The Essential Role of Growth Deficiency in the Diagnosis of FASD

Susan Astley PhD

Julia Bledsoe MD

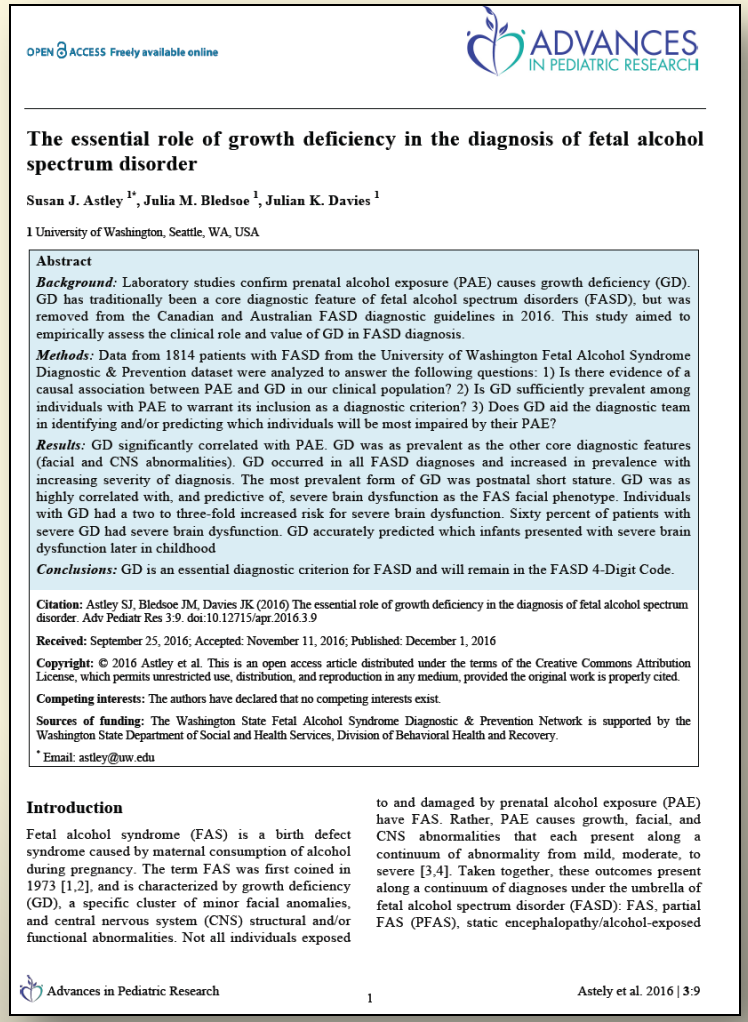
Julian Davies MD

Members of the FAS DPN FASD Diagnostic Team

University of Washington
Seattle WA

Published in Advances in Pediatric Research
An open access journal

http://depts.washington.edu/fasdpn/pdfs/Astley-Growth2016Abstract.pdf



OPEN ACCESS Freely available online

ADVANCES IN PEDIATRIC RESEARCH

The essential role of growth deficiency in the diagnosis of fetal alcohol spectrum disorder

Susan J. Astley [1*], Julia M. Bledsoe [1], Julian K. Davies [1]

1 University of Washington, Seattle, WA, USA

Abstract

Background: Laboratory studies confirm prenatal alcohol exposure (PAE) causes growth deficiency (GD). GD has traditionally been a core diagnostic feature of fetal alcohol spectrum disorders (FASD), but was removed from the Canadian and Australian FASD diagnostic guidelines in 2016. This study aimed to empirically assess the clinical role and value of GD in FASD diagnosis.

Methods: Data from 1814 patients with FASD from the University of Washington Fetal Alcohol Syndrome Diagnostic & Prevention dataset were analyzed to answer the following questions: 1) Is there evidence of a causal association between PAE and GD in our clinical population? 2) Is GD sufficiently prevalent among individuals with PAE to warrant its inclusion as a diagnostic criterion? 3) Does GD aid the diagnostic team in identifying and/or predicting which individuals will be most impaired by their PAE?

Results: GD significantly correlated with PAE. GD was as prevalent as the other core diagnostic features (facial and CNS abnormalities). GD occurred in all FASD diagnoses and increased in prevalence with increasing severity of diagnosis. The most prevalent form of GD was postnatal short stature. GD was as highly correlated with, and predictive of, severe brain dysfunction as the FAS facial phenotype. Individuals with GD had a two to three-fold increased risk for severe brain dysfunction. Sixty percent of patients with severe GD had severe brain dysfunction. GD accurately predicted which infants presented with severe brain dysfunction later in childhood

Conclusions: GD is an essential diagnostic criterion for FASD and will remain in the FASD 4-Digit Code.

Citation: Astley SJ, Bledsoe JM, Davies JK (2016) The essential role of growth deficiency in the diagnosis of fetal alcohol spectrum disorder. Adv Pediatr Res 3:9. doi:10.12715/apr.2016.3.9

Received: September 25, 2016; Accepted: November 11, 2016; Published: December 1, 2016

Competing interests: The authors have declared that no competing interests exist.

Sources of funding: The Washington State Fetal Alcohol Syndrome Diagnostic & Prevention Network is supported by the Washington State Department of Social and Health Services, Division of Behavioral Health and Recovery.

* Email: astley@uw.edu

Introduction

Fetal alcohol syndrome (FAS) is a birth defect syndrome caused by maternal consumption of alcohol during pregnancy. The term FAS was first coined in 1973 [1,2], and is characterized by growth deficiency (GD), a specific cluster of minor facial anomalies, and central nervous system (CNS) structural and/or functional abnormalities. Not all individuals exposed to and damaged by prenatal alcohol exposure (PAE) have FAS. Rather, PAE causes growth, facial, and CNS abnormalities that each present along a continuum of abnormality from mild, moderate, to severe [3,4]. Taken together, these outcomes present along a continuum of diagnoses under the umbrella of fetal alcohol spectrum disorder (FASD): FAS, partial FAS (PFAS), static encephalopathy/alcohol-exposed

Background

Although growth deficiency (GD) has traditionally been a core diagnostic feature of FASD since 1973, GD was removed from the Canadian and Australian FASD diagnostic guidelines in 2016.

Should the 4-Digit Code follow suit?

To guide this decision, we conducted the following study to empirically assess the clinical role and value of GD in the diagnosis of FASD.

Methods / Objectives

Data from 1,814 patients with FASD from the University of Washington Fetal Alcohol Syndrome Diagnostic & Prevention dataset were analyzed to answer the following 3 questions:

1) Is GD sufficiently prevalent among individuals with PAE to warrant its inclusion as a diagnostic criterion?

2) Laboratory studies confirm prenatal alcohol exposure (PAE) causes growth deficiency (GD).

   Is there evidence of a causal association between prenatal alcohol exposure (PAE) and growth deficiency (GD) in our clinical population?

3) Does GD aid the diagnostic team in identifying and/or predicting which individuals will be most impaired by their PAE?

What is Fetal Alcohol Syndrome (FAS)?

