### The North Dakota Integrated Developmental Disorders Study Plan

**Larry Burd, Ph.D., Department of Pediatrics, University of North Dakota School of Medicine & Health Sciences**

<table>
<thead>
<tr>
<th>Disorder / Condition</th>
<th>Case-Control Birth Certificates</th>
<th>12 Year Outcome</th>
<th>Cost Studies</th>
<th>Service Use</th>
<th>Developmental Comorbidity</th>
<th>Risk Factors</th>
<th>Bio-Markers</th>
<th>Prevention</th>
<th>Treatment</th>
<th>Recurrence Risk</th>
<th>Mortality</th>
<th>Genomics</th>
<th>Enviromics</th>
<th>Brain Registry</th>
<th>Cohort Comparisons</th>
<th>Prevalence</th>
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FASD — Fetal Alcohol Spectrum Disorder  
ADHD — Attention Deficit - Hyperactivity Disorder  
SIDS — Sudden Infant Death Syndrome  
SED — Severely Emotionally Disturbed
FASD: Why Can’t We See It?

Larry Burd, PhD
Director, North Dakota Fetal Alcohol Syndrome Center
larry.burd@med.und.edu    701-777-3683
A Note on the Influence of Maternal Inebriety on the Offspring

By W. C. Sullivan, M.D., and Stewart Scholar in Mental Disease, R.U.I., Deputy Medical Officer, H.M. Convict Prison, Parkhurst (July, 1899)
Two Hundred and Fifty-Eight Cases of Suffocation of Infants

By Charles Templeman, M.D.,
B.Sc. (Pub. Health), Surgeon of Police;
Surgeon to the Royal Infirmary, Dundee.

(Read before the Medico-Chirurgical Society of Edinburgh,
1st June 1892.)
Five Things That Are Just Not So!

1. Many women drink during pregnancy - just not the ones I see
2. Asking about drinking will complicate my relationship with my patient
3. Drugs are a bigger problem here.
4. We are already doing everything that needs to be done
5. FASD is just too much stigma
The UK had 365,606 women using alcohol during pregnancy in 2018

Heavy uses (6%) who drink all 40 weeks of pregnancy = 21,936

How many are identified?
Alcohol Elimination Kinetics

- Absorption
- Dispersion
- Metabolism
- Excretion

- First in to last out
Architecture of Exposure Episodes

- Drinking days
- Drinks per day
- Cumulative exposure
- Polysubstance exposure
- Multiplicative effect of combined exposure

Dosimetry and cumulative exposure effects

- Smoking days
- Cigarettes per day
- Cumulative exposure
Fetal Compartment

1. Exposure: First in - to - last out
2. Teratogenic Fraction
3. Cumulative Dosimetry
Exposure Assessment

How We Do It

Exposure

Risk Stratification

When was your last drink?

<table>
<thead>
<tr>
<th>Before</th>
<th>Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-awareness</td>
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<tr>
<td></td>
<td>Post-awareness</td>
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<table>
<thead>
<tr>
<th>Unexposed</th>
<th>Exposed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exposed &amp; High Risk</td>
</tr>
</tbody>
</table>

Charting PAE During Pregnancy

On average, how many days per week did you drink during pregnancy? _____ (a)

On an average drinking day during pregnancy, how many drinks did you have? _____ (b)

How many days per month did you have 4 or more drinks during pregnancy? _____ (c)

What is the most you had to drink on any one day during pregnancy? _____ (d)

What is a drink? Alcohol %_____ Drink vol _____
Fetal Exposure Assessment

Screening for Prenatal Alcohol Exposure

When Was Your Last Drink?

<table>
<thead>
<tr>
<th>Before</th>
<th>During Pregnancy</th>
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<tr>
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<td>Unexposed</td>
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<tr>
<td></td>
<td>Pre-awareness</td>
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Risk Stratification

<table>
<thead>
<tr>
<th>What is a drink?</th>
</tr>
</thead>
<tbody>
<tr>
<td>No use reported, but concerns remain</td>
</tr>
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</table>

Maternal Risk Score

- Age over 25 years
- Unmarried, divorced, widow, living with partner
- On TANF, WIC, Social Security or income < $15,000/year
- Did not graduate from high school
- Poor diet
- Smokes more than 1 pack per day

Score Adjustment for any score checked

- Drinks less than 2 drinks/week & less than 2 drinks drinking day
- Age first drink—less than 15 years
- In treatment over three times
- In treatment in last 12 months
- Previous child with FASD, birth defect or developmental disability
- Previous child died
- Children out of home (foster care or adopted)

