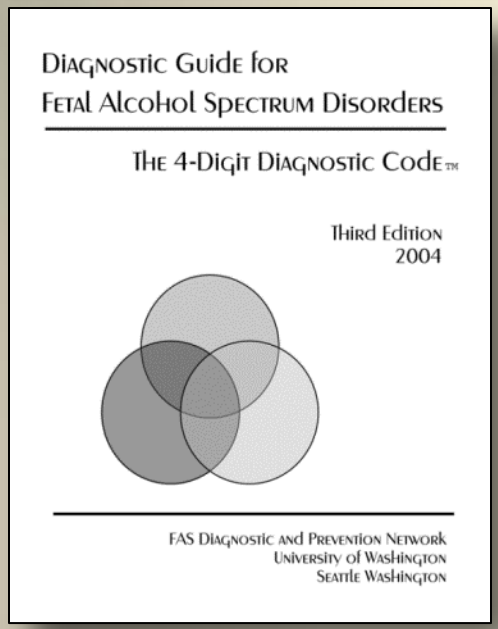
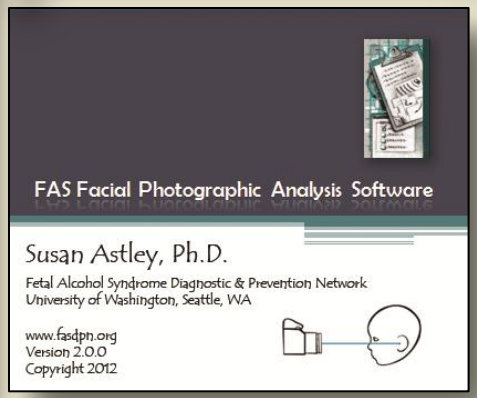
WA State FAS Diagnostic & Prevention Network (fasdpn.org)





Validation of the FASD 4-Digit Diagnostic Code

Susan Astley PhD
Professor Epidemiology/Pediatrics
Director WA FAS DPN
University of Washington
2013

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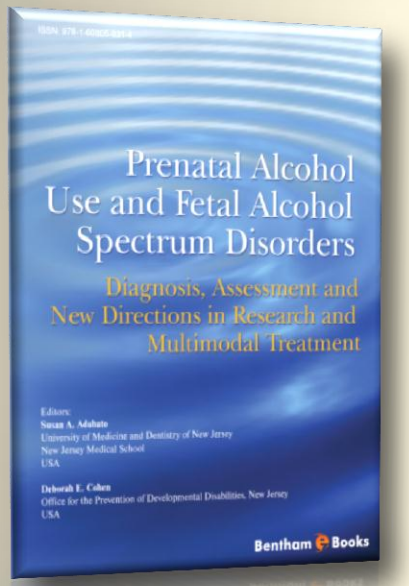
select 'play file' to listen to narration.

Diagnosing FASD: 2011 Chapter[2]



(Submitted for publication in 2009)

CHAPTER 1

Diagnosing Fetal Alcohol Spectrum Disorders (FASD)

Susan. J Astley*

Departments of Epidemiology and Pediatrics, University of Washington, Seattle, Washington, U.S.A.

While we try to teach our children about life, our children teach us what life is all about

Angela Schwindt

Abstract: Fetal Alcohol Syndrome (FAS) is a permanent birth defect syndrome caused by maternal consumption of alcohol during pregnancy. Almost four decades have passed since the term FAS was first coined. The condition is now recognized as a spectrum of disorders: Fetal Alcohol Spectrum Disorders (FASD). Substantial progress has been made in developing specific criteria for delineating diagnoses under the umbrella of FASD. In the 14 years since the publication of the seminal report on FAS by the Institute of Medicine in 1996, clear consensus has been reached on two fundamental issues: 1) an FASD diagnostic evaluation is best conducted by a team of professionals from multiple disciplines (medicine, psychology, speech-language, occupational therapy) and 2) the team should use rigorously case-defined and validated FASD diagnostic guidelines. This chapter will provide a brief overview of the discovery of FASD, diagnostic challenges, how diagnostic guidelines and clinical models have evolved over time to address these challenges, and how new technology may influence the future of FASD diagnosis.

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http://depts.washington.edu/fasdpn/pdfs/astley-FASD-chapter2011.pdf

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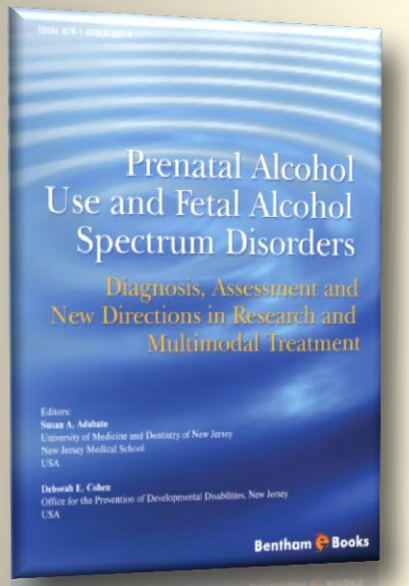

Prenatal Alcohol Use and FASD: Diagnosis, Assessment and New Directions in Research and Multimodal Treatment, 2011, 3-29 3

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CHAPTER 1

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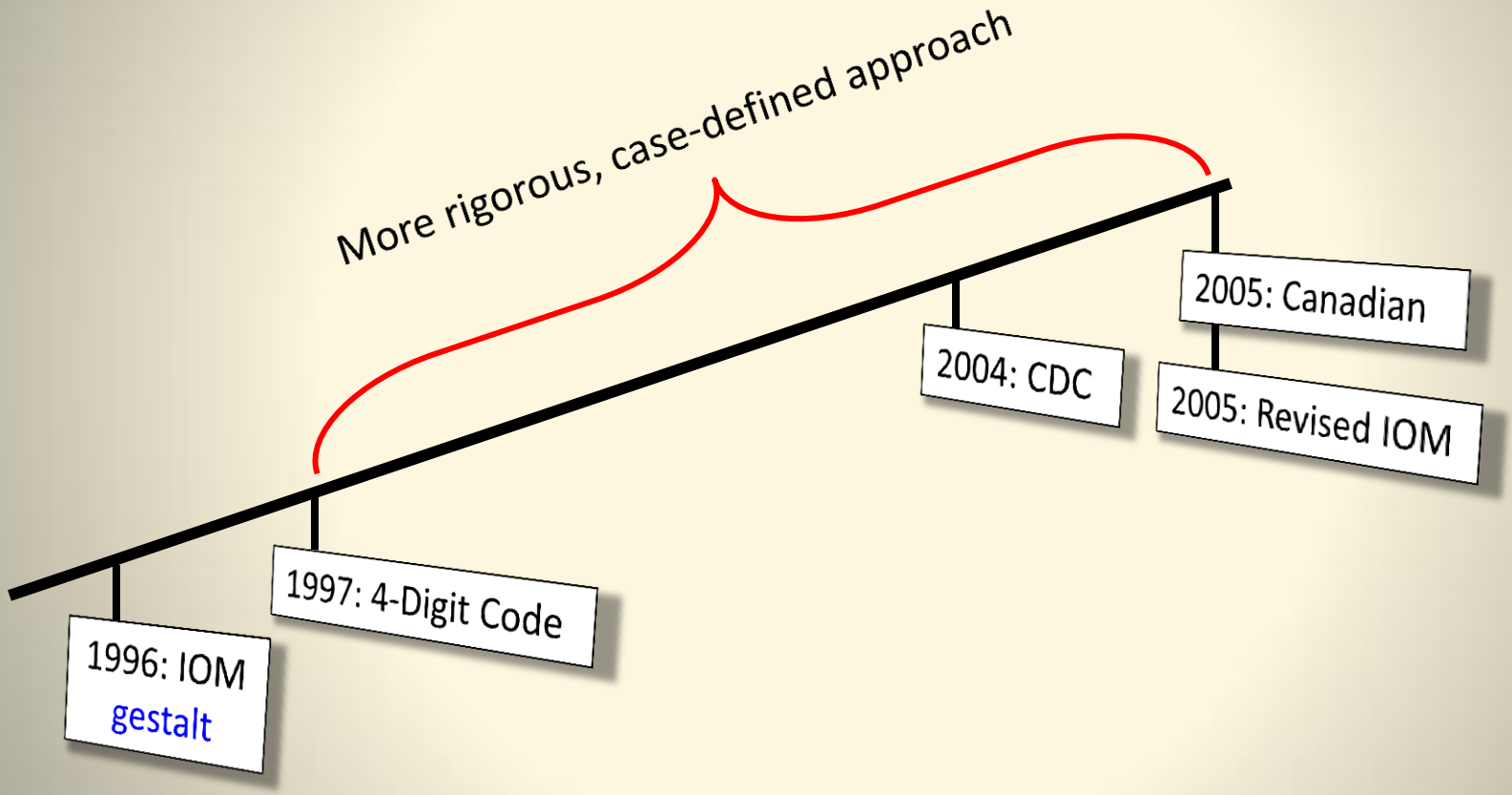
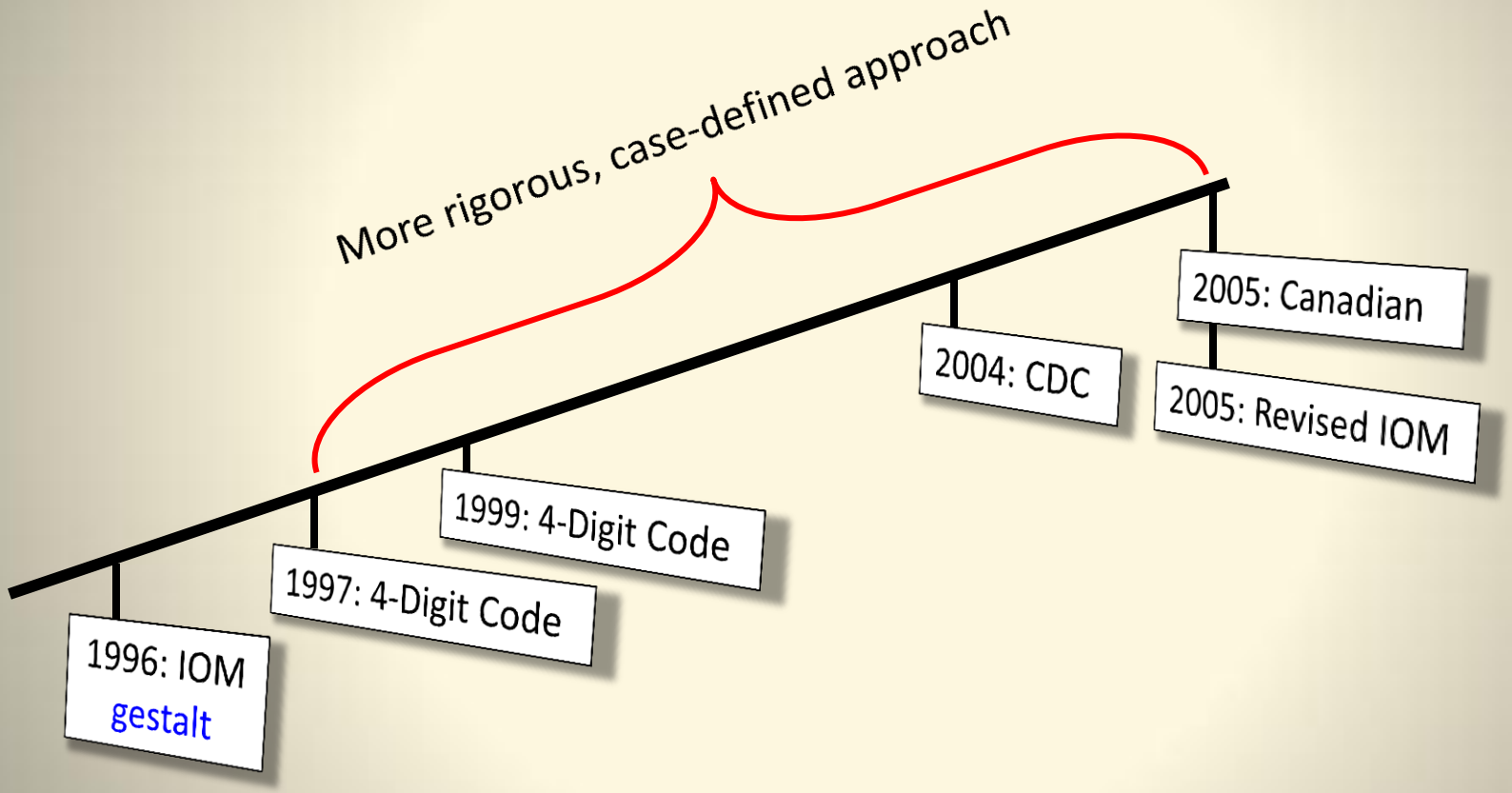
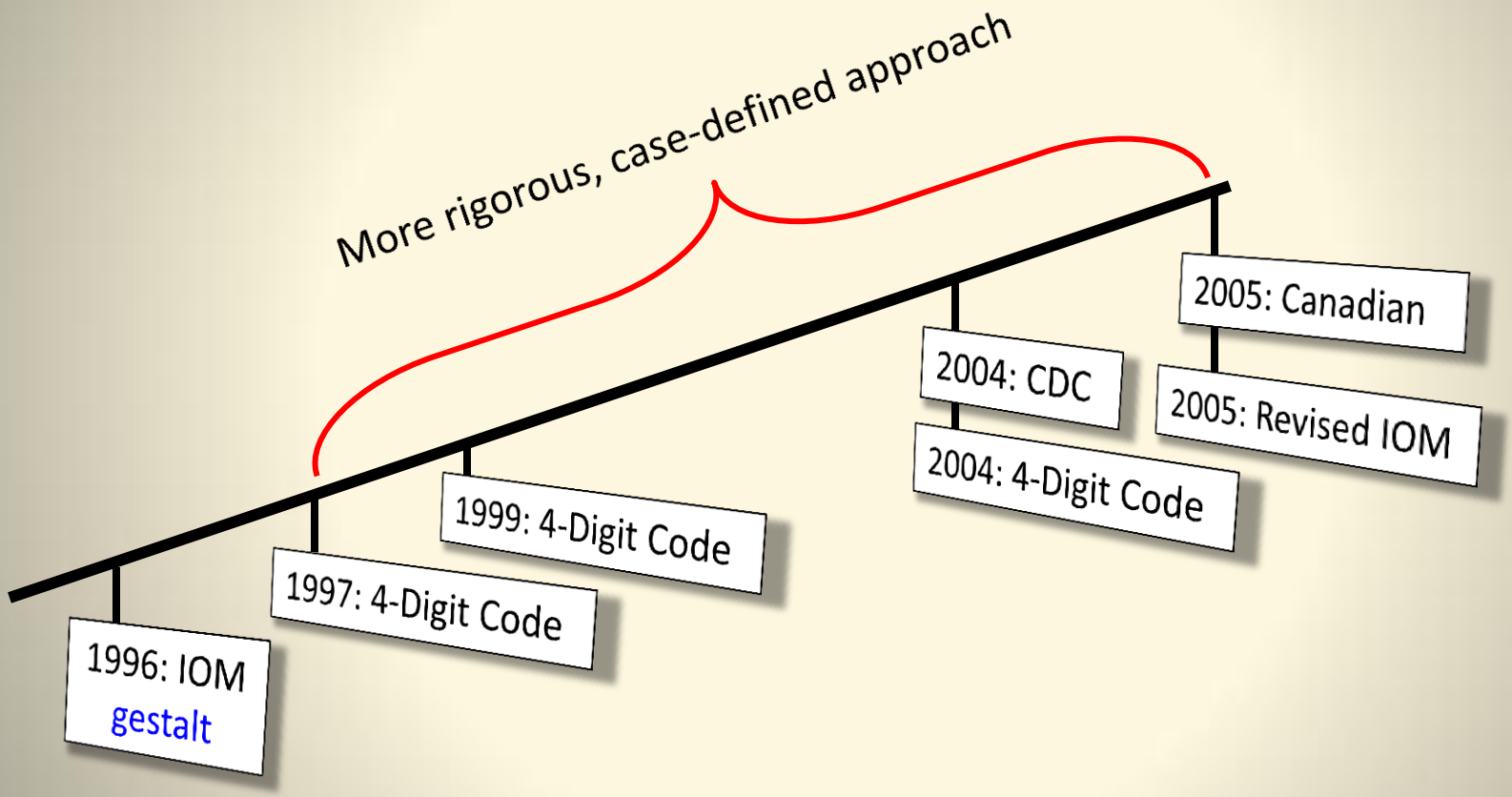
FAS/D Diagnostic Guidelines: Timeline[2]



FAS/D Diagnostic Guidelines: Timeline[2]



FAS/D Diagnostic Guidelines: Timeline[2]



Diagnosing FASD: Chapter (Astley, 2011)[2]

FAS

Table 1. FAS diagnostic criteria: Comparison across the five most current FAS/D diagnostic guidelines.

	4-Digit Code (2004)[38]	CDC (2004) [36]	Canadian (2005) [37]	Hoyme (2005)[19]	IOM (1996)[1]
Growth	Prenatal and/or postnatal height or weight ≤ 10th percentile (Growth Ranks 2-4)	Prenatal and/or postnatal height or weight ≤ 10th percentile (Growth Ranks 2-4)	At least 1 of the following: • Prenatal and/or postnatal height or weight ≤ 10th percentile • Weight-to-height ratio (≤10th percentile) (Growth Ranks 2-4)	Prenatal and/or postnatal height or weight ≤ 10th percentile (Growth Ranks 2-4)	At least 1 of the following: • Low birth weight • Low weight for height • Decelerating weight (Growth Ranks 1-4)
Face	All 3 of the following at any age: • PFL ≤ 3rd percentile • Smooth philtrum Rank 4 or 5 • Thin upper lip Rank 4 or 5 (Face Rank 4)	All 3 of the following: • PFL ≤ 10th percentile • Smooth philtrum Rank 4 or 5 • Thin upper lip Rank 4 or 5 (Face Ranks 3-4)	All 3 of the following at any age: • PFL ≤ 3rd percentile • Smooth philtrum Rank 4 or 5 • Thin upper lip Rank 4 or 5 (Face Rank 4)	2 or more of the following: • PFL ≤ 10th percentile • Smooth philtrum Rank 4 or 5 • Thin upper lip Rank 4 or 5 (Face Ranks 2-4)	Characteristic pattern that includes features such as short PFL, flat upper lip, flattened philtrum, and flat midface. (Face Ranks 1-4)
CNS	At least 1 of the following: • Structural/Neurological: (e.g., OFC ≤ 3rd percentile, abnormal structure, seizure disorder, hard signs) • Severe Dysfunction: (3 or more domains[a] of function with impairment 2 or more SDs below the mean) (CNS Rank 3 and/or 4)	At least 1 of the following: • Structural/Neurological: (e.g., OFC ≤ 10th percentile, abnormal structure, seizure disorder, hard/soft signs) • Dysfunction[b]: ○ 3 or more domains of function with impairment 1 or more SDs below the mean ○ Global deficit (2 or more SDs below the mean) (CNS Ranks 2-4)	At least 3 of the following Structure/Neurological/ Functional domains with impairment[c]: • Hard/soft signs, structure, cognition, communication, academic achievement, memory, executive functioning, abstract reasoning, ADD, adaptive behavior, social skills, or communication (CNS Ranks 3 and/or 4)	At least 1 of the following: • Structural ○ OFC ≤ 10th percentile ○ Abnormal structure (CNS Rank 1 or 4)	At least 1 of the following: • Structural/Neurological: ○ Decreased cranial size at birth ○ Abnormal structure (e.g., microcephaly, partial/complete agenesis of the corpus callosum, cerebellar hypoplasia) ○ Neurological hard/soft signs (CNS Rank 4?)
Alcohol	Confirmed or Unknown (Alcohol Ranks 2,3 or 4)	Confirmed or Unknown (Alcohol Ranks 2,3 or 4)	Confirmed or Unknown (Alcohol Ranks 2,3 or 4)	Confirmed-excessive or Unknown (Alcohol Ranks 2 or 4)	Confirmed-excessive or Unknown (Alcohol Ranks 2 or 4)

Astley

Examples of Contrasts between the Diagnostic Guidelines[2]

An example where the Revised IOM Guidelines differ from the other FASD Diagnostic Guidelines.

Patient Outcomes (10 years old)	
Growth:	Height 10th percentile, weight 95th percentile
Face:	PFL : 10th percentile Philtrum: Somewhat smooth, Rank 4 Upper Lip: Thick, Rank 1
CNS:	OFC 10th percentile, IQ 100, No evidence of dysfunction
Alcohol:	Unknown
Diagnostic Classifications	
IOM:	Unable to classify. Not sufficiently case-defined
4-Digit Code:	Not FASD, Code 2212
Canadian:	Not FASD
CDC:	Not FAS
Revised IOM:	FAS / Alcohol Unknown

Examples of Contrasts between the Diagnostic Systems[2]

An example where the Canadian Guidelines differ from the other FASD Diagnostic Guidelines.

Patient Outcomes (2 years old)	
Growth	Height 1st percentile, weight 1st percentile
Face	PFL: 1st percentile Philtrum: Smooth, Rank 5 Upper Lip: Thin, Rank 5
CNS	OFC 1st percentile, BSID outcomes low-normal
Alcohol	Intoxicated weekly throughout pregnancy
Diagnostic Classifications	
IOM	FAS/PFAS
4-Digit Code	FAS / Alcohol Exposed (Code = 4444)
Canadian	Not FASD
CDC	FAS / Alcohol Exposed
Revised IOM	FAS / Alcohol Exposed

Examples of Contrasts between the Diagnostic Systems[2]

An example where the 4-Digit Code differs from the other FASD Diagnostic Guidelines.

Patient Outcomes (10 years old)	
Growth	Height 50th percentile, weight 50th percentile
Face	PFL: Normal, 50th percentile Philtrum: Normal, Rank 2 Upper lip: Normal, Rank 2
CNS	2 Domains of significant dysfunction (ADHD, Memory) No CNS structural or neurological abnormalities.
Alcohol	Binge drinking weekly throughout pregnancy.
Diagnostic Classifications	
IOM	Not FASD
4-Digit Code	Neurobehavioral Disorder/Alcohol Exposed (Code = 1124)
Canadian	Not FASD
CDC	Not FAS
Revised IOM	Not FASD

Validation

How well an instrument measures what it purports to measure.

The performance (validity)

of a FASD Diagnostic System

must be rigorously assessed, *not assumed*.

As you assess the performance of FASD Diagnostic Guidelines, ask the following questions:

1. Have properly designed studies been published to confirm the FAS Face is highly specific (>95%) to FAS and alcohol (e.g. observed only among individuals with prenatal alcohol exposure and FAS)?

2. Were data used to empirically derive the diagnostic guidelines? Was the data drawn from a large, representative population base?

3. Individuals are born with FAS/D. Can the diagnostic system identify FAS/D at birth and across the lifespan?

4. Growth, face, brain, and alcohol exposure all present along clinically meaningful continuums. The FAS face is not just present or absent. The brain is not just normal or abnormal. Do the Guidelines recognize/incorporate these important continuums?

5. Do the guidelines produce clinically distinct subgroups across the full spectrum (FAS, PFAS, SE/AE, ND/AE)?
   A. Do MRI studies identify statistically significant contrasts between the FASD subgroups?
   B. Individuals with FAS have more severe CNS dysfunction than individuals with "ARND". Do the Guidelines generate FAS and "ARND" groups that demonstrate this important contrast?
   C. Do individuals who meet the criteria for FAS actually have FAS?

6. Can the guidelines detect unique alcohol exposure patterns between the FASD subgroups?

7. Are the guidelines confirmed to be reproducible? If two clinics use the guidelines, do they render the same diagnoses?

8. Do families report high satisfaction/confidence with the diagnostic process/outcome?

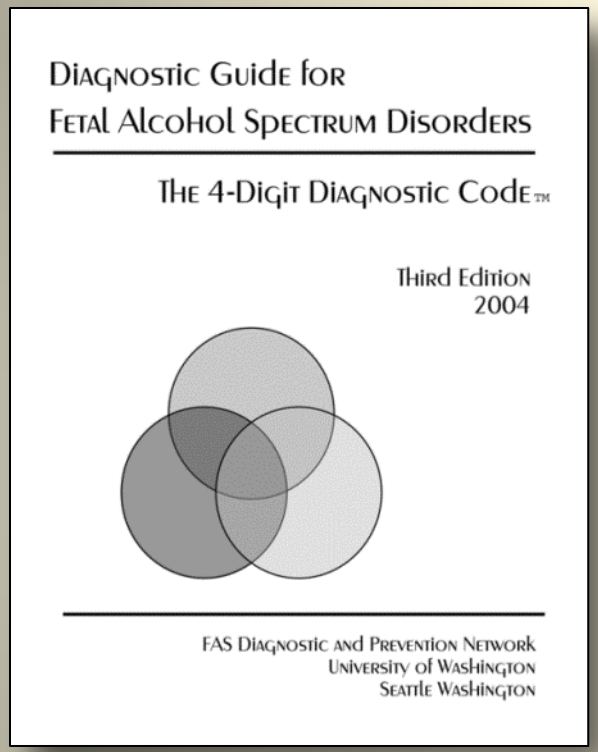
9. Do diagnoses under the umbrella of FASD qualify patients for intervention services that lead to improved outcomes?

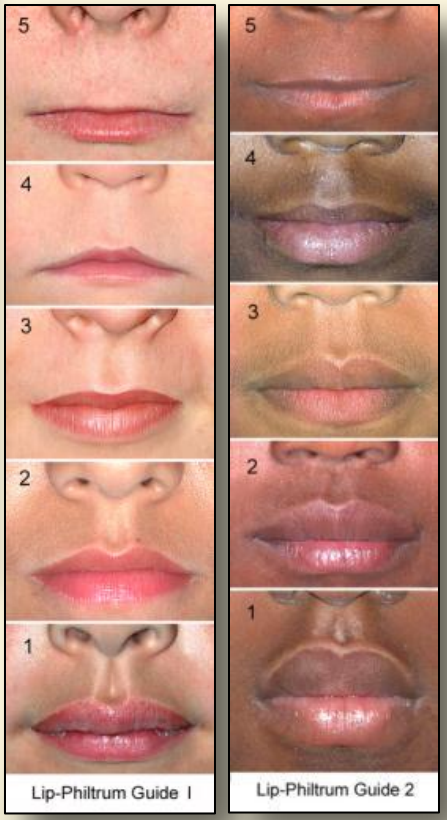
The answers to all of these questions are YES for the 4-Digit Code[1-18].

