Prevalence of Fetal Alcohol Spectrum Disorders in Child Care Settings: A Meta-analysis

abstract

BACKGROUND: Children often enter a child-care system (eg, orphanage, foster care, child welfare system) because of unfavorable circumstances (eg, maternal alcohol and/or drug problems, child abuse/neglect). Such circumstances increase the odds of prenatal alcohol exposure, and thus this population can be regarded as high risk for fetal alcohol spectrum disorders (FASD). The primary objective was to estimate a pooled prevalence for fetal alcohol syndrome (FAS) and FASD in various child-care systems based on data from existing studies that used an active case ascertainment method.

METHODS: A systematic literature review, using multiple electronic bibliographic databases, and meta-analysis of internationally published and unpublished studies that reported the prevalence of FAS and/or FASD in all types of child-care systems were conducted. The pooled prevalence estimates and 95% confidence intervals (CIs) were calculated by using the Mantel-Haenszel method, assuming a random effects model. Sensitivity analyses were performed for studies that used either passive surveillance or mixed methods.

RESULTS: On the basis of studies that used active case ascertainment, the overall pooled prevalence of FAS and FASD among children and youth in the care of a child-care system was calculated to be 6.0% (60 per 1000; 95% CI: 38 to 85 per 1000) and 16.9% (169 per 1000; 95% CI: 109 to 238 per 1000), respectively.

CONCLUSIONS: The results confirm that children and youth housed in or under the guardianship of the wide range of child-care systems constitute a population that is high-risk for FASD. It is imperative that screening be implemented in these at-risk populations. Pediatrics 2013;132:e980–e995

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KEY WORDS

adoption, child-care settings, fetal alcohol spectrum disorder(s), fetal alcohol syndrome, meta-analysis, orphanages, prevalence, systematic literature review

ABBREVIATIONS

ACA—active case ascertainment
ARBD—alcohol-related birth defects
ARND—alcohol-related neurodevelopmental disorder
CI—confidence interval
FAS—fetal alcohol syndrome
FASD—fetal alcohol spectrum disorders
IOM—Institute of Medicine
pFAS—partial fetal alcohol syndrome

Ms Lange contributed to study design and the development of the data collection instruments, performed data collection and extraction, assisted in data interpretation, wrote the first draft of the manuscript and revised the manuscript; Mr Shield performed the statistical analysis, assisted in data interpretation, and contributed to revising the manuscript; Dr Rehm contributed to data interpretation and reviewed and revised the manuscript; Dr Popova led conception and design of the study, led the data collection instruments, led data collection, led data interpretation, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

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Children who come into the care of a child-care system often do so because of unfavorable circumstances, such as parental alcohol and/or drug problems, child abuse and/or neglect, child abandonment, and young maternal age. Such circumstances are likely to increase the odds that a child was exposed to alcohol in utero.1,2

Children and youth in the care of various child-care settings (eg, orphanage, foster care, boarding school, adoption center, or child welfare system) represent a unique population with disproportionately increased rates of developmental disabilities, congenital malformations, and mental health diagnoses.3–7 In addition, children in care have an increased prevalence of social maladjustment6 and greater difficulty forming secure attachment relationships than do home-reared infants.9 Internationally adopted children experience high levels of deprivation before adoption. They tend to be undernourished, receive poor medical care, receive little attention, and lack quality interactions.10 Maternal alcohol abuse has been identified as a main reason for leaving a child in an orphanage.11 Thus, the risk of fetal alcohol spectrum disorders (FASD) in this population is likely to be high. FASD is the non-diagnostic umbrella term used to characterize the full range of damage caused by prenatal alcohol exposure, varying from mild to severe, and encompassing a broad array of physical defects and cognitive, behavioral, emotional, and adaptive functioning deficits. FASD includes the following 4 diagnoses: fetal alcohol syndrome (FAS), partial FAS (pFAS), alcohol-related neurodevelopmental disorder (ARND), and alcohol-related birth defects (ARBD), all of which may include congenital anomalies, such as malformations and dysplasia of the cardiac, skeletal, renal, ocular, auditory, and other systems.

The severity of FASD and its associated disability is a significant and direct predictor of removing children from their birth home and placing them in foster care. For example, Kvigne et al12 compared the outcomes of children with full-blown FAS and pFAS with those without FAS. Among their sample of Northern Plains American Indian children, children with full-blown FAS13 were 64 times more likely to be removed from their homes and children with pFAS were 14 times more likely compared with children without FAS. Furthermore, children with full-blown FAS were 28 times more likely to be placed in foster care and 13.5 times more likely to be placed with their relatives, and children with pFAS were 5 times more likely to be placed in foster care and twice as likely to be placed with relatives compared with children without FAS.

Further attesting to the likely over-representation of FASD in the various child-care systems, Elgen et al14 reported that 21.3% of their Norwegian cohort with FASD,15 referred by pediatric and clinical psychiatry departments, had been adopted, and 66% were in foster care. A Canadian study conducted by Habbick et al16 reported that 8.7% of children with FAS13,17 were in temporary foster care, 23.2% were in permanent foster care, 18.4% were adopted, and 6.3% were residing in a long-term residential placement.

In addition, it appears that the prevalence of FASD in child-care settings, as well as in general, is a self-perpetuating problem; that is to say, women with FASD are likely to drink while pregnant, give birth to a child with FASD, and do not generally maintain custody of their children. In a sample of 415 patients with FASD, 30 females gave birth to a child; of these, 57% no longer had the child in their care, 40% were drinking during pregnancy, 17% had children diagnosed with FASD, and an additional 13% had children who were suspected of having FASD.18

It is clear that children and youth in care represent a significant population with special needs,3–9 and a better understanding of their deficits and impairments is needed to target interventions and provide appropriate services.

