ascertainment[a]	Prevalence (*n*/*N* per 1,000 live births)
CDC (2002)	1998 to 2002	1 to 3	United States	General population	Passive surveillance	FAS Alaska, white non-Hispanic = 0.26 (5/19,007); FAS Alaska, black = 0.00 (0/1,341); FAS Alaska, Hispanic = 0.00 (0/1,287); FAS Alaska, Asian/Pacific Islander = 0.00 (0/1,493); FAS Alaska, American Indian/Alaska Native = 5.62 (40/7,117); FAS Alaska, other/unknown = 0.00 (0/39); FAS Arizona, white non-Hispanic = 0.13 (15/114,851); FAS Arizona, black = 0.57 (4/7,054); FAS Arizona, Hispanic = 0.20 (16/80,626); FAS Arizona, Asian/Pacific Islander = 0.23 (1/4,371); FAS Arizona, American Indian/Alaska Native = 2.49 (39/15,685); FAS Arizona, other/unknown = 0.00 (0/456); FAS Colorado, white non-Hispanic = 0.17 (11/63,653); FAS Colorado, black = 0.91 (5/5,508); FAS Colorado, Hispanic = 0.37 (8/21,579); FAS Colorado, Asian/Pacific Islander = 0.00 (0/2,556); FAS Colorado, American Indian/Alaska Native = 0.57 (1/1,744); FAS Colorado, other/unknown = 0.00 (0/96); FAS New York, white non-Hispanic = 0.26 (18/68,932); FAS New York, black = 1.56 (21/13,455); FAS New York, Hispanic = 0.00 (0/3,635); FAS New York, Asian/Pacific Islander = 0.00 (0/1,693); FAS New York, American Indian/Alaska Native = 1.60 (1/627); FAS New York, other/unknown = 0.00 (0/447)
Chávez and colleagues (1988)	1981 to 1986	*Not reported*	United States	General population	Passive surveillance	FAS 0.00 (4,617,613 * 0.926 * 0.093)
Druschel and Fox (2007)[c]	1995 to 1999	*Not reported*	United States	General population	Passive surveillance	FAS Erie, White, non-Hispanic = 0.34 (15/44,200); FAS Monroe, white, non-Hispanic = 0.18 (6/32,807); FAS Erie, black = 3.35 (36/10,731); FAS Monroe, black = 0.41 (4/9,870)
Duimstra and colleagues (1993)[d]	1987 to 1990	*Not reported*	United States	General population	Passive surveillance	FAS 3.91 (4/1,022)
Egeland and colleagues (1998)	1977 to 1992	0 to 16.1	United States	General population	Passive surveillance	FAS Alaska Native, noted, 1977 to 1980 = 2.37 (17/7,160); FAS Alaska Native, cases, 1977 to 1980 = 1.40 (10/7,160); FAS Alaska non-Native, noted, 1977 to 1980 = 0.18 (5/28,092); FAS Alaska non-Native, cases, 1977 to 1980 = 0.07 (2/28,092); FAS Alaska Native, noted, 1981 to 1984 = 5.91(53/8,971); FAS Alaska Native, cases, 1981 to 1984 = 3.79 (34/8,971); FAS Alaska non-Native, noted, 1981 to 1984 = 0.19 (7/37,301); FAS Alaska non-Native, cases, 1981 to 1984 = 0.11 (4/37,301); FAS Alaska Native, noted, 1985 to 1988 = 6.70 (68/10,150); FAS Alaska Native, cases, 1985 to 1988 = 4.14 (42/10,150); FAS Alaska non-Native, noted, 1985 to 1988 = 0.18 (7/38,010); FAS Alaska non-Native, cases, 1985 to 1988 = 0.16 (6/38,010); FAS Alaska Native, noted, 1989 to 1992 = 5.15 (57/11,065); FAS Alaska Native, cases, 1989 to 1992 = 2.53 (28/11,065); FAS Alaska non-Native, noted, 1989 to 1992 = 0.44 (16/36,016); Alaska non-Native, cases, 1989 to 1992 = 0.31 (11/36,016)
Fox and Druschel (2003)[c]	1995 to 1998	<2.0	United States	General population	Passive surveillance	FAS 0.37 (20/54,054)

Continued.

