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RESEARCH ARTICLE

Comparing diagnostic outcomes of children with fetal alcohol syndrome in South Africa with diagnostic outcomes when using the updated Institute of Medicine diagnostic guidelines

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Introduction: During fetal alcohol spectrum disorder (FASD) prevalence studies in South Africa, cases of fetal alcohol syndrome (FAS) were identified that presented differently from the 2016 Hoyme et al. modified Institute of Medicine (IOM) criteria. We compared diagnostic outcomes of children diagnosed with FAS using a combination of the 2005 Hoyme et al. criteria and the "gestalt method" in South Africa to the diagnosis they would have received using the latest Hoyme et al. criteria. The frequency with which dysmorphic features presented was compared to the frequency with which they were reported in the revised criteria which drew on a larger sample.

Methods: Data were gathered from four South African FASD prevalence studies. Dysmorphology data, anthropometric data, and final diagnosis for participants ($N = 917$) were extracted.

Results: Of the 390 participants with diagnoses of "full FAS," 175 would not have received a "full FAS" diagnosis using the 2016 criteria. Of these, 21 would have received a pFAS diagnosis, and 154 would have received a diagnosis of ARND or a "no-FASD" diagnosis. The frequency of all but five dysmorphic features differ significantly between this sample and the sample examined for the 2016 criteria. There is more variability in the features present in the current sample.

Discussion: Differences regarding diagnostic outcomes and prevalence of dysmorphic features suggest that strict application of the diagnostic criteria may miss children who present with FAS. We recommend including gestalt-based screening in a research setting where the clinical experience is available to inform future guidelines.

KEYWORDS

diagnostic criteria, dysmoprhic features, FASD screening, fetal alcohol spectrum disorder, fetal alcohol syndrome

1 | INTRODUCTION

The impact of the teratogenicity of alcohol can present in various forms. Initially, only the most severely affected cases were recognized in children of alcoholic mothers (Jones, Smith, Ulleland, Streissguth, & Streissguth, 1973; Lemoine, Harousseau, Borteyru, & Menuet, 2003), and these children were diagnosed with fetal alcohol syndrome (FAS). FAS had to be a diagnosis of exclusion as there are other genetic and teratogenic conditions that share features with FAS (Hoyme et al., 2016). With the recognition that there are children affected by prenatal alcohol exposure (PAE) that do not meet the diagnostic criteria of FAS, the possible diagnoses were expanded to include partial fetal alcohol syndrome (pFAS), alcohol-related neurodevelopmental disorder (ARND), and alcohol-related birth defects (ARBD) (Institute

of Medicine [IOM], 1996). The aforementioned were grouped together under the term fetal alcohol spectrum disorder (FASD).

There are biomarkers that can be used to confirm prenatal alcohol use shortly after pregnancy (Kulaga, Pragst, Fulga, & Koren, 2009; Pichini et al., 2012). This is an improvement over the current self-report method (Lange, Shield, Koren, Rehm, & Popova, 2014) and a step in the direction of more objective diagnostic criteria. Even with recent advances in epigenetic studies (Laufer et al., 2015; Masemola, van der Merwe, Lombard, Viljoen, & Ramsay, 2015; Portales-Casamar et al., 2016), there are currently no objective biomarkers against which a diagnosis of FASD can be validated. The diagnosis therefore remains a clinical one and no set of diagnostic criteria can be objectively validated as yet.

There is also evidence of a dose–response effect with regards to alcohol consumption during pregnancy (O'Leary et al., 2010; Sood et al., 2001). The timing of, and the amount of, alcohol consumption during pregnancy impacts on how the disorder presents (Ernhart et al., 1987). Due to this variability, with the exception of FAS, there is as yet no definitive clinical picture of all forms of FASD.

Recent studies have highlighted issues with the convergent validity of the various diagnostic systems. There is significant disagreement between the various diagnostic systems, to such an extent that there is only "fair" to "moderate" agreement on diagnoses when the same participants are diagnosed using the various systems (Coles et al., 2016). These discrepancies complicate the comparison of prevalence figures, the evaluation of interventions, and make it difficult to validate FASD diagnoses (Chudley, 2017). With the progress being made in working toward clinical criteria for diagnosis (Astley & Clarren, 2000; Hoyme et al., 2016), it is important to not lose sight of the fact that the pool of individuals on whom the diagnostic criteria are based, may not represent the full picture of how the impact of PAE presents. Even if the criteria are being based on larger databases of participants, there are still ethnic groups with different phenotypes that have never been included in FASD research. In this article, we will report on the dysmorphic and other features of children diagnosed with FASD, who would normally not have been included in the screening phase of a study using the IOM criteria as modified by Hoyme et al. (2005, 2016).