As seen from the individual studies in the literature, the prevalence of FASD in various child-care systems is high; however, a systematic overview of the available literature on the prevalence of FASD in existing child-care systems was absent. Therefore, the objectives of the current study were as follows: (1) to perform a comprehensive literature review of studies reporting the prevalence of FAS and FASD in various child-care systems using world literature, (2) to perform a meta-analysis to estimate a pooled prevalence for FAS and FASD as measured by studies using an active case ascertainment (ACA) method (generally considered the most accurate method of measuring the prevalence of FAS and FASD),19,20 and (3) to perform a meta-analysis to estimate a pooled prevalence for FAS and FASD as measured by studies using other methods of ascertainment.

METHODS

The systematic literature review and meta-analysis were conducted and reported according to the standards set out in Preferred Reporting Items for Systematic Reviews and Meta-Analyses21 (PRISMA; http://www.prisma-statement.org).

Search Strategy and Study Selection

A systematic literature search was performed to identify published and unpublished studies that have estimated the prevalence of FAS and/or FASD in various child-care settings. The search included articles in scholarly peer-reviewed journals, conference proceedings, publicly
available unpublished research, government reports, and books.

The search was conducted in multiple electronic bibliographic databases, including: Ovid Medline, PubMed, Embase, Web of Science (including Science Citation Index, Social Sciences Citation Index, Arts and Humanities Citation Index), PsycINFO, ERIC, Episodhost, CINAHL, Campbell Collaboration, the Cochrane Database of Systematic Reviews, CSA Sociological Abstracts, Social Work Abstracts, Canadian Centre on Substance Abuse Library Collection Database, National Institute on Alcohol Abuse and Alcoholism’s Alcohol Alert, Scopus, Centre for Addiction and Mental Health Library Database, and Google Scholar. The search was also conducted by using electronic catalogs available in the countries of the former Soviet Union in the Russian language, including but not limited to Sigla, eLibrary, Journals.medi, Bing, Nigma, Medpoisk, Mednavigator, Medlinks, Medicinskiikatalog, ZdravInform, ConsiliumMedicum, and Infamed. In addition, other Web sites were searched for relevant literature.

The search was conducted by using multiple combinations of the following key words: FASD, FAS, pFAS, ARND, ARBD, fetal alcohol effects, prenatal alcohol exposure, prevalence, incidence, occurrence, frequency, orphanage(s), orphans, foster care, foster homes, group homes, adoptees, adopted children, youth, adoption(s), boarding school(s), (residential) institution(s), residential treatment centers, institutionalized, institutional care, group homes, charity homes, social services, child welfare (system), child-care (systems), baby houses, boarding schools, and children in care.

In addition, manual reviews of the content pages of the major epidemiologic journals and of citations in the relevant articles were conducted. The search was not limited geographically or by language of publication and was conducted up to the end of June 2012.

**Inclusion Criteria**

Articles were retained if they met the following inclusion criteria: (1) consisted of original, quantitative research published in a peer-reviewed journal or unpublished scholarly report; (2) involved a measurement of either FAS or FASD; (3) assessed the prevalence of FAS and/or FASD among children in a child-care setting using an ACA method, passive surveillance, or both; and (4) provided a measure of uncertainty for the prevalence of FAS and/or FASD or provided a count of individuals who were identified as having FAS and/or FASD.

**Quality Criteria**

The minimum quality criteria for inclusion of studies were as follows: (1) cases of FAS and/or FASD were diagnosed and/or documented and (2) the method of surveillance was clearly stated.

**Challenges of “Measuring” FAS and FASD**

Since the first description of FAS by Jones and Smith22 in 1973, the diagnostic guidelines and recommendations have changed numerous times, affecting the prevalence estimates reported in epidemiologic studies over the years. Currently, there are several commonly accepted FASD diagnostic systems: Institute of Medicine (IOM) diagnostic criteria25; University of Washington FASD 4-Digit Diagnostic Code24; Center for Disease Control and Prevention (CDC) FAS Diagnostic guidelines15; Hoyme clarification of the IOM diagnostic criteria26; and the Canadian guidelines for diagnosis.26 Other diagnostic guidelines that have been used in the past include those published by Sokol and Clarren,13 the criteria of the FASD Study Group of the Research Society on Alcoholism,17 and those of Smith’s Recognizable Patterns of Human Malformations27; however, such guidelines are not considered sufficiently specific to ensure diagnostic accuracy.28 The FAS Screen29 has also been used to identify individuals with FAS; however, this is a screening tool and should not be used in replacement of a diagnostic system.

Although the criteria for FASD diagnoses have been described thoroughly in the foregoing guidelines, the diagnosis of FASD is challenging, and the specific assessment techniques used to make the definitive diagnosis are still debated, especially for ARND.30 In addition, the various existing methods of surveillance can produce an apparent discrepancy in the prevalence estimates obtained, with each approach yielding different data sets with its own implications and limitations.19 The 3 main approaches to studying the prevalence of FASD are (1) passive surveillance, (2) clinic-based studies, and (3) ACA. Passive surveillance is the use of existing record collections (eg, birth certificates, special registries, medical charts, adoption records) in a particular geographic catchment area to look for documented or probable cases of FASD. Clinic-based studies are prospectively conducted in prenatal clinics or hospitals. At-risk newborns are identified by screening the biological mothers and are examined and diagnosed if they are shown to have FASD. ACA is an approach in which researchers actively seek, find, and recruit children who may have FASD within a given population. Once identified as possible cases, clinical specialists examine these cases and assess the children for a final diagnosis of FASD. There are also mixed-method approaches, which use 2 of these 3 approaches (usually ACA and passive surveillance). The epidemiologic surveillance methods tend to
provide different prevalence estimates. ACA has been demonstrated to produce the highest prevalence estimates.\textsuperscript{19,20} Furthermore, the measurement of alcohol consumption during pregnancy is difficult and is typically based on maternal self-report; therefore, findings, by nature, may be imprecise due to recall and social desirability biases.