Table 1. (Continued)

References	Study year	Age range (in years)	Country	Sample method	Case ascertainment[a]	Prevalence (*n*/*N* per 1,000 live births)
Fox and colleagues (2015)						FAS Arizona, white non-Hispanic = 0.12 (14/112,784); FAS Arizona, black non-Hispanic = 0.37 (4/10,756); FAS Arizona, Hispanic = 0.10 (12/118,792); FAS Arizona, Asian/Pacific Islander or other non-Hispanic = 0.18 (3/16,607); FAS Arizona, American Indian/Alaska Native non-Hispanic = 1.93 (25/12,956); FAS Colorado, white non-Hispanic = 0.27 (17/62,672); FAS Colorado, black non-Hispanic = 0.48 (3/6,197); FAS Colorado, Hispanic = 0.18 (7/38,617); FAS Colorado, Asian/Pacific Islander or other non-Hispanic = 0.00 (0/9,694); FAS Colorado, American Indian/Alaska Native non-Hispanic = 2.06 (1/485); FAS New York, white non-Hispanic = 0.50 (29/57,753); FAS New York, black non-Hispanic = 1.83 (22/12,014); FAS New York, Hispanic = 0.84 (6/7,155); FAS New York, Asian/Pacific Islander or other non-Hispanic = 0.37 (2/5,478); FAS New York, American Indian/Alaska Native non-Hispanic = 3.82 (2/524)
Harris and Bucens (2003)	1999 to 2000	<2 to 10		General population	Passive surveillance	Nonindigenous FAS 0.00 (0/16,132); pFAS 0.00 (0/16,132); ARND 0.00 (0/16,132); FAS alcohol not confirmed 0.00 (0/16,132); Indigenous FAS 1.87 (17/9,077); pFAS 2.31 (21/9,077); ARND 0.44 (4/9,077); FAS alcohol not confirmed 0.11 (1/9,077)
Leversha and Marks (1995)	1993	<10	New Zealand	General population	Passive surveillance	FAS 0.11 (63/10 *60,000)
Mutch and colleagues (2014)	1980 to 2010	0 to 0		General population	Passive surveillance	FASD Aboriginal, 1980 to 1989 = 2.58 (32/(32/(2.58/1,000))); FASD Aboriginal, 1990 to 1999 = 2.79 (42/(42/(2.79/1,000))); FASD Aboriginal, 2000 to 2010 = 6.12 (114/(114/(6.12/1,000))); FASD Nonaboriginal, 1980 to 1989 = 0.01 (4/(4/(0.01/1,000))); FASD Nonaboriginal, 1990 to 1999 = 0.03 (7/(7/(0.03/1,000))); FASD Nonaboriginal, 2000 to 2010 = 0.04 (11/(11/(0.04/1,000))).
Thanh and colleagues (2013)	2012	0 to 9	Canada	General population	Passive surveillance	FAS 4.20 (5,145/510,300); FASD 32.66 (16,666/510,300); FASD related 28.46 (14,521/510,300)
Williams and colleagues (1998)	1994	2	Canada	General population	Passive surveillance	FAS 6.71 (5/745)

ARBD, alcohol-related birth defects; ARND, alcohol-related neurodevelopmental disorder; aFAS, atypical FAS; FAS, fetal alcohol syndrome; FASD, fetal alcohol spectrum disorders; FAE, fetal alcohol effects.

[a]Case ascertainment methods are categorized according to May and Gossage (2001).

[b]Overlapping cohort with May and colleagues (2011) and will be excluded for further analysis.

[c]Overlapping cohort with CDC (2002) and will be excluded for further analysis.

[d]Overlapping cohort with CDC (1993), Alaska and will be excluded for further analysis.

This table presents the raw prevalence estimates per 1,000 live births. For the column *study year* the period was data collection was mentioned. If this was not available for extraction, the year of publication was reported. For all samples with the notification not reported, the data was not explained and or mentioned in the publication.

diagnosis providers were pediatricians[1] (21 samples, 12.6%), followed by dysmorphologists[1] (13 samples, 7.8%). Clinicians were reported in 3 samples (1.8%). One sample reported that geneticists provided the diagnosis (0.6%), and in 3 samples, diagnosis providers were unclear, and could be either a geneticist or a dysmorphologist[1] (1.8%; note that these are often considered to describe the same profession). Other publications reported that diagnosis was based on case conference including multiple disciplines (11 samples, 6.6%; for details, see https://osf.io/cguji).