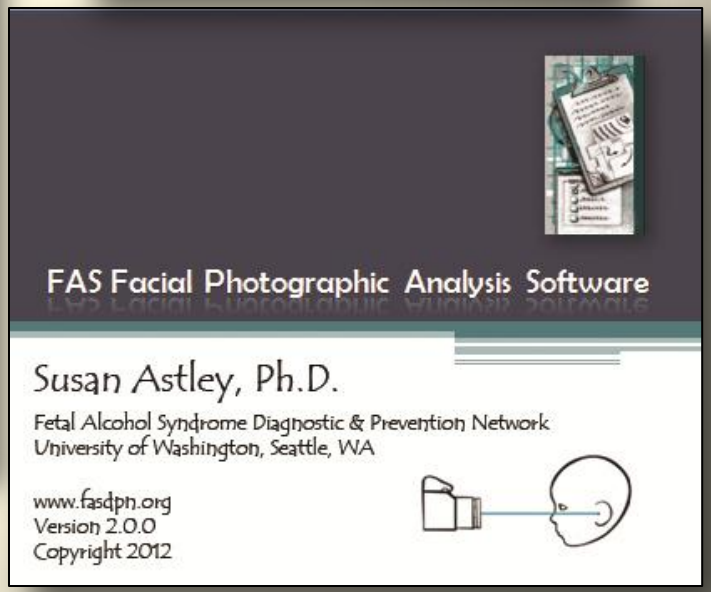
Astley

Introduction to the FASD 4-Digit Code

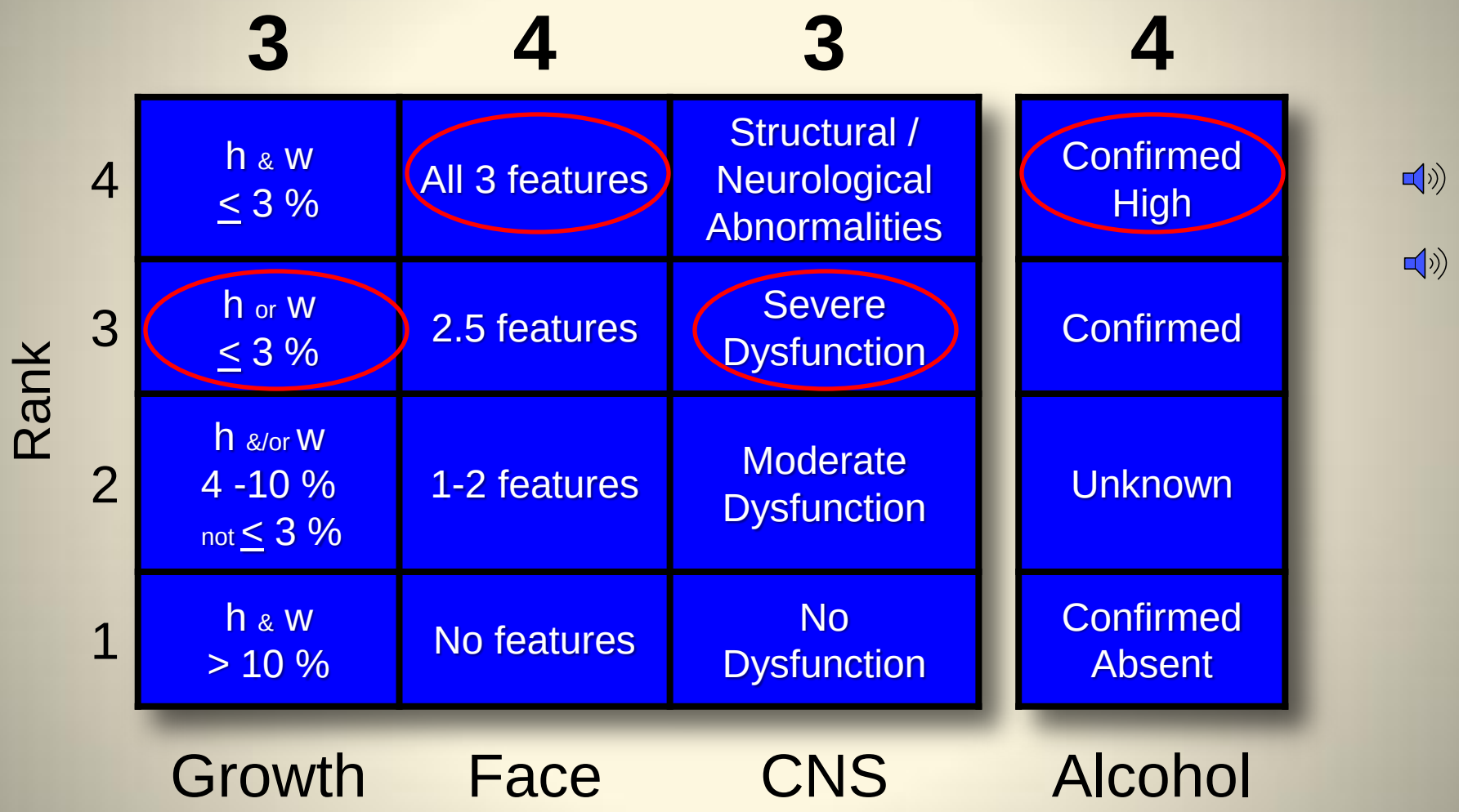
FASD 4-Digit Diagnostic Code[11,18]







Abbreviated Case-Definitions of 4-Digit Code[11]



3434 is one of twelve 4-Digit Codes for FAS

Astley

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

4-Digit Code produces FOUR Diagnostic Subgroups[3]

Diagnosis		Growth	FAS Face	CNS		Alcohol
1. FAS	Fetal Alcohol Syndrome	growth	face	severe		alc
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

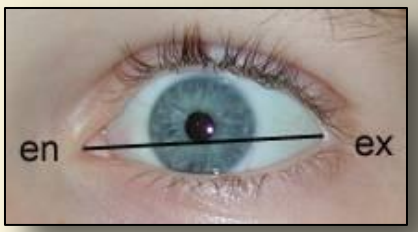
4-Digit Code produces FOUR Diagnostic Subgroups[3]

Diagnosis		Growth	FAS Face	CNS		Alcohol
1. FAS	Fetal Alcohol Syndrome	growth	face	severe		alc
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

SE/AE = severe “ARND”
ND/AE = moderate “ARND”

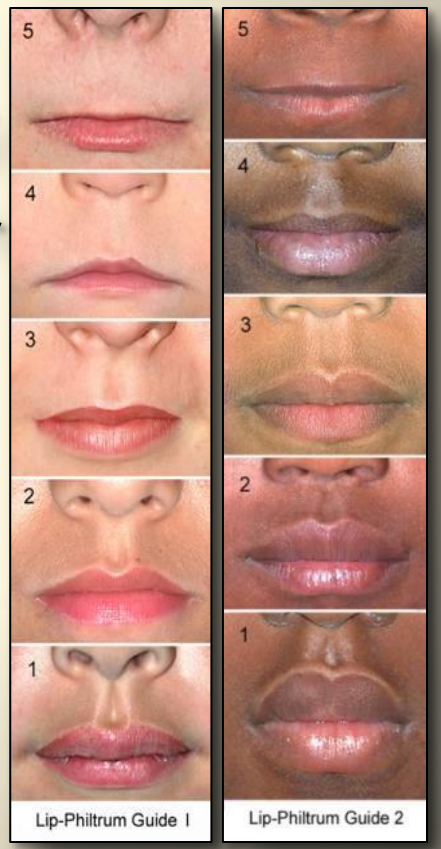
4-Digit Code FAS Face (Rank 4)[11-13]

1)	Short PFL	≤ -2 SD
2)	Smooth Philtrum	Rank 4 or 5
3)	Thin Upper Lip	Rank 4 or 5



Palpebral fissure length (PFL) = endocanthion to exocanthion

FAS



The 4-Digit Code Used Worldwide for 16 years .

The University of Washington FASDPN has trained[18]:

- 144 diagnostic teams from 16 countries
- 4,864 professionals have completed the Seattle 1-day clinic observation training.
- 731 professionals worldwide have completed the FASD 4-Digit Diagnostic Code Online Course.

The Code is simple to use and understand[1-3]:

- 86% of families report it is easy to understand.
- 93% of professionals describe it as clear.
- 99% of professionals report they would recommend it to others.

All Diagnostic tools are distributed for free or at cost[18].

- 4,642 Diagnostic Guides (hard copy) and 635 Facial Software distributed to date.
- > 10,000 Diagnostic Guides (pdf) downloaded for free.
- Instructional videos/animations posted on fasdpn.org

Validation of the FASD 4-Digit Code

The 4-Digit Code is a simple, comprehensive, evidence-based, validated diagnostic system.

The performance of the 4-Digit Code was validated before it was published in 1997 and continues to be extensively assessed (validated) to this day.

Before Publication in 1997:

1. The FAS facial phenotype was empirically case-defined. Sensitivity and specificity confirmed to be >95% across race and age by direct and 2D photographic measurement[12,13].
2. The Code itself was tested in the FASD clinic on 1,014 patients over 4 years before it was released[10].

After Publication in 1997:

Performance extensively assessed (validated) over 20 years on over 7,000 patients and research subjects.

1. MRI/fMRI/MRS studies confirm brains of FAS/PFAS, SE/AE, and ND/AE are clinically distinct[6-9].
2. 10-year Foster Care FAS Screening Program confirms FAS can be accurately screened from a 2D digital facial photograph (>95% screened with a Rank 4 FAS facial photograph received a diagnosis of FAS)[15,16].
3. Analysis of 2,550 patients confirms: face predicts brain; diagnoses have unique alcohol exposure patterns; FAS can be diagnosed at birth; stable homes lead to better outcomes, and growth, face, brain and alcohol all present along clinically important continuums[1-17].
4. Diagnostic reproducibility > 93% for 677 patients diagnosed by the WA FASD Clinics over 18 years[1-3].
5. Patient satisfaction surveys over 20 years reveal : 86% report the 4-Digit Code is easy to understand, 89% report it allows them to better understand and meet their child's needs . 86% report access to effective interventions is equally high across all diagnostic subgroups FAS, SE/AE, and ND/AE . 99% of families report they would recommend the interdisciplinary FASD clinic to other families[1-3].

Validation Publications: Astley (1995 1996 1999 2000 2001 2006 2009a 2009b 2009c 2009d 2010 2010a 2010b 2011 2012 2013)

Evidence Validating the Performance of the FASD 4-Digit Code[1-18]

1. The Rank 4 FAS Face:
   A. Is confirmed to be highly specific (>95%) to FAS and alcohol[12,13,15].
   B. Is uniquely correlated with significantly smaller frontal lobes and lower choline levels[7,8].
   C. Serves as the most efficient/effective way to screen for FAS in population-based samples[15,16]

2. The Facial Phenotype:
   A. Presents on a continuum that is significantly correlated with (predictive of) abnormal brain structure and function[1-18].
   B. Can be measured easily and accurately from a 2-D photo using the FAS Facial Photographic Analysis Software[13,15].
   C. Presents across all races and ages and does not diminish with age [3, 12,13].

3. The 4-Digit Code method for Ranking brain dysfunction correlates with underlying brain structure.
   A. The more severe the CNS dysfunction Rank (1,2,3), the smaller the caudate[3,7].

4. The diagnoses FAS/PFAS, SE/AE, and ND/AE are clinically and statistically distinct[1-18] .
   A. Only FAS/PFAS have the FAS face, small frontal lobes, reduced choline[3,7,8].
   B. Only FAS/PFAS and SE/AE have small caudates[3,8.]
   C. FAS/PFAS have more severe CNS dysfunction than SE/AE[3,6].
   D. ND/AE have CNS structural abnormalities underlying their moderate CNS dysfunction[3,7].
   E. Even families detect/report clear distinctions between the diagnostic subgroups[1-3].

5. Alcohol exposure patterns differ between diagnostic subgroups.
   A. Exposure patterns among FAS/PFAS distinct from SE/AE and ND/AE[1-3].

6. The 4-Digit Code is reproducible across clinics. Of 677 patients diagnosed at the 5 WA FASD Clinics, >93% received a diagnosis that matched the diagnosis rendered by the Seattle Clinic[1,3].

7. Patient surveys over 18 years confirm the diagnostic subgroups FAS/PFAS, SE/AE, ND/AE provide equal access to effective interventions, confirming the term ARND (that inappropriately implies a causal link with alcohol) is unnecessary[1].

Initial Evidence of Improved Performance[10] 4-Digit Code vs Gestalt (1997)

First 454 patients in FAS DPN diagnosed by both Gestalt Method and 4-Digit Code:

Gestalt method of diagnosis produced a highly variable FAS group.

69 patients received a gestalt diagnosis of FAS.

In the absence of rigorous guidelines, this group was very heterogeneous.

Of the 69 subjects with a gestalt diagnosis of FAS:

- only 32 had growth deficiency ($\leq 10^{th}$ percentile).
- only 27 had the Rank 4 FAS face.
- only 40 had significant CNS structural/functional abnormalities.

When the more rigorous 4-Digit Code was applied to the 69 with Gestalt FAS:

- Only 9 of the 69 retained a diagnosis of FAS.
- 12 were reclassified to PFAS
- 18 were reclassified to Static Encephalopathy /Alcohol Exposed
- 26 were reclassified to Neurobehavioral Disorder / Alcohol Exposed
- 4 were not even on the spectrum (exposure unknown)

Correlations that should be detected between growth, face, brain, and alcohol:

- Were totally absent when gestalt method was used.
- Were strongly significant when 4-Digit Code was used.

The Quintessential Role of the FAS Facial Phenotype

4-Digit Code (Rank 4) FAS Face is highly specific to FAS/Alcohol

Rank 4 FAS Facial Phenotype

Short PFL	≤ -2 SD (≤ 2%)
Smooth Philtrum	Rank 4 or 5
Thin Upper Lip	Rank 4 or 5

F
A
S

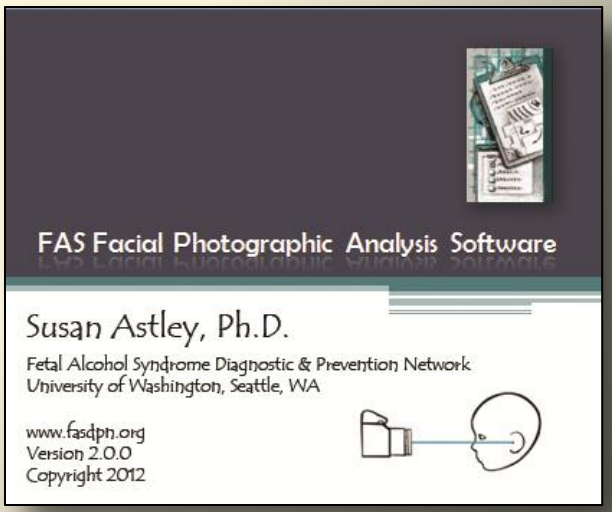
1. The Rank 4 FAS Facial Phenotype is > 95% specific to prenatal alcohol exposure and FAS[12,13]:
   - This high specificity is the only reason a diagnosis of FAS (alc unknown) can be made! The Rank 4 face is the only FAS facial phenotype specific enough to alcohol exposure to serve as the confirmation of exposure[2].
   - The Rank 4 face is so specific to FAS, it alone can be used to screen for FAS (as demonstrated in a 10-yr FAS screening of foster care in Seattle)[15,16].
2. The Rank 4 FAS Face has never been observed in a child with confirmed absence of prenatal alcohol exposure[1,3].
3. The Rank 4 FAS face was derived empirically through scientific studies, not just clinical opinion[12,13].
4. When these facial criteria are relaxed, the face is no longer specific to FAS and alcohol. If it is not specific to alcohol, a valid diagnosis of FAS (alcohol unknown) cannot be made[4].

10-Year Foster Care FAS Screening using 2D Photos

10-Year Photo screening confirmed Rank 4 FAS face is HIGHLY specific.

- > 95% of children with Rank 4 FAS face had FAS.
- 1 out of every 100 children in foster care had FAS.

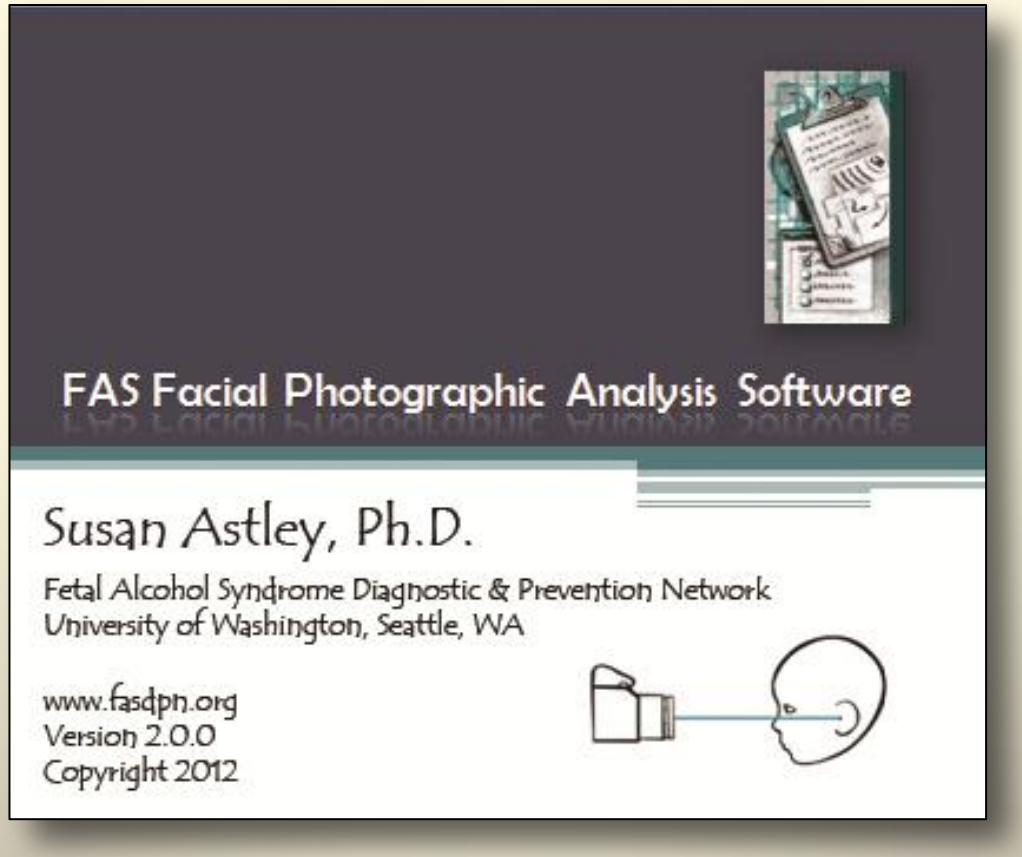
(2,500 foster children screened over 10 years with 98% participation rate.)



FAS Facial Software: Used to screen and diagnose facial features

$60 software, >10,000 2D photos measured since 2004

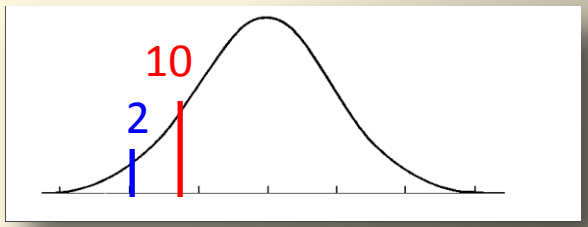
Click here for video demonstration of the software



Evidence that the FAS PFL criteria should be kept at 2%, not relaxed to 10%

Feldman et al., 2012 (Study of 922 subjects)

- 1st trimester alcohol exposure correlated with smooth philtrum and thin upper lip.
- No pattern of prenatal alcohol exposure correlated with a PFL ≤ 10%. (the authors noted this was an unexpected finding).



Astley (Study of 1,400 subjects)[1]

- When the definition of a "short" PFL was relaxed to ≤ 10%, NO correlations were found with any pattern of prenatal alcohol exposure.
- When the definition of a "short" PFL was strengthened to ≤ 2%, Strong, significant correlations were found with many patterns of alcohol exposure (1st trimester, binge, 5 days/wk).

Evidence that the FAS Facial criteria require all 3 features, not just 2 of the 3

The Revised-IOM criteria for the "FAS face"

- relaxed the PFL to the 10th percentile and
- requires only 2 of the 3 facial features be present.

A 2006 study [4] confirmed these relaxations in the 4-Digit Code criteria rendered the Revised-IOM FAS facial phenotype non-specific to FAS and prenatal alcohol exposure.

When the Revised-IOM FAS facial criteria were applied to a population of:

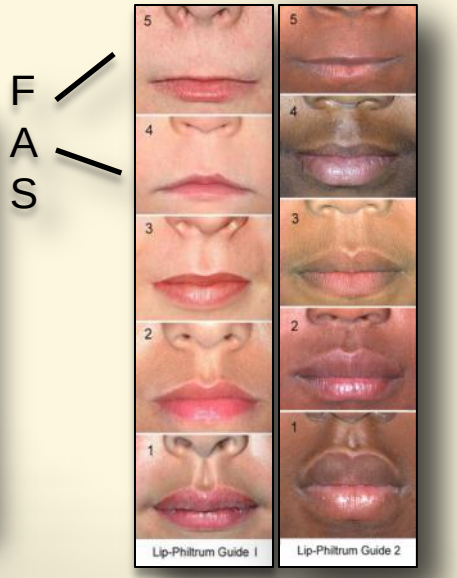
- Healthy, high functioning children (mean IQ = 120)
- With confirmed absence of prenatal alcohol exposure.

25% met the Revised-IOM criteria for the full FAS facial phenotype.

FAS Face: 4-Digit Code (Rank 4) vs Revised IOM[4]

4-Digit Code (Rank 4) FAS Face

1)	Short PFL	≤ -2 SD (≤ 2 %)
2)	Smooth Philtrum	Rank 4 or 5
3)	Thin Upper Lip	Rank 4 or 5



Revised IOM FAS Face

When the facial criteria are relaxed:

- PFL ≤ 10%
- And only 2 of 3 features required

The phenotype moves well into the normal range (both in definition and appearance) and is no longer specific to FAS or alcohol.

Example of a healthy, normal child (IQ 105) with confirmed absence of prenatal alcohol exposure who meets the Revised IOM criteria for the FAS face.

PFL 5%, Philtrum Rank 4, Lip Rank 1

The Quintessential Role of the FAS Facial Phenotype[1-3]

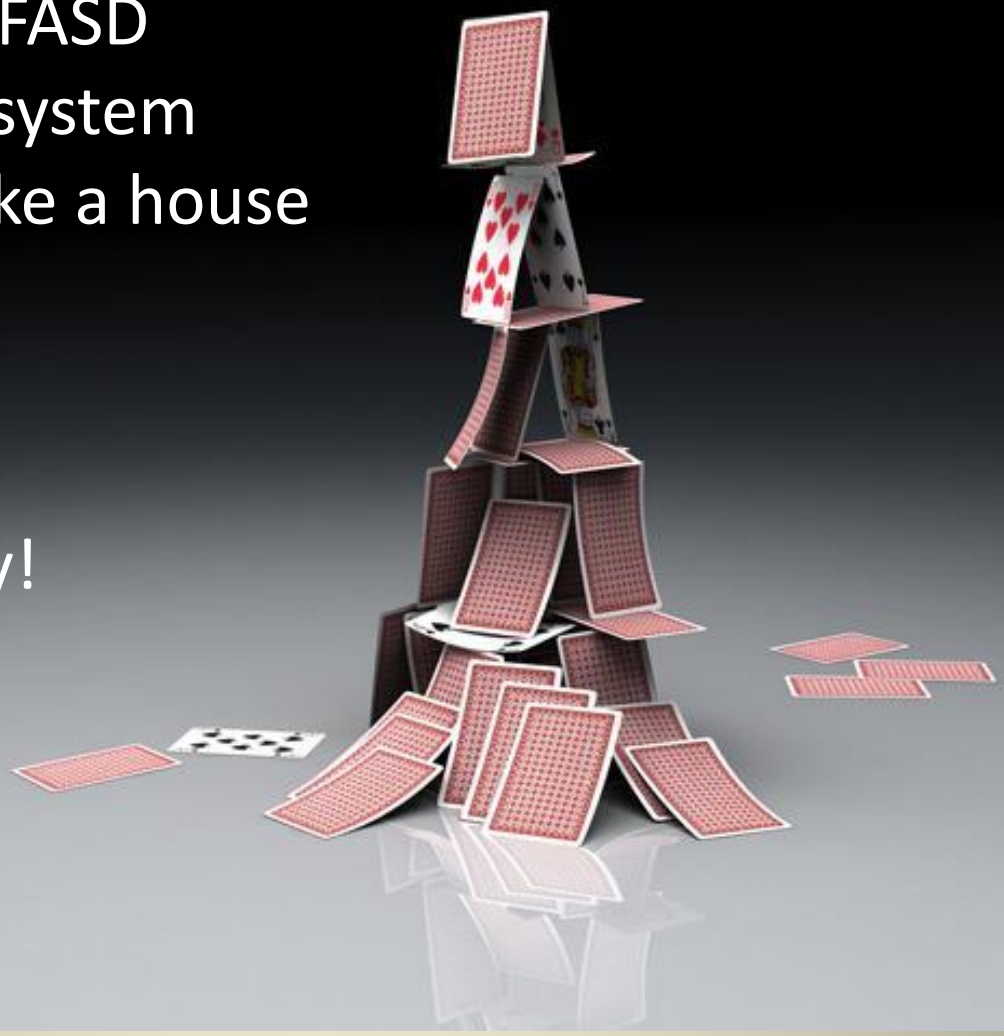
Why are the criteria used to define the FAS facial phenotype
so important to the medical validity of **all** diagnoses under the umbrella of FASD,
not just the diagnosis of FAS?

- When one makes a diagnosis of FAS, one is stating implicitly that the individual has a syndrome caused by prenatal alcohol exposure.
- One is also stating implicitly that the biological mother drank alcohol during pregnancy and, as a result, harmed her child.
- These are bold conclusions to draw and are not without medical, ethical, and even legal consequences.

What happens when the FAS face is not Specific to FAS and Prenatal Alcohol Exposure?

The whole FASD diagnostic system collapses like a house of cards.

Here is why!



The Quintessential Role of the FAS Facial Phenotype[1]

If the FAS Facial Phenotype is not CONFIRMED to be at least 95% specific to FAS and alcohol exposure the entire FASD diagnostic system breaks down.

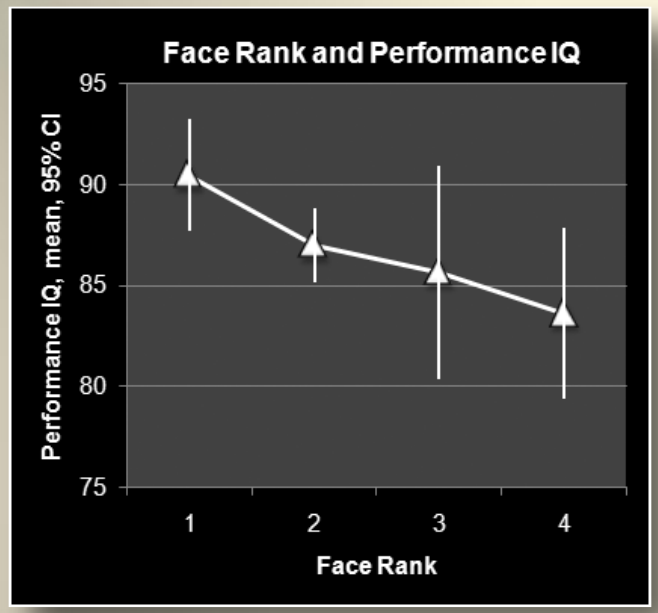
1. The term (FAS) is rendered invalid.
   If the face is NOT specific to (caused only by) alcohol, you can no longer call the condition FAS. You can no longer confirm alcohol is causally linked to any of the outcomes (growth, brain, OR FACE) in an individual patient.

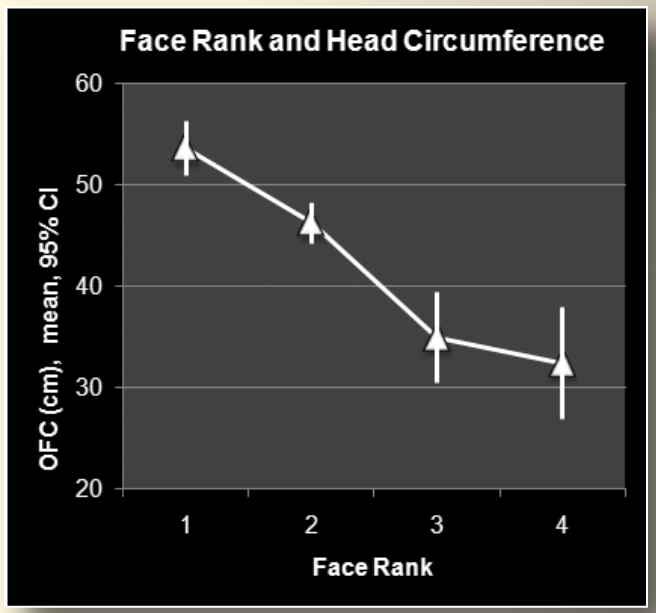
2. The diagnosis (FAS/alcohol exposure unknown) is also rendered invalid.
   The FAS face can no longer serve as the confirmation of alcohol exposure when the exposure history is unknown.

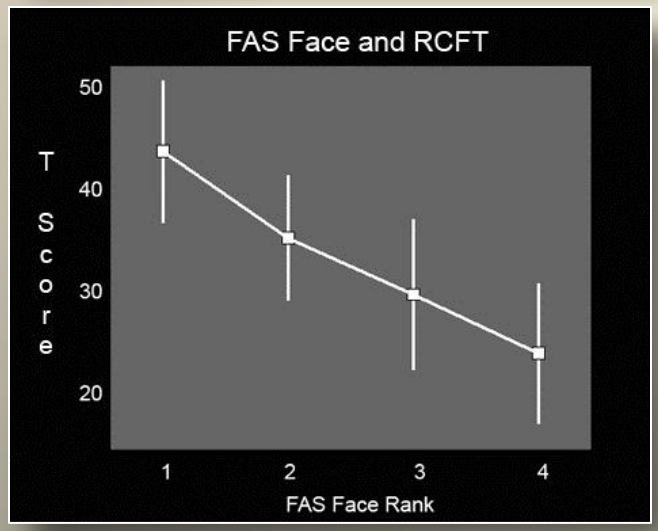
3. FAS is no longer distinct from ARND.
   ARND is "FAS without the face". But if there is no FAS face, there is no distinction between FAS and ARND. Thus, one can no longer justify classifying FAS and ARND separately.

4. The term "ARND" remains invalid.
   Since ARND has no feature specific to prenatal alcohol, you are in no position to declare the Neurodevelopmental Disorder is "Alcohol-Related" (ARND) in an individual patient.

Strong correlations between the 4-Digit FAS Face and brain support the validity of the 4-Digit Code FAS Facial Phenotype[1-18]



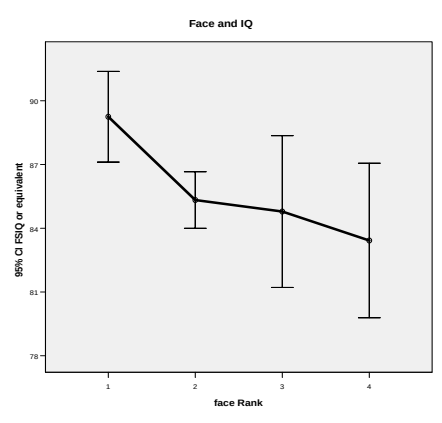




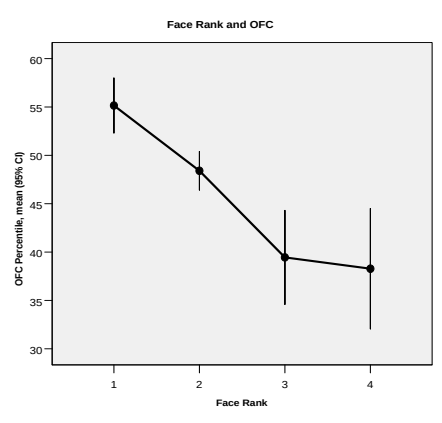
- The FAS facial phenotype presents along a <u>clinically meaningful continuum</u>. It is not simply present or absent.
- The more severe the FAS face, the more severe the CNS structural/functional abnormality.