**Data Extraction**

One member of the study team independently extracted the data from the available articles, and a second investigator checked table entries for accuracy against the original articles. All discrepancies were reconciled by team discussion. Data were extracted for the country in which the study took place (as well as for provinces, territories or states, if data were available), year(s) the study took place, the total number of study participants, the age range of the study participants, the gender of the participants (reported as percentage of male participants), the number of FAS cases, the number of FASD cases (inclusive of the 4 FASD diagnoses [FAS, pFAS, ARND, and ARBD]), the prevalence of FAS and/or FASD in the sample population and a measure of uncertainty for this prevalence, the method of case ascertainment used (ie, ACA method and/or passive surveillance), and the percentage of cases of FAS and/or FASD with documented prenatal alcohol exposure.

**Meta-analysis**

The meta-analysis aimed to combine prevalence estimates, and because meta-analyses methods assume that data are normal distributed, a double arcsine transformation was applied to the prevalence data so that the data followed a normal distribution.\textsuperscript{31} The double arcsine-transformed prevalence estimates were weighted by the inverse variance of the double arcsine-transformed prevalence. The pooled prevalence estimates were calculated separately for each method of surveillance used, as well as for all methods of surveillance combined, using the Mantel-Haenszel method, assuming a random effects model.\textsuperscript{32} Heterogeneity between studies was assessed using the Cochrane $Q$ test and the $I^2$ statistic.\textsuperscript{33,34} Results of the meta-analysis were displayed using a Forest plot.

Publication bias (the possibility that studies that measured the prevalence of FAS and/or FASD were not published because their results differed greatly from previous estimations) was tested by visually inspecting a funnel plot for a skewed distribution. Publication bias in studies measuring FAS and/or FASD was deemed by the authors to be unlikely because an observed prevalence of FAS and/or FASD that was substantially different than had previously been estimated would likely be published. The funnel plots presented are scatter plots of the double arcsine-transformed prevalence estimates from individual studies plotted against the SE of the double arcsine-transformed prevalence estimates. The larger, most powerful studies that provided the most precise transformed prevalence estimates are plotted at the top of the funnel plot, and the smaller, less powerful studies that provided the least precise transformed prevalence estimates are plotted at the bottom. If random effects are not present, the spread of the estimates narrows as the studies become more powerful (ie, the transformed prevalence estimates have a narrower spread for the more powerful studies compared with the studies with the least power). Thus, under the central limit theorem, in the absence of unequal bias, and between study heterogeneity, the funnel plot will resemble a symmetrical inverted funnel centered on the summary estimate (with the sides of the triangle defined by extending the SE multiplied by 1.96). Additionally, 95% of the study estimates should fall within the pseudo 95% confidence intervals (CI) if heterogeneity across studies is large (the study estimates are assumed to have a fixed effect). See the Discussion for additional explanations of why study estimates (when plotted in a funnel plot) may not form a funnel shape. Publication bias was also assessed using a ranked correlation test,\textsuperscript{35} and by using a weighted regression test.\textsuperscript{36} The trim and fill method was then used to adjust for potential publication bias.\textsuperscript{37} Furthermore, the stability of the results and the influence of studies were tested using a leave-one-study-out sensitivity analysis.\textsuperscript{38}

All analyses were performed using Stata version 11.0.\textsuperscript{39}

**RESULTS**

**Characteristics of the Included Studies**

Initially, the electronic searches yielded 534 publications regarding the prevalence of FAS and/or FASD in various child-care settings; 251 duplicate articles were removed. Seventeen additional articles were identified through manual review of the content pages of the major epidemiologic journals and of citations in the relevant articles, and 300 articles were screened using titles and abstracts. Sixty-nine full-text articles were retrieved for additional consideration. Thirty-four articles (representing 33 studies) contained relevant data and were selected for data extraction. A schematic diagram of the search strategy is depicted in Fig 1.

Data on the prevalence of FAS and/or FASD in child-care systems were available from only 8 countries, as follows: Brazil (1 study),\textsuperscript{40} Chile (2 studies),\textsuperscript{41,42} Canada (3 studies),\textsuperscript{43,44} Israel (1 study),\textsuperscript{45} Russia (10 studies),\textsuperscript{46–55} Spain (1 study),\textsuperscript{56} Sweden (3 studies),\textsuperscript{57–59} and...
One study reported on the prevalence of FAS among preadoption children from Eastern Europe (Romania, Ukraine, Moldova). 71 Twenty-seven articles were published in English, 4 articles were published in Russian, and 3 articles were published in Spanish. In the identified studies, the prevalence of FAS and/or FASD was reported for the following 6 major settings: boarding schools, child welfare agencies, foster care, homes for children with mental deficiencies, orphanages, and mixed-care setting. A boarding school is a school in which some or all students study and live during the school year; children in boarding schools remain in the custody of their parents. Child welfare agencies, foster care, and adoption agencies all fall under child protection services, a set of usually government-run services designed to protect children and young people who are underage. An orphanage can be defined as a public institution created to provide care and protection for children without parents. Fourteen studies reported the prevalence of FAS and/or FASD among adoptees, and the 19 remaining studies reported the prevalence of FAS and/or FASD among preadoptees.

The prevalence of FAS and/or FASD also varied greatly depending on the child-care setting in which the study was conducted. The prevalence of FAS and/or FASD was observed among children in the child welfare system in the United States (5.3 per 1000) 61 whereas the highest FAS prevalence was reported among

FIGURE 1
Flow diagram depicting the search strategy. Thirty-four articles were retained, representing 33 studies. PS, passive surveillance. Country Codes: BRA, Brazil; CHL, Chile; CAN, Canada; EUR, Eastern Europe; ESP, Spain; ISR, Israel; MDA, Moldova; ROU, Romania; RUS, Russia; SWE, Sweden; UKR, Ukraine; USA, United States of America.