FAS is characterized by:

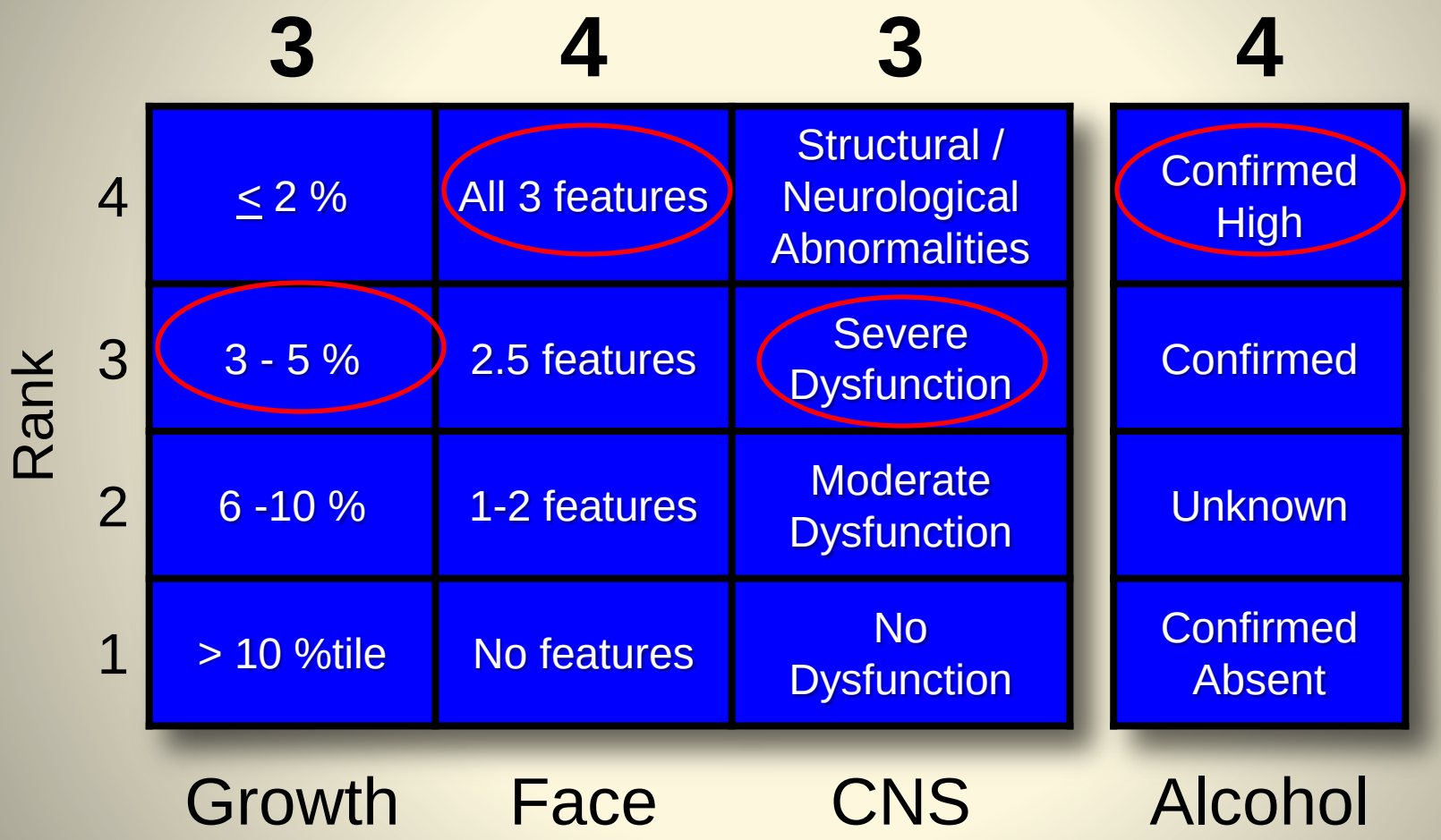
1. Growth deficiency
2. Unique facial features
3. CNS abnormalities (evidence of structural, neurological and/or functional abnormalities)
4. Prenatal alcohol exposure

Prevalence: 1 to 3 per 1,000 live births (equivalent to down syndrome).

Leading known cause of developmental disabilities.

Entirely preventable.

Abbreviated Case-Definitions of 4-Digit Code



3434 is one of twelve 4-Digit Codes for FAS

Example of 4-Digit Codes for FAS and PFAS[11]

A. **FAS (alcohol exposed)**

2433	3433	4433
2434	**3434**	4434
2443	3443	4443
2444	3444	4444

B. **FAS (alcohol exposure unknown)**

2432	3432	4432
2442	3442	4442

C. **Partial FAS (alcohol exposed)**

1333	1433	2333	3333	4333
1334	1434	2334	3334	4334
1343	1443	2343	3343	4343
1344	1444	2344	3344	4344

What is Fetal Alcohol Spectrum Disorder (FASD)?

FASD is an umbrella term.
FASD reflects the full range of outcomes caused by prenatal alcohol exposure.
The 4-Digit Code generates four diagnoses under the umbrella of FASD:

Diagnosis		Growth	FAS Face	CNS		Alcohol
1. FAS	Fetal Alcohol Syndrome	growth	face	severe		alc or unk
2. PFAS	Partial FAS		face	severe		alc
3. SE/AE*	Static Encephalopathy / Alc Exposed			severe		alc
4. ND/AE	Neurobehavioral Disorder / Alc Exposed				moderate	alc

* Also referred to as:

- Alcohol Related Neurodevelopmental Disorder (ARND) or
- Neurodevelopmental Disorder Prenatal Alcohol Exposed (ND-PAE)

What is Fetal Alcohol Spectrum Disorder (FASD)?

FASD is an umbrella terr
FASD reflects the full range of outcomes obse viduals
with prenatal alcohol expo
The 4-Digit Code generates four diagnoses und of FASD:

PFAS:
FAS without the growth deficiency

Diagnosis		Growth	FAS Face	CNS		Alcohol
1. FAS	Fetal Alcohol Syndrome	growth	face	severe		alc or unk
2. PFAS	Partial FAS		face	severe		alc
3. SE/AE*	Static Encephalopathy / Alc Exposed			severe		alc
4. ND/AE	Neurobehavioral Disorder / Alc Exposed				moderate	alc

* Also referred to as:

- Alcohol Related Neurodevelopmental Disorder (ARND) or
- Neurodevelopmental Disorder Prenatal Alcohol Exposed (ND-PAE)

What is Fetal Alcohol Spectrum Disorder (FASD)?

FASD is an umbrella ter
FASD reflects the full range of outcomes obse viduals
with prenatal alcohol expo
The 4-Digit Code generates four diagnoses und of FASD:

SE/AE
Category F

Diagnosis		Growth	FAS Face	CNS		Alcohol
1. FAS	Fetal Alcohol Syndrome	growth	face	severe		alc or unk
2. PFAS	Partial FAS		face	severe		alc
3. SE/AE*	Static Encephalopathy / Alc Exposed			severe		alc
4. ND/AE	Neurobehavioral Disorder / Alc Exposed				moderate	alc

* Also referred to as:

- Alcohol Related Neurodevelopmental Disorder (ARND) or
- Neurodevelopmental Disorder Prenatal Alcohol Exposed (ND-PAE)

What is Fetal Alcohol Spectrum Disorder (FASD)?

FASD is an umbrella ter
FASD reflects the full range of outcomes obse viduals
with prenatal alcohol expo
The 4-Digit Code generates four diagnoses und of FASD:

SE/AE
Category K

Diagnosis		Growth	FAS Face	CNS		Alcohol
1. FAS	Fetal Alcohol Syndrome	growth	face	severe		alc or unk
2. PFAS	Partial FAS		face	severe		alc
3. SE/AE*	Static Encephalopathy / Alc Exposed	growth		severe		alc
4. ND/AE	Neurobehavioral Disorder / Alc Exposed				moderate	alc

* Also referred to as:

- Alcohol Related Neurodevelopmental Disorder (ARND) or
- Neurodevelopmental Disorder Prenatal Alcohol Exposed (ND-PAE)

What is Fetal Alcohol Spectrum Disorder (FASD)?

FASD is an umbrella ter
FASD reflects the full range of outcomes obse viduals
with prenatal alcohol expo
The 4-Digit Code generates four diagnoses und of FASD:

ND/AE
Category H

Diagnosis		Growth	FAS Face	CNS		Alcohol
1. FAS	Fetal Alcohol Syndrome	growth	face	severe		alc or unk
2. PFAS	Partial FAS		face	severe		alc
3. SE/AE*	Static Encephalopathy / Alc Exposed			severe		alc
4. ND/AE	Neurobehavioral Disorder / Alc Exposed				moderate	alc

* Also referred to as:

- Alcohol Related Neurodevelopmental Disorder (ARND) or
- Neurodevelopmental Disorder Prenatal Alcohol Exposed (ND-PAE)

What is Fetal Alcohol Spectrum Disorder (FASD)?