The more severe the 4-Digit Code FAS face,
the more severe the abnormalities in brain structure, function, even development[1-3,7,14].

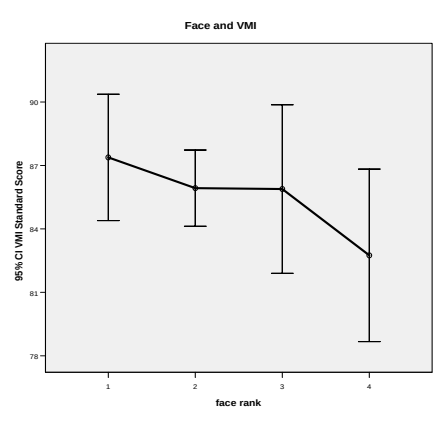
The more severe the FAS face….



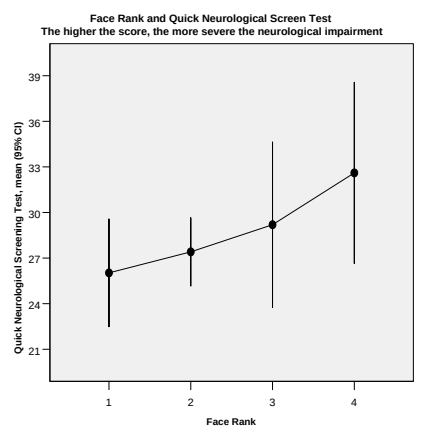
the lower the IQ



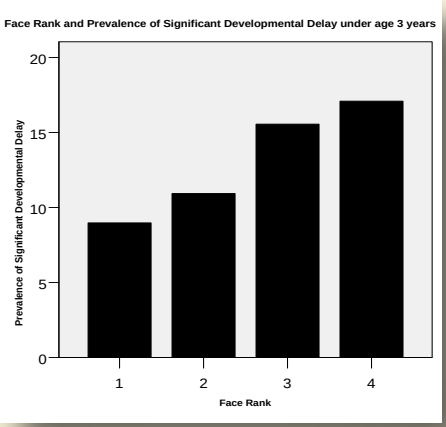
the smaller the OFC



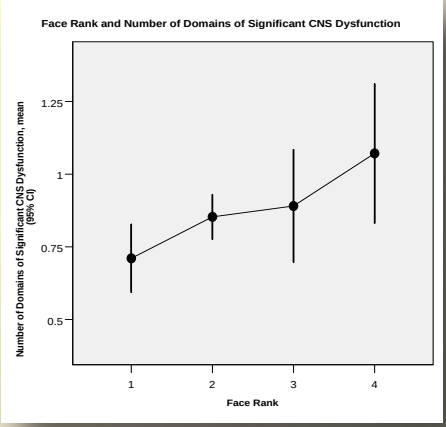
the greater the impairment in visual motor integration



the greater the neurological impairment

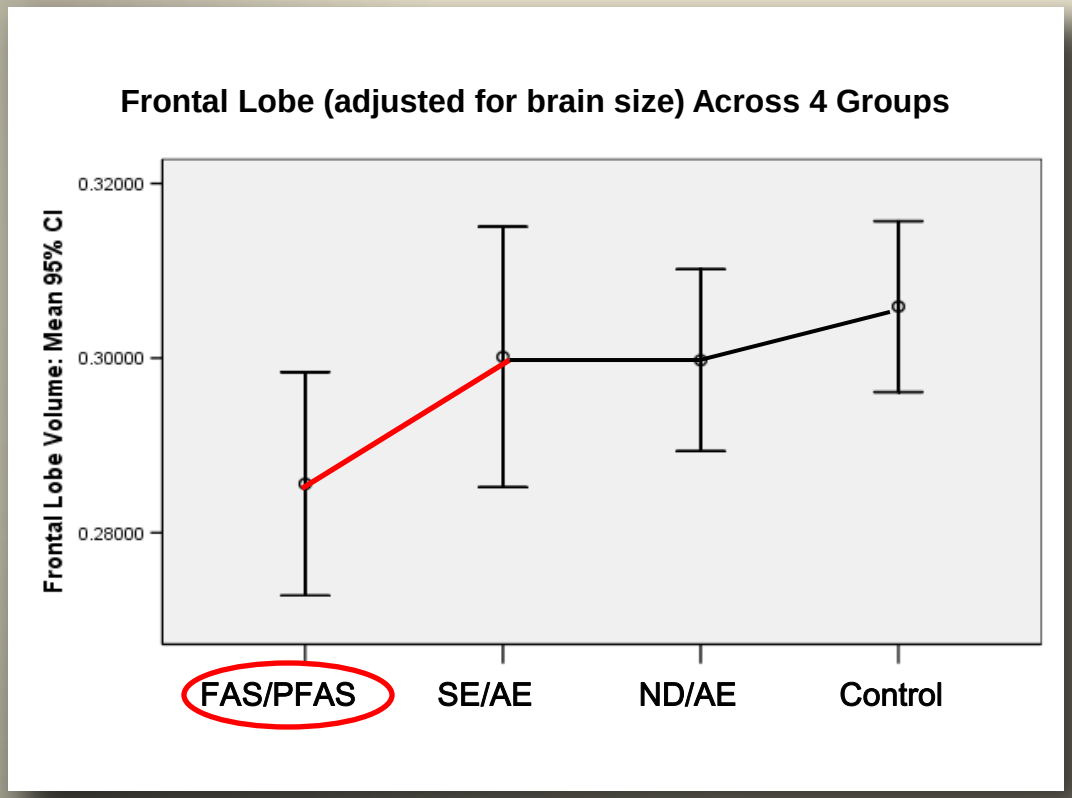


the higher the prevalence of developmental delay under age 3

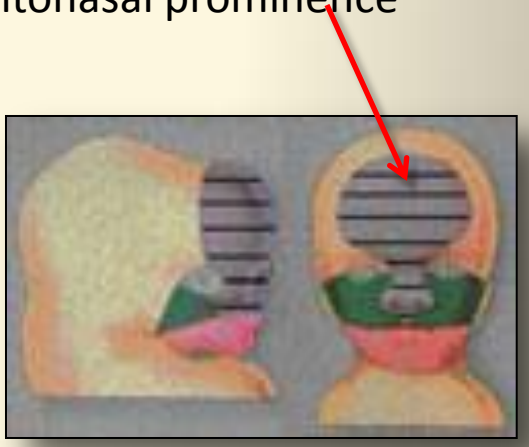


the more domains of significant dysfunction

Only those with the Rank 4 FAS Face have Disproportionately Smaller Frontal Lobe Volumes[1-3,7]

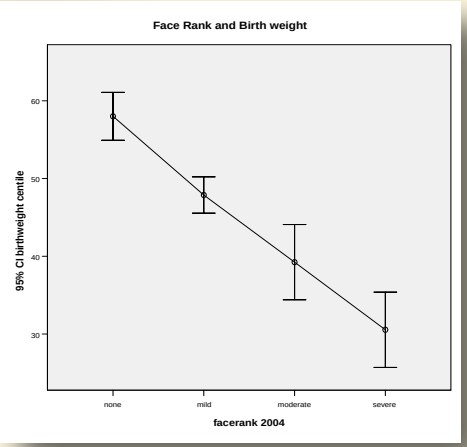


This is particularly compelling since the morphogenesis of the middle and upper face is heavily influenced by signals emanating from the forebrain to the frontonasal prominence

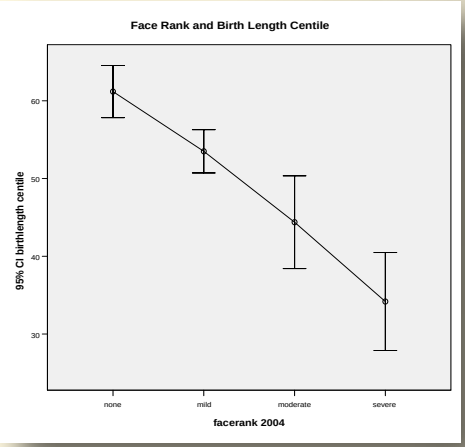


The more severe the 4-Digit Code FAS face, the more severe the Growth Deficiency[1]

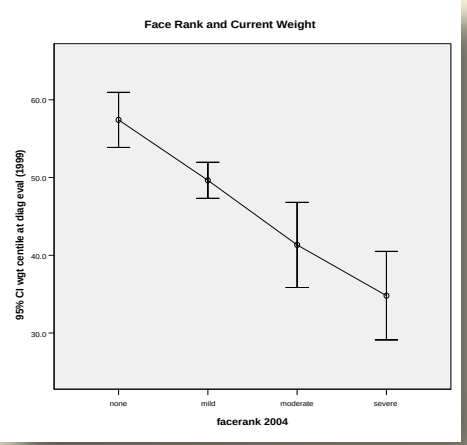
The more severe the FAS face



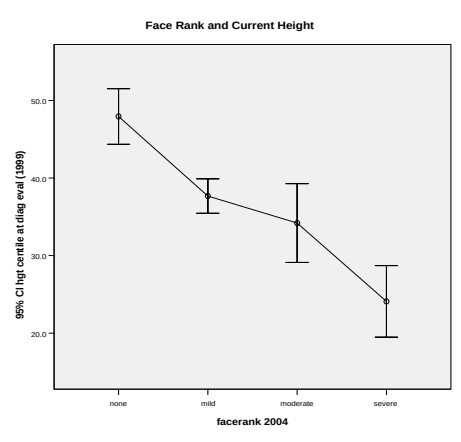
the lower the birth weight



the lower the birth length



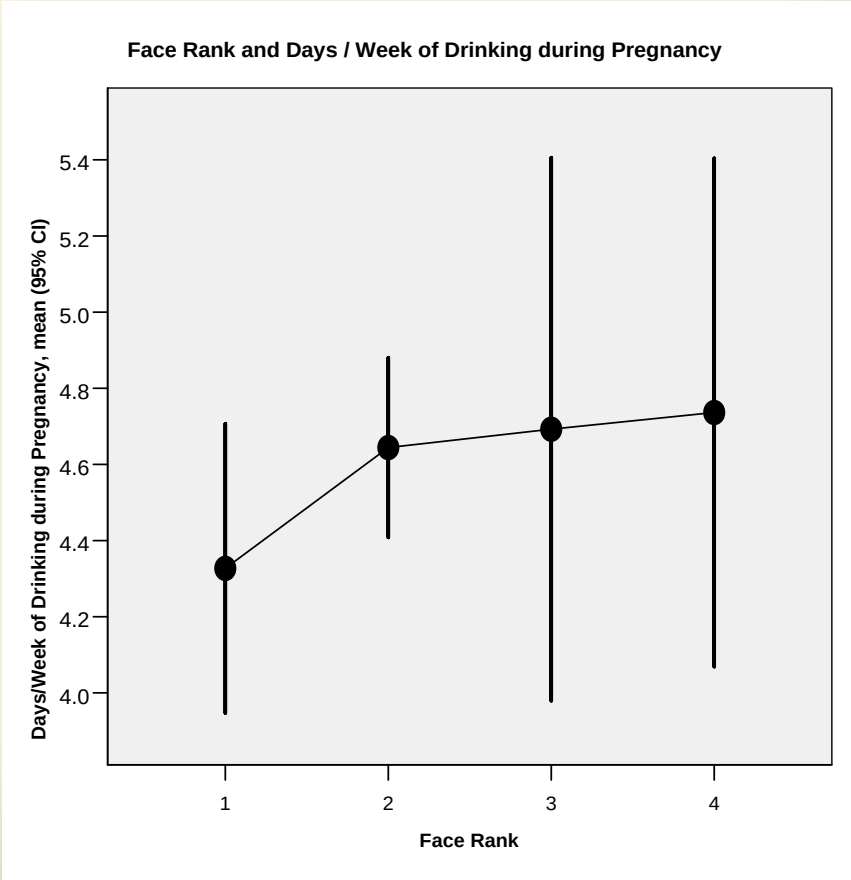
the lower the current weight



the lower the current height

The more severe the 4-Digit Code FAS face, the higher the Alcohol Exposure[1-3]

The more severe the FAS face….



The greater the number of days per week of drinking during pregnancy

4-Digit Code FAS Facial Phenotype: Facts

1. Empirically identified and case-defined 18 years ago (1995)[12-14].
2. Presents along a clinically meaningful continuum [1-3,12-14]
   (absent, mild, moderate, severe: Ranks 1,2, 3, 4).
3. This continuum is significantly correlated with (predictive of) brain damage [1-3,12-14]
   (the more severe the face, the more severe the brain damage/dysfunction).
4. This face can be identified across all ages and races and does NOT diminish with age[1-3,12-15].
   Measured in 1,958 Whites, 596 Blacks, 360 Native Americans, 254 Hispanics, 48 Asians
5. The Rank 4 FAS Face is confirmed to be highly specific to (caused only by) prenatal alcohol exposure. This high specificity (>95%) is the only reason a diagnosis of FAS to be rendered when exposure is unknown[1-4].
6. If any of the criteria for the Rank 4 FAS Face (PFL 2%, Rank 4-5 Lip and Philtrum) are relaxed, the face is no longer specific to prenatal alcohol exposure. The University of Washington already relaxed the criteria as far as possible without losing specificity [4].
7. A diagnosis of (FAS/Alcohol Exposure Unknown) cannot be made if the FAS facial phenotype used to render that diagnosis is not specific to alcohol. Specificity must be scientifically confirmed, not assumed[12,13].
8. The full continuum of the 4-Digit Code FAS facial phenotype is easily and accurately measured from a 2D digital photo using a $60 piece of software (FAS Facial Photographic Analysis Software). This ease, accuracy, and low cost of measurement is why 2D was selected over 3D[1-3,13-16].
9. The most accurate and efficient method to screen for full FAS is to identify the Rank 4 facial phenotype from a 2D digital facial photo (as demonstrated by a published 10-year FAS screening of foster care in Seattle)[15,16].

Lets look at the 4-Digit Code's Method for Classifying

CNS Dysfunction

CNS Ranks 1, 2, and 3

CNS Dysfunction is Ranked on a 3-Point Scale

Rank	Growth (3)	Face (4)	CNS (3)	Alcohol (4)
4	h & w ≤ 3 %	All 3 features	Structural / Neurological Abnormalities	Confirmed High
3	h or w ≤ 3 %	2.5 features	3. Severe Dysfunction	Confirmed Moderate
2	h &/or w 4 -10 % not ≤ 3%	1-2 features	2. Moderate Dysfunction	Unknown
1	h & w > 10 %	No features	1. No Dysfunction	Confirmed Absent

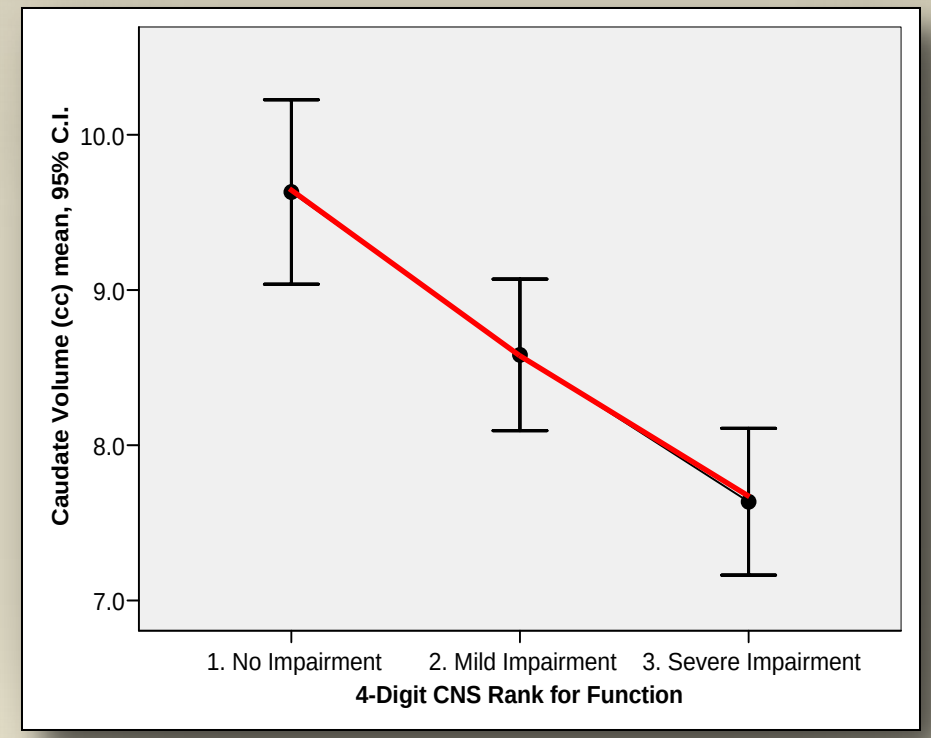
The 3 CNS Ranks in the 4-Digit Code were case-defined to predict increasing likelihood of underlying structural brain abnormality[10].

Alcohol is a teratogen that interferes with the structural development of the fetal brain. This, in turn, can lead to abnormal function.

We postulated in 1997… The greater the dysfunction, the higher the probability of underlying structural brain abnormality. In 2009, MRI proved this to be true!

CNS Rank	Label	Case-Definition	Likelihood of underlying structural brain abnormality
3	Severe Dysfunction	3 or more domains, 2 SDs below the mean	Probable
2	Moderate Dysfunction	1-2 domains , 2 SDs below the mean	Possible
1	No Dysfunction	No evidence of dysfunction	Unlikely

CNS Ranks 1, 2, 3 Correlate with Decreasing Caudate Volume[7]



This is powerful evidence that the CNS Ranking system used by the 4-Digit Code is clinically and scientifically valid (*Construct Validity*).

Construct Validity refers to the ability of a measurement tool (e.g., a survey, scoring system, etc) to actually measure the physiological concept being assessed.

Does the 4-Digit Code produce diagnostic subgroups with significantly distinct CNS structural/functional abnormalities?

Yes!

FAS/PFAS, SE/AE, and ND/AE are clinically and statistically distinct[1-3,6-9].

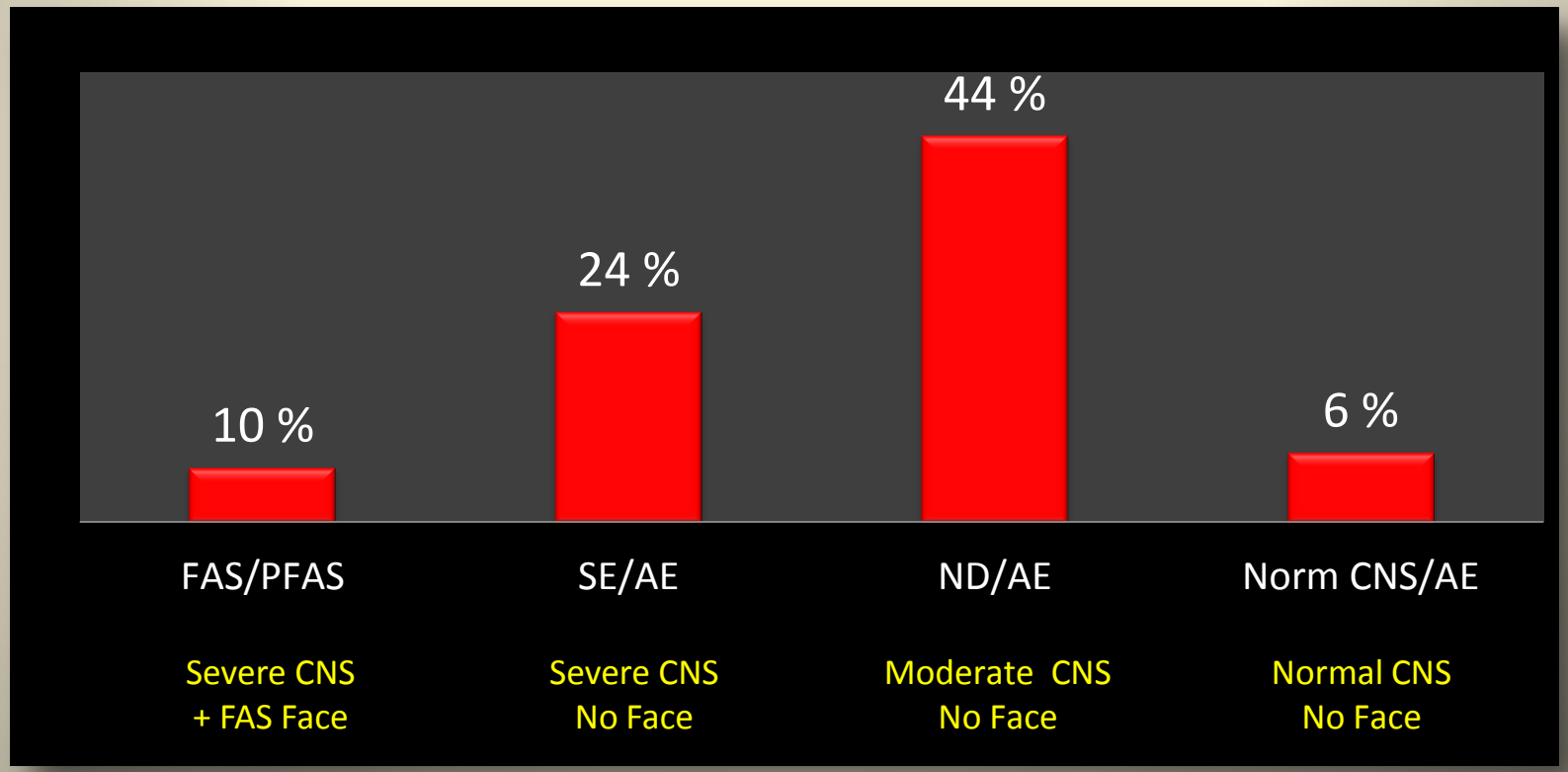
1. Only FAS/PFAS have the FAS face, small frontal lobes, reduced choline.
2. Only FAS/PFAS and SE/AE have small caudates.
3. FAS/PFAS have more severe CNS dysfunction than SE/AE.
4. SE/AE has more severe CNS dysfunction than ND/AE.
5. ND/AE has CNS structural abnormalities underlying their moderate CNS dysfunction.

Here is the evidence….

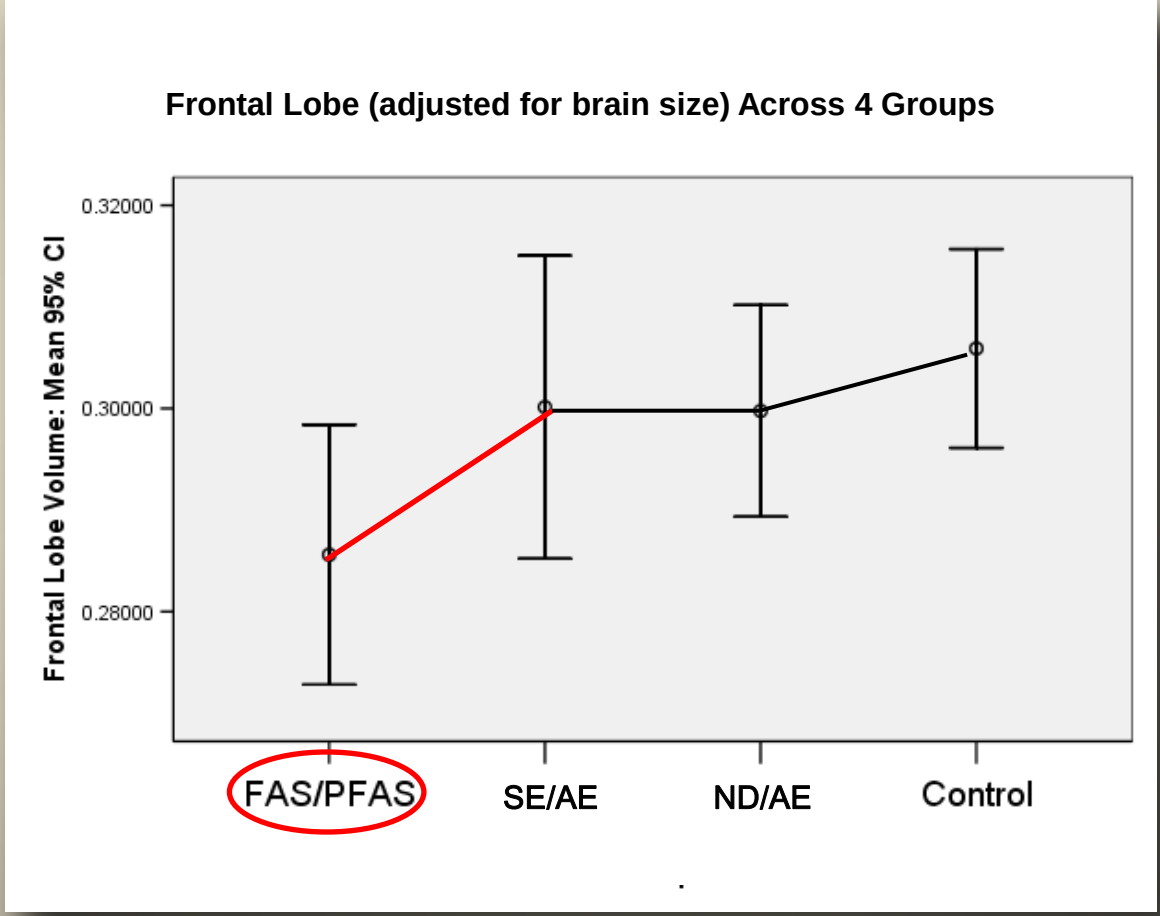
Sociodemographic Profile of 2,550 Patients with FASD diagnosed in the WA FAS DPN clinics[1,3]

Characteristic		%
Gender:	male	57
Race:	White	52
	Black	7
	Native American	8
	Other	33
Age at diagnosis (yrs):	0-3	18
	4-5	16
	6-10	36
	11-15	20
	16+	10

FASD Diagnostic Outcomes for 2,550 Patients with Confirmed Prenatal Alcohol Exposure evaluated at the WA FASD Diagnostic Clinics[1,3]



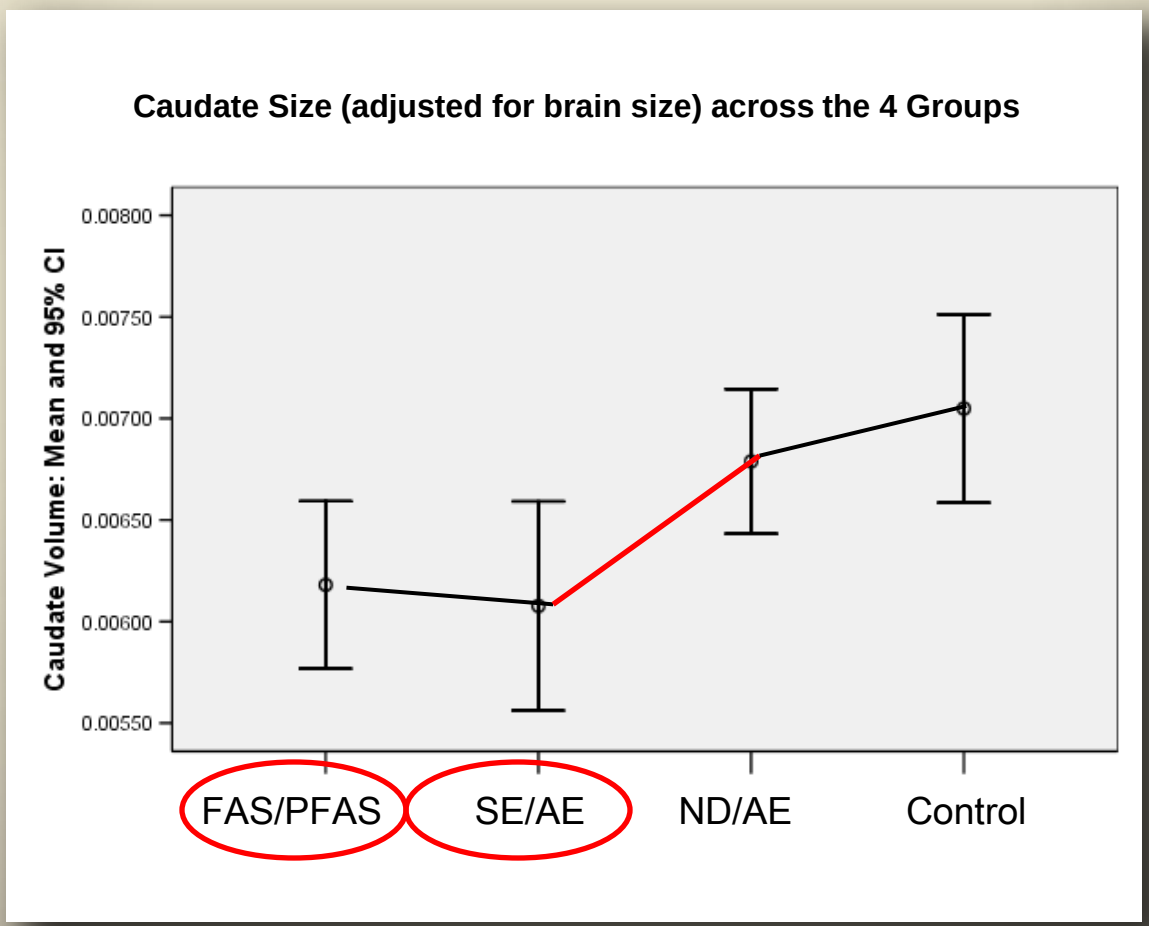
Only those with FAS/PFAS (with the Rank 4 FAS face) had disproportionately smaller frontal lobe volumes[7]



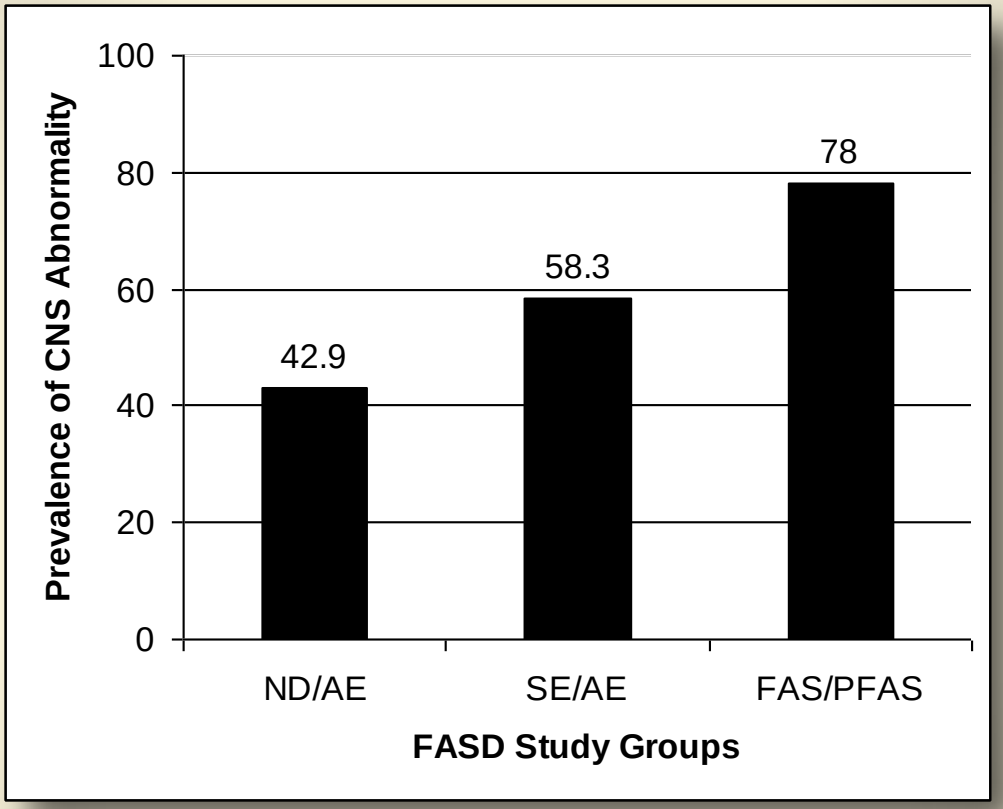
Only those with FAS/PFAS and SE/AE

(those with severe Rank 3 dysfunction)

had disproportionately smaller caudate volumes[7].