This article will not attempt to give an overview of the evolution of the FASD diagnosis, but will rather touch on points relevant to the current argument. Tracing the development of the diagnostic criteria of FASD back to its inception, the impact of PAE was initially described as a pattern of malformation in children (Jones et al., 1973; Lemoine et al., 2003). With further clarification came, the requirements for diagnosis that a patient must present with, namely, (a) pre- and/or postnatal growth retardation, (b) central nervous system involvement (of which microcephaly is one possible indicator), and—of particular interest to this article—(c) a *qualitatively* described pattern of dysmorphic features (Sokol & Clarren, 1989). This was expanded upon when the Institute of Medicine (IOM) set out their criteria. The IOM acknowledged once again that the diagnosis requires a qualitative appraisal by a suitably experienced clinician of the dysmorphic facial features of an individual. This set of criteria also included descriptions of pFAS, ARND, and ARBD. The IOM highlighted the fact that the refinement of the diagnostic criteria is a circular process in the absence of objective verification of the diagnoses (IOM, 1996).

The IOM criteria were critiqued by various groups for lacking specificity and quantitative guidelines for diagnosis (Astley & Clarren, 2000; Hoyme et al., 2005). It was rightly argued that to have practical value, diagnostic criteria need to enable nonspecialist clinicians to reliably diagnose FASD. It is argued that the diagnosis and treatment of FASD cannot remain solely the responsibility of dysmorphologist and geneticists. The magnitude of the problem necessitates the involvement of clinicians from other spheres as well. To this end, various clinical guidelines have been proposed including the four-digit diagnostic code (Astley, 2013; Astley & Clarren, 2000) and modified versions of the IOM criteria (Hoyme et al., 2005, 2016).

The majority of prevalence studies in South Africa have used the IOM, or a modified version of the IOM criteria (May et al., 2000, 2007, 2013; Olivier, Urban, Chersich, Temmerman, & Viljoen, 2013; Urban et al., 2008, 2015, 2016; Viljoen et al., 2005). The first South African studies were however only conducted well after the formulation of the IOM guidelines which were based on case reports from the United States and Europe (Clarren & Smith, 1978; Institute of Medicine, 1996). Only in later modifications of these criteria were data from South African populations included, with 92 predominantly Colored (mixed ancestry) children added to a sample of 72 Native-American children for analysis (Hoyme et al., 2005). These criteria were then later updated to standardize and set out clear diagnostic guidelines for clinicians using data from more than 10,000 children participating in epidemiological studies (Hoyme et al., 2016).

From the perspective of the current authors, the above raises two areas of concern. First, only children from the Western Cape Province, who were predominantly Colored (mixed ancestry), were included in the 2005 guidelines. It is possible that children from other population groups in South Africa may present differently. Even the updated lip/-philtrum guides for South Africa are only aimed at Colored (mixed ancestry) populations (Hoyme et al., 2015). Second, while the critiques of the original IOM model are valid and while its utility in a clinic setting is doubtful, the fact that all the current criteria for diagnosis can be traced back to qualitative appraisal of children affected by alcohol in utero remains (Clarren & Smith, 1978; Jones et al., 1973; Lemoine

et al., 2003). In a *research* setting, it can be of value to have expert dysmorphologists and geneticist screen for the FAS gestalt as described in the initial IOM guidelines (1996) and examine children identified in this way. This is especially important now that our understanding of the spectrum of damage cause by PAE has increased.

The characteristic pattern of facial abnormalities and dysmorphic features are key aspects of a FASD diagnosis. Some of these features of FAS are however open to interpretation by a clinician. Features that are not measured include midfacial hypoplasia, prognathism, smooth philtrum, and thin vermillion border. Guidelines exist for the philtrum and vermillion border abnormalities (Astley, 2013; Hoyme et al., 2015, Hoyme et al., 2016), but even so it is dependent on clinical judgment. In South Africa, there are a number of ethnic phenotypes that need to be taken into account when drawing conclusions, and what may seem dysmorphic on one context may be normal in a different ethnic group. One possible solution to this subjectivity is the work being done on 3-D photogrammetry which can provide objective measures of the dysmorphic features (Douglas & Mutsvangwa, 2010; Mutsvangwa, Meintjes, Viljoen, & Douglas, 2010).