FASD is an umbrella ter
FASD reflects the full range of outcomes obse viduals
with prenatal alcohol expo
The 4-Digit Code generates four diagnoses und of FASD:

ND/AE
Category I

Diagnosis		Growth	FAS Face	CNS		Alcohol
1. FAS	Fetal Alcohol Syndrome	growth	face	severe		alc or unk
2. PFAS	Partial FAS		face	severe		alc
3. SE/AE*	Static Encephalopathy / Alc Exposed			severe		alc
4. ND/AE	Neurobehavioral Disorder / Alc Exposed	growth			moderate	alc

* Also referred to as:

- Alcohol Related Neurodevelopmental Disorder (ARND) or
- Neurodevelopmental Disorder Prenatal Alcohol Exposed (ND-PAE)

Interdisciplinary FASD Diagnostic Clinic

An FASD diagnosis is best conducted:

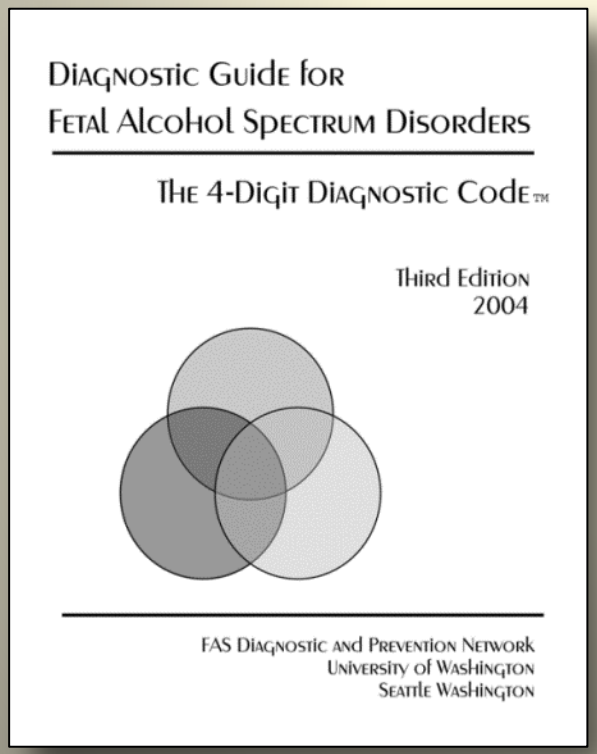
- by an interdisciplinary team
- using validated diagnostic guidelines.

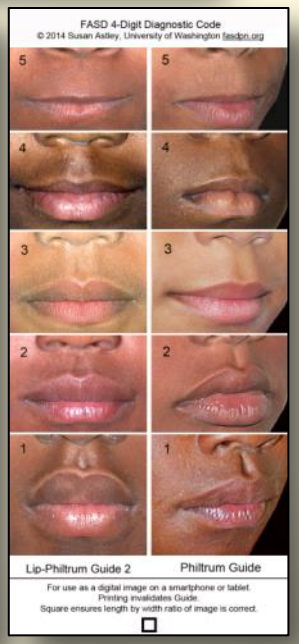
Interdisciplinary team typically includes:

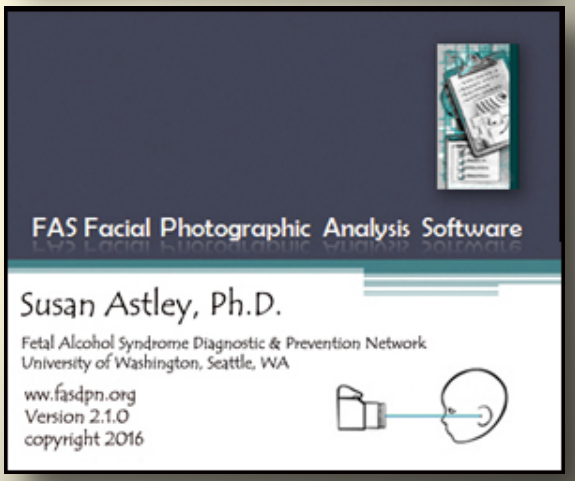
- Pediatrician
- Psychologist
- Speech Language Pathologist
- Occupational Therapist
- Social Worker
- Family Advocate

FASD Diagnostic Tools

All tools available at
fasdpn.org







Ranking Growth with the 4-Digit Code

What type of GD are we looking for?

We are looking for GD characteristic of a teratogenic insult, not of postnatal environmental factors such as nutritional deprivation or chronic or acute illness. We want to answer the question

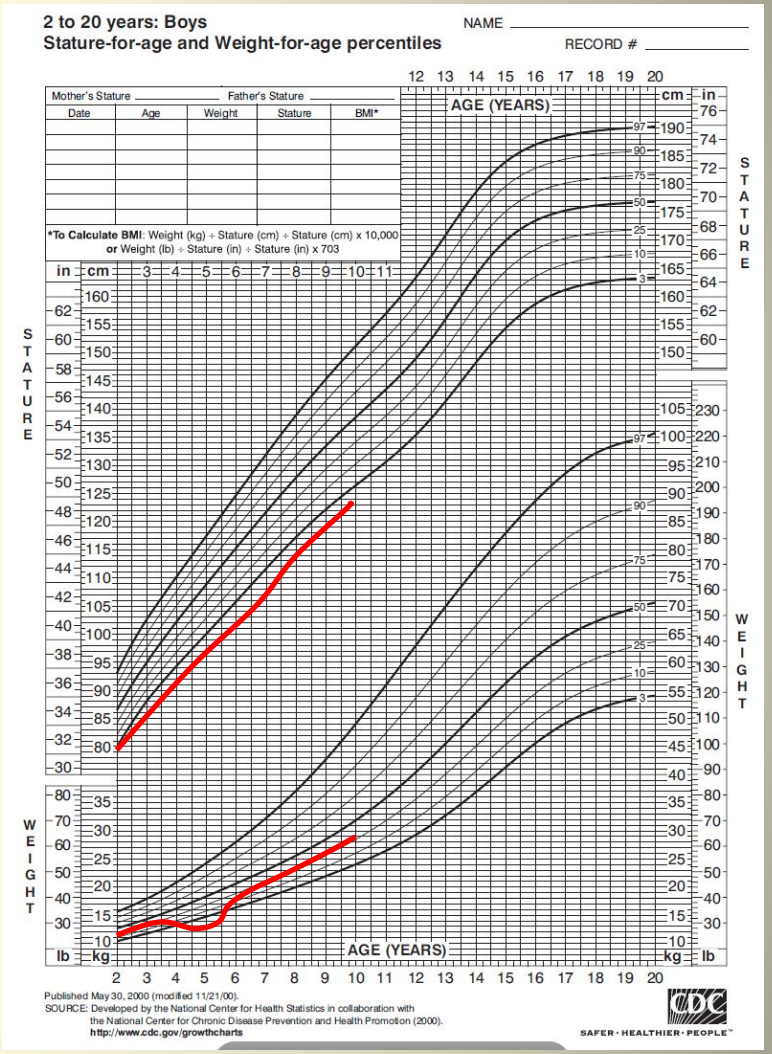
'What is the patient's growth potential after controlling for parental height and postnatal environmental influences?'

GD of teratogenic origin is likely to present as a relatively consistent impairment over a period of time (i.e., the patient's growth follows the normal curve, but is below genetic expectation for family background).

In contrast, GD caused by postnatal environmental influences is likely to present as periodic fluctuations in the curve.

In the next slide you will see that the 4-Digit Code method for Ranking growth deficiency places emphasis on height deficiency over weight deficiency.

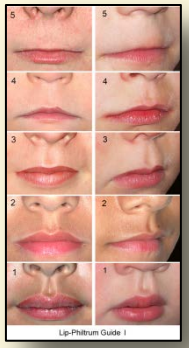
This is because weight gain and loss are more easily influenced by other risk factors such as nutrition and illness.



Ranking Growth with the 4-Digit Code

First, divide the growth record into two parts:

1. prenatal (birth measures)
2. postnatal (all measures after birth).



Second, select and rank the part of the growth record with the greatest deficiency in height percentile?