Prevalence of CNS Structural Abnormalities increases with increasing severity of 4-Digit FASD diagnosis[1-3,7].

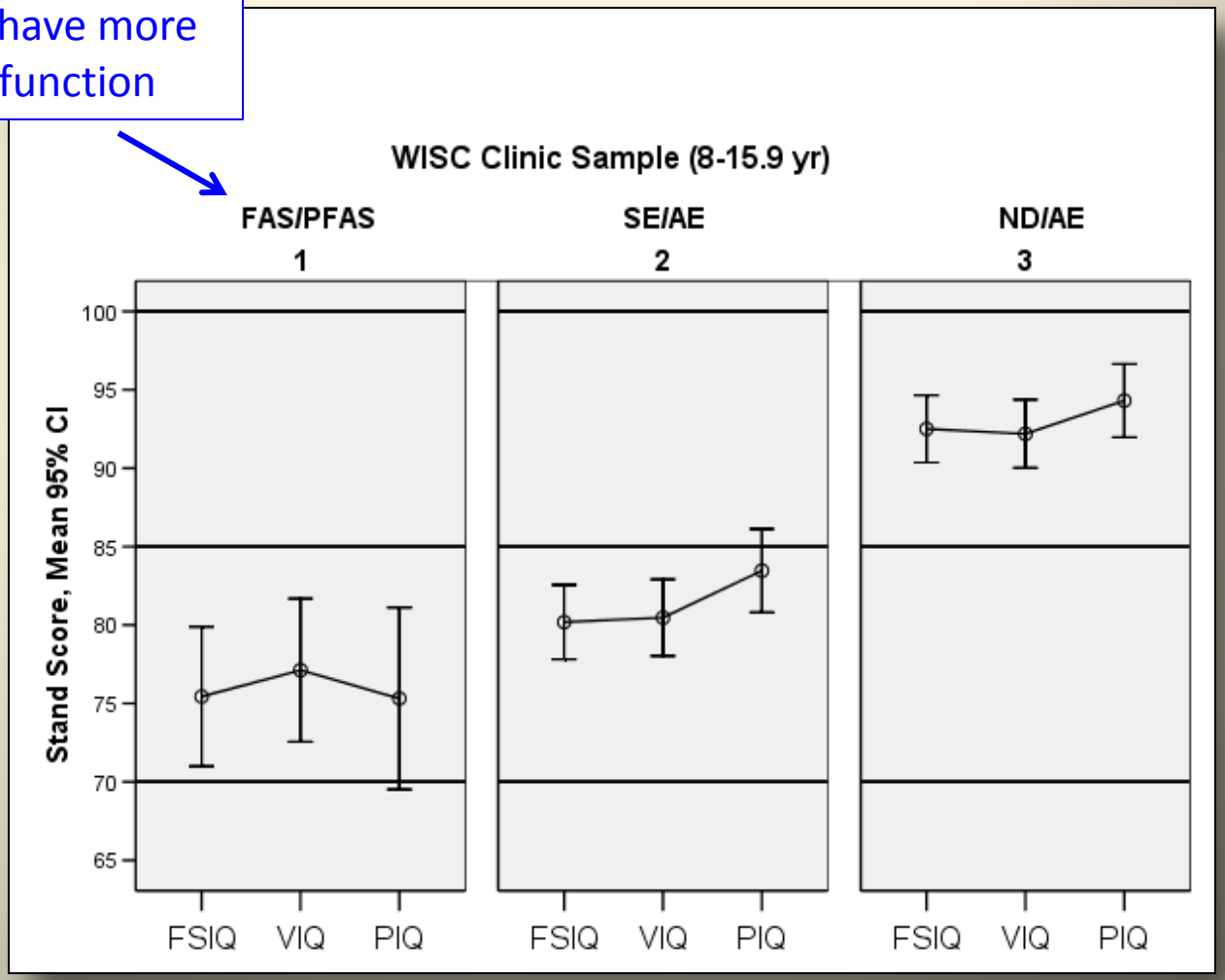


The prevalence of subjects with 1 or more brain regions that were significantly smaller than a healthy unexposed control group increased as severity of FASD diagnostic classification increased.

Even the ND/AE group with moderate dysfunction (CNS Rank 2) had structural abnormalities!

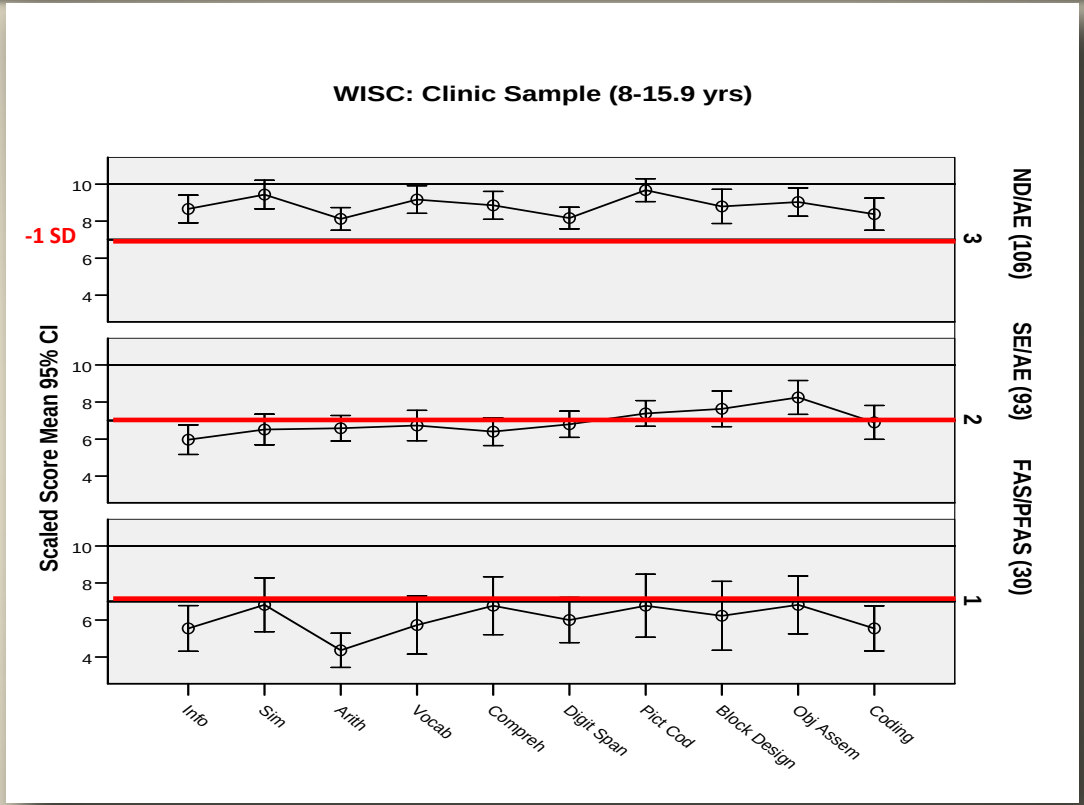
WISC IQ decreases with increasing severity of the 4-Digit Code FASD diagnosis[1-3,6]

Those with the Rank 4 FAS face DO have more severe dysfunction



WISC subtest scores decrease with increasing severity of 4-Digit Code FASD diagnosis[1-3,6].

WISC Subtests



ND/AE
Above -1 SD line

SE/AE
At -1 SD line

FAS
Below -1 SD line

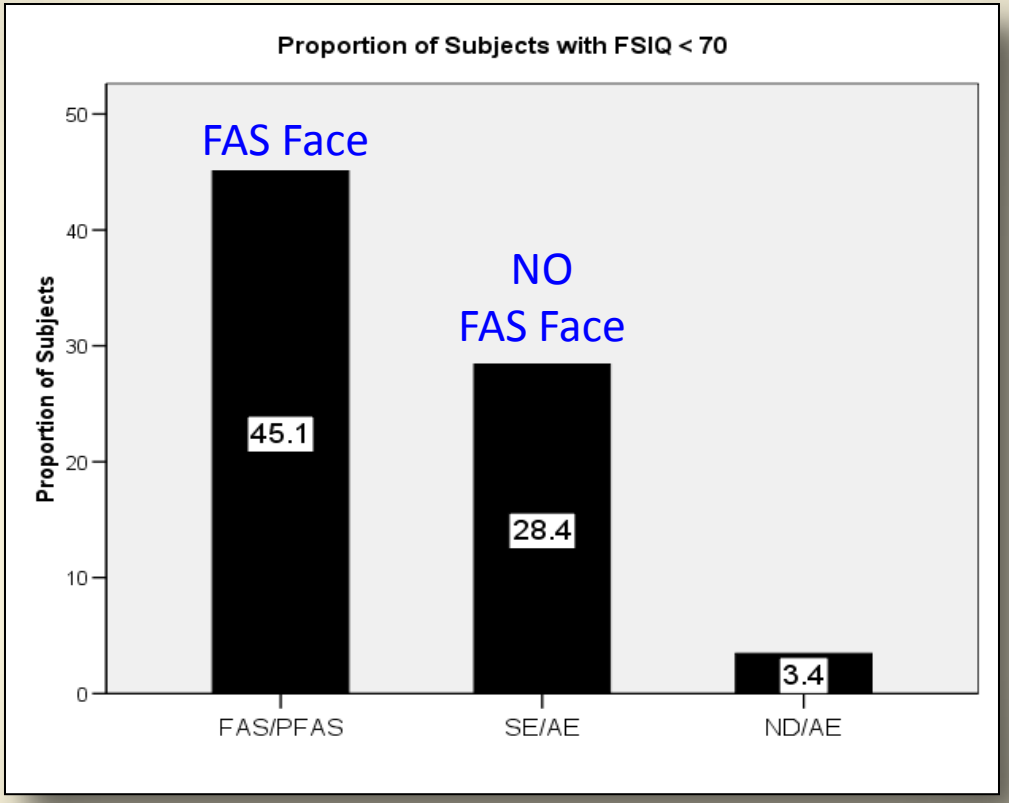
FAS/PFAS and SE/AE must meet the same diagnostic threshold for severe dysfunction.

That said ….

Those who meet that threshold and have the FAS Face (FAS/PFAS) have more severe dysfunction than those who meet that threshold and do not have the FAS face (SE/AE).

Proportion of subjects with FSIQ < 70 increases with increasing severity of 4-Digit Code FASD diagnosis[1-3,6].

FSIQ < 70



FAS/PFAS and SE/AE must meet the same diagnostic threshold for severe dysfunction.

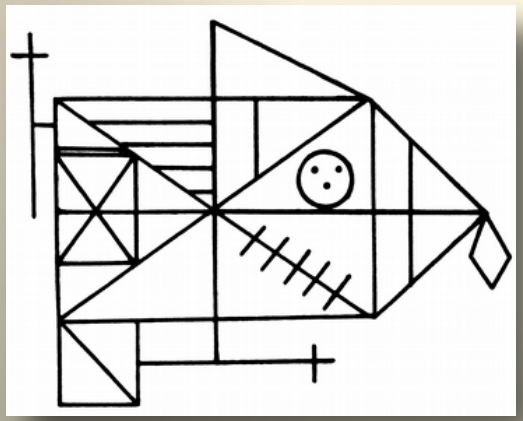
That said ….

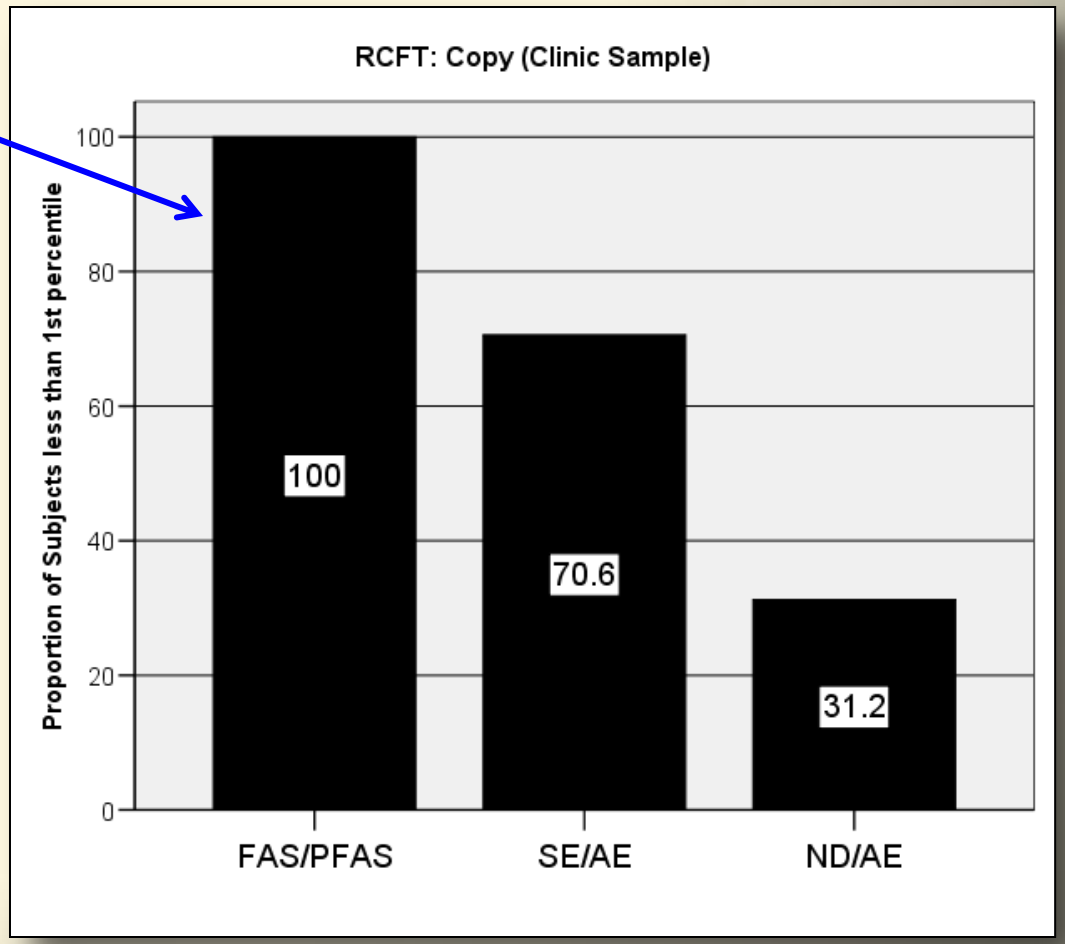
Those who meet that threshold and have the FAS Face (FAS/PFAS) have more severe dysfunction than those who meet that threshold and do not have the FAS face (SE/AE).

Proportion of subjects who fail the RCFT increases with increasing severity of 4-Digit Code FASD diagnosis[1-3,6].

Note: in every slide, those with the Rank 4 FAS Face DO have more severe dysfunction than those with SE/AE or ND/AE (severe and moderate "ARND")

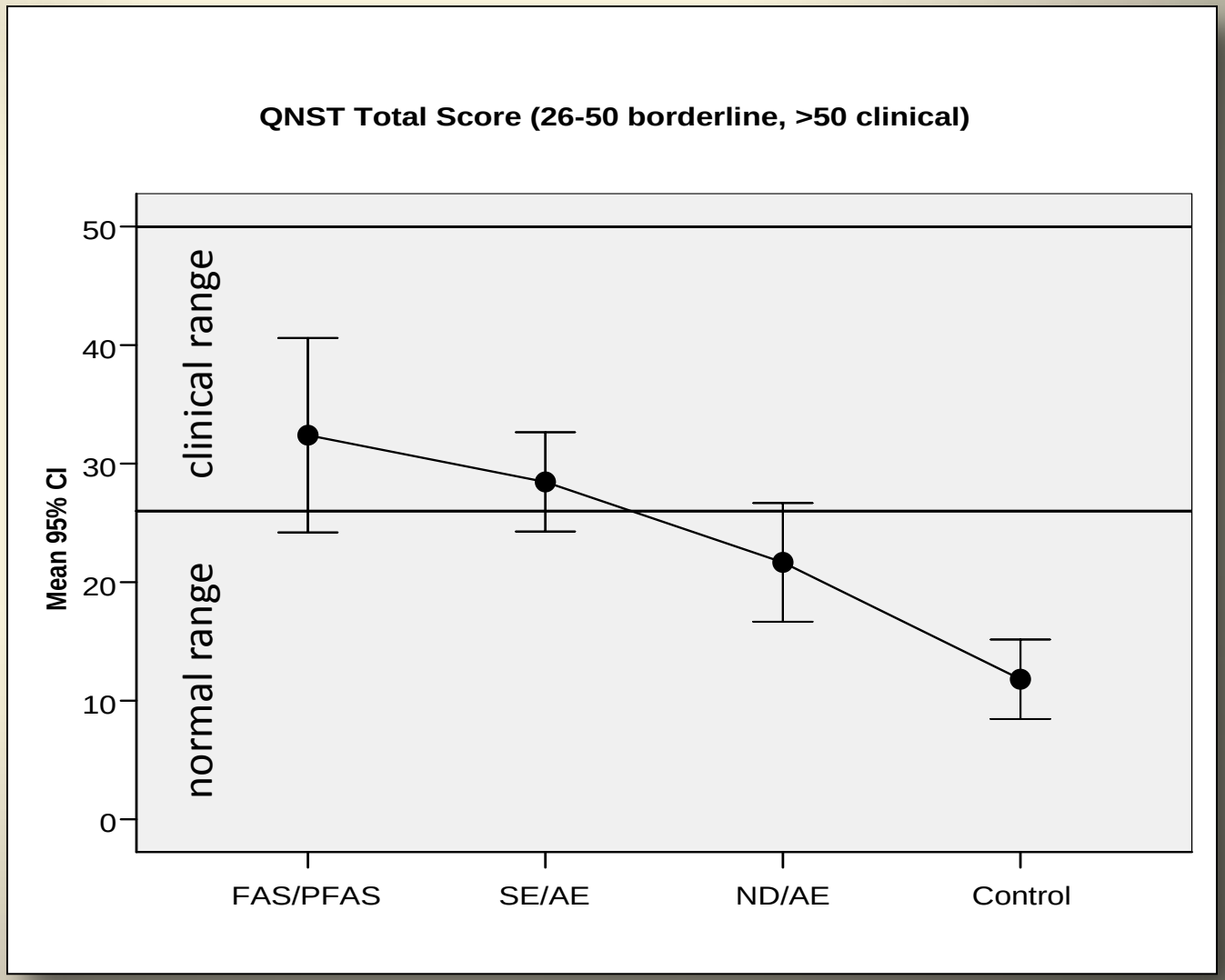
Rey Complex Figure Test





Performance on the Quick Neurological Screen Test decreases with increasing severity of 4-Digit Code FASD diagnosis[1-3,6].

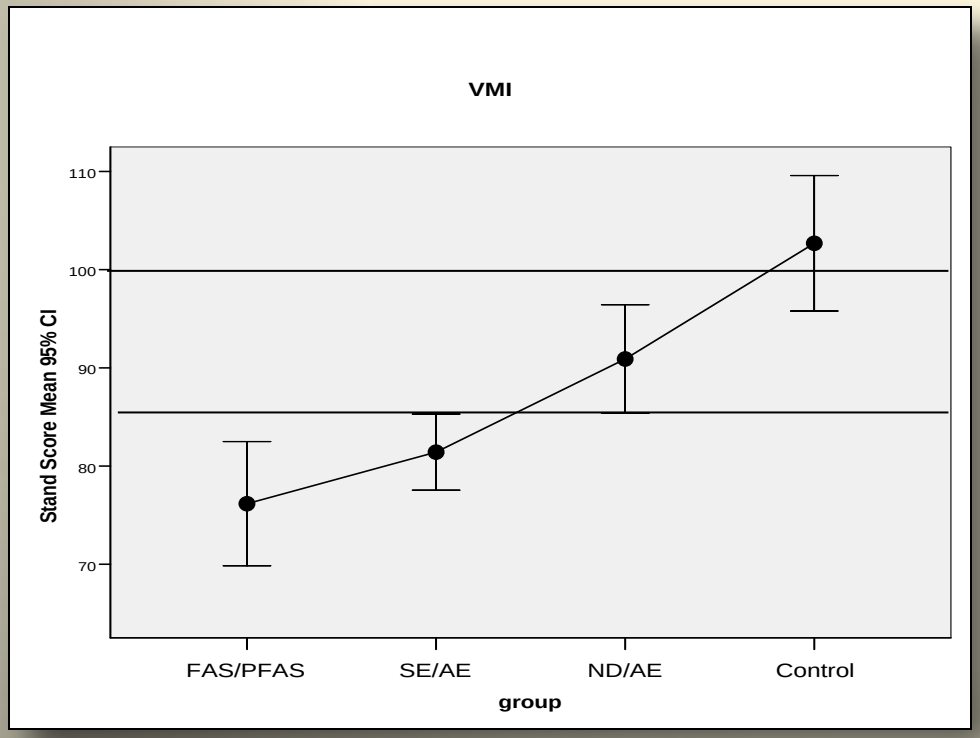
Quick Neurological Screen Test



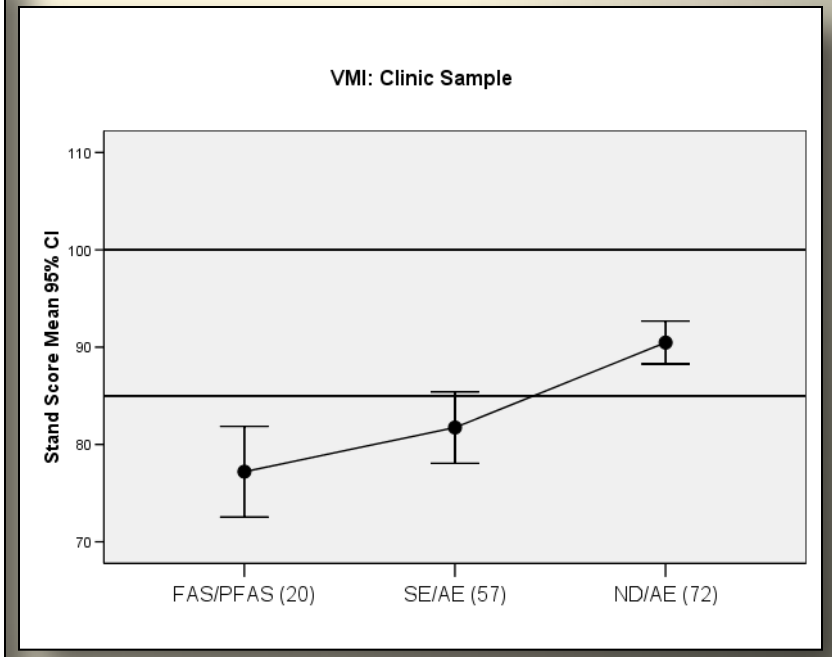
Performance on Visual Motor Integration decreases with increasing severity of 4-Digit Code FASD diagnosis[1-3,6].