Meta-Analyses. The prevalence rates were highly heterogeneous (I^2 ranging from 97.675 for ARBD to 99.997 for FASD, all Qs > 65, all ps < 0.001; note that detailed heterogeneity statistics for every conducted meta-analysis are available in the Supporting Information at https://osf.io/cguji) and therefore both CIs and PIs were reported, conform to the recommendation by Riley and colleagues (2011). First a meta-analysis was conducted using all estimates (i.e., combining estimates from samples from the general population with estimates in suspected high-prevalence subpopulations such as orphanages). As expected, samples from high-prevalence subpopulations yielded significantly and substantially higher prevalence estimates. For example, for FAS, the general population had a PI from 0 to 39.65 per 1,000 births, versus 0 to 805.02 for high-prevalence subpopulations. This is consistent with the fact that estimates from these latter samples are biased upward given that these samples were studied precisely because FAS prevalence was suspected to be particularly high. Therefore, subsequent meta-analyses were conducted only on the general population samples (see https://osf.io/cguji; for interested readers: note that the forest plots presented there show which studies were included in each meta-analysis).

We started by conducting 1 unmoderated meta-analysis per syndrome category to get a global prevalence estimate. Subsequent meta-regressions including all moderators for which sufficient data were available showed that country consistently and strongly contributed to the substantial heterogeneity observed in the global prevalence estimates (see Table 2). Because of these considerable differences in prevalence between countries, we will not discuss the global prevalence estimates further. Instead, we followed up with separate meta-analyses per syndrome category per country (see Table 2), and where possible, we explored whether the remaining heterogeneity was accounted for by other moderators (specifically, descent, case identification method, adherence to IOM 1996 and 2005 criteria, study year, start age, and age range; see Table 3) using bivariate meta-regressions, as very few samples remained for each combination of syndrome category and country. To enable interpreting the effects of these moderators, we conducted meta-analyses per subgroup. For continuous moderators, ad hoc subgroups were created to enable these analyses and thereby facilitate interpretation of the association between the moderators and prevalence. The following subgroups were created. For year of data collection, samples before 1990, between 1990 and 2000, and after 2000 were distinguished. For IOM 1996 and 2005, samples with mean adherence scores between 1 and 2, between 2 and 3, and between 3 and 4 were analyzed. For start age samples that started from birth from those that started later were identified. Finally, for age range, we distinguished studies spanning <5 years from those spanning 5 to 10, 10 to 15, 15 to 20, and more than 20 years. Start age (i.e., the age of the youngest participants in the sample) and age range were correlated (CI [−0.52 to −0.27], $r = -0.41$, $p < 0.001$): samples with a later start age had shorter age ranges.

FAS—For FAS, South Africa showed a particularly high prevalence, with a PI from 18.42 to 110.38 per 1,000 (point estimate 55.42). This lower bound is higher than the upper bounds for the PIs for all other countries, except Canada and Croatia, which reported the next highest prevalence estimates, with PIs ranging from 0 to 398.08 per 1,000 (point estimates of 11.73 and 37.19, respectively). Other countries showed largely overlapping PIs, but with much lower prevalence estimates with point estimates ranging from 0.11 to 8.2 per 1,000. For FAS, there were only sufficient samples available to enable bivariate moderator analysis in Australia, South Africa and the United States (see Table 3). In Australia, although descent was significantly associated to

