Two Recent Approaches to FASD Diagnosis: An Issue Paper

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Overview

Over the last 50 years, a significant amount of research and clinical expertise has been devoted to characterizing the effects of prenatal alcohol exposure on the developing fetus. Simultaneously, a variety of systems and approaches have also emerged to provide diagnostic guidance for the related diagnoses. Fetal Alcohol Spectrum Disorder (FASD) is now widely used to describe the resultant sequelae associated with prenatal alcohol exposure.

Despite ongoing pressure to develop a consensus around diagnostic approaches for FASD, different multidisciplinary diagnostic systems continue to emerge.[1-5] Recently, significant differences in diagnostic sensitivity and specificity were revealed after comparing the 2005 Canadian diagnostic guidelines[1] and the Diagnostic and Statistical Manual of Mental Disorders, 5th edition diagnosis Neurobehavioural disorder associated with prenatal alcohol exposure (ND-PAE).[6] Although considerable overlap was identified between both sets of criteria, the neurobehavioural domains assessed for a ND-PAE diagnosis limited the identification of patients with FASD.[7]

Similarly, two recent publications that describe revised diagnostic approaches for outcomes resulting from prenatal alcohol exposure are now available: the revised Canadian guidelines[8] and an updated IOM approach.[9] The Canadian publication documents a national process, which included representation from multidisciplinary experts in the field,[8] while the other was developed by a group of leading specialists and researchers from the United States.[9] Though the two publications share some commonalities, several significant differences are noted and described further in this issue paper. Both publications arose in response to emergent data in the field that supported improvements and changes to the diagnostic process. Although, both approaches continue to underscore the need for a multidisciplinary team approach, comprised of individuals with specific expertise and experience in the field of FASD, ***three*** specific differences were apparent: 1) the craniofacial criteria; 2) the clinical cut-off for neuropsychological impairment; and 3) the diagnostic nomenclature.

Methodology

The methodological approaches of the two diagnostic systems differed in their approach and external consultation processes. The updated Institute of Medicine (IOM) approach included a thorough literature review and reflected the collective expertise of the authors. In contrast, the Canadian guidelines used the AGREE II framework, in which a 14 member steering committee led the development of the guideline and included input from 35 diagnostic clinics across Canada. Extensive consultations from national and international experts was obtained via 6 in-person focus groups + a 2-day international workshop. A systematic review of the literature was conducted and appraised using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE)[10] system for rating quality of evidence and grading the strength of each recommendations.

Prenatal Alcohol Exposure

Documented prenatal alcohol exposure (PAE) is challenging in the clinical setting, as studies have shown that women tend to under-report (or not report) their alcohol consumption during pregnancy.[11-13] Many factors influence obtaining reliable antenatal records (i.e., moving between healthcare providers; national or international adoption; medical records lost or destroyed over time), which can confound and delay the diagnostic process. The effects of PAE are complex, multifaceted and vary by individual. They have

been described as growth deficits, physical defects, craniofacial dysmorphology and central nervous system (CNS) dysfunction, the latter of which is considered the most debilitating and persistent, necessitating life-long supports and resources. Although FASD results from PAE, the contribution of other determinants of health (environment, socioeconomic status, genetics, adverse life experiences, mental and physical health) have been extensively reviewed for their contribution to the severity and prevalence of FASD. [14]

In the updated IOM guidelines, any <u>one</u> of the following constitutes documented PAE: reliable clinical observation; self-report; reports by reliable source; medical records; alcohol treatment; social, legal or medical problems; positive alcohol-exposure biomarker(s); increased risk assessed by a validated screening tool; drinking levels reported by the mother 3 months before her pregnancy/positive pregnancy test.[9] In the Canadian approach, the criteria are: Reliable clinical observation; self-report; reports by reliable source; medical records; alcohol treatment; social, legal or medical problems.[8] An important difference between the two guidelines is the lower cut-off values for weekly and binge drinking in the updated IOM guideline compared to the Canadian guidelines (Table 1).

Table 1.

