r

INSTITUTE OF HEALTH ECONOMICS
ALBERTA CANADA

SYSTEMATIC REVIEW ON THE PREVALENCE OF FETAL ALCOHOL SPECTRUM DISORDERS

MARIA OSPINA, MSC, PHD (C)

LIZ DENNETT, MLIS

Edmonton, April 2013

ACKNOWLEDGEMENTS

We thank Dr. Bing Guo for her assistance with title study selection and risk of bias assessments and Ms. Debra Hass and Ms. Janelle Prytula for their assistance with article retrieval.

COMPETING INTEREST

Competing interest is considered to be financial interest, either direct or indirect, that would be affected by the research contained in this report, or creation of a situation where an author's and/or external reviewer's judgment could be unduly influenced by a secondary interest such as personal advancement.

Based on the statement above, no competing interest exists with the author(s) of this report.

Production of this document has been made possible by a financial contribution from Alberta Health. The views expressed herein do not necessary represent the official policy of Alberta Health.

ABSTRACT

Background

Fetal alcohol spectrum disorders (FASD) constitutes a national public health problem with serious education, social and economic implications for society as those affected suffer a lifelong disability and may need lifelong support. An understanding of the epidemiological aspects of FASD may provide essential knowledge to map the burden of the condition in a variety of settings and populations.

Objectives

To conduct a systematic review and meta-analysis of the existing research-based evidence on the prevalence of FASD in a variety of settings (community, schools, foster care system, correctional systems and specialized care).

Methods

Electronic searches in biomedical electronic databases were conducted from database inception to December 2012. In addition, reference lists of reviews and retrieved articles, scientific meeting proceedings, government documents, theses and dissertations were sought to identify additional studies. Included in the review were primary studies assessing the prevalence of FASD, fetal alcohol syndrome (FAS), partial fetal alcohol syndrome (pFAS), alcohol-related neurodevelopmental disorders (ARND) or alcohol-related birth defects (ARBD) in children, youth or adult populations in communities, schools, foster care or correctional systems. Studies must have reported numeric data to enable the calculation of prevalence rates for the conditions of interest. Whenever possible (i.e., in absence of statistical heterogeneity across the studies), meta-analyses of the prevalence of FASD were conducted separately for each FASD category (i.e., FAS, pFAS, ARND, ARBD, and FASD-overall, including composite definitions of the condition).

Results

The literature searches identified a total of 1872 citations. After screening and applying the eligibility criteria, 54 unique studies were included in the review. The majority of studies have been conducted between 1980 and 2012, with most of them published in peer-reviewed journals.

The majority of studies on FASD prevalence have been conducted in North America and Europe. Countries that individually accounted for the largest number of studies were the USA (15 studies) and South Africa (12 studies). Nine studies assessing the prevalence of FASD in Canada were identified in this review.

Seven studies evaluated the prevalence of the entire FASD spectrum as a whole, whereas 18 studies evaluated the prevalence of FASD as a composite of certain subtypes (e.g., FAS plus pFAS; FAS plus ARND and ARBD). Among the different FASD subtypes, estimates of FAS prevalence were reported in the vast majority of the studies (46 studies) followed by pFAS (19 studies), ARND (10 studies) and ARBD (four studies) prevalences.

Substantial heterogeneity in FASD prevalence estimates were identified across the studies included in the review. Some of the variations in prevalence across the studies can be attributed to many factors, including differences in the methods of case ascertainment and diagnostic criteria, study

participants' age, and methodological characteristics of the studies, among others. Variation in prevalence are also likely to reflect true variations in different geographic and or sub populations.

Prevalence of FASD in the community. Studies assessing the prevalence of FASD in community and population-based samples reported estimates that ranged from 0.02% to 0.5% which translate to FASD rates of 0.2 to 5 per 1000 population. Prevalence estimates were substantially heterogeneous for FAS (0.0006% to 0.3%), as the studies used different methods for case identification that included birth certificates and medical chart review (which reported the lowest prevalence rates) as well as active case ascertainment methods. Similar heterogeneity was identified for pFAS (0.0006% to 0.3%) and both ARND and ARBD estimates (1.08% and 0.37%).

Prevalence of FASD in schools. Results of this review found wide variations in the rate of overall FASD in studies conducted in school settings, ranging from 0.5% to 10.7%. Meta-analyses of the prevalence of specific FASD subtypes provided more reliable information after controlling for potential sources of heterogeneity. A meta-analysis of FAS studies excluding those conducted in South Africa (which are recognized for reporting systematically higher rates of FASD in a region with one of the highest rates of alcohol consumption per capita in the world) yielded a pooled estimate of 0.36% which translates to a rate of 3.6 per 1000 population. The pooled prevalence of pFAS in school settings was higher after adjusting for inadequate sampling strategies: 2.9%, which translates to a rate of 29 per 1000 population. The pooled prevalence of ARND was calculated in 0.23%, for a rate of 2.3 per 1000 population.

Prevalence of FASD among children in foster care. Prevalence estimates of overall FASD in foster care settings ranged from 30.5% to 52%, which translate to FASD rates of 305 to 520 per 1000 population in foster care settings. For FAS alone, a meta-analysis of studies using formal diagnostic criteria for case identification showed that approximately 21% of children in foster care are likely to have the condition. Prevalence estimates for other subtypes such as pFAS, ARND and ARB were also high, ranging from 2% to 14% depending on the methods of diagnosis and case ascertainment.

Prevalence of FASD in prisons and correctional facilities. Estimates of FASD prevalence in correctional systems were derived from studies conducted in Canada and the USA with numbers ranging between 9.8% and 23.3%. More reliable data using active case ascertainment strategies yielded estimates of 1.04% for FAS, 10% for pFAS and 4.1 to 8.7% for ARND.

Prevalence of FASD in Aboriginal populations. Prevalence estimates of overall FASD in Aboriginal populations varied greatly according to the setting in which the studies were conducted. The majority of studies that assessed FASD prevalence in Aboriginal peoples were conducted in Canada. FASD prevalence estimates were higher among Aboriginal youth in correctional facilities (26.9%) and lower in community samples (0.17%). A pooled estimate of FAS prevalence in Aboriginal peoples was calculated in 0.2% (95% CI: 0.1, 0.3, six studies) for a rate of 2 FAS cases per 1000 population, which is not substantially higher than those identified in community samples of the general population. Estimates from two studies on pFAS in Aboriginal populations ranged from 0.13% to 3.9%. Prevalence of ARND in Aboriginal peoples in one study reported a rate of 0.02% (relative to the total population), which translates to a rate of 0.2 per 1000 live births.

Prevalence of FASD in other specialized settings. Composite estimates of FASD in special education settings ranged from 2.1% to 8.8%. A meta-analysis of the prevalence of FAS among children in special education yielded a pooled FAS prevalence rate of 4.9% (95% CI: 2.5, 7.3), whereas the prevalence of pFAS among children attending special education schools was 5.4%.

Conclusions

FASD prevalence rates have been evaluated in a variety of settings including the community, schools, foster care systems, prisons and correctional systems. The magnitude of FASD prevalence vary according to the setting in which it was evaluated, with higher estimates identified in foster and justice systems compared to those obtained from community and school samples. All of them, however, deserve attention for the planning and organization of prevention strategies. The epidemiology of FASD does not seem to be isolated into a specific region and impacts many communities around the world. There is a need for continued good quality research on the prevalence of FASD to provide a basis for health policy and resource allocation for prevention initiatives and clinical and social services.

ABBREVIATIONS

AEP = alcohol exposed pregnancy

ARND = alcohol-related neurodevelopmental disorder

ARBD = alcohol-related birth defects

ASI = Addiction Severity Index

CDC = Center for Disease Control

CI = confidence interval

FAS = fetal alcohol syndrome

FASD = fetal alcohol spectrum disorder

ICD-9 = International Classification of Diseases, 9th Revision

IOM = Institute of Medicine

IQR = interquartile range

NA = not applicable

NOS = New Castle Ottawa Scales

NR = not reported

pFAS = partial fetal alcohol syndrome

USA = United States of America

yr = year(s)

GLOSSARY

Allocation: The process by which an individual is assigned to an intervention or a control group in a randomized controlled trial. Ideally, the investigators should not know which comparison group individual patients have been placed into.

Bias: Defined as a systematic deviation from the truth. In studies, it refers to systematic errors in measurement or assessment that cause either an overestimation or underestimation of the results.

Blinding: A strategy used in research in which people involved in a study (whether researchers, participants, or other person) are prevented from knowing certain information about the study process. Blinding is a basic tool to prevent conscious as well as subconscious bias in research that can be introduced by knowing which intervention group the participants belong to.

Cochrane Q: A common test for heterogeneity that assumes the null hypothesis that all the apparent variability between individual study results is due to chance. Cochrane Q generates a probability, presented as a *P* value, based on a X^2 distribution, that between-study differences in results equal to or greater than those observed are likely to occur simply by chance.

Confidence interval (CI): A statistical term for the range of values that includes the true value (usually a mean, proportion, relative risk, or odds ratio) of the unknown quantity being measured. The interval is usually quantified as either 90% or 95% to represent the degree of confidence. In

general, a higher degree of confidence will require a larger interval. CIs are smaller when estimates are based on larger sample sizes.

Cross-sectional study: A type of observational design in which exposure and outcome are determined simultaneously for each subject. It is often described as taking a "snapshot" of a group of individuals.

Fetal Alcohol Spectrum Disorders: It is the term used to describe the range of harms that can result from prenatal alcohol exposure, including vision and hearing problems, as well as slow growth and brain damage that result in lifelong problems with attention, memory, reasoning, and judgment.

I^2 statistic: The I^2 statistic is a test of heterogeneity that describe the proportion of variation in prevalence estimates that is due to genuine variation in prevalence rather than sampling error. I^2 can be calculated from Cochrane *Q* (the most commonly used heterogeneity statistic) according to the formula: I^2 = 100% × (Cochrane *Q* – degrees of freedom) / Cochran *Q*. Any negative values of I^2 are considered equal to 0, so that the range of I^2 values is between 0% and 100% (I^2 less than 25 percent = small; I^2 between 26 and 74 percent = moderate; 75 percent and above = high).

Meta-analysis: The combination of quantitative evidence from a number of studies.

Methodological quality: The extent to which the design and conduct of a study are likely to have prevented systematic errors (bias). Variation in quality can explain variation in the results of studies included in a systematic review. More rigorously designed (better 'quality') studies are more likely to yield results that are closer to the 'truth'.

P value (e.g. $P < 0.05$): A statistical term for the probability that the results of a particular study (e.g. an observed mean difference) could have been produced by chance in the absence of a real difference. By scientific convention, P values of <0.05 or <0.01 indicate a low probability that the difference is by chance and are used by scientists as a guideline for determining when an observed difference can be considered real.

Prospective cohort study: A type of observational design in which a group of participants (a cohort) that have been exposed to a characteristic of interest are followed over a period of time to asses outcomes. They are longitudinal and go forward over time.

Retrospective analytical cohort study: A type of observational design in which a group of participants (a cohort) is assembled based on his previous exposure to a characteristic of interest. They are longitudinal and go backward over time.

Statistical significance: The likelihood that a finding or a result is caused by something other than just chance.

Systematic review: Summaries of research evidence that address a clearly formulated question using systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyze data from the studies that are included in the review.

TABLE OF CONTENTS

INTRODUCTION

Fetal alcohol spectrum disorder (FASD) is an umbrella term that refers to a spectrum or range of clinical conditions associated with prenatal alcohol exposure.[1] Four types of FASD have been described (Table 1) that are characterized by prenatal and postnatal growth retardation, a unique cluster of facial anomalies, and central nervous system impairments (neurological, cognitive, and behavioural).[2]

Table 1: Fetal alcohol spectrum disorder subtypes

Subtypes	Description
Fetal alcohol syndrome (FAS)	Diagnostic classification for individuals who were prenatally exposed to alcohol and who present with growth deficiency, with height or weight below the 10th percentile, facial characteristics (e.g., small eyes, smooth philtrum, and thin upper lip), central nervous system damage (structural, neurological, and/or functional impairment)
Partial Fetal Alcohol Syndrome (pFAS)	Diagnostic classification for individuals who were prenatally exposed to alcohol and who present with some but not all of the physiological symptoms of full FAS
Alcohol-Related Neurodevelopmental Disorder (ARND)	Diagnostic classification for individuals who were prenatally exposed to alcohol, have symptoms of central nervous system damage associated with FAS but do not present the facial features typical of FAS
Alcohol-Related Birth Defects (ARBD)	Diagnostic classification for individuals who were prenatally exposed to alcohol and who have physical defects such as malformations of the heart, bone, kidney, vision, or hearing systems

FASD results from maternal alcohol use during pregnancy.[3] It is one of the leading causes of birth defects and developmental disabilities in Canadian children, along with spina bifida and Down syndrome,[4,5] and is the only one of the three that is considered to be largely preventable.[6,7]

FASD constitutes a national public health problem with serious education, social, and economic implications for society as those affected suffer a lifelong disability and may need lifelong support. An understanding of the epidemiological aspects of FASD may provide essential knowledge to map the burden of the condition in a variety of settings and populations. This information is crucial as it helps to inform public policy and planning resource allocation to alleviate its social impact, particularly for populations in which the burden of the condition is high.

In past decades, investigators from all regions of the world have made substantial efforts to determine the prevalence of FASD. Several literature reviews have reported highly variable rates of FASD depending on the setting in which the condition has been evaluated: community, schools,[8] correctional systems,[9] and those conducted in populations traditionally considered at a high risk of developing the condition (i.e., Aboriginal populations.[10] The reasons for variability in FASD prevalence rates across studies remain poorly understood. Factors related to differences in FASD case definition and diagnostic methods, as well as geographical and population factors have been hypothesized as sources of variability across the estimates.

Previous systematic reviews on the prevalence of FASD have been mainly descriptive and have not included a quantitative synthesis of the evidence or explored potential sources of heterogeneity in FASD prevalence estimates across the studies.

With these considerations in mind, the aim of this study was to conduct a systematic review and meta-analysis of the scientific literature on the prevalence of FASD in a variety of populations and settings. Through a strict methodological approach, the review provides FASD prevalence information that can help to inform policy makers regarding the allocation of health services for FASD.

OBJECTIVE

1. To conduct a systematic review and meta-analysis of the existing research-based evidence on the prevalence of FASD in a variety of settings (community, schools, foster care system, correctional systems and specialized care).
2. To examine a variety of factors that may be implicated in the heterogeneity of FASD prevalence estimates.

METHODOLOGICAL APPROACH

Literature Searches

Electronic searches in biomedical electronic databases listed in Table 2 were conducted from database inception to December 2012 with no date limits applied. The search strategy was designed by one of the IHE Research Librarians and comprised of both subject headings and keywords relating to FASD and prevalence of the condition (See Appendix A for detailed search strings). In addition, reference lists of reviews and retrieved articles were checked for relevant studies. Scientific meeting proceedings, government documents, theses and dissertations were sought to identify unpublished studies. Language restrictions were not imposed in the searches.

Table 2: Electronic databases searched for relevant studies

Database	Years/issues searched	Date of search
MEDLINE (Ovid Interface)	1946-2012	Dec 5, 2012
Embase (Ovid Interface)	1974-2012	Dec 5, 2012
PsycINFO (Ovid interface)	1806 – 2012	Dec 5, 2012
CINAHL (EBSCO interface)	1937-2012	Dec 5, 2012
SocINDEX (EBSCO interface)	1908-2012	Dec 5, 2012
Criminal Justice Abstracts (EBSCO interface)	1968-2012	Dec 5, 2012
Sociological Abstracts (Proquest interface)	1952-2012	Dec 5, 2012
Social Services Abstracts (Proquest interface)	1979-2012	Dec 5, 2012
ABI/Inform Global (Proquest interface)	1970-2012	Dec 5, 2012
British Humanities Index (Proquest interface)	1962-2012	Dec 5, 2012
Canadian Research Index (Proquest interface)	1982-2012	Dec 5, 2012
CBCA Complete (Proquest interface)	1971-2012	Dec 5, 2012

CBCA Fulltext Education (Proquest interface)	1977-2012	Dec 5, 2012
CBCA Reference and Current Events (Proquest interface)	1982-2012	Dec 5, 2012
Dissertations and Theses (Proquest interface)	1861-2012	Dec 5, 2012
ERIC (Proquest interface)	1966-2012	Dec 5, 2012
National Criminal Justice Reference Service (Proquest interface)	1970-2012	Dec 5, 2012
Web of Science (ISI Interface Licensed Resource)	1899-2012	Dec 5, 2012

Criteria for Selection of Studies

For inclusion in the systematic review, primary studies were to use cross-sectional or cohort (prospective or retrospective) designs to assess the prevalence of FASD, FAS, pFAS, ARND or ARBD in children, youth, or adult populations. The studies were to assess the prevalence of the condition in communities, schools, foster care, or correctional systems. Studies must have reported numeric data to enable the calculation of prevalence rates for the conditions of interest. Studies that used denominator data from other studies for calculating prevalence rates were not considered for inclusion. Studies were not excluded on the basis of language of publication. Table 3 summarizes the eligibility criteria for the review.

Table 3: Criteria for inclusion of studies in the review

Category	Criteria
Population	Children, youth, adults (no restrictions by age)
Condition	FASD, FAS, pFAS, ARND, ARBD
Study design	Cross-sectional studies, prospective and retrospective cohort studies
Outcomes of interest	Prevalence rates
Study settings	Community, schools (for regular and special education), foster care system/orphanages, prisions/correctional facilities,
Source	Scientific literature. Peer-reviewed studies, conference abstracts, government reports, thesis/dissertations

Two reviewers independently screened the titles and abstracts generated from the search strategies to identify potentially relevant articles. The full text of papers deemed relevant and of those whose abstracts and titles provided insufficient information were retrieved for a closer inspection by two independent reviewers who determined study eligibility for the review. Studies that did not satisfy the selection criteria at this stage were excluded and the reasons for exclusion were documented. Disagreements about inclusion and exclusion of studies were resolved through discussions among reviewers until consensus was reached. Multiple publications were not considered to be unique studies and any information that they provided was incorporated to the information reported in the main study.

Evaluation of the Methodological Quality of the Studies

The review approach to methodological quality focused on assessing the internal validity of the individual studies, which is defined as the extent to which study design, conduction, and reporting prevent or reduce bias in the results.

Two quality assessment tools were used in this systematic review: study quality of cross-sectional studies was assessed with an eight-items rating system developed by Loney et al.[11] that evaluated the methods of sampling, sampling frame, sample size, outcome measurement, outcome assessment, response rate, statistical reporting, and interpretation of study results. Each item is assigned a score of one or zero points to generate an overall single quality score that ranges from zero to eight (the maximum score possible). Loney quality ratings from one to three points indicate poor quality, ratings between four and six points are considered as of moderate quality and those between seven to eight indicate high methodological quality.[11]

The methodological quality of cohort studies was assessed with the Newcastle-Ottawa Scales (NOS),[12] an eight-item instrument that evaluates the methods of participants' selection, the comparability between cohorts, and outcomes ascertainment. Overall, NOS quality scores range from zero to nine (zero to four points = poor quality; five to seven points = moderate quality; and eight to nine points = high quality).[12]

An individual components approach based on study susceptibility to bias was adopted to report the results of the methodological quality assessment rather than reporting the overall quality scores only.[13] Two reviewers independently assessed study quality, with disagreements resolved by consensus.

Data Collection

One reviewer extracted information from included studies onto a pretested data extraction form and double-entered it for accuracy and completion. The following information was extracted from individual studies, where possible: country of first author, publication year, country where the study was conducted, study design, geographical location (i.e., rural, urban, mixed), study settings (i.e., community, schools, foster care/orphanages, prison/correctional facilities, other), sample size, average age, case ascertainment method/diagnostic sequence and diagnostic criteria. Similarly, information on the number of individuals diagnosed with FASD, FAS, pFAS, ARND and ARBD was obtained.

Data Analysis and Synthesis of Results

Key details of the included studies (article's source, study design and methods, study population characteristics, diagnostic criteria, and prevalence rates) were presented in evidence tables sorted by study setting and then by first author and year of publication (Appendix 2.C). Characteristics of the individual studies were presented in a narrative way to describe the populations, settings and case definitions for which the prevalence estimates apply.

Meta-analysis of prevalence data. Unadjusted prevalence estimates of FASD, FAS, pFAS, ARND, ARBD (number of cases/sample size) were re-calculated along with standard errors and study variance based on the information on crude numerators and denominators provided in the individual studies. Prevalence estimates were obtained from studies conducted in community settings, schools, foster care, prisons, and correctional facilities. Similarly, prevalence estimates obtained from special populations (e.g., Aboriginal, special education groups) were also calculated.

Meta-analyses of the prevalence of FASD were conducted separately for each FASD category (i.e., FAS, pFAS, ARND, ARBD, and FASD-overall, including broad definitions of the condition). For all meta-analyses, individual studies were weighted (w) by the inverse of its variance. Weighted prevalence estimates were obtained by multiplying each prevalence rate by the study weight under a single effect model. Prevalence estimates for each individual study were reported with 95% confidence intervals (95% CI) around these estimates. Forest plots were used to visualize the data

and examine the extent of heterogeneity among the studies. Statistical heterogeneity across the studies was evaluated using the Cochran's Q test under the null hypothesis that the true prevalences were identical in every study. Statistical heterogeneity was indicated by a p-value less than 0.05 for the Cochran's Q test.[14]

Since heterogeneity was expected a priori, a measure of the degree of inconsistency across the studies, the I^2 statistic,[14] was calculated to describe the proportion of variation in prevalence estimates that was due to genuine variation in prevalences rather than sampling error. Consistency of prevalence estimates across the studies was characterized as small (I^2 less than 25 percent), moderate (I^2 between 26 and 74 percent) and high (75 percent and above).[14]

If statistical heterogeneity was low, meta-analysis of prevalence estimates was conducted using a random-effects model[15] assuming that the different studies are estimating different, yet related prevalence estimates.

Methodological and clinical characteristics (e.g., participant characteristics, country where studies were conducted, methods of case ascertainment and diagnosis criteria) were explored qualitatively as potential sources of heterogeneity. Where appropriate, sensitivity analyses by study quality and subgroup analysis based on relevant sources of heterogeneity were conducted.

Finally, pooled prevalence rates were expressed as number of cases per 1000 people in the population, when appropriate.

Study selection, methodological quality assessment, and data extraction were managed with Microsoft® Excel® 2008 for Mac, Version 12.1.5 (Microsoft Corporation, Redmond, WA).

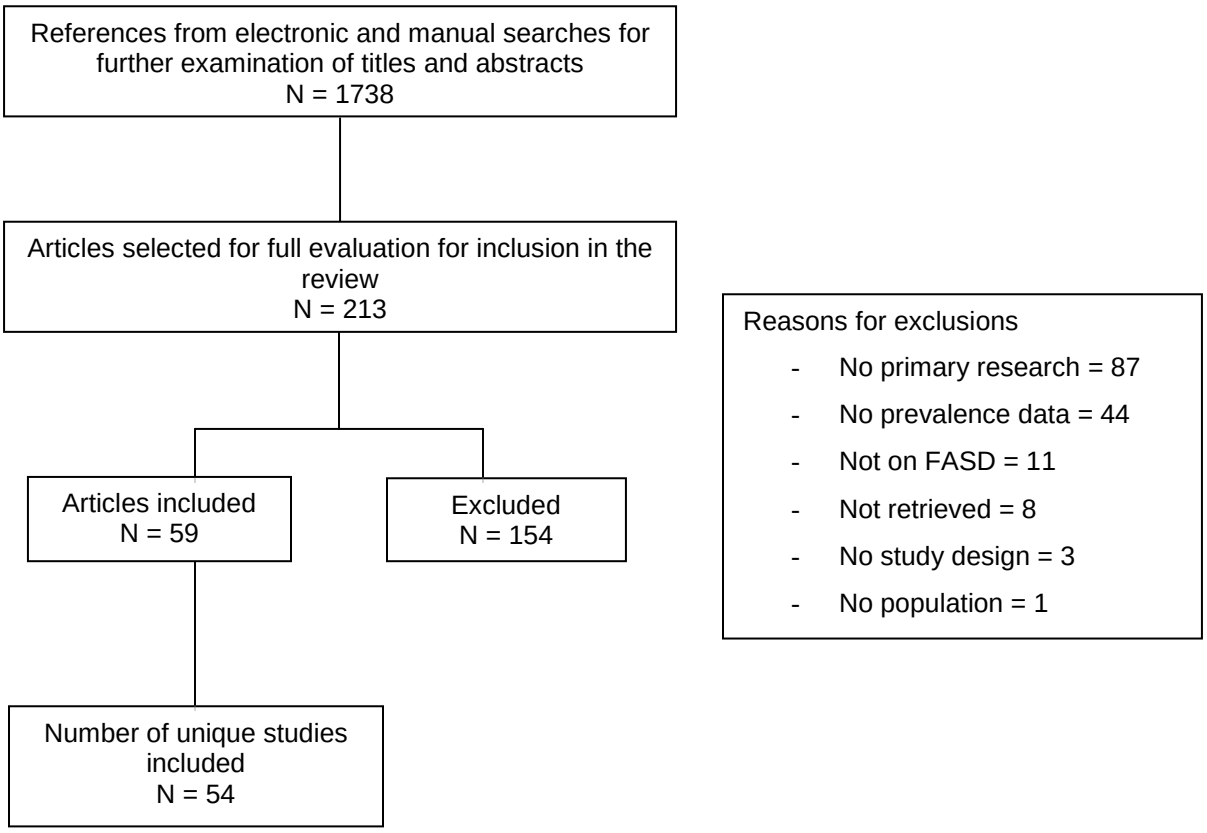
Descriptive statistical analyses were undertaken using Predictive Analysis Software Statistics for Mac® (PASW® version 18.0, IBM SPSS, Somers NY). Meta-analysis were conducted in Excel using the macros developed by Neyeloff et al.[16]

RESULTS

Search Results

The systematic search (electronic, grey literature and manual searches) identified 1872 citations. After screening of titles and abstracts, and removal of duplicates, 213 studies were judged as potentially relevant, with 59 of them satisfying the eligibility criteria. Of these, five references were multiple publications and therefore, the review included 54 unique studies reported in 59 publications (Figure 1). Figure 3 outlines study retrieval and selection for the review. The complete list of excluded studies and reasons for exclusion is described in Appendix B.