Visual Motor Integration

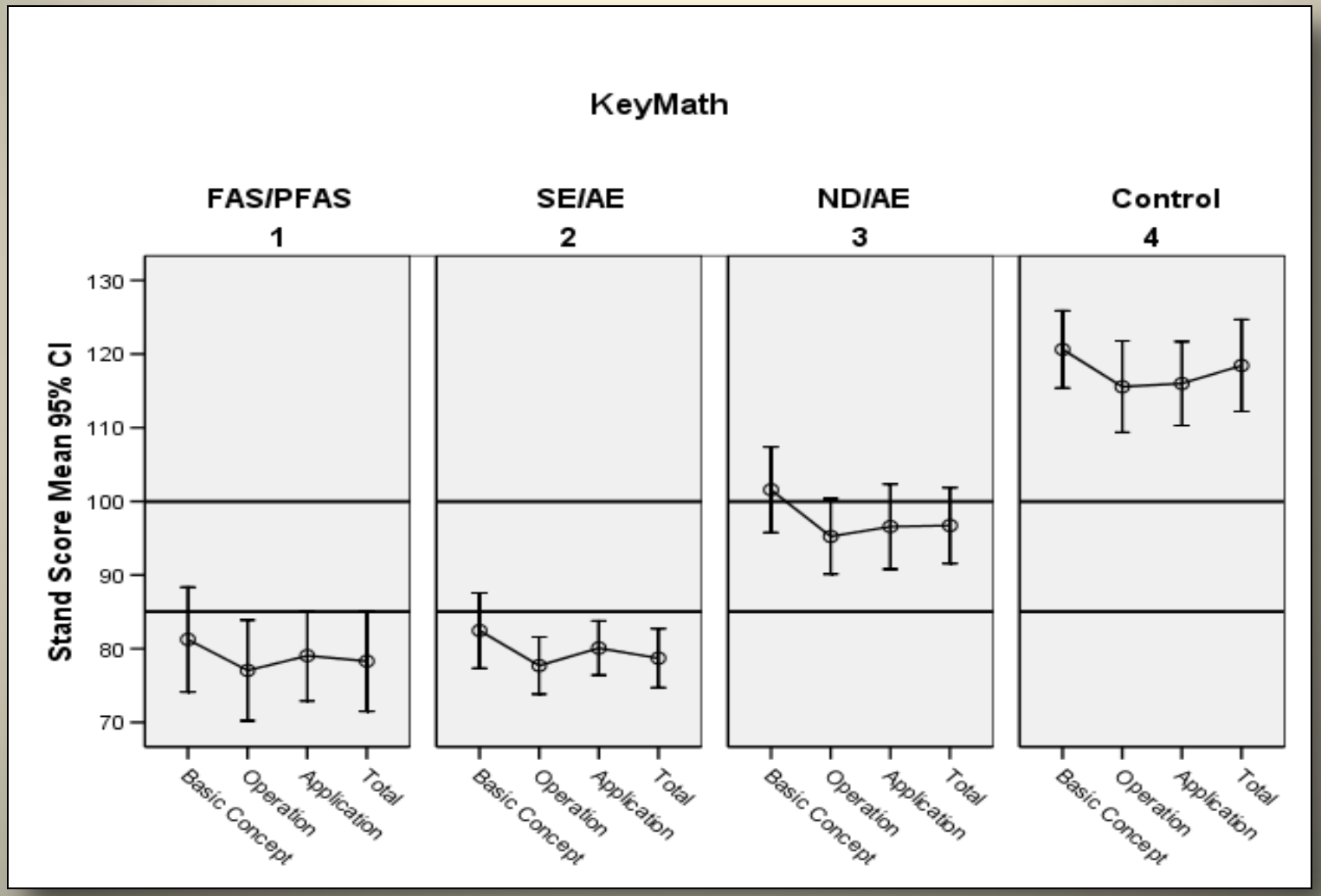
MRI Study



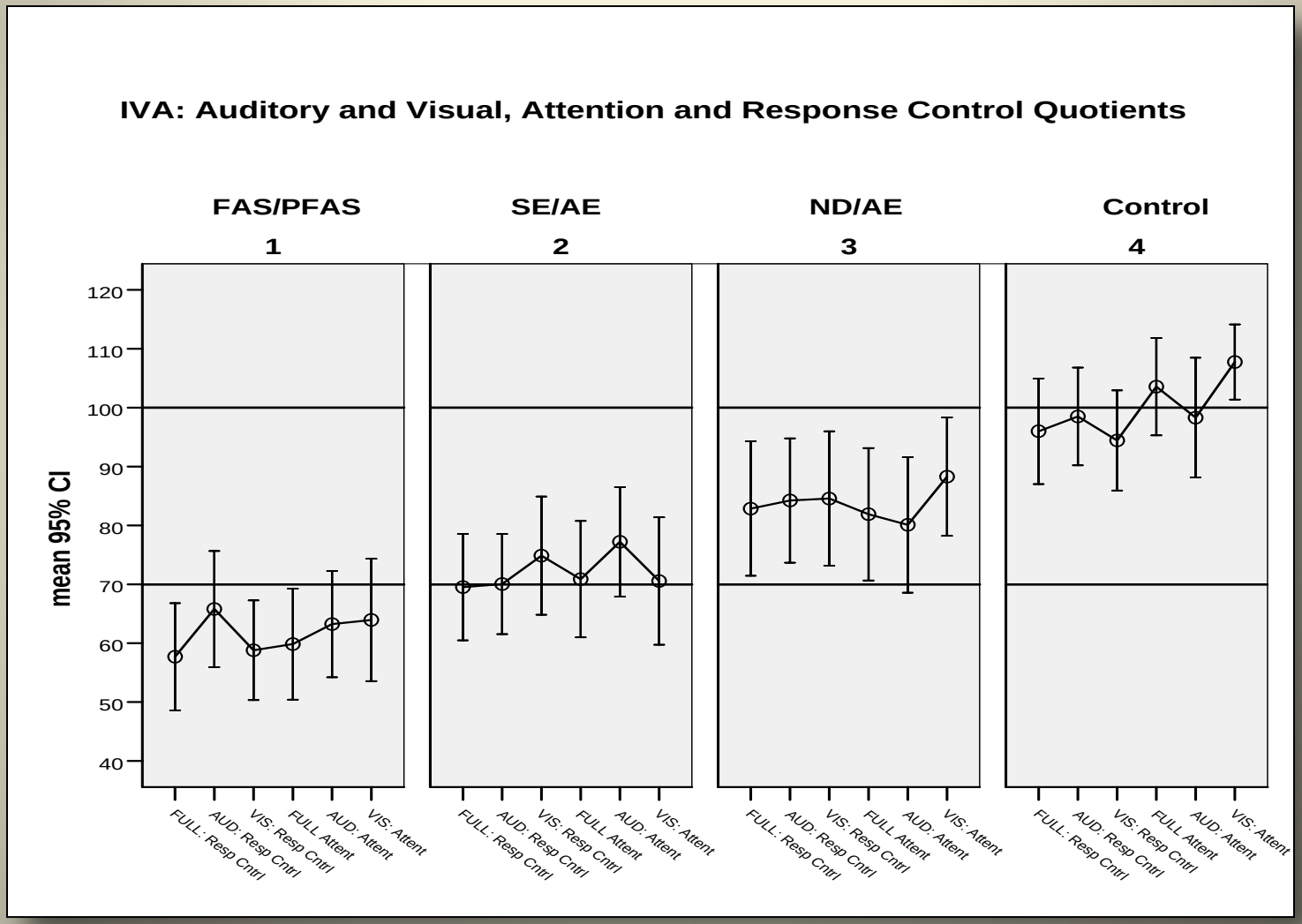
Clinic Sample



Performance on KeyMath comparably impaired among FAS/PFAS and SE/AE[1-3,6].

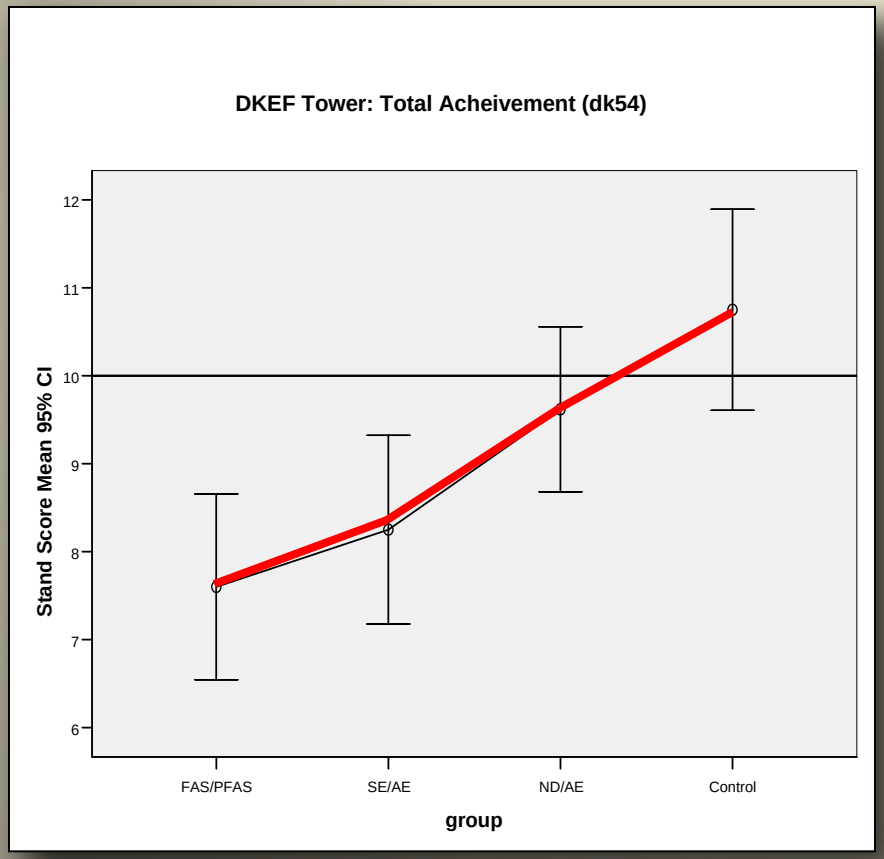


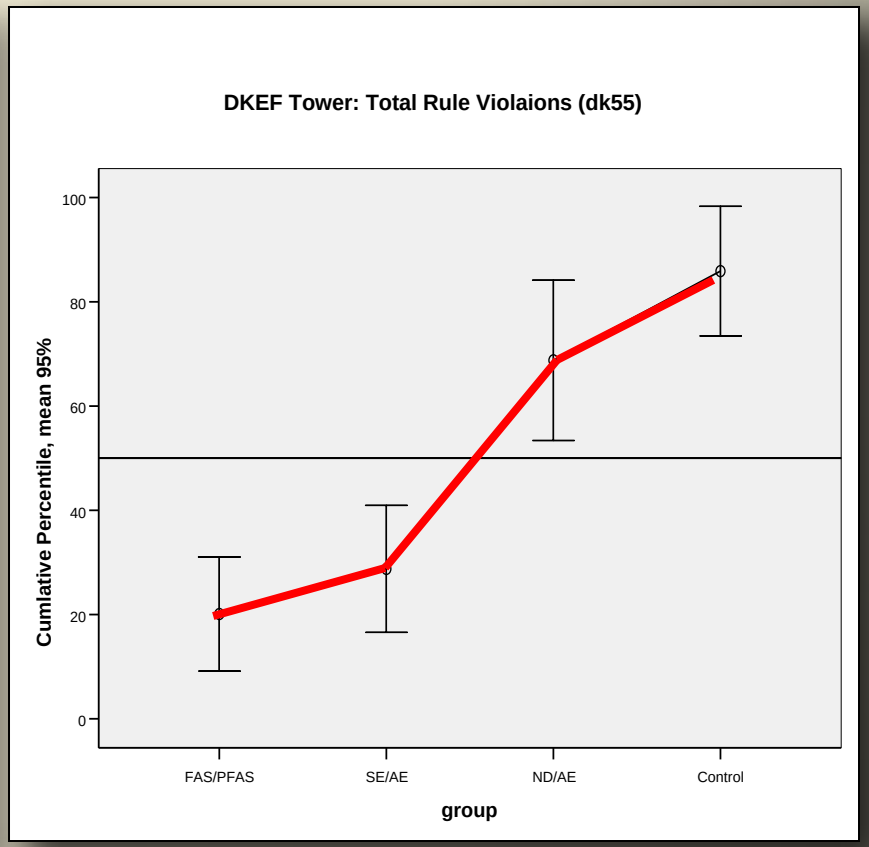
Performance on Continuous Performance Test (IVA) decreases with increasing severity of 4-Digit Code FASD diagnosis[1-3,6].



Performance on Executive Function task decreases with increasing severity of 4-Digit Code FASD diagnosis[1-3,6].

Delis-Kaplan Executive Function System: Tower Test



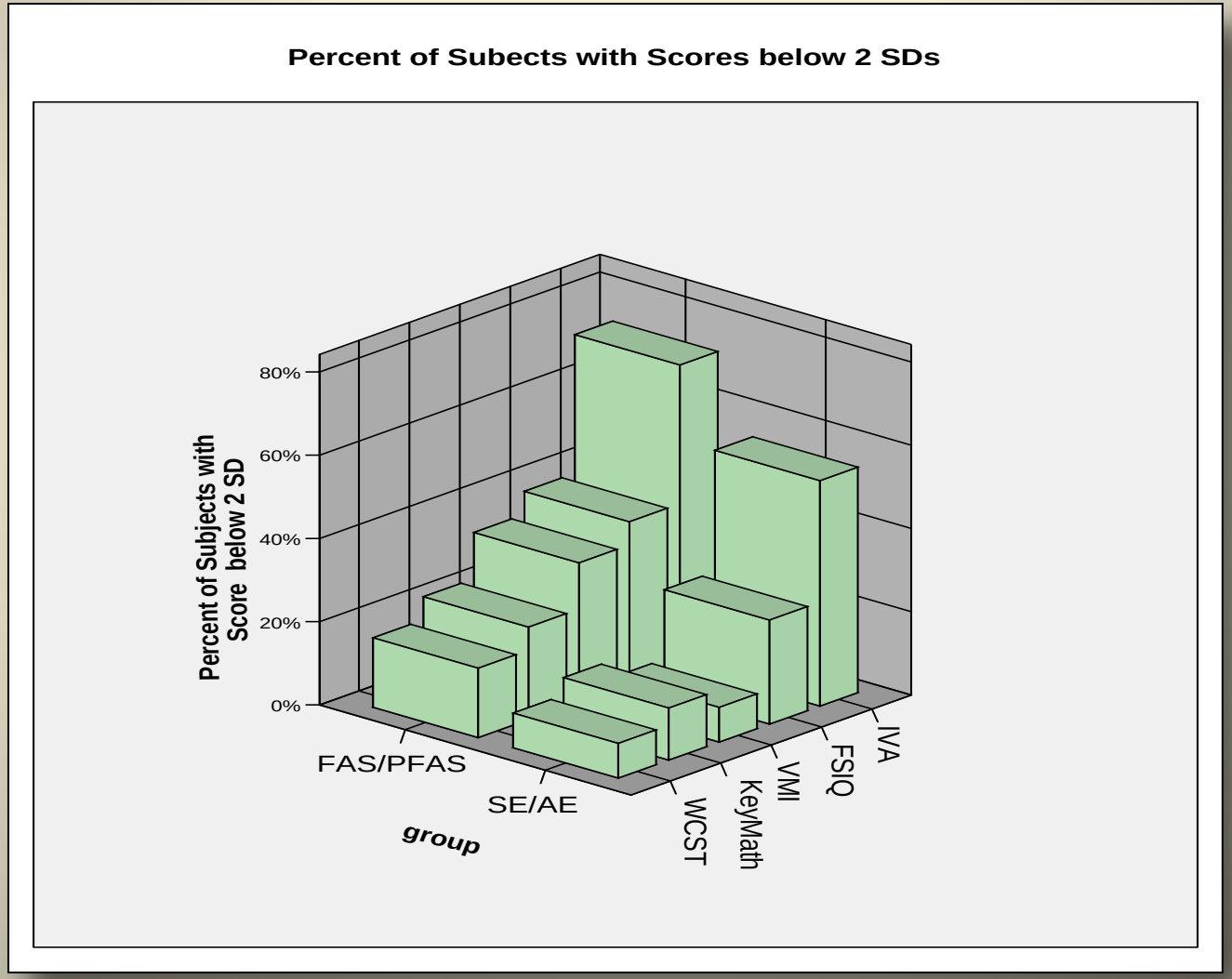


Significant Differences between FAS/PFAS and SE/AE[1-3,6-9]

FAS/PFAS and SE/AE must meet the same diagnostic threshold for severe dysfunction (CNS Rank 3 or 4).
That said ….
Those who meet that threshold and have the FAS Face (FAS/PFAS) have more severe outcomes than those who meet that threshold and do not have the FAS face (SE/AE).

	FAS/PFAS	SE/AE
FAS Face	Yes	No
Alcohol: More days/week	6 days / week	4 days / week
Alcohol: All 3 trimesters	77%	59%
Smaller OFC	30th percentile	43rd percentile
Microcephalic	49% of subjects	27% of subjects
Frontal lobe	Disproportionately smaller	
Choline: Frontal/Parietal	Significantly lower	
WISC PIQ	76	82
WISC Arith	4	6
WISC mazes	3	7
Key Math estimation	5	6.4
VMI	77	89
RCFT Copy	100% failure	70% failure
IVA Full Response Quot.	58	70

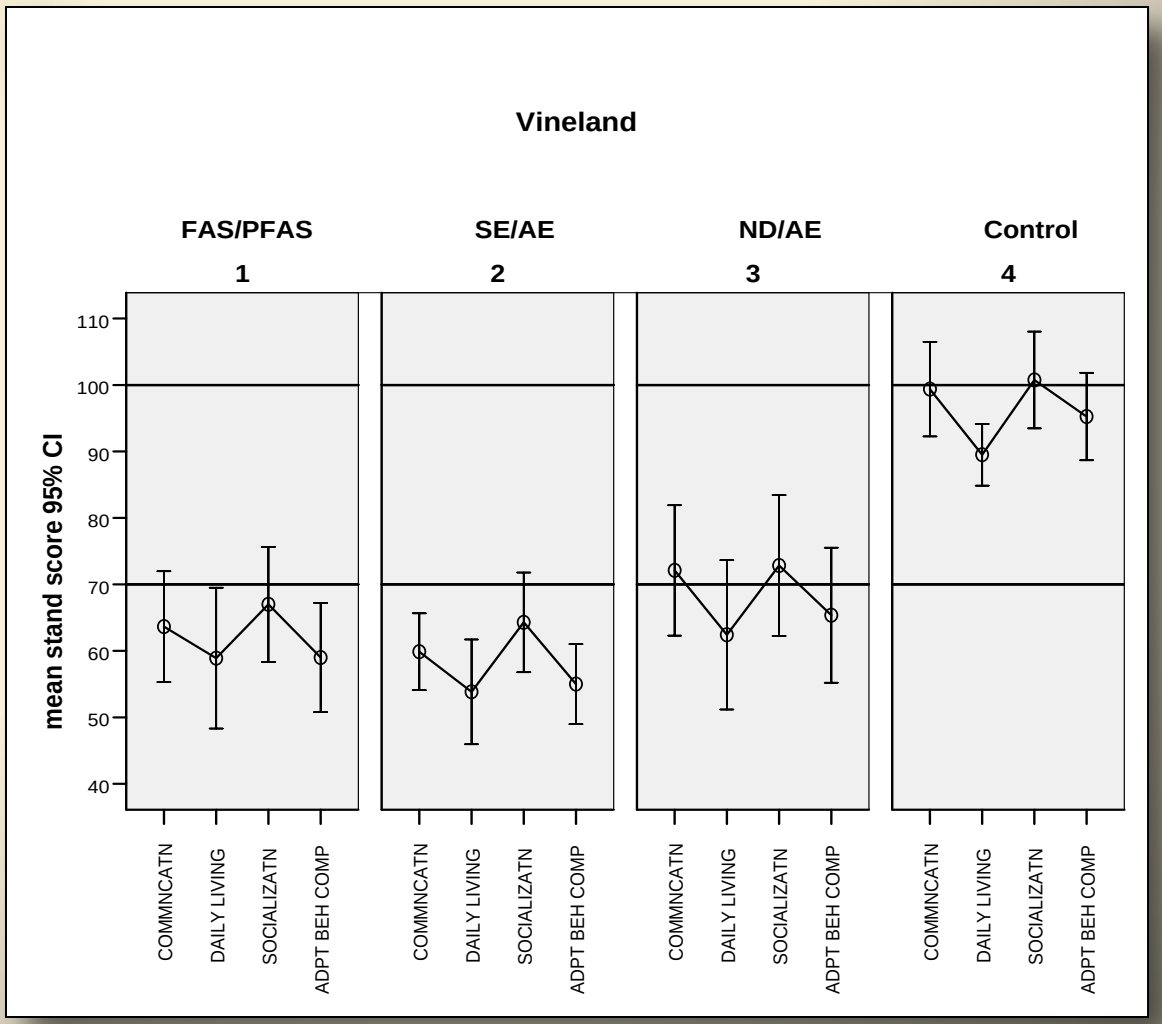
FAS/PFAS significantly more severe than SE/AE[1-3]



One domain in which FAS/PFAS, SE/AE, and ND/AE are Comparably Impaired: Adaptive Function[1-3,7]

Vineland Adaptive Behavior Scales

All 3 FASD groups are 2 SDs below the mean



Even parents can detect behavioral differences between the 4-Digit Code Diagnoses

FAS/PFAS, SE/AE, ND/AE

A structured 2-hour interview is conducted with the parents by the MD and Psychologist using the 4-Digit Code Parent Interview Form (p.6 of the Diagnostic Form[11]).

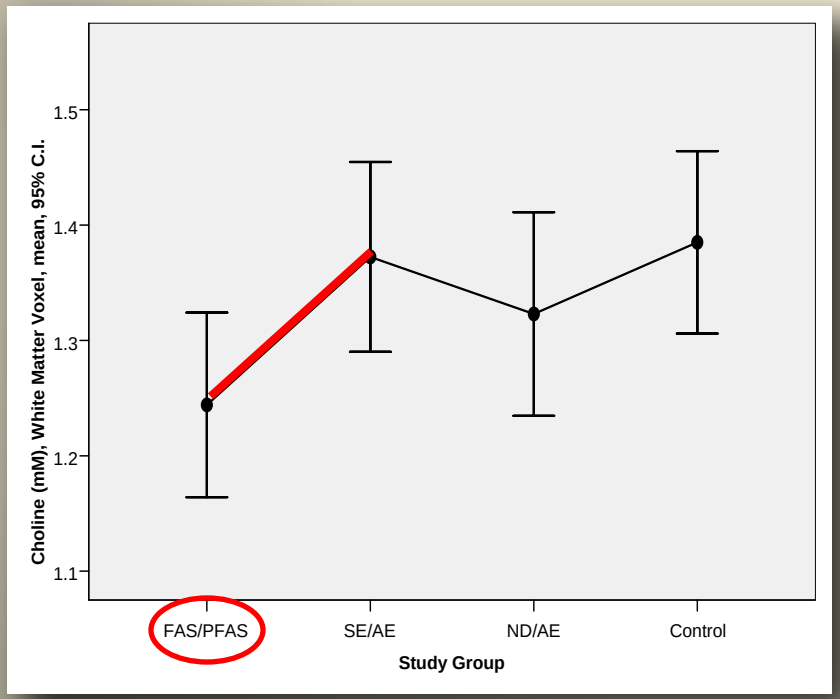
The interview takes place before a diagnosis has been rendered and before the clinicians have even met the child. Thus the results are not biased.

This is a powerful example of construct validity[3].

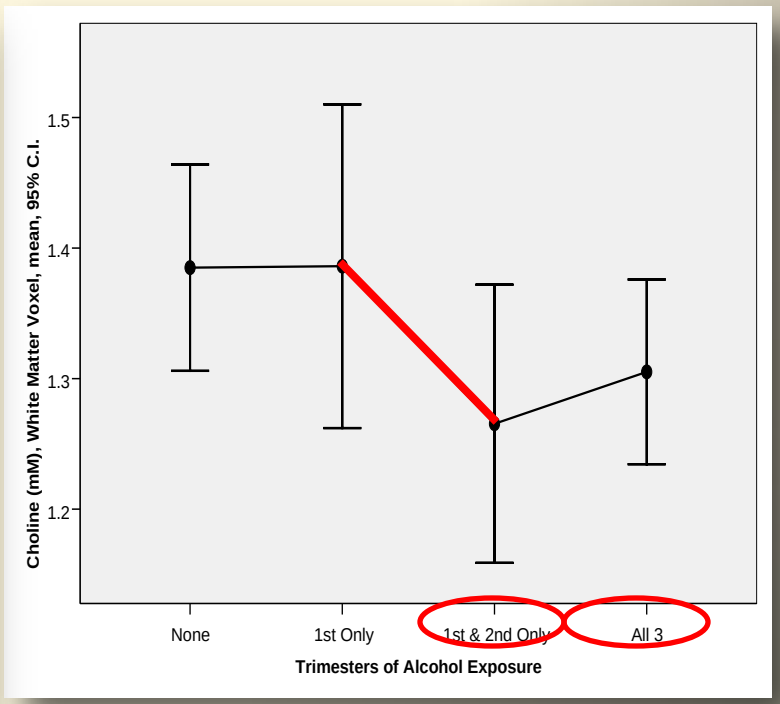
Outcomes of 1,400 parent interviews during FASD evaluation

MRS Study confirms Choline Significantly Lower among FAS/PFAS[8]

- Choline is significantly lower among FAS/PFAS (may be a marker for white matter deficit).
- Choline lower among those with alcohol exposure through the 2nd or 3rd trimesters.



Choline lower in FAS/PFAS



Choline lower with more trimesters of exposure

Is the 4-Digit Code Practical (Simple) to Use?

Clinicians and families report the 4-Digit Code is simple to use and easy to understand[1-3]

Surveys of 100s of Clinicians and Families over 20 years confirm:

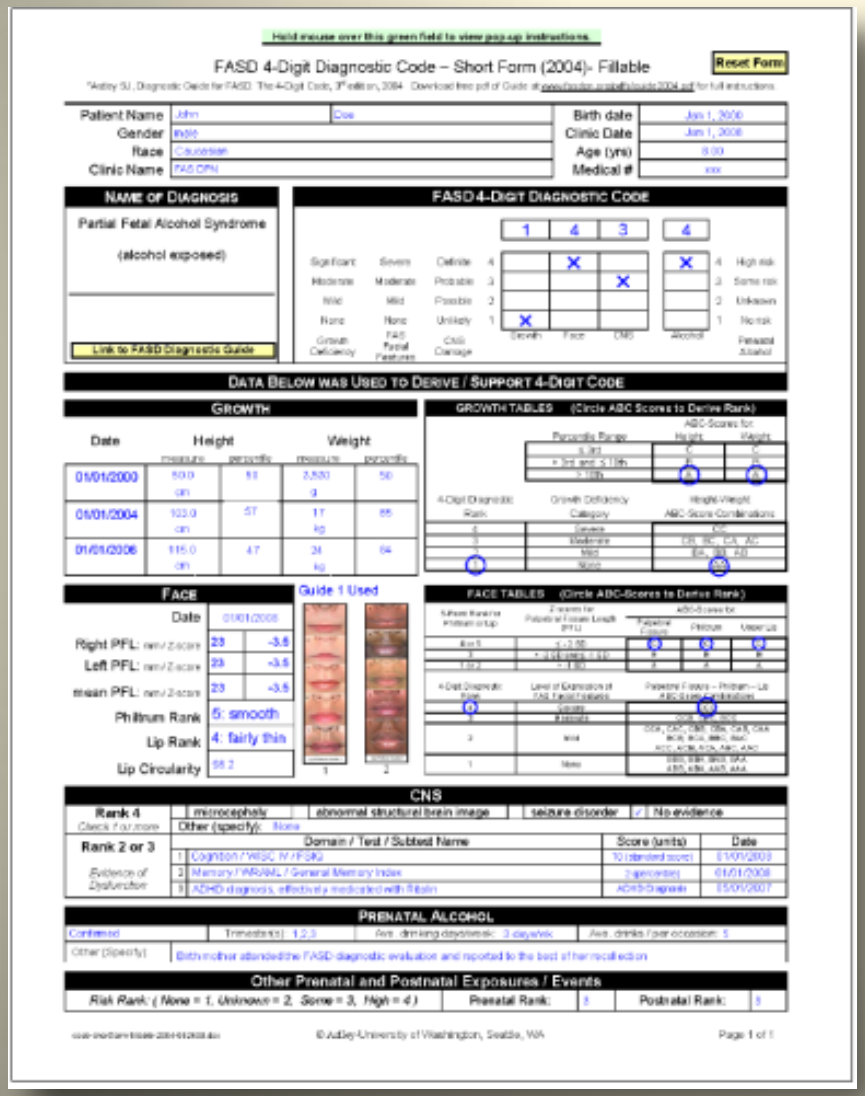
86% of families report it is easy to understand.

93% of professionals describe it as clear.

99% of professionals report they would recommend the 4-Digit Code to others.

Clinics worldwide have been using it since 1997.

4-Digit Code is simple to use [1-3]



FASD 4-Digit Diagnostic Code – Short Form (2004)- Fillable

Reset Form

Patient Name: John Doe
Gender: Male
Race: Caucasian
Clinic Name: FAS CPN
Birth date: Jan 1, 2000
Clinic Date: Jan 1, 2008
Age (yrs): 8.00
Medical #: xxx

NAME OF DIAGNOSIS

Partial Fetal Alcohol Syndrome

(alcohol exposed)

Link to FASD Diagnostic Guide

FASD 4-DIGIT DIAGNOSTIC CODE

1	4	3	4

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

DATA BELOW WAS USED TO DERIVE / SUPPORT 4-DIGIT CODE

GROWTH

Date	Height measure	Height percentile	Weight measure	Weight percentile
01/01/2000	50.0 cm	51	3,500 g	50
01/01/2004	103.0 cm	57	17 kg	65
01/01/2006	115.0 cm	47	24 kg	64

GROWTH TABLES (Circle ABC Scores to Derive Rank)

Percentile Range | ABC Scores for Height | ABC Scores for Weight
≤ 3rd and ≥ 97th | A | A
> 3rd and ≤ 10th | B | B
> 10th and < 90th | C | C

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

FACE

Guide 1 Used

	Date	01/01/2008	
Right PFL: raw / Z-score	23	-3.5
Left PFL: raw / Z-score	23	-3.5
mean PFL: raw / Z-score	23	-3.5
Philtrum Rank	5: smooth	
Lip Rank	4: fairly thin	
Lip Circularity	55.2	

FACE TABLES (Circle ABC-Scores to Derive Rank)

Philtrum Rank or Philtrum Lip | Z-scores for Palpebral Fissure Length (PFL) | ABC-Scores for Palpebral Fissures | Philtrum | Upper Lip
5 | ≤ -1.65 | A | A | A
4 | > -1.65 and ≤ -0.82 | B | B | B
1 to 3 | > -0.82 | C | C | C

4-Digit Diagnostic Rank | Level of Expression of FAS Facial Features | Palpebral Fissure – Philtrum – Lip ABC-Score Combinations
4 | Severe | CCA, CAC, CBB, CBA, CAB, CAA, BCC, BCB, BBC, BBB, BBA, BAC, BAB, BAA, ACC, ACB, ACA, ABC, ABB, ABA, AAC, AAB, AAA
3 | Moderate | CCB, CCC, CBC, CBB, CAC, CAB, CAA, BCC, BCB, BBC, BBB, BBA, BAC, BAB, BAA, ACC, ACB, ACA, ABC, ABB, ABA, AAC, AAB, AAA
2 | Mild | BBB, BBA, BAC, BAB, BAA, ABC, ABB, ABA, AAC, AAB, AAA
1 | None | BBC, BBB, BBA, BAC, BAB, BAA, ABC, ABB, ABA, AAC, AAB, AAA

CNS

Rank 4 Check 1 or more	microcephaly	abnormal structural brain image	seizure disorder	No evidence
	Other (specify): None			

Rank 2 or 3 Evidence of Dysfunction	Domain / Test / Subtest Name	Score (units)	Date
1	Cognition / WISC IV / FSIQ	70 (standard score)	01/01/2003
2	Memory / WRAML / General Memory Index	(age-norms)	01/01/2008
3	ADHD diagnosis, effectively medicated with Ritalin	ADHD Diagnosis	05/01/2007

PRENATAL ALCOHOL

Confirmed	Trimester(s): 1,2,3	Ave. drinking days/week: 3 days/wk	Ave. drinks / per occasion: 5
Other (specify):	Birth mother attended the FASD diagnostic evaluation and reported to the best of her recollection		

Other Prenatal and Postnatal Exposures / Events

Risk Rank: (None = 1, Unknown = 2, Some = 3, High = 4) | Prenatal Rank: 1 | Postnatal Rank: 1

© Astley-University of Washington, Seattle, WA | Page 1 of 1

The Code can be administered using nothing more than:

1. Our 1-page diagnostic form programmed to derive the 4-Digit Code from the data you enter. (pdf available free online[18])

2. And a $4 Lip-Philtrum Guide.

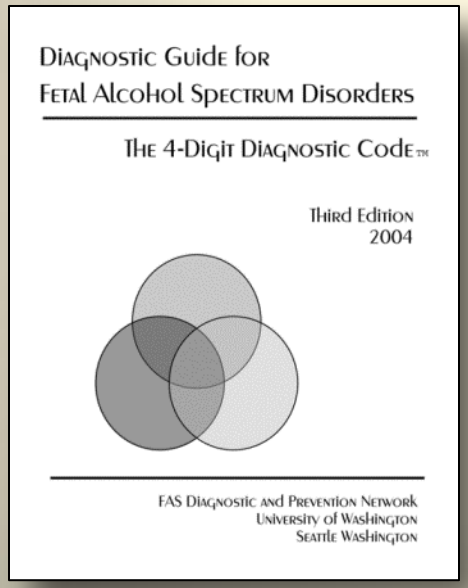
The 4-Digit Code provides an objective method for recording prenatal alcohol exposure

---

The 4-Digit Code can detect distinct patterns of alcohol exposure between the diagnostic subgroups

FAS/PFAS, SE/AE and ND/AE

4-Digit Code Form used to Document Alcohol Exposure[11]



Posted free online
www.fasdpn.org

Alcohol Exposure

Please fill in this information as completely as possible.
This information is critical to the evaluation of the patient.