The United States (USA; 11 studies60–70). One study reported on the prevalence of FAS among preadooption children from Eastern Europe (Romania, Ukraine, Moldova). 71 Twenty-seven articles were published in English, 4 articles were published in Russian, and 3 articles were published in Spanish. In the identified studies, the prevalence of FAS and/or FASD was reported for the following 6 major settings: boarding schools, child welfare agencies, foster care, homes for children with mental deficiencies, orphanages, and mixed-care setting. A boarding school is a school in which some or all students study and live during the school year; children in boarding schools remain in the custody of their parents. Child welfare agencies, foster care, and adoption agencies all fall under child protection services, a set of usually government-run services designed to protect children and young people who are underage. An orphanage can be defined as a public institution created to provide care and protection for children without parents. Fourteen studies reported the prevalence of FAS and/or FASD among adoptees, and the 19 remaining studies reported the prevalence of FAS and/or FASD among preadoptees.

Of the 33 studies analyzed, 27 reported the age of the children and youth included in their study. The overall age range was 0 to 20 years. Twenty-three of the studies reported the gender distribution of the children and youth included in their respective samples, which ranged from 31% to 67% male (the study by Miller and Hendrie62 is excluded from this reported range because 98% of their sample was female). Less than half of the studies (ie, 15) reported the percentage of individuals with documented prenatal alcohol exposure, which ranged from 8% to 100%. The 2 countries with the highest reported prevalence of FAS among children and youth in child-care settings were Russia54,55 and Sweden,58 427 to 680 per 1000 (orphanage for children with special needs) and 296 per 1000 (adoptees from Eastern Europe), respectively, whereas Eastern Europe71 (preadoption children from Romania, Ukraine, Moldova) and the United States62 (adoptees from China) had a reported prevalence for FAS of 0 per 1000. As with FAS, the 2 countries with the highest reported prevalence of FASD among children and youth in child-care settings were Russia47 and Sweden,58 397 per 1000 (orphanage) and 521 per 1000 (adoptees from Eastern Europe), respectively, and 40 per 1000 was reported for Israel45 (foster care and preadoption children) and the United States64,68 (adoptees from Eastern Europe).

It is important to note that in all instances in which the sample is made up of adoptees, the country in which the study was based was not the country of origin for the sample (ie, the children sampled were born in a different country and adopted into the country in which the study was conducted). The prevalence of FAS and/or FASD also varied greatly depending on the child-care setting in which the study was conducted. The lowest FAS prevalence was observed among children in the child welfare system in the United States (5.3 per 1000) 61 whereas the highest FAS prevalence was reported among...
children residing in an orphanage for children with special needs in Russia (680 per 1000)\(^{54,55}\). Two studies reported 0 cases of FAS among their samples drawn from orphanages and foster care in Eastern Europe\(^{71}\) and adoptees from China\(^{62}\) respectively. The prevalence of FASD was the lowest among foster and preadoptive children in Israel\(^{60}\) and adoptees from Eastern Europe\(^{58}\) (40 per 1000) and was the highest among adoptees in Sweden from Eastern Europe\(^{62}\) (521 per 1000).

The included studies used different methods of case ascertainment. ACA was used in 18 studies (55%), the passive method was used in 8 studies (24%), and a mixed-methods approach (both ACA and passive surveillance) was used in 7 studies (21%).

Of the studies that used an ACA approach (ie, those that used ACA solely, as well as those that used a mixed-methods approach), 10 studies\(^{40–42,49–51,62,64,69–71}\) did not report the system used for diagnosing FAS and/or FASD. Of those studies that did report the diagnostic system used, 7 studies\(^{44,56–58,71}\) used the 4-Digit Diagnostic Code\(^{24}\), 2 studies\(^{48,58}\) used the IOM diagnostic criteria\(^{25}\), 2 studies\(^{37,68}\) used the CDC FAS Guidelines\(^{15}\), 1 study\(^{66}\) used the FASD Study Group criteria\(^{17}\), and 1 study\(^{63}\) used the Smith's Recognizable Patterns of Human Malformations\(^{27}\). One study\(^{45}\) used a modified version of the IOM diagnostic criteria\(^{25}\) in combination with a modified version of the Canadian Guidelines\(^{26}\) and 1 study\(^{62}\) used a modified version of the 4-Digit Diagnostic Code\(^{24}\) along with the FAS Screen\(^{29}\).

Table 1 presents the data extracted from the examined studies.

**Pooled Prevalence Meta-analysis**

The pooled prevalence estimates of FAS and FASD among children and youth in various child-care settings by method of case ascertainment are presented in Table 2 (the estimates obtained from Legon'kova\(^{54}\) and Pal'chik and Legon'kova\(^{45}\) were excluded from the meta-analysis because no sample size or SE was provided and thus, the uncertainty of these estimates could not be ascertained).

The random effects analysis of the 16 studies that used an ACA methodology indicated an overall pooled prevalence of 6.0% (60 per 1000; 95% CI: 38 to 85 per 1000) for FAS. Figure 2 depicts the Forest plot for the meta-analysis of the double arcsine-transformed prevalence of FAS with the studies presented in the order they appear in Table 1. The boxes in the Forest plot represent the point estimate of the double arcsine-transformed prevalence from each study and the bars that extend from these estimates are the 95% CIs. In the Forest plot, the size of the box is proportional to the weight given to each study when the combined estimate (represented as a diamond) was calculated. Tests demonstrate that heterogeneity in these estimates was present ($Q_{16} = 305.99, P = .000; \hat{\tau}^2 = 95.1%, P = .000$) for the pooled analysis of double arcsine of FAS. The funnel plot (see Fig 3) of all FAS studies that used ACA formed a random scatter plot; because random effects were present, the funnel plot could be used to determine if publication bias was present (because the assumption of a fixed effect was not proven).\(^{72}\) Additionally, the Begg rank correlation test\(^{35} (P = .685)$ and the Egger weighted regression test\(^{36} (P = .401)$ both indicated that publication bias was not present; however, this finding may be due to studies exceeding the pseudo 95% CI (see funnel plot). The trim and fill analysis\(^{37}$ indicated that a small study effect was not present and did not need to be adjusted for.

