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REVIEW ARTICLE

Screening approaches for identifying fetal alcohol spectrum disorder in children, adolescents, and adults: A systematic review

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Abstract

Background: Fetal alcohol spectrum disorder (FASD) is a prevalent neurodevelopmental disorder that is caused by prenatal alcohol exposure (PAE) and associated with a range of cognitive, affective, and health concerns. Although the identification of FASD can facilitate the provision of interventions and support, and plays a protective role against adverse outcomes, there are high rates of missed detection. The identification of FASD via screening may improve its recognition across settings. The current systematic review examined the available evidence on FASD screening tools and approaches across age groups and settings.

Methods: A systematic search was carried out for both peer-reviewed studies and gray literature sources published between January 1990 and May 2020 and was preregistered with PROSPERO (#CRD42019122077). Studies included in the review focused on human applications of FASD screening in children, adolescents, and adults. The quality of the studies was assessed using the QUADAS-2 and GRADE frameworks.

Results: The search yielded 20 screening tools and approaches across 45 studies, broadly characterized in 2 groups. The first group included approaches currently in use that aim to identify individuals at risk of FASD using a range of markers ($n = 19$) or associated sentinel dysmorphic facial features ($n = 6$). Another group of studies, characterized as emerging, focused on identifying promising biomarkers of PAE/FASD ($n = 20$). Overall, we identified limited research supporting the psychometric properties of most screening approaches. The quality review provided evidence of bias due to the common use of case–control designs and lack of adequate reference standards.

Conclusions: Although several FASD screening tools and approaches are available for use across a range of age groups and settings, the overall evidence base supporting their psychometric properties is weak, with most studies demonstrating significant risk of bias. Service providers should exercise caution in selecting and implementing FASD screening tools given these limitations. It is critically important to accurately identify individuals with FASD across ages and settings to support healthy outcomes. Thus, there is a pressing need for additional research in this area, particularly validation studies in large and representative samples using robust methodological approaches.

KEYWORDS
fetal alcohol spectrum disorder, identification, prenatal alcohol exposure, screening

INTRODUCTION

Fetal alcohol spectrum disorder (FASD) is a common neurodevelopmental disorder resulting from prenatal alcohol exposure (PAE) associated with wide-ranging impairments in neurodevelopmental functioning, affect and behavior regulation, physical health concerns, and in some cases, facial dysmorphology and growth restriction (Cook et al., 2016; Hoyme et al., 2016; Mattson et al., 2019)[1]. Although many individuals with FASD experience various difficulties, with wide-ranging inter- and intraindividual profiles, they also have many unique strengths and can achieve healthy and positive outcomes with appropriate supports (Ali et al., 2018; Carmichael Olson & Sparrow, 2021; Flannigan et al., 2018; Mattson et al., 2019; McLachlan et al., 2017, 2020). FASD is one of the most common neurodevelopmental disorders, with conservatively estimated prevalence in North America ranging from 2 to 5%, and higher rates in child welfare, special education, and criminal justice settings (May et al., 2014, 2018; Popova et al., 2019a, 2019b). The social and economic costs associated with FASD are substantial, with lifetime costs for 1 individual with FASD estimated to be $2 million USD, and estimates of annual costs associated with FASD in Canada range from $1.3 to 2.3 billion CAD (Lupton et al., 2004; Popova et al., 2016).

Early identification, assessment, and/or diagnosis of FASD, coupled with the provision of individualized intervention services and supports, have been identified as key protective factors that mitigate adverse outcomes experienced by individuals with FASD (McLachlan et al., 2020; Popova et al., 2020; Streissguth et al., 2004). Formal recognition and/or diagnosis of FASD in children and adolescents may also confer additional important benefits, including easier access to appropriate supports, better understanding of an individual's strengths and challenges, formation of peer and caregiver support networks, and improved communication among the circle of care (Doak et al., 2019; Helgesson et al., 2018). Identification of FASD remains critical in adulthood given the life-course nature of the difficulties experienced by those with FASD, and because evidence suggests that adult-oriented interventions can lead to valuable outcomes, such as reductions in substance use and improved relationships (Brintnell et al., 2019; Denys et al., 2011). Despite the recognized importance of identification, FASD continues to be misidentified and underrecognized (Chasnoff et al., 2015; McLachlan et al., 2020; Popova et al., 2020).

Several barriers complicate timely identification of individuals with FASD. These include the relatively "hidden" nature of the disorder, with a large proportion of those with FASD presenting with no overt outward physical signs (~90%), as well as underreporting of alcohol use during pregnancy due to substantial stigma and fear of repercussions (Astley, 2010; Corrigan et al., 2019). Additional barriers include a continued lack of system-level resources, complex and variable clinical presentations, and limited FASD knowledge and awareness among professionals needed to effectively recognize, assess, and provide support to individuals with FASD and their families (Astley Hemingway et al., 2019; Corrigan et al., 2019; McLachlan et al., 2020; Wedding et al., 2007). Guidelines for diagnosing FASD also range considerably across countries with respect to criteria and diagnostic nosology, which continue to change over time (see Coles et al., 2016, for a review). This complicates identification of individuals with FASD, as well as research efforts to establish valid FASD screening tools and approaches. Improved capacity to identify FASD through screening has been proposed as an important step toward ensuring that individuals with the disability are recognized and provided appropriate assessment, intervention, and resources, ultimately supporting improved outcomes and reducing adverse societal and economic costs (Clarren et al., 2011; Goh et al., 2008; Hopkins et al., 2008).

In 2008, Goh et al. completed a comprehensive review of FASD screening tools and developed a screening toolkit comprising 4 approaches identified as promising, including the Neurobehavioural Screening Tool (NST)[2] for children ages 6 to 18 years, the Medicine Wheel tool for use with children ages 4 to 14 years, the Asante Centre Probation Officer Tool for justice-involved youth (12 to 18 years), and meconium analysis of fatty acid ethyl esters in newborns. However, with the exception of meconium analysis, sparse empirical support for these tools was identified, and synthesis relied primarily on correspondence with the communities and institutions using the tools to gain sufficient information to describe and characterize them. Thus, there was limited evidence regarding the psychometric properties and clinical utility of the tools. A subsequent review aiming to update evidence supporting the toolkit identified no new tools, and only 2 additional peer-reviewed studies (Koren et al., 2014).

Several factors need to be considered in selecting and implementing appropriate and evidence-based FASD screening tools. Psychometric considerations include a tool's ability to produce consistent results (reliability) and measure the intended construct (validity), in this case, FASD (Litwin, 1995). Additional key metrics that speak to the clinical utility or predictive power of screening tools include sensitivity, specificity, positive predictive value, and negative predictive value (Trevethan, 2017). These clinical metrics require consideration of the proportion of screening decisions that result in correct classification relative to a reference standard or a validated approach for classification (Maxim et al., 2014; Trevethan, 2017). Although the reference standard may often be a diagnosis of FASD, this will vary based on the intended construct of measurement (e.g., a specific PAE-related diagnosis, presence of PAE-associated sentinel facial features), as well as both population and setting. Variation in reference standards also further complicates the generalizability

of psychometric characteristics, predictive power, tool validation, and consolidation of the evidence base across screening approaches (Meehl & Rosen, 1955; Wilson & Reichmuth, 1985).

Although many FASD screening tools and approaches have been developed and implemented with the aim of improving identification across a range of settings and populations, to our knowledge, systematic consideration of the evidence base supporting the utility, reliability, and validity of these tools is lacking. Thus, the aim of this review was to provide a systematic overview of the available evidence on FASD screening tools and approaches in school-aged children, adolescents, and adults, across a range of settings. Identifying gaps in the literature and potentially promising approaches to FASD screening can serve to inform future research and practice needs in this important area.

METHODS

The current systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and was preregistered with PROSPERO, an international prospective register of systematic reviews (Registration #CRD42019122077).[3]

Search strategy and study selection

Studies were selected for inclusion if they: (a) involved an empirical evaluation of instruments, protocols, or other tools designed to screen or identify FASD in human models from school-aged years (≥ 5 years) through adulthood; (b) had a title and abstract available in English; (c) offered a novel contribution via new empirical data to the state of the evidence; and (d) had undergone academic peer review.[4] Studies characterizing tiered approaches or identification strategies rather than evaluating a single unified tool or approach, such as those commonly described in prevalence ascertainment studies and decision trees, were not included in the review (e.g., Goh et al., 2016; May et al., 2014; Popova et al., 2019a).