Figure 1: PRISMA flow diagram for study retrieval and selection for the review



Characteristics of Included Studies

General characteristics

Fifty four studies (35 cross-sectional studies,[17-51] 13 retrospective cohort studies,[52-64] and six prospective cohort studies,[65-70]) provided data on the prevalence of FASD. Tables C1 to C6 of Appendix C summarize the overall key characteristics of the studies included in the review. The studies were published between 1980 and 2012, with a median year of publication of 2004 (interquartile range [IQR]: 1997, 2010). Most of the studies (n = 41) were published in peer-reviewed journals, 11 were presented at scientific conferences, one was a government report, and one was a thesis. Authors of primary studies were from a variety of countries, including the USA (20 studies), Canada (nine studies), Australia (six studies), South Africa (four studies), Chile (three studies), France (two studies), Croatia, Germany, Israel, Italy, Lithuania, Poland, Spain, Sweden, and Taiwan (one study each).

The prevalence of FASD has been investigated in a variety of countries: USA,[17,18,20,21,32,37,48,54,56,57,60,65,68-70] South Africa,[35,36,38,44,50,51] Canada,[19,24,27,31,42,46,58,62,64] Australia,[23,52,53,59,61,63] Chile,[39-41,66] France (including the Reunion Island),[47,55] Italy,[33,34] Croatia,[45] Germany,[25] Israel,[49] Lithuania,[29] Norway,[22] Poland and the Netherlands,[26] Russia,[43] South Korea,[30] Sweden,[67] and Taiwan.[28]

Characteristics of study populations

The majority of studies evaluated the prevalence of FASD in community samples of children[22,23,37,46,47,52-54,56-61,63-66,69,70] and in samples of children enrolled in schools.[20,21,28,30,32-36,38,40,41,44,45,50,51,68] Other studies were conducted in samples of children from the foster care system,[17,25,26,29,39,43,49,67] and among youth and adults in prisons and correctional facilities.[18,19,24,31,42,62] A smaller proportion of studies included samples from maternity wards[55] and centers for developmental problems.[48] The median number of individuals sampled in cross-sectional studies was 782 (IQR 324 to 1976), whereas sample sizes in prospective and retrospective cohort studies were larger (median of 6522 individuals; IQR: 814 to 93813).

Prevalence data for other special populations of interest in this review were provided in the individual studies. Twelve studies reported data on the frequency of FASD among Aboriginal children[27,37,46,53,57-59,63-65] and youth,[62] with five studies conducted in reserves.[27,37,46,63,65] One study[54] reported FASD prevalence data among minority racial groups. Three studies[30,40,41] reported FASD prevalence data among children attending special education programs.

FASD conditions evaluated

FASD was defined in many ways in the studies. Some of them evaluated the prevalence of the entire FASD spectrum as a whole, whereas other studies evaluated the prevalence of FASD as a composite of certain condition types. Seven studies evaluated the prevalence of the entire FASD spectrum,[22,26,44,62,63,67,70] whereas 18 studies summed up the frequency of particular FASD types (i.e, FAS + pFAS,[23,27,32,35,40,45,48,50,66,68] FAS + pFAS + ARND,[24,29,33,59] FAS + ARND,[28] FAS + ARND + ARBD,[47] FAS + pFAS + ARND + ARBD,[34] and pFAS + ARND[31]) to define the overall prevalence of FASD.

The vast majority of the studies (46 studies[17-25,27-30,32-43,45-47,50-60,64-70]) reported estimates of the prevalence of FAS. Nineteen studies[21,23,24,27,29,31-36,40,45,49,50,59,66-68] assessed the prevalence of pFAS, ten studies[24,28,29,31,33,34,36,47,59,67] reported on ARND and four studies on ARBD.[34,47,61,67]

Methods for FASD diagnosis and case ascertainment

A variety of FASD case definitions were used in the studies. They included the 1996 Institute of Medicine (IOM) criteria for the diagnosis of FASD[23,24,27,32,36,38,47,50,61,64,67] or modifications of the IOM criteria.[29,33-35,44,45,51] Other diagnostic criteria used in the studies were the 4-Digit Diagnostic Code,[17,20,43,58,59,66] the Canadian Taskforce Guidelines on FASD,[21,30] and the CDC Guidelines.[22] One study[49] combined the IOM criteria and the Canadian Taskforce Guidelines on FASD for FASD diagnosis.

Some studies used other methods for defining FASD cases: Six studies[39-41,46,65,69] used the criteria of the Fetal Alcohol Study Group from the Research Society of Alcoholism, whereas two studies[56,60] used the FASSNet methodology and one study[70] used the Wisconsin Fetal Alcohol Syndrome Screening Project case definition. Some studies relied on questionnaires such as the Fetal Alcohol Syndrome questionnaire[25,26] and the FAS Screen[68] to identify the cases. In some instances, the diagnosis of FASD was based on self-reported physician diagnosis of the condition.[18,19,42,62] Finally, two studies[54,57] used the International Classification of Diseases, 9th Revision (codes 760.71 and 760.7) and for one study,[52] the diagnostic criteria used was unclear.

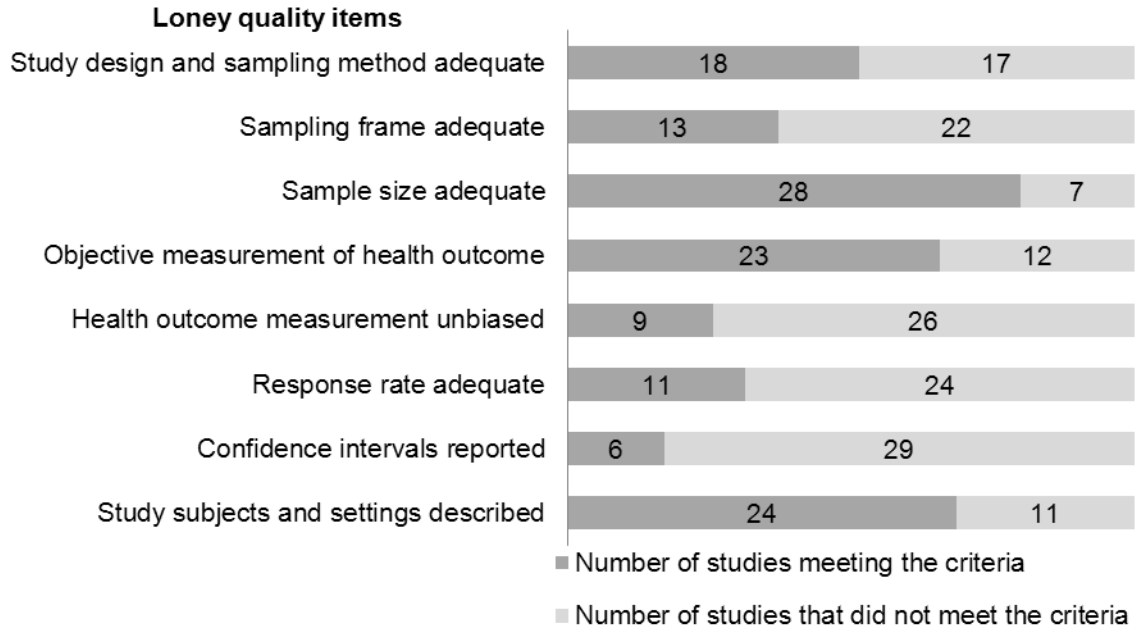
Diagnostic sequences for case identification included a variety of methods. Passive case ascertainment methods included audits of vital statistics databases, birth defects registries, and medical records audit.[48,52-63] Studies that used active strategies for case identification,[17-47,49-51,64-70]

included a combination of strategies such as medical examination, dysmorphological assessments, neurobehavioural assessments, interviews or chart reviews to establish maternal drinking during pregnancy, medical and school records audit and case conferences to establish a final diagnosis.

Methodological quality of the studies

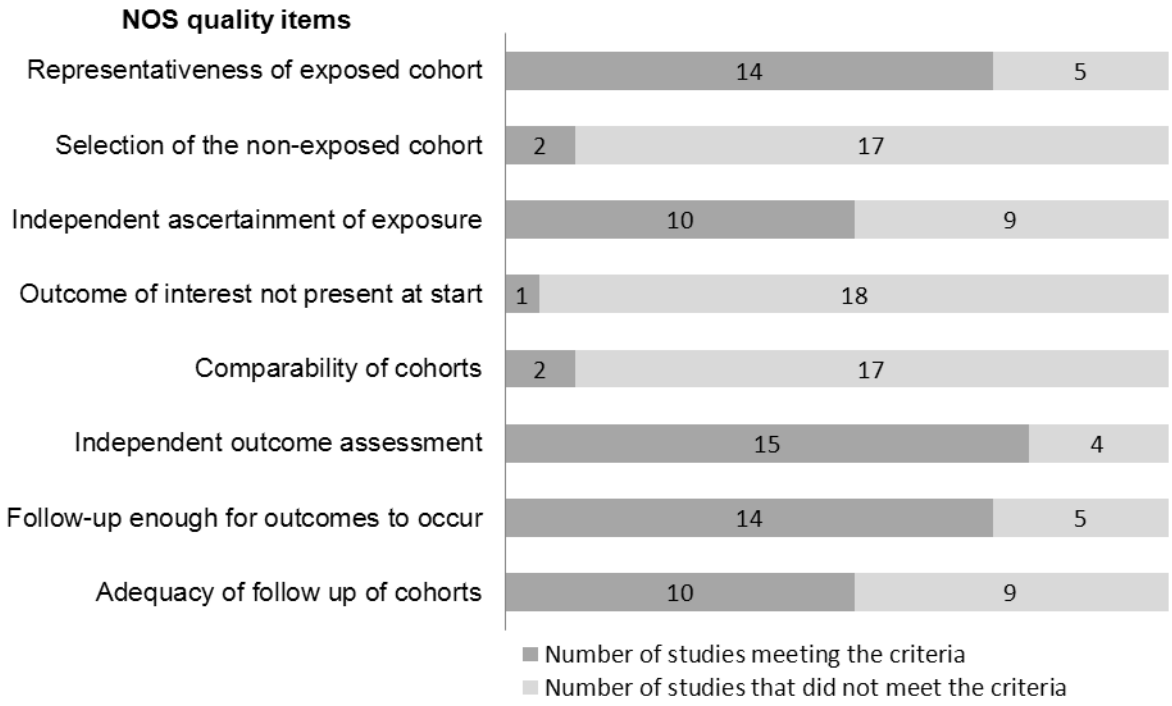
Cross-sectional studies. Overall, cross-sectional studies were of moderate methodological quality (median Loney score: 4; IQR: 2, 6). Of the 35 cross-sectional studies, 16 were considered of poor methodological quality, 14 were of moderate quality, and five were of strong methodological quality. Figure 2 provides a summary of how well cross-sectional studies were able to address issues related with sampling methods, sample size, validity and blinding of outcome assessment, response rate, and generalizability of study results.

Figure 2: Methodological quality of cross-sectional studies assessing the prevalence of FASD



Cohort studies. Overall, the 19 cohort studies were of poor methodological quality (median NOS score: 4; IQR: 2 to 5). Thirteen cohort studies were of poor quality, whereas five were of moderate quality. Only one cohort study was of high methodological quality. To note, many of the cohort studies were descriptive; that is to say, they did not include a comparison group in the design and, therefore, issues such as comparability of cohorts and selection of non-exposed cohorts were naturally not applicable, leading to lower ratings of the methodological quality. Figure 3 provides a summary of how cohort studies controlled for factors related with selection bias, validity of methods for ascertainment of exposure and outcome, and completeness of data at follow-up.

Figure 3: Methodological quality of cohort studies assessing the prevalence of FASD



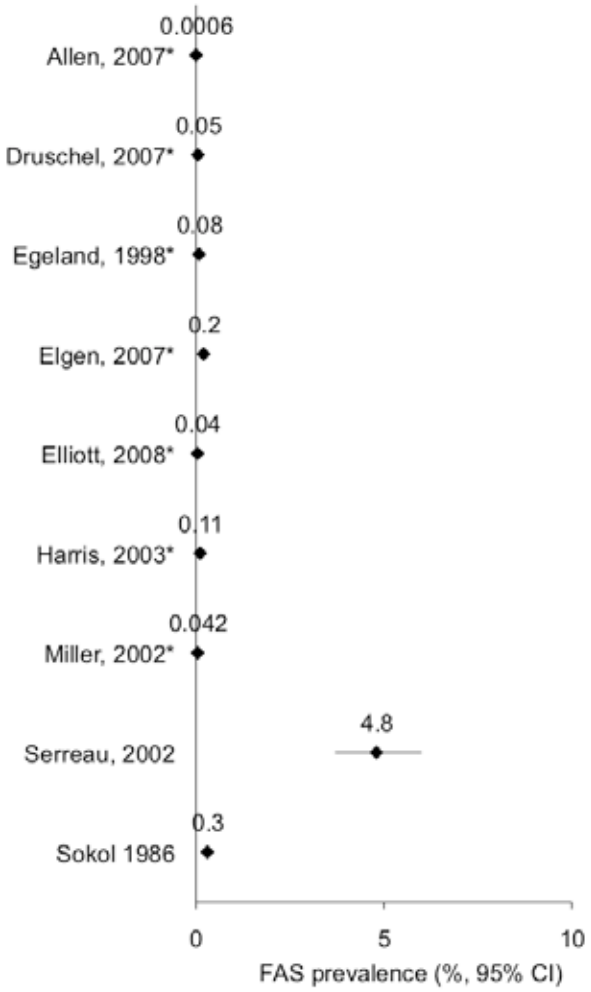
Analysis of the Prevalence of FASD

Data on FASD prevalence is analyzed and reported separately according to the study population and settings: communities, children attending schools, children under foster care, individuals in prisons and correctional facilities, and special groups comprising Aboriginal peoples and children attending special education school or specialized clinics for developmental disorders. Similarly, FASD prevalence estimates are reported separately for FAS, pFASD, ARND and ARBD.

Prevalence of FASD in the community

FAS prevalence. Nine studies (six cohort studies[52,56,57,59,60,69] and three cross-sectional studies[22,23,47] evaluated the prevalence of FAS in community settings (Figure 4). FAS prevalence data was reported without 95% CI in all but two studies[47,69] as they calculated the prevalence for the entire population.

Figure 4: Studies assessing FAS prevalence in community samples

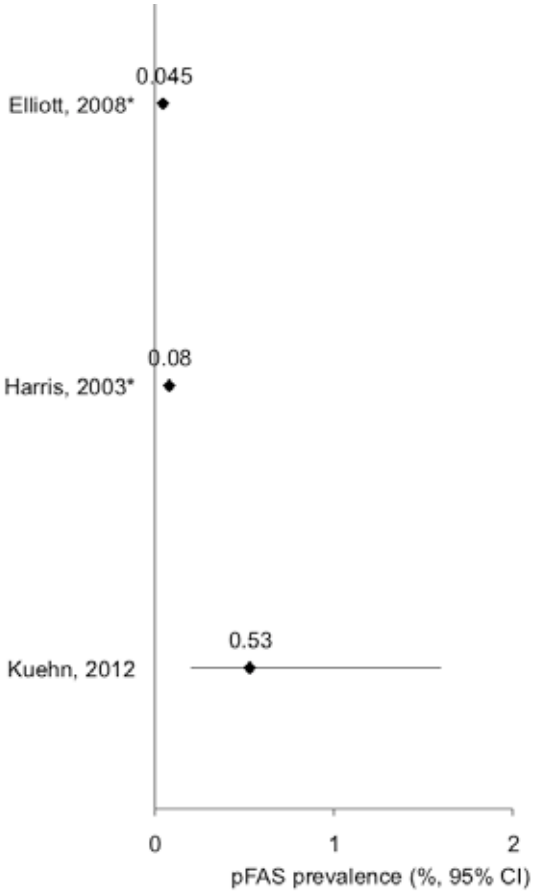


* 95% CI not calculated

Two studies[22,52] did not provide denominator data for calculating FAS prevalence rates and therefore, they were excluded from the meta-analysis. There was evidence of heterogeneity between the studies ($p<0.05$; $I^2 = 94.6\%$) and, therefore, a pooled estimate of FAS prevalence was not calculated. Sources of heterogeneity were explored. Heterogeneity was not removed after subgroup analysis by study and population characteristics were conducted. Overall, prevalence estimates of FAS in the community typically ranged from 0.0006% to 0.3%. An outlier estimate of 4.85% obtained in a sample of children attending primary care centres in the Reunion Island was the highest FAS estimate obtained in community samples.

pFAS prevalence. One cross-sectional study[23] and two cohort studies[59,66] reported on the prevalence of pFAS in community settings (Figure 5). pFAS prevalence estimates ranged from 0.045% to 0.53%.

Figure 5: Studies assessing pFAS prevalence in community samples

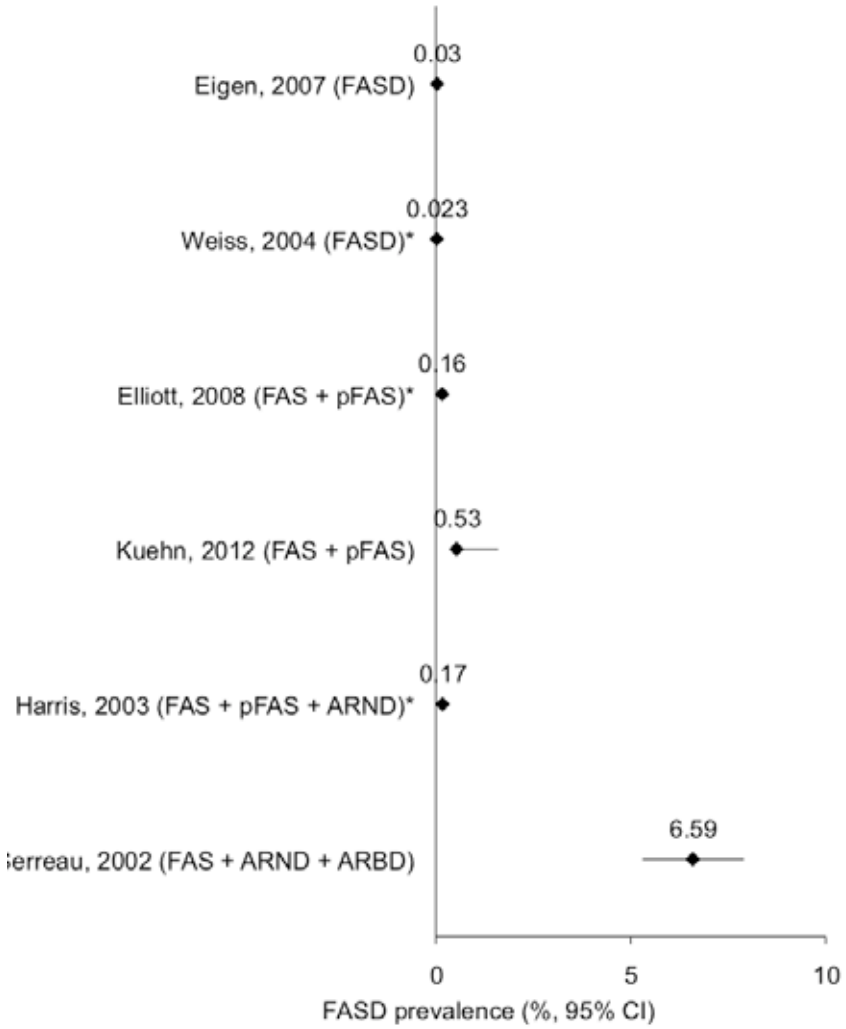


* 95% CI not calculated

ARND and ARBD prevalence. One cross-sectional study[47] and one cohort study[59] assessed the prevalence of ARND in community settings. ARND prevalence was calculated in 0.01% and 1.06%, respectively. One cross-sectional study[47] and one cohort study[61] assessed the prevalence of ARBD in community settings. ARBD prevalence in the studies were 1.08% and 0.37%.

FASD prevalence from composite definitions. Six studies (three cross-sectional studies[22,23,47] and three cohort studies[59,66,70] reported composite measures of FASD prevalence in the community. Three studies[23,59,70] did not provide information on the denominator to calculate 95% CIs around the prevalence estimate. Definitions of what constituted FASD varied across the studies. Two studies[22,70] evaluated the prevalence of FASD as a single entity. Two studies[23,66] defined FASD as FAS and pFAS combined, one study[59] considered FAS, pFAS and ARND in the definition, whereas another study defined FASD as FAS, ARND and ARBD combined.[47] Combining prevalence estimates based on such a heterogeneous set of FASD definitions deemed inappropriate, and therefore, a graphic display of individual FASD estimates is provided (Figure 6) along with a description of the definition of FASD applied in the studies. Apart from one study conducted in the Reunion Island,[47] community prevalence estimates of overall FASD ranged from 0.02% to 0.5%, which translate to FASD rates of 0.2 to 5 per 1000 population.

Figure 6: Studies assessing composite measures of FASD prevalence in community samples

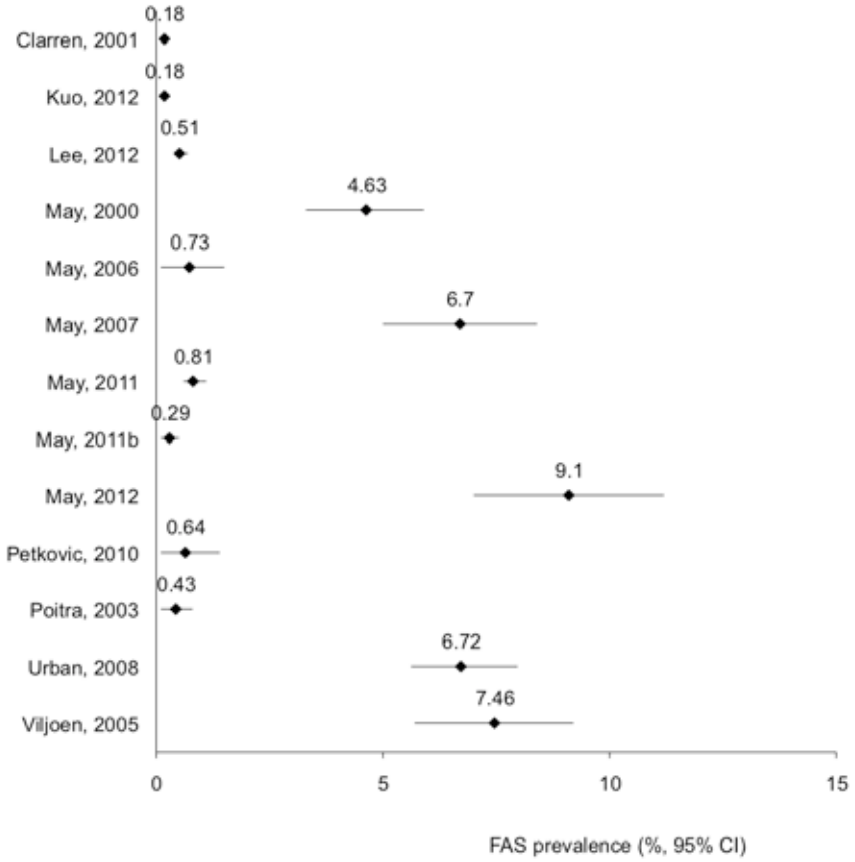


* 95% CI not calculated

Prevalence of FASD in schools

FAS prevalence. Thirteen studies (12 cross-sectional studies[20,28,30,32-36,38,45,50,51] and one prospective cohort study[68] totaling 26,340 children provided data for the analysis of the prevalence of FAS in school settings (Figure 7). There was evidence of heterogeneity between the studies ($p<0.05$; $I^2 = 96.5\%$) and therefore, a pooled estimate of FAS prevalence was not calculated. Sources of heterogeneity were explored.

Figure 7: Studies assessing FAS prevalence in schools



A subgroup analysis based on study location showed moderate homogeneity ($p>0.05$; $I^2 = 71.7\%$) among eight studies[20,28,30,32-34,45,68] that reported FAS prevalence for countries other than South Africa, which is recognized to have the highest prevalence estimates of all countries (Figures 8 and 9). After excluding the studies conducted in South Africa, the pooled prevalence of FAS in school settings was calculated in 0.36% (95% CI: 0.21, 0.50; 8 studies), which translates to a rate of 3.6 per 1000 population. In contrast, a pooled analysis of FAS prevalence from the five studies[35,36,38,50,51] conducted in South Africa yielded a pooled FAS prevalence of 6.7% (95% CI: 5.4, 8.1), which translates to a rate of 67 per 1000 population. The studies were moderately homogeneous ($p>0.05$; $I^2 = 71.9\%$).