The pooled prevalence for FASD was 19.8% (198 per 1000; 95% CI: 135 to 270 per 1000) when the 10 studies that used an ACA methodology were summarized. Figure 4 depicts the Forest plot for the meta-analysis of the double arcsine-transformed prevalence estimates of FASD with the studies presented in the order they appear in Table 1. Tests demonstrate that heterogeneity in these estimates was present ($Q_{18} = 216.58, P = .000; \hat{\tau}^2 = 95.8%, P = .000$) for the pooled analysis of double arcsine of FASD. The funnel plot (see Fig 5) of all FASD studies that used ACA formed a random scatter plots; because random effects were present, the funnel plot could be used to determine if publication bias was present (because the assumption of a fixed effect was not proven).\(^{72}\) Additionally, the Begg rank correlation test\(^{35} (P = .419)$ and the Egger weighted regression test\(^{36} (P = .460)$ indicated that publication bias was not present; however, the trim and fill analysis indicated publication bias was present. When corrected for publication bias using a trim and fill method (using a random effects model), the prevalence of FASD was estimated to be 16.9% (189 per 1000; 95% CI: 109 to 238 per 1000). To be conservative, publication bias was corrected for.

The pooled prevalence for FAS was 3.3% (33 per 1000; 95% CI: 5 to 101 per 1000) and the pooled prevalence for FASD was 6.3% (63 per 1000; 95% CI: 15 to 136 per 1000) when a summary of the studies using passive surveillance was completed. The pooled analysis of the studies that used a mixed-methods approach to case ascertainment indicated a pooled prevalence of 5.1% (51 per 1000; 95% CI: 1 to 341 per 1000) for FAS and 7.2% (72 per 1000; 95% CI: 6 to 186 per 1000) for FASD. Publication bias was not observed for the prevalence of FAS or FASD when pooling the studies that used a passive surveillance approach or a mixed-methods approach.