Several databases were searched to identify peer-reviewed studies (ERIC, CINAHL, Medline, PsycINFO, PubMed, Social Services Abstracts, and Web of Science) using the following search terms: ("fetal alcohol spectrum disorder*" OR "FASD" OR "foetal alcohol spectrum disorder*" OR "fetal alcohol syndrome" OR "foetal alcohol syndrome" OR "alcohol related neurodevelopmental disorder*" OR "ARND") AND (screening OR screen OR biomarker OR neurobiomarker OR identification OR detection OR "biological marker*" OR questionnaire OR measure OR instrument). The search was conducted in 2 stages, including an initial search for studies published between January 1, 1990, and January 11, 2019, and a follow-up search bringing the review to May 2020. A parallel grey literature search using the same search terms across several databases (Open Grey, Open Government Canada, ProQuest, and PsycExtra) was conducted to identify tools or approaches that may be currently in use in the field but not reflected in the peer-reviewed literature.[5] We also searched published proceedings, abstracts from relevant conferences, websites, reference lists of relevant publications, Google, a custom search engine for Canadian government documents, and studies from the original database search that did not meet the peer-reviewed requirement.

All identified studies were uploaded to Covidence, an online software platform for facilitating systematic literature reviews. All studies were evaluated for inclusion and selection at both the title/abstract and full-text review stages by at least 2 independent reviewers, and conflicts were resolved through consensus, with input from the senior author (KM).

Data extraction, quality assessment, and synthesis

Data extraction elements relating to population characteristics (e.g., age, setting, ethnicity), study design (e.g., case-control, prospective case ascertainment), reference standard (e.g., diagnostic outcome), and key findings (e.g., classification accuracy, sensitivity, specificity) were independently extracted by 2 members of the research team. Discrepancies were discussed and resolved via consensus. The QUADAS-2 framework (Whiting et al., 2011) was used to evaluate study quality and bias risk, with precedence for use in screening studies (e.g., Hirota et al., 2018). Given the varying approaches, age groups, and settings covered in the current review, applicability of study samples to the research question was assessed qualitatively. The Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) system (Goldet & Howick, 2013) was used to assess the quality of the overall body of evidence supporting the recommendation of FASD screening tools or approaches currently available for use across ages and settings.

RESULTS

Study selection and characteristics

We identified 3392 unique studies, and 45 were included in the qualitative synthesis (Figure 1). Details and key outcomes of individual studies are reported in Tables 1–3. Across studies, 20 unique screening tools or approaches were characterized, and were most commonly published using data from Canada (49%), the United States (27%), South Africa (9%) and other countries (16%).[6] Included studies were published between 1995 and 2020, with sample sizes ranging from 20 to 3740 participants. Most studies used case–control ($n = 27$) or cross-sectional designs ($n = 18$). A narrative and descriptive approach was undertaken to synthesize findings given the number of tools/approaches, age groups, settings, and heterogeneity of studies included in the review. We identified 2 broad categories to facilitate narrative review. The first included screening tools and/or approaches considered to be currently available, including a subset that relied on a range of indicators to identify individuals who may have FASD, as well as a subset that focused more narrowly on

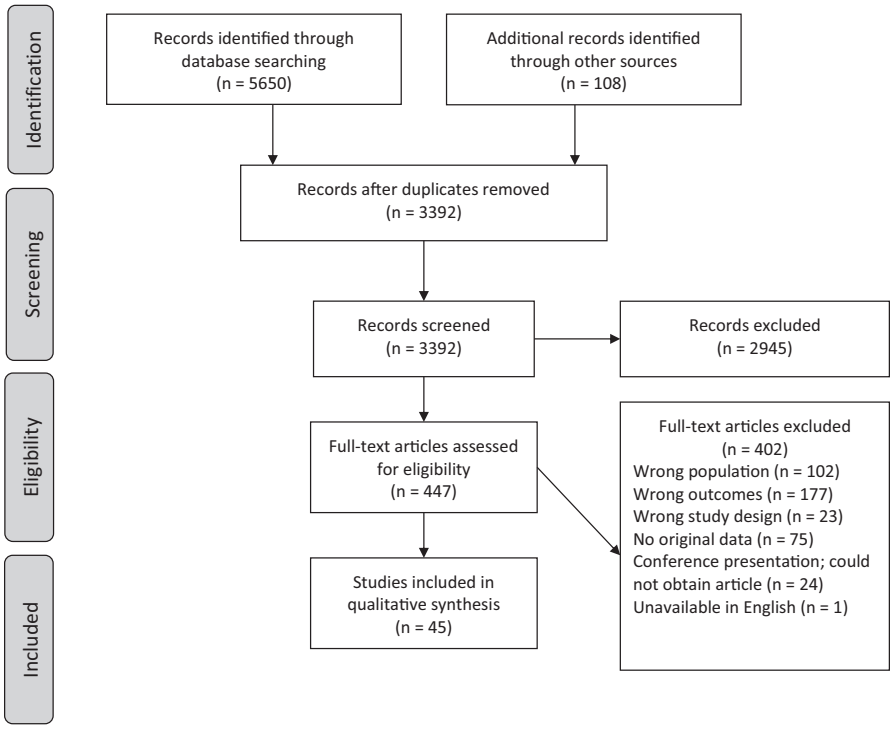

FIGURE 1 Flow chart depicting study selection

identifying the sentinel dysmorphic facial features associated with PAE/FASD. The second category included emerging biomarkers thought to have promising potential for FASD screening purposes.

Details relevant to screening tool format and application (e.g., intended age of individuals to be screened, response format, number of items, informant, tool development, and other considerations), are available in Table S1. The domains screened across each tool (e.g., PAE, sentinel facial features, neurodevelopmental impairment, history) are characterized in Table S2.

Summary and synthesis

Tools and approaches available for use across the FASD spectrum

Children and youth

Several screening tools in the form of questionnaires or checklists have been developed to identify FASD in children and adolescents across school and clinical settings. These tools are focused on a range of features, including facial dysmorphology, growth, developmental and behavioral indicators, and parent characteristics (see Tables S1 and S2).

To date, the Neurobehavioural Screening Tool (NST; Nash et al., 2006) has undergone the most study with respect to psychometric characteristics and classification accuracy (Breiner et al., 2013; Haynes et al., 2014; LaFrance et al., 2014; Nash et al., 2006, 2011; Patel et al., 2020). Notwithstanding variable scoring thresholds applied across studies, the NST has shown good sensitivity and specificity in distinguishing children and adolescents with FASD from neurotypically developing youth based on neurodevelopmental and behavioral indicators not specific to PAE/FASD. Among the limited number of studies evaluating differential identification, attenuated sensitivity and/or specificity was found when comparing youth with FASD to those with attention-deficit/hyperactivity disorder (ADHD), and poor item differentiation for FASD versus conduct disorder (Haynes et al., 2014; Nash et al., 2006, 2011).