	Height	Weight
Birth	20%	30%
10 yrs old	5%	15%

GROWTH TABLES

Percentile Range	ABC-Scores for: Height	Weight
≤ 3rd	C	C
> 3rd and ≤ 10th	B	B
> 10th	A	A

4-Digit Diagnostic Rank	Growth Deficiency Category	Height-Weight ABC-Score Combinations
4	Severe	CC
3	Moderate	CB, BC, CA, AC
2	Mild	BA, BB, AB
1	None	AA

4-Digit Diagnostic Code Grid

(See instructions in Diagnostic Guide for FASD)

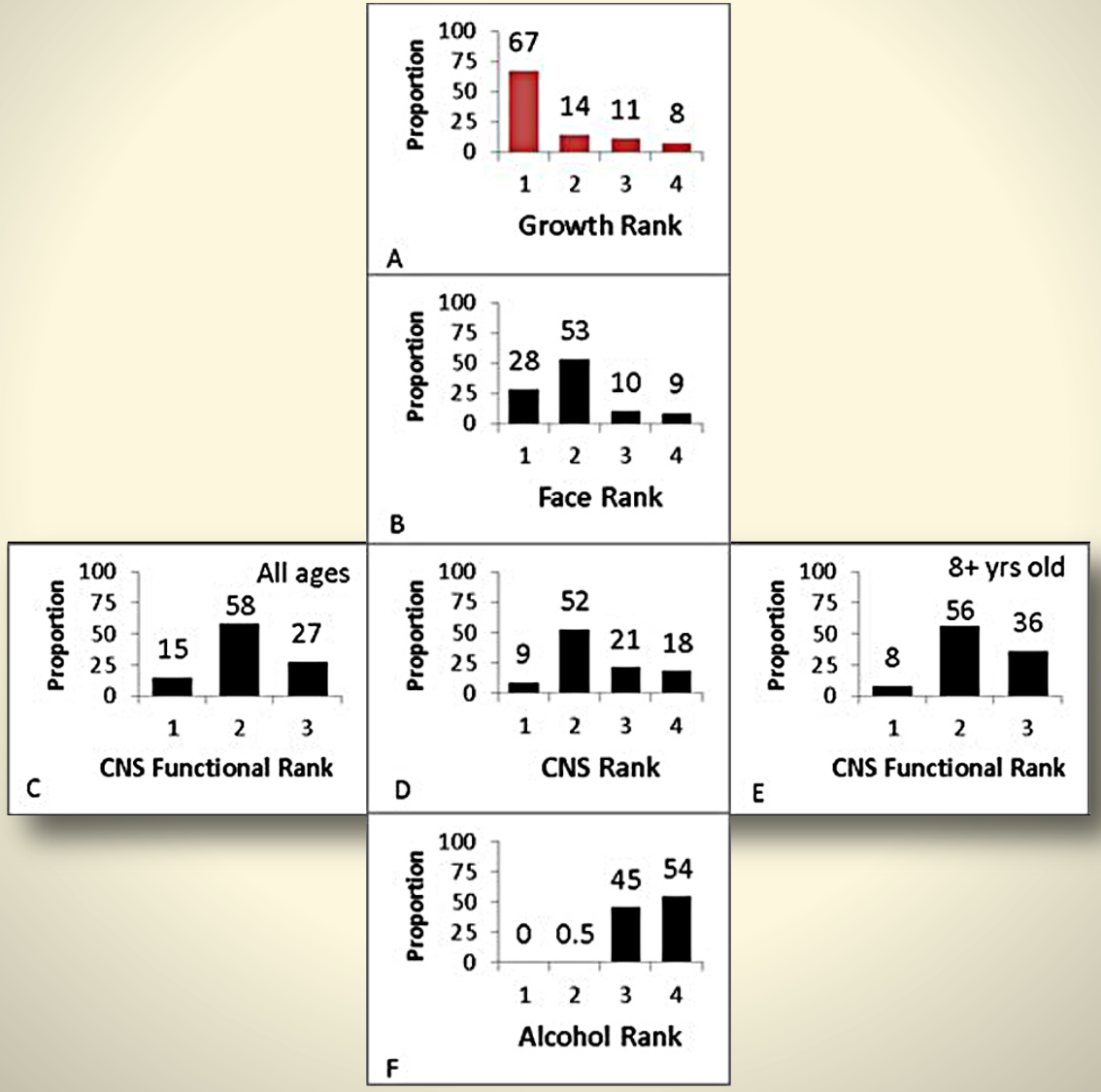
2

				Growth	Face	CNS	Alcohol		
Significant	Severe	Definite	4					4	High risk
Moderate	Moderate	Probable	3					3	Some risk
Mild	Mild	Possible	2	X				2	Unknown
None	None	Unlikely	1					1	No risk
Growth Deficiency	FAS Facial Features	CNS Damage							Prenatal Alcohol

Sociodemographics of the 1,814 Consecutively Evaluated Patients

	N	Valid %
GENDER		
Female	760	42
RACE		
Caucasian	872	48
African American	139	8
Native American/Canadian	158	9
Other including mixed race	637	37
AGE AT DIAGNOSIS (years)		
0–2	226	13
3–5	420	23
6–7	297	16
8–12	508	28
13–18	281	15
19–51	82	5
Mean (SD) min–max	8.9 (6.1)	0.2–50.9
FASD DIAGNOSES		
FAS	82	5
PFAS	123	7
SE/AE	504	28
ND/AE	943	52
SPF/AE	40	2
No abnormalities/AE	122	7

Growth, Face, CNS, and Alcohol Ranks for the 1,814 Patients



Key Findings: GD is as Prevalent as the Face and CNS Abnormalities

Study Question 1:
Is GD sufficiently prevalent among individuals with PAE
to warrant its inclusion as a diagnostic criterion?

Answer:
GD is as prevalent as the other core diagnostic features of FASD.
(the FAS facial features and CNS abnormalities)

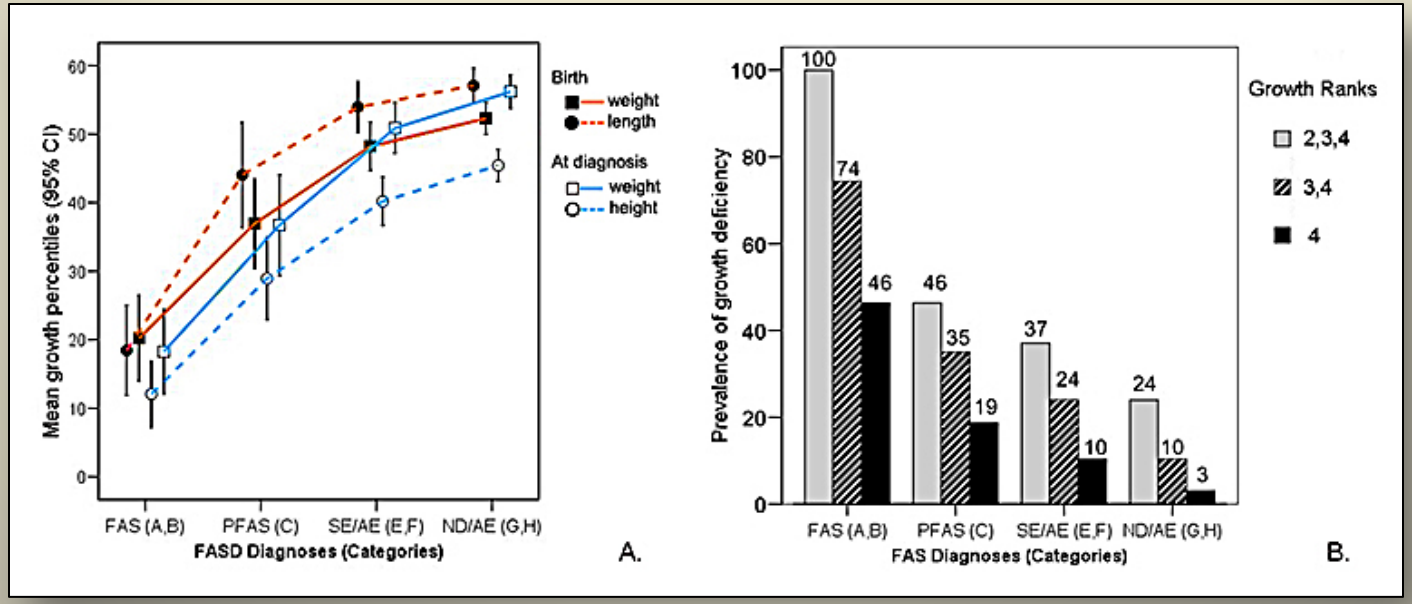
1. 19% had GD ≤ 3rd percentile (Growth Ranks 3 and 4)
   - 19% had the FAS facial features (Face Ranks 3, 4)
   - 18% had CNS structural/neurological abnormalities (CNS Rank 4)

2. 33% had GD ≤ 10th percentile (Growth Ranks 2, 3 and 4)
   - 36% had severe CNS dysfunction (CNS Rank 3)

Key Findings: GD occurs across the full spectrum of FASD

GD ≤ 10th percentile occurs across the full spectrum of FASD diagnoses, <u>not just among those with full FAS</u>.