The pooled analysis of all studies combined indicated a pooled prevalence...
<table>
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<th>Country (province, territory or state, if available)</th>
<th>Reference</th>
<th>Study year(s)</th>
<th>Total Sample Size</th>
<th>Age (range)</th>
<th>Gender (% male)</th>
<th>Type of Institution/ Country of Origin for Adoptees</th>
<th>Case Ascertainment Method</th>
<th>Diagnostic System Used</th>
<th>Number of FAS Cases</th>
<th>Prevalence of FAS (per 1000)</th>
<th>Number of FASD Cases</th>
<th>Prevalence of FASD (per 1000)</th>
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<td>EUR (ROU 73%, UKR 22%, MDA 5%)</td>
<td>Diamond et al48</td>
<td>1999–2001</td>
<td>82</td>
<td>2 mo to 4 y</td>
<td>51</td>
<td>Preadoption—orphans (84.1%) and foster care (15.9%)</td>
<td>ACA</td>
<td>Not specified</td>
<td>0</td>
<td>0</td>
<td>n/a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISR</td>
<td>Tenenbaum et al49</td>
<td>n/a</td>
<td>100</td>
<td>0.5 mo–2 y</td>
<td>42</td>
<td>Preadoption and foster care</td>
<td>ACA</td>
<td>IOM diagnostic criteria25 with modif. based on the Canadian guidelines26</td>
<td>2</td>
<td>20</td>
<td>4</td>
<td>40</td>
<td>8%</td>
</tr>
<tr>
<td>RUS</td>
<td>Aronson46</td>
<td>1994–1997</td>
<td>131</td>
<td>n/a</td>
<td>n/a</td>
<td>Preadoption—orphans</td>
<td>ACA and PS</td>
<td>Criteria defined by the FASOSG of the Society on Alcoholism</td>
<td>2</td>
<td>15</td>
<td>n/a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RUS, Ekaterinburg</td>
<td>Bubnov47</td>
<td>2005–2009</td>
<td>445</td>
<td>0–4 y</td>
<td>n/a</td>
<td>Orphanage</td>
<td>ACA</td>
<td>CDC FAS diagnostic guidelines17</td>
<td>67</td>
<td>151</td>
<td>177</td>
<td>397</td>
<td>n/a</td>
</tr>
<tr>
<td>RUS, Moscow</td>
<td>Warren et al50</td>
<td>n/a</td>
<td>184</td>
<td>8.5–17 y</td>
<td>67</td>
<td>Boarding schools and orphanage</td>
<td>ACA</td>
<td>IOM diagnostic criteria25</td>
<td>26</td>
<td>141.3</td>
<td>n/a</td>
<td></td>
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<td>Country (province, territory or state, if available)</td>
<td>Reference</td>
<td>Study year(s)</td>
<td>Total Sample Size</td>
<td>Age (range)</td>
<td>Gender (% male)</td>
<td>Type of Institution/ Country of Origin for Adoptees</td>
<td>Case Ascertainment Method</td>
<td>Diagnostic System Used</td>
<td>Number of FAS Cases</td>
<td>Prevalence of FAS (per 1000)</td>
<td>Number of FASD Cases</td>
<td>Prevalence of FASD (per 1000)</td>
<td>% of Sample With Documented PAE</td>
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<tr>
<td>RUS, Moscow</td>
<td>Riley et al&lt;sup&gt;39&lt;/sup&gt; (see Mattson et al)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1999</td>
<td>2352</td>
<td>n/a</td>
<td>n/a</td>
<td>Boarding schools and orphanages for children with mental deficiencies</td>
<td>ACA</td>
<td>Not specified</td>
<td>186</td>
<td>79.1</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>RUS, Moscow</td>
<td>Konovalova et al&lt;sup&gt;40&lt;/sup&gt;; Marintcheva et al&lt;sup&gt;41&lt;/sup&gt;</td>
<td>n/a</td>
<td>3675</td>
<td>7–17 y</td>
<td>n/a</td>
<td>41 institutions (boarding schools with special needs programs for those with mental deficiencies, regular and special needs orphanages, and schools of the social welfare system)</td>
<td>ACA</td>
<td>Not specified</td>
<td>320</td>
<td>87</td>
<td>557</td>
<td>152</td>
<td>n/a</td>
</tr>
<tr>
<td>RUS, Murmansk</td>
<td>Miller et al&lt;sup&gt;42&lt;/sup&gt;</td>
<td>n/a</td>
<td>234</td>
<td>1.5 mo–6 y</td>
<td>52</td>
<td>Orphanages (&quot;baby homes&quot;)</td>
<td>ACA</td>
<td>Modified 4-Digit Diagnostic Code&lt;sup&gt;24&lt;/sup&gt; and FAS Screen&lt;sup&gt;29&lt;/sup&gt;</td>
<td>17</td>
<td>72.7 &quot;alcohol fetopathy&quot;</td>
<td>40%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RUS, St. Petersburg</td>
<td>The St. Petersburg: USA Orphanage Research Team&lt;sup&gt;33&lt;/sup&gt;</td>
<td>2004–2005</td>
<td>193</td>
<td>0–6 y</td>
<td>54</td>
<td>Orphanages</td>
<td>PS</td>
<td>Not specified</td>
<td>9–10</td>
<td>46.6–51.8</td>
<td>39%</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>RUS, St. Petersburg</td>
<td>Miller et al&lt;sup&gt;11&lt;/sup&gt;</td>
<td>1997–2002</td>
<td>1167</td>
<td>n/a</td>
<td>n/a</td>
<td>Orphanages</td>
<td>PS</td>
<td>Not specified</td>
<td>112</td>
<td>96</td>
<td>n/a</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>RUS, St. Petersburg</td>
<td>Legon'kova&lt;sup&gt;54&lt;/sup&gt;; Pal'chik and Legon'kova&lt;sup&gt;53&lt;/sup&gt;</td>
<td>2000–2009</td>
<td>n/a</td>
<td>0–7 y</td>
<td>n/a</td>
<td>Orphanages for children with neuropsychological disabilities</td>
<td>ACA and PS</td>
<td>4-Digit Diagnostic Code&lt;sup&gt;24&lt;/sup&gt;</td>
<td>n/a</td>
<td>46–55</td>
<td>n/a</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>RUS, St. Petersburg</td>
<td>Legon'kova&lt;sup&gt;54&lt;/sup&gt;; Pal'chik and Legon'kova&lt;sup&gt;53&lt;/sup&gt;</td>
<td>2006–2009</td>
<td>n/a</td>
<td>0–7 y</td>
<td>n/a</td>
<td>Orphanages for children with physical and mental delays</td>
<td>ACA and PS</td>
<td>4-Digit Diagnostic Code&lt;sup&gt;24&lt;/sup&gt;</td>
<td>n/a</td>
<td>427–680</td>
<td>n/a</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>SWE</td>
<td>Landgren et al&lt;sup&gt;57&lt;/sup&gt;</td>
<td>n/a (adopted: 1993–1997)</td>
<td>76</td>
<td>5 mo–7 y</td>
<td>58</td>
<td>Adoptees from EUR (POL 57%, RUS 30%,</td>
<td>PS</td>
<td>Not specified</td>
<td>4</td>
<td>32.6</td>
<td>29%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> FAS = fetal alcohol syndrome; FASD = fetal alcohol spectrum disorder; PAE = prenatal alcohol exposure; EUR = Europe; POL = Poland; RUS = Russia; SWE = Sweden; USA = United States; PS = Psychiatric Symptoms; ACA = Adoption Case Analysis; n/a = not available.
<table>
<thead>
<tr>
<th>Country (province, territory or state)</th>
<th>Reference</th>
<th>Study year(s)</th>
<th>Total Sample Size</th>
<th>Age (range)</th>
<th>Gender (% male)</th>
<th>Type of Institution/Country of Origin for Adoptees</th>
<th>Case Ascertainment Method</th>
<th>Diagnostic System Used</th>
<th>Number of FAS Cases</th>
<th>Prevalence of FAS (per 1000)</th>
<th>Number of FASD Cases</th>
<th>Prevalence of FASD (per 1000)</th>
<th>% of Sample With Documented PAE</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWE</td>
<td>Landgren et al(^{58,e})</td>
<td>n/a 6 y after adoption</td>
<td>71</td>
<td>4.8–10.5 y</td>
<td>56</td>
<td>Adoptees from EUR (EST, LVA, POI, ROU, RUS)</td>
<td>ACA</td>
<td>IOM diagnostic criteria(^{25})</td>
<td>21</td>
<td>295.8</td>
<td>37</td>
<td>521</td>
<td>34% (probable)</td>
</tr>
<tr>
<td>SWE</td>
<td>Grönlund et al(^{59,e})</td>
<td>n/a 6 y after adoption</td>
<td>72</td>
<td>4.8–10.5 y</td>
<td>57</td>
<td>Adoptees from EUR (EST, LVA, POI, ROU, RUS)</td>
<td>ACA and PS</td>
<td>4-Digit Diagnostic Code(^{24})</td>
<td>15</td>
<td>208.3</td>
<td>80%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA, Washington State</td>
<td>Astley et al(^{60})</td>
<td>1999–2001</td>
<td>600</td>
<td>0.6–15.3 y</td>
<td>52</td>
<td>Foster care</td>
<td>ACA</td>
<td>Smith's Recognizable Pattern's of Human Malformations(^{27})</td>
<td>6–9</td>
<td>10–15</td>
<td>15%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>Ringeisen et al(^{61})</td>
<td>1999–2000</td>
<td>5496</td>
<td>0–14 y</td>
<td>50</td>
<td>Child welfare system</td>
<td>PS</td>
<td>Not specified</td>
<td>29</td>
<td>5.3</td>
<td>n/a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>Miller and Hendrie(^{62})</td>
<td>1991–1998</td>
<td>452</td>
<td>2 mo–12.4 y</td>
<td>2</td>
<td>Adoptees from CHN</td>
<td>ACA</td>
<td>Not specified</td>
<td>0</td>
<td>0</td>
<td>n/a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>Albers et al(^{63})</td>
<td>1991–1995</td>
<td>56</td>
<td>2.5 mo–9 y</td>
<td>46</td>
<td>Adoptees from EUR (ALB 7%, BGR 2%, KAZ 2%, LVA 2%, MDA 12%, POL 2%, RUS 64%, UKR 9%)</td>
<td>ACA</td>
<td>Not specified</td>
<td>1</td>
<td>17.9</td>
<td>11%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>Miller et al(^{64})</td>
<td>n/a</td>
<td>50</td>
<td>8–11 y</td>
<td>52</td>
<td>Adoptees from EUR (BGR 2%, EST 6%, LVA 2%, MDA 6%, ROU 29%, RUS 52%, UKR 8%)</td>
<td>ACA and PS</td>
<td>Not specified</td>
<td>2</td>
<td>40</td>
<td>n/a</td>
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<tr>
<td>USA</td>
<td>McGuinness et al(^{65})</td>
<td>1997</td>
<td>105</td>
<td>6–9 y</td>
<td>48</td>
<td>Adoptees from EUR (SUN)</td>
<td>PS</td>
<td>Not specified</td>
<td>7</td>
<td>66.7</td>
<td>41%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>Miller et al(^{66})</td>
<td>1988–2004</td>
<td>103</td>
<td>n/a</td>
<td>53</td>
<td>Adoptees from GTM (orphanage, foster care, mixed-care settings)</td>
<td>ACA and PS</td>
<td>4-Digit Diagnostic Code(^{24})</td>
<td>19</td>
<td>184.5</td>
<td>n/a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>Johnson et al(^{67})</td>
<td>n/a</td>
<td>252</td>
<td>0–103 y</td>
<td>n/a</td>
<td>Adoptees from EUR (BLG 2%, POI 1%, ROU 4%, RUS 76%, other SUN countries 17%)</td>
<td>PS</td>
<td>Not specified</td>
<td>6</td>
<td>25.8</td>
<td>17%</td>
<td></td>
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<tr>
<td>USA</td>
<td>Loman et al(^{68})</td>
<td>n/a</td>
<td>200</td>
<td>8–11 y</td>
<td>46.5</td>
<td>Adoptees (post-institutionalized and foster care) from EUR 21%, BGR 25%,</td>
<td>ACA and PS</td>
<td>CDC FAS diagnostic guidelines(^{15})</td>
<td>8</td>
<td>40</td>
<td>n/a</td>
<td></td>
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<tr>
<td>Country (province, territory or state, if available)</td>
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<td>Study year(s)</td>
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<td>Prevalence of FAS (per 1000)</td>
<td>Number of FASD Cases</td>
<td>Prevalence of FASD (per 1000)</td>
<td>% of Sample With Documented PAE</td>
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<tr>
<td>USA</td>
<td>Miller et al&lt;sup&gt;60&lt;/sup&gt;</td>
<td>2004–2007</td>
<td>138</td>
<td>7.5 mo–5 y</td>
<td>51</td>
<td>Adoptees from Eastern Europe</td>
<td>ACA</td>
<td>Not specified</td>
<td>10</td>
<td>75.8</td>
<td>n/a</td>
<td>3.4</td>
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<tr>
<td>USA</td>
<td>Farina et al&lt;sup&gt;70&lt;/sup&gt;</td>
<td>n/a</td>
<td>29</td>
<td>16 mo–7.5 y</td>
<td>48</td>
<td>Adoptees from Russia</td>
<td>ACA</td>
<td>Not specified</td>
<td>10</td>
<td>344.8</td>
<td>n/a</td>
<td>3.4</td>
<td></td>
</tr>
</tbody>
</table>