Three tools have been developed for the purpose of larger-scale population screening of FASD in children and youth in specific settings. The FAS Screen (Burd et al., 1999) is aimed at identifying children and adolescents with FAS[7] in schools, and 2 studies demonstrated generally high sensitivity, specificity, and overall accuracy (Burd et al., 1999; Poitra et al., 2003). However, Burd et al. (1999) also reported low positive predictive value of the FAS Screen, suggesting that few children who screened positive ultimately received a diagnosis. The tool also heavily emphasizes facial dysmorphology and growth indicators, and there are no data on whether the tool can identify children on the FASD spectrum without any physical signs. Clarren et al. (2001) evaluated the feasibility and effectiveness of another FASD screening program in a school setting. Findings suggested that application of widespread FASD screening programs in schools may be feasible, but few indicators of accuracy for the screening procedure were reported, and there was notably better participation in the program when a passive versus active consent approach to enrolment was used. Finally, the Children's Aid Society of Toronto (CAST) FASD screening tool (Steinhart, 2016) was developed to identify youth with FASD in a child welfare setting. In the single study published on this tool, youth with and without FASD

TABLE 1 Characteristics and outcomes of studies for screening across the FASD spectrum

Author/Year/Country	Participants (age; *N*; % male)	Outcome screened	Recruitment setting	Study design	Outcomes/psychometric properties
Neurobehavioural Screening Tool					
Breiner et al., 2013 (Canada)	4–6 y; *N* = 60; % male NR	FASD	FASD clinic and previous research participants	Case–control diagnostic accuracy	Se = 94%, Sp = 96%
Haynes et al., 2014 (Canada)	6–12 y; *N* = 71; 46.5% male	FASD	Clinical and research program	Case–control diagnostic accuracy	Participants were children born to women with and without clinical depression , of which none screened positive for FASD
LaFrance et al., 2014 (Canada)	6–17 y; *N* = 102; 44.1% male	FASD	FASD service program, previous research participants, and community settings	Case–control diagnostic accuracy	5-item threshold for FASD and controls: Se = 62.5%, Sp = 100%, PPV = 100%, NPV = 64% 5-item threshold for PAE and controls: Se = 50%, Sp = 100%, PPV = 100%, NPV = 74.4% Trend toward higher sensitivity among adolescents (70.8%) over children (54.2%) 4-item threshold for FASD and controls: Se = 89.6%, Sp = 90.6%
Nash et al., 2006 (Canada)	6–16 y; *N* = 90; % male NR	FASD and ARND	FASD clinics, previous research participants, and community settings	Matched case–control diagnostic accuracy	FASD and controls: Se = 86%, Sp = 82% FASD and ADHD: Se = 81%, Sp = 72%
Nash et al., 2011 (Canada)	6–18 y; *N* = 220; 64.1% male	FASD	FASD clinics, outpatient treatment centers, and previous research participants	Case–control diagnostic accuracy	FASD and controls: Se = 98%, Sp = 42% FASD and ADHD: Se = 89%, Sp = 54% FASD and CD/ODD: 1 item differed between groups
Patel et al., 2020 (Canada)	3–15 y; *N* = 106; 50% male	FASD	Care settings	Cross-sectional diagnostic accuracy	Of those who screened positive, PPV = 78%
FASD screening program					
Clarren et al., 2001 (US)	Grade 1; *N* = 3740; % male NR	Alcohol-related conditions	Schools	Cross-sectional diagnostic accuracy	Nearly all eligible children were screened when consent was passive compared with 25% screened when consent was active; 40% who screened positive and attended a diagnostic clinic were identified as having an alcohol-related condition
FAS Screen					
Burd et al., 1999 (US)	3–14 y; *N* = 1013; % male NR	FAS	Schools	Cross-sectional diagnostic accuracy	Se = 100%, Sp = 94.1%, PPV = 9.1%, NPV = 100%, Ac = 94%
Poitra et al., 2003 (US)	Kindergarten; *N* = 1384; % male NR	FAS and pFAS	Schools	Cross-sectional diagnostic accuracy	Se = 100%, Sp = 95.43%, Ac = 95%
Children's Aid Society of Toronto screening tool					
Steinhart, 2016[†] (Canada)	7–15 y; *N* = 75; 57% male	FASD	Care settings	Case-control	One item differed between the FASD and control groups Use of the tool was unsupported

(Continues)

TABLE 1 (Continued)

Author/Year/Country	Participants (age; N; % male)	Outcome screened	Recruitment setting	Study design	Outcomes/psychometric properties
Fetal Alcohol Behaviour Scale					
Streissguth et al., 1998 (US)	2–51 y; N = 739; 60.6% male	FAS and FAE	Fetal alcohol and drug unit, corrections, and general practice waiting rooms	Case-control and cross sectional	FAS/FAE reference sample, Cronbach's α = 0.91 Normative sample, Cronbach's α = 0.89 Test–retest reliability, r = 0.69 36-item version: ~80% of FAS/FAE group scored >11 or 12 26-item version: 85% of FAS/FAE group scored >6 or 7; 85% of adults in corrections scored <6 or 7 Adults with higher FABS scores more likely to be living dependently
Life History Screen					
Grant et al., 2013 (US)	>18 y; N = 549; 0% male	FASD	Community program for women with substance abuse	Case-control diagnostic accuracy	Se = 80.8%, Sp = 65.5%, LR+ = 2.34, LR- = 0.29, Ac = 67.6%
Structured for Success Project screening tool					
Wilson, 2006† (Canada)	Adults; N = 65; % male NR	FASD	FASD family support programs	Cross-sectional	Internal consistency, Cronbach's α 0.91 Test–retest r = 0.748*
Brief Screen Checklist					
Forrester et al., 2015† (Canada)	<35 y; N = 23; 0% male	FASD	Corrections	Cross-sectional diagnostic accuracy	Se = 100%, Sp = 82%, PPV = 67%, NPV = 100% Cronbach's α = 0.94
MacPherson et al., 2011† (Canada)	<30 y; N = 91; 100% male	FASD	Corrections	Cross-sectional diagnostic accuracy	Se = 78%, Sp = 85%, PPV = 41%, NPV = 97%, Ac = 84% Cronbach's α 0.89
McLachlan, 2017† (Canada)	18–40 y; N = 80; 85% male	FASD	Corrections	Cross-sectional diagnostic accuracy	Se = 92.3%, Sp = 70.4%, PPV = 44.8%, NPV = 97.4%
FAS BeST					
Mushlitz, 2020† (US)	21–77 y; N = 44; 41.4% male	Risk of PAE	Drug court treatment program and social media	Cross-sectional	Split-half reliability: Court group (top-bottom), RMt (10) = 0.268; Social media group (top-bottom), RMt (28) = 5.825*; Social media group (odd-even), RMt (28) = 11.257* Self-report and adult-other versions completed with the court group were correlated; however, total scores were significantly different, RMt (10) = 2.235*
FASD Screening and Referral Tool for Youth Probation Officers					
Conry & Asante, 2010† (Canada)	Youth; N = NR; % male NR	FASD	Youth corrections	NR	Over a 2-year period, 21 screened positive and completed assessment, 81% of whom received a diagnosis under the FASD umbrella
McLachlan, 2017† (Canada)	18–40 y; N = 80; 85% male	FASD	Corrections	Cross-sectional diagnostic accuracy	Few items were endorsed High rates of incomplete screens limited further evaluation
Singal et al., 2018† (Canada)	12–18 y; N = 323; % male NR	FASD	Youth corrections	Cross-sectional diagnostic accuracy	Se = 34%, Sp = 84% 215 of the 323 charts had insufficient data to properly complete the screens (therefore classified as negative screens)

(Continues)

TABLE 1 (Continued)

Author/Year/Country	Participants (age; N; % male)	Outcome screened	Recruitment setting	Study design	Outcomes/psychometric properties
Red Flag Method					
Singal et al., 2018† (Canada)	12-18 y; $N = 323$; % male NR	FASD	Youth corrections	Cross-sectional diagnostic accuracy	70.9% agreement on cases between the Red Flag Method and the FASD Screening and Referral Tool for Youth Probation Officers

Abbreviations: Ac, accuracy; ADHD, attention-deficit/hyperactivity disorder; ARND, alcohol related neurodevelopmental disorder; CD, conduct disorder; FABS, Fetal Alcohol Behaviour Scale; FAE, fetal alcohol effects; FAEE, fatty acid ethyl esters; FAS, fetal alcohol syndrome; FASD, fetal alcohol spectrum disorder; LR-, negative likelihood ratio; LR+, positive likelihood ratio; NPV, negative predictive value; NR, not reported; ODD, oppositional defiant disorder; PAE, prenatal exposure to alcohol; pFAS, partial fetal alcohol syndrome; PPV, positive predictive value; Se, sensitivity; Sp, specificity.

*$p < 0.05$.

†Not peer reviewed.

were compared on a subset of items (12 of 15) via retrospective chart review. Only 1 item (alcohol abuse in the family/caregiver) differentiated the groups, and no further psychometric characteristics were reported.