Table 2. Meta-Regressions for Global and Local FASD Prevalence Estimates

	FAS	pFAS	ARND	ARBD	FASD
Global prevalence	$2.89_{k=94}$ (0 to 39.65)	$11.22_{k=17}$ (0 to 76.12)	$5.19_{k=6}$ (0 to 54.2)	$3.52_{k=5}$ (0 to 17.81)	$22.77_{k=13}$ (0 to 176.77)
Local prevalence					
Australia	$1.33_{k=11}$ (0 to 37.61)	$0.8_{k=3}$ (0 to 6.3)	$0.12_{k=2}$ (0 to 1.76)	$10.82_{k=1}$ (8.05 to 13.99)	$1.06_{k=6}$ (0 to 10.05)
Canada	$37.19_{k=3}$ (0 to 398.08)				$30.52_{k=2}$ (23.81 to 38.04)
Croatia	$11.73_{k=2}$ (1.23 to 31.26)	$43.01_{k=2}$ (25.41 to 64.85)			
Italy	$8.2_{k=1}$ (3.35 to 14.99)	$36.89_{k=1}$ (25.9 to 49.69)	$1.03_{k=1}$ (0 to 4.4)	$1.03_{k=1}$ (0 to 4.4)	$47.13_{k=1}$ (34.66 to 61.38)
New Zealand	$0.11_{k=1}$ (0.08 to 0.13)				$113.22_{k=3}$ (7.04 to 319.21)
South Africa	$55.42_{k=8}$ (18.42 to 110.38)	$28.29_{k=5}$ (0 to 108.22)	$20.25_{k=2}$ (0 to 148.23)		
United States	$0.67_{k=68}$ (0 to 5.44)	$2.22_{k=6}$ (0 to 17.09)	$9.07_{k=1}$ (4.73 to 14.73)	$2.58_{k=3}$ (0 to 15.79)	$33.5_{k=1}$ (24.76 to 43.48)

ARBD, alcohol-related birth defects; ARND, alcohol-related neurodevelopmental disorder; FAS, fetal alcohol syndrome; FASD, fetal alcohol spectrum disorders.

This table represents global FASD prevalence estimates including the associated prediction intervals followed by local FASD prevalence estimates whereby k is the number of samples. Parentheses signify confidence intervals (as opposed to prediction intervals).

Table 3. Multivariate Moderated Meta-Analysis for Global and Local FASD Predictors

	FAS				pFAS				FASD			
	Global[a]	Australia	SA	US	Global[a]	Australia	SA	US	Global[a]	Australia	SA	US
Descent	✗	✓	•	✓	✗	✗	•	✗	✗	✓	•	•
Case identification method	✓	✗	•	✓	✓	✗	•	✗	✓	•	•	•
IOM96	✓	✗	✗	✗	✗	✗	✗	✗	•	•	•	•
IOM05	✗	✗	✗	✗	✗	✗	✗	✗	•	•	•	•
Study year	✗	✓	✗	✗	✓	✗	✗	✗	✓	•	✗	•
Start age	✗	✓	✗	✗	✗	•	•	✗	✗	•	•	•
Age range	✗	✓	✗	✓	✓	✗	•	✗	✗	•	•	•

FAS, fetal alcohol syndrome; FASD, fetal alcohol spectrum disorders; pFAS, partial fetal alcohol syndrome.

[a]This represents a multivariate moderated meta-analysis for FAS and pFAS in comparison to 3 countries as there were too few samples to run analysis; • = too few samples to run analysis or all samples have the same value, ✓ = significant moderator, ✗ = nonsignificant moderator; SA = South Africa, US = United States; IOM95 and IOM05 represent adherence to the Institute of Medicine guidelines in 1996 and the revised guidelines in 2005.

prevalence, the overlapping PIs imply that this difference between the point estimates must be interpreted with caution. For the nonnative population, a prevalence estimate was found to be 0.04 per 1,000, with a PI from 0 to 0.46. For the native population this estimate was higher, with a PI from 0 to 113.79 per 1,000 (point estimate 8.66). Moreover, study year, start age, and age range were also significantly associated to prevalence. Prevalence estimates were highest for studies conducted after the year 2000 (PI from 0 to 158.09 per 1,000, point estimate 9.84), studies including ages starting after the first year of life (PI from 0 to 280.04 per 1,000, point estimate 40.91), and studies employing an age range from 0 to 5 years (PI from 0 to 280.04 per 1,000, point estimate 40.91). For South Africa, none of the moderators was significant. In the United States, descent, case ascertainment, and age range were significantly associated to prevalence, but again, PIs overlapped. For nonnative samples, prevalence was estimated to be 0.06 per 1,000, with a PI from 0 to 1.33. For the native population this estimate was higher, with a PI from 0.7 to 7.64 per 1,000 (point estimate 3.29). The estimated prevalence based on active case ascertainment samples was 3.24 per 1,000, with a PI from 0 to 14.97. For passive surveillance, this was much lower, with a PI from 0 to 4.8 (point estimate 0.54). Finally, prevalence estimates were highest for studies employing an age range from 10 to 15 years, with a PI from 0.02 to 11.32 (point estimate 3.44; note that age range refers to the number of years between the youngest and oldest participants in the sample, not to their ages). Prevalence estimates from studies using other age ranges showed overlapping PIs from 0 to 9.32.

pFAS—For pFAS, South Africa, Croatia, and Italy showed high-prevalence estimates, with PIs from 0 to 108.22 per 1,000 (point estimates between 28.29 and 43.01). Other countries showed largely overlapping PIs, but with much lower prevalence estimates with point estimates ranging from 0.80 to 2.22 per 1,000. For pFAS, there were only sufficient samples available to enable bivariate moderator analysis in Australia, South Africa, and United States. However, none of the moderators was significant (see Table 3).