Score Adjustment for any score checked

- Heavy drinker (drinks 3 or more drinks/day for 3 or more days per week, or more than 5 drinks/day on 6 or more occasions)
- Uses inhalants, sniff, huff or illegal drugs

Score

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Recommendations</th>
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<tbody>
<tr>
<td>0 None</td>
<td>Standard prenatal care</td>
</tr>
<tr>
<td>5 Low</td>
<td>Standard prenatal care</td>
</tr>
<tr>
<td>20-40 Moderate</td>
<td>Standard prenatal care and patient education on FASD</td>
</tr>
<tr>
<td>45-50 High</td>
<td>High risk pregnancy, prompt in office intervention or alcohol drug abuse treatment</td>
</tr>
<tr>
<td>55-105 Very High</td>
<td>High risk pregnancy, alcohol drug abuse treatment</td>
</tr>
</tbody>
</table>

Exposure Risk Markers

- History of maternal substance abuse
- Premature birth (<36 weeks)
- Congenital Defects
- Family history of substance abuse
- Emergency room visit with concerns about substance abuse
- Mother smokes
- Mother has been in jail or prison

Assessment of Exposure During Pregnancy

Chart These

- On average, how many days per week did you drink during pregnancy? (a)
- On an average drinking day during pregnancy, how many drinks did you have? (b)
- How many days per month did you have 4 or more drinks during pregnancy? (c)
- What is the most you had to drink on any one day during pregnancy? (d)
- What is a drink? Alcohol % _______ Drink vol _______ (e)
- How many cigarettes/day? (f)
- How many days per week? (g)

Calculate Exposure Parameters

**Cumulative exposure during pregnancy**

**Pregnancy Drinking Days**

\[ \text{Pregnancy Drinking Days} = (a \times 40) \]

Estimates number of drinking days during pregnancy.

**Percentage of Days Exposed During Pregnancy**

\[ \text{Percentage of Days Exposed During Pregnancy} = \frac{(e - 280)}{(e - 280) + (e \times 9)} \]

Estimates days exposed during pregnancy.

**Number of Binge Days**

\[ \text{Number of Binge Days} = (c \times 9) \]

(4 or more drinks in 1 day)

Estimates number of binge days.

**Number of Drinks During Pregnancy**

\[ \text{Number of Drinks During Pregnancy} = (a \times b) \]

Estimates cumulative number of drinks during pregnancy.

**Ounces of absolute alcohol**

\[ \text{Ounces of absolute alcohol} = (f \times 2) \]

Estimates cumulative absolute alcohol exposure during pregnancy.

Smoking days exposed

Maternal Alcohol Use History

**Confirmed Exposure**

- Maternal Report
- Medical Chart
- Criminal Record

**Confirmed No Exposure**

- Reliable Reporter of Exposure
- No Reporter
- Child in Foster Care
- Mother is Dead
- Adopted - no history

- Maternal Report
- Quit Before Pregnancy
- Never Drinker
Do not ask more than one exposure question at a time!
Days from Conception to Last Known Drink

Blood Alcohol Concentration

First Visit; r = .513
Second Visit; r = .434
Third Visit; r = .069
Average; r = .266
<table>
<thead>
<tr>
<th>Drinks</th>
<th>Maternal BAC</th>
<th>Alcohol Accumulation in Fetal Compartment</th>
<th>Alcohol Elimination to 0</th>
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Alcohol Elimination Rates (AER) in Ten Mother - Newborn Pairs

Burd et al., 2012
No deaths at BAC <96 mg/dl
## What About My Mom?

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>FASD Mothers</th>
<th>Sample Size</th>
<th>Mortality Proportion (95% CI)</th>
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<td>Astley et al.</td>
<td>2010</td>
<td>9</td>
<td>154</td>
<td>5.84 (2.12, 9.56)</td>
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<td>Astley et al.</td>
<td>2000</td>
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<td>10.51 (6.75, 14.26)</td>
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<td>Olivier et al.</td>
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<td>Spohr et al.</td>
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<td>Urban et al.</td>
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<td>May et al.</td>
<td>1983</td>
<td>15</td>
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<td>Streissguth et al.</td>
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<td>Viljoen et al.</td>
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<td>Li et al.</td>
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<td>Kugne et al.</td>
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<td>May et al.</td>
<td>2007</td>
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<td>May et al.</td>
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<td><strong>Overall</strong></td>
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<td>1268</td>
<td>11.25 (7.58, 14.92)</td>
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The estimated mortality proportion is calculated using the standard error and confidence interval provided in each study. The overall ratio (RR) is 39, indicating a significant increase in mortality risk.
The FASD Family