Updated IOM Definition	Canadian Definition
≥6 drinks/week for ≥ 2 weeks during pregnancy; ≥3 drinks per occasion on ≥ 2 occasions during pregnancy	≥7 drinks/week during pregnancy; ≥4 drinks per occasion on ≥ 2 occasions during pregnancy

Growth

The Canadian diagnostic guidelines have removed growth as a diagnostic criterion; the updated IOM guidelines have not. The recommendation to remove growth as a diagnostic criterion was based on historical clinical reports, basic science and clinical research.[15, 16] Growth, *per se*, is neither sensitive nor sufficiently specific to indicate a FASD diagnosis. In the latter, growth at ≤ 10th percentile is indicative of growth restriction.

Facial Dysmorphology

A significant difference between the updated IOM guidelines and Canadian guidelines are the criteria for positive facial evaluation (Table 2). The concomitant presentation of the three sentinel facial features of FASD (short palpebral fissures, poorly formed philtrum and flat vermilion border of the upper lip) have been reportedly specific to PAE. [16] Of the triad of clinical facial features associated with prenatal alcohol exposure, the updated IOM guideline only require 2 of 3 for positive facial evaluation while the Canadian guidelines require all 3.

Table 2.

Updated IOM	Canada
-Short Palpebral Fissure: ≤ 10th percentile -Smooth Philtrum: 4 or 5 score on guide -Thin Vermilion Border of upper lip: 4 or 5 score on guide	-Short Palpebral Fissure: ≥ 2 SDs below the mean (< 3rd percentile) -Smooth Philtrum: 4 or 5 score on guide -Thin Vermilion Border of upper lip: 4 or 5 score on guide

Neurodevelopmental Assessment and Neuropsychological Evaluation

Both diagnostic guidelines recommend standardized tests for conducting the neurodevelopmental assessment; however, the clinical cut-off for diagnosis is ≥ 1.5 SD below the mean in the updated IOM guidelines; and ≥ 2 SD below the mean in the Canadian guidelines. All diagnoses must include neurobehavioural impairment in 1-2 domains in the updated IOM guidelines; there must be evidence of neurodevelopmental impairment in 3 or more brain domains (or for infants and young children, microcephaly) in the Canadian guidelines based on the following brain domains (Table 3):

Table 3.

Updated IOM	**Canada**
Brain Domains: 1. Global Intellectual 2. Cognition 3. Behaviour and Self-Regulation 4. Adaptive Skills	**Brain Domains:** 1. Motor Skills 2. Neuroanatomy/Neurophysiology 3. Cognition 4. Language 5. Academic Achievement 6. Memory 7. Attention 8. Executive Function 9. Affect regulation 10. Adaptive Behaviour, Social Skills or Social Communication

Nomenclature

The updated IOM diagnostic terminology maintains the original 4 diagnostic categories (FAS; pFAS; ARND; ARBD) that were introduced by the IOM, with the disclaimer that ARND cannot be diagnosed in children < 3 years. They report that the ARBD diagnosis is necessary, although uncommon and that changing the nomenclature introduces confusion. An importance clarifier is the suffix added to each diagnostic category: "with cognitive impairment" or "with behavioural impairment". In contrast, the Canadian guidelines have recommended using FASD as a diagnostic term to simplify the understanding of a diagnosis. FASD is further categorized as "with sentinel facial features" or "without sentinel facial features" based on the presence of absence of facial features, respectively. Additionally, the Canadian approach have recommended the use of an "at-risk" designation that is not a diagnosis, but identifies clients who need to be reassessed at a later date.

Patient Population

The targeted diagnostic population for the updated IOM guidelines was 0-21 years; while the Canadian guidelines provided recommendations for diagnosis across the lifespan.

