SCREENING AND REFERRAL TO IDENTIFY CHILDREN AT RISK FOR FASD: SEARCH FOR NEW METHODS 2006-2013

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ABSTRACT

As part of the ***Canadian Association of Paediatric Health Centres Taskforce on FASD Screening*** commitment to further pilot, validate and evaluate the multiple components of the Canadian FASD Screening Tool Kit, it was deemed necessary that recent developments and/or improvements in FASD screening were identified and considered. In 2008 a literature review of methods for screening for FASD was published until 2006 and identified five tools which met pre-set criteria. A review of all new papers was published from the period January 2006 until July 1, 2013.

Out of 1392 papers, two new screening methods met the inclusion criteria: Clarren et al's new norms for palpebral fissure length by age in Canada; and Breiner et al's extension of the Neurobehavioral Screening Test (NST) to age 4 years. Further work is needed to validate these methods in other settings.

INTRODUCTION

As part of the Public Health Agency of Canada FASD Screening Taskforce's commitment to further pilot, validate and evaluate the multiple components of the Canadian FASD Screening Tool Kit, it deemed necessary that recent developments and/or improvements in FASD screening were identified and considered. In 2008 a literature review of methods for screening for FASD identified five tools which met pre-set criteria. The criteria, the process and results have been published by Goh, et al. (http://www.caphc.org/documents_programs/fasd/final_fasd_lit_review.pdf). Since then, the Tool Kit has been widely distributed and accessed through the CAPHC Knowledge Exchange Network (KEN) and extensive testing of the tools has taken place.

To ensure that the latest information on FASD screening is considered and evaluated, a subsequent literature review has been undertaken using a similar approach to the original one. This was an iterative process that built on existing knowledge in order to enrich and maintain the scientific relevance of the Tool Kit.

METHODS

FASD screening methods published since 2007 to the present were reviewed. This process included searching in the English language using PubMed-Medline and Embase databases, as well as Google. Because full papers were needed for this process, abstracts of meetings were not included. The key words included were FASD, alcohol, pregnancy, and screening.

As a basic rule, reports that describe methods already approved by the Steering Committee in 2008 were not searched (e.g. screening for maternal drinking) but rather new ideas for screening, not covered by the existing methods. The identified papers were evaluated based on the criteria established by the Steering Committee in 2006. The Epidemiological Evidence criteria had to be satisfied for inclusion. Methods that appeared promising, but yet did not have epidemiological proof of their ability to distinguish children affected by FASD from other children, have been retained for future evaluation.