**THE DADS**
- Age: 30.8
- Education: 10.9
- Unmarried: 63%
- Alcoholic: 12 + years
- Heavy Drinker: +
- Treatment: < 3
- Low SES: +

**Previous Terminations** ↑
**Number of Prenatal Visits** ↓
**Number of Prenatal Complications** ↑
**Birth Weight** ↓

**THE CHILDREN**
- Age Diagnosis: 7.1 Years
- Older Sibs: 2
- Younger: 2
- Mean Birth Weight: -701 grams
- Birth Defects: 50%
- Cerebral Palsy: 6%
- Intellectual Disability: 40%
- ADHD: 75%
- Out of Home: 85%
- Head Injury: 15%
- If FAS Diagnosis: 1 dead sibling (9%)
- 2 dead siblings (2%)
- 3 dead siblings (5%)

**Mortality Rate**
- FASD = 5.4%
- FAS Sibling = 11.4%
- Sibling Controls = 2.0%
- RR = 530%
- Infection OR = 13.7
- SIDS OR = 10.2

**THE MOMS**
- Age: 27.4
- Education: 10.6
- Unmarried: 63%
- Smoker: 82%
- Alcoholic: 10 + years
- Treatment: > 3 (45%)
- Low SES: +
- Poor Diet: +
- Parity: 3
- Prenatal Visits: < 5 (56%)
- 1st Prenatal: > 1st tri (56%)
- Mortality: 4.9%

**Mortality**
- FASD Mothers: 4.9%
- Controls: 0.11%
- OR = 44.82
- 87% Died age 50 < (41.5%)
- Cancer
- Alcohol Related Accidents: 67%
- 31.3 YPLL per case

**Number of Prenatal Complications** ↑
**Number of Prenatal Visits** ↓
**Late Start Prenatal Care** ↑
**Birth Weight** ↓
**Number of Malformations** ↑
<table>
<thead>
<tr>
<th>What PAE Forecasts</th>
<th>Prenatal</th>
<th>Labor &amp; Delivery</th>
<th>Post Natal</th>
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</table>
| Prenatal           | • Smoking  
                      • Drug Use  
                      • Late and Infrequent Prenatal Care  
                      • Depression  
                      • Inadequate Nutrition | • Stillbirth  
                      • Prematurity  
                      • Birth Defects  
                      • Hospitalizations | • Neglect  
                      • Abuse  
                      • Birth Defects  
                      • Poor Nutrition  
                      • Smoking  
                      • Parental Substance Abuse  
                      • Violence  
                      • Depression  
                      • SIDS |
Fetal Alcohol Spectrum Disorders (FASD)

See PAE, Think Impairment

ARND: Risk Factors Ahead

Exit 1  Abuse/Neglect
Exit 2  Mental Disorders
Exit 3  School Problems
Exit 4  Legal Problems
Exit 5  Substance Abuse
Exit 6  Dependent Living
Neurobehavioral Expression of FASD

“No, I won’t.”

“Let’s wait; I want to talk this over…”

“OK!”
FASD

Diagnosis = Phenotype Detection
Behind the Face of FASD: We See

- ADHD
- Depression
- Cognitive Impairment
- Intellectual Disability
- Learning Disabilities
- Substance Abuse
- Judgment Deficits
FASD has important neurocognitive features which effect treatment

What we first see

BEHAVIOR + IMPAIRMENT

What we should see

LESS BEHAVIOR + MORE IMPAIRMENT

Most children have fewer behaviors and more impairments than we first suspect.
1) These scores or performances are not useful because they are not reproducible

2) This day will determine much of the rest of the person’s life
FASD in UK

- Annual Births: 731,213
- Annual FASD Births (1%): 7,311
- Recurrent Cases (20%): 1,462
- 10% will recur in families with multiple affected children: 731
- Start Prevention With These Mothers or in These Families

- Birth – 18 - Population: 131,599
Cost and Service Burden of FASD in UK

- The Daily Cost: GBP 1,263,451
- Annual Cost of Care: GBP 2.7 billion
- Foster Care (5 years per case): 36,555 years
- Special Education: 18,277 years
- Juvenile Corrections: 5,848 years
- Developmental Disabilities: 98,698 years
- Mental Health: 219,330 years
All FASD