Several tools have been designed for use in community and correctional settings to identify FASD among youth who are justice-involved. The FASD Screening and Referral Tool for Youth Probation Officers[8] (Conry & Asante, 2010) comprises a screening checklist and case management/referral planning guide and is designed to support youth probation officers in identifying FASD in this population. Conry and Asante (2010) reported that over a 2-year period, 81% of youth who screened positive using the tool and who completed an FASD assessment received a diagnosis under the FASD umbrella. The brief nature of the empirical report, however, limits interpretation of these findings. Classification accuracy of the tool remains unknown as further evaluations were hindered by insufficient access to information to complete the screening items in youth and adult corrections, signaling a need for additional psychometric evaluation of the tool (McLachlan, 2017; Singal et al., 2018). Next, the Red Flag Method is an FASD referral screening approach used by youth probation officers to aid in referring youth who are justice-involved to the Manitoba FASD Youth Justice Program. Based on a retrospective chart review, Singal et al. (2018) found reasonable screening outcome concordance (70.9%) for the Red Flag Method and the FASD Screening and Referral Tool for Youth Probation Officers. Nevertheless, limited information was reported regarding administration methods, psychometric properties, or screening accuracy based on a validated reference standard.

Lifespan

We identified only 1 tool developed for potential lifespan application in identifying PAE-related diagnoses (FAS, FAE), the Fetal Alcohol Behaviour Scale (FABS; Streissguth et al., 1998). Data was reported for several versions of the FABS across multiple samples. Results indicated high item-to-scale reliability and reasonable test–retest reliability among a subset of children and adults with FAS/FAE. Although estimates of sensitivity/specificity were not reported, a greater proportion of this group scored higher on the FABS compared with other samples (i.e., adults in corrections, children from general practice waiting rooms), and adults with high FABS scores were more likely to be living dependently.

Adults

The review yielded 2 screening tools developed to identify FASD in adults. First, the Life History Screen (LHS; Grant et al., 2013) is designed to support clinicians in identifying neurodevelopmental impairments, including FASD, that may affect outcomes for adults in substance use treatment programs. Using a subset of LHS items (those in common with the Addiction Severity Index; McLellan et al., 1992) during intake for addictions treatment, Grant et al. (2013) found reasonable sensitivity; however, specificity was low and overall classification accuracy was only slightly better than chance in terms of identifying women with possible FASD. Second,

the Structured for Success Project (SFSP) Screening Tool (Wilson, 2006) demonstrated high internal consistency and good test–retest reliability among parents with confirmed or suspected FASD/PAE, though estimates of sensitivity and specificity were not reported.

Two tools included in the review were applied in justice contexts with adults. Several versions of the Brief Screen Checklist (BSC; MacPherson et al., 2011) were developed to screen for FASD in adults who are federally incarcerated. Although collateral versions of this tool have been developed, data have most consistently been reported for the self-report version of the BSC, with small variations in total items and item wording across studies. Despite this limitation, 3 studies have been undertaken in institutional and community settings with adults who are justice-involved, and despite conservative sample sizes, all studies used methodologically rigorous prospective case-ascertainment designs (Forrester et al., 2015; MacPherson et al., 2011; McLachlan, 2017). These yet unpublished findings related to the BSC suggest strong internal consistency, with moderate-to-high sensitivity and specificity, and promising overall screening accuracy. McLachlan (2017) also reported strong preliminary sensitivity, specificity, and classification accuracy for an abbreviated 8-item version of the BSC in a single sample of adults with justice involvement. An additional study was identified in which adult adaptations of the Fetal Alcohol Syndrome Behavior Survey (FAS BeST; self-report and adult-other versions) where characterized and applied in 2 adult samples, one within a correctional context and the other with online participants with unknown justice involvement (Mushlitz, 2020). Results indicated mixed support for the structure and reliability of the tool between samples. Although positive correlations between versions were reported, total scores were significantly different, and indicators of sensitivity, specificity, and classification accuracy were not characterized.

Tools and approaches available for use based on facial features

Three studies were identified in which manual measurements of facial features indicative of PAE were evaluated (Astley & Clarren, 1995; Lee et al., 2016; Moore et al., 2001). Two studies used discriminant analysis to identify facial features that best distinguished children and adults with and without FAS/pFAS using a known-groups design, and results indicated excellent sensitivity and good specificity (Astley & Clarren, 1995; Moore et al., 2001). Another study implemented a screening protocol for children, based on manual measurement of facial features and growth, in high-risk settings (e.g., institutions and special education programs for those with intellectual and developmental disabilities, orphanages; Lee et al., 2016). Of those children who screened positive, a small percentage (14.9%) were identified as having FAS[9], and half were inconclusive, suggesting lower specificity in these settings.

An additional 3 studies were identified evaluating the Facial Photographic Analysis Software, a commercially available tool involving a computerized analysis of 2D facial images to assess facial features associated with PAE (Astley & Clarren, 1996; Astley et al., 2002; Avner et al., 2014). Results across child and adult samples demonstrated excellent sensitivity for identifying dysmorphic facial features associated with PAE. Specificity and classification accuracy were very high in 2 of the 3 studies (Astley & Clarren, 1996; Astley et al., 2002). Avner et al. (2014) also compared manual measurement and 2D analysis approaches and found mixed classification agreement, with the 2D analysis approach erring on the side of overestimating short palpebral fissure length, ultimately lowering specificity.

Emerging approaches: biomarkers associated with FASD

The search revealed 20 studies spanning 7 potentially promising biomarker approaches for identifying FASD or PAE, best considered "emerging" given the early state of the evidence and feasibility for implementation to date. Serum sample proteins were analyzed in 2 studies, with results demonstrating concentration differences for 10 proteins among children with and without PAE/FAS (Andreu-Fernández et al., 2019; Robinson et al., 1995). In 2 studies, findings indicated significant differences in several dermatoglyphic measurements (i.e., fingerprints and lines of the hand) between children with and without PAE/FASD (Andreu-Fernández et al., 2020; Planas et al., 2018). One study found differences in neural activity between children and adolescents with and without PAE using near-infrared spectroscopy, an indirect measure of neural activity utilizing near-infrared light to detect changes in oxygenated and deoxygenated hemoglobin levels (Barrett et al., 2019). Results of this study indicated group differences in the left and medial prefrontal cortex, as well as the right prefrontal cortex during a working memory task. Respiratory sinus arrhythmia (RSA), or the relation between breathing and heart rate, was evaluated as a biomarker for FASD in the context of an intervention trial (Reid et al., 2019). Results indicated lower RSA in children with FASD prior to a mindfulness exercise compared with children without FASD.

Classification accuracy has been explicitly evaluated for 3 additional emerging biomarker approaches, including 3D facial image analysis, eye movement control, and DNA methylation. Six studies were conducted to evaluate 3D facial image analysis for detecting facial dysmorphology associated with PAE (Douglas et al., 2003; Fang et al., 2008; Grobbelaar & Douglas, 2007; Meintjes et al., 2002; Suttie et al., 2013, 2017). Three of these studies provided evidence supporting the validity of 3D image analysis for identifying specific sentinel dysmorphic facial features associated with PAE in children, such as palpebral fissure length (Douglas et al., 2003; Grobbelaar & Douglas, 2007; Meintjes et al., 2002). An additional 3 studies demonstrated high sensitivity, specificity, and classification accuracy in discriminating children with and without PAE/FAS using full 3D facial scans (Fang et al., 2008; Suttie et al., 2013, 2017). Some studies have suggested that this method may hold promise in identifying additional subtle facial dysmorphology resulting from PAE, with the ultimate goal of developing more sensitive tools capable of

TABLE 2 Characteristics and outcomes of studies for screening based on sentinel facial features