Figure 8: Non-South African studies assessing FAS prevalence in schools

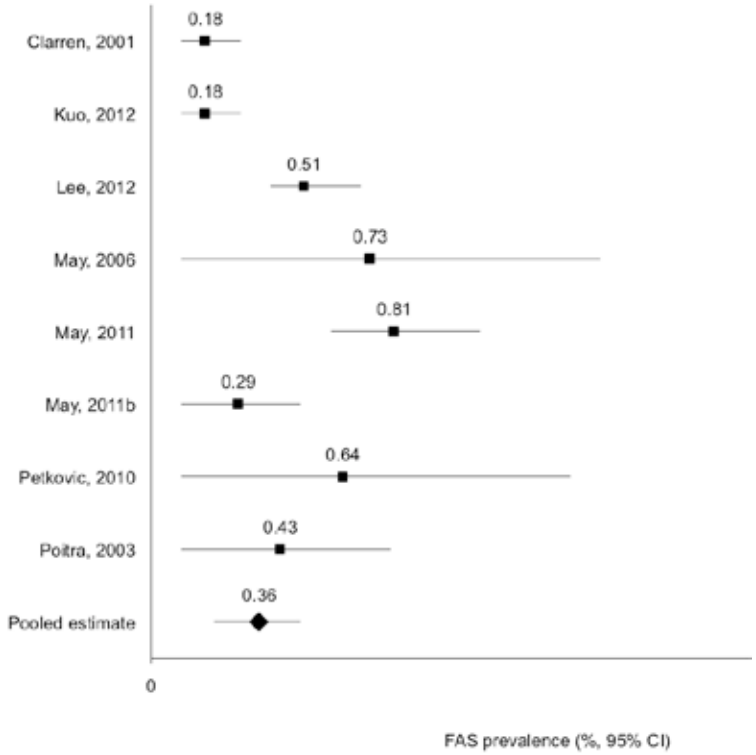
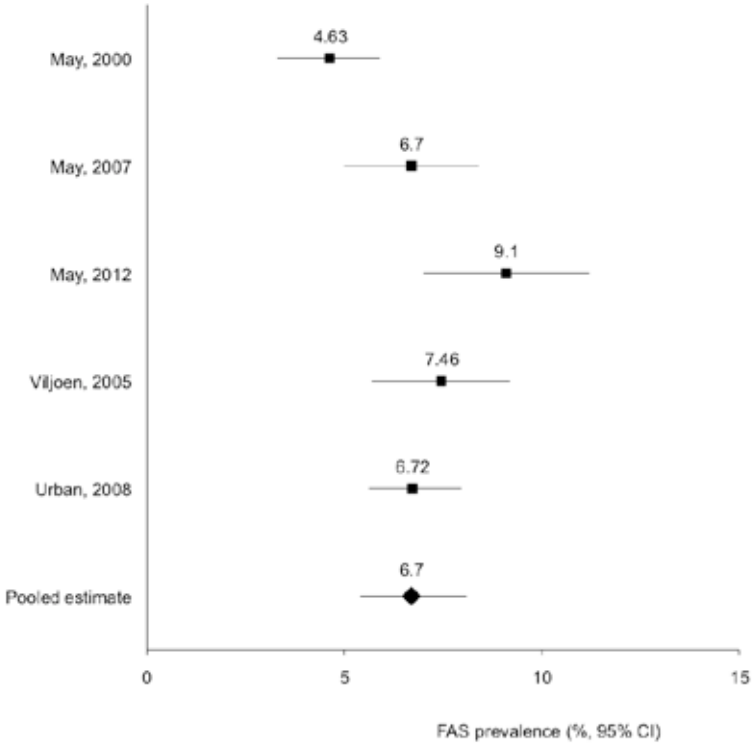
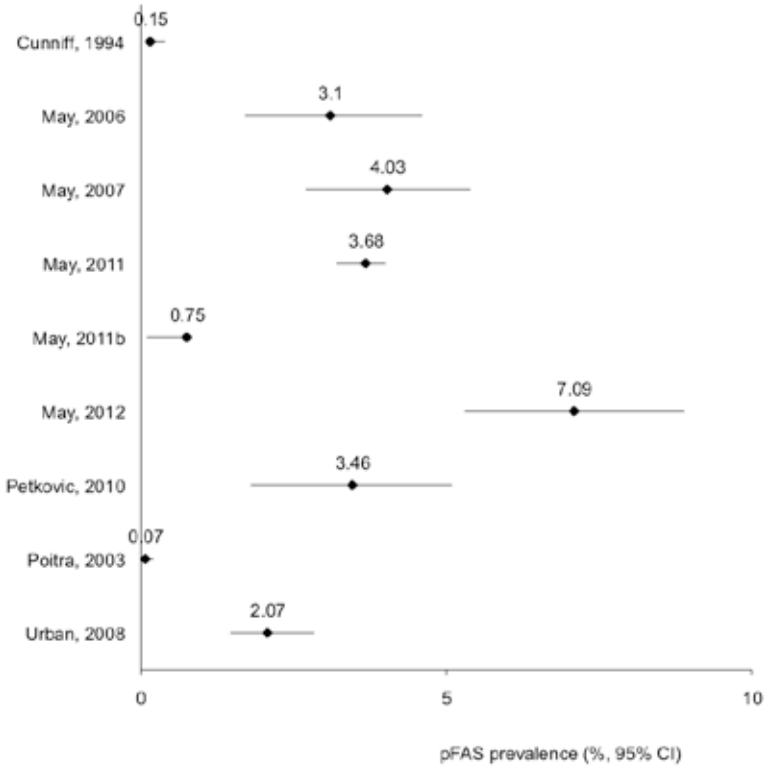


Figure 9: South African studies assessing FAS prevalence in schools



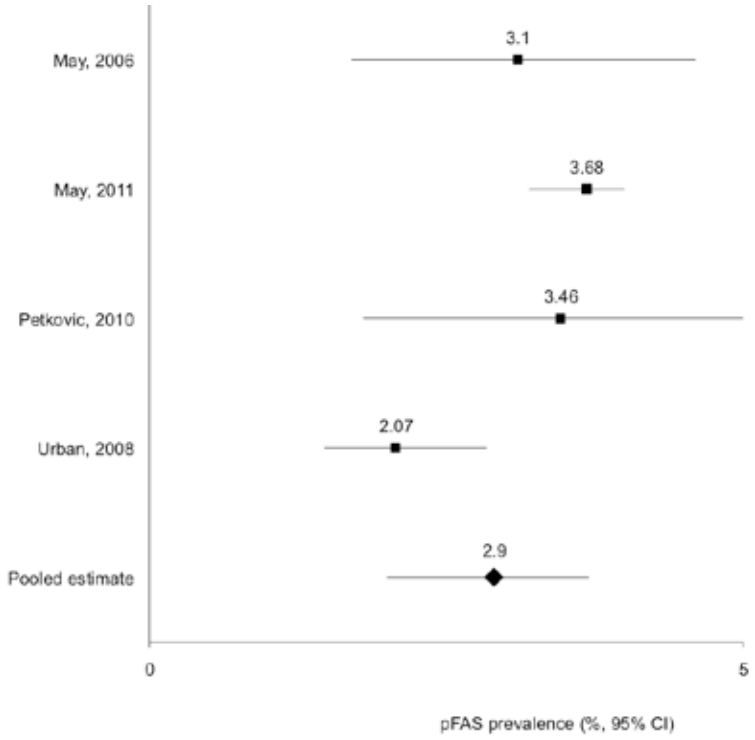
pFAS prevalence. Nine studies (eight cross-sectional studies[21,32-36,45,50] and one prospective cohort study[68] totaling 9809 children provided data for the analysis of the prevalence of pFAS in school settings (Figure 10). There was substantial heterogeneity across the studies ($p<0.05$; $I^2 = 94.9\%$) and therefore, a pooled estimate of pFAS prevalence was not calculated.

Figure 10: Studies assessing pFAS prevalence in schools



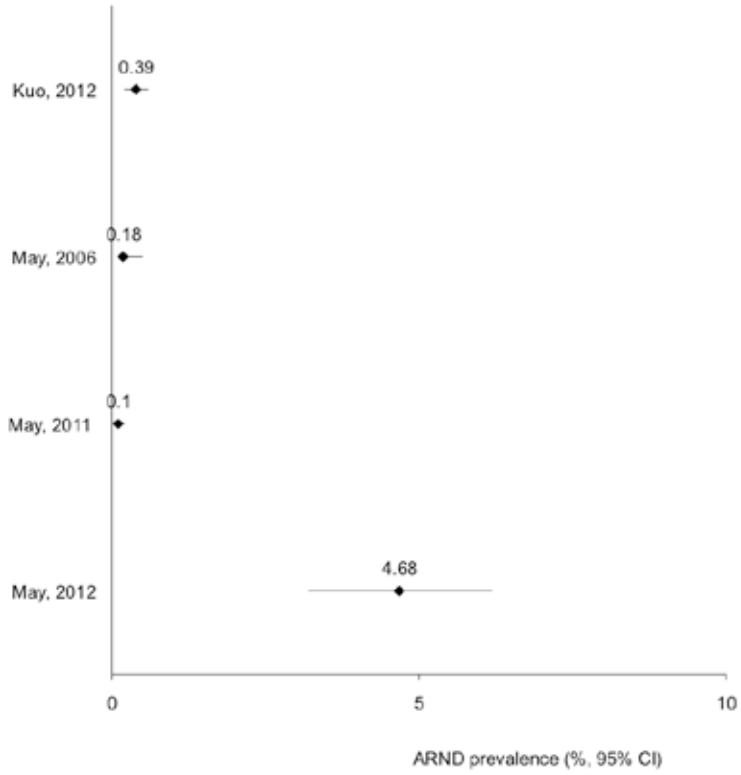
Examination of potential sources of heterogeneity found that studies that did not describe their sampling strategies[21,32,36] or used convenience samples[35,68] accounted for substantial heterogeneity in the results. After removing these studies, the pooled prevalence of pFAS in schools was 2.9% (95% CI: 2.0, 3.7; four studies) (Figure 11), which translates to a rate of 29 per 1000 population. The studies were moderately homogeneous ($p>0.05$; $I^2 = 42.6\%$).

Figure 11: Studies assessing pFAS prevalence in schools obtained from random samples or the total population



ARND and ARBD prevalence. Four cross-sectional studies[28,33,34,36] totaling 6083 children provided data for the analysis of the prevalence of ARND in school settings (Figure 12). Substantial heterogeneity across the studies ($p<0.05$; $I^2 = 91.5\%$) precluded the calculation of a pooled estimate. After qualitative analysis of heterogeneity, it was found that the study conducted in South Africa[36] accounted for a considerable proportion of heterogeneity across the studies. After removing this study from the meta-analysis, a pooled estimate of ARND prevalence of 0.23% (95% CI: 0.03, 0.4) was obtained, for a rate of 2.3 per 1000 population. The studies were moderately homogeneous ($p>0.05$; $I^2 = 52\%$).

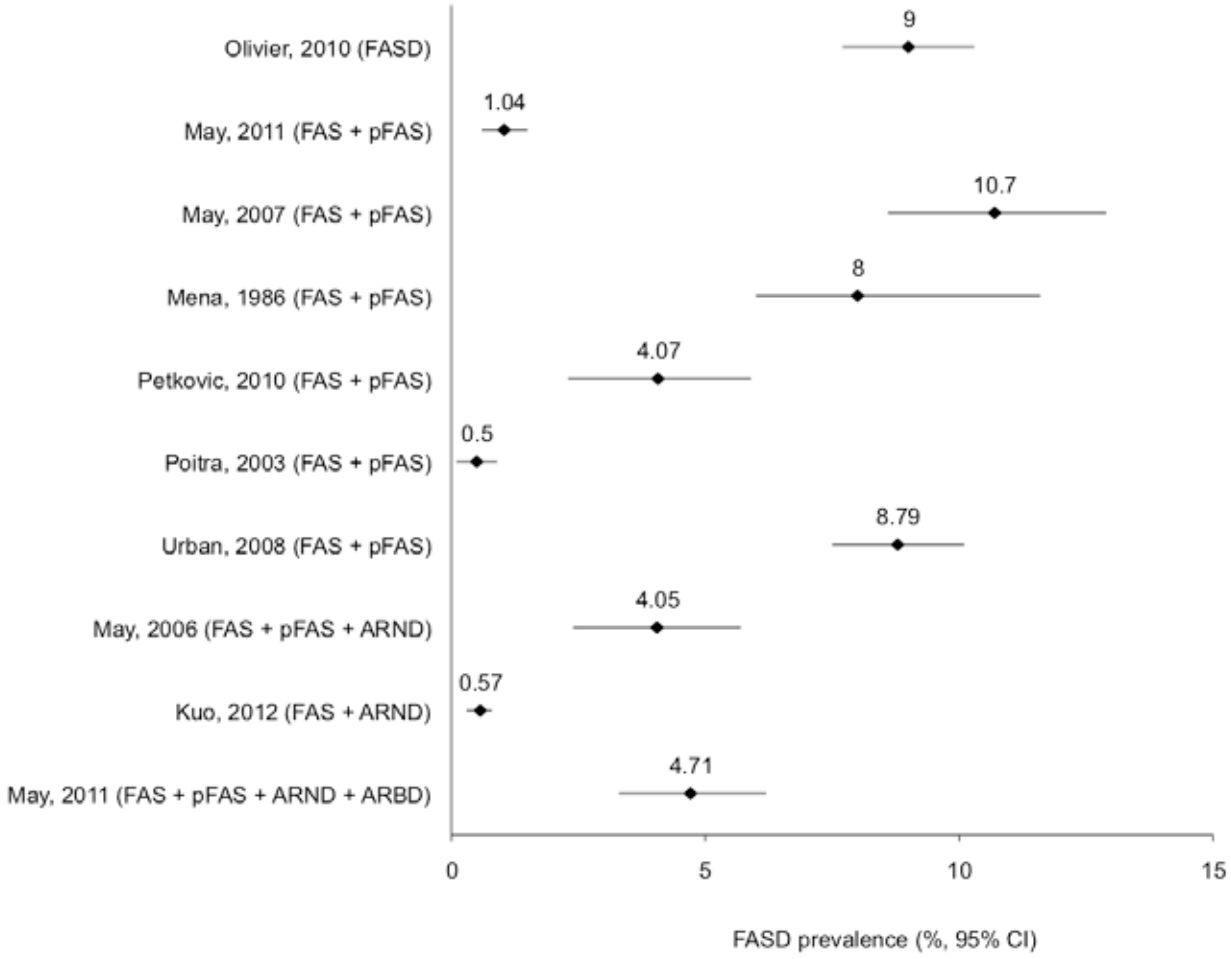
Figure 12: Studies assessing ARND prevalence in schools



One cross-sectional study assessed the prevalence of ARBD among Italian schools and identified a rate of 1 ARBD case per 1000 school children.

FASD prevalence from composite definitions. Ten studies (nine cross-sectional studies[28,32-35,40,44,45,50] and one cohort study[68] reported composite measures of FASD prevalence in school settings. FASD definitions varied across the studies. One study[44] evaluated the prevalence of FASD as a single entity. Six studies[32,35,40,45,50,68] defined FASD as FAS and pFAS combined; one study[33] considered FAS, pFAS and ARND in the definition, one study included FAS and ARND[28] whereas another study[34] included the full spectrum of FAS, pFAS, ARND and ARBD. A summary of FASD estimates from the individual studies is provided on Figure 13, along with a description of the definition of FASD that was applied. School-based prevalence estimates of overall FASD ranged from 0.5% to 10.7%, which translate to FASD rates of 5 to 107 per 1000 population in school settings.

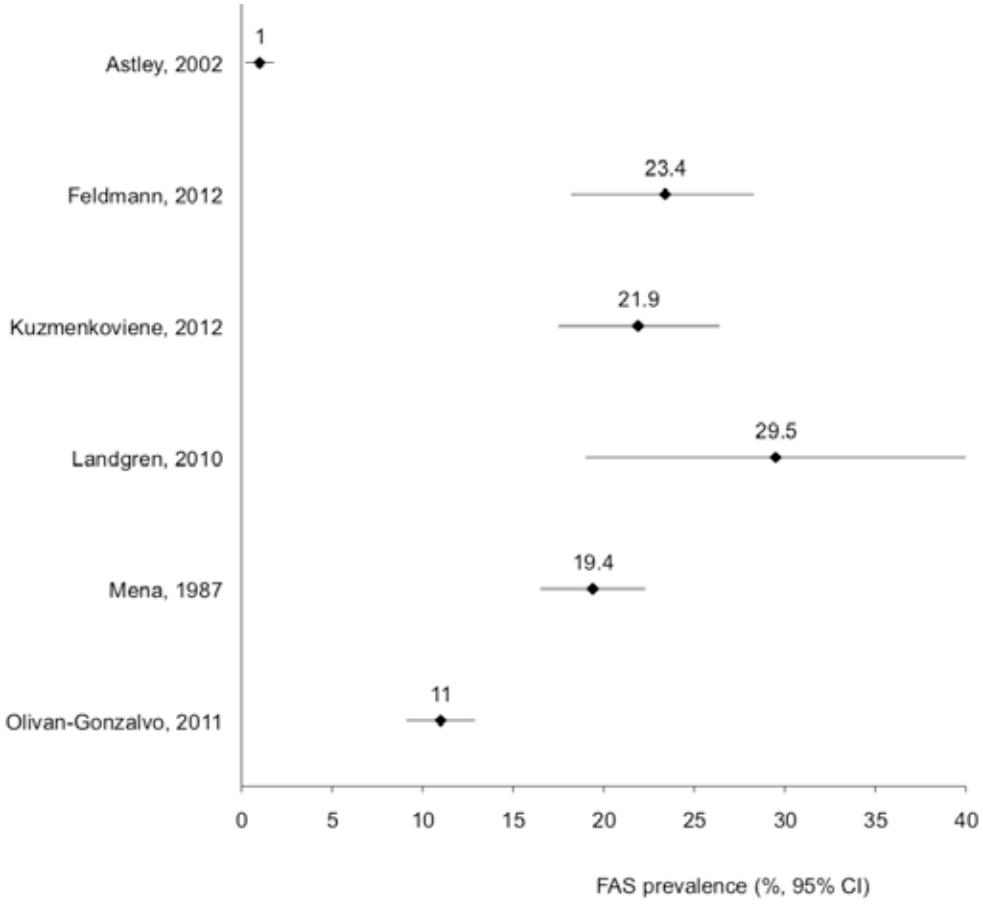
Figure 13: Studies assessing composite measures of FASD prevalence in school samples



Prevalence of FASD among children in foster care

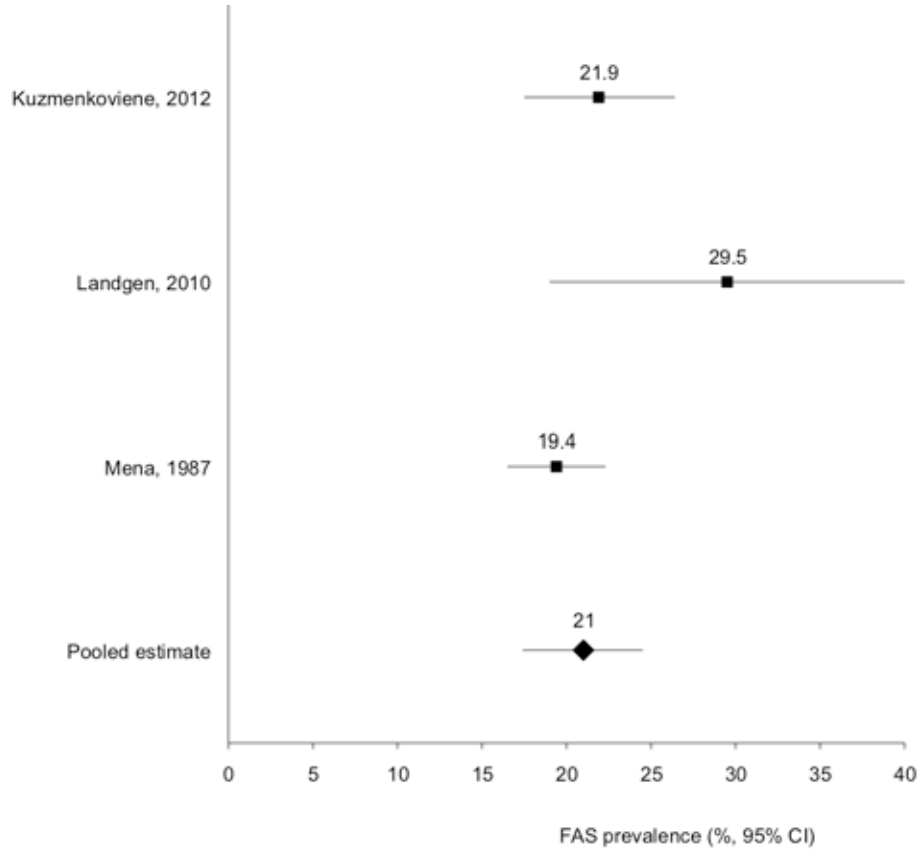
FAS prevalence. Six studies (five cross-sectional studies[17,29,39,43,71] and one prospective cohort study[67] totaling 3038 children reported on the prevalence of FAS among children in foster care (Figure 14). There was substantial heterogeneity between the studies ($p<0.05$; $I^2 = 98.3\%$) and therefore, a pooled estimate of FAS prevalence was not calculated.

Figure 14: Studies assessing FAS prevalence in foster care



The type of diagnostic criteria for FAS used in the studies was identified as an important source of heterogeneity. A meta-analysis of studies that applied formal diagnostic criteria such as the IOM criteria,[67] the Hoyme criteria[29] and the guidelines of the Fetal Alcohol Study Group of the Research Society of Alcoholism[39] for case identification yielded a pooled FAS prevalence estimate of 21% (95% CI: 17.4, 24.5), which translates to a rate of 210 per 1000 population. The results were moderately homogeneous ($p>0.05$; $I^2 = 26.9$) (Figure 15).

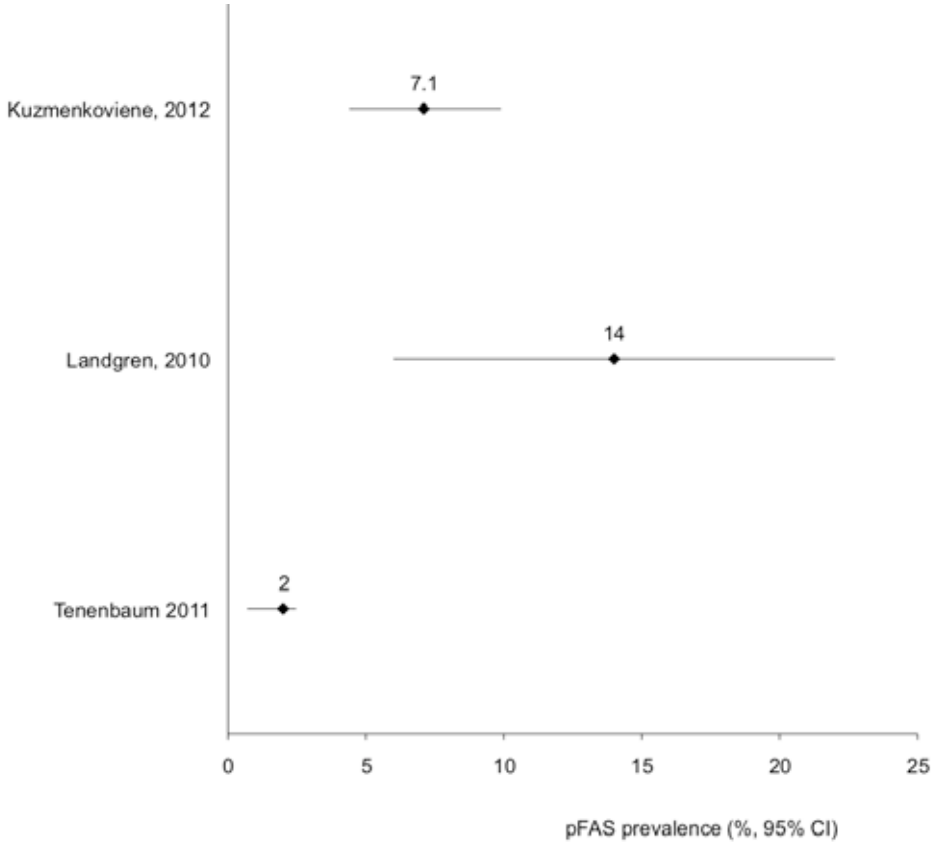
Figure 15: Studies assessing FAS prevalence in foster care using formal diagnostic criteria



Prevalence estimates from the two studies[17,43] that used the 4-Digit system to identify FAS cases were not pooled due to substantial heterogeneity.

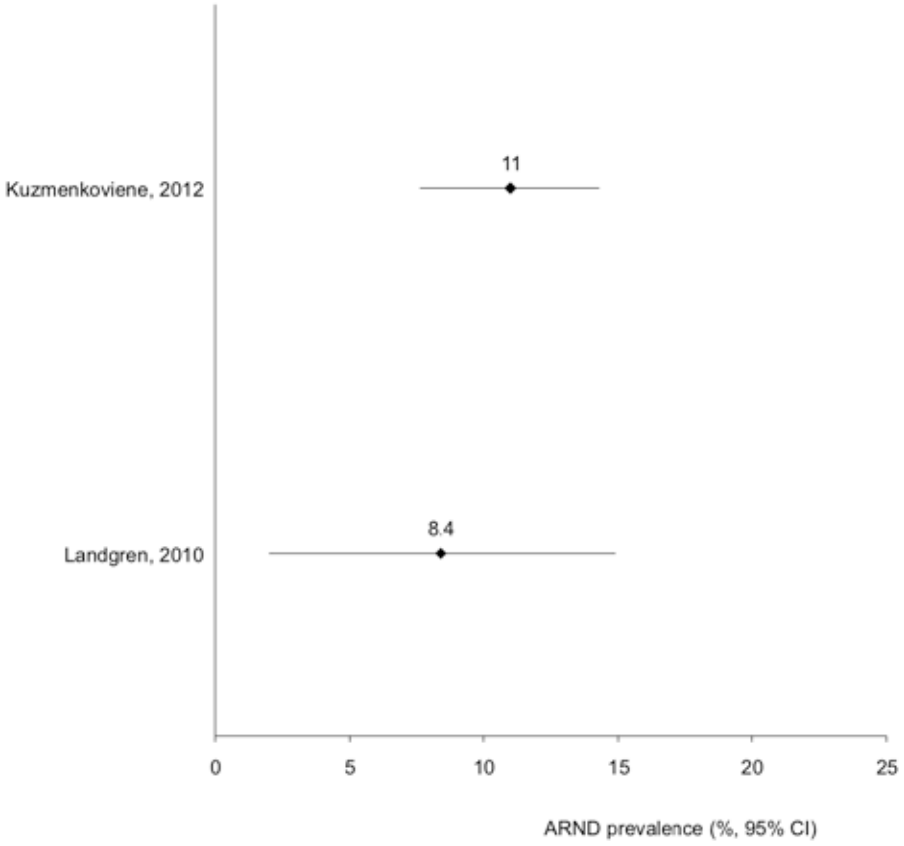
pFAS prevalence. Two cross-sectional studies[29,49] and one prospective cohort study[67] totaling 508 children assessed the prevalence of pFAS among children in foster care (Figure 16). Prevalence estimates were substantially heterogeneous across the studies ($p<0.05$; $I^2 = 81.4\%$) and were not pooled. Due to the small number of studies, subgroup analyses by potential sources of heterogeneity were not conducted. Estimates of pFAS across the three studies ranged from 2% to 14%.