GD increases significantly in prevalence with increasing severity of diagnosis.

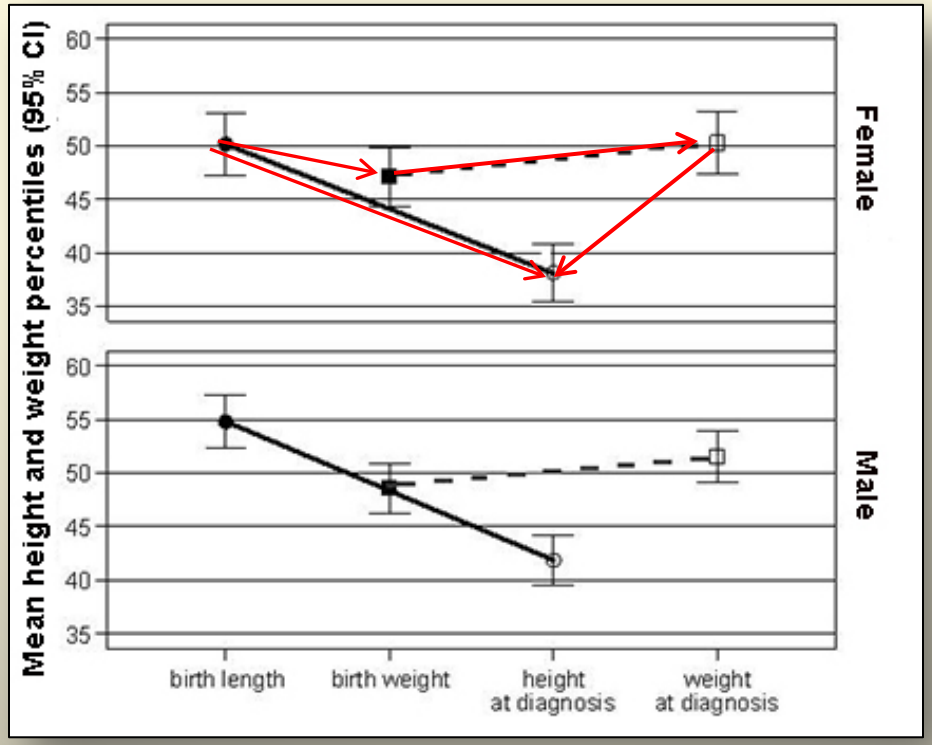


H or W ≤ 10th %
H or W ≤ 3rd %
H & W ≤ 3rd %

Key Findings: GD Changes with Age. Postnatal Short Stature Most Prevalent

The profile of GD changes with age, with the most prevalent form being postnatal short stature.

- Weight is more deficient (by 5 percentile points) than length at birth.
- Height is more deficient (by 11 percentile points) than weight later in life (infant to adult).
- The mean weight percentile increases slightly and significantly (by 3 percentage points) with age.
- The mean height percentile decreases substantially and significantly (by 13 percentage points) with age.
- These patterns are comparable between males and females.



Key Findings: The most prevalent form of GD was postnatal short stature

The 4-Digit Code uses a unique method for documenting GD across a patient's lifespan.

Growth is ranked based on the section of the patient's growth curve that has the lowest height percentile.

- prenatal (birth) or
- postnatal (infancy-adulthood)

The 4-Digit Code emphasizes height deficiency because weight gain and loss is more easily influenced by other risk factors such as nutrition and illness.

Using this approach on the 1,162 patients with growth measures at birth and diagnosis:

- 72% of 4-Digit Growth Ranks were based on postnatal growth.
- The height percentile was lowest at birth in only 28% of subjects.

Key Findings: The 4-Digit Growth Rank documents the GD associated with PAE

Study Question 2:

Is there evidence of a causal association between prenatal alcohol exposure (PAE) and growth deficiency (GD) in our clinical population?

Answer: Yes

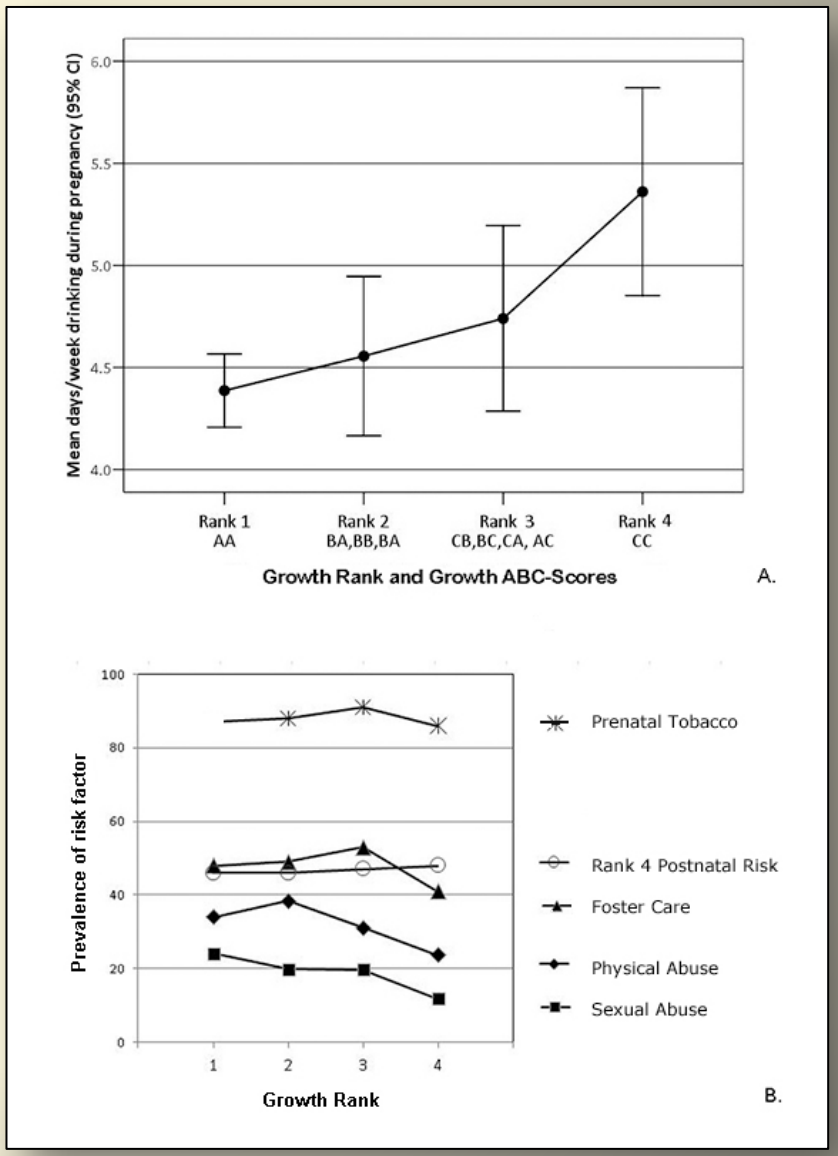
Although GD is caused by many risk factors including prenatal tobacco exposure, the 4-Digit Code Growth Rank uniquely captures the GD associated with PAE because:

- Prenatal tobacco exposure impairs prenatal growth, not postnatal growth. This is reported in the literature and observed in our dataset.
- PAE's primary impact is on postnatal growth, not prenatal growth, with its greatest impact on postnatal short stature. This is reported in the literature and observed in our dataset.
- Since the 4-Digit Code ranks growth based on the age when the height percentile was lowest, this resulted in 82% of the growth ranks for 1,814 subjects being derived from postnatal measures of growth.
- Since tobacco does not influence postnatal growth, this explains why the 4-Digit Growth Rank is significantly correlated with PAE and not with prenatal tobacco exposure in our dataset.
- Postnatal risks (neglect, abuse, multiple home placements) did not impact the 4-Digit Growth Rank because they were effectively removed from the Ranking process.