There are guidelines for South Africa's Colored (mixed ancestry) population for diagnosing lip/philtrum abnormalities (Hoyme et al., 2015), yet no such guidelines exist for other ethnic groups. There is also significant heterogeneity within the Colored population depending on their ancestry (Suttie et al., 2017). To use Khoisan ancestry as an example, clinical experience (DV) has shown that a phenotype exists that is slightly closer to the phenotype of FAS than in other ethnic groups. The Khoisan phenotype may include epicanthic folds and shorter palpebral fissure length (PFL) in children not exposed to alcohol in utero. This is not to say that the phenotype would be confused with FAS, the diagnosis of dysmorphic features may however vary in degree based on the familiarity of the dysmorphologist with the phenotype.

These issues are not confined to mixed ancestry groups however. There is for example a significant difference in how the vermillion border and philtrum present in Caucasian and Colored groups as opposed to Black population groups. A vermillion border that is seen as normal for Caucasian or Colored groups may in fact be thin for a child from a Black population. Clinical experience is therefore important when working in a context with heterogenous populations. Dysmorphic criteria based on a large international sample like the 2016 Hoyme et al. criteria may therefore also not be accurate in all population groups.

Dysmorphology scores are not used as the basis for a diagnosis of FASD, yet assessing the prevalence of the various dysmorphic features can indicate whether there are grounds to re-evaluate which features should be classified as cardinal features. Currently short PFL, a thin vermillion border, and a smooth philtrum are seen as the most important facial anomalies. Without objective confirmation, and with the circular nature of how these criteria are refined, this assertion should be checked in different settings and population as it remains possible that FAS could present differently.

When it comes to diagnosing the whole spectrum of FASD, in addition to the above concerns, the difficulty in accurately establishing maternal alcohol use also needs to be taken into account. As mentioned, there are ways of establishing alcohol use soon after birth, but in school-based active case-ascertainment studies, the method predominantly used in South Africa, this is not possible. Even if alcohol use can be confirmed, the timing of and amount of alcohol use in pregnancy is not always reliable (Lange et al., 2014).

This study retrospectively analyzed data gathered during prevalence studies in the Western-, Northern-, and Eastern Cape provinces. The goal was to compare the frequency with which dysmorphic features appeared in these samples with the frequency reported in the latest modified IOM criteria (Hoyme et al., 2016). The features in the 2016 Hoyme et al. criteria were based on the features of a sample of 370 of the children in the international cohort.

2 | METHODS

2.1 | FASD diagnostic process

Dysmorphology and anthropometric data were gathered from four FASD prevalence studies conducted by the Foundation for Alcohol Related Research (FARR). The studies focused on children of school-entry age (between 6 and 8 years old) and used active case-ascertainment methods. Two studies were conducted in the Northern Cape, one in the Western Cape and one in the Eastern Cape. All four studies followed the same procedure based on the modified IOM criteria (Hoyme et al., 2005). A tiered screening method was used, with primary health care (PHC) nurses conducting anthropometric screening on all children taking part in the study. Participants with height and weight ≤10th percentile for age (Centers for Disease Control and Prevention & National Center for Health Statistics, 2000) and/or a head circumference (occipitofrontal circumference [OFC]) ≤10th percentile (Rollins, Collins, & Holden, 2010) were referred for an evaluation by a clinician.

During the anthropometric screening, the PHC nurses also conducted brief health screenings as an additional service to the participants. Where required, nurses would make referrals to clinics for any identified health problems. Based on their discretion, they would also refer children to the clinician in the study for further examination. Examples of these referrals include evidence of moderate to severe infections, eye disorders, deformities (facial clefts or limb anomalies) and other miscellaneous anomalies. Regardless of the grounds for referral to the clinician, these participants would