Figure 16: Studies assessing pFAS prevalence in foster care



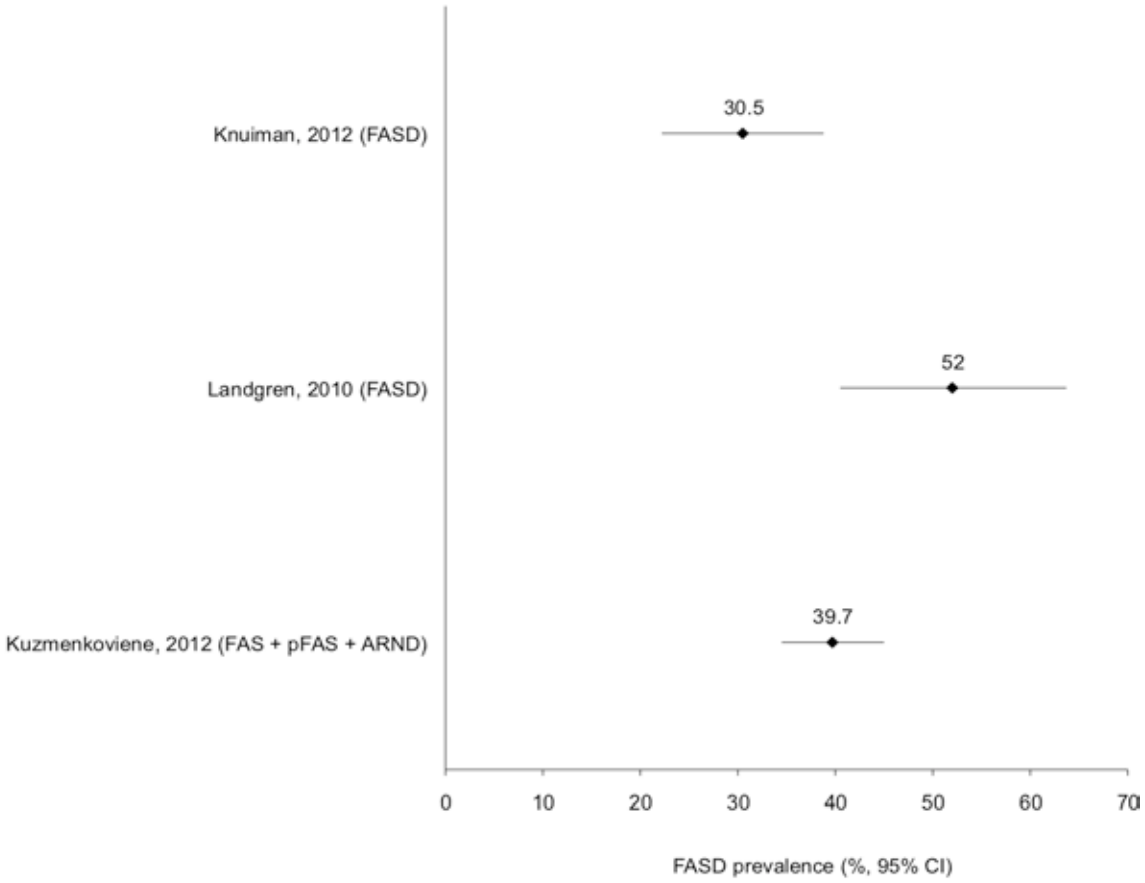
ARND and ARBD prevalence. Two studies (one cross-sectional study[29] and one prospective cohort study[67] totaling 408 children provided data for the analysis of the prevalence of ARND in foster care (Figure 17). Due to the small number of studies, a meta-analysis of ARND prevalence was not conducted. Prevalence values of ARND were 8.4% and 11% in these two studies. One prospective cohort study[67] that evaluated the prevalence of ARBD among children in foster care yielded an estimate of 11.26% (95% CI: 3.9, 18.6).

Figure 17: Studies assessing ARND prevalence in foster care



FASD prevalence from composite definitions. Three studies (two cross-sectional studies[26,29] and one cohort study[67]) reported composite measures of FASD prevalence in foster care settings. Two studies[26,29] evaluated the prevalence of FASD as a single entity, whereas one study[67] included FAS, pFAS and ARND in the definition. A summary of FASD estimates from the individual studies is provided on Figure 18, along with a description of the definition of FASD that was applied. Prevalence estimates of overall FASD in foster care settings ranged from 30.5% to 52%, which translate to FASD rates of 305 to 520 per 1000 population in foster care settings.

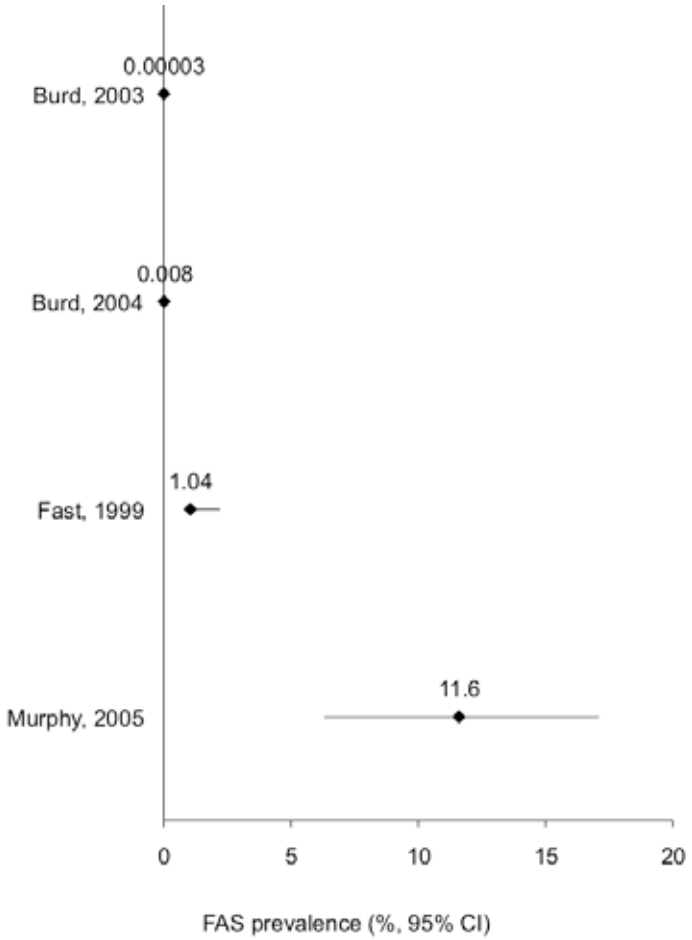
Figure 18: Studies assessing composite measures of FASD prevalence in foster care samples



Prevalence of FASD in prisons and correctional facilities

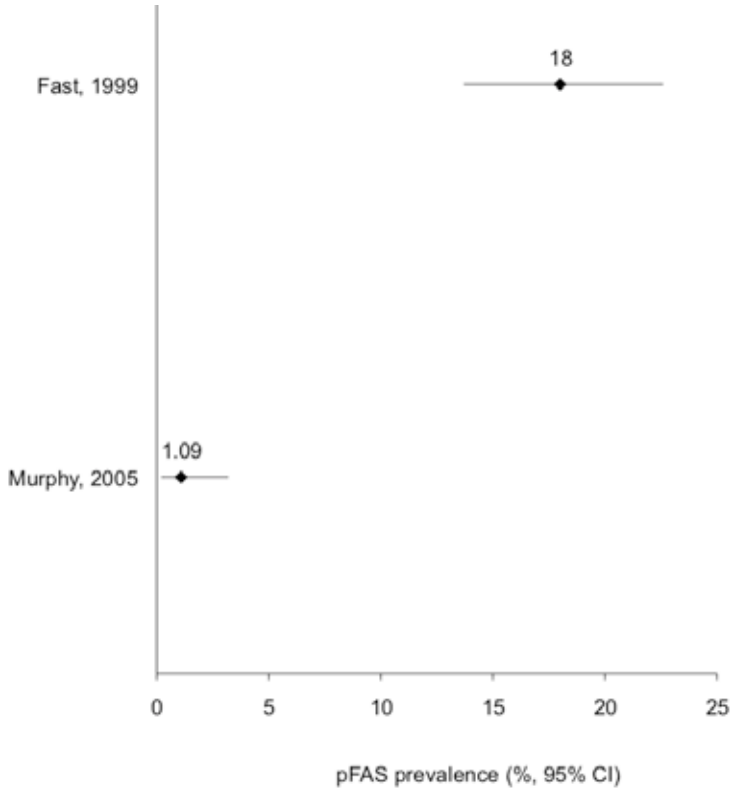
FAS prevalence. Four cross-sectional studies[18,19,24,42] evaluated the prevalence of FAS in prisons, forensic and correctional services (Figure 19). FAS prevalence estimates across the studies were substantially heterogeneous ($p<0.05$; $I^2 = 90.5\%$) and were not combined. FAS estimates in prisons and correctional systems based on self-reporting of FAS diagnoses ranged dramatically from 0.0003% in one study[18] to 11.6% in another study.[42] These FAS prevalence estimates should be interpreted with caution. More reliable data on the true prevalence of FAS in prisons and correctional facilities is derived from one study[24] that used an active case ascertainment strategy to identify FAS cases based on the IOM criteria (1.04%; 95% CI:1.0, 2.2).

Figure 19: Studies assessing FAS prevalence in prisons and correctional facilities



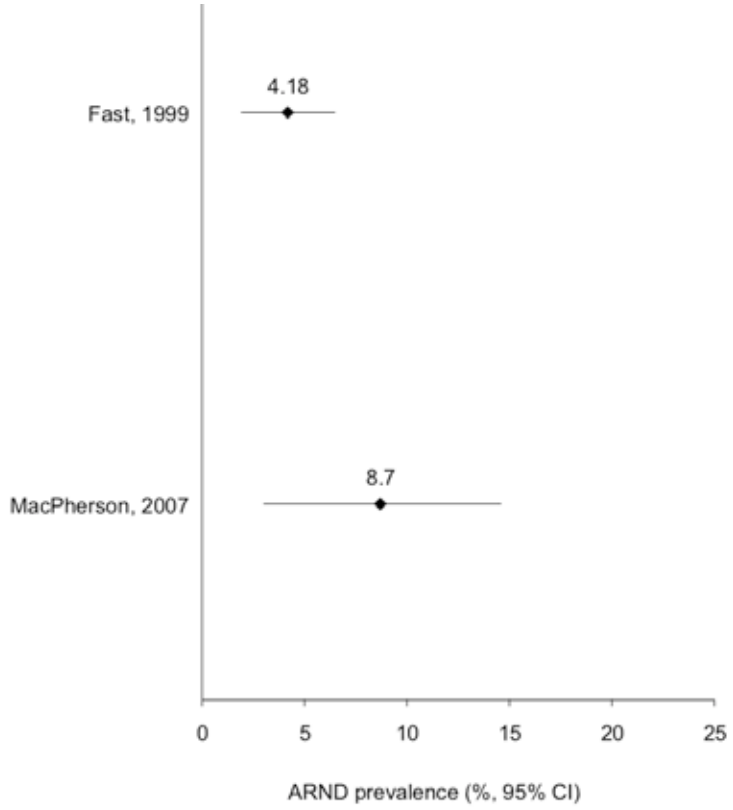
pFAS prevalence. Two cross-sectional studies[24,31] totaling 424 individuals assessed the prevalence of pFAS among youth and adult in prisons and correctional systems (Figure 20). Due to the small number of studies, a meta-analysis of pFAS prevalence was not conducted. The two studies yielded substantially different prevalence estimates. One study conducted with youth in correctional systems that used case ascertainment methods in the context of forensic assessments obtained a pFAS prevalence estimate of 18% (95% CI: 13.7, 22.6), whereas one study that examined individuals in both prisons and correctional facilities reported a pFAS prevalence of 1.09% (95% CI: 1.0, 3.2). We explored a variety of study characteristics to understand the source of differences in the study results. Both studies were conducted in Canada and use similar methods for case surveillance. The main differences were related to the methods of sampling and the diagnostic criteria for pFAS. Whereas one study[24] applied the IOM criteria for case definition and included the total population in correctional systems; the methods for case definition and sampling in the other study[31] were unclear. Based on this, we considered that the estimate provided by the study that used a formal set of criteria for pFAS was more reliable (18%).

Figure 20: Studies assessing pFAS prevalence in prisons and correctional facilities



ARND and ARBD prevalence. Two cross-sectional studies[24,31] totaling 424 individuals analyzed the prevalence of ARND in prisons and correctional facilities (Figure 21). Due to the small number of studies, a meta-analysis of ARND prevalence was not conducted. Prevalence values of ARND were 4.1% and 8.7% in these two studies. None of the studies evaluated the prevalence of ARBD among youth and adults in prisons and correctional facilities.

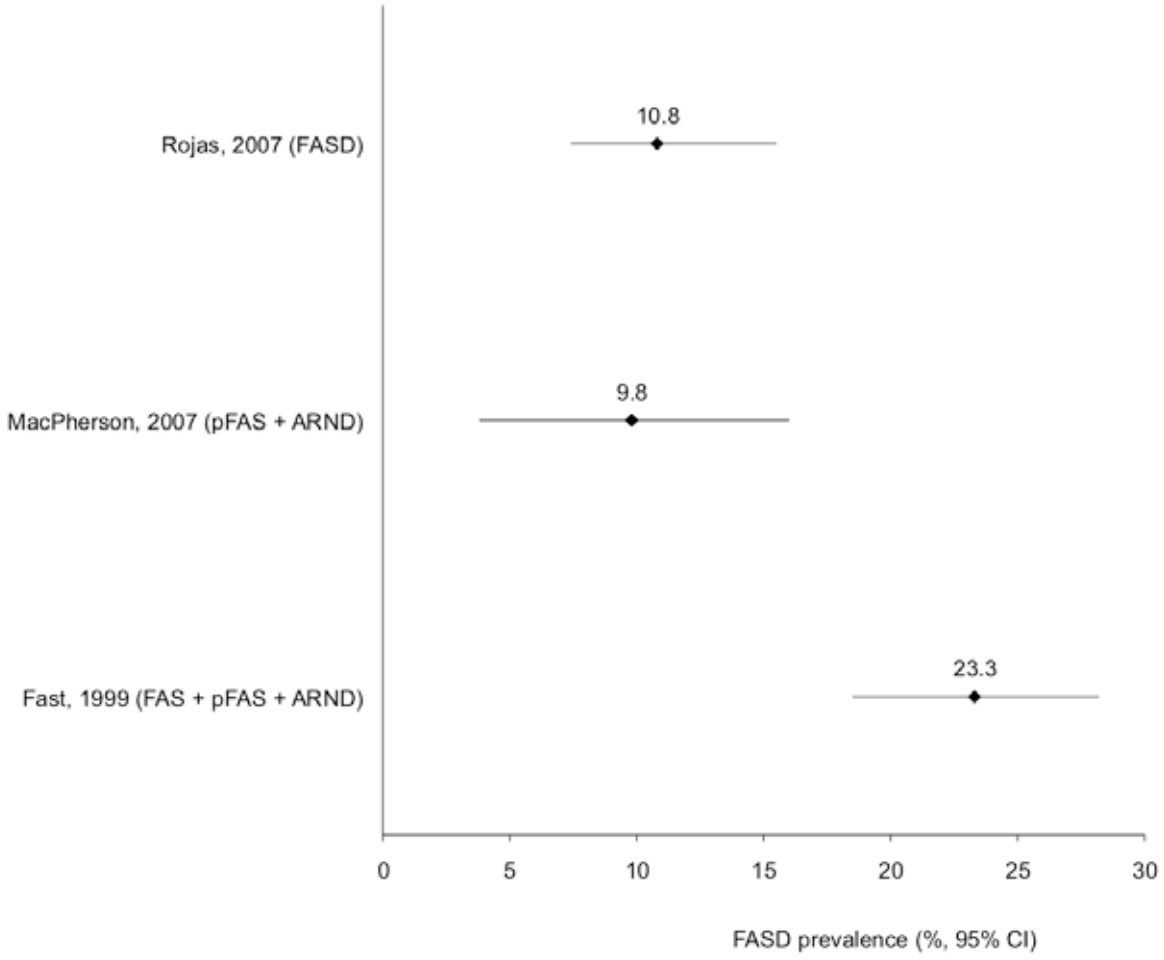
Figure 21: Studies assessing ARND prevalence in prisons and correctional facilities



FASD prevalence from composite definitions. Three studies (two cross-sectional studies[24,31] and one cohort study[62] reported composite measures of FASD prevalence in prisons and correctional facilities.

One study[62] evaluated the prevalence of FASD as a single entity. One study[31] defined FASD as pFAS and ARND whereas another study[24] FAS, pFAS, and ARND. A summary of FASD estimates from the individual studies is provided on Figure 22, along with a description of the definition of FASD that was applied. Prevalence estimates of overall FASD in prisons and correctional facilities ranged from 9.8% to 23.3%, which translate to FASD rates of 98 to 233 per 1000 population in prisons and correctional settings.

Figure 22: Studies assessing composite measures of FASD prevalence in prison and correctional facilities



Prevalence of FASD in special populations

Aboriginal populations. Eleven studies (eight cohort studies[53,57-59,62-65] and three cross-sectional studies[27,37,46] provided data for the analysis of the prevalence of FASD in aboriginal populations. The majority of studies that assessed FASD prevalence in Aboriginal peoples were conducted in Canada.[27,46,58,62,64] Aboriginal peoples from the USA[37,57,65] and Australia[53,59,63] were also evaluated. All the studies except one conducted in correctional facilities[62] derived their samples from the community (including reserves[27,37,46,63]). Ten studies[27,37,46,53,57-59,63-65] evaluated the prevalence of FAS among Aboriginal peoples. Two studies[27,59] evaluated the prevalence of pFAS and one study(59) reported on the prevalence of ARND. None of the studies reported data on the prevalence of ARBD in Aboriginal populations.

FAS prevalence. From the ten studies that assessed the prevalence of FAS, two studies[53,58] did not report the denominators for which the prevalence rates were estimated and therefore, they were excluded from the quantitative analysis. FAS rates reported for Aboriginal groups in these two studies were 2.76 per 1000 live births[53] and 0.58 per 1000 live births, respectively. Heterogeneity in FAS prevalence estimates across the other eight studies (Figure 23) was substantial ($p<0.05$; $I^2 =$ 86.7%), with two studies that had sample sizes of less than 200 individuals27,46 accounting for a

great portion of the heterogeneity. After exclusion of the two studies with small sample size, a pooled estimate of FAS prevalence in Aboriginal peoples was calculated in 0.2% (95% CI: 0.1, 0.3), which translates to a rate of 2 FAS cases per 1000 population (Figure 24).

Figure 23: Studies assessing FAS prevalence in Aboriginal peoples

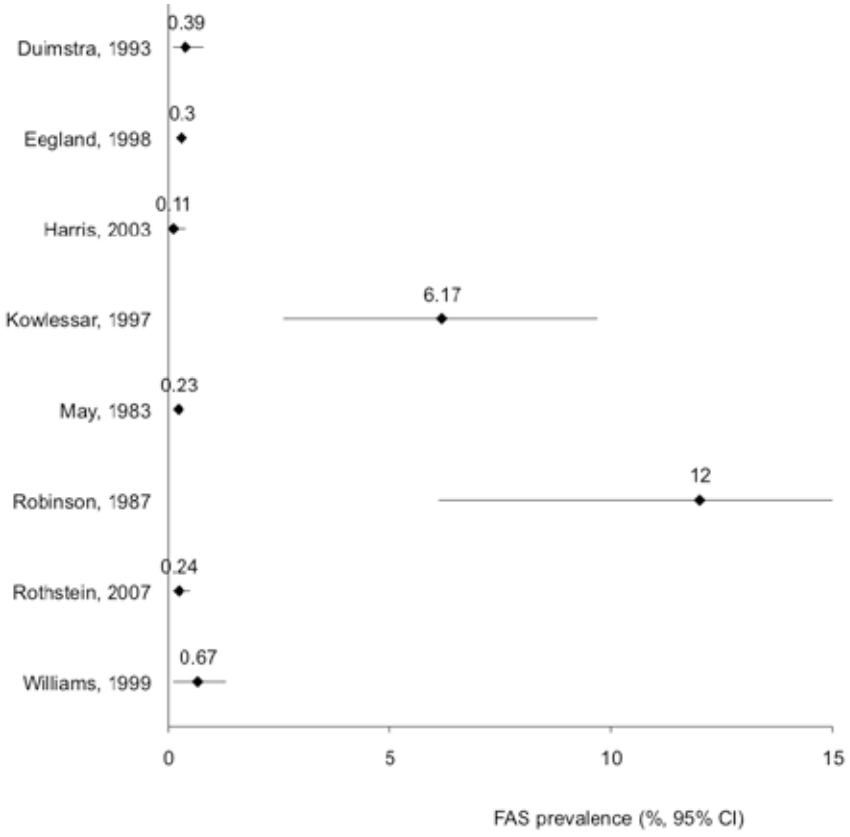
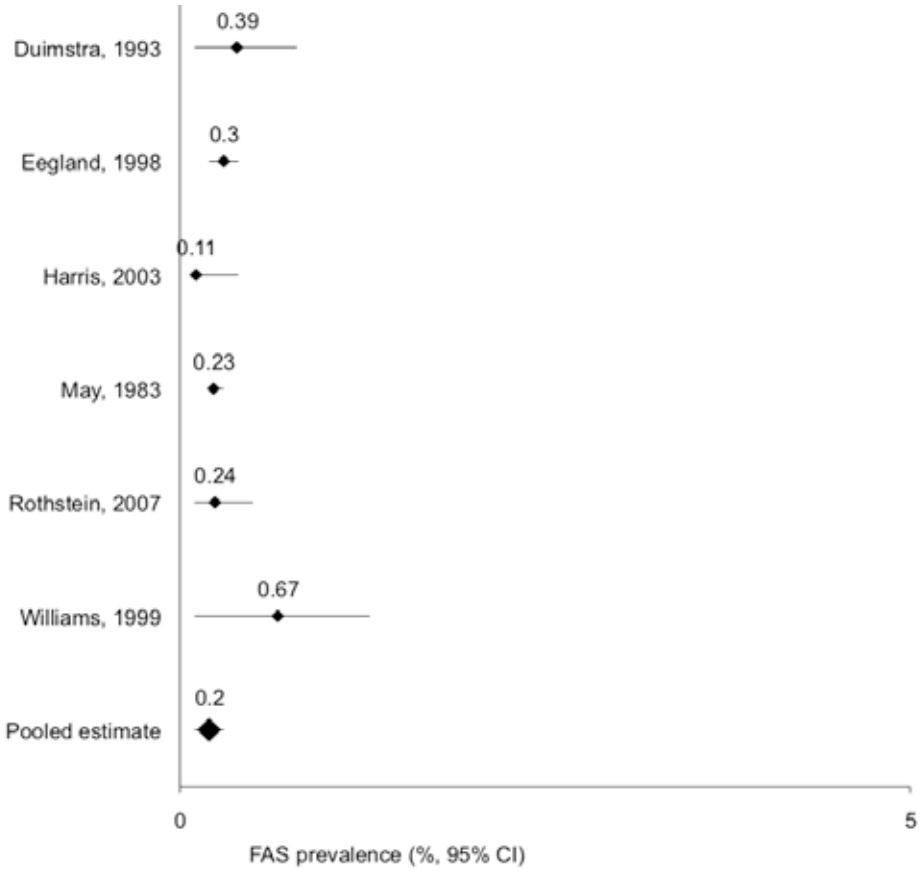


Figure 24: FAS prevalence in Aboriginal peoples based on studies with sample sizes greater than 200 individuals



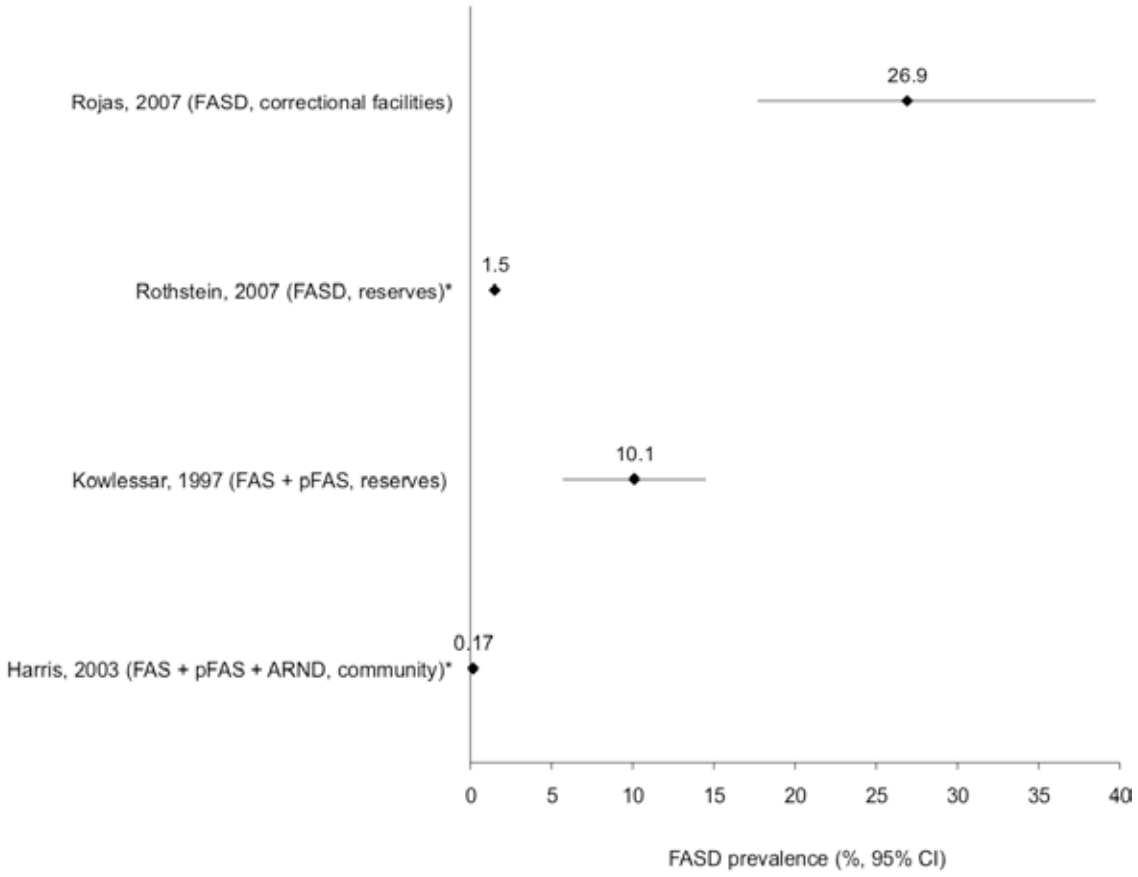
pFAS prevalence. One cohort study[59] and one cross-sectional study[27] reported on the prevalence of pFAS among Aboriginal peoples. Estimates from these two studies ranged from 0.13% (relative to the total population)[59] to 3.9% (95% CI:1.1, 6.8).[27]

ARND and ARBD prevalence. One retrospective cohort study[59] evaluated the prevalence of ARND in Aboriginal peoples and reported a rate of 0.02% (relative to the total population), which translates to a rate of 0.2 per 1000 live births. None of the studies reported on the prevalence of ARBD in Aboriginal peoples.