Conclusion

Although both guidelines recommend a multidisciplinary approach to diagnosis, the goal of the updated IOM guidelines were to improve sensitivity and increase inclusion of children in the complete continuum of FASD (but could lead to overdiagnosis). The Canadian guidelines were intended to provide specific guidance for diagnosing infants/young children and adults; to improve clarity of the nomenclature and to refine the criteria for the neurodevelopmental assessment. Moving forward, universal agreement on a diagnostic system for FASD would provide the opportunity to more accurately determine the true prevalence and incidence of FASD on a national and international scale, as well as the comparison of data sets from different diagnostic centres.

References

1. Chudley AE, Conry J, Cook JL, Loock C, Rosales T, LeBlanc N, et al. Fetal alcohol spectrum disorder: Canadian guidelines for diagnosis. CMAJ. 2005;172:S1-S21. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15738468.

2. 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. Available from: PM:15629980.

3. Landgraf MN, Nothacker M, Heinen F. Diagnosis of fetal alcohol syndrome (FAS): German guideline version 2013. Eur J Paediatr Neurol. 2013;17:437-46. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23618613.

4. Stratton K, Howe C, Battaglia. Fetal Alcohol Syndrome: Diagnosis, Epidemiology, Prevention, and Treatment. Institute of Medicine (IOM). National Academy Press; 1996.

5. Watkins RE, Elliott EJ, Wilkins A, Mutch RC, Fitzpatrick JP, Payne JM, et al. Recommendations from a consensus development workshop on the diagnosis of fetal alcohol spectrum disorders in Australia. BMC Pediatr. 2013;13:156. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24083778.

6. APA. Diagnostic and statistical manual of mental disorders, Fifth edition. Arlington: 2013.

7. Sanders JL, Breen RE, Netelenbos N. Comparing diagnostic classification of neurobehavioral disorder associated with prenatal alcohol exposure with the Canadian fetal alcohol spectrum disorder guidelines: a cohort study. CMAJ Open. 2017;5:E178-E83. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28401132.

8. Cook JL, Green CR, Lilley CM, Anderson SM, Baldwin ME, Chudley AE, et al. Fetal alcohol spectrum disorder: a guideline for diagnosis across the lifespan. CMAJ. 2016;188:191-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26668194.

9. Hoyme HE, Kalberg WO, Elliott AJ, Blankenship J, Buckley D, Marais AS, et al. Updated Clinical Guidelines for Diagnosing Fetal Alcohol Spectrum Disorders. Pediatrics. 2016;138. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27464676.

10. GRADE Working Group, Schünemann H, Brożek J, Guyatt G, Oxman A, (editors). The GRADE Handbook http://gdt.guidelinedevelopment.org/app/handbook/handbook.html 2013.

11. Morrow-Tlucak M, Ernhart CB, Sokol RJ, Martier S, Ager J. Underreporting of alcohol use in pregnancy: relationship to alcohol problem history. Alcohol Clin Exp Res. 1989;13:399-401. Available from: https://www.ncbi.nlm.nih.gov/pubmed/2665555.

12. Jacobson SW, Jacobson JL, Sokol RJ, Martier SS, Ager JW, Kaplan MG. Maternal recall of alcohol, cocaine, and marijuana use during pregnancy. Neurotoxicol Teratol. 1991;13:535-40. Available from: https://www.ncbi.nlm.nih.gov/pubmed/1758408.

13. Ernhart CB, Morrow-Tlucak M, Sokol RJ, Martier S. Underreporting of alcohol use in pregnancy. Alcohol Clin Exp Res. 1988;12:506-11. Available from: https://www.ncbi.nlm.nih.gov/pubmed/3056071.

14. Esper LH, Furtado EF. Identifying maternal risk factors associated with Fetal Alcohol Spectrum Disorders: a systematic review. Eur Child Adolesc Psychiatry. 2014;23:877-89. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25164262.

15. O'Leary CM, Nassar N, Kurinczuk JJ, Bower C. The effect of maternal alcohol consumption on fetal growth and preterm birth. BJOG. 2009;116:390-400. Available from: PM:19187371.

16. Astley SJ. Validation of the fetal alcohol spectrum disorder (FASD) 4-Digit Diagnostic Code. J Popul Ther Clin Pharmacol. 2013;20:e416-67. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24323701.