TABLE 1 Comparison of weighted dysmorphology scoring systems

	FARR	2005 Hoyme et al.	2016 Hoyme et al.
Height < 10%	1	1	2
Weight < 10%	2	2	1
OFC < 10%	3	3	3
PFL < 10%	3	3	3
Hyperactivity	3	1	N/A
Fine and gross motor skills	3	1	N/A
Hypoplastic midface	2	2	2
"Railroad track" ears	2	1	1
Strabismus	2	0	1
Ptosis	3	2	1
Epicanthal folds	1	1	2
Flat nasal bridge	1	1	2
Anteverted nares	1	2	2
Long philtrum	3	2	2
Smooth philtrum	3	3	3
Thin vermilion	3	3	3
Prognathism	2	0	1
Heart murmur	3	1	1
Limited elbow supination	3	2	1
Clinodactyly	1	1	2
Camptodactyly	2	1	2
Altered palmar crease	1	1	2
Hypertrichosis	2	1	1
Inter canthal distance	N/A	0	2
Hypoplastic nails	N/A	0	1
Total possible score	50	35	41

receive a dysmorphology exam as a matter of course. The clinician (DV) who conducted the majority of examinations and oversaw the remainder has extensive experience in diagnosing FASD among various clinical populations (May et al., 2000; Urban et al., 2008, 2016; Viljoen, Craig, Hymbaugh, Boyle, & Blount, 2003; Viljoen, Croxford, Gossage, Kodituwakku, & May, 2002; Viljoen et al., 2005), and has been involved in FASD research in South Africa since the first epidemiological study was conducted in 1998 (May et al., 2000).

The dysmorphic features of participants were recorded using a scoring system, similar to the one developed during the clarification of the IOM criteria (Hoyme et al., 2005). Both the FARR and 2005 Hoyme et al. criteria's scoring systems were developed by assigning weight to frequently appearing dysmorphic features in children with FASD based on clinical experience. The first author on this article (DV) was involved in the development of both these criteria. Only the latest 2016 Hoyme et al. version of the adapted IOM criteria has been based on the frequency of these features appearing in a clinical sample (Hoyme et al., 2016). Please see Table 1 for details on the scoring systems. Aside from the weight given to the various features, the main differences between the scoring systems is that the FARR system excludes inter canthal distance and hypoplastic nails, and they are scored 0 in the 2005 Hoyme et al. system. In the 2016 Hoyme et al. system inter canthal distance and hypoplastic nails are included and scored 2 and 1, respectively. The 2016 Hoyme et al. criteria exclude hyperactivity and motor function which are present in the FARR and 2005 Hoyme et al. versions, as these are seen as neurobehavioral and not dysmorphic features. Last, a confirmed heart defect is not noted separately from a heart murmur in the FARR system.

All children who advance to the clinical screening phase receive neurodevelopmental assessments and interviews are conducted with their biological mother or a proxy informant. Diagnoses are made at a case conference based on the outcomes of the clinical examinations, neurodevelopmental assessments and maternal interviews.

As with the Hoyme et al. (2005) modified criteria, a diagnosis of FAS required evidence of prenatal and/or postnatal growth retardation and evidence (height or weight ≤10th percentile), evidence of deficient brain growth (OFC ≤10th percentile), and the presence of the characteristic pattern of facial features. A diagnosis of FAS could be made without confirmed maternal alcohol use, yet maternal history was always considered where available. Furthermore, a child's cognitive functioning is also taken into consideration as part of the diagnostic process. Performance 2 or more standard deviations below the expected means on the relevant assessments is treated as a significant developmental delay.

The major difference between the 2005 Hoyme et al. criteria and the diagnostic process followed by FARR is in the weighting of the dysmorphic features. Palpebral fissure length, a narrow vermillion border and smooth philtrum were not treated as cardinal features of FAS by FARR. Due to concerns about the limited pool of subjects these criteria were based on, and due to the large variations in facial morphology in the various South African ethnic groups, the dysmorphologist could still give a diagnosis of FAS based on clinical experience. A diagnosis of FAS could be given if the FAS gestalt was present and if it was supported by the neurodevelopmental assessment and maternal interview.

2.2 | Data collection

All clinical examination forms from the four South African prevalence studies were included in the dataset. All children advancing to the clinical screening phase were therefore included in the study. In addition to clinical data, the final diagnosis of the participants was included. This yielded 917 records.