FASD prevalence from composite definitions. Four studies (one-cross-sectional study[27] and three cohort studies[59,62,63]) reported composite measures of FASD prevalence among Aboriginal peoples, including children in the community and youth from correctional facilities. Two studies (one conducted in Aboriginal children[63] and the other in a sample of Aboriginal youth sex offenders[62]) evaluated the prevalence of FASD as a single entity. FASD definitions in the other two studies included FAS and pFAS combined[27] and FAS, pFAS and ARND.[59]

Prevalence estimates of overall FASD in Aboriginal populations (Figure 25) varied greatly according to the setting in which the studies were conducted. FASD prevalence estimates were higher among Aboriginal youth in correctional facilities (26.9%) and lower in community samples 0.17%). Prevalence of FASD in reserves greatly differ (1.5% and 10.1%) in two studies that used different case definitions.

Figure 25: Studies assessing composite measures of FASD prevalence in Aboriginal peoples



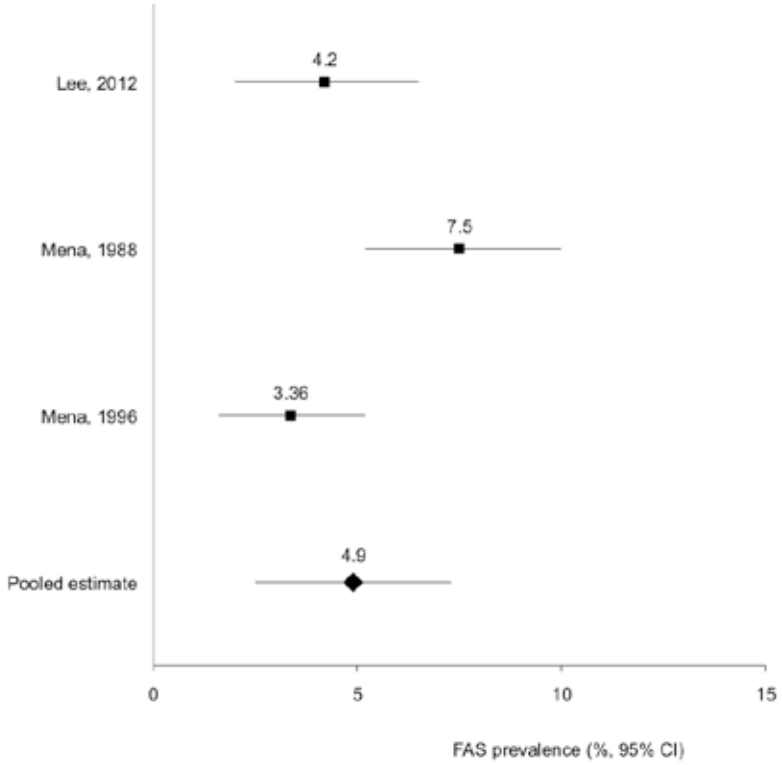
* 95% CI not calculated

Other ethnic groups: One retrospective cohort study[54] evaluated the prevalence of FAS across a variety of ethnic groups. The study did not provide denominators to re-calculate the prevalence rates and therefore, FAS rates per 1000 live births reported in the study were: 0.6 for African Americans; 0.08 for Hispanics; 2.9 for American Indians; 0.03 for Asians, compared to the white population in the USA (0.09).

Special education and clinical settings. Three cross-sectional studies[30,40,41] reported on the prevalence of FASD,[40] FAS[30,40,41] and pFAS[40] among children attending special education programs. None of the studies assessed the prevalence of ARND or ARBD in this population. One cross-sectional study[48] reported a composite measure of the prevalence of FAS and pFAS in a sample of children attending a specialized clinic for developmental disorders.

FAS prevalence. A meta-analysis of the prevalence of FAS among children in special education settings that totaled 1168 participants (Figure 26) yielded a pooled FAS prevalence rate of 4.9% (95% CI: 2.5, 7.3; four studies). Results across the studies were moderately homogeneous ($p>0.05$; $I^2 = 72\%$).

Figure 26: Studies assessing FAS prevalence in children in special education settings



pFAS prevalence: One study[40] that evaluated the prevalence of pFAS among children attending special education schools yielded an estimate of 5.4% (95% CI: 3.2, 7.7) for a rate of 54 per 1000 population.

Finally, one cross-sectional study that evaluated the prevalence of FAS and pFAS combined in a sample if children attending a clinic for developmental problems yielded a prevalence estimate of 2.1% (95% CI 1.2, 3.1).

FASD prevalence from composite definitions. Two cross-sectional studies conducted in children attending special education programs[40] and children attending a specialized clinic for developmental disorders[48] estimated the prevalence of FASD. The two studies defined FASD as FAS and pFAS combined and yielded estimates of 8.8% (95% CI:6.0, 11.6)[40] and 2.1% (95% CI: 1.2, 3.1).[48]

SUMMARY OF THE OVERALL RESULTS

Table 4 summarizes the results of the analysis of the prevalence of FASD in community, schools, foster care, prisons and correctional facilities and special populations. Prevalence is using ranges (when more than one study not combined into a meta-analysis provided prevalence data) or pooled estimates (when the estimate was derived from a meta-analysis). Translations to rates per 1000 population are also provided.

Table 4: Synthesis of individual study results

Setting		Community	Schools	Foster care	Prison and correctional facilities	Aboriginal peoples	Special education and clinical care
FAS	%	Range: 0.0006 - 0.3 (9 studies)	- Pooled (no South African studies): 0.36 (95% CI: 0.21, 0.50; 8 studies) - South African studies: 6.7 (95% CI: 5.4, 8.1, 5 studies)	Pooled: 21 (95% CI: 17.4, 24.5; 4 studies)	1.04 (1 study)	Pooled: 0.2 (95% CI: 0.1, 0.3, six studies)	Pooled: 4.9 (95% CI: 2.5, 7.3; four studies)
	Rate per 1000 population	0.006 – 3	- Non-South African studies: 3.6 - South African studies: 67	210	10.4	2	49
pFAS	%	Range: 0.045 - 0.53 (3 studies)	Pooled: 2.9 (95% CI: 2.0, 3.7; four studies)	2 - 14 (3 studies)	18 (1 study)	Range: 0.13 - 3.9 (2 studies)	5.4% (95% CI: 3.2, 7.7; one study)
	Rate per 1000 population	0.4 – 5.3	29	20 - 140	180	1.3 - 39	54
ARND and ARBD	%	Range: 0.37 - 1.08 (2 studies)	Pooled (no South African study): 0.23 (95% CI: 0.03, 0.4; 3 studies)	- ARND: 8.4 -11 (2 studies) - ARBD: 11.26 (1 study)	Range: 4.1 - 8.7 (2 studies)	ARND: 0.02 (1 study)	NR
	Rate per 1000 population	3.7 – 10.8	2.3	-ARND: 84 – 110 -ARBD: 112.6	41 - 87	0.2	
FASD - composite definitions	%	Range: 0.02 - 0.5 (six studies)	Range: 0.5 - 10.7 (10 studies)	Range: 30.5 - 52 (3 studies)	Range: 9.8 - 23.3 (3 studies)	- In correctional facilities: 26.9 - In community: 0.17 - In reserves (range): 1.5 - 10.1	Range: 2.1 - 8.8 (2 studies)
	Rate per 1000 population	Range: 0.2 - 5	5 - 107	305 - 520	98 - 233	- In correctional facilities: 269 - In community: 1.7 - In reserves (range): 15 - 101	21 - 88

95% CI: 95% confidence interval; ARBD = alcohol-related birth defect (s); ARND = alcohol-related neurodevelopmental disorder(s); FAS = fetal alcohol syndrome; FASD = fetal alcohol spectrum disorder(s); pFAS: partial fetal alcohol spectrum disorder

DISCUSSION

This systematic review has summarized the evidence from 54 studies on the prevalence of FASD with a synthesis of estimates for different subtypes of FASD applicable to important settings and populations. To our knowledge, this is the broadest systematic review on this subject to date that has conducted a quantitative synthesis of FASD prevalence data.

The review has revealed that the majority of studies assessing the prevalence of FASD have been published in peer-reviewed journals, with most of them published after the introduction of the 1996 IOM criteria. Our search strategy identified original studies of FASD prevalence conducted in all continents, with most of the studies being conducted in North America (USA and Canada) and Europe (France, Italy, Croatia, Germany, Lithuania, Norway, Poland, the Netherlands, Russia, and Sweden). Countries that individually accounted for the largest number of studies were the USA (15 studies) and South Africa (12 studies). Nine studies assessing the prevalence of FASD in Canada were identified in this review.

The wide representation of countries in which FASD studies have been conducted indicates that FASD is a well-studied disorder, a matter of concern and challenges for researchers worldwide for which its prevalence rate has been estimated in several different cultures. Although the objective of this review was not to provide a profile of the distribution of FASD by countries around the world, it is clear that FASD crosses all boundaries; it does not seem to be isolated into a specific region and impacts many communities around the world.

Seven studies evaluated the prevalence of the entire FASD spectrum as a whole, whereas 18 studies evaluated the prevalence of FASD as a composite of certain subtypes (e.g., FAS plus pFAS; FAS plus ARND and ARBD). Among the different FASD subtypes, estimates of FAS prevalence were reported in the vast majority of the studies (46 studies) followed by pFAS (19 studies), ARND (10 studies) and ARBD (four studies) prevalence. The greater interest in assessing the prevalence of FAS is not unexpected, as it has been largely considered as the most severe manifestation of the spectrum of FASD conditions.

The prevalence of FASD and its subtypes have been evaluated in a variety of settings including the community, schools, foster care systems, prisons, and correctional facilities. Similarly, some groups in the population (i.e., Aboriginal peoples) have been particularly targeted in the study of FASD prevalence. The interest in studying the prevalence of FASD in Aboriginal groups results of a public health concern stemming from knowledge of higher rates of heavy alcohol drinking among women in Aboriginal groups compared to their non-Aboriginal counterparts (e.g., 10.2% versus 3.3% in Canada),[72] but also because of the recognition of significant social, economical and political inequalities that have historically affected Aboriginal peoples and that constitute important determinants of their health status.

Substantial variations and inconsistencies in FASD prevalence estimates were identified across the studies included in the review. Heterogeneity among studies can be attributed to many causes, including differences in the methods of case ascertainment and diagnostic criteria, study participants' age and varying degrees of public awareness about FASD. Similarly, a large variation in FASD prevalence estimates has been shown across different study settings as a result of the sample composition across the studies. For example, prevalence estimates of FASD were lower in community, population-based samples compared to those obtained from studies including individuals at a higher risk of having developmental disorders detected (i.e., foster case system and

prisons and correctional facilities). Results of studies conducted in different study settings are discussed separately below.

Prevalence of FASD in the community

Studies assessing the prevalence of FASD in community and population-based samples reported estimates that ranged 0.02% to 0.5% which translate to FASD rates of 0.2 to 5 per 1000 population. Prevalence estimates were substantially heterogeneous for FAS (0.0006% to 0.3%), which is not unexpected as the studies used different methods for case identification, ranging from birth certificates and medical chart review (which reported the lowest prevalence rates) to active case ascertainment methods. Similar heterogeneity was identified for pFAS (0.0006% to 0.3%) and ARND and ARBD estimates (1.08% and 0.37%).

Prevalence of FASD in schools

Studies on FASD prevalence conducted in school settings provide a unique opportunity to use active ascertainment methods for case identification in representative samples of children from local populations.[8] Results of this review found wide variations in the rate of overall FASD in studies conducted in school settings, ranging from 0.5% to 10.7%; however, meta-analyses of the prevalence of specific FASD subtypes provided more reliable information after controlling for potential sources of heterogeneity. A meta-analysis of FAS studies excluding those conducted in South Africa (which are recognized for reporting systematically higher rates of FASD in a region with one of the highest rates of alcohol consumption in the world) yielded a pooled estimate of 0.36% which translates to a rate of 3.6 per 1000 population. The pooled prevalence of pFAS in school settings was higher after adjusting for inadequate sampling strategies: 2.9%, which translates to a rate of 29 per 1000 population. The pooled prevalence of ARND was calculated in 0.23%, for a rate of 2.3 per 1000 population. These estimates are within the range of those reported by May et al.[8] in a review of in-school studies on the prevalence of FASD.

Prevalence of FASD among children in foster care

Evidence from a limited number of studies suggest that a large proportion of children with FASD (up to 80%) live in institutional or foster placements or are under adoption care.[73] Results from this review indicate that prevalence estimates of overall FASD in foster care settings ranged from 30.5% to 52%, which translate to FASD rates of 305 to 520 per 1000 population in foster care settings. For FAS alone, a meta-analysis of studies using formal diagnostic criteria for case identification showed that approximately 21% of children in foster care have likely to have the condition. Prevalence estimates for other subtypes such as pFAS, ARND and ARB were also high, ranging from 2% to 14% depending on the methods of diagnosis and case ascertainment. Because it is not always possible to establish a history of maternal drinking for children in foster placements or among children that have been adopted, it is likely that these estimates are underreported.

Prevalence of FASD in prisons and correctional facilities

The frequency of FASD among individuals within correctional and justice systems have received considerable attention in recent years. Estimates of FASD prevalence in correctional systems were derived from studies conducted in Canada and the USA with numbers ranging between 9.8% to 23.3%, which translate to FASD rates of 98 to 233 per 1000 population in prisons and correctional settings. Estimates of FASD subtypes were heterogeneous and those based on self-reported diagnosis of the condition should be interpreted with caution due to potential misclassification bias. More reliable data using active case ascertainment strategies yielded estimates of 1.04% for FAS, 10% for pFAS and 4.1 to 8.7% for ARND. Because it is very difficult to accurately establish a

history of maternal drinking in youth and adult populations in prisons and correctional facilities, it is likely that the true prevalence of FASD is underestimated. The magnitude of the estimates of FASD prevalence in correctional systems identified in this review allow to conclude, in line with the review by Popova et al.[74] that FASD is a substantial problem among youth and adults in correctional facilities and constitute an area that deserves further attention in the criminal justice system.

Prevalence of FASD in Aboriginal populations

Prevalence estimates of overall FASD in Aboriginal populations varied greatly according to the setting in which the studies were conducted. FASD prevalence estimates were higher among Aboriginal youth in correctional facilities (26.9%) and lower in community samples (0.17%). This review was not aimed at making formal direct comparisons of FASD prevalence between Aboriginal and non-Aboriginal populations; however, rates of FASD between Aboriginal and non-Aboriginal people in correctional systems or the community were similar. A pooled estimate of FAS prevalence in Aboriginal peoples was calculated in 0.2% (95% CI: 0.1, 0.3, six studies) for a rate of 2 FAS cases per 1000 population, which is not substantially higher than those identified in community samples of the general population. Estimates from two studies on pFAS among Aboriginal populations ranged from 0.13% to 3.9%. Prevalence of ARND in Aboriginal peoples in one study reported a rate of 0.02% (relative to the total population), which translates to a rate of 0.2 per 1000 live births.

Prevalence of FASD among children living in reserves ranged from 1.5% to 10.1%. Results from studies conducted in individual reserves are likely not representative of the Aboriginal population as a whole and may rather reflect the impact of socio-economic factors that interplay with levels of maternal intake of alcohol in deprived settings.

Prevalence of FASD in other specialized settings

Composite estimates of FASD in special education ranged from 2.1% to 8.8%. A meta-analysis of the prevalence of FAS among children in special education settings yielded a pooled FAS prevalence rate of 4.9% (95% CI: 2.5, 7.3), whereas the prevalence of pFAS among children attending special education schools was 5.4%.

Difficulties in estimating FASD prevalence

Prevalence estimates of FASD reported in this review should be interpreted with caution because of the large variability found in all analyses. Estimating the prevalence of FASD was hampered by a number of methodological challenges, differences in case definition, and inherent bias in the study designs of the individual studies. Significant heterogeneity in prevalence measures of FASD, which was incompletely explained by subgroup analyses, was identified by graphic representation of estimates and by several indices of heterogeneity. Despite wide variation, we were able to provide some pooled estimates of FASD that are useful to indicate the public health burden of the condition.

It is important, however, to describe some of the potential sources of heterogeneity that may have accounted for differences in FASD estimates across the studies for all the study settings studied in this review.

First, the wide variation in FASD prevalence can result from different methods of diagnosis and case identification. Self-reported physician diagnoses and data derived from birth certificates and chart reviews appear to underestimate FASD prevalence. For many FASD conditions studied, a variety of diagnostic criteria with different levels of precision were used. Possible effects of differences in the methods of diagnosis and case definition result in some true FASD cases never

being diagnosed, and other cases being over estimated as a result of clinical ambiguity. This is particularly important, when signs of FAS are interpreted irrespective of the knowledge of maternal exposure to alcohol.

Misclassification of FASD risk is another important factor. Verification of maternal drinking can be often challenging and biomarkers to accurately classify alcohol exposure in newborn and infants are under development. Similarly, different levels of consent for alcohol screening during pregnancy and newborn alcohol screening may have biased the results of individual studies.

Another important source of heterogeneity include the age of the study population. Although studies conducted in school and foster care settings included children from similar age ranges (between 7 and 12 years approximately), studies conducted in correctional systems and the community included a wide diversity of age ranges. Manifestations of FASD may be more or less obvious depending on the age of the individual. In some instances, early manifestations of FAS can be more accurately detected at birth, with some phenotypical characteristics becoming less pronounced over time. On the other hand, the identification of neurodevelopmental, learning disabilities and behavioural problems associated with FASD are more likely to be identified in older children.

Differences in the methodological quality and reporting of the studies included in the review also limited the comparability of the studies and the utility of some data extracted. Finally study sample size is another factor that can explain variability in FASD estimates with studies based on smaller sample sizes identifying a smaller number of cases.

Strengths and Limitations

One of the main strengths of this systematic review is the comprehensive search strategy including multiple electronic databases. This systematic review update is likely to have identified most of the peer-reviewed scientific literature on the prevalence of FASD that has been published up to December 2012. It is possible, however, that some studies were not identified in the searches if they were not published in mainstream journals. Similarly, there may have been some time lag bias, with smaller studies or studies with unremarkable results being published slower than larger studies and therefore, they may have not been captured in the searches.

We adopted a rigorous approach to select studies for inclusion in the review. Similarly, we appraised the methodological quality of individual studies using standard quality assessment tools. Another important strength of this systematic review is that we controlled for the impact of multiple-publication bias in the analysis of the results. A total of five studies were identified as multiple publications of unique studies included in the review. Identifying multiple publications in this review avoided the inclusion of duplicate publication of data in the meta-analyses that may have skewed the interpretation of the prevalence estimates.

The differences in study methodologies, case definition, population sizes, study date, and the country in which the studies were performed all render meaningful comparisons and pooling of data difficult and approximate. Our analyses of heterogeneity and calculation of confidence intervals relied on the completeness of data published in the original studies.

A formal assessment of the impact of publication bias on the review results was not conducted as funnel plots were not considered appropriate due to the large degree of variation across the studies. Eight studies that were potentially eligible were not retrieved; however, it is unlikely that the lack of availability of data from these studies is a direct consequence of the FASD prevalence that they may

have observed. Therefore, the impact of publication bias related to the lack of retrieval of this set of studies is expected to be low.

Research Directions in the Evaluation of FASD Prevalence

The current review helps consolidate current knowledge of FASD prevalence and perhaps more importantly, it makes evident the gaps in knowledge that still exist concerning the epidemiology of FASD in Canada. Future studies assessing FASD prevalence should use more uniform case definitions and ascertainment methods and provide prevalence values standardized to the Canadian population to facilitate comparisons across provinces. Canada serves as an ideal territory for the study of FASD epidemiology due to the presence of a growing community of FASD researchers and publicly-funded, universally accessible health care. Establishment of sustained active surveillance systems for the condition would further strengthen such research efforts.

CONCLUSIONS

FASD prevalence rates have been evaluated in a variety of settings including the community, schools, foster care systems, prisons, and correctional systems. The magnitude of FASD prevalence vary according to the setting in which it was evaluated, with higher estimates identified in foster and justice system compared to those obtained from community and school samples. All of them, however, deserve attention for the planning and organization of prevention strategies. The epidemiology of FASD does not seem to be isolated into a specific region and impacts many communities around the world. There is a need for continued good quality research on the prevalence of FASD to provide a basis for health policy and resource allocation for prevention initiatives and clinical and social services.

REFERENCES

1. Sokol RJ, aney-Black V, Nordstrom B. Fetal alcohol spectrum disorder. *JAMA* 2003;290(22):2996-9.
2. Astley SJ, Clarren SK. Diagnosing the full spectrum of fetal alcohol-exposed individuals: introducing the 4-digit diagnostic code. *Alcohol Alcohol* 2000;35(4):400-10.
3. Abel EL. Prenatal effects of alcohol. *Drug and Alcohol Dependence* 1984;14(1):1-10.
4. Public Health Agency of Canada. It's your health. Available from: *http://www.hc-sc.gc.ca/hl-vs/iyh-vsv/diseases-maladies/fasd-etcaf-eng.php* 2009 [accessed 3 Feb, 2013].
5. Abel EL, Sokol RJ. Fetal alcohol syndrome is now leading cause of mental retardation. *Lancet* 1986; 2(8517):1222.
6. Abel EL, Sokol RJ. Incidence of fetal alcohol syndrome and economic impact of FAS-related anomalies. *Drug and Alcohol Dependence* 1987;19(1):51-70.
7. Abel EL, Hannigan JH. Maternal risk factors in fetal alcohol syndrome: provocative and permissive influences. *Neurotoxicology and Teratology* 1995;17(4):445-62.
8. May PA, Gossage JP, Kalberg WO, Robinson LK, Buckley D, Manning M, et al. Prevalence and epidemiologic characteristics of FASD from various research methods with an emphasis on recent in-school studies. *Developmental Disabilities Research Reviews* 2009;15(3):176-92.
9. Chiodo LM, Janisse J, aney-Black V, Sokol RJ, Hannigan JH. A metric of maternal prenatal risk drinking predicts neurobehavioral outcomes in preschool children. *Alcoholism* 2009 Apr;33(4):634-44.
10. Burd L, Moffatt ME. Epidemiology of fetal alcohol syndrome in American Indians, Alaskan Natives, and Canadian Aboriginal peoples: a review of the literature. *Public Health Reports* 1994;109(5):688-93.
11. Loney PL, Chambers LW, Bennett KJ, Roberts JG, Stratford PW. Critical appraisal of the health research literature: prevalence or incidence of a health problem. *Chronic Diseases of Canada* 1998;19(4):170-6.
12. Wells GA, Shea B, O'Connell D, Petersen J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. Available from: *http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp* (accessed 28 Feb, 2013).
13. Juni P, Witschi A, Bloch R, Egger M. The hazards of scoring the quality of clinical trials for meta-analysis. *JAMA* 1999;282:1054-60.
14. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine* 2002;21:1539-58.
15. Berkey CS, Hoaglin DC, Mosteller F, Colditz GA. A random-effects regression model for meta-analysis. *Statistics in Medicine* 1995;14:395-411.
16. Neveloff J, Fuchs SC, Moreira LB. Meta-analysis and forest plots using a Microsoft Excel spreadsheet: step-by-step guide focusing on descriptive data analysis. *BMC Research Notes* 2012;5(52).

17. Astley SJ, Stachowiak J, Clarren SK, Clausen C. Application of the fetal alcohol syndrome facial photographic screening tool in a foster care population. *Journal of Pediatrics* 2002;141(5):712-7.

18. Burd L, Selfridge R, Klug M, Bakko S. Fetal alcohol syndrome in the United States corrections system. *Addiction Biology* 2004;9(2):169-76.

19. Burd L, Selfridge RH, Klug MG, Juelson T. Fetal alcohol syndrome in the Canadian Corrections system. *Journal of FAS International* 2013;2003(e14).

20. Clarren SK, Randels SP, Sanderson M, Fineman RM. Screening for fetal alcohol syndrome in primary schools: a feasibility study. *Teratology* 2001;63(1):3-10.

21. Cunniff C, Markley R, Feild CR. Fetal Alcohol Syndrome Surveillance - Epsdt Screening. *Pediatric Research* 1994;35(4):A91.

22. Elgen I, Bruaroy S, Laegreid LM. Lack of recognition and complexity of foetal alcohol neuroimpairments. *Acta Paediatrics* 2007;96(2):237-41.

23. Elliott EJ, Payne J, Morris A, Haan E, Bower C. Fetal alcohol syndrome: a prospective national surveillance study. *Archives of Diseases in Children* 2008;93(9):732-7.

24. Fast DK, Conry J, Loock CA. Identifying fetal alcohol syndrome among youth in the criminal justice system. *Journal of Developmental and Behavioral Pediatrics* 1999;20(5):370-2.

25. Feldmann R. Prevalence of FAS in Germany. *Journal of Population Therapeutics and Clinical Pharmacology* 2012;19(3):e421.

26. Knuiman S, Rijk C, Hoksbergen R, Van BA. Fetal Alcohol Spectrum Disorders in children adopted from Poland: neurobehavioral functioning and early detection. *Journal of Population Therapeutics and Clinical Pharmacology* 2012;19(3):e415-6.

27. Kowlessar DL. *An examination of the effects of prenatal alcohol exposure on school-age children in a Manitoba First Nation Community: a study of fetal alcohol syndrome prevalence and dysmorphology.* Canada: Winnipeg, MB: The University of Manitoba; 1997.