Moldova, MDA 0.5%, POL 0.5%, RUS 0.5%, RUS 5%, South America 21.5% (BOL 0.5%, BRA 1%, COL 9%, ECU 1%, GTM 8.5%, PRY 1%, SSV 0.5%), Asia 57% (CHN 11.5%, IND 7.5%, KHM 0.5%, KOR 34.5%, PHI 15%, VNM 1.5%), Africa 0.5% (ETH 0.5%).

Table 1 Continued

CDC, Centers for Disease Control and Prevention; modif., modifications; n/a, not available; PAE, Prenatal Alcohol Exposure; PI, postinstitutionalized; PS, passive surveillance; Country Codes: ALB, Albania; BGR, Bulgaria; BLR, Belarus; BOL, Bolivia; BRA, Brazil; CAN, Canada; CHL, Chile; CHN, China; COL, Colombia; ECU, Ecuador; ESP, Spain; EST, Estonia; ETH, Ethiopia; EUR, Eastern Europe; GEO, Georgia; GTM, Guatemala; IND, India; ISR, Israel; KAZ, Kazakhstan; KHM, Cambodia; KOR, Korea; LTU, Lithuania; LVA, Latvia; MDA, Moldova; PHI, Philippines; POL, Poland; PRY, Paraguay; ROU, Romania; RUS, Russia; SVK, El Salvador; SUN, Former Soviet Union; SWE, Sweden; SK, Slovakia; UKR, Ukraine; USA, United States of America; VNM, Vietnam; YUG, Yugoslavia.

<sup>a</sup> Country of birth. The first column indicates the country into which the children have been adopted (the country where the study was based).

<sup>b</sup> For whom data were available.

<sup>c</sup> Konolova et al<sup>50</sup> and Marintcheva et al<sup>51</sup> were published in iteration.

<sup>d</sup> Legon'kova<sup>54</sup> and Pačík and Legon'kova<sup>55</sup> were published in iteration.