Alcohol use by the birth mother

- **Before pregnancy:** average number of drinks per drinking occasion: 12
  maximum number of drinks per occasion: 12
  average number of drinking days per week: 4 to 5
  Type(s) of alcohol: x wine, x beer, x liquor, ___ unknown, ___ other (specify) ___

- **During pregnancy:** average number of drinks per drinking occasion: 12
  maximum number of drinks per occasion: 12
  average number of drinking days per week: 4 to 5
  Type(s) of alcohol: x wine, x beer, x liquor, ___ unknown, ___ other (specify) ___

Which trimester(s) did the mother drink alcohol? x 1st x 2nd ___ 3rd ___ Unknown

	No	Yes	Unknown
Was the birth mother ever reported to have a problem with alcohol?	___	x	___
Was the birth mother ever diagnosed with alcoholism?	___	x	___
Did the birth mother ever receive treatment for alcohol addiction?	___	x	___

If the above information is unknown, please provide any information that might help describe the mother's level of alcohol use DURING pregnancy The drinking was pretty regular up until a couple of weeks into the second trimester. From that time the drinks were used to help post-acute withdrawal symptoms and finally stopped when I went into a treatment center.

What is the source(s) of this information on alcohol use? birth mother

Did the birth mother use any of the following substances during pregnancy?

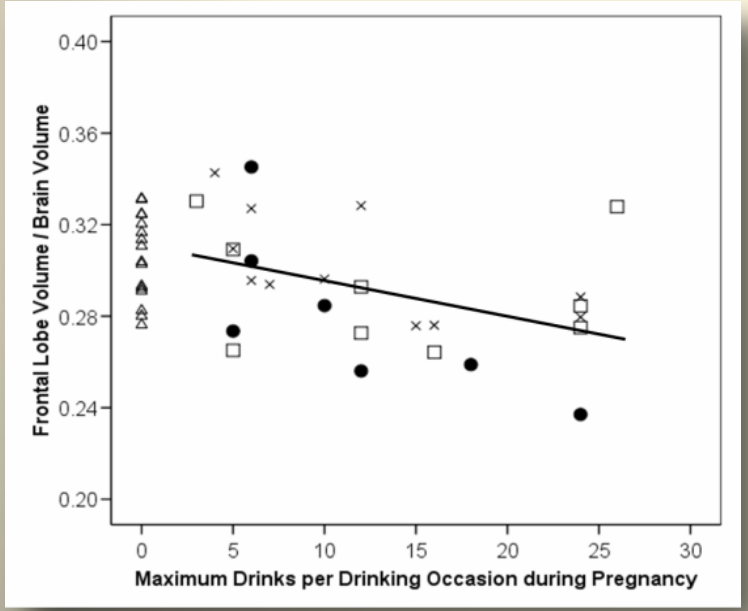
Yes	No	Unknown	Type	Please List Specific Substance(s)	Month(s) of Pregnancy
___	x	___	Drugs	___	___
x	___	___	Tobacco	cigarettes	6
x	___	___	Medications	tylenol with codeine, vicadin	4
___	x	___	X-rays	___	___

Frontal Lobe Volume and Alcohol Exposure[1-3,7]

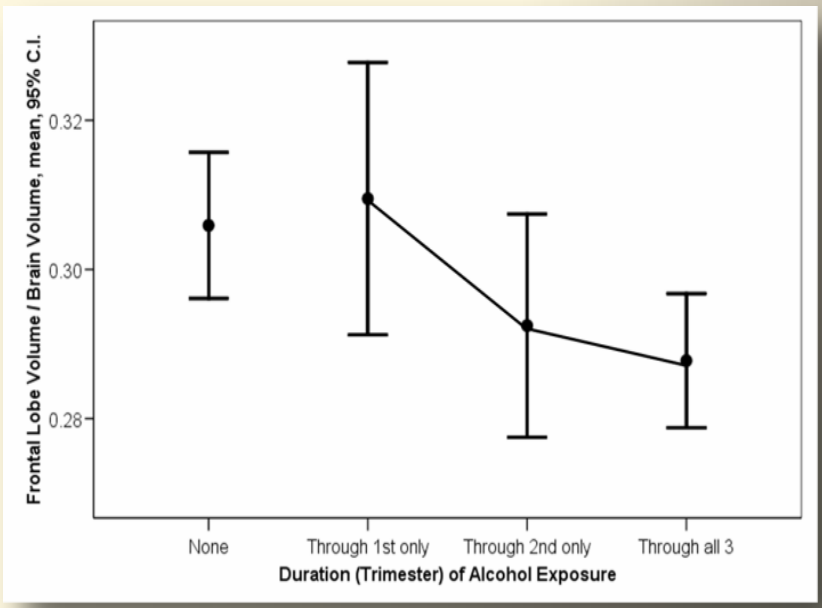
4-Digit Code method for documenting prenatal alcohol exposure allows important at-risk patterns of exposure to be detected.

The frontal lobe volume decreases significantly with:

increasing number of drinks and increasing duration of exposure.



Number of Drinks



Trimesters of Exposure

Significant Differences in Alcohol Exposure Patterns detected between FAS/PFAS and SE/AE[1-3]

FAS/PFAS and SE/AE must meet the same diagnostic threshold for severe dysfunction.
That said ….

Those who meet that threshold and have the FAS Face (FAS/PFAS) have significantly

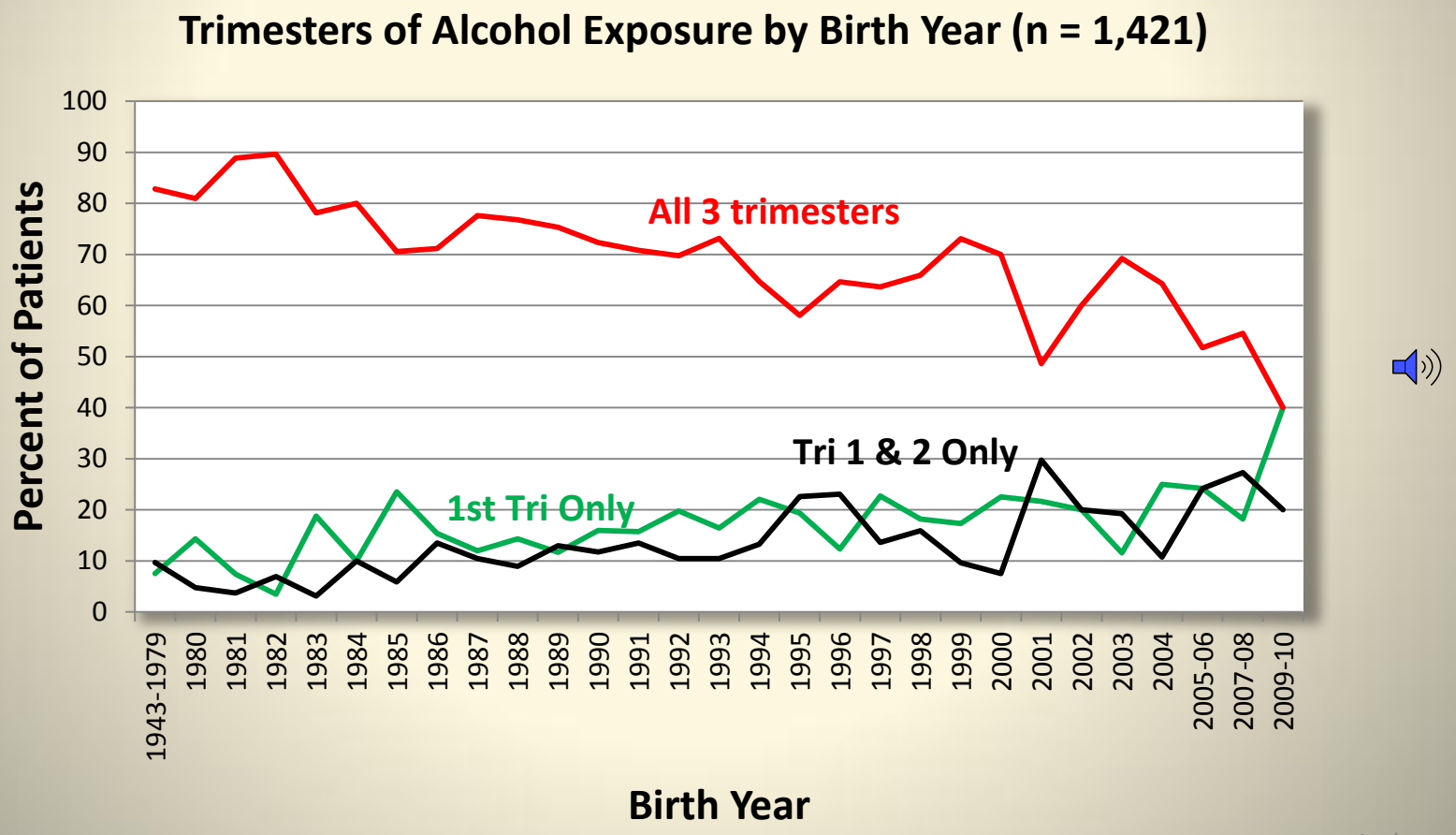
- more days/week of alcohol exposure and
- are more likely to have exposure all 3 trimesters

than those who meet that threshold and do not have the FAS face (SE/AE).

	FAS/PFAS	SE/AE
FAS Face	Yes	No
Alcohol: More days/week	6 days / week	4 days / week
Alcohol: All 3 trimesters	77%	59%

Can even detect reduction in alcohol exposure over 30 years in WA FASDPN Clinics

Of the 1,421 patients with prenatal alcohol exposure reported by trimester, the percent of pregnancies with reported exposure all 3 trimesters decreased significantly from 82% to 40% across birth cohorts spanning 1943-2010.



Should Thresholds of Alcohol Use be Required? NO [1-3]

Here is why:

Inaccurate: The accuracy of reported exposure can never be confirmed, even when reported directly by the birth mother (recall error, not comfortable reporting).

Not Available: Among 1,400 patients with confirmed exposure, **less than 50%** were able to report details like quantity/frequency/duration.

Sends the wrong public health message: "Are you implying exposure below the threshold is SAFE?"

Risk varies by individual: This is well documented in twins.

Alcohol Use "Reported" During Pregnancy among 1,400 Patients			
Reported Drinking Pattern during Pregnancy	FAS (n=154)	SE/AE (n=334)	ND/AE (n = 722)
Quantity: Max drinks per occasion mean (range) N	13 (1-60) 56	13 (1-72) 169	13 (1-128) 275
Frequency: Days per week mean (range) N	5.6 (1-7) 81	4.3 (1-7) 227	4.4 (1-7) 409
Duration: Trimesters 1st only (1st + 2nd) all 3, %	14 (14) 72	17 (12) 67	12 (11) 72

Are the guidelines confirmed to be reproducible?

If two clinics use the guidelines, do they render the same diagnoses?

The 4-Digit Code is simple to use with > 93% reproducibility[1].

The FAS DPN provides a free, 1-page, electronic pdf that is programmed to automatically derive the 4-Digit Code based on the growth, face, brain and alcohol data you enter into the form.

The WA FASD Network Clinics use this form. They rendered the correct FASD diagnosis in > 93% of the 677 FASD diagnostic evaluations they conducted over 18 years. Most common source of error was facial measurement when software not used.

Form is available free online
http://depts.washington.edu/fasdpn/pdfs/FASD-4digit-shortform-fillable-2004-052508.pdf

Hold mouse over this green field to view pop-up instructions.

FASD 4-Digit Diagnostic Code – Short Form (2004)- Fillable

Reset Form

*Astley SJ, Diagnostic Guide for FASD: The 4-Digit Code, 3rd edition, 2004 - Download free pdf of Guide at www.fasdpn.org/pdfs/guide2004.pdf for full instructions.

Patient Name	John	Doe	
Gender	male		
Race	Caucasian		
Clinic Name	FAS DPN		

Birth date	Jan 1, 2000
Clinic Date	Jan 1, 2008
Age (yrs)	8.00
Medical #	xxx

NAME OF DIAGNOSIS

Partial Fetal Alcohol Syndrome

(alcohol exposed)

Link to FASD Diagnostic Guide

FASD 4-DIGIT DIAGNOSTIC CODE

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

DATA BELOW WAS USED TO DERIVE / SUPPORT 4-DIGIT CODE

GROWTH

Date	Height measure	Height percentile	Weight measure	Weight percentile
01/01/2000	50.0 cm	50	3,520 g	50
01/01/2004	103.0 cm	57	17 kg	65
01/01/2006	115.0 cm	47	24 kg	84

GROWTH TABLES (Circle ABC Scores to Derive Rank)

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

FACE

Guide 1 Used

Date	01/01/2008	
Right PFL: mm / Z-score	23	-3.5
Left PFL: mm / Z-score	23	-3.5
mean PFL: mm / Z-score	23	-3.5
Philtrum Rank	5: smooth	
Lip Rank	4: fairly thin	
Lip Circularity	98.2	

FACE TABLES (Circle ABC-Scores to Derive Rank)

5-Point Rank for Philtrum or Lip	Z-scores for Palpebral Fissure Length (PFL)	ABC-Scores for: Palpebral Fissure	Philtrum	Upper Lip
4 or 5	≤ -2 SD	C	C	C
3	> -2 SD and ≤ -1 SD	B	B	B
1 or 2	> -1 SD	A	A	A

4-Digit Diagnostic Rank	Level of Expression of FAS Facial Features	Palpebral Fissure – Philtrum – Lip ABC-Score Combinations
4	Severe	CCC
3	Moderate	CCB, CBC, BCC
2	Mild	CCA, CAC, CBB, CBA, CAB, CAA BCB, BCA, BBC, BAC ACC, ACB, ACA, ABC, AAC
1	None	BBB, BBA, BAB, BAA ABB, ABA, AAB, AAA

CNS

Rank 4	microcephaly	abnormal structural brain image	seizure disorder	✓	No evidence
Check 1 or more	Other (specify): None				

Rank 2 or 3 Evidence of Dysfunction		Domain / Test / Subtest Name	Score (units)	Date
	1	Cognition / WISC IV / FSIQ	70 (standard score)	01/01/2008
	2	Memory / WRAML / General Memory Index	2 (percentile)	01/01/2008
	3	ADHD diagnosis, effectively medicated with Ritalin	ADHD Diagnosis	05/01/2007

PRENATAL ALCOHOL

Confirmed	Trimester(s): 1,2,3	Ave. drinking days/week: 3 days/wk	Ave. drinks / per occasion: 5
Other (Specify):	Birth mother attended the FASD diagnostic evaluation and reported to the best of her recollection		

Other Prenatal and Postnatal Exposures / Events

Risk Rank: (None = 1, Unknown = 2, Some = 3, High = 4)	Prenatal Rank:	3	Postnatal Rank:	3

code-shortform-fillable-2004-052508.doc © Astley-University of Washington, Seattle, WA Page 1 of 1

Do families report a high level of satisfaction / confidence in the FASD 4-Digit Diagnostic Code?

Are the names of the diagnoses (FAS, SE/AE, ND/AE) valid and ethical?

Do the diagnoses qualify patients for intervention services that lead to improved outcomes?

20 years of Patient Satisfaction Surveys confirm families have a high level of satisfaction /confidence in the 4-Digit Code and ALL diagnoses provided access to services that led to improved outcomes[1-3].

University of Washington Patient Survey by mail (n = 577)	FAS/PFAS %	SE/AE %	ND/AE %
Easy to understand	83	84	84
Confident in diagnosis	98	97	98
Provided information not received elsewhere	96	92	90
Successful at finding/accessing recommended services	81	87	85
Services met some to all of my needs	91	81	86
Would recommend clinic to other families with similar needs	100	99	99

University of Washington Patient Survey by phone (all patients in 2012)	%
Received what you hoped to gain from clinic. Yes	98
Clinic helped you better understand your child and their needs. Yes	98
Clinic helped you better meet your child needs. Yes	97
You were somewhat to very successful at finding recommended services	89
You were somewhat to very successful at accessing recommended services	89
Confident in usefulness of the recommendations	97

Can FAS be Diagnosed at Birth?

Is microcephaly alone a sufficient CNS criteria?

Lets revisit the issue of microcephaly as a CNS criteria for FAS

- Microcephaly alone is sufficient to meet the CNS criteria for FAS in all guidelines except the Canadian Guidelines.

- The Canadian Guidelines are the only guidelines that require severe CNS dysfunction be present to render a diagnosis of FAS.

Patient Outcomes (2 years old)	
Growth	Height 1st percentile, weight 1st percentile
Face	PFL: 1st percentile Philtrum: Smooth, Rank 5 Upper Lip: Thin, Rank 5
CNS	OFC 1st percentile, BSID outcomes low-normal
Alcohol	Intoxicated weekly throughout pregnancy
Diagnostic Classifications	
IOM	FAS/PFAS
4-Digit Code	FAS / Alcohol Exposed (Code = 4444)
Canadian	Not FASD
CDC	FAS / Alcohol Exposed
Revised IOM	FAS / Alcohol Exposed

Astley

Evidence that microcephaly (≤ 3rd percentile) is sufficient for FAS

- The 4-Digit Code's CNS criteria for FAS requires evidence of structural and/or functional abnormality. Microcephaly alone IS sufficient.
- The Canadian CNS criteria for FAS requires evidence of severe functional abnormality. Microcephaly alone is NOT sufficient.
  - This prevents a diagnosis of FAS from being rendered in a child under the age of 6 years (because they are too young to engage in the required functional assessments). But children with FAS are born with FAS.
  - Why was microcephaly alone not sufficient? The concern was "*What if an infant with microcephaly grew up to have 'normal' brain function*?" We know in the general population that not everyone with microcephaly has severe brain dysfunction.
  - But delaying a diagnosis of FAS until 6 years of age will adversely impact early intervention, prevention, and surveillance efforts.

It turns out, the combination of
microcephaly (≤ 3rd percentile) AND the Rank 4 FAS Face
is highly predictive of severe CNS dysfunction[1,2]

In the FAS DPN Clinic

Among 50 patients 1-23 years of age with microcephaly AND the Rank 4 FAS Face

All over 6 years of age had severe CNS dysfunction (CNS Rank 3)

Brain Function	0-6 yrs old	7-23 yrs old
CNS 1: normal	68%	0%
CNS 2: moderate dysfunction	18%	0%
CNS 3: severe dysfunction	15%	100%

The Problem with the Term ARND

How to fix the problem

The Problem with the terms FAE and ARND[2,10]

The field continues to struggle with what to label the condition characterized by prenatal alcohol exposure and CNS abnormalities when the FAS facial phenotype is absent.

The problem with the diagnostic terms used to date:

- Fetal Alcohol Effects (FAE) and
- Alcohol-Related Neurodevelopmental Disorder (ARND)

They imply that the patient's outcomes are *alcohol effects or alcohol-related.*
They imply *alcohol caused the patient's* outcomes.

But this presumption in an individual patient is medically invalid because the CNS abnormalities are not specific to (caused only by) prenatal alcohol exposure.

There are many other known and unknown risk factors that may be partly or even fully responsible for the patient's outcome.

In the absence of the FAS facial phenotype, current medical technology has no ability to confirm or rule-out the causal role of alcohol in an *individual patient.*

And…It is NEVER just alcohol[1-3].

There are many other known and unknown risk factors that may be partly or even fully responsible for the patient's outcome.

Risk Factors Among 2,550 FASD Patients	
Prenatal alcohol exposure	100%
No prenatal care	31 %
Maternal learning disabilities	36 %
Other adverse prenatal exposures	93 %
Prenatal tobacco	62 %
Prenatal crack/cocaine	37 %
Perinatal difficulties	53 %
Foster/adoptive care	85 %
Physical abuse	34 %
Sexual abuse	24 %
Neglect	64 %
Home placements (average #)	3

Solution: Replace ARND with ND/AE and SE/AE [11]

- In 1995, Aase, Jones, & Clarren proposed discontinuation of the term Fetal Alcohol Effects (FAE).

> " We propose abandoning the clinical use of the term FAE with its implications of causation. A diagnosis that implies causation should not be applied unless the relationship can be proven. If prenatal alcohol exposure has taken place, but FAS cannot be substantiated, the exposure still should be indicated, and any nonspecific abnormalities or problems noted. Several unfortunate consequences may result from inappropriately using the term FAE: Women are stigmatized for having damaged their children by drinking during pregnancy when it is by no means certain that they have done so."

- But, in 1996, the term Alcohol Related Neurodevelopmental Disorder (ARND) was introduced with all the same limitations of FAE (IOM, 1996).

- In 1997, the 4-Digit Code introduced the following terms to replace ARND (Astley, Clarren, 1997) :
  - ND/AE Neurobehavioral Disorder / Alcohol Exposed
  - SE/AE Static Encephalopathy / Alcohol Exposed

- One need not confirm a causal link between a patient's alcohol exposure and neurodevelopmental disorder to provide effective intervention (Bertrand et al, 2009, Olson et al.,2007) and prevention (Astley et al., 2004).

- Access to services should be based on a person's disability, not on what caused their disability (Aase et al., 1995, Astley 2011).

The slippery slope of ARND[2]

When you use a term like ARND, you find yourself wanting/needing to require an excessive exposure to alcohol to increase the odds that the child's impairments might in fact be caused, at least in part, by their alcohol exposure.

This is a dangerous road to go down.

1. Setting a threshold of excessive exposure for Alcohol Related Neurodevelopmental Disorder (ARND) does not confirm the patient's Alcohol exposure is Related to their Neurodevelopmental Disorder.

2. Alcohol is NEVER the only risk contributing to the neurodevelopmental disorder.

3. You are sending a dangerous message that lower levels of alcohol exposure are safe?

4. You are blaming a woman for harming her child, when you have no ability to make/defend such a claim. These claims have consequences.

"ARND" has been diagnosed effectively for 20 years, without calling it ARND[1-3]

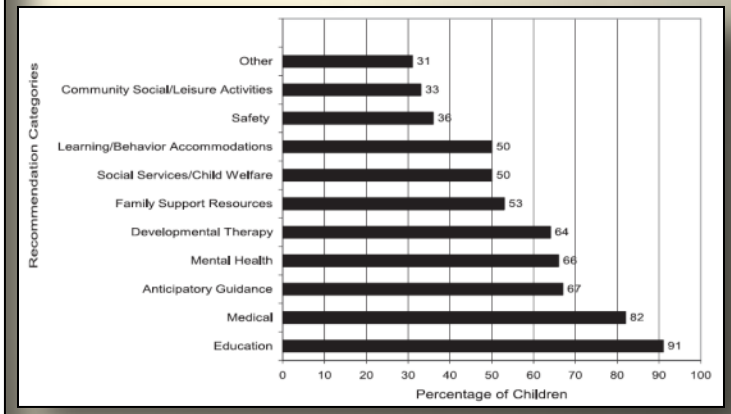
- Washington State has effectively case-defined, diagnosed, and referred children with "ARND" for intervention services using the 4-Digit Code for 20 years.
- 1,730 diagnosed to date.
  - 1,122 Neurodevelopmental Disorder / Alcohol Exposed (ND/AE) "moderate ARND"
  - 612 Static Encephalopathy / Alcohol Exposed (SE/AE) "severe ARND"
- 100% have confirmed exposure , most as high as those with FAS.
- All risk factors are documented and reported in the medical record, not just the alcohol.
- All receive comprehensive intervention recommendations. (Jirikowic, et al, 2010)
- It is a child's disability, not their exposure, that qualifies them for services.
- 84% of families report the intervention services met all or most of their needs.[3]

Final Diagnosis: **(1) Static encephalopathy**
(2) Alcohol exposed

Fetal Alcohol Syndrome (FAS) is defined by evidence of growth deficiency, a specific set of subtle facial anomalies, and evidence of central nervous system (CNS) damage/dysfunction occurring in patients exposed to alcohol during gestation. Not all individuals exposed to alcohol during gestation have FAS.

In this patient's case, no growth deficiency or characteristic set of facial features were found so the patient does not have FAS, but there was evidence of significant CNS damage/dysfunction as you will see noted on the attached pages. There was also a clear history of exposure to significant amounts of alcohol during gestation. In this situation, we use the term "static encephalopathy" to describe the patient's condition. On the attached sheets are the specific findings in this patient's case that led us to this conclusion. The diagnosis of static encephalopathy does not mean that alcohol is the only cause of the problem. A number of other factors could be contributing to the present issues such as the patient's genetic background, other potential exposures or problems during pregnancy, and various experiences since birth. These kinds of differences may partly explain why there is so much variability in the kinds of specific difficulties that patients with static encephalopathy face.

Individuals with significant CNS abnormalities have structural, neurological, and/or cognitive/behavioral evidence of CNS damage/dysfunction, and should be viewed as individuals with disabilities. The diagnosis of static encephalopathy has implications for educational planning, societal expectations, and health. On the attached sheet you will find a list of specific problems that have been identified that need attention.



Astley

The term ARND is not needed to qualify for services[1]

There tends to be a strong belief among families and some clinicians that the only diagnosis that will qualify a child for services is FAS.

Along the same lines, it is also believed that the outcome must be blamed on (linked to) the alcohol (e.g., ARND) for a child to qualify for services.

20 years of family surveys in the WA State FASD clinics confirm that a diagnosis of FAS or ARND is not required to access and benefit from services.

Families whose children received a diagnosis of:

- Static Encephalopathy / Alcohol Exposed (SE/AE) or
- Neurodevelopmental Disorder / Alcohol Exposed (ND/AE)

were as likely to access and benefit from services as families whose children received a diagnosis of FAS/PFAS.

Patient Satisfaction Survey (N = 577)	FAS/PFAS %	SE/AE %	ND/AE %
Somewhat to very successful at finding/accessing recommended services	81	87	85
Services met some to all of my needs	91	81	86

Should ND/AE be included under the umbrella of FASD?

YES

Here is why

ARND presents along a continuum.

Static Encephalopathy / Alcohol Exposed (SE/AE) = Severe ARND
Neurobehavioral Disorder / Alcohol Exposed (ND/AE) = Moderate ARND

Other Guidelines do not include this “moderate ARND” group under the umbrella of FASD.

Example of Contrasts between the Diagnostic Systems

An example where the 4-Digit Code differs from the other FASD Diagnostic Guidelines.