28. Kuo HT, Wu HP, Li Q, Zhou FC, Morisky DE, Lee ML. *In-school study of prevalence of fetal alcohol spectrum disorder in east Taiwan.* Alcohol Clin Exp Res Conference: 35th Annual Scientific Meeting of the Research Society on Alcoholism, RSA; 2012 Jun 23-27; San Francisco, CA.

29. Kuzmenkoviene E, Prasauskiene A, Endziniene M. The prevalence of fetal alcohol spectrum disorders and concomitant disorders among orphanage children in Lithuania. *Journal of Population Therapeutics and Clinical Pharmacology* 2012; 19(3):e423.

30. Lee HK. Epidemiology of Fetal Alcohol Syndrome in Korea. *Alcoholism, Clinical and Experimental Research* 2012;36:34A.

31. MacPherson P., Chudley, AE. Fetal Alcohol Spectrum Disorder (FASD): Screening and estimating incidence in an adult correctional population. 2nd International Conference on Fetal Alcohol Spectrum Disorder: Research, Policy, and Practice around the World, Victoria BC, March 7-10, 2007. Available from: *events.onlinebroadcasting.com/fas/09707/ppts/correctional.ppt* (accessed October 6th, 2011).

32. May PA, Gossage JP. Epidemiological Analysis of Three Waves of Data About Children with Fetal Alcohol Spectrum Disorders and Controls in A Small City in the Northern Plains. *Alcoholism, Clinical and Experimental Research* 2011;35(6):137A.

33. May PA, Fiorentino D, Phillip GJ, Kalberg WO, Eugene HH, Robinson LK, et al. Epidemiology of FASD in a province in Italy: Prevalence and characteristics of children in a random sample of schools. *Alcoholism* 2006;30(9):1562-75.

34. May PA, Fiorentino D, Coriale G, Kalberg WO, Hoyme HE, Aragon AS, et al. Prevalence of children with severe fetal alcohol spectrum disorders in communities near Rome, Italy: new estimated rates are higher than previous estimates. *International Journal of Environmental Research & Public Health* 2011;8(6):2331-51.

35. May PA, Gossage JP, Marais AS, Adnams CM, Hoyme HE, Jones KL, et al. The epidemiology of fetal alcohol syndrome and partial FAS in a South African community. *Drug and Alcohol Dependence* 2007;88(2-3):259-71.

36. May PA, Marais A-S, Barnard R, Seedat S, Blankenship J, Gossage JP. An epidemiology of diagnosing the full spectrum of FASD. *Alcoholism, Clinical and Experimental Research* 2012;36:212.

37. May PA, Hymbaugh KJ, Aase JM, Samet JM. Epidemiology of fetal alcohol syndrome among American Indians of the Southwest. *Social Biology* 1983;30(4):374-87.

38. May PA, Brooke L, Gossage JP, Croxford J, Adnams C, Jones KL, et al. Epidemiology of fetal alcohol syndrome in a South African community in the Western Cape Province. *American Journal of Public Health* 2000;90(12):1905-12.

39. Mena M, Nazal R, Fernandez E, Munoz M, Mora F, Olivo G, et al. Prevalence of fetal alcohol syndrome in foster homes of the Servicio Nacional de Menores, VIII region, Chile. *Revista Médica de Chile* 1987;115(12):1218-25.

40. Mena M, Casanueva V, Fernandez E, Carrasco R, Perez H. Fetal alcohol syndrome at schools for mentally handicapped children in Concepcion, Chile. *Bulletin of the Pan American Health Organization* 1986;20(2):157-69.

41. Mena M, Nazal R, Albornoz C, Pettinelli H, Velasquez P, Soza G. Fetal alcohol syndrome: prevalence in 4 special education schools in Chile. *Revista Médica de Chile* 1988;116(12):1252-6.

42. Murphy A, Chittenden M. *Time out II: a profile of BC youth in custody.* Vancouver, BC: The McGeary Centre Society; 2005.

43. Olivan-Gonzalvo G. Frequency of fetal alcohol syndrome in institutionalized children of eastern European countries. *Revue Neurologique* 2011;53(2):127-8.

44. Olivier L, Chersich M, Urban M, Viljoen D. *The evaluation of maternal risk factors and epidemiology of FASD in Two populations within the Northern Cape Province of South Africa.* Alcohol Clin Exp Res Conference: 33rd Annual Scientific Meeting of the Research Society on Alcoholism, RSA; 2010 Jun 26-30; San Antonio, TX:212A.

45. Petkovic G, Barisic I. FAS prevalence in a sample of urban schoolchildren in Croatia. *Reproductive Toxicology* 2010;29(2):237-41.

46. Robinson GC, Conry JL, Conry RF. Clinical profile and prevalence of fetal alcohol syndrome in an isolated community in British Columbia. *CMAJ* 1987;137(3):203-7.

47. Serreau R, Maillard T, Verdier R, Bouchara L, Catteau C, Herve C, et al. Clinical study and prevalence of fetal alcohol syndrome in medico-social institutions of the Reunion Island. *Archives de Pédiatrie* 2002;9(1):14-20.

48. Shanske AL. Prevalence of the Fetal Alcohol Syndrome in A Developmental Clinic Population. *American Journal of Human Genetics* 1980;32(6):A128.

49. Tenenbaum A, Hertz P, Dor T, Castiel Y, Sapir A, Wexler ID. Fetal alcohol spectrum disorder in Israel: increased prevalence in an at-risk population. *The Israel Medical Association Journal* 2011;13(12):725-9.

50. Urban M, Chersich MF, Fourie LA, Chetty C, Olivier L, Viljoen D. Fetal alcohol syndrome among grade 1 schoolchildren in Northern Cape Province: prevalence and risk factors. *South African Medical Journal* 2008;98(11):877-82.

51. Viljoen DL, Gossage JP, Brooke L, Adnams CM, Jones KL, Robinson LK, et al. Fetal alcohol syndrome epidemiology in a South African community: a second study of a very high prevalence area. *Journal of Studies on Alcohol* 2005;66(5):593-604.

52. Allen K, Riley M, Goldfeld S, Halliday J. Estimating the prevalence of fetal alcohol syndrome in Victoria using routinely collected administrative data. *Australian and New Zealand Journal of Public Health* 2007;31(1):62-6.

53. Bower C, Silva D, Henderson TR, Ryan A, Rudy E. Ascertainment of birth defects: the effect on completeness of adding a new source of data. *Journal of Paediatrics and Child Health* 2000;36(6):574-6.

54. Chavez GF, Cordero JF, Becerra JE. Leading Major Congenital Malformations Among Minority Groups in the United States, 1981-1986. *MMWR CDC Surveillance Summaries* 1988;37(3):17-24.

55. Dehaene P, Samaille-Villette C, Boulanger-Fasquelle P, Subtil D, Delahousse G, Crepin G. Diagnosis and prevalence of fetal alcoholism in maternity. *Presse Medicale* 1991;20(21):1002.

56. Druschel CM, Fox DJ. Issues in estimating the prevalence of fetal alcohol syndrome: examination of 2 counties in New York State. *Pediatrics* 2007;119(2):e384-90.

57. Egeland GM, Perham-Hester KA, Gessner BD, Ingle D, Berner JE, Middaugh JP. Fetal alcohol syndrome in Alaska, 1977 through 1992: an administrative prevalence derived from multiple data sources. *American Journal of Public Health* 1998;88(5):781-6.

58. Habbick BF, Nanson JL, Snyder RE, Casey RE, Schulman AL. Foetal alcohol syndrome in Saskatchewan: unchanged incidence in a 20-year period. *Canadian Journal of Public Health* 1996; 87(3):204-7.

59. Harris KR, Bucens IK. Prevalence of fetal alcohol syndrome in the Top End of the Northern Territory. *Journal of Paediatrics and Child Health* 2003;39(7):528-33.

60. From the Centers for Disease Control and Prevention. Fetal alcohol syndrome--Alaska, Arizona, Colorado, and New York, 1995-1997. *JAMA* 2002;288(1):38-40.

61. O'Leary CM, Nassar N, Kurinczuk JJ, de KN, Geelhoed E, Elliott EJ, et al. Prenatal alcohol exposure and risk of birth defects. *Pediatrics* 2010;126(4):e843-50.

62. Rojas EY, Gretton HM. Background, offence characteristics, and criminal outcomes of Aboriginal youth who sexually offend: a closer look at Aboriginal youth intervention needs. *Sexual abuse: a Journal of Research and Treatment* 2007;19(3):257-83.

63. Rothstein J, Heazlewood R, Fraser M, Paediatric Outreach Service. Health of Aboriginal and Torres Strait Islander children in remote Far North Queensland: findings of the Paediatric Outreach Service. *Medical Journal of Australia* 2007;186(10):519-21.

64. Williams RJ, Odaibo FS, McGee JM. Incidence of fetal alcohol syndrome in northeastern Manitoba. *Canadian Journal of Public Health* 1999;90(3):192-4.

65. Duimstra C, Johnson D, Kutsch C, Wang B, Zentner M, Kellerman S, et al. A fetal alcohol syndrome surveillance pilot project in American Indian communities in the Northern Plains. *Public Health Reports* 1993;108(2):225-9.

66. Kuehn D, Aros S, Cassorla F, Avaria M, Unanue N, Henriquez C, et al. A prospective cohort study of the prevalence of growth, facial, and central nervous system abnormalities in children with heavy prenatal alcohol exposure. *Alcoholism* 2012;36(10):1811-9.

67. Landgren M, Svensson L, Stromland K, Andersson GM. Prenatal alcohol exposure and neurodevelopmental disorders in children adopted from eastern Europe. *Pediatrics* 2010;125(5):e1178-85.

68. Poitra BA, Marion S, Dionne M, Wilkie E, Dauphinais P, Wilkie-Pepion M, et al. A school-based screening program for fetal alcohol syndrome. *Neurotoxicology and Teratology* 2003;25(6):725-9.

69. Sokol RJ, Ager J, Martier S, et al. Significant determinants of susceptibility to alcohol teratogenicity. *Annals of the New York Academy of Science* 1986;477:87-102.

70. Weiss M, Cronk CE, Mahkorn S, Glysch R, Zirbel S. The Wisconsin Fetal Alcohol Syndrome Screening Project. *WMJ: Official Publication of the State Medical Society of Wisconsin* 2004;103(5):53-60.

71. Chaudhuri JD. Alcohol and the developing fetus: a review. *Medical Science Monitor* 2000;6(5):1031-41.

72. Health Canada. *A statistical profile of the health of First Nations in Canada: determinants of health, 1999 to 2003.* Ottawa, ON: Health Canada; 2009.

73. Streissguth AP, Bookstein FL, Barr HM, Sampson PD, O'Malley K, Young JK. Risk factors for adverse life outcomes in fetal alcohol syndrome and fetal alcohol effects. *Journal of Developmental and Behavioral Pediatrics* 2004;25(4):228-38.

74. Popova S, Lange S, Bekmuradov D, Mihic A, Rehm J. Fetal alcohol spectrum disorder prevalence estimates in correctional systems: a systematic literature review. *Canadian Journal of Public Health* 2011; 102(5):336-40.

APPENDIX A: METHODOLOGY

Search Strategy

Comprehensive searches of psychological, sociological, and biomedical electronic databases listed in Table A1 were conducted from database inception) to December 5, 2012. The search strategy was designed by an Information Specialist at the IHE and comprised of both controlled vocabulary and keywords. In addition, reference lists of reviews and retrieved articles were browsed for relevant studies.

Table A1: Databases searched for relevant studies

Database	Edition or date searched	Search Terms ††
Core Databases		
Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946	1946 – Dec 5, 2012	1. fetal alcohol syndrome/ 2. f?etal alcohol.tw. 3. ((alcohol* or ethanol) adj5 (birth defects or congenital malformations or neurodevelopmental)).tw. 4. ((fas and (alcohol* or ethanol or (drinking not drinking water))) not (fatty acid adj2 synt*)).tw. 5. (fasd or fae or arbd or arnd).tw. 6. or/1-5 7. Fetal Alcohol Syndrome/ep [Epidemiology] 8. Incidence/ 9. Prevalence/ 10. Population surveillance/ 11. Mass Screening/ 12. (incidence or prevalen*).tw. 13. epidemiolog*.tw. 14. epidemiologic studies/ 15. epidemiologic methods/ 16. cross-sectional studies/ 17. surveillance.tw. 18. chart review.tw. 19. (case* adj5 (identif* or ascertain* or finding)).tw. 20. "door to door".tw. 21. or/7-20 22. 6 and 21 23. animals/ 24. (rat or rats or mouse or mice or rodent*).ti. 25. 22 not (23 or 24) 26. case reports/ or clinical trial/ or clinical trial, phase i/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or controlled clinical trial/ or randomized controlled trial/ or in vitro/ or twin study/ 27. 25 not 26
Embase (Ovid Interface)	1974 – Dec 5, 2012	1. fetal alcohol syndrome/ 2. f?etal alcohol.tw. 3. ((alcohol* or ethanol) adj5 (birth defects or congenital malformations or neurodevelopmental)).tw. 4. ((fas and (alcohol* or ethanol or (drinking not drinking water))) not (fatty acid adj2 synt*)).tw. 5. (fasd or fae or arbd or arnd).tw. 6. or/1-5 7. Fetal Alcohol Syndrome/ep 8. Incidence/ 9. Prevalence/ 10. disease surveillance/ 11. mass screening/ or developmental screening/ or newborn screening/ 12. (incidence or prevalen*).tw.

		13. epidemiolog*.tw. 14. epidemiology/ 15. cross-sectional studies/ 16. "medical record review"/ 17. surveillance.tw. 18. (case* adj5 (identif* or ascertain* or finding)).tw. 19. "door to door".tw. 20. or/7-19 21. 6 and 20 22. (exp vertebrate/ or animal/ or exp experimental animal/ or nonhuman/ or animal.hw.) not (exp human/ or human experiment/) 23. (rat or rats or pig or pigs or porcine or mouse or mice or hamster or hamsters or animal or animals or dog or dogs or cats or bovine or sheep or murine or primate*).ti,ab,sh. not (exp human/ or human experiment/) 24. 21 not (22 or 23) 25. clinical trial/ or controlled clinical trial/ or phase 1 clinical trial/ or phase 2 clinical trial/ or phase 3 clinical trial/ or phase 4 clinical trial/ or clinical study/ or case report/ or case study/ or intervention study/ or major clinical study/ or exp in vitro study/ 26. 24 not 25
PsycINFO (Ovid interface)	1806 – Dec 5, 2012 (November Week 4 2012)	1. fetal alcohol syndrome/ 2. f?etal alcohol.tw. 3. ((alcohol* or ethanol) adj5 (birth defects or congenital malformations or neurodevelopmental)).tw. 4. ((fas and (alcohol* or ethanol or (drinking not drinking water))) not (fatty acid adj2 synt*)).tw. 5. (fasd or fae or arbd or arnd).tw. 6. or/1-5 7. (incidence or prevalen*).tw. 8. epidemiolog*.tw. 9. epidemiology/ 10. surveillance.tw. 11. (case* adj5 (identif* or ascertain* or finding)).tw. 12. "door to door".tw. 13. screening.tw. 14. cross sectional.tw. 15. chart review.tw. 16. or/7-15 17. 6 and 16 18. animals/ 19. 17 not 18 20. experimental design/ or clinical trials/ or experimental methods/ 21. case report/ 22. 19 not (20 or 21)
CINAHL (EBSCO interface)	1937- Dec 5, 2012	S1: fetal alcohol OR foetal alcohol OR fasd OR fae OR arbd OR arnd S2: alcohol n8 birth defect* S3: alcohol n8 neurodevelopmental S4: alcohol n8 malformation* S5: S1 OR S2 OR S3 OR S4 S6: (MH "Fetal Alcohol Syndrome/EP") S7: prevalen* or incidence or epidemiolog* or surveillance or cross-sectional or screening S8: case* n5 identif* OR case* n5 ascertain* OR case* n5 finding S9: S6 OR S7 OR S8 S10: S5 AND S9 S11: ((MH "Clinical Trials+") OR (MH "Nonrandomized Trials") OR (MH "One-Shot Case Study") OR (MH "Community Trials")) OR (case study or case report* or case series) S12: S10 NOT S11
SocINDEX with Full Text (EBSCO interface)	1908 - Dec 5, 2012	S1: fetal alcohol OR foetal alcohol OR fasd OR fae OR arbd OR arnd S2: alcohol n8 birth defect* S3: alcohol n8 neurodevelopmental S4: alcohol n8 malformation* S5: S1 OR S2 OR S3 OR S4 S6: prevalen* or incidence S7: epidemiolog* or surveillance or cross-sectional S8: case* n5 identif* OR case* n5 ascertain* OR case* n5 finding S9: screening

		S10: number w10 fetal alcohol OR number w10 foetal alcohol OR number w10 fasd OR number w10 birth defects OR number w10 malformations OR number w10 arbd OR number w10 arnd OR number w10 neurodevelopmental OR number w10 FAS S11: percentage* w10 fetal alcohol OR Percentage* w10 foetal alcohol OR Percentage* w10 fasd OR Percentage* w10 birth defects OR Percentage* w10 malformations OR Percentage* w10 arbd OR Percentage* w10 arnd OR Percentage* w10 neurodevelopmental OR Percentage* w10 fas S12: rate* w10 fetal alcohol OR rate* w10 foetal alcohol OR rate* w10 fasd OR rate* w10 birth defects OR rate* w10 malformations OR rate* w10 arbd OR rate* w10 arnd OR rate* w10 neurodevelopmental OR rate* w10 fas S13: (estimate* w10 fetal alcohol OR estimate* w10 foetal alcohol OR estimate* w10 fasd OR estimate* w10 birth defects OR estimate* w10 malformations OR estimate* w10 arbd OR estimate* w10 arnd OR estimate* w10 neurodevelopmental OR estimate* w10 fas) S14: (frequen* w10 fetal alcohol OR frequen* w10 foetal alcohol OR frequen* w10 fasd OR frequen* w10 birth defects OR frequen* w10 malformations OR frequen* w10 arbd OR frequen* w10 arnd OR frequen* w10 neurodevelopmental OR frequen* w10 fas) S15: S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 S16: S5 AND S15 S17: (clinical trial OR case report OR case study OR case series OR controlled trial) OR intervention*.ti. S18: S16 NOT S17
Criminal Justice Abstracts (EBSCO interface)	1968 - Dec 5, 2012	S1: fetal alcohol OR foetal alcohol OR fasd OR fae OR arbd OR arnd S2: alcohol n8 birth defect* S3: alcohol n8 neurodevelopmental S4: alcohol n8 malformation* S5: S1 OR S2 OR S3 OR S4 S6: prevalen* or incidence S7: epidemiolog* or surveillance or cross-sectional S8: case* n5 identif* OR case* n5 ascertain* OR case* n5 finding S9: screening S10: number w10 fetal alcohol OR number w10 foetal alcohol OR number w10 fasd OR number w10 birth defects OR number w10 malformations OR number w10 arbd OR number w10 arnd OR number w10 neurodevelopmental OR number w10 FAS S11: percentage* w10 fetal alcohol OR Percentage* w10 foetal alcohol OR Percentage* w10 fasd OR Percentage* w10 birth defects OR Percentage* w10 malformations OR Percentage* w10 arbd OR Percentage* w10 arnd OR Percentage* w10 neurodevelopmental OR Percentage* w10 fas S12: rate* w10 fetal alcohol OR rate* w10 foetal alcohol OR rate* w10 fasd OR rate* w10 birth defects OR rate* w10 malformations OR rate* w10 arbd OR rate* w10 arnd OR rate* w10 neurodevelopmental OR rate* w10 fas S13: (estimate* w10 fetal alcohol OR estimate* w10 foetal alcohol OR estimate* w10 fasd OR estimate* w10 birth defects OR estimate* w10 malformations OR estimate* w10 arbd OR estimate* w10 arnd OR estimate* w10 neurodevelopmental OR estimate* w10 fas) S14: (frequen* w10 fetal alcohol OR frequen* w10 foetal alcohol OR frequen* w10 fasd OR frequen* w10 birth defects OR frequen* w10 malformations OR frequen* w10 arbd OR frequen* w10 arnd OR frequen* w10 neurodevelopmental OR frequen* w10 fas) S15: S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 S16: S5 AND S15 S17: (clinical trial OR case report OR case study OR case series OR controlled trial) OR intervention*.ti. S18: S16 NOT S17

Proquest Interface searching the following databases simultaneously: Sociological Abstracts (1952-) Social Services Abstracts (1979 -) ABI/Inform Global (1970-) British Humanities Index (1962-) Canadian Research Index (1982 -) CBCA Complete (1971 -) CBCA Fulltext Education (1977 -) CBCA Reference and Current Events (1982 -) Dissertations and Theses (1861-) ERIC (1966-) National Criminal Justice Reference Service (1970-)	Database inception - Dec 5, 2012	(TI(fetal alcohol OR foetal alcohol OR FASD OR FAE OR ARBD OR ARND OR alcohol related neurodevelopmental OR alcohol related birth defects) OR AB(fetal alcohol OR foetal alcohol OR FASD OR FAE OR ARBD OR ARND OR alcohol related neurodevelopmental OR alcohol related birth defects) OR SU(fetal alcohol)) AND (TI(prevalen* or incidence* or epidemiology OR surveillance OR cross-sectional) OR AB(prevalen* or incidence* or epidemiology OR surveillance OR cross-sectional))
Web of Science ISI Interface Licensed Resource	1899 - Dec 5, 2012	#1 TS=(fetal alcohol OR foetal alcohol OR FASD OR FAE OR ARBD OR ARND OR alcohol related neurodevelopmental OR alcohol related birth defects) AND TS=(prevalen* or incidence* or epidemiology OR surveillance OR cross-sectional) #2 TS=(clinical trial or case study or case series or case report or controlled trial or in vitro) #3 TS=(mouse OR mice OR murine OR rat OR rats OR pig OR pigs OR porcine OR sheep) #4 #1 NOT (#2 OR #3)

Note:

†† "*", "# ", and "?" are truncation characters that retrieve all possible suffix variations of the root word e.g. surg* retrieves surgery, surgical, surgeon, etc.

Searches separated by semicolons have been entered separately into the search interface

APPENDIX B: EXCLUDED STUDIES, MULTIPLE PUBLICATIONS AND STUDIES PENDING OF FULL PUBLICATION

Excluded Research Studies

The application of the selection criteria resulted in 154 studies excluded from the systematic review. The primary reasons for the exclusion of studies were as follows: 1) the study was not original research (e.g., narrative review, commentary, editorial) (n = 87); 2) the study did not report measurable data for the outcomes of interest (prevalence) (n = 44); 3) the study was not on FASD prevalence (n = 11); 4) the study was not retrieved (n = 8); 5) the study did not use any of the study designs considered in the review (n = 3); and 6) the study did not target the populations of interest (n = 1);. Table B1 lists the excluded studies and the reason for their exclusion from the systematic review.

Table B1: Excluded research studies

Main reason for exclusion: **The study was not original research (N = 87)**
1. Update: Trends in fetal alcohol syndrome - United States, 1979-1993. JAMA 1995;273:1406.
2. High rate of FAS seen in South Africa. Medical Letter on the CDC [Internet] c2003;14. Available from: http://www.highbeam.com/doc/1G1-106430748.html [accessed 2013 Feb 5].
3. Manitoba study suggests one in ten prisoners has fetal alcohol syndrome. Canadian Press NewsWire [Internet] c2007. Available from: http://login.ezproxy.library.ualberta.ca/login?url=http://search.proquest.com/docview/359960358?accountid=14474 [accessed 2013 Feb 5].
4. Population-based birth defects surveillance data from selected states, 2001-2005. Birth Defects Res, Part A 2008;82:831-61.
5. Abel EL, Sokol RJ. Incidence of fetal alcohol syndrome and economic impact of FAS-related anomalies. *Drug* Alcohol Depend 1987;19:51-70.
6. Abel EL. Fetal alcohol syndrome in families. Neurotoxicol Teratol 1988;10:1-2.
7. Abel EL, Sokol RJ. A revised conservative estimate of the incidence of FAS and its economic impact. Alcoholism 1991;15:514-24.
8. Abel EL. An update on incidence of FAS: FAS is not an equal opportunity birth defect. Neurotoxicol Teratol 1995;17:437-43.
9. Abel EL. Fetal alcohol syndrome: the 'American Paradox'. Alcohol Alcohol 1998;33:195-201.
10. Abel EL. Fetal alcohol syndrome: a cautionary note. Curr Pharm Des 2006;12:1521-9.
11. Armstrong EM. Diagnosing moral disorder: the discovery and evolution of fetal alcohol syndrome. Soc Sci Med 1998;47:2025-42.
12. Armstrong EM, Abel EL. Fetal alcohol syndrome: the origins of a moral panic. Alcohol Alcohol 2000;35:276-82.
13. Bateman C. FASD: De Aar mums get beyond the 'tippling point'. SAfr Med J 2010; 100:4567.
14. Beckett CD. Fetal alcohol spectrum disorders: a Native American journey to prevention. Fam Community Health 2011;34:242-5.
15. Bray DL, Anderson PD. Appraisal of the epidemiology of fetal alcohol syndrome among Canadian native peoples. Can J Public Health 1989;80:42-5.
16. Burd L, Moffatt ME. Epidemiology of fetal alcohol syndrome in American Indians, Alaskan Natives, and Canadian Aboriginal peoples: a review of the literature. Public Health Rep 1994;109:688-93.