<sup>e</sup> Grönlund et al<sup>59</sup> and Landgren et al<sup>57,58</sup> are reporting on the same sample of individuals.
The prevalence of FAS in child-care settings (60 per 1000) was found to be ∼9 to 60 times higher than the prevalence of FAS in the general population of North America, for example, which is reported to range from 2 to 7 cases per 1000 individuals in the United States20 and 1 per 1000 in Canada.73

The pooled prevalence of FASD in child-care settings (169 per 1000, based on studies that used ACA), was found to be ∼17 to 19 times higher than the prevalence of FASD in the general population.

### DISCUSSION

This study revealed that the vast majority of existing studies report that the prevalence of FAS and FASD in child-care settings in various countries is extremely high. On the basis of the findings of studies using ACA, the prevalence of FAS in child-care settings (60 per 1000) was found to be ∼9 to 60 times higher than the prevalence of FAS in the general population of North America, for example, which is reported to range from 2 to 7 cases per 1000 individuals in the United States20 and 1 per 1000 in Canada.73

The pooled prevalence of FASD in child-care settings (169 per 1000, based on studies that used ACA), was found to be ∼17 to 19 times higher than the prevalence of FASD in the general population.
of North America, which is reported to be 9 to 10 per 1000 individuals.\textsuperscript{19,74} It is important to note, however, that the prevalence obtained from orphanages for children with physical and mental delays in Russia was the highest among all studies (42.7\%-68.0\%)\textsuperscript{54,55}; if it were feasible to include these 2 studies in the analysis of studies using a mixed-method approach, the estimated pooled FAS prevalence would be much higher.

This study is limited by the poor performance of the trim and fill method in instances in which there is substantial between-study heterogeneity.\textsuperscript{75,76} Additionally, the funnel plots assume that unequal bias and random effects are not present among the studies being examined. The funnel plots (for the FAS and FASD meta-analyses) had an excess number of estimates exceeding the pseudo 95\% confidence limits, indicating that the measures used in the meta-analyses either arose from different populations; had data irregularities (biases), such as location biases (eg, language bias); were subject to selective outcome reporting and/or poor methodologic design; or arose by chance.\textsuperscript{77}

![Funnel plot of the 16 studies that measured the prevalence of FAS using ACA methods used in the meta-analysis with pseudo 95\% CIs.](image1)

![Forest plot of the 10 studies that reported the prevalence of children and youth with FASD in care of the various child-care settings using ACA. The size of the box around the point estimate is representative of the weight of the estimate used in calculating the aggregated point estimate. Weights are from random effects analysis.](image2)
Given that ACA is recognized as the method from which a more rigorous and valid estimate of the prevalence of FAS and FASD would be obtained compared with passive and clinic-based methods, these estimates as determined by ACA have been highlighted here as the most important findings.

The observed differences in the prevalence reported among the various child-care settings, as well as between studies, are notable. Unfortunately, it cannot be definitively stated as to why these differences exist; however, it could be the result of the systems of care in each country. For instance, in the United Kingdom, when children become a ward of the state, they will be placed in foster care, yet if they display behavioral disorders, they will be placed in a group home. As such, one would expect to see more cases of FASD in the latter setting.

Another possible reason for the observed differences is that they could be due to the diagnostic system (or combination of systems) used in each of the studies. Each diagnostic system is likely to affect the reported prevalence; the direction of this effect depends on the sensitivity and specificity of the diagnostic systems themselves.

Individuals housed under the guardianship of the wide range of child-care systems clearly constitute a population that is at high-risk for prenatal alcohol exposure and FASD. Screening for FASD in this high-risk population is necessary to facilitate early diagnosis. In general, early FASD diagnosis can improve the quality of life of children with FASD by facilitating timely interventions and reducing the odds of developing secondary disabilities (eg, school failure and dropout, mental health problems, addictions, trouble with the law, incarceration). Early diagnosis and providing an appropriate environment improves outcomes and decreases the risk for secondary disabilities by up to fourfold.

Specifically, in the context of child-care settings, early FASD diagnosis can (1) help establish appropriate placements, (2) allow foster/adoptive parents to be better prepared to meet their child’s needs and improve parenting by increasing their understanding of the deficits and behavioral problems displayed by individuals with FASD, (3) reduce the likelihood of multiple failed placements, and (4) increase awareness and understanding of both caregivers and caseworkers of the consequences of prenatal alcohol exposure.

FASD is not widely recognized by health care practitioners and, as such, is underdiagnosed. This has been attributed predominantly to a lack of training of health care practitioners; however, lack of time, as well as the idea that a diagnosis will not make a difference for the individual have also been noted as barriers to FASD diagnosis. Efforts need to be made to increase the capacity of primary care pediatricians and physicians all over the world with regard to FASD recognition and diagnosis. This will not only raise awareness of FASD in general but will also raise awareness of the severe consequences of prenatal alcohol exposure and, it is hoped, prevent subsequent alcohol-exposed pregnancies.

Given that prenatal alcohol exposure increases an exposed child’s risk of chronic physical, developmental, behavioral, and/or emotional conditions, children and youth prenatally exposed to alcohol have special health care needs, and such needs place demands on the health care system that far exceed those of non-alcohol-exposed children. Thus, continuous, lifelong developmental and behavioral surveillance of such prenatally alcohol-exposed children and youth should be provided by their primary health care provider to facilitate their ongoing treatment and referral needs.

It is important to point out that having a known history of prenatal alcohol exposure can have a significant impact on whether a child is diagnosed with FASD (with the exception of FAS, which can be diagnosed without confirmation of prenatal alcohol exposure); this can pose a significant problem in the diagnosis of the current population of at-risk individuals because this information is commonly unavailable or unverifiable. With regard to the
current study, the availability of the prenatal history can have a significant impact on reported prevalences, especially when case ascertainment is passive.

It should be noted that the findings of the current study are not generalizable to the general population of the respective countries because individuals housed under the guardianship of the wide range of child-care systems are at a higher risk of prenatal alcohol exposure and FASD.

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Prevalence of Fetal Alcohol Spectrum Disorders in Child Care Settings: A Meta-analysis
Shannon Lange, Kevin Shield, Jürgen Rehm and Svetlana Popova
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