Author/Year/Country	Participants (age; *N*; % male)	Outcome screened	Recruitment Setting	Study design	Outcomes/psychometric properties
Manual Measurements					
Astley & Clarren, 1995 (US)	0–10 y; *N* = 194; 55.7% male	FAS	FAS clinic	Cross-sectional diagnostic accuracy	Se = 100%, Sp = 89%, False-positive rate = 9% 71% of false positives were PFAE
Lee et al., 2016 (South Korea)	4–18 y; *N* = 307; 65.5% male	Facial features	High-risk settings	Cross-sectional	Of those who screened positive, 14.9% met criteria for facial features of FAS, 50.6% were deferred, and 34.5% were classified as No FAS
Moore et al., 2001 (US)	3 w->40 y; *N* = 131; 58% male	FAS and pFAS	FAS support centers and research centers	Case–control diagnostic accuracy	PAE vs. Non-PAE: Se = 98%, Sp = 90%, Ac = 96% FAS vs. pFAS vs. controls: Se = 86%, Sp = 94%, Ac = 88%
Facial Photographic Analysis Software					
Astley & Clarren, 1996 (US)	0–27 y; *N* = 126; 66.7% male	FAS	FAS image database and previous research participants	Matched case–control diagnostic accuracy	Se = 100%, Sp = 100%, Ac = 100%
Astley et al., 2002 (US)	0–12 y; *N* = 600; 52% male	FAS	Care settings	Cross-sectional diagnostic accuracy	Se = 100%, Sp = 99.8%, PPV = 85.7%, NPV = 100%, Ac = 99.8%
Avner et al., 2014 (Canada)	2 m–15 y; *N* = 40; 60% male	Short PFL and philtrum smoothness	FAS clinic	Cross-sectional diagnostic accuracy	Se = 100%, Sp = 64%

Abbreviations: Ac, accuracy; FAS, fetal alcohol syndrome; FASD, fetal alcohol spectrum disorder; NPV, negative predictive value; PAE, prenatal exposure to alcohol; PFAE, partial fetal alcohol effects; pFAS, partial fetal alcohol syndrome; PFL, palpebral fissure length; PPV, positive predictive value; Se, sensitivity; Sp, specificity.

detecting a larger proportion of individuals across the FASD spectrum (e.g., Suttie et al., 2013). Seven studies were identified where differences in eye movement control were evaluated as a possible biomarker of FASD, demonstrating promising sensitivity and classification accuracy in differentiating children and adolescents with FASD from neurotypically developing children (Green et al., 2009; Paolozza et al., 2014a, 2014b, 2014c, 2017; Tseng et al., 2013; Zhang et al., 2019). Further, 1 study demonstrated high accuracy for differentiating children with FASD from those with ADHD (Tseng et al., 2013). Finally, in 1 study, differences in DNA methylation patterns for children and adolescents with and without FASD were assessed, with results demonstrating good preliminary sensitivity and classification accuracy (Lussier et al., 2018).

Quality assessment

Results of the quality assessment for individual studies in the review using the QUADAS-2 indicated that most demonstrated a high risk of bias (Table 4). This can primarily be explained by patient selection due to the prevalence of case–control designs, lack of rigorous or consistent reference standards, and flow and timing. Many studies relied on either known or *a priori* diagnostic outcomes to classify the groups, few included prospective interdisciplinary FASD assessment following screening, and few characterized follow-up assessment for those who screened negative, with limited information provided with respect to how PAE/FASD was ruled out for the non-PAE/FASD groups. Results from the GRADE evaluation regarding the strength of the evidence for recommending screening tools and approaches that are currently available for use to detect FASD across the diagnostic spectrum were deemed very low, indicating that estimates of efficacy are uncertain at present (see Table 5). Some tools appear to have more support, such as the NST and BSC, owing to the presence of a greater number of studies with fewer concerns regarding risk of bias. However, overall strong recommendations cannot presently be made for specific screening tools or approaches across settings and age groups. Similarly, strong recommendations cannot currently be made regarding screening tools based on facial features of PAE, as these studies also demonstrated high risk of bias based on the QUADAS-2, owing largely to the use of case–control designs and a lack of preestablished thresholds.

DISCUSSION

We aimed to review and synthesize the evidence of available and emerging screening tools and approaches for identifying FASD in school-aged children, adolescents, and adults. Consistent with previous reviews, our results highlighted an array of tools currently available for use ($n = 11$) and designed to identify individuals across the FASD spectrum using various administration methods, including self-report questionnaires, checklists, and interview strategies (Goh et al., 2008). Most of these tools were focused on FASD screening in children and/or adolescents ($n = 6$) across various contexts such as schools (e.g., FAS Screen; Burd et al., 1999), following referral to an FASD diagnostic clinic (e.g., NST; Nash et al., 2006), and in youth justice settings (e.g., FASD Screening and Referral Tool for Youth Probation Officers; Conry & Asante, 2010). Fewer tools were available for use with adults ($n = 4$) and those currently available are all designed for use in focused settings, including adult corrections (e.g., MacPherson et al., 2011), family support programs (e.g., Wilson, 2006), and substance use treatment programs (Grant et al., 2013). There was also 1 tool intended for both children and adults in multiple contexts (e.g., diagnostic and correctional contexts; Streissguth et al., 1998). Although results highlighted several potentially useful tools, the overall evidence base regarding psychometric properties is limited. Most studies in the review lacked evaluation of tool reliability, and many tools were evaluated at a single site, in a single sample, or solely evaluated by the tool developers, limiting the generalizability of study findings. Additionally, many studies had methodological weaknesses, including conservative sample sizes, evaluation of only a subset of proposed screening items, and limited access to information by respondents. Importantly, we found significant risk of bias across studies which limits the interpretability of findings. Therefore, at this time, none of the tools currently available can be deemed to have strong evidence for detecting individuals across the FASD spectrum, and there is need for additional rigorous research in this area.

Across studies, there is a marked lack of evidence supporting classification accuracy of tools to identify individuals with FASD. Regarding sensitivity, some tools demonstrated seemingly good ability to detect individuals with FASD. However, several studies included well-defined known groups, relying on a previous diagnosis (or lack thereof). Among these case–control studies, as well as many other cross-sectional studies, most lacked comprehensive assessment of PAE/FASD as a reference standard, particularly for those who screened negative. Without evaluation of those who screen negative, there are no means of verifying that individuals with FASD were not missed by the screening tool (i.e., false negatives), potentially inflating sensitivity estimates. Further, false negatives may lead to a delayed or missed diagnosis, possibly resulting in individuals and caregivers not receiving critically needed supports and services (Maxim et al., 2014).

Similarly, findings suggest a lack of evidence supporting the specificity of the tools to accurately identify FASD. Although some approaches demonstrated good accuracy in differentiating individuals with FASD from neurotypically functioning individuals (e.g., the NST, eye movement control, DNA methylation), lack of real-world application may potentially overinflate estimates of specificity and classification accuracy as compared to application in more heterogenous samples, including individuals with other neurodevelopmental or comorbid disorders. Few studies applied screening tools in real-world contexts using prospective designs, and those that did were limited by application in research contexts (e.g., participants had to consent to participate, leading to potential selection bias). Further,

TABLE 3 Characteristics and outcomes of studies based on emerging biomarker approaches