17. Burd L. Special issue: the Four State Fetal Alcohol Consortium: Clinical and epidemiologic findings - Introduction. Neurotoxicol Teratol 2003;25:641.
18. Burd L. Fetal alcohol syndrome. Am J Med Genet 2004;127C; 1-2.
19. Centers for Disease Control and Prevention (CDC). Linking multiple data sources in fetal alcohol syndrome surveillance: Alaska. MMWR 1993;42:312-4.
20. Centers for Disease Control and Prevention (CDC). Fetal alcohol syndrome: United States, 1979-1992. MMWR 1993;42:339-41.
21. Centers for Disease Control and Prevention (CDC). Birth certificates as a source for fetal alcohol syndrome case ascertainment: Georgia, 1989-1992. MMWR 1995;44:251-3.
22. Centers for Disease Control and Prevention (CDC). Update: trends in fetal alcohol syndrome--United States, 1979-1993. MMWR 1995;44:249-51.
23. Centers for Disease Control and Prevention (CDC). Use of international classification of diseases coding to identify fetal alcohol syndrome: Indian Health Service facilities, 1981-1992. MMWR 1995;44:253-5.
24. Centers for Disease Control and Prevention (CDC). Surveillance for fetal alcohol syndrome using multiple sources: Atlanta, Georgia, 1981-1989. MMWR 1997;46:1118-20.
25. Centers for Disease Control and Prevention (CDC). Fetal alcohol syndrome: Alaska, Arizona, Colorado, and New York, 1995-1997. MMWR 2002;51:433-5.
26. Centers for Disease Control and Prevention (CDC). Fetal alcohol syndrome: South Africa, 2001. MMWR 2003;52:660-2.
27. Chambers C. Measuring worldwide incidence of FASD. Neurotoxicol Teratol 2007;29:400.
28. Chambers CD. Measuring worldwide incidence of FASD. Birth Defects Res Part A 2007;79:384.
29. Chudley AE, Kilgour AR, Cranston M, Edwards M. Challenges of diagnosis in fetal alcohol syndrome and fetal alcohol spectrum disorder in the adult. Am J Med Genet 2007;Part C, Seminars in Medical Genetics. 145C:261-72.
30. Cordero JF, Floyd L, Martin ML, Davis M. Tracking the prevalence of FAS. Alcohol Health Res W 1994;18(1):82-95.
31. de Plevitz LR, Gould JS, Smith TM. Fetal alcohol syndrome and fetal alcohol spectrum disorder in indigenous schoolchildren. Med J Australia 190: 286-7.
32. Duerbeck NB. Fetal alcohol syndrome. Compr Ther 1997;23:179-83.
33. Elliott AJ, Hanson JD. Fetal alcohol syndrome in South Dakota. SD Med 2006;59:341-2.
34. Elliott E. Fetal alcohol syndrome: Where did APSU surveillance lead? J Paediatr Child Health 2011;47:4
35. Elliott EJ, Bower C. FAS in Australia: fact or fiction? Journal of Paediatr Child Health 2004;40:8-10.
36. Fitzgerald P. FAS persists despite broad public awareness. Michigan Med 1988;87:262-4.
37. Foxhall K. FAS receives attention at NIAAA session: US prevalence much higher than anticipated. Contemp Pediatr 2011;28:16.
38. Glasgow G. The incidence of fetal alcohol syndrome in New Zealand. NZ Med J 1996;109:18.
39. Grinfeld H, Goldenberg S, Segre CA, Chadi G. Fetal alcohol syndrome in Sao Paulo, Brazil. Paediatr Perinat Ep 1999;13:496-7.
40. Huebert K, Raftis C. Fetal alcohol syndrome and other alcohol-related birth defects. 2nd ed. Edmonton, AB: Alberta Alcohol & Drug Abuse Commission; 1996.
41. Hymbaugh K. Foetal alcohol syndrome case finding and surveillance in the USA. J Intellect Disabil Res 2000;44:328.
42. Kalberg WO, Marais A-S, Hoyme EH, May PA. Prospective ascertainment of infants in two communities in the Western Cape: identifying predictors of fetal alcohol spectrum disorders in infancy. Proceedings of the 35th Annual Scientific Meeting of the Research Society on Alcoholism, RSA 2012 Jun 23-27; San Francisco, CA United States.

43. Khoury MJ, Boyle C, Decoufle P, Floyd L, Hymbaughm K. The interface between dysmorphology and epidemiology in the "diagnosis" and surveillance for fetal alcohol effects. Pediatrics 1996;98:315-6.
44. Koening A, Muller RL, Osorio MCN. Fetal alcohol syndrome. Revista do Hospital de Clinicas de Porto Alegre 1985;5:33-7.
45. Koren G, Nulman I, Chudley AE, Loocke C. Fetal alcohol spectrum disorder. CMAJ 2003;169:1181-5.
46. Kyskan CE, Moore TE. Global perspectives on fetal alcohol syndrome: assessing practices, policies, and campaigns in four English-speaking countries. Can Psychol 2005;46:153-65.
47. Leonard BJ, Boettcher LM, Brust JD. Alcohol-related birth defects. Minnesota's response to a critical health problem. Minn Med 1991;74:23-5.
48. Little RE, Wendt JK. The effects of maternal drinking in the reproductive period: An epidemiologic review. J Subst Abuse 1991;3:187-204.
49. Maillard T, Lamblin D, Lesure JF, Fourmaintraux A. Incidence of fetal alcohol syndrome on the southern part of Reunion Island (France). Teratology 1999;60:51-2.
50. Marti HM, Cabrera Lopez JC, Calvo HF, Toledo BL, Calvo Rosales LJ, Hernandez MM. Fetal alcohol syndrome: diagnostic criteria and findings in 13 cases. Acta Pediatr Esp 2004; 62:224-8.
51. Mathis MP. Birth certificates as a source for fetal alcohol syndrome case ascertainment - Georgia, 1989-1992. Addict Nurs1995;7:47-8.
52. May PA, Gossage JP. Estimating the prevalence of fetal alcohol syndrome: a summary. Alcohol Res Health 2001;25:159-67.
53. May PA, Gossage JP, Kalberg WO, Robinson LK, Buckley D, Manning M, et al. Prevalence and epidemiologic characteristics of FASD from various research methods with an emphasis on recent in-school studies. Dev Disabil Res Rev 2009;15:176-92.
54. May PA. Report on outreach efforts and analysis of approach: a pilot project on fetal alcohol syndrome for American Indians. Rockville, MD: Indian Health Service (PHS/HSA);1981.
55. May PA. Fetal alcohol effects among North American Indians: evidence and implications for society. Alcohol Health Res W 1991;15:239-48.
56. May PA, McCloskey J, Gossage JP. Fetal alcohol syndrome among American Indians: epidemiology, issues, and research review. In: Mail PD, Heurtin-Roberts S, Martin SE, Howard J, editors. Alcohol use among American Indians and Alaska Natives: multiple perspectives on a complex problem. Bethesda, MD: U.S. Dept. of Health and Human Service; 2002.
57. McKinstry J. Using the past to step forward: Fetal alcohol syndrome in the Western Cape Province of South Africa. Am J Public Health 2005;95:1097-9.
58. Meaney FJ, Miller LA, FASSNet Team. A comparison of fetal alcohol syndrome surveillance network and birth defects surveillance methodology in determining prevalence rates of fetal alcohol syndrome. Birth Defects Res 2003;67:819-22.
59. Miller L, Montgomery A. Foetal alcohol syndrome surveillance in Colorado, USA. J Intellect Disabil Res 2000;44:395.
60. Nayak RB, Murthy P. Fetal alcohol spectrum disorder. Indian Pediatrics 2008;45:977-83.
61. Neugut RH. Epidemiological appraisal of the literature on the fetal alcohol syndrome in humans. Early Hum Dev 1981;5:411-29.
62. Nobile L, Mathias L, He YK, Martins JA. Alcohol in pregnancy: epidemiology and fetal effects. J Bras Psiquiatr 1984;33:347-51.
63. Nulman I, Ickowicz A, Koren G, Knittel-Keren D. Fetal alcohol spectrum disorder. In: Brown I, Percy M, editors. A comprehensive guide to intellectual and developmental disabilities. Baltimore, MD: PH Brookes; 2007
64. O'Leary C, Bower C, Payne J, Elliott E. Fetal alcohol syndrome. Aust Fam Physician 2006;35:184.
65. Orakwue N, McNicholas F, O'Malley K. Fetal alcohol spectrum disorders: an Irish perspective. Irish J Psychol Med 2010;27(4):i-v.

66. Paintner A, Williams AD, Burd L. Fetal alcohol spectrum disorders: implications for child neurology, part 1: prenatal exposure and dosimetry. J Child Neurol 2012;27:258-63.
67. Palmer C. Fetal alcohol effects: incidence and understanding in the Cape. S Afr Med J 1985;68(:779-80.
68. Pancratz DR. Fetal alcohol syndrome and fetal alcohol effects in child development. Washington (D.C): ERIC Clearinghouse, 1993.
69. Phillipson R. The Fetal Alcohol Syndrome: recent international statistics. Aust NZ J Dev Disabil 1988;14:211-7.
70. Pinto S, Schub T. Fetal alcohol syndrome. Glendale, California ; 2012.
71. Podvin D. Foetal alcohol syndrome surveillance network: prevalence in Alaska. J Intellect Disabil Res 2000;44:430.
72. Popova S, Lange S, Bekmuradov D, Mihic A, Rehm J. Fetal alcohol spectrum disorder prevalence estimates in correctional systems: a systematic literature review. Can J Public Health 2011;102:336-40.
73. Ripabelli G, Cimmino L, Grasso GM. Alcohol consumption, pregnancy and fetal alcohol syndrome: implications in public health and preventive strategies. Annali di Igiene 2006;18:391-406.
74. Rolland M, Regnier C. Infants born to alcoholic mothers. Rev Pediatr 1985;21:81-9.
75. Sampson PD, Streissguth AP, Bookstein FL, Little RE, Clarren SK, Dehaene P, et al. Incidence of fetal alcohol syndrome and prevalence of alcohol-related neurodevelopmental disorder. Teratology 1997;56:317-26.
76. Sokol RJ, aney-Black V, Nordstrom B. Fetal alcohol spectrum disorder. JAMA 2003;290:2996-9.
77. Square D. Fetal alcohol syndrome epidemic on Manitoba reserve. CMAJ 1997;157:59-60.
78. Streissguth AP. Fetal alcohol syndrome: an epidemiologic perspective. Am J Epidemiol 1978;107:467-78.
79. Streissguth AP, LaDue RA. Fetal alcohol. Teratogenic causes of developmental disabilities. Monogr Am Assoc Ment Defic 1987;(8):1-32.
80. Viljoen D. Fetal alcohol syndrome: A South African epidemic. Int J Gynecol Obstetr 2009;107:S89-S90.
81. Viljoen D. Fetal alcohol syndrome. S Afr Med J 1999;89:958-60.
82. Wallace P. Prevalence of fetal alcohol syndrome largely unknown. Iowa Med 1991;81:381.
83. Warren KR, Calhoun FJ, May PA, Viljoen DL, Li TK, Tanaka H, et al. Fetal alcohol syndrome: an international perspective. Alcoholism 2001;25:202S-6S.
84. Warren KR, Foudin LL. Alcohol-related birth defects--the past, present, and future. Alcohol Res Health 2001;25:153-8.
85. Welty T, Selva K, Confield LR. Use of international classification of diseases coding to identify fetal alcohol syndrome: Indian health service facilities, 1981-1992. Addict Nurs1995;7:49-51.
86. Wilson M. Fetal alcohol syndrome--the American scene. Nurs Times 1981;77:1832-5.
87. Yaltonskaya A, Yaltonsky V, Kolpakov Y, Abrosimov I, Derevnina A, Rehm J, et al. What is happening in the Russian Federation in terms of research on fetal alcohol spectrum disorder and prenatal alcohol exposure? J Popul Ther Clin Pharmacol 2012;19:e438.

Main reason for exclusion:

The study did not report measurable data for the outcomes of interest (prevalence) (N = 44)

1. Alvear J, Andreani S, Cortes F. Fetal alcohol syndrome and fetal alcohol effects among children in a secondary nutritional recovery centre. Rev Med Chile 1998;126:407-12.
2. Amendah DD, Grosse SD, Bertrand J. Medical expenditures of children in the United States with fetal alcohol syndrome. Neurotoxicol Teratol 2011;33:322-4.
3. Asante KO, Nelmes-Matzke J. Report on the survey of children with chronic handicaps and fetal alcohol syndrome in the Yukon and northwest British Columbia. Ottawa, ON: Health and Welfare Canada;1985.

4. Astley SJ. Profile of the first 1,400 patients receiving diagnostic evaluations for fetal alcohol spectrum disorder at the Washington State Fetal Alcohol Syndrome Diagnostic & Prevention Network. Can J Clin Pharmacol 2010;17:e132-64.
5. Autti-Ramo I. The outcome of children exposed to alcohol in utero: A prospective follow-up study during the first three years. Helsinki:University of Hensinki, 1993.
6. Bower C, Rudy E, Callaghan A, Quick J, Nassar N. Age at diagnosis of birth defects. Birth Defects Res 2010;88:251-5.
7. Burd L, Cox C, Poitra B, Wentz T, Ebertowski M, Martsolf JT, et al. The FAS Screen: a rapid screening tool for fetal alcohol syndrome. Addict Biol 1999;4:329-36.
8. Burd L, Martsolf JT, Klug M. Children with fetal alcohol syndrome in North Dakota: a case control study utilizing birth certificate data. Addict Biol 1996;1:181-9.
9. Cadle RG, Dawson T, Hall BD. The prevalence of genetic disorders, birth defects and syndromes in central and eastern Kentucky. J K y Med Assoc 1996;94:237-41.
10. Cannon MJ, Dominique Y, O'Leary LA, Sniezek JE, Floyd RL, FASSNet Team. Characteristics and behaviors of mothers who have a child with fetal alcohol syndrome. Neurotoxicol Teratol 2012;34:90-5.
11. Ceccanti M, Alessandra SP, Tarani L, Luisa AM, Chessa L, Mancinelli R, et al. Clinical delineation of fetal alcohol spectrum disorders (FASD) in Italian children: comparison and contrast with other racial/ethnic groups and implications for diagnosis and prevention. Neurosci Biobehav R 2007;31:270-7.
12. Clarren SK, Lutke J. Building clinical capacity for fetal alcohol spectrum disorder diagnoses in western and northern Canada. Can J Clin Pharmacol 2008;15:e223-37.
13. Fiorentino D, Coriale G, Spagnolo PA, Prastaro A, Attilia ML, Mancinelli R, et al. Fetal alcohol syndrome disorders: experience on the field. The Lazio study preliminary report. Ann Ist Super Sanita 2006;42:53-7.
14. Fitzpatrick JP, Elliott EJ, Latimer J, Carter M, Oscar J, Ferreira M, et al. The Lililwan Project: study protocol for a population-based active case ascertainment study of the prevalence of fetal alcohol spectrum disorders (FASD) in remote Australian Aboriginal communities. BMJ Open 2012;2:e000968. doi:10.1136/bmjopen-2012-000968
15. Habbick BF, Nanson JL, Snyder RE, Casey RE. Mortality in foetal alcohol syndrome. Can J Public Health 1997;88:181-3.
16. Hansen C, O'Leary L, Dominique Y, Fershteyn Z, Correa A, Miller L. Age when fetal alcohol syndrome criteria were met: the Fetal Alcohol Syndrome Surveillance Network (FASSNet). Birth Defects Res Part A. Proceedings of the 36th Annual Meeting of the International Clearinghouse for Birth Defects Surveillance and Research Salt 2009 Sep 11-15; Lake City, United States:507.
17. Hoyme HE, May PA, Kalberg WO, Kodituwakku P, Gossage JP, Trujillo PM, et al. A practical clinical approach to diagnosis of fetal alcohol spectrum disorders: clarification of the 1996 institute of medicine criteria. Pediatrics 2005;115:39-47.
18. Hymbaugh K, Miller LA, Druschel CM, Podvin DW, Meaney FJ, Boyle CA, et al. A multiple source methodology for the surveillance of fetal alcohol syndrome: the Fetal Alcohol Syndrome Surveillance Network (FASSNet). Teratology 2002;66:S41-9.
19. Iosub S, Fuchs M, Bingol N, Rich H, Stone RK, Gromisch DS, et al. Familial fetal alcohol syndrome: incidence in blacks and hispanics. Alcohol Clin Exp Res 1985;9(2):185.
20. Iosub S, Fuchs M, Bingol N, Stone RK, Gromisch DS, Wasserman E. Familial fetal alcohol syndrome: incidence in blacks and hispanics. Pediatr Res 1985;19:A202.
21. Jones KL, Smith DW, Streissguth AP, Myrianthopoulos NC. Incidence of the fetal alcohol syndrome in offspring of chronically alcoholic women. Pediatr Res 1974;8 440.
22. Kapalanga J, Wong D, Gandy A, Avind SA, Bhoka G. Ecogenetic and epigenetic influences in FASD. J Popul Ther Clin Pharmacol. Proceedings of the 12th Annual Fetal Alcohol Canadian Expertise, FACE, Research Roundtable; 2011 Sep 13; Stanhope, Canada:e421.

23. Larkby CA, Goldschmidt L, Hanusa BH, Day NL. Prenatal alcohol exposure is associated with conduct disorder in adolescence: findings from a birth cohort. J Am Acad Child Adolesc Psychiatry 2011;50:262-71.
24. Leversha AM, Marks RE. The prevalence of fetal alcohol syndrome in New Zealand. NZ Med J 1995;108:502-5
25. May PA, Marais AS, Gossage JP, Viljoen DL. Epidemiological analysis of a third wave of data about children with fetal alcohol spectrum disorders and controls in the Western Cape Province, South Africa. Alcohol Clin Exp Res 2005;29:43A.
26. May PA, Gossage JP, Smith M, Tabachnick BG, Robinson LK, Manning M, et al. Population differences in dysmorphic features among children with fetal alcohol spectrum disorders. J Dev Behav Pediatr 2010;31:304-16.
27. May PA, Tabachnick BG, Adnams CM, et al. Neuropsychological development among children with fetal alcohol spectrum disorders in South Africa: a structural equation model. Alcohol Clin Exp Res 2007;31:247A.
28. May PA, Tabachnick BG, Gossage JP. Structural equation modeling of physical features of fetal alcohol spectrum disorders among children in South Africa. Alcohol Clin Exp Res 2007;31:247A.
29. May PA, Tabachnick BG, Gossage JP, Kalberg WO, Marais AS, Robinson LK, et al. Maternal risk factors predicting child physical characteristics and dysmorphology in fetal alcohol syndrome and partial fetal alcohol syndrome. Drug Alcohol Depend2011;119:18-27.
30. Miller LA, Shaikh T, Stanton C, Montgomery A, Rickard R, Keefer S, et al. Surveillance for fetal alcohol syndrome in Colorado. Public Health Rep 1995;110:690-7.
31. Miller LC, Chan W, Litvinova A, Rubin A, Comfort K, Tirella L, et al. Fetal alcohol spectrum disorders in children residing in Russian orphanages: a phenotypic survey. Alcoholism 2006;30:531-8.
32. Miller LC, Chan W, Litvinova A, Rubin A, Tirella L, Cermak S. Medical diagnoses and growth of children residing in Russian orphanages. Acta Paediatr 2007;96:1765-9.
33. Morleo M, Woolfall K, Dedman D, Mukherjee R, Bellis MA, Cook PA. Under-reporting of foetal alcohol spectrum disorders: an analysis of hospital episode statistics. BMC Pediatr 2011;11:14.
34. Oconnor TA, Kilbride HW, Hayen LK. Incidence of fetal alcohol syndrome among infants with intrauterine cocaine exposure. J Matern Fetal Investig 1993;3:29-31.
35. O'Malley K. Foetal alcohol spectrum disorders in an Irish context. J Intellect Disabil Res 2007;51:664.
36. Olegard R, Sabel KG, Aronsson M, Sandin B, Johansson PR, Carlsson C, et al. Effects on the child of alcohol abuse during pregnancy: retrospective and prospective studies. Acta Paediatr Scand 1979;275:112-21.
37. Olivier L, Chersich MF, Urban M, Davies L-A, Chetty C, Viljoen D. Universal prevention is associated with lower prevalence of FASD in Northern Cape, South Africa: a multicentre before-after study. J Popul Ther Clin Pharmacol 2012;19:e393.
38. Pensak M, Cunniff C, Meaney FJ. Foetal alcohol syndrome surveillance network: Experience in Arizona, USA. J Intellect Disabil Res 2000;44:426.
39. Rajani H, O'Riordan T, Cameron K. FASD multidisciplinary diagnostic clinic model in a rural Canadian setting and the use of "MAP" (Multi-Action Plan) for assigning responsibility and monitoring follow up of recommendations and utilization of resources. J Popul Ther Clin Pharmacol 2012;19:e428-9.
40. Robert M, Carceller A, Domken V, Ramos F, Dobrescu O, Simard MN, et al. Physical and neurodevelopmental evaluation of children adopted from Eastern Europe. Can J Clin Pharmacol 2009;16:e432-e440.
41. Robinson M, Oddy WH, McLean NJ, Jacoby P, Pennell CE, de Klerk NH, et al. Low-moderate prenatal alcohol exposure and risk to child behavioural development: a prospective cohort study. BJOG 2010;117:1139-50.
42. Russell M. Incidence of Conditions Associated with Fetal alcohol syndrome in children born to women with a history of alcohol-abuse. Am J Epidemiol 1975;102:437.
43. Senecky Y, Inbar D, Diamond G, Basel-Vanagaite L, Rigler S, Chodick G. Fetal alcohol spectrum disorder in Israel. IMAJ 2009;11:619-22.

44. Vitez M, Koranyi G, Gonczy E, Rudas T, Czeizel A. A semiquantitative score system for epidemiologic studies of fetal alcohol syndrome. Am J Epidemiol 1984;119:301-8.
Main reason for exclusion: **The study did not assessed FASD (N = 11)**
1. Alati R, Van DK, Najman JM, Williams GM, Clavarino A. Early weaning and alcohol disorders in offspring: biological effect, mediating factors or residual confounding? Addiction 2009;104:1324-32.
2. Centers for Disease Control and Prevention (CDC). Alcohol consumption among pregnant and childbearing-aged women--United States, 1991 and 1995. MMWR 1997;46:346-50.
3. de C, I, Llorca PM, Ughetto S, Vendittelli F, Boussiron D, Sapin V, et al. Is pregnancy the time to change alcohol consumption habits in France? Alcoholism 2008;32:868-73.
4. Godel JC, Lee BE, McCallum DE, Lee SL, Macneil CW, Liddell GA, et al. Exposure to alcohol in utero: influence on cognitive function and learning in a northern elementary school population. Paediatr Child Health 2000;5:93-100.
5. Hagberg B, Hagberg G, Lewerth A, et al. Mild mental retardation in Swedish school children. I. Prevalence. Acta Paediatr Scand 1981;70:441-4.
6. Hingson R, Scotch N, Goldman E. Impact of the Rand Report on alcoholics, treatment personnel and Boston residents. J Stud Alcohol 1977;38:2067-76.
7. Langlois PH, Scheuerle A. Using registry data to suggest which birth defects may be more susceptible to artifactual clusters and trends. Birth Defects Res 2007;79:798-805.
8. Mullally A, Cleary BJ, Barry J, Fahey TP, Murphy DJ. Prevalence, predictors and perinatal outcomes of peri-conceptional alcohol exposure: retrospective cohort study in an urban obstetric population in Ireland. BMC Pregnancy Childbirth 2011;11:27.
9. Ouellette E, Rosett J, Rosman N, Weiner L. Adverse effects on offspring of maternal alcohol abuse during pregnancy. NEJM 1977;297:528-30.
10. Schneider M, Norman R, Parry C, Bradshaw D, Pluddemann A, South African Comparative Risk Assessment Collaborating Group. Estimating the burden of disease attributable to alcohol use in South Africa in 2000. S Afr Med J 2007;97:664-72.
11. Schulman J, Edmonds LD, McClearn AB, Jensvold N, Shaw GM. Surveillance for and comparison of birth defect prevalences in two geographic areas--United States, 1983-88. MMWR 1993;42:1-7.
Main reason for exclusion: **The full text of the study was not retrieved (N = 8)**
1. Centers for Disease Control and Prevention. Update: trends in fetal alcohol syndrome: United States, 1979-1993. JAMA1995;273:1406.
2. Dehaene P, Crepin G, Delahousse G, Querleu D, Walbaum R, Titran M, et al. Epidemiological aspects of the foetal alcoholism syndrome. 45 cases. Nouv Presse Med1981;10:2639-43.
3. Majewski F, Bierich JR, Seidenberg J. Prevalency and pathogenesis of fetal alcohol syndrome. Monatssch Kinderh 1978;126:284-5.
4. Maritz W. Fetal alcohol syndrome update. S Afr Med J 1997;87:975-6.
5. Quaid J, Kirkpatrick J, Nakamura Rea. Establishing the occurrence of FAS/FAE in a rural community. Provider 1993;18:71-5.
6. Robinson GC. Appraisal of the epidemiology of fetal alcohol syndrome among Canadian native peoples. Can J Public Health1989;80:382
7. van WH, Letteboer TG, Pereira RR, de RS, Balemans WA, Lindhout D. Diagnosis of fetal alcohol spectrum disorders. Ned Tijdsch Genees 2010;154:A331
8. Wong N. British Columbia Surveillance Registry. Vancouver BC: BC Ministry of Health; 1983.

Main reason for exclusion: **The study did not use any of the study designs considered in the review (N = 3)**
1. Chersich MF, Urban M, Olivier L, Davies LA, Chetty C, Viljoen D. Universal prevention is associated with lower prevalence of fetal alcohol spectrum disorders in Northern Cape, South Africa: a multicentre before-after study. Alcohol Alcohol 2012;47:67-74
2. Fernandez-Mayoralas DM, Fernandez-Jaen A, Munoz-Jareno N, Calleja PB, rroyo-Gonzalez R. Fetal alcohol syndrome, Tourette syndrome, and hyperactivity in nine adopted children. Pediatr Neurol 2010;43:110-6.
3. Olivier L, Urban M, Chersich M, Viljoen D. Holistic interventions are effective in reducing the prevalence of FASD in the Northern Cape Province of South Africa: A multi-centre before-after study. Alcohol Clin Exp Res 2010;34(6):212A.
Main reason for exclusion: **The study did not target the populations of interest (N = 1)**
1. Astley SJ. Comparison of the 4-digit diagnostic code and the Hoyme diagnostic guidelines for fetal alcohol spectrum disorders. Pediatrics 2006;118:1532-45.

Multiple Publications of Studies Included in the Review

Of the 59 included articles, five articles were identified as multiple publications; that is, cases in which the same study was published more than once or part of the data from an original report was republished. The multiple publications were not considered to be unique studies, and any information that they provided was included with the data reported in the main study.