Key Findings: The 4-Digit Growth Rank documents the GD associated with PAE

Growth deficiency was significantly correlated with PAE after control for other risk factors, including tobacco.

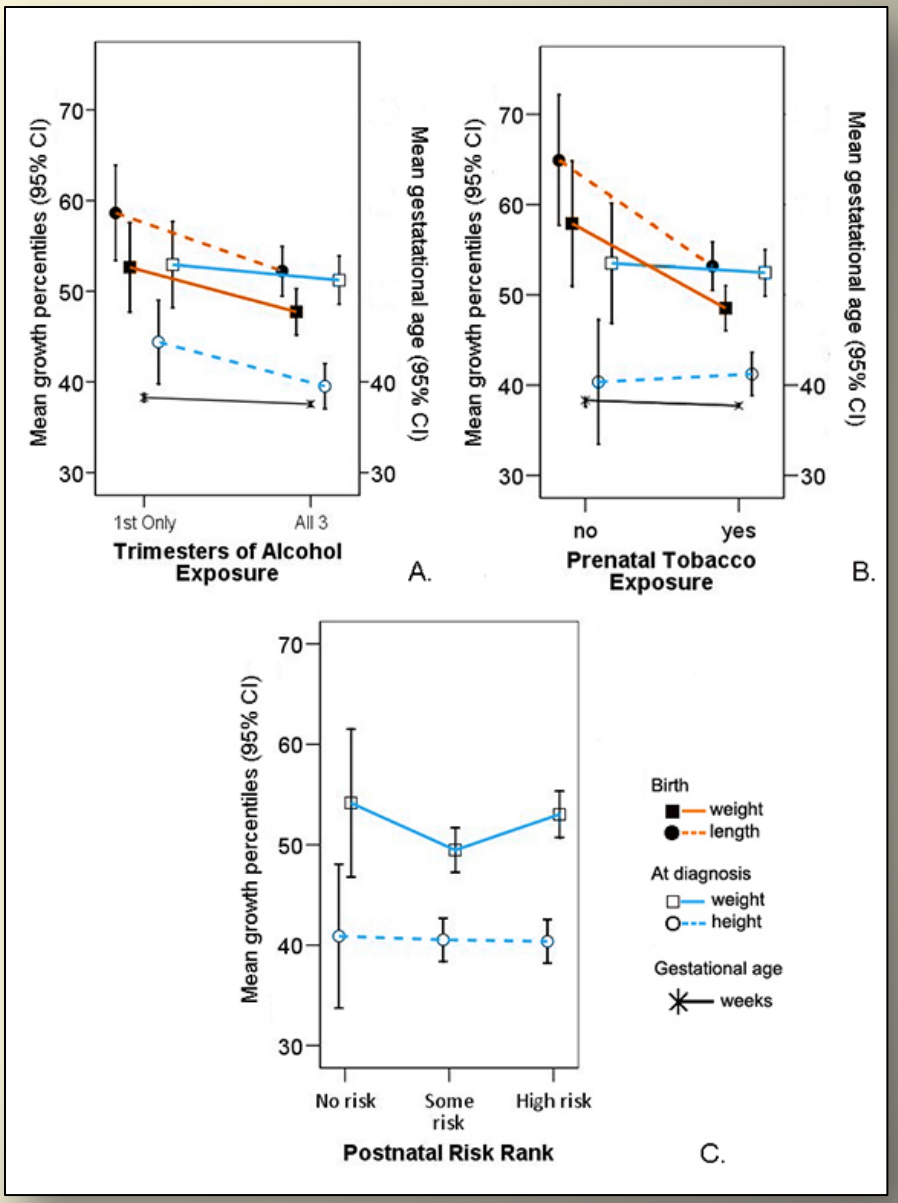
The absence of an association between the Growth Rank and other postnatal risk factors demonstrates the clinical team effectively avoided using deficient growth measures caused by other risk factors when deriving the FASD 4-Digit Rank for Growth.



Key Findings: The 4-Digit Growth Rank documents the GD associated with PAE

Although both alcohol and tobacco were associated with decreased prenatal growth …

Only alcohol was associated with decreased postnatal growth (short stature).



Key Findings: The 4-Digit Growth Rank documents the GD associated with PAE

Postnatal short stature was the most prevalent form of GD in our clinical population, and was significantly correlated with PAE after controlling for these other risk factors

Among the 639 with height or weight $\leq 10^{th}$ percentile at birth or at diagnosis		At birth		At diagnosis	
		n	%	n	%
Proportion with height deficiency	639	164	38.2	443	69.3
Proportion with weight deficiency	639	213	41.4	285	44.6

Our finding are remarkably consistent with the literature, both past and present.

Key Findings: Our Findings are Consistent with Published Empirical Studies

Greene et al. as far back as 1991 found:

> *PAE to negatively affect average preschool height, but not weight. This difference persisted after controlling for the use of other substances and background factors*.

Habbick et al. 1998 concluded:

> "*despite retarded bone age readings, children with FAS do not show significant catch-up growth in height, although they do show relative gain in weight. Short stature can be used as a diagnostic criterion in individuals with FAS beyond childhood, whereas thinness is a less reliable feature.*"

Nordstrom-Klee et al (2002) report:

> *while growth deficits caused solely by prenatal cigarette exposure are unlikely to persist beyond infancy, the effects of prenatal exposure to alcohol on growth continue well into childhood.*

Carter et al. (2016)] most recently reported that, among children with heavy PAE:

> "*children born small for gestational age (SGA) with postnatal growth restriction (height ≤ 10th percentile) were most heavily exposed. Exposure was intermediate for those born SGA with catch-up growth and lowest for those without prenatal or postnatal growth restriction. Effects on neurocognition were strongest in children with both prenatal and long-term growth restriction, more moderate in those with fetal growth restriction and postnatal catch-up, and weakest in those without growth restriction".*

Key Findings: Our Findings are Consistent with Published Empirical Studies

Carter et al. (2016)] most recently reported that, among children with heavy PAE:

> "*children born small for gestational age (SGA) with postnatal growth restriction (height ≤ 10th percentile) were most heavily exposed. Exposure was intermediate for those born SGA with catch-up growth and lowest for those without prenatal or postnatal growth restriction. Effects on neurocognition were strongest in children with both prenatal and long-term growth restriction, more moderate in those with fetal growth restriction and postnatal catch-up, and weakest in those without growth restriction".*

This is a good segue way into our final question….

Study Question 3

Does GD aid the diagnostic team in identifying and/or predicting which individuals will be most impaired by their PAE?

Answer:

Yes!

Key Findings: GD is as Highly Correlated with CNS Dysfunction as the FAS Face

GD is as highly correlated with severe CNS dysfunction as the FAS facial phenotype.