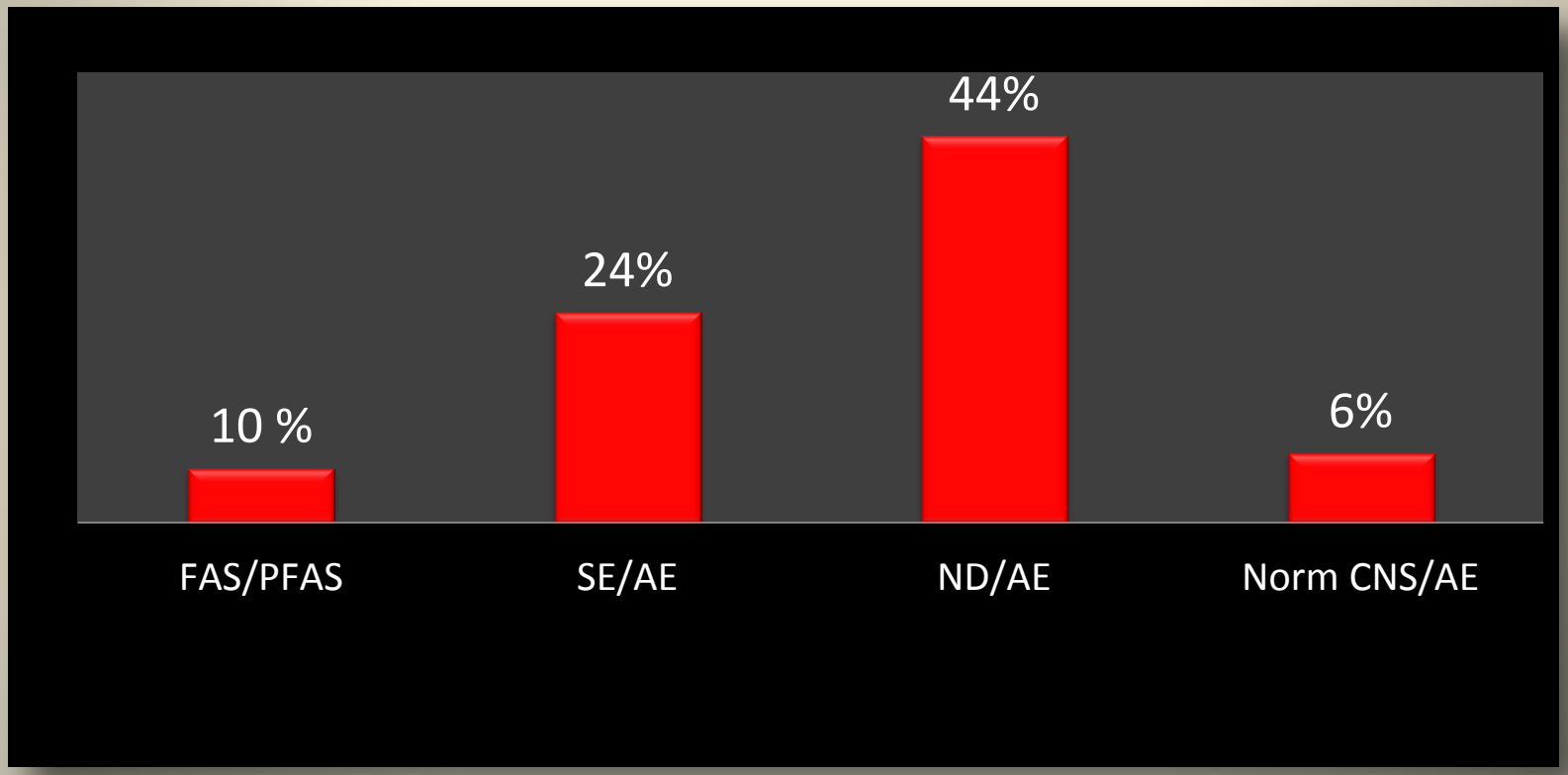
Patient Outcomes (10 years old)	
Growth	Height 50th percentile, weight 50th percentile
Face	PFL: Normal, 50th percentile Philtrum: Normal, Rank 2 Upper lip: Normal, Rank 2
CNS	2 Domains of significant dysfunction (ADHD, Memory) No CNS structural or neurological abnormalities.
Alcohol	Binge drinking weekly throughout pregnancy.
Diagnostic Classifications	
IOM	Not FASD
4-Digit Code	Neurobehavioral Disorder/Alcohol Exposed (Code = 1124)
Canadian	Not FASD
CDC	Not FAS
Revised IOM	Not FASD

Should thresholds or patterns of Alcohol use be required?[2]

Table 3. ARND (or its equivalent: Static Encephalopathy/Alcohol Exposed or Neurobehavioral Disorder/Alcohol Exposed) diagnostic criteria. Comparison across the five most current FAS/D diagnostic guidelines.

	4-Digit Code (1997-2004)	CDC[a] (2004)	Canadian (2005)	Hoyme (2005)	IOM (1996)
Growth	Normal to deficient (Growth Ranks 1-4)	--	No growth deficiency (Growth Rank 1)	No growth deficiency (Growth Rank 1)	No growth deficiency (Growth Rank 1)
Face	No more than 1 of the following: • PFL ≤ 3rd percentile • Philtrum Rank 4 or 5 • Lip Rank 4 or 5 (Face Ranks 1-2)	--	No FAS facial phenotype (Face Rank 1)	No FAS facial phenotype (Face Rank 1)	Presumably no components of the pattern of FAS characteristic facial anomalies. (Face Rank 1)
CNS	Criteria for "Static Encephalopathy" At least 1 of the following: • Structural/Neurological: (e.g., OFC ≤ 3rd percentile, abnormal structure, seizure disorder, hard signs) • Severe Dysfunction: (3 or more domains of function with impairment 2 or more SDs below the mean) (CNS Rank 3 and/or 4) Criteria for "Neurobehavioral Disorder" • No Structural/Neurological abnormalities. • Moderate Dysfunction: (1-2 domains of function with impairment ≥ 1.5 SDs below the mean) (CNS Rank 2)	--	At least 3 of the following Structure/Neurological/Functional domains with significant impairment: • Hard/soft signs, structure, cognition, communication, academic achievement, memory, executive functioning, abstract reasoning, ADD, adaptive behavior, social skills, or communication (CNS Ranks 3-4)	At least 1 of the following: • Structural ○ OFC ≤ 10th percentile ○ Abnormal structure • Dysfunction ○ Complex pattern of behavior / cognitive abnormalities (CNS Ranks 1-4)	At least 1 of the following: • Structural/Neurological: ○ Decreased cranial size at birth ○ Abnormal structure ○ Hard/soft signs • Dysfunction ○ Complex pattern of behavior / cognitive abnormalities (CNS Ranks 2-4)
Additional Criteria	The term ARND is not used. The following terms are used in lieu of ARND: Static Encephalopathy (Severe dysfunction) Neurobehavioral Disorder (Moderate dysfunction)	--			
Alcohol	Confirmed (Alcohol Ranks 3 or 4)	--	Confirmed (Alcohol Ranks 3 or 4)	Confirmed-excessive (Alcohol Rank 4)	Confirmed-excessive (Alcohol Rank 4)

FASD Diagnostic Outcomes for 2,550 Patients[1-3]



ND/AE represents 44% of our alcohol-exposed clinic population.

ND/AE have alcohol exposures as high as FAS/PFAS[3]

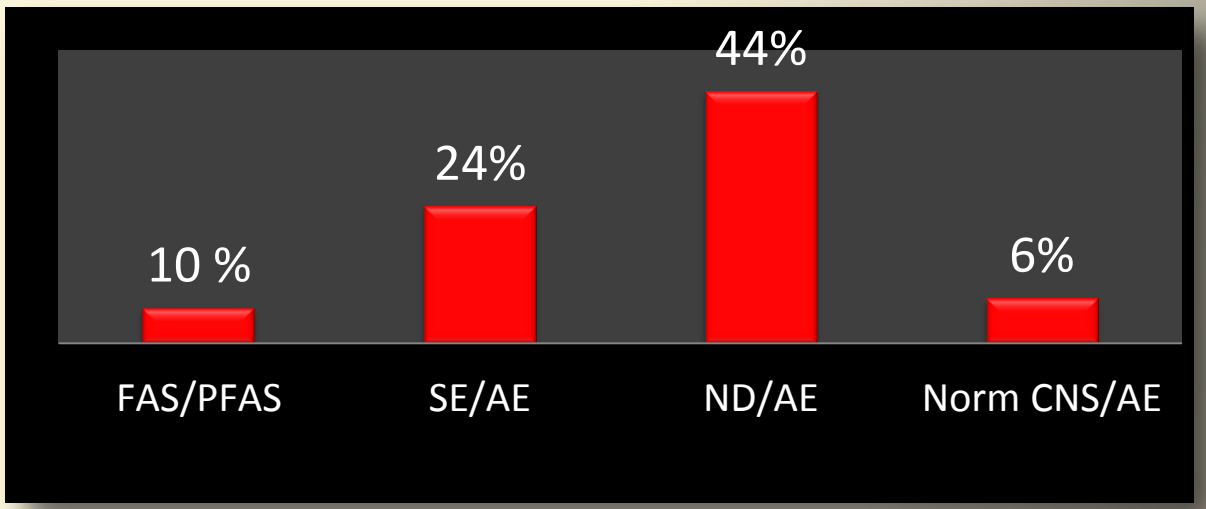
During Pregnancy	FAS	SE/AE	ND/AE
Ave # drinks	8.2	9.8	9.3
Max # drinks	12.5	12.9	13.3
Ave days/week	5.6	4.3	4.4

Alcohol does cause moderate dysfunction (ND/AE)

FASDPN Clinic:

44 % of 2,550 patients had ND/AE, but many other risk factors were present.

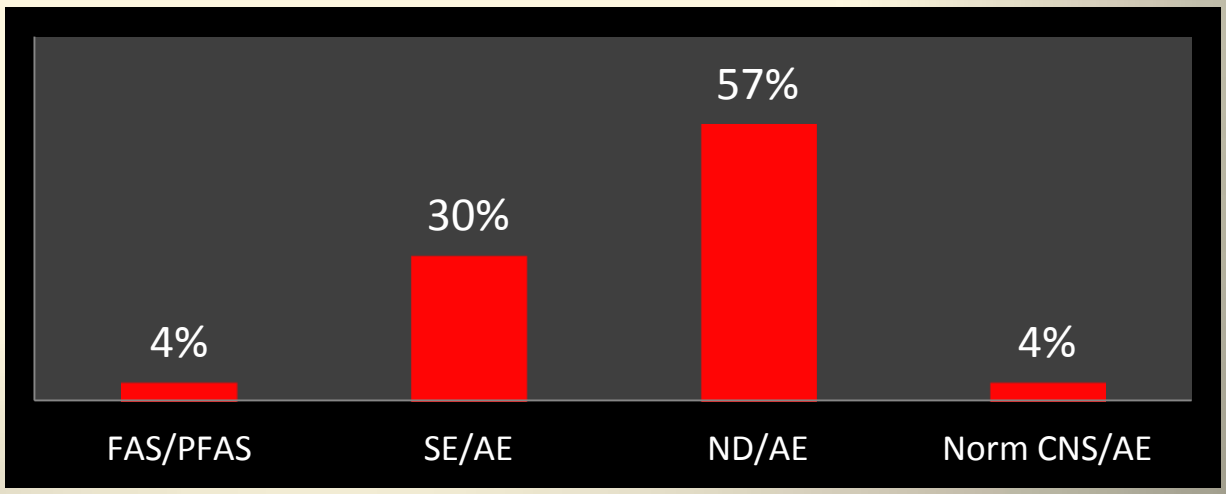
(Astley, 2010)



Primate Study:

57 % had ND/AE, and NO other risk factors were present.

(Clarren et al., 1992)

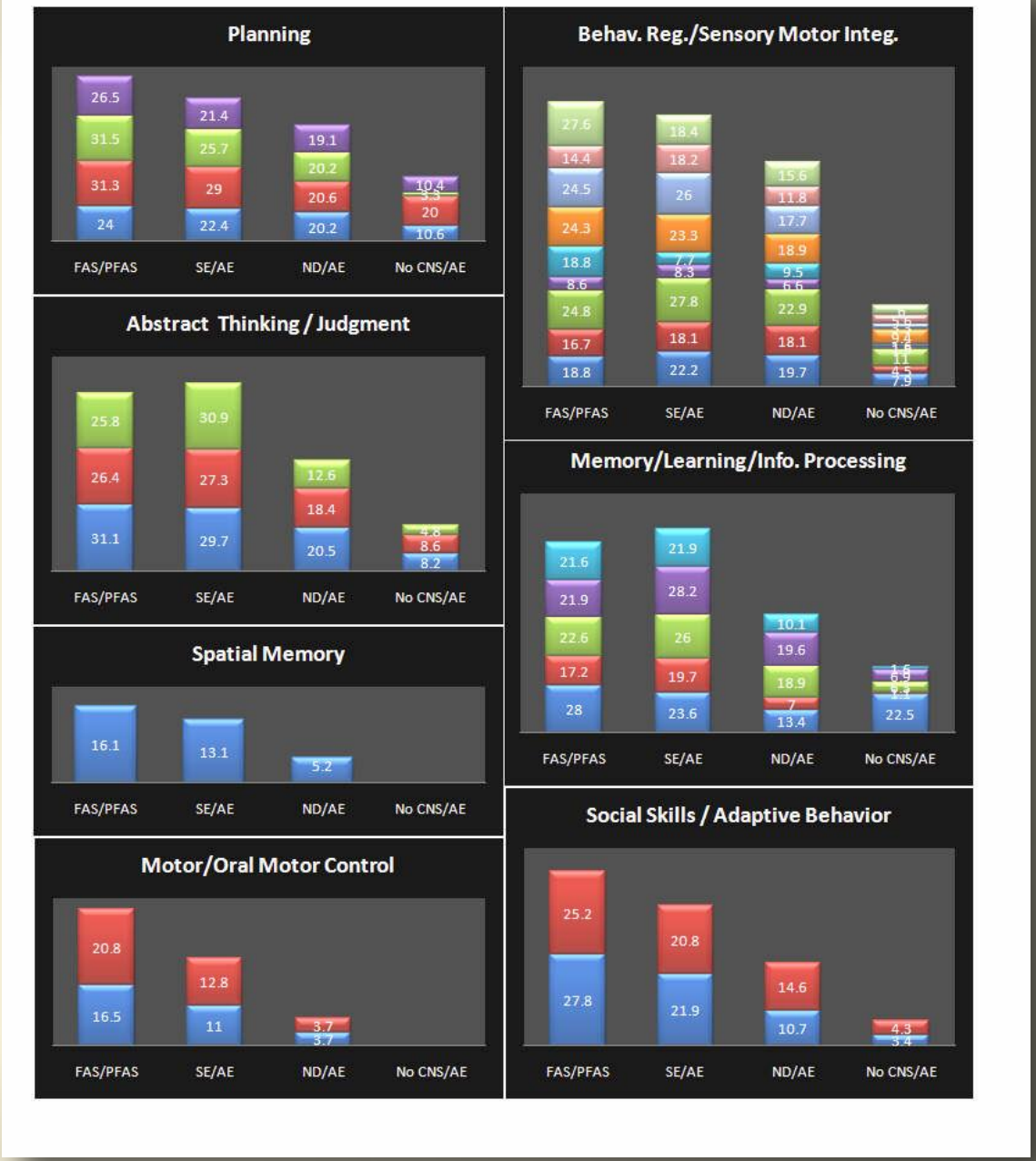


Among 1,122 Patients with ND/AE[1-3]

Proportion of Patients with Significant Dysfunction	
Cognition	3 %
Achievement	36 %
Executive Function	18 %
Language	17 %
Motor / Sensory	29 %
Development	35 %
ADHD	45 %
Adaptation	36 %

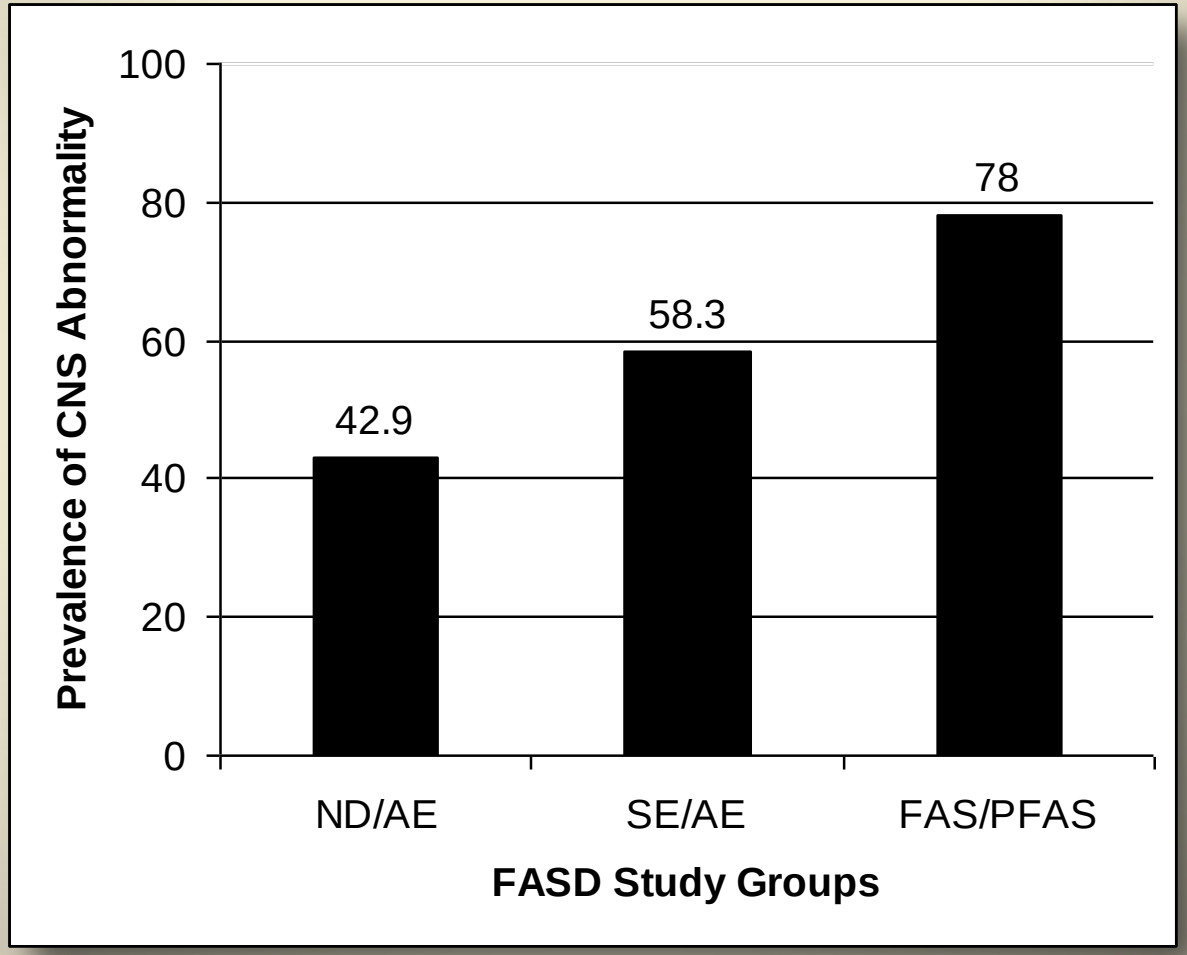
Parents view children with ND/AE as having significant challenges across all domains[3].

Parent's Report of Child's Behavior
via
Parent Interview with Psychologist and MD



Parent interview (page 6) of the Diagnostic Form

At least 43% of the ND/AE group have CNS structural abnormalities! [3]



Bottom line…

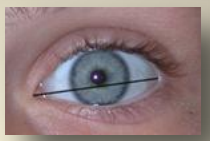
Neurobehavioral Disorder / Alcohol Exposed (ND/AE) should be included in FASD Diagnostic Guidelines.

By calling it ND/AE,
we are accurately declaring the child:

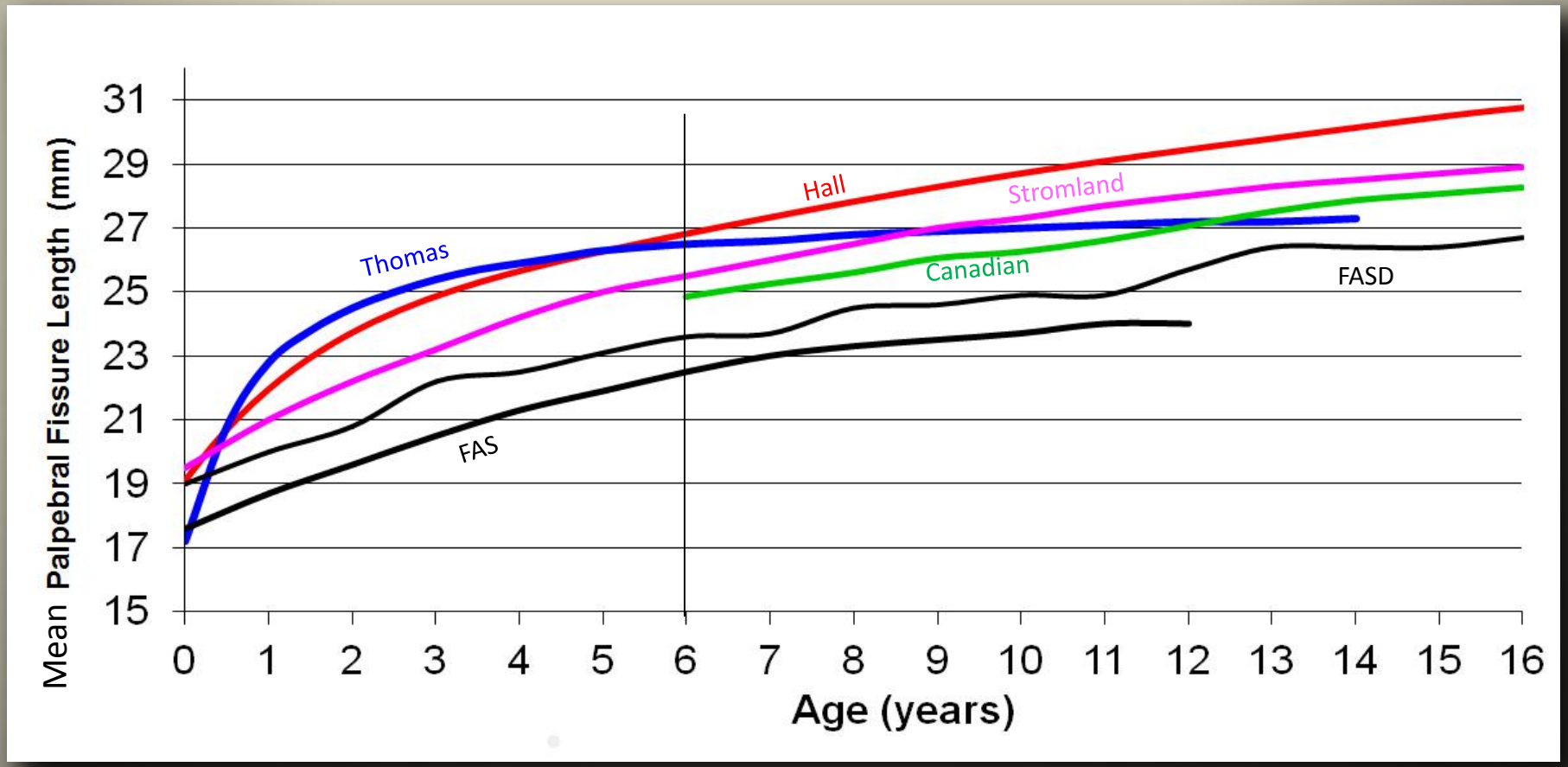
1. has a Neurobehavioral Disorder and
2. was exposed to a teratogen (alcohol)

Which PFL Charts to Use

Which PFL Chart to Use[5]

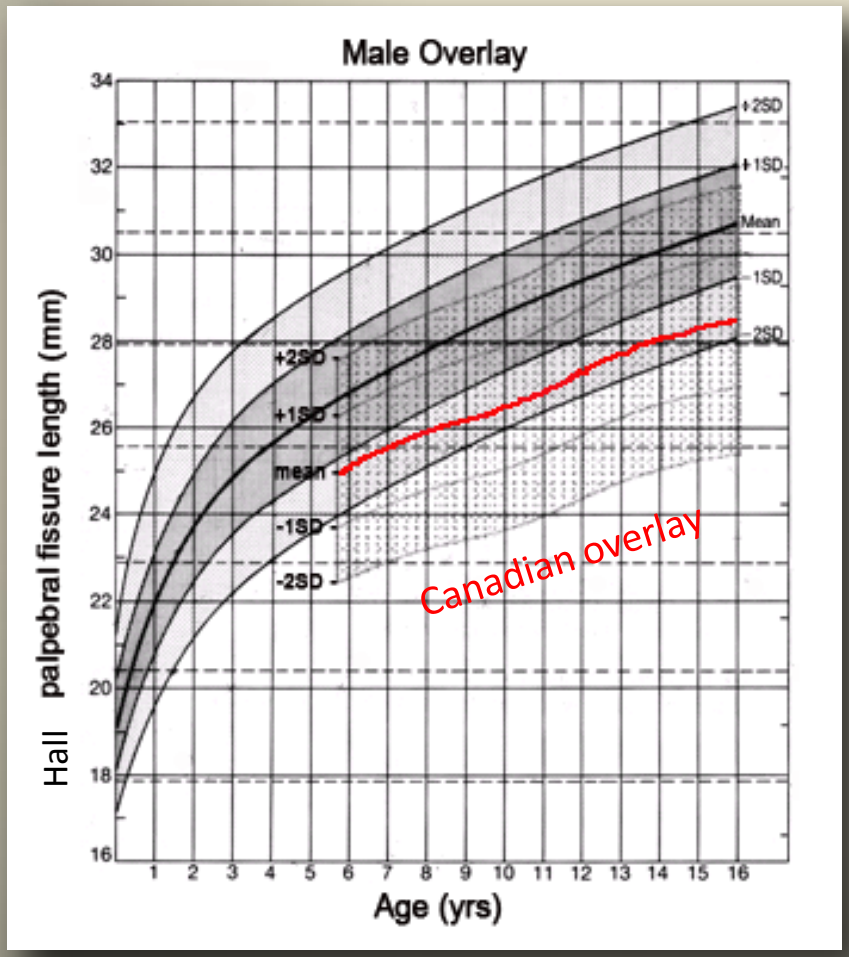


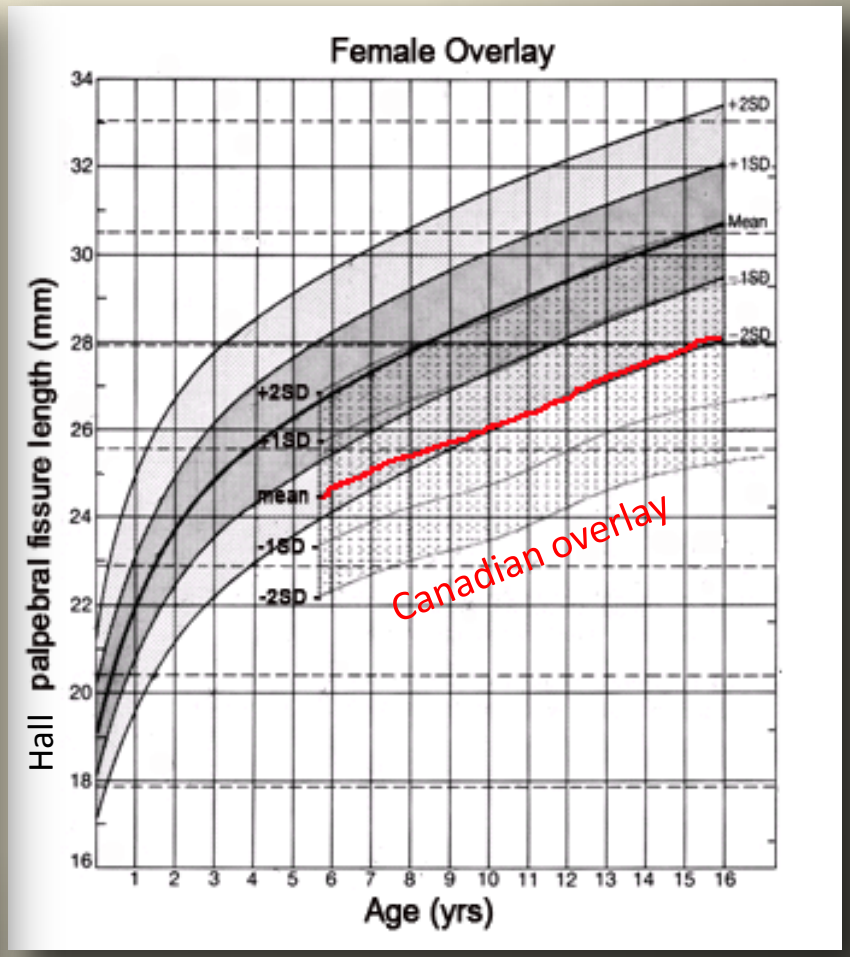
Thomas	Poor fit. Curve does not match true growth trajectory from birth to 16.
Hall	Good curve fit, but PFL too large.
Canadian	Good curve fit, PFL correct size, but chart starts at 6 years of age.
Stromland	Good curve fit, PFL correct size, chart extends across the full age range.