Author/Year/Country	Participants (age; *N*; % male)	Outcome Screened	Recruitment Setting	Study Design	Outcomes/Psychometric Properties
Serum Protein Analysis					
Andreu-Fernández et al., 2019 (Spain)	8–12 y; *N* = 150; 56% male	FASD and PAE	Previous research participants and adoptees with PAE	Case-control	Participants with IGF-II concentration below the 5th %ile: FASD = 14%, PAE = 6.5%, controls = 0% Participants with IGF-II concentration below the 50th %ile: FASD = 43%, PAE = 19.4%, controls = 3.2% Correlations found between IGF-II and some neuropsychological measures
Robinson et al., 1995 (US)	FAS Female: *M* = 10.1 ± 2.0 y FAS Male: *M* = 9.5 ± 1.7 y Control Female: *M* = 10.7 ± 1.5 Control Male: *M* = 10.0 ± 0.6 y; *N* = 20; 35% male	FAS	Hospital setting	Case-control	21 proteins were significantly different between those with and without FAS, of which 8 may be useful as biomarkers due to significant differences in protein concentration 4 groups of protein spots were able to distinguish FAS from controls with 100% accuracy
Dermatoglyphics					
Andreu-Fernández et al., 2020 (Spain)	FASD: *M* = 10.7 ± 3.7 y No FASD: *M* = 12.0 ± 3.4 y *N* = 185; 62.7% male	FASD	Previous research participants	Case-control	Significant correlations found between FASD diagnosis and TABRC, FA_{ABCR}, TATD, and FA_{ATD}
Planas et al., 2018 (Spain)	PAE: *M* = 9.48 y, Controls: *M* = 9.76 y *N* = 50; 52% male	PAE	Hospital setting	Case-control	Higher FA_{ABRC} levels in those with the highest FAEE compared with low FAEE and nonexposed
Functional Near-Infrared Spectroscopy					
Barret et al., 2019 (US)	6–18 y; *N* = 71; 45.8% male	PAE	FASD clinics and community settings	Case-control	Main effect of group found in levels of oxygenated and deoxygenated hemoglobin in the left and medial prefrontal cortex during a working memory task Main effects of group found in the right prefrontal cortex for oxygenated hemoglobin during the inhibitory condition of a working memory task
Respiratory Sinus Arrhythmia					
Reid et al., 2019 (Australia)	6–10 y; *N* = 34; 47.1% male	FASD	FASD clinic and schools	Case-control	Trend toward group effects with lower RSA in the FASD group prior to mindfulness intervention
3D Facial Photographic Analysis					
Douglas et al., 2003 (South Africa)	6–7 y; *N* = 46; % male NR	Facial measurements	Previously collected data	Cross-sectional diagnostic accuracy	Mean differences between automatic and manual measurements (mm): PFL = 0.66, IPD = 0.27, ICD = 1.19, OCD = 1.17
Fang et al., 2008 (South Africa and Finland)	2.8–21.0 y; *N* = 149; 45.6% male	FAS facial features	Previously collected data	Case–control diagnostic accuracy	Caucasian: Se = 88.2%, Sp = 100%, Ac = 92.6% Cape colored: Se = 91.7%, Sp = 90%, Ac = 90.9% Combined: Se = 82.75% Sp = 76.2% Ac = 80.0%

(Continues)

TABLE 3 (Continued)

Author/Year/Country	Participants (age; *N*; % male)	Outcome Screened	Recruitment Setting	Study Design	Outcomes/Psychometric Properties
Grobbelaar & Douglas, 2007 (South Africa)	6–7 y; *N* = 48; % male NR	Facial measurements	Previously collected data	Cross-sectional	Mean difference between manual and algorithmic marking (mm): PFL = −0.40, IPD = −0.18, ICD = 0.14, OCD = 0.05, ULW = 0.19, ULH = −0.02 95% of differences fell within acceptable limits
Meintjes et al., 2002 (South Africa)	Gr. 1; *N* = 44; % male NR	FAS facial features	Previously collected data from a community setting	Cross-sectional	Mean differences between automatic and manual measurements (mm): PFL = 0.1, IPD = 2.9*, ICD = 2.3* Test–retest mean differences (mm): PFL = 0.0, IPD = 0.0, ICD = 0.5*
Suttie et al., 2013 (South Africa)	FAS: *M* = 10.6 ± 2.4 y pFAS: *M* = 10.0 ± 1.5 y HE: *M* = 10.4 ± 2.7 y Controls: *M* = 10.1 ± 2.6 y; *N* = 192; 50% male	Facial dysmorphology	Antenatal clinics and schools	Case–control diagnostic accuracy	FAS vs. nonexposed: Ac = 97 – 100% for the face, 92% for the profile FAS/pFAS vs. nonexposed: Ac = 90% for the face, 92% for the profile
Suttie et al., 2017 (US, South Africa, and Europe)	3–18 y; *N* = 415; 53.7% male	Facial dysmorphology	Previously collected data and community settings	Case–control diagnostic accuracy	Caucasian: Ac = 96% Cape colored: Ac = 98%
Eye Movement Control					
Green et al., 2009 (Canada)	8–15 y; *N* = 181; 46.4% male	FASD	Community settings	Case-control	Group differences between FASD and controls: PS SRT (*d* = 0.64)*, PS coefficient of variation (*d* = 0.59)*, PS express saccades (*d* = 0.07)*, PS direction errors (*d* = 0.60)*, AS SRT (*d* = 0.69)*, AS coefficient of variation (*d* = 0.99)*, AS direction errors (*d* = 0.92)*
Paolozza et al., 2014a (Canada)	5–17 y; *N* = 202; 49.7% male	FASD and PAE	FASD clinics and community settings	Case-control	FASD performed worse than controls on all psychometric and eye movement measures, including: PS endpoint (*d* = −0.47)*, antisaccade endpoint (*d* = −.63)*, and sequence errors (*d* = −0.86,)* Correlations found between some eye movement tasks and psychometric measures
Paolozza et al., 2014b (Canada)	5–17 y; *N* = 232; 39.7% male	FASD and PAE	FASD clinics and community settings	Case-control	FASD performed worse than controls on all psychometric and eye movement measures: direction errors (*d* = −0.5)*, timing errors (*d* = −0.7)*; auditory attention (*d* = 0.6)*, response set (*d* = 0.6)*, inhibition: naming (*d* = 0.8)*, inhibition: inhibition (*d* = 1.2)*, inhibition: switching (*d* = 1.4)* FASD had negative correlations between direction errors and: inhibition (*r* = −0.31)*, and switching (*r* = −0.36)*

(Continues)

TABLE 3 (Continued)

Author/Year/Country	Participants (age; *N*; % male)	Outcome Screened	Recruitment Setting	Study Design	Outcomes/Psychometric Properties
Paolozza et al., 2014c (Canada)	7–18 y; *N* = 78; 47.4% male	FASD	FASD clinics and community settings	Case-control	FASD performed worse than controls on: AS SRT ($t = 2.4$)*, AS anticipatory saccades ($t = 2.4$)*, AS direction errors ($t = 2.8$), MGS sequence errors ($t = 2.1$)* and MGS timing errors ($t = 0.9$)*
Paolozza et al., 2017 (Canada)	5–18 y; *N* = 136; 44.1% male	PAE	FASD clinics and community settings	Case-control	Several correlations between DTI and eye movement outcomes in the control group but not the PAE group
Tseng et al., 2013 (Canada)	Control children: $M = 10.7 \pm 1.8$ ADHD: $M = 11.2 \pm 1.8$ FASD: $M = 12.3 \pm 2.1$; *N* = 52; 57.4% male	FAS, pFAS and ARND	NR	Case–control diagnostic accuracy	FASD vs. ADHD vs. control children Ac = 77.3% FASD vs. control children Ac = 79.2% ADHD vs. FASD Ac = 90.4% FASD Se = 73%; Sp = 91%
Zhang et al., 2019 (Canada)	5–18 y; *N* = 207; 46.9% male	FASD	FASD clinics and community settings	Case–control diagnostic accuracy	PS and natural viewing: Se = 77.27%, Sp = 79.17%, Ac = 78.26% PS, AS, natural viewing and short battery of neuropsychological tests: Se = 81.8%, Sp = 87.5%, Ac = 84.78%
DNA Methylation					
Lussier et al., 2018 (Canada)	3.5–18 y; *N* = 227; 54.2% male	FASD	Previously collected data and FASD clinics	Matched case–control diagnostic accuracy	Se = 91.7%, Sp = 75%, PPV = 90%, NPV = 78.6%, Ac = 83.3%

Abbreviations: Ac, accuracy; ARND, alcohol-related neurodevelopmental disorder; AS, antisaccade; DTI, diffusion tensor imaging; FA_{ABCR}, fluctuating asymmetry from the a-b ridge count; FA_{ATD}, fluctuating asymmetry from the ATD angle; FAE, fetal alcohol effects; FAEE, fatty acid ethyl esters; FAS, fetal alcohol syndrome; FASD, fetal alcohol spectrum disorder; HE, heavily exposed; ICD, inner canthal distance; IGF, insulin growth factor; IPD, interpupillary distance; MGS, memory guided saccade; NPV, negative predictive value; NR, not reported; OCD, outer canthal distance; PAE, prenatal exposure to alcohol; pFAS, partial fetal alcohol syndrome; PFL, palpebral fissure length; PPV, positive predictive value; PS, prosaccade; RSA, respiratory sinus arrhythmia; Se, sensitivity; Sp, specificity; SRT, saccadic reaction time; TABRC, total a-b ridge count; TATD, total ATD angle; ULH, upper lip height; ULW, upper lip width.