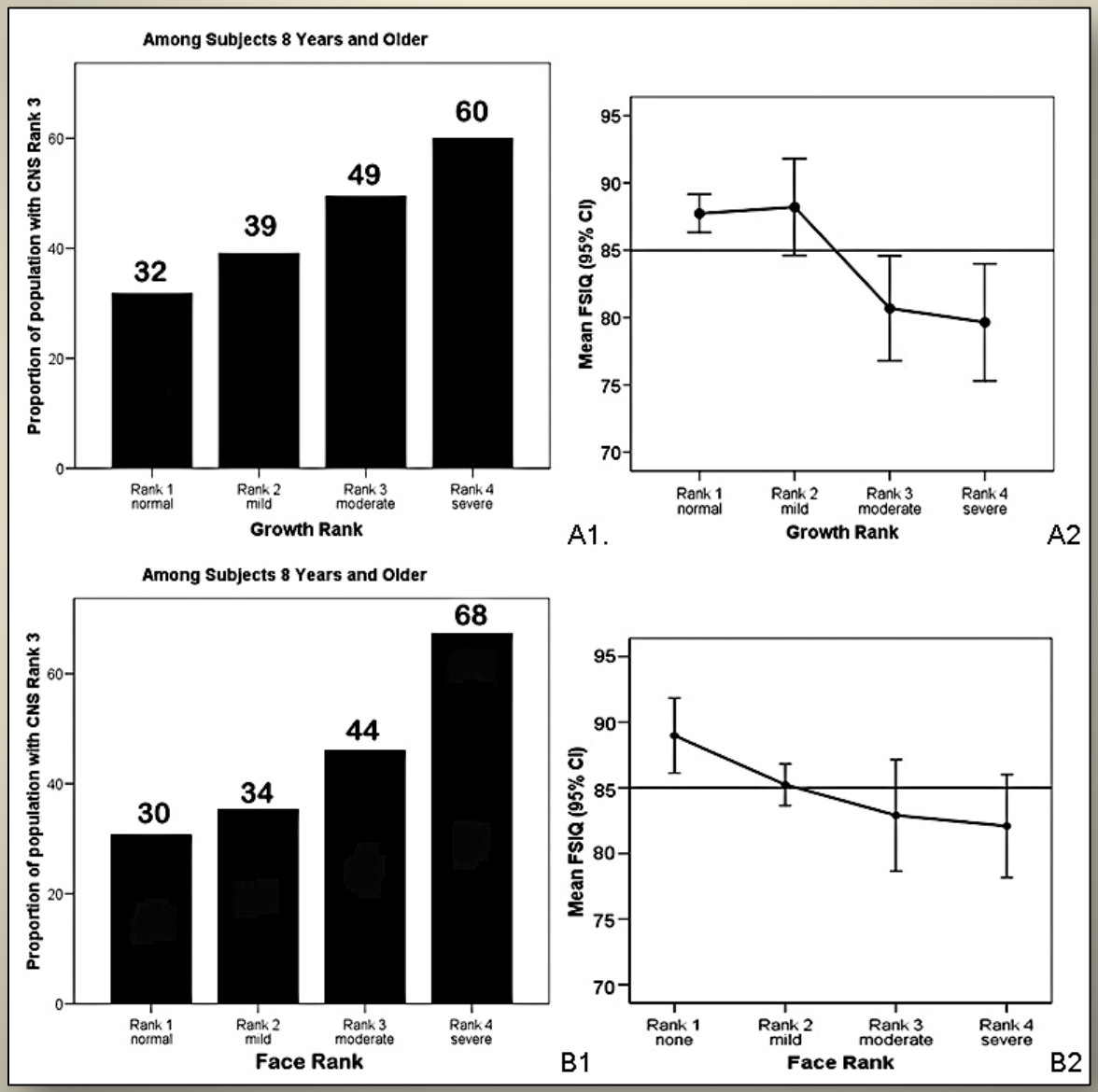
- The prevalence of severe CNS dysfunction (CNS Rank 3) increased significantly and linearly with increasing Growth Deficiency Rank :

	Severe CNS Dysfunction
Growth Rank 1: Normal	32 %
Growth Rank 2: Mild	39 %
Growth Rank 3: Moderate	49 %
Growth Rank 4: Severe	60 %

- The prevalence of severe CNS dysfunction (CNS Rank 3) increased significantly and linearly with increasing Face Rank:

	Severe CNS Dysfunction
Face Rank 1: Normal	30 %
Face Rank 2: Mild	34 %
Face Rank 3: Moderate	44 %
Face Rank 4: Severe FAS	68%

Key Findings: GD is as Highly Correlated with CNS Dysfunction as the FAS Face



Growth

Face

Key Findings: GD is as Predictive of Severe CNS Dysfunction as the 4-Digit FAS Face

Growth Rank is as predictive of severe CNS dysfunction as the 4-Digit Code FAS Face Rank.

- Individuals with Growth Ranks 3 and 4 (height and/or weight ≤ 3rd percentile) had a 2- to 3-fold increased risk for severe CNS dysfunction. This finding was statistically significant.

- Individuals with Face Ranks 3 and 4 (2.5 to all 3 of the FAS facial features) had a 2- to 5-fold increased risk for severe CNS dysfunction. This finding was statistically significant.

- GD was especially powerful in predicting which infants/toddlers with PAE and normal early development presented with severe CNS dysfunction later in childhood.

Key Findings: GD is as Predictive of Severe CNS Dysfunction as the 4-Digit FAS Face

Table 8. Individuals with growth deficiency or facial features were over 2-fold more likely to have severe CNS dysfunction

		Severe CNS Dysfunction CNS Rank 3	Unadjusted		Adjusted for Face or Growth	
	N	n (%)	OR	95% CI	OR	95% CI
Growth Rank						
1	517	162 (31%)	Referent 1.0			
2	96	36 (38%)	1.32	0.84–2.07	1.25	0.79–1.98
3	79	39 (49%)	2.14	1.32–3.45	1.77	1.07–2.91
4	43	24 (56%)	2.77	1.47–5.20	1.96	1.01–3.81
Face Rank						
1	182	52 (29%)	Referent 1.0			
2	439	144 (33%)	1.22	0.84–1.78	1.12	0.76–1.64
3	55	26 (47%)	2.24	1.21–4.16	1.93	1.03–3.63
4	59	39 (66%)	4.88	2.60–9.13	3.82	1.98–7.33

Key Findings: GD is as Predictive of Severe CNS Dysfunction as the 4-Digit FAS Face

Among 46 subjects with two evaluations when they were on average 4 and 10 years of age, respectively,

those with

- growth deficiency,
- FAS facial features, or
- microcephaly

at their 1st diagnostic evaluation

were more likely to present with

- severe CNS dysfunction (CNS Rank 3)

at their 2nd diagnostic evaluation.

Table 9. Infants/toddlers with sentinel physical features were most at risk for severe CNS dysfunction later in childhood†

Sentinel physical feature	CNS Rank increased to Rank 3 at the second diagnostic evaluation	
	No n (%)	Yes n (%)
Growth Rank at first evaluation*		
1 (normal)	18 (54)	15 (46)
2 (mild)	3 (43)	4 (57)
3 (moderate)	1 (33)	2 (67)
4 (severe)	0 (0)	3 (100)
Face Rank at first evaluation**		
1 (normal)	10 (83)	2 (17)
2 (mild)	7 (39)	11 (61)
3 (moderate)	2 (33)	4 (67)
4 (severe)	3 (30)	7 (70)
Microcephaly at first evaluation ***		
Normal OFC	21 (51)	20 (49)
Microcephaly	1 (20)	4 (80)

Key Findings: GD is as Predictive of Severe CNS Dysfunction as the 4-Digit FAS Face

The more sentinel physical features, the greater the risk for severe CNS dysfunction.

Table 10. Prevalence of severe CNS dysfunction among 854 subjects† that presented with sentinel physical features

Sentinel physical feature(s) present	Proportion with CNS Rank 3: severe dysfunction			
	Growth Ranks 2,3,4 Height and/or weight ≤ 10th %		Growth Ranks 3,4 Height and/or weight ≤ 3%	
	%	n	%	n
None	30	153/514	31	182/594
Growth deficiency only	41*	63/153	47*	34/73
Growth and face	56*	20/36	68*	13/19
Growth, face, and microcephaly	67*	18/27	68*	17/25

Key Findings: GD is Highly Correlated, but not Concordant with the FAS Face and Microcephaly

GD is highly correlated, but not highly concordant, with the FAS facial phenotype and microcephaly.

- GD increased significantly with increasing severity of the FAS facial phenotype.
- GD increased significantly with increasing severity of microcephaly.
- Despite these significant correlations, most patients with GD (83% and 71%, respectively) do not have the Rank 4 FAS facial phenotype or microcephaly.

Thus, documenting GD is an essential component of an FASD diagnostic evaluation.