2.3 | Data analysis

The dysmorphology data were extracted for those children who had an FASD diagnosis and the number of dysmorphic

features present was calculated. The weighted score was not used in this calculation, only the presence or absence of a feature was noted. Three data sets were extracted from these records, (a) children diagnosed with full FAS by FARR, (b) children diagnosed with FAS by FARR who would have received an FAS diagnosis according to a strict application of the 2016 Hoyme et al. criteria, and (c) children diagnosed with FAS by FARR who would not have received an FAS diagnosis according to a strict application of the 2016 Hoyme et al. criteria. These data sets were then compared based on dysmorphic features present. The percentage of children diagnosed with FAS, presenting with each feature in this dataset, was compared to the results published in the latest update on the IOM model (Hoyme et al., 2016).

3 | RESULTS

Of the initial 917 participants, 451 received an FASD diagnosis during the prevalence studies. Of the children diagnosed 390 had a diagnosis of full FAS, of which only 215 would have received a diagnosis of full FAS using the updated IOM criteria. Of the 175 who would not have received an FAS diagnosis, 21 would have received a pFAS diagnosis. The remaining 154 would likely either have received a diagnosis of ARND or a diagnosis of "no-FASD" based on these criteria (Table 2).

TABLE 2 Diagnosis of participants using 2016 Hoyme et al. updated IOM criteria

Dysmorphic feature	FAS diagnosis ($n = 215$)	Other diagnosis ($n = 175$)
Height < 10%	201 (93.48%)	133 (76%)
Weight < 10%	210 (97.67%)	150 (85.71%)
OFC < 10%	176 (81.86%)	151 (86.28%)
PFL < 10%	183 (85.11%)	74 (42.28%)
Hyperactivity	15 (6.97%)	18 (10.28%)
Fine and gross motor skills	2 (0.93%)	1 (0.57%)
Hypoplastic midface	25 (11.62%)	17 (9.71%)
"Railroad track" ears	2 (0.93%)	2 (1.14%)
Strabismus	7 (3.25%)	5 (2.85%)
Ptosis	7 (3.25%)	8 (4.57%)
Epicanthal folds	69 (32.09%)	60 (34.28%)
Flat nasal bridge	91 (42.32%)	74 (42.28%)
Anteverted nares	16 (7.44%)	12 (6.85%)
Long philtrum	135 (62.79%)	119 (68%)
Smooth philtrum	213 (99.06%)	106 (60.57%)
Thin vermilion	80 (37.2%)	10 (5.71%)
Prognathism	10 (4.65%)	5 (2.85%)
Heart murmur	6 (2.79%)	13 (7.42%)
Limited elbow supination	5 (2.32%)	2 (1.14%)
Clinodactyly	91 (42.32%)	63 (36%)
Camptodactyly	22 (10.23%)	10 (5.71%)
Altered palmar crease	85 (39.53%)	77 (44%)
Hypertrichosis	3 (1.39%)	3 (1.71%)

Note. Hypoplastic nails and inter canthal distance not included.

TABLE 3 Comparison of frequency of dysmorphic features

Dysmorphic feature	FAS diagnosis FARR ($n = 390$)	FAS diagnosis Hoyme et al., 2016 ($n = 370$)
Height < 10%	334 (85.64%)	327 (88.37%)
Weight < 10%	360 (92.3%)	322 (87.02%)
OFC < 10%	327 (83.84%)	354 (95.67%)
PFL < 10%	257 (65.89%)	313 (84.59%)
Hypoplastic midface	42 (10.76%)	216 (58.37%)
"Railroad track" ears	4 (1.02%)	57 (15.4%)
Strabismus	12 (3.07%)	35 (9.45%)
Ptosis	15 (3.84%)	64 (17.29%)
Epicanthal folds	129 (33.07%)	204 (55.13%)
Flat nasal bridge	165 (42.3%)	179 (48.37%)
Anteverted nares	28 (7.17%)	118 (31.89%)
Long philtrum	254 (65.12%)	122 (32.97%)
Smooth philtrum	319 (81.79%)	307 (82.97%)
Thin vermilion	90 (23.07%)	293 (79.18%)
Prognathism	15 (3.84%)	21 (5.67%)
Heart murmur	19 (4.87%)	50 (13.51%)
Limited elbow supination	7 (1.79%)	31 (8.37%)
Clinodactyly	154 (39.48%)	149 (40.27%)
Camptodactyly	32 (8.2%)	114 (30.81%)
Altered palmar crease	162 (41.53%)	173 (46.75%)
Hypertrichosis	6 (1.53%)	19 (5.13%)

Note. Hypoplastic nails and inter canthal distance, hyperactivity, and motor skills not included.