*$p < 0.05$.

TABLE 4 Quality assessment of studies using the Quadas-2 framework

Study	Risk of bias			
	Patient selection	Index test	Reference standard	Flow and timing
Screening across the FASD spectrum				
Neurobehavioural Screening Tool				
Breiner et al. (2013)	H	H	L	U
Haynes et al. (2014)	L	H	NA	L
LaFrance et al. (2014)	U	H	U	H
Nash et al. (2006)	H	H	L	L
Nash et al. (2011)	H	H	L	U
Patel et al. (2020)	L	L	H	H
FASD Screening Program				
Clarren et al. (2001)	H	L	H	H
FAS Screen				
Burd et al. (1999)	H	L	H	H
Poitra et al. (2003)	L	L	H	H
Children's Aid Society of Toronto Screening Tool				
Steinhart (2016)	H	H	L	U
Fetal Alcohol Behaviour Scale				
Streissguth et al. (1998)	H	H	L	H
Life History Screen				
Grant et al. (2013)	H	H	H	H
Structured for Success Project Screening Tool				
Wilson (2006)	H	H	NA	L
Brief Screen Checklist				
Forrester et al. (2015)	L	H	L	L
MacPherson et al. (2011)	L	H	L	H
McLachlan (2017)	L	H	L	H
FAS BeST				
Mushlitz (2020)	H	H	H	H
FASD Screening and Referral Tool for Youth Probation Officers				
Conry & Asante (2010)	U	U	U	U
Singal et al. (2018)	L	L	H	H
Screening based on sentinel facial features				
Manual measurements				
Astley & Clarren (1995)	H	H	L	L
Lee et al. (2016)	L	L	H	H
Moore et al. (2001)	H	H	L	L
Facial Photographic Analysis Software				
Astley & Clarren (1996)	H	H	L	L
Astley et al. (2002)	L	L	H	H
Avner et al. (2014)	H	H	U	L
Emerging biomarker approaches				
Serum Protein Analysis				
Andreu-Fernández et al. (2019)	H	H	L	L
Robinson et al. (1995)	H	H	L	L

(Continues)

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TABLE 4 (Continued)

Study	Risk of bias			
	Patient selection	Index test	Reference standard	Flow and timing
Dermatoglyphics				
Andreu-Fernández et al. (2020)	H	H	L	H
Planas et al. (2018)	H	L	L	H
Functional Near-Infrared Spectroscopy				
Barrett et al. (2019)	H	H	L	H
Respiratory Sinus Arrhythmia				
Reid et al. (2019)	H	H	L	H
3D Facial Photographic Analysis				
Douglas et al. (2003)	U	H	H	L
Fang et al. (2008)	H	L	L	L
Grobbelaar & Douglas (2007)	U	L	L	L
Meintjes et al. (2002)	U	L	L	L
Suttie et al. (2013)	H	H	L	H
Suttie et al. (2017)	H	L	L	L
Eye Movement Control				
Green et al. (2009)	H	H	L	H
Paolozza et al. (2014a)	H	L	L	H
Paolozza et al. (2014b)	H	L	L	H
Paolozza et al. (2014c)	H	L	L	H
Paolozza et al. (2017)	H	H	L	H
Tseng et al. (2013)	H	H	L	U
Zhang et al. (2019)	H	H	L	U
DNA Methylation				
Lussier et al. (2018)	U	H	L	H

Note: L = low risk, H = high risk, U = unclear.

studies using cross-sectional designs rarely reported sample characteristics with respect to differential diagnosis, thereby greatly limiting the interpretability of specificity estimates. Poor or unclear specificity at screening may ultimately return higher than expected rates of false positive results, which, in the case of FASD, may lead to adverse consequences for individuals and families, including psychological distress stemming from associated stigma, delayed identification of the true nature of identified difficulties, or provision of inappropriate supports. Potentially harmful consequences for biological parents, and women in particular, whose children are identified as having FASD also require consideration (Maxim et al., 2014; Miranda et al., 2013; Zizzo et al., 2013). Additionally, the follow-up assessment and care needs required following a positive FASD screen can be expensive and time-consuming, potentially contributing to misuse of limited resources (Clarren et al., 2011; Maxim et al., 2014; Popova et al., 2013, 2020).

Notably limited across many tools were accessible and detailed descriptions of tool/item construction or refinement procedures. Several tools were reported to have been developed based on FASD diagnostic criteria, expert experience, or characteristics commonly observed in individuals with FASD (but not necessarily specific to PAE/FASD). Although many tools were described as intending to identify FASD, their item content ranged considerably (see Table S2). Some tools explicitly considered the presence of PAE or related risk indicators (e.g., history of difficulties related to maternal alcohol use), but many did not, and rather focused more broadly on behavioral, developmental, or neurocognitive deficits frequently characterized in both individuals with FASD, but also other neurodevelopmental and mental health disorders. For instance, many of the checklist/questionnaire approaches included items commonly associated with ADHD (e.g., difficulty concentrating, misunderstanding expectations) and oppositional defiant/conduct disorder (e.g., stealing, lack of guilt). Similarly, some tools included personal life events (e.g., not being raised by biological parents, employment history) and parental characteristics (e.g., few social supports, mental health difficulties) which, while common in this population, are not causally related, and may be neither sensitive, nor specific to FASD. Ultimately, these considerations highlight the need for more careful examination of intended screening targets and goals. Tools that do not consider PAE risk at

TABLE 5 Quality assessment of currently available screening tools/approaches across settings and ages using the GRADE system

No. of Studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Quality
Screening across the FASD spectrum							
19	Low	Serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	No publication bias detected	Very low
Screening based on sentinel facial features							
6	Low	Serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	No publication bias detected	Very low

screening may serve to identify a range of important functional and need indicators, but may be less likely to produce screening outcomes specific to FASD, particularly in the absence of a unique profile of strengths and needs (Lange et al., 2019; Mattson et al., 2019; McLachlan et al., 2017). Through clear operationalization of intended screening construct(s) and targets (e.g., FASD, PAE, adverse experiences, functional/clinical needs), as well as the characterization of methods used in item/tool development, evaluation, and refinement, the field will be better supported not only in improving the rigor of research efforts to validate FASD screening tools, but also in achieving more tailored implementation of measures appropriate for the context.

Lack of consistency in the approaches used to define and diagnose FASD over time may also complicate efforts to validate screening tools and identification processes. Since FASD first appeared in the literature, various diagnostic labels and criteria have been proposed, implemented, and updated (e.g., Benz et al., 2009; Cook et al., 2016; World Health Organization, 2005). Research has shown that evaluating the same individual using different diagnostic systems can result in conflicting diagnostic outcomes, both in terms of the specific label applied (e.g., FAS vs. ARND), as well as whether or not a PAE-related diagnosis should be made (Astley Hemingway et al., 2019; Coles et al., 2016). Regarding the present review, many of the included studies relied on a previous diagnosis of FASD as their reference standard, with no information regarding which guidelines were followed to make the diagnosis. Thus, estimates of the psychometric properties of the screening tools may be skewed due to differences in diagnostic categorization as a result of varying diagnostic systems. Additionally, items for some of the screening tools were selected based on diagnostic criteria, which may limit the effectiveness of the tool to screen for individuals with FASD in regions where other diagnostic guidelines are followed. Screening tools and approaches will need to be validated across the diagnostic systems for which their use is intended, and re-evaluated as more is understood about the impacts of alcohol on fetal development and as FASD diagnostic guidelines are updated.