ARND—For ARND, South Africa showed again a particularly high prevalence, with a PI from 0 to 148.23 per 1,000 (point estimate 20.25). The United States reported the second highest prevalence estimates, with a CI from 4.73 to 14.73 (point estimate 9.07; note that PIs cannot be computed based on 1 sample). Other countries showed largely overlapping PIs, but with much lower prevalence estimates with point estimates ranging from 0.12 to 1.03 per 1,000. For ARND, there were insufficient samples available to enable further moderator analyses.

ARBD—For ARBD, Australia reported the highest prevalence estimate, with a CI from 8.05 to 13.99 (point estimate 10.82). Other countries showed largely overlapping PIs, but with much lower prevalence estimates with point estimates ranging from 1.03 to 2.58 per 1,000. Again, insufficient samples were available to enable further moderator analyses.

FASD—For FASD, South Africa showed again a particularly high prevalence, with a PI from 7.04 to 319.21 per 1,000 (point estimate 113.22). Canada, Italy, and the United States reported overlapping PIs but with much lower prevalence estimates with point estimates ranging from 30.52 to 47.13 per 1,000. Australia showed an exceptionally low prevalence, with a PI from 0 to 10.05 (point estimate 1.06). For FASD, there were only sufficient samples available to enable bivariate moderator analysis in Australia and South Africa (see Table 3). In Australia, descent was significantly associated to prevalence. For the nonnative population a PI was observed from 0 to 0.07 (point estimate 0.02 per 1,000). For the native population this estimate was higher, with a PI from 0.72 to 8.93 per 1,000 (point estimate 3.69).

Publication Bias. Although prevalence reports generally do not involve null hypothesis significance testing and therefore seem less prone to publication bias, we inspected funnel plots nonetheless (these are available at https://osf.io/cguji). For FAS, the funnel plot mainly showed the considerably heterogeneity in reported prevalence, with most samples showing quite low prevalence rates, and some showing

higher prevalence; and although the higher prevalence samples had slightly higher standard errors, these were not clearly associated to prevalence. For pFAS, a clear pattern emerged: samples with lower prevalence estimates had smaller standard errors. Note that the variance of the double arcsine transformed proportion is equal to $1/(4n + 2)$, where n is the total number of individuals in the sample. Therefore, as sample sizes increase, the standard error of the prevalence estimates decreases exponentially. This implies that for pFAS, studies with lower sample sizes report higher prevalence rates. To verify this, we computed the correlation coefficient between sample size and prevalence estimate. The outcome ($r = -0.35$, CI = [−0.74 to 0.22], $p = 0.220$, $n = 13$ samples) was consistent with this hypothesis. The funnel plots for ARND and FASD showed the same pattern, with correlations of −0.43 and −0.35, respectively. In each other syndrome category, the number of samples was too low to warrant inspection of the funnel plots. Overall, there were no clear indications of publication bias.

Confounding. Although publication bias seemed unlikely, analysis of associations between study year, geography, methodology and reported prevalence rates revealed a number of patterns. The cross tables and tests of their significance are available in the Supplementary Materials (https://osf.io/cguji), but the most remarkable patterns will be discussed here. First, most studies were from the United States and Australia, which were the only 2 countries in which most studies used passive rather than active case ascertainment ($\chi^2_{18} = 214.93$, $p < 0.001$). Passive case ascertainment was associated to lower prevalence estimates. Also, for pFAS and FASD, study year was significantly associated to prevalence estimate, with more recent studies reporting higher estimates. Study year was also associated to geography: for example, all South African studies were conducted recently (after 2000; $\chi^2_{18} = 93.23$, $p < 0.001$). More recent studies also employed active case ascertainment more frequently ($\chi^2_4 = 84.39$, $p < 0.001$). These associations make it hard to establish whether higher prevalence estimates were reported as better methods were used or over time.