Using the table of the revised dysmorphology score in the Hoyme et al. (2016) article to calculate the percentage of children presenting with each feature, a comparison was made with the total sample of children diagnosed with FASD in FARR's prevalence studies. Significant differences in the frequency of dysmorphic features were found (see Table 3 for details).

The anthropometric features remain prominent as is to be expected as they remain a part of the screening criteria. The cardinal features of FAS as per the updated IOM criteria (palpebral fissure length, smooth philtrum, and thin vermillion border) are however not as prevalent in the FARR sample as in the IOM sample (see Table 3 for details). While the prevalence of a smooth philtrum was not significantly different ($X^2[1, N = 760] = 0.18, p = .670$), there were major differences in the prevalence of short palpebral fissures ($X^2[1, N = 760] = 35.40, p < .001$) and thin vermillion borders ($X^2[1, N = 760] = 239.14, p < .001$; Figure 1).

Comparing the frequency of the remaining dysmorphic features in the two criteria, using chi square tests, all but five features (height, flat nasal bridge, altered palmar crease, clinodactyly, and prognathism) differ significantly (Figure 1). There was a wider spread of features present in the FARR sample than in the Hoyme et al. (2016) sample and all features, except weight and long philtrum, were less frequent in the FARR sample.

4 | DISCUSSION

It is concerning that of 390 children diagnosed with full FAS by the clinicians involved in these studies, 175 would have missed a diagnosis of FAS based on a strict application of the 2016 Hoyme et al. criteria. Only 21 of these children would have received a diagnosis of pFAS using these criteria as all the cardinal features were not present. The remaining 154 children would have received a diagnosis of "no-FASD" or a diagnosis of ARND. A further 28 children would not have qualified for a clinical assessment based on the anthropometric criteria. Going back to the initial description of FASD and the gestalt method of diagnosis, based on the clinicians experience the pattern of dysmorphology and growth deficits, do however warrant a diagnosis of full FAS.

A diagnosis of ARND should not be seen as a lesser form of FASD. The impact on the affected individual can be as severe in terms of intellectual ability (Rasmussen, 2005). With ARND, the facial features of FAS are largely absent, and it requires a more stringent diagnostic approach. We agree with Hoyme et al. that where PAE is confirmed, it would be prudent to screen for the whole spectrum of FASD (2016).

As FARR used the rather subjective gestalt method and the strict 2005 Hoyme et al. criteria, it was difficult to compare the frequency of dysmorphic features in the FARR and