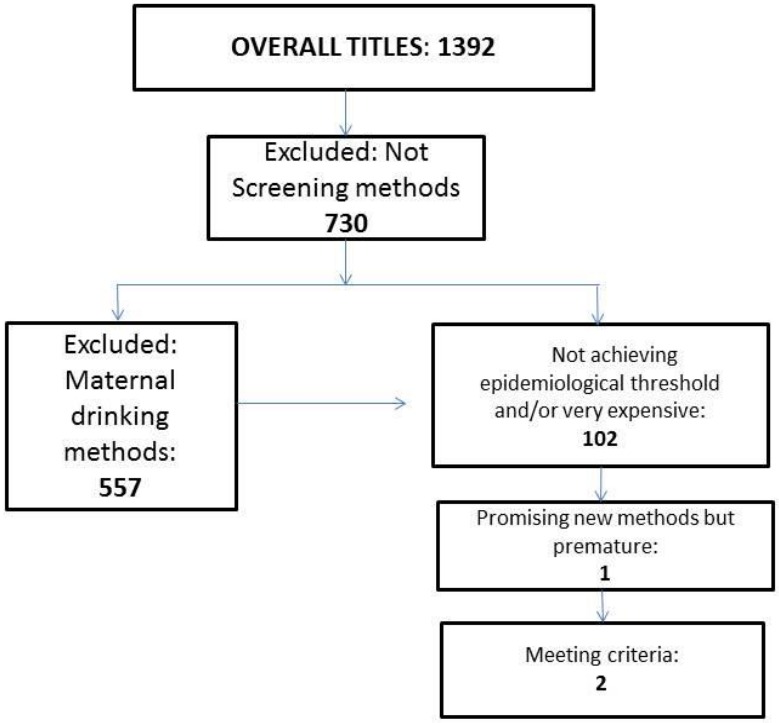
RESULTS

A total of 1392 titles were identified and their abstracts were reviewed for meeting the inclusion criteria. The vast majority did not describe screening methods for FASD, but rather mentioned the term *screening* to quote the need for screening, or describe existing methods. By far, the most commonly mentioned screening method was Maternal drinking (see Figure 1).

The published screening methods were classified as follows:

- Premature but potentially promising;
- Not meeting epidemiological threshold and/or very expensive;
- Meeting Criteria.

FIG. 1 Literature Evaluation Process



Premature but potentially promising screening methods

One study was considered potentially promising but premature. This study examined the feasibility and cost of neonatal screening for prenatal alcohol exposure by measuring phosphatidylethanol in dried blood spots.[1] Phosphatidylethanol is a metabolite of alcohol that can be identified in baby's blood if exposure occurred near term. This group measured the feasibility of obtaining an additional dried blood spot card to measure this metabolite. This work shows feasibility, but at this stage they did not measure the metabolite and establish its predictive value.

Screening methods not meeting epidemiological threshold and /or very expensive

Several studies were reviewed that did not meet the epidemiological threshold and/or they were considered too expensive at this time to be feasible screening methods.

A study which examined saccadic eye movements in children with FASD[2] was reviewed. Saccadic eye movement is a powerful tool for assessing sensory, motor and cognitive function. The cerebellum has frequently been reported to be damaged by prenatal alcohol exposure. This study tested the hypothesis that children with FASD will exhibit deficits in the accuracy of saccades.

Results of the study suggest that children with FASD may have deficits in eye movement control and sensory-motor integration including cerebellar circuits, thereby impairing saccade accuracy. However, this method did not meet the inclusion criteria due to its prohibitive cost and the need for complex laboratory equipment that precludes wide use in the community and even in academic centres.

An increasing number of neuro-imaging studies have assessed brain structure and function of children with FASD compared to healthy controls. Four of these studies were evaluated. The results point to various degrees of statistical differences, but with large overlap and poor sensitivity and specificity. Due to the huge costs of these tests, other criteria were not further assessed (e.g. references 3-4).

Meeting Criteria

Two studies reviewed met the criteria for consideration as FASD screening tools. The first study examined palpebral fissures (PF) length. Shortened PF's are key physical markers for identifying children with FAS. There was concern that normative data on PF's now available may not reflect all racial/ethnic groups and be inaccurate in general. A large population-based study was completed to determine normative PF values across the full diversity of the Canadian school population.[5]

A normative sample of school age children was identified in Vancouver, British Columbia and Winnipeg, Manitoba to reflect the diversity of racial and national groups in Canada. The sample included students in grades 2, 4, 6, 8, and 10 from 17 schools in Vancouver and 31 schools in Winnipeg. Schools were selected based on racial diversity obtained from data from the 2001 Statistics Canada census. 1064 students in Vancouver and 1033 students in Winnipeg were photographed in a standardized way. Photographs were analyzed using a computerized method.

Analysis demonstrated that PFs do grow with age and there is a slight but meaningful difference between boys and girls in each age group. Most importantly, this study has demonstrated that it is possible to define Canadian standards without references to racial or ethnic origin.

The second study to meet the criteria explored a screening method for younger children that could potentially lead to early diagnosis and intervention. Most children with FASD do not display the typical facial changes, making the diagnosis much more challenging due to poor specificity of the brain dysfunction exhibited by these children. The Neurobehavioural Screening Tool (NST) is one of the five tools in the Tool Kit which uses items from the Child Behaviour Checklist. Through this project, the NST has been validated in several populations. This tool has high sensitivity and specificity in separating children aged 6-13 years that are at risk for FASD from those with ADHD and from healthy controls.