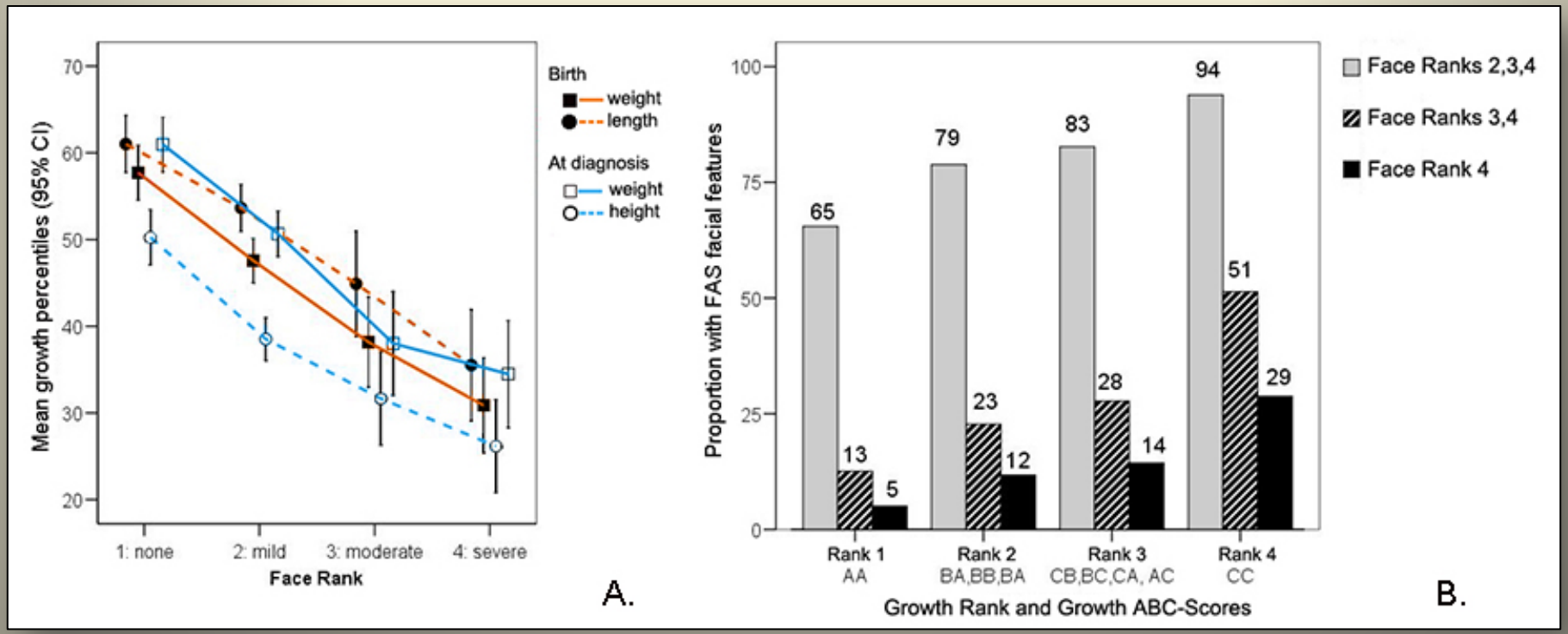
If you not document GD, you would fail to identify the majority of individuals (especially infants/toddlers) at highest risk for severe CNS dysfunction.

Microcephaly and the FAS face may be highly correlated with GD, but they cannot be used in lieu of growth measures to identify all infant/toddlers at risk for severe CNS dysfunction.

Key Findings: GD is Highly Correlated with the 4-Digit FAS Face

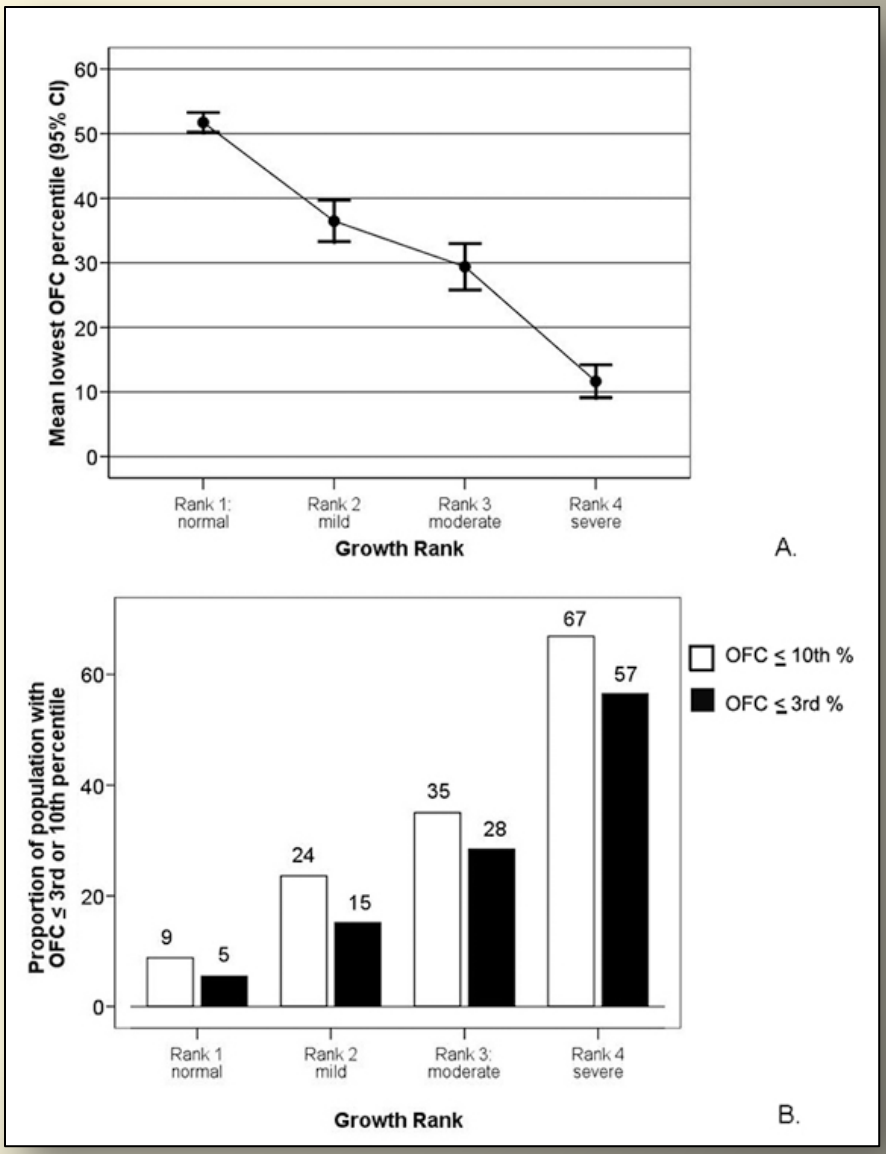
The more severe the growth deficiency,
the more severe the FAS facial phenotype.

<u>Since the 4-Digit FAS face is specific to PAE,
the correlation between the FASD Face and GD
supports PAE as a causal factor for GD.</u>



Key Findings: GD is Highly Correlated with Microcephaly

The more severe the growth deficiency, the smaller the head circumference



Conclusions

The outcomes of this study empirically confirm and illustrate the essential role of GD in the diagnosis of, and early intervention for, FASD. We will continue to include GD as a core diagnostic feature of FASD in the 4-Digit Code for the following reasons:

1. Laboratory studies confirm PAE causes GD. The 4-Digit Code Growth Rank documents GD (postnatal short stature) attributable to PAE.
2. GD is not only prevalent across the full spectrum of FASD; it is as prevalent as the other core diagnostic features (e.g., the FAS facial features and CNS abnormalities).
3. GD is not only highly correlated with severe CNS dysfunction, but is highly predictive of severe CNS dysfunction.

   In fact, GD is so highly predictive of severe CNS dysfunction, it should be used to identify those infants/toddlers with PAE who are at high risk for severe CNS dysfunction, and qualify them for early intervention services – despite apparently normal early development.

Action

Since the discovery of FAS in 1973, GD has been a core diagnostic feature.

Based on the findings of this empirical study and near identical findings published by Carter et al. (2016) we recommend that GD should remain a core diagnostic feature of FASD.

Carter RC, Jacobson JL, Molteno CD, Dodge NC, Meintjes EM, Jacobson SW. Fetal alcohol growth restriction and cognitive impairment. Pediatrics. 2016;138(2):e20160775.

And will remain a core diagnostic feature in the FASD 4-Digit Code