Hall PFL Chart with Canadian Overlays[5]

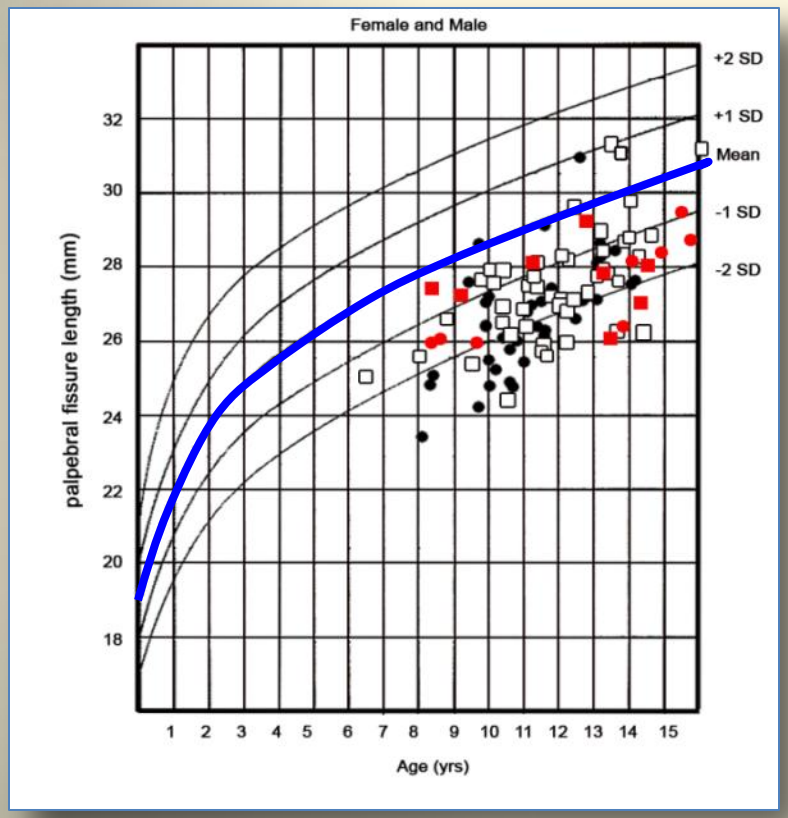
Hall PFL chart over estimates true PFL by 2mm.
The Canadian mean PFL is 2 SDs below the Hall mean PFL.

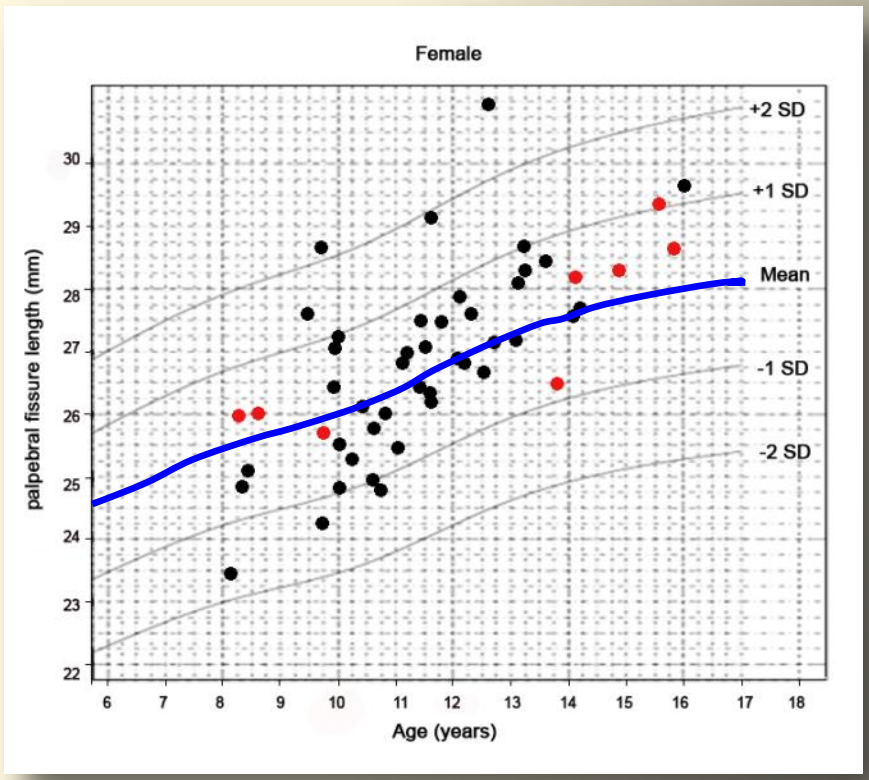




U.S. Caucasians good fit on Canadian PFL Charts[5]

106 healthy school children plotted on Hall and Canadian PFL charts





Hall Chart:
U.S. population falls 1.5 SDs below mean.

Canadian Chart:
U.S. population clusters around mean.

Use of Hall Charts did not generate inaccurate FAS diagnoses[5]

Since the Hall PFL Chart over estimates the true size of a PFL, it will over estimate the number of children with short PFLs.

This could lead to an inaccurate over diagnosis of FAS.

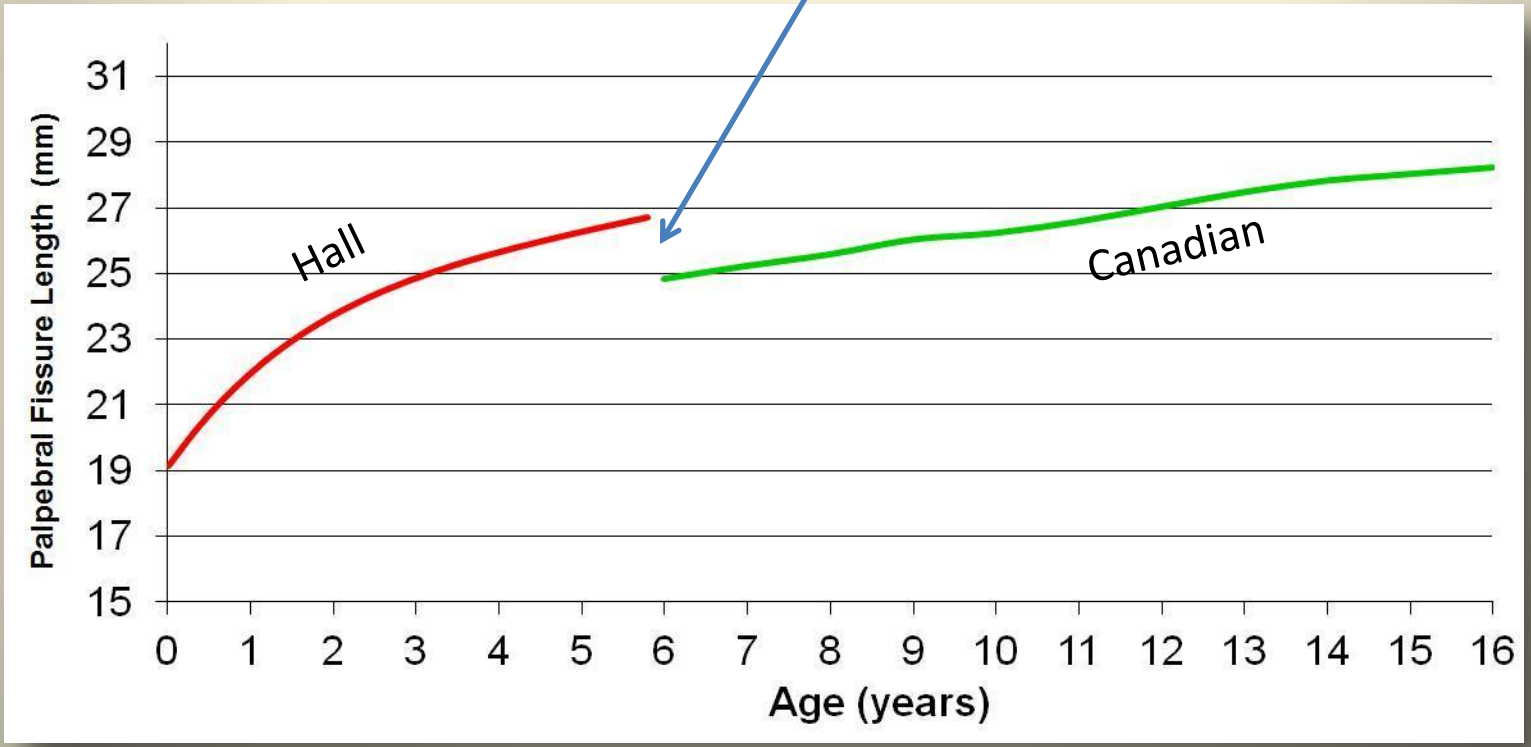
To test this concern, all patients who received a diagnosis of FAS in the past 18 years at the FAS DPN clinic had their PFL z-scores recomputed using the Canadian PFL Charts.

No patient lost their diagnosis of FAS. All continued to meet the PFL criteria of 2 SDs below the mean.

4-Digit Code PFL Criteria for FAS	2.0 SDs below the mean
Mean PFL for all patients with FAS using Hall	3.9 SDs below the mean
Mean PFL for all patients with FAS using Canadian	2.4 SDs below the mean

Canadian PFL starts at 6 years old[5]

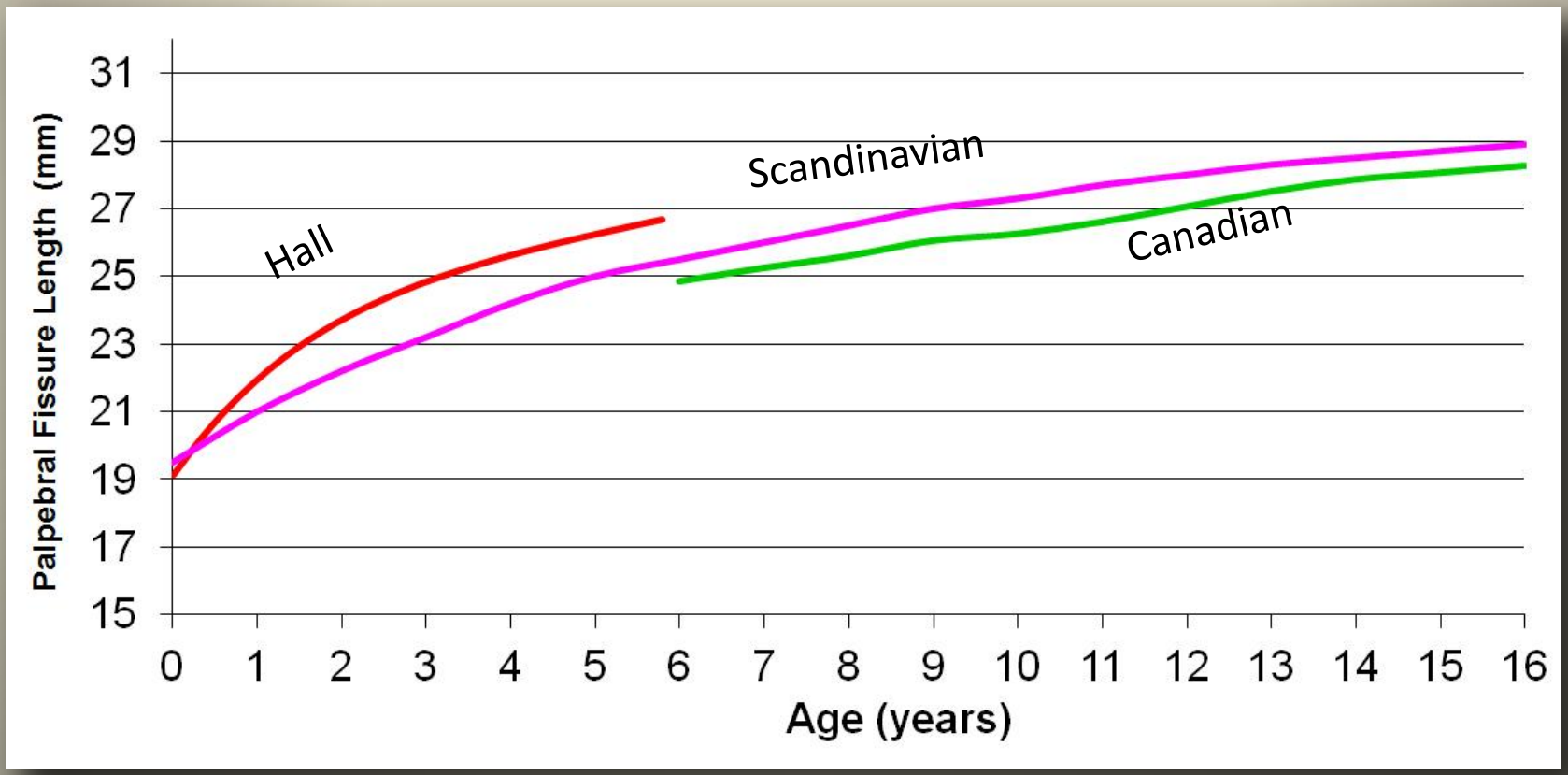
Thus, a 5.9 year-old on Hall chart has PFLs 2 mm larger than a 6.0 year old on Canadian chart.



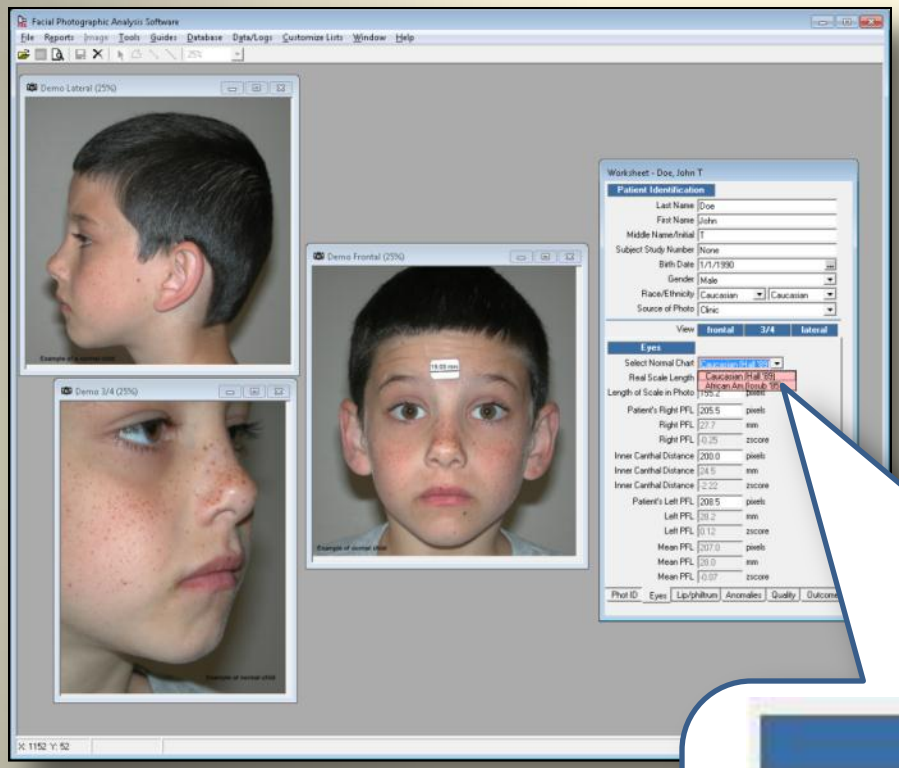
Stromland Scandinavian PFL Chart Covers Full Age Range

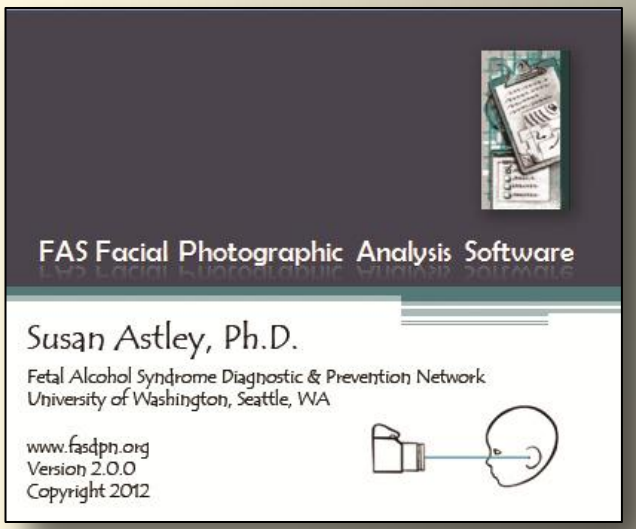
University of Washington FASD Clinic uses the Stromland PFL Chart to avoid inaccurate leap in PFL for children < 6 years old.

(35% of our FASD Clinic population is < 6 years old)

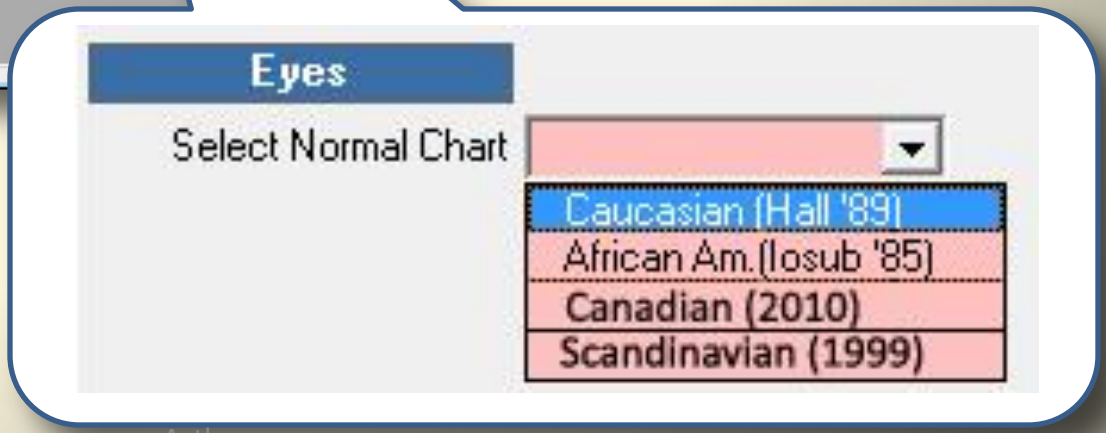


Canadian and Scandinavian PFL Charts added to Facial Software, Version 2.0[18]





Version 2.0 Software released Nov, 2012.



The Lip-Philtrum Guides

When is a Philtrum Rank 4 or 5?

The facial phenotype of FAS includes a Rank 4 or 5 philtrum.

Too often, I observe clinician's coding a Rank 3 philtrum as a Rank 4 philtrum.

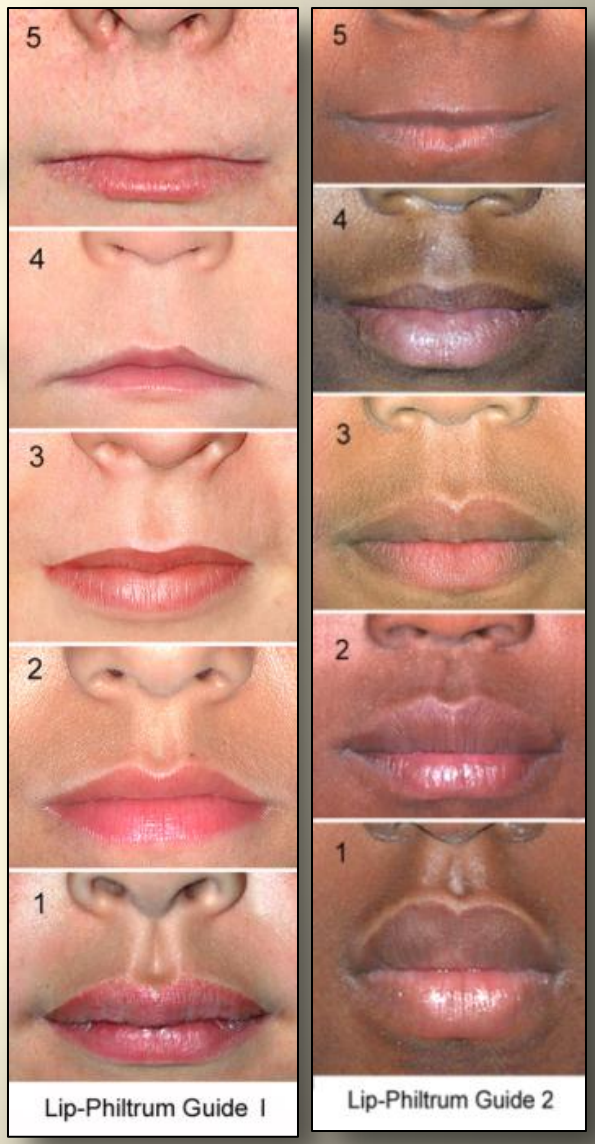
The philtrum is the vertical groove between the nose and upper lip

In the slides below, I have provided detailed descriptions and photographs of Rank 4 and 5 philtrums.

These additional aids should help you:

- differentiate a Rank 4 from a Rank 5,
- differentiate a Rank 3 from a Rank 4.

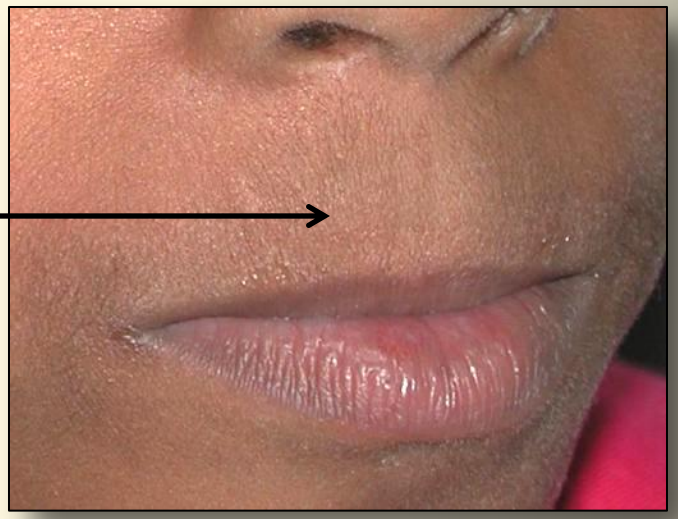
FAS



Definitions and Pictorial Examples of Rank 5 and Rank 4 Philtrums[18]

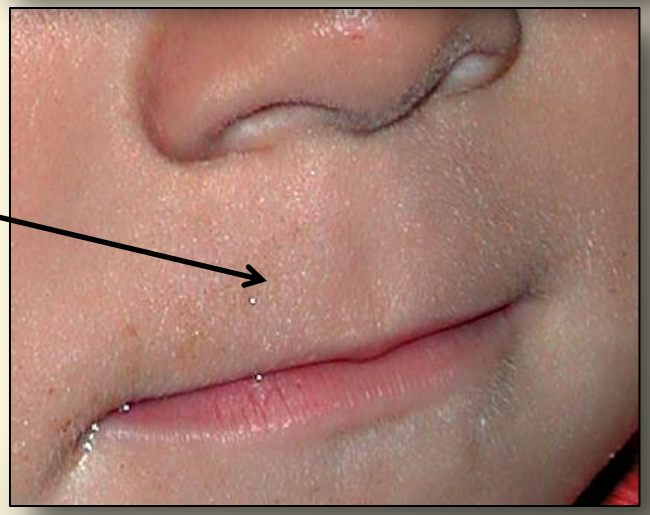
Definition of a Rank 5 Philtrum:

- **Absolutely smooth**. No hint of a philtrum depression, no matter what angle you view it at.



Definition of a Rank 4 Philtrum:

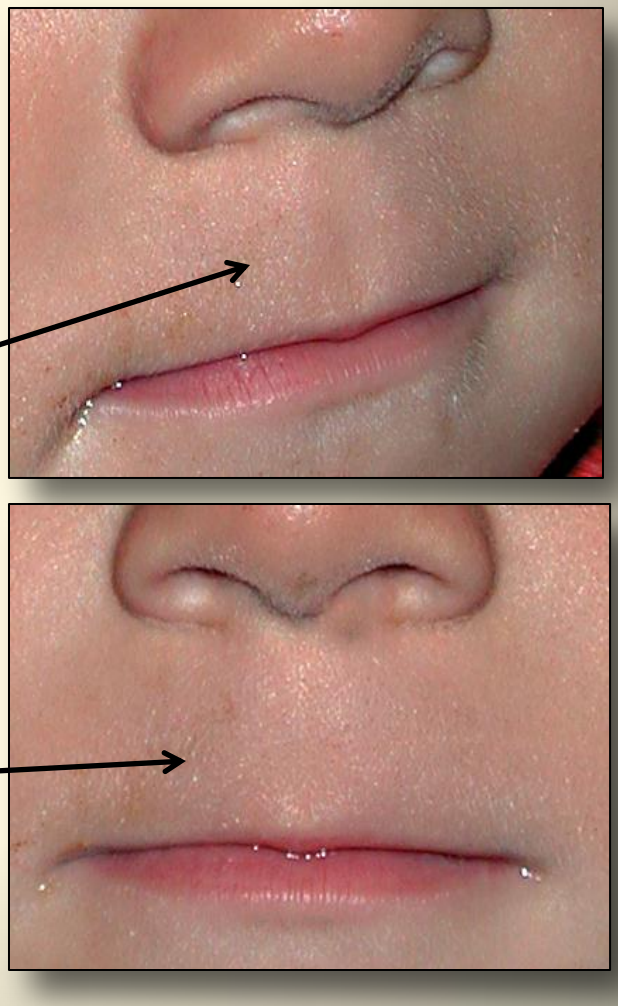
- **Just the bare semblance of a depression** exists. You typically have to view the philtrum from an angle to detect it. A Rank 4 philtrum is so close to being smooth, it is often difficult to detect in a frontal photograph.



These photos are posted on fasdpn.org

Angle and Frontal Views of a Child with a Rank 4 Philtrum[18]

Angle and Frontal Views of a child with a Rank 4 Philtrum



Definition of a Rank 4 Philtrum:

Just the bare semblance of a depression exists.

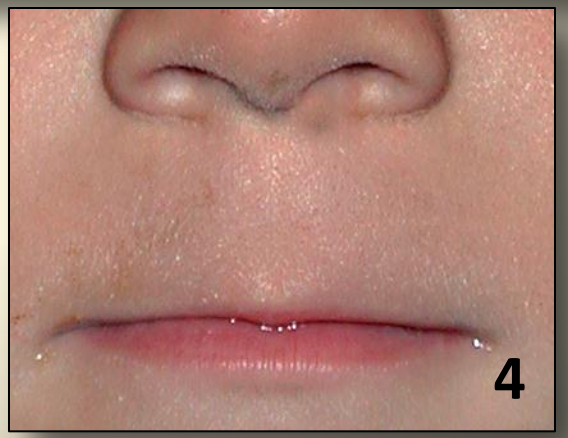
- You typically have to view the philtrum from an angle to detect it.

- A Rank 4 philtrum is so close to being smooth, it is often difficult to detect in a frontal photograph.

Angle and Frontal views of Rank 5 and Rank 4 Philtrums

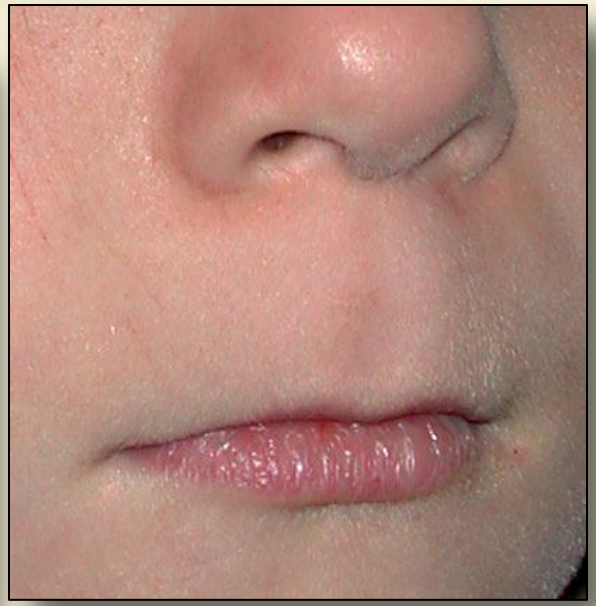
Rank 5

Rank 4



Astley

Further examples of angle and frontal views of Rank 4 Philtrums



Conclusion (Astley, 2011)[2]

Accurate, reliable, diagnoses across the full continuum of FASD have been available to families and clinicians for over a decade. As medical technology and our understanding of FASD advance, so must our diagnostic methods and tools. It is imperative that advancements in diagnostic methods be guided by an evidence base of rigorously designed, implemented, and peer-reviewed research. When a diagnosis under the umbrella of FASD is made, two individuals are affected directly; the child and the birth mother. The consequences of an incorrect diagnosis for both mother and child must be considered carefully. Diagnostic guidelines should guide professionals in rendering an accurate diagnosis. A diagnosis reflects the condition of a patient; however, because a diagnosis serves many purposes (eg, treatment, prevention, communication among specialists, and qualification for services), the process of rendering a diagnosis can sometimes be influenced by those different purposes. The only diagnosis that serves all purposes most effectively is a correct diagnosis. Access to services should be based on an individual's disabilities and not on what caused their disabilities. Therefore, services should be available for individuals across the full continuum of FASD and not just those with FAS.

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17. Jirikowic T, Gelo J, Astley S Children and youth with fetal alcohol spectrum disorders: Summary of intervention recommendations after clinical diagnosis. Intellectual and Developm Disabilities 2010;48(5):330-344.
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All literature referenced in this presentation is available at: www.fasdpn.org/htmls/literature.htm