We identified a number of studies ($n = 12$) evaluating the screening utility of identifying the sentinel facial features specifically associated with PAE, including manual measurements, 2D photographic analysis, and the emerging application of 3D analytic approaches. Computerized analysis of photographic images in particular may allow for efficient and objective screening for facial dysmorphology specifically associated with PAE. Although 2D measurements of the sentinel facial features demonstrate high sensitivity, specificity, and classification accuracy, such approaches only detect the small proportion of individuals with FASD with facial features. Emerging evidence suggests that computerized analysis of 3D facial images may hold promise in identifying more subtle and nuanced dysmorphic alterations indicative of PAE, thereby widening screening application. Notably, there was limited research evaluating these approaches in adults, highlighting the need for additional studies in this area. This is of particular importance given that while some facial features may persist into adulthood for some individuals, they may also diminish

with age in others and thus be more difficult to detect (Moore & Riley, 2015). Additionally, facial differences across ethnic groups may influence facial measurements and classification accuracy, suggesting the potential need for representative normative samples (e.g., Moore et al., 2007). While screening based on facial features may be very effective at detecting sentinel facial dysmorphology, these approaches may be most useful when applied in combination with other screening tools, or to aid in the diagnostic process, along with the identification of other key deficits and needs commonly experienced by individuals with FASD.

The search identified several additional emerging approaches for detecting FASD or PAE based on potential biomarkers. Some advocates suggest that biomarkers may facilitate earlier identification and provide more objective evaluation compared with approaches that rely on observation and informant report, yet others have highlighted that they may be overly resource intensive, requiring a great deal of specialized equipment, time, and expertise to administer (Lakhan et al., 2010; Mayeux, 2004). Further, as with other screening tools, biomarkers are also susceptible to bias, and both false-positive and false-negative outcomes (Mayeux, 2004; Miranda et al., 2013). While biomarker approaches may prove more expensive per administration compared with questionnaire/checklist approaches, they may nevertheless yield significant cost savings over time compared with a no-screening approach or missed identification (Berrigan et al., 2019; Zhang et al., 2019). Additionally, some of the identification approaches, such as 3D facial image analysis, dermatoglyphics, and analysis of eye movement control, may eventually be administered by a range of professionals with proper training. Most of the approaches identified in this review are best considered to be in the initial stages of either development or validation. Screening based on 3D facial analysis and eye movement control appears to have the potential for more proximal application, with preliminary evidence suggesting good sensitivity, specificity, and classification accuracy. However, there was some variability in whether studies targeted PAE or FASD as the intended screening outcome. Many individuals with PAE do not go on to develop FASD, nor the full spectrum of adverse outcomes associated with the disorder (Kuehn et al., 2012). Thus, approaches that identify PAE versus FASD may have different clinical applications. For instance, while PAE-based screening measures may not necessarily be specific to FASD, they may be sensitive in identifying those at risk, which may prove useful given the continued high rates of missed detection of individuals with FASD and the clinical challenges inherent in confirming PAE during diagnosis (Chasnoff et al., 2015; Cook et al., 2016; Freeman et al., 2019). However, the studies reviewed presented with serious risk of bias, and there is insufficient information to determine the accuracy of screening tools in heterogenous populations, signifying a need for further research.

Ultimately, results of this review indicate that additional research is needed to characterize the psychometric properties and accuracy of many screening tools that are currently available, as well as emerging approaches, to guide practitioners in making evidence-based decisions. Specifically, future studies would benefit from employing larger, more representative, and clearly phenotyped samples, including individuals with other neurodevelopmental and/or comorbid disorders. Studies should be conducted across multiple sites and in collaboration with research teams beyond the instrument developers. Evaluation of additional implementation indicators is also needed, such as information regarding the costs and training requirements associated with screening, ease of use among raters, and stakeholder acceptability, using collaborative approaches that include individuals with FASD and their care providers (Goh et al., 2008). Including individuals with lived experience in the research process will prove particularly important in ensuring ethical, sensitive, and supportive screening experiences across populations, also taking into consideration the gender, cultural, and trauma-informed needs of many individuals with FASD (Esmail et al., 2015; Slattery et al., 2020). Understanding additional outcomes beyond screening accuracy is also important, such as the impact of screening on clinical or organizational practices and referral patterns, and the health and well-being of those undergoing screening and their care providers (Adriaensen et al., 2013; Dobrow et al., 2018).

Limitations

The current review was not without limitations. First, these results do not represent an exhaustive list of FASD screening tools and approaches currently being used in the field. For instance, inclusion and exclusion criteria applied during the search may have limited consideration of studies that did not explicitly state a potential screening application. In addition, many tools in use may not have met the criteria requiring novel empirical data, but may nevertheless hold promise for FASD screening (e.g., Burd et al., 2004). Relatedly, while we believe this was a comprehensive search that included various terms used to refer to FASD, it is possible that studies could have been missed as some terms were not included in the search strategy (e.g., alcohol-related birth defects, fetal alcohol effects, neurobehavioral disorder associated with prenatal alcohol exposure).

We found that some tools were not evaluated with representative samples, including culturally and/or ethnically diverse samples. This may have been impacted by restricting inclusion criteria to English language studies and signals a potential gap with respect to studies published in other languages. As such, studies which may have extended the generalizability of the tools to other ethnic or cultural groups may have been missed. Further, our search did not yield any screening tools designed to detect neurodevelopmental disabilities or developmental needs more broadly, with data reported specifically for individuals with FASD, highlighting the need for additional research to assess whether these instruments may hold potential for earlier identification of this vulnerable population.

Last, we did not consider tools or approaches focused on identifying women at risk of having an alcohol-exposed pregnancy. Given

their unique needs and considerations, this remains a critical area of need in terms of supporting healthy outcomes and ultimately, prevention efforts (e.g., Cook et al., 2017; Graves et al., 2020).

CONCLUSIONS

Identification of individuals with FASD across the lifespan, coupled with the provision of appropriate intervention and supports, plays a critical role in promoting healthy outcomes (Pei et al., 2019; Streissguth et al., 2004). Several tools and approaches for identifying FASD in children, adolescents, and adults, designed for use in specific settings are currently available for use by a range of professionals . Some tools show early potential promise for use in identifying individuals who may have PAE or FASD. However, limited overall evidence regarding the validity, reliability, and utility of screening tools and approaches, combined with methodological limitations across studies to date, render it difficult to consider any individual tool or approach as being psychometrically established. More research is needed to adequately assess not only the psychometric properties of these tools, but also other critical implementation indicators and outcomes, particularly in more representative and heterogenous populations using rigorous designs and methodologies, and participatory approaches.

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CONFLICTS OF INTEREST

The authors have no financial or other conflicts to declare.

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ENDNOTES

[1] Although FASD is the diagnostic term currently used according to the Canadian diagnostic guideline (Cook et al., 2016), other terms have been used to describe individuals impacted by PAE, either historically or as part of other diagnostic systems. These terms include fetal alcohol syndrome (FAS), partial fetal alcohol syndrome (pFAS), alcohol-related neurodevelopmental disorder (ARND), fetal alcohol effects (FAE), alcohol-related birth defects (ARBD), foetal alcohol syndrome, and foetal alcohol spectrum disorder (see Coles et al., 2016 for a review).

[2] At the time of publication of the review by Goh et al., (2008), the NST was referred to as a modified version of the Child Behavior Checklist.

[3] The initial preregistered protocol included consideration of animal models and screening in neonates, infants, and preschool-aged children. Following an initial search and study selection, we opted to narrow the scope of the review and focus on postnatal clinical models in older children, adolescents, and adults, given the importance of identifying screening tools and approaches during later developmental years when individuals with FASD frequently go unidentified in everyday settings and contexts.

[4] The peer-reviewed criterion was required for studies identified through databases searches. Studies identified through the grey literature search were not required to have undergone academic peer review.

[5] Due to system constraints, the following search terms were used for Open Government Canada: "('Fetal alcohol spectrum disorder' OR FASD) AND screen."

[6] Other countries included South Korea, Spain, Australia, and studies comprising data from multiple countries/continents.

[7] FAS is a diagnostic term for individuals with PAE who demonstrate sentinel facial features of PAE along with central nervous system deficits (Chudley et al., 2005).

[8] The FASD Screening and Referral Tool for Youth Probation Officers has also been referred to as the Asante FASD Screening Tool (McLachlan, 2017), the Asante Centre Probation Officer Tool (Goh et al., 2008) and the Asante Centre for Fetal Alcohol Syndrome Probation Officer Screening and Referral Tool (Singal et al., 2018).

[9] Based solely on growth and facial indicators, without evaluation of neurodevelopmental/cognitive functioning.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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