This current study tested the validity of the NST for children aged 4-6 years in order to help facilitate diagnosis of FASD in young children.[6] In this pilot study, the NST has shown very high sensitivity and specificity and has demonstrated that it can be used to identify children who are very likely to be diagnosed with FASD.

TABLE 1 FASD Screening Methods Evaluation Criteria

CRITERIA **1=most difficult; 5= very easy**
Critical Criterion: **Epidemiological evidence (sensitivity, specificity)**
Ease of Use (1-5)
Accessibility (1-5)
Expertise needed (1-5)
Feasibility of implementation (1-5)
Cost (1-5)
Cultural appropriateness (1-5)

Evaluation of Accepted Studies

Steering Committee members were asked to rate the two selected papers using the criteria developed in 2007. On a scale of 1-5 the studies were rated in terms of ease of use, accessibility, expertise needed, feasibility of implementation, cost, and cultural appropriateness.

The quantitative evaluation of the criteria for the two evaluable papers by Steering Committee members is presented as mean and range:

Clarren et al[5]

The study did not describe a new screening method per se, but Steering members agreed that it provides an essential baseline for using this method in a Canadian population. Overall the tool was highly endorsed. There was larger variability in evaluating the expertise needed to measure accurately palpebral fissure (see Table 2).

Breiner et al[6]

Overall the tool was highly endorsed. There was larger variability on epidemiological evidence due to the relatively small sample size (see Table 3).

TABLE 2 Distribution of palpebral fissure lengths in Canadian school age children. Clarren et al[5]

Criteria	**Mean score**	**Range**
Epidemiological evidence	4.0	3-5
Ease of Use	3.9	3-5
Expertise needed	3.5	2-5
Feasibility of implementation	4.6	4-5
Cost	4.5	3-5
Cultural sensitivity	4.7	4-5
OVERALL ASSESSMENT: 4.3		

TABLE 3 Identifying the neurobehavioral phenotype of fetal alcohol spectrum disorder in young children. Breiner, et al[6]

Criteria	Mean score	Range
Epidemiological evidence	3.5	2-5
Ease of Use	5.0	5
Expertise needed	4.6	4-5
Feasibility of implementation	4.8	4-5
Cost	4.8	4-5
Cultural sensitivity	3.9	1-5
OVERALL ASSESSMENT: 4.6		

DISCUSSION

The aim of this study was to expand our initial identification of screening methods for FASD to potential new methods published after 2006. Interesting new approaches have been developed based on the physiology of eye movement, brain imaging and measuring alcohol metabolites in neonatal blood. However, none of these methods have presented sufficient epidemiological evidence of sensitivity and specificity.

Overall, two new methods have met our taskforce threshold: The measurement of palpebtal fissure (PF) length and the neurobehavioral screening test for age 4-6 years.

A PF shorter than 2 standard deviation from the mean for age is pathognomonic of FASD, and it could be argued that one cannot use a key sign of the syndrome as a screener for the same condition. Moreover, it is acknowledged that the vast majority of children with FASD do not display short PF. However, this sign is highly specific, with a very short differential diagnosis[7], and it is agreed among physicians that a child displaying PF shorter than 2 standard deviations for his/her age should be examined for FASD.

The second method is the extension of the neurobehavioral neurobehavioral test established and validated in the past[8] to 4 years of age. Based on the Child Behavior Checklist, the original NST appears to have high sensitivity and specificity.

The younger version of the CBCL misses 2 of the questions endorsed above age 6, however, despite this, the test appears to maintain its sensitivity and specificity.[6]

Future studies will need to corroborate these methods, as is true for the first wave of screening tests, in order to expand their use and make them part of the public health means to combat FASD.

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