DISCUSSION

This systematic literature review and meta-analysis revealed that prevalence rates were available for only 10 countries. Prevalence data were sampled from the general population ($n = 135$ or 81.3%) and from suspected high-prevalence subpopulations ($n = 31$ or 18.7%). Prevalence estimates from suspected high-prevalence subpopulations were not included in the meta-analysis as these rates are biased upward given the sample selection. Reported prevalence estimates displayed considerable heterogeneity, which was largely explained by country and descent. In meta-analyses per country, descent, case ascertainment method, and age range also emerged as moderators. On the basis of the findings from studies that sampled in the general population (conducted in Australia, Canada, Croatia, Italy, New Zealand, South Africa, and the United States), the pooled prevalence rates were particularly high in South Africa for FAS (55.42 per 1,000), ARND (20.25 per 1,000), and FASD (113.22 per 1,000). For pFAS high rates were found in Croatia (43.01 per 1,000), Italy (36.89 per 1,000), and South Africa (28.29 per 1,000). In the case of ARBD, a prevalence of 10.82 per 1,000 was found in Australia. Other notable findings were that native populations showed higher prevalence estimates for FAS in Australia and the United States and for FASD in Australia. Moreover, samples based on active case ascertainment showed higher prevalence estimates for FAS in the United States. It is important to note that although some studies report prevalence of a diagnostic category such as ARND, the methodology for obtaining that information is not sufficient to give a true prevalence estimate in that general population as many of these active case ascertainments were focused on identifying FAS-related physical features first and only secondarily identifying neurobehavioral abnormalities (May et al., 2013). Another important conclusion is that there is a high discrepancy in quality of reported diagnosis and poor consensus regarding diagnostic tools used to establish FASD diagnosis.

Limitations

The outcomes of the meta-analyses should be interpreted with caution. Substantial variation was found in the CIs and PIs. This was caused by a high degree of heterogeneity among studies (e.g., varying prevalence rates per country). Prevalence estimates were available for only 10 countries, precluding establishing a global prevalence estimate. Furthermore, a considerable proportion of the included studies used selective sampling in suspected high-prevalence subpopulations, and could therefore not contribute prevalence estimates for the general population. Individual publications showed substantial differences in methodology, and did not always describe their methods in detail. We also observed a marked lack of consensus regarding methods to obtain the FASD diagnosis. For example, although most conformed with the revised IOM criteria (Hoyme et al., 2005) where the FASD spectrum consists of 4 diagnostic categories, the included publications reported in addition different other syndrome categories (e.g., aFAS or FAE). Limited reporting sometimes made identifying and coding the used methodology and diagnostic process challenging. For example, FASD diagnosis were reported but not explained in terms of who made the diagnosis or what cutoff scores were used for diagnosing. Moreover, prevalence rates were reported but often without their denominator. This caused complications in data analysis and interpretation, especially inability to explain heterogeneity sufficiently. Finally, our search strategy was based around combining queries in bibliographic databases with sources included in previous reviews. This means that we did not systematically search for gray literature, which means we may have missed a number of prevalence

studies. Fortunately, because the risk of publication bias is low in prevalence studies, this is unlikely to have biased the results.

Strengths

These limitations may reflect the fact that this is the first comprehensive systematic literature review to examine worldwide FASD prevalence estimates. The comprehensive approach ameliorated the risk of bias as a consequence of the described limitations. First, the iterative query development procedure makes it unlikely that relevant keywords were missed. Second, the systematic, independent screening procedure made erroneous exclusion of publications unlikely, and necessary exclusions were further limited by contacting authors to obtain full text articles when these were not available. Third, the ascendancy and descendancy approaches were applied. Fourth, authors' responses (in combination with their high response rate) show that roughly 80% approved our interpretation of their data. Compared to previous reviews on prevalence estimates of FASD, this is the first study performed so thoroughly and systematically. Another major strength is the combination of qualitative literature review and quantitative meta-analysis and the separations of data per diagnostic outcome of FASD. Finally, the unmoderated meta-analysis followed by meta-regressions including all moderators enabled a better understanding of the observed heterogeneity.