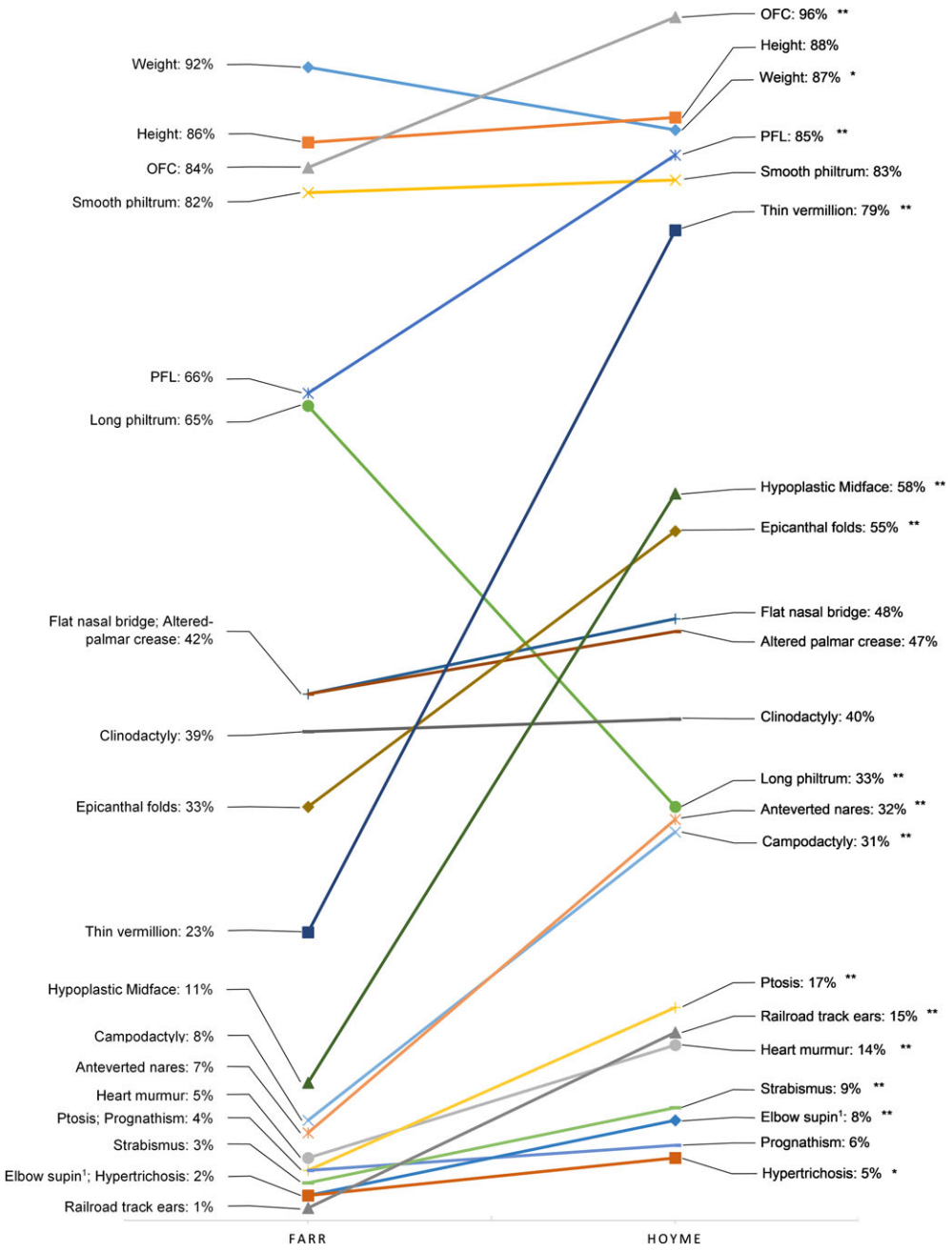

FIGURE 1 Comparison of dysmorphic features' rank between criteria used by FARR and Hoyme et al. (2016). *$p > .05$; **$p > .001$; [1]Limited elbow supination

2016 Hoyme et al. samples. Additional dysmorphologists, with the clinical experience and a background in the gestalt method, would need to examine the same participants in *research* setting to strengthen the comparison. The differences between the two groups could also be due to the Hoyme et al. (2016) group being drawn from an even more heterogenous group than the FARR sample. The 370 children in the Hoyme et al. (2016) sample are not confined to one geographic area or country as opposed to FARR's purely South African sample.

The largest differences in frequency are, as can be expected, in the features where there is some measure of subjectivity. This supports the argument that there may be individuals who can be diagnosed with FAS, but do not fit the current dysmorphic profile. This highlights the need for further research. Some of the variation could also be explained due ethnic differences in the expression of the FASD phenotype.

The large differences in the frequency of dysmorphic features do suggest that strict cut-offs in the diagnostic criteria should be treated with caution. In a *clinical* setting, it is important to not misdiagnose FASD, and in these instances, the updated IOM criteria provide unambiguous guidelines that can be used by specialists and nonspecialists alike. In the context of *research* in new and varied populations, it may be of value to loosen the anthropometric criteria so as to include more edge-cases in the clinical screening. Where experienced clinicians with a background in genetics and dysmorphology are available, it would be valuable if the use of the IOM criteria is supplemented by the gestalt method. It needs to be emphasized that the current approach is not intended to replace the modified versions of the IOM criteria (Hoyme et al., 2005, 2016), but rather to identify FAS and FASD cases that present differently which can inform the continuing process of finding universally applicable and validated guidelines (Chudley, 2017; Coles et al., 2016; Del Campo & Jones, 2017).

This article does not suggest a new set of guidelines for FASD diagnosis. It rather serves to highlight the fact that with no objective biomarkers for FASD, a conclusive "checklist" for diagnosis is difficult to establish. There should always be an avenue for additional features of FASD to be identified and added to our current knowledge base.

We therefore recommend that, where the expertise is available, the diagnostic cut-off points are not applied in an overly strict fashion, but rather that the screening criteria be relaxed to over sample participants and thereby to identify FASD cases that would normally slip through the process.

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CONFLICT OF INTEREST

The authors have conflict of interest to declare.

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