Table B2: Multiple publications

Multiple publications of studies included in the review (N = 5)
1. Egeland GM, Perham-Hester KA, Hook EB. Use of capture-recapture analyses in fetal alcohol syndrome surveillance in Alaska. Am J Epidemiol 1995;141:335-41. **Associated publication of Egeland et al.**[57]
2. Fox DJ, Druschel CM. Estimating prevalence of fetal alcohol syndrome (FAS): effectiveness of a passive birth defects registry system. Birth Defects Res 2003;67:604-8. **Associated publication of Druschel et al.**[56]
3. Randels SP, Clarren SK, Sanderson M, Gaudino J, Hymbaugh K, Fineman RM. Population-Based Fetal Alcohol Syndrome (Fas) Surveillance at Elementary-School Entrance. American Journal of Human Genetics 1995;57:1734. **Associated publication of Clarren et al.**[20]
4. Tenenbaum A, Hertz P, Dor T, Castiel Y, Sapir A, Wexler ID. Fetal Alcohol Spectrum Disorder in a preadoption clinic in Israel-the tip of the iceberg? J Popul Ther Clin Pharmacol 2012;19:e422. **Associated publication of Tenenbaum et al.**[49]
5. Viljoen D, Fourie L, Chetty CM, Urban M, Nero M, Josephs J, et al. The epidemiology of fetal alcohol spectrum disorder in the northern cape province of south Africa. Alcohol Clin Exp Res 2007;31:188A. **Associated publication of Olivier et al.**[44]

APPENDIX C: CHARACTERISTICS OF STUDIES INCLUDED IN THE REVIEW

Table C1: Studies on the prevalence of FASD in the community

Study	Country	Design	Sampling	Sample size	Age (mean or range)	Diagnostic sequence	Diagnostic criteria	FASD Prevalence	Summary of quality rating
Allen, 2007[52]	Australia	RCS	Total population	nr	nr	1) Medical records audit	nr	FAS: 3/nr; FAS rate: 0.006 per 1000 births	Low
Druschel, 2007[56]	USA	RCS	Total population	106,336	nr	1) Vital statistics records; 2) Medical records audit	FASSNet	FAS: 63/106336 (0.05%; 95% CI: na; FAS rate: 0.5 per 1000 births)	Low
Egeland, 1998[57]	USA	RCS	Total population	176,765	8.4 mo	1) Vital statistics records; 2) Medical records audit	ICD-9 codes 760.71, 760.7	FAS: 145/176765 (FAS rate per 1000 live births: 0.8)	Low
Elgen, 2007[22]	Norway	CSS	Total population	nr	< 15 yr	1) Physicians' referral; 2) Chart review; 3) Dysmorphological assessment; 4) Neurobehavioural assessment	CDC	FASD: 13/nr (0.33 to 1.5 per 1000); FAS: 0.2 per 1000; FAS/FASD: 0.3 per 1000) FAS: 5/nr (rate 0.3 to 1.2 per 1000)	Low
Elliott, 2008[23]	Australia	CSS	Total population	55,392	3.3 yr	1) Physicians' report card	IOM	FAS: 25/55392 (0.045; 95% CI nr); pFAS: 65/55392 (0.11%; 95% CI nr); FAS + pFAS: 90/55392 (0.16%; 95% CI nr)	Moderate
Harris, 2003[59]	Australia	RCS	Total population	25,209	nr	1) Medical records audit	4-Digit system	FASD: 43/25209 (0.17; 95% CI: nr; rate per 1000 live births: 1.7); FAS: 18/25209 (0.07%; 95% CI: nr; rate per 1000 live births: 0.7); pFAS: 21/25209 (0.08; 95% CI: nr; rate per 1000 live births: 0.8); ARND: 4/25209 (0.01%; 95% CI: nr; rate per 1000 live births: 0.15)	Low
Kuehn, 2012[66]	Chile	PCS	Unknown	189	<8.5 yr	1) Interview/maternal risk; 2) Dysmorphological assessment; 3) Neurobehavioural assessment; 4) Case conference	4-Digit system	FAS: 0; pFAS overall: 1/189 (0.53%; 95% CI: 0.5, 1.6); FAS + pFAS: 1/189 (0.53%; 95% CI: 0.5, 1.6)	High
Miller, 2002[60]	USA	RCS	Total population	437,252	nr	1) Vital statistics records; 2) Medical records audit	FASSNet	FAS: 185/437252 (0.042%; rate per 1000 live births: 0.42)	Low
O'Leary, 2010[61]	Australia	RCS	Random	4,714	<6 yr	1) Interview/maternal risk; 2) Birth defects registry	IOM	ARBD: 51/4714 (1.08%; 95% CI: 0.8, 1.4)	Low
Serreau, 2002[47]	France (Reunion Island)	CSS	Total population	1,320	< 20 yr	1) Interview/maternal risk; 2) Dysmorphological assessment; 3) Case conference	IOM	FAS: 64/1320 (4.8%; 95% CI: 3.7, 6.0); ARND: 14/1320 (1.06%; 95% CI: 0.5, 1.6); ARBD: 5/1320 (0.37; 95% CI: 0.1, 0.7); ARBD + ARND: 4/1320 (0.3; 95% 95: 0.1, 0.6); FASD: 87/1320 (6.59%; 95% CI: 5.3, 7.9)	Moderate

Sokol, 1986[69]	USA	PCS	Consecutive	8,331	nr	1) Interview/maternal risk; 2) Dysmorphological assessment	FASG - RSA	FAS: 25/8331 (0.3%; 95% CI: 0.2, 0.4)	Moderate
Weiss, 2004[70]	USA	PCS	Total population	56,247	2-3 yr	1) Medical records audit; 2) Neurobehavioural assessment; 3) Dysmorphological assessment	WFASS	FASD: 13/56247 (0.023%; 95% CI: na; FASD rate: 0.23 per 1000 births)	Low

95% CI = 95% confidence interval; ARBD = alcohol-related birth defects; ARND = alcohol-related neurodevelopmental disorders; CSS = cross-sectional study; CDC = Center for Disease Control; CSS = cross-sectional study; FAS = fetal alcohol syndrome; FASD = fetal alcohol spectrum disorders; FASG = Fetal Alcohol Study Group; IOM = Institute of Medicine; ICD-9 = International Classifications of Disease, 9th Revision; mo = month(s); nr = not reported; PCS = prospective cohort study; pFAS = partial fetal alcohol syndrome; RCS = Retrospective cohort study; RSA = Research Society of Alcoholism; WFASS = Wisconsin Fetal Alcohol Syndrome Screening Project case definition ; yr(s): years

Table C2: Studies on the prevalence of FASD in school settings

Study	Country	Design	Sampling	Sample size	Age (mean or range)	Diagnostic sequence	Diagnostic criteria	FASD Prevalence	Summary of quality rating
Clarren, 2001[20]	USA	CSS	Total population	3,740	nr	1) Dysmorphology assessment; 2) Interview/maternal risk	4-Digit system	FAS: 7/3740 (0.18%; 95% CI: 0.1, 0.3)	Moderate
Cunniff, 1994[21]	USA	CSS	Unknown	660	nr	1) Medical examination; 2) Dysmorphological assessment	FASD Canadian Diagnostic Guidelines	AS: 0/660; pFAS: 1/660 (0.15; 95% CI:0.1, 0.4)	Low
Kuo, 2012[28]	Taiwan	CSS	Unknown	3,817	3-15 yr	1) Interview/maternal risk; 2) Dysmorphological assessment; 3) Neurobehavioural assessment; 4) Case conference	nr	FASD: 22/3817 (0.57; 95% CI: 0.3, 0.8; FASD rate per 1000 live births: 5.7); FAS: 7/3817 (0.18%; 95% CI: 0.1, 0.3; FAS rate per 1000 live births 1.8); ARND: 15/3817 (0.39; 95% CI: 0.2, 0.6; ARND rate per 1000 live births: 3.93)	Low
Lee, 2012[30]	South Korea	CSS	Convenience	8,092	nr	1) Medical examination; 2) Dysmorphological assessment	FASD Canadian Diagnostic Guidelines	FAS: 40/7785 (0.51%; 95% CI: 0.4, 0.7)	Low
May, 2011[34]	Italy	CSS	Random	976	79.5 mo	1) Dysmorphology assessment; 2) Neurobehavior screening; 3) Interview/maternal risk; 4) Case conference	Hoyme	FASD: 46/976 (4.71%; 95% CI: 3.3, 6.2; rate per 1000: 47.1); FAS: 8/976 (0.81%; 95% CI: 0.6, 1.1; rate per 1000: 8.2); pFAS: 36/976 (3.68%; 95% CI: 3.2, 4.0; rate per 1000: 36.8); ARND: 1/976 (0.1%; 95% CI:nr; rate per 1000: 1); ARBD: 1/976 (0.1%; 95% CI:nr; rate per 1000: 1);	High
May, 2006[33]	Italy	CSS	Random	543	80.4 mo	1) Dysmorphology assessment; 2) Neurobehavior screening; 3) Interview/maternal risk; 4) Case conference	Hoyme	FASD: 22/543 (4.05%; 95% CI: 2.4, 5.7); FAS: 4/543 (0.73; 95% CI: 0.1, 1.5); pFAS: 17/543 (3.1%; 95% CI:1.7, 4.6); ARND: 1/543 (0.18%; 95% CI:0.1, 0.5)	Moderate
May, 2012[36]	South Africa	CSS	Unknown	747	81.4 mo	1) Dysmorphology assessment; 2) Neurobehavior screening; 3) Interview/maternal risk; 4) Case conference	IOM	FASD: 156/747 (20.8; 95% CI: 18, 23.8); FAS: 68/747 (9.1%; 95% CI:7.0, 11.2); pFAS: 53/747 (7.09; 95% CI: 5.3, 8.9); ARND: 35/747 (4.68; 95% CI: 3.2, 6.2)	Low
May, 2000[38]	South Africa	CSS	Convenience	992	6.6 yr	1) Dysmorphology assessment; 2) Neurobehavior screening; 3) Interview/maternal risk; 4) Case conference	IOM	FAS: 46/992 (4.63; 95% CI: 3.3, 5.9)	High
May, 2007[35]	South Africa	CSS	Convenience	818	7.3 yr	1) Dysmorphology assessment; 2) Neurobehavior screening; 3) Interview/maternal risk; 4) Case conference	Hoyme	FAS: 55/818 (6.7%; 95% CI: 5.0, 8.4); pFAS: 33/818 (4.03; 95% CI: 2.7, 5.4) ; FAS + pFAS: 88/818 (10.7%; 95% CI: 8.6, 12.9)	High

May, 2011[32]	USA	CSS	Unknown	2,334	7.1 yr	1) Medical examination; 2) Dysmorphological assessment; 3) Neurobehavioural assessment	IOM	FAS: 7/2385 (0.29%; 95% CI: 0.1, 0.5); pFAS: 18/2385 (0.75; 95% CI: 0.4, 0.11); FASD (FAS + pFAS): 25/2385 (1.04; 95% CI:0.6, 1.5)	Low
Mena, 1988[41]	Chile	CSS	Convenience	475	nr	1) Interview/maternal risk; 2) Medical examination; 3) Dysmorphology assessment; 4) Neurobehavioural assessment	FASG - RSA	FAS: 36/475 (7.5%; 95% CI: 5.2, 10)	Moderate
Mena, 1986[40]	Chile	CSS	Convenience	386	nr	1) School records audit; 2) Maternal/risk assessment; 3) Medical records audit; 4) Dysmorphology assessment; 5) Neurobehavioural assessment	FASG - RSA	FAS: 13/386 (3.36%; 95% CI: 1.6, 5.2); pFAS: 21/386 (5.4%; 95% CI: 3.2, 7.7); FAS + pFAS: 34/386 (8.8%; 95% CI:6.0, 11.6)	Moderate
Olivier, 2010[44]	South Africa	CSS	Unknown	1,788	nr	1) Dysmorphology assessment; 2) Neurobehavior screening; 3) Interview/maternal risk	Hoyme	FASD: 161/1788 (9%; 95% CI: 7.7, 10.3)	Low
Petkovic, 2010[45]	Croatia	CSS	Random	466	8.8 yr	1) Interview/maternal risk; 2) Dysmorphology assessment	Hoyme	FAS + pFAS: 19/466 (4.07%; 95% CI: 2.3, 5.9); FAS: 3/466 (0.64%; 95% CI: 0.1, 1.4); pFAS: 16/466 (3.46%; 95% CI: 1.8, 5.1)	Moderate
Poitra, 2003[68]	USA	PCS	Convenience	1,384	nr	1) Screening; 2) Dysmorphologic assessment; 3) Interview/maternal risk; 4) Case conference	FAS Screen	FAS: 6/1384 (0.43%; 95% CI:0.1, 0.8; FAS rate: 4.3 per 1000); pFAS: 1/1384 (0.07%; 95% CI: 0.01, 0.2; pFAS rate: 0.72 per 1000) , FAS + pFAS: 7/1384 (0.5; 95% CI: 0.1, 0.9)	Moderate
Urban, 2008[50]	South Africa	CSS	Total population	1,830	7.05 yr	1) Dysmorphology assessment; 2) Neurobehavior screening; 3) Interview/maternal risk; 4) Case conference	IOM	FAS: 123/1830 (6.72%; 95% CI: 5.62, 7.97); pFAS: 38/1830 (2.07%; 95% CI: 1.47, 2.84); FAS + pFAS: 161/1830 (8.79%; 95% CI: 7.5, 10.1)	High
Viljoen, 2005[51]	South Africa	CSS	Convenience	857	6.5 yr	1) Dysmorphology assessment; 2) Neurobehavior screening; 3) Interview/maternal risk; 4) Case conference	Hoyme	FAS: 64/857 (7.46; 95% CI: 5.7, 9.2)	Moderate

95% CI = 95% confidence interval; ARBD = alcohol-related birth defects; ARND = alcohol-related neurodevelopmental disorders; CSS = cross-sectional study; FAS = fetal alcohol syndrome; FASD = fetal alcohol spectrum disorders; FASG = Fetal Alcohol Study Group; IOM = Institute of Medicine; mo = month(s); nr = not reported; PCS = prospective cohort study; pFAS = partial fetal alcohol syndrome; RSA = Research Society of Alcoholism; yr = year(s)

Table C3: Studies on the prevalence of FASD in foster care settings

Study	Country	Design	Sampling	Sample size	Age (mean or range)	Diagnostic sequence	Diagnostic criteria	FASD Prevalence	Summary of quality rating
Astley, 2002[17]	USA	CSS	Total population	600	5.8 yr	1) Dysmorphology assessment; 2) Clinical records review; 3) Clinical examination	4-Digit system	FAS: 6/600 (1%; 95% CI: 0.2, 1.8)	High
Feldmann, 2012[25]	Germany	CSS	Unknown	267	nr	1) Interview/questionnaire	FASQ	FAS: 62/267 (23.4%; 95% CI: 18.2, 28.3)	Low
Knuiman, 2012[26]	Poland/ Netherlands	CSS	Unknown	118	10 yr	1) Interview/questionnaire	FASQ	FASD: 36/118 (30.5%: 95% CI: 22.2, 38.8)	Low
Kuzmenkoviene, 2012[29]	Lithuania	CSS	Unknown	337	nr (pre-school children)	1) Dysmorphology assessment; 2) Neurobehavior screening; 3) Medical examination	Hoyme	FASD: 134/337 (39.7%; 95% CI: 34.5, 45); FAS: 74/337 (21.9%; 95% CI: 17.5, 26.4); pFAS: 24/337 (7.1%; 95% CI: 4.4, 9.9); ARND: 37/337 (11%; 95% CI:7.6, 14.3)	Low
Landgren, 2010[67]	Sweden	PCS	Total population	71	7.5 yr	1) Medical records audit/maternal risk; 2) Dysmorphological assessment; 3) Neurobehavioural assessment; 4) Case conference	IOM	FASD: 37/71 (52%; 95% CI:40.5, 63.7); FAS: 21/71 (29.5%; 95% CI: 19,40); pFAS: 10/71 (14%; 95% CI: 6, 22); ARND: 6/71(8.4%; 95% CI: 2.0, 14.9); ARBD: 8/71 (11.26; 95% CI: 3.9, 18.6)	Low
Mena, 1987[39]	Chile	CSS	Unknown	701	nr	1) Interview/maternal risk; 2) Medical examination; 3) Dysmorphology assessment; 4) Neurobehavioural assessment	FASG - RSA	FAS: 136/701 (19.4%; 95% CI: 16.5, 22.3)	Moderate
Olivan-Gonzalvo, 2011[43]	Russia	CSS	Unknown	1,062	27 mo	1) Telemedicine case conference	4-Digit system	FAS: 117/1062 (11.01%; 95% CI: 9.1, 12.9)	Low
Tenenbaum, 2011[49]	Israel	CSS	Consecutive	100	5.9 mo	1) Medical examination	IOM and FASD Canadian Diagnostic Guidelines combined	p FAS: 2/100 (2%; 95% CI: 0.7, 4.7); ARND: 0; ARBD: 0	Low

95% CI = 95% confidence interval; ARBD = alcohol-related birth defects; ARND = alcohol-related neurodevelopmental disorders; CSS = Cross-sectional study; FAS = fetal alcohol syndrome; FASD = fetal alcohol spectrum disorders; FASG = Fetal Alcohol Study Group; FASQ = Fetal Alcohol Syndrome Questionnaire; IOM = Institute of Medicine; mo = month(s); nr = not reported; PCS = Prospective cohort study; pFAS = partial fetal alcohol syndrome; RSA = Research Society of Alcoholism; yr = year(s)

Table C4: Studies on the prevalence of FASD in prisons and correctional facilities

Study	Country	Design	Sampling	Sample size	Age (mean or range)	Diagnostic sequence	Diagnostic criteria	FASD Prevalence	Summary of quality rating
Burd, 2004[18]	USA	CSS	Total population	3'080,904	>15 yr	1) Interview/questionnaire	Self-reported dx	FAS: 1/3080904 (0.0003 per 1000)	Moderate
Burd, 2003[19]	Canada	CSS	Total population	148,797	>15 yr	1) Interview/questionnaire	Self-reported dx	FAS: 13/148797 (0.008%; 0.087 per 1000 population)	Moderate
Fast, 1999[24]	Canada	CSS	Total population	287	14.8 yr	1) Dysmorphology assessment; 2) Neurobehavior screening; 3) Clinical records/maternal risk; 4) Case conference	IOM	FASD: 67/287 (23.3%; 95% CI: 18.5, 28.2); FAS: 3/287 (1.04%; 95% CI:1.0, 2.2); pFAS: 52/287 (18%; 95% CI: 13.7, 22.6); ARND: 12/287 (4.18; 95% CI: 1.9, 6.5)	Moderate
MacPherson, 2007[31]	Canada	CSS	Unknown	91	<30 yr	1) Neurobehavioural assessment; 2) Dysmorphological assessment; 3) Chart review/maternal risk; 4) Case conference	nr	FASD: 9/91 (9.8%; 95% CI: 3.8, 16); pFAS: 1/91 (1.09%; 9% CI: 1.0, 3.2); ARND: 8/91 (8.79; 95% CI: 3.0, 14.6)	Low
Murphy, 2005[42]	Canada	CSS	Total population	137	14-19 yr	1) Interview/questionnaire	Self-reported dx	FAS:16/137 (11.6%; 95% CI: 6.3, 17.1)	Low
Rojas, 2007[62]	Canada	RCS	Total population	230	15.91 yr	1) Medical records audit	Self-reported dx	FASD: 25/230 (10.8%; 95% CI: 7.4, 15.5)	Moderate

95% CI = 95% confidence interval; ARND = alcohol-related neurodevelopmental disorders; CSS = Cross-sectional study; dx = diagnosis; FAS = fetal alcohol syndrome; FASD = fetal alcohol spectrum disorders; FASG = Fetal Alcohol Study Group; IOM = Institute of Medicine; mo = month(s); nr = not reported; pFAS = partial fetal alcohol syndrome; RCS = retrospective cohort study; RSA = Research Society of Alcoholism; yr = year(s)

Table C5: Studies on the prevalence of FASD in Aboriginal peoples and minority groups

Study	Country	Design	Sampling	Sample size	Age (mean or range)	Diagnostic sequence	Diagnostic criteria	FASD Prevalence	Summary of quality rating
Bower, 2000[53]	Australia	RCS	Total population	nr	nr	1) Birth defects registry	nr	FAS: 67/nr (FAS rate per 1000 live births: 2.76)	Moderate
Duimstra, 1993[65]	USA	PCS	Total population	1,022	nr	1) Medical records audit; 2) Neurobehavioural assessment; 3) Dysmorphological assessment; 4) Interview/maternal risk	FASG - RSA	FAS: 4/1022 (0.39%; 95% CI: 0.1, 0.8; FAS rate per 1000: 3.9)	Moderate
Egeland, 1998[57]	USA	RCS	Total population	176,765	8.4 mo	1) Vital statistics records; 2) Medical records audit	ICD-9 codes 760.71, 760.7	FAS: 114/37346 (0.30%; 95% CI 0.2, 0.4; FAS rate per 1000 live births: 3.0)	Low
Habbick, 1996[58]	Canada	RCS	Convenience	nr	nr	1) Vital statistics records; 2) Medical records audit	4-Digit system	FAS rate per 1000 live births: 0.585 (86% aboriginal)	Low
Harris, 2003[59]	Australia	RCS	Total population	25,209	nr	1) Medical records audit	4-Digit system	FAS: 18/16132 (0.11; 95% CI: nr; rate per 1000 live births: 1.11); pFAS: 21/16132 (0.13%; 95% CI: nr; rate per 1000 births: 1.3); ARND: 4/16132 (0.02%; 95% CI: nr; rate per 1000 live births: 0.2); FASD: 43/16132 (0.26%; 95% CI: nr; rate per 1000 live births: 2.6)	Low
Kowlessar, 1997[27]	Canada	CSS	Convenience	178	5-15 yr	1) Interview/maternal risk; 2) Chart review; 3) Dysmorphological assessment; 4) Neurobehavioural assessment	IOM	FAS: 11/178 (6.17; 95% CI:2.6, 9.7); pFAS: 7/178 (3.9; 95% CI:1.1, 6.8); FAS + pFAS: 18/178 (10.1; 95% CI: 5.7, 14.5)	Moderate
May, 1983[37]	USA	CSS	Convenience	22,963	0-14 yr	1) Dysmorphological assessment; 2) Chart review/maternal risk; 3) Case conference	nr	FAS: 55/22963 (0.23%; 95% CI: 0.2, 0.3; FAS rate per 1000: 2.3)	Low
Robinson, 1987[46]	Canada	CSS	Total population	116	3-18 yr	1) Interview/maternal risk; 2) Neurobehavioural screening; 3) Medical examination	FASG - RSA	FAS:14/116 (12%; 95% CI: 6.1, 18; FAS rate per 1000: 140)	Moderate
Rojas, 2007[62]	Canada	RCS	Total population	230	15.91	1) Medical records audit	Self-reported dx	FASD: 18/67 (26.9%; 95% CI: 17.7, 38.5)	Moderate
Rothstein 2007[63]	Australia	RCS	Unknown	1,995	7.6 yr	1) Medical records audit	nr	FAS: 5/1995 (0.24%; 95% CI 0.1, 0.5; rate per 1000: 2.4)	Low
Williams, 1999[64]	Canada	RCS	Total population	745	<2 yr	1) Medical records/audit; 2) Dysmorphological assessment	IOM	FAS: 5/745 (0.67; 95% CI: 0.1, 1.3)	Low

Chavez, 1988[54] **Other ethnic minorities**	USA	RCS	Total population	4'617,613	nr	1) Medical records audit	ICD-9 codes (nr)	FAS: African americans: 0.6 per 1000 live births; Hispanics: 0.08 per 1000; American Indians: 2.9 per 1000; Asians: 0.03 per 1000; Whites: 0.09 per 1000	Low

95% CI = 95% confidence interval; ARBD = alcohol-related birth defects; ARND = alcohol-related neurodevelopmental disorders; CSS = cross-sectional study; CSS = cross-sectional study; FAS = fetal alcohol syndrome; FASD = fetal alcohol spectrum disorders; FASG = Fetal Alcohol Study Group; IOM = Institute of Medicine; ICD-9 = International Classifications of Disease, 9th Revision; mo = month(s); nr = not reported; PCS = prospective cohort study; pFAS = partial fetal alcohol syndrome; RCS = Retrospective cohort study; RSA = Research Society of Alcoholism; yr(s): years

Table C6: Studies on the prevalence of FASD in special education and clinical settings

Study	Country	Design	Sampling	Sample size	Age (mean or range)	Diagnostic sequence	Diagnostic criteria	FASD Prevalence	Summary of quality rating
Lee, 2012[30]	South Korea	CSS	Convenience	8,092	nr	1) Medical examination; 2) Dysmorphological assessment	FASD Canadian Diagnostic Guidelines	FAS-13/307 (4.2%; 95% CI: 2.0, 6.5)	Low
Mena, 1988[41]	Chile	CSS	Convenience	475	nr	1) Interview/maternal risk; 2) Medical examination; 3) Dysmorphology assessment; 4) Neurobehavioural assessment	FASG - RSA	FAS: 36/475 (7.5%; 95% CI: 5.2, 10)	Moderate
Mena, 1986[40]	Chile	CSS	Convenience	386	nr	1) School records audit; 2) Maternal/risk assessment; 3) Medical records audit; 4) Dysmorphology assessment; 5) Neurobehavioural assessment	FASG - RSA	FAS: 13/386 (3.36%; 95% CI: 1.6, 5.2); pFAS: 21/386 (5.4%; 95% CI: 3.2, 7.7); FAS + pFAS: 34/386 (8.8%; 95% CI:6.0, 11.6)	Moderate
Shanske AL, 1980[48] **Specialized clinic**	USA	CSS	Unknown	900	< 7 yr	1) Medical records audit	nr	FAS + pFAS combined: 19/900 (2.1%; 95% CI: 1.2, 3.1)	Low

95% CI = 95% confidence interval; CSS = cross-sectional study; FAS = fetal alcohol syndrome; FASD = fetal alcohol spectrum disorders; FASG = Fetal Alcohol Study Group; nr = not reported; pFAS = partial fetal alcohol syndrome; RSA = Research Society of Alcoholism