Conclusions and Policy Implications

The present study synthesized current global FASD prevalence rates. Data were only available for a limited number of countries. In some countries the emerging pooled prevalence rates were relatively high (e.g., South Africa), whereas other countries had relatively low rates (e.g., New Zealand). Prevalence estimates were significantly related to various variables such as geography, quality of diagnosis, and age of diagnosis. We offer several recommendations to optimize the degree to which prevalence estimates from different studies can be meaningfully aggregated.

The first recommendation involves sampling methods. Only random sampling from the general population enables establishing prevalence rates for that general population. Studying subpopulations where particularly high prevalence is suspected makes sense in many situations, but not when estimating population prevalence as such studies will lead to overestimates.

The second recommendation involves guidelines for FASD diagnosis. Various guidelines have been used to establish FASD diagnoses, which hinders meta-analysis. In addition to the guidelines reported in the literature so far, the recent inclusion of fetal alcohol exposure in the DSM-5 was accompanied by a novel guideline (American Psychiatric Association, 2013; Sanders, 2013). The negative consequences of prenatal alcohol exposure are described as a diagnosis of neurobehavioral disorder associated with prenatal alcohol exposure (ND-PAE). However, this diagnosis only covers 2 domains namely, CNS dysfunction and confirmation of alcohol exposure. We recommend that future studies use the revised IOM guidelines (Hoyme et al., 2005), as these have been most widely employed so far, thereby maximizing comparability to past data. It remains arguable whether maternal drinking history is required for an FASD diagnosis. It is recommended that maternal drinking history should be obtained whenever possible. Also, underreporting of alcohol consumption is common and therefore evidence-based methods should be considered for detecting prenatal alcohol use (Ernhart et al., 1988; Sarkar et al., 2010). When maternal drinking history is omitted, relevant considerations should be disclosed.

A third recommendation concerns the method of case identification. Each method of case identification has specific advantages and disadvantages (May and Gossage, 2001) and the estimates they provide seem to differ. It is therefore important that method of case identification is reported and taken into account in future meta-analyses. Fourth, we reiterate the recommendation of Mason and colleagues (2005) regarding incidence versus prevalence: as FASD is a birth defect, prevalence estimates are preferred over incidence estimates. In addition, all reports should include not only the estimated prevalence rate, but also the numerator and denominator to enable meta-analysis.

Fifth, it is recommended that every FASD prevalence study report at least the following: (i) sampling method used, and if there was no random sampling from the general population, the considerations to select the chosen subpopulation; (ii) method used to identify FASD cases (active case ascertainment, passive surveillance, or clinic-based); (iii) the recruitment context (e.g., schools, adoption agencies, hospital records); (iv) which professionals were included in the diagnostic team or were consulted; (v) who provided the FASD diagnoses; (vi) which diagnostic guidelines were followed, and if the revised IOM guidelines (Hoyme et al., 2005) were not followed, why not; (vii) which cutoff scores were used in the diagnostic process, and again, if deviating from the IOM guidelines, why; (viii) whether maternal drinking was assessed (and if not, why not; note that diagnosis preferably follows the revised IOM guidelines (Hoyme et al., 2005), considering the confirmation of maternal drinking history when available and reliable); (ix) the ages of the youngest and oldest participants; (x) mean age; (xi) the begin and end year of data collection; (xii) the total number of FASD cases (the numerator in the prevalence formula); and (xiii) the total sample size (the denominator in the prevalence formula).

Future FASD studies will benefit from considering these recommendations and contribute to a better insight in FASD prevalence estimates around the world. There is an urgent need for more prevalence studies, in many more countries, following the same methodology and in any case clearly reporting their used methodology. Nonetheless, the results

from this review make it clear that FASD is an important public health topic with implications for both prevention and clinical management strategies. The present meta-analysis reveals the areas of concerns which is a first step of a needs assessment necessary for planning evidence-based health promotion programs (Bartholomew et al., 2011).

CONTRIBUTORS

Authors SR, GJYP, GK, LC designed the study and directed its implementation, including quality assurance and control. Authors DT and JN helped supervising the field activities. Authors SR and GJYP conducted the literature review and analyses and prepared the Materials and Methods and the Discussion sections of the text. All other co-authors contributed to successive drafts. All authors gave significant input in preparation of the article and approved the manuscript and submission.

FUNDING

This research received no specific grant.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA SHARING STATEMENT

All materials are publicly available (https://osf.io/cguji).

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