Facial Features
Brain Impairments
Confirmed Exposure

Diagnosed <1%

Undiagnosed = 99%

ARND
ND-PAE

1 in 800 (.00125%) Diagnosed
Nuthun Special About Me

### FASD and Mental Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>How much more prevalent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychotic Disorder</td>
<td>24.5</td>
</tr>
<tr>
<td>ADHD</td>
<td>10</td>
</tr>
<tr>
<td>Intellectual Disability</td>
<td>22</td>
</tr>
<tr>
<td>Oppositional Defiant Disorder</td>
<td>4.9</td>
</tr>
<tr>
<td>Reactive Attachment Disorder</td>
<td>9.3</td>
</tr>
<tr>
<td>Learning Disability</td>
<td>2</td>
</tr>
<tr>
<td>Depression</td>
<td>4</td>
</tr>
<tr>
<td>Bipolar Disorder</td>
<td>3.2</td>
</tr>
<tr>
<td>Anxiety Disorder</td>
<td>11.2</td>
</tr>
<tr>
<td>PTSD</td>
<td>.5</td>
</tr>
<tr>
<td>Obsessive Compulsive Disorder</td>
<td>4.1</td>
</tr>
</tbody>
</table>
The Neurodevelopmental Disorder Behavioral Checklist

In order to complete this checklist:
1) Behaviors must be impaired for the age of the person being assessed.
2) Interviewer needs to have known the person being assessed for at least one month.
3) After the interviewer fills out the form, the clinician then adds other observed behaviors not already reported.

CHECK ALL THAT APPLY FOR THE APPROPRIATE AGE RANGE

<table>
<thead>
<tr>
<th>BEHAVIOR</th>
<th>3-6 Yrs.</th>
<th>7 Yrs.+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperactive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor attention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Impulsive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disorganized</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seems unaware of consequences of actions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No fear</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Would leave with a stranger</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor social skills</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Few friends</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Will talk or interact with anyone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Easily manipulated and set up by others</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Socially inept (inappropriate speech or touching)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difficulty staying on topic during conversation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Always talking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cocktail speech - little content</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Too loud</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Can’t remember from one day to the next</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below average IQ (&lt;85)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor school performance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suspended or expelled from school</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor sleeper</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Can’t follow routine - needs reminders to get dressed, brush teeth, etc.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temper tantrums</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extreme mood swings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Requires constant supervision</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Been in trouble with the law</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inpatient treatment for mental health, substance abuse, or in jail</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inappropriate sexual behavior</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor motor skills</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Has or needs glasses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Had foster care or was adopted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication for behavior - ever</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother used alcohol or drugs during pregnancy (OPTIONAL)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4) Calculate total score.

<table>
<thead>
<tr>
<th>TOTAL CHECKED:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>16</td>
</tr>
</tbody>
</table>

(Continue assessment if score is greater than or equal to above.)
Table 1. Prevalence of ten ACE items for children with and without FAS.
Sexual abuse and In residential care not included in total ten-item ACE score.

<table>
<thead>
<tr>
<th>ACE</th>
<th>FASD N</th>
<th>FASD %</th>
<th>Non-FASD N</th>
<th>Non-FASD %</th>
<th>RR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parents Divorced/Separated</td>
<td>71</td>
<td>72.45</td>
<td>48</td>
<td>45.71</td>
<td>1.86</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Drinking/Drugs in Home</td>
<td>83</td>
<td>84.69</td>
<td>24</td>
<td>22.86</td>
<td>4.96</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Neglect</td>
<td>85</td>
<td>86.73</td>
<td>15</td>
<td>14.29</td>
<td>6.73</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Unloving Family</td>
<td>67</td>
<td>68.37</td>
<td>12</td>
<td>11.43</td>
<td>3.39</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Depression</td>
<td>32</td>
<td>32.65</td>
<td>37</td>
<td>35.24</td>
<td>0.94</td>
<td>.810</td>
</tr>
<tr>
<td>Physical Abuse</td>
<td>49</td>
<td>50.00</td>
<td>10</td>
<td>9.52</td>
<td>2.44</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Verbal Abuse</td>
<td>46</td>
<td>46.94</td>
<td>8</td>
<td>7.62</td>
<td>2.44</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>In Prison</td>
<td>35</td>
<td>35.71</td>
<td>8</td>
<td>7.62</td>
<td>2.07</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mother Abused</td>
<td>32</td>
<td>32.65</td>
<td>9</td>
<td>8.57</td>
<td>1.92</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sexual Abuse</td>
<td>23</td>
<td>23.47</td>
<td>6</td>
<td>5.71</td>
<td>1.84</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>In Foster Care</td>
<td>89</td>
<td>90.82</td>
<td>17</td>
<td>16.19</td>
<td>9.05</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>In Residential Care</td>
<td>19</td>
<td>19.39</td>
<td>3</td>
<td>2.86</td>
<td>1.98</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>None or One</td>
<td>10</td>
<td>10.20</td>
<td>61</td>
<td>58.10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Two to six</td>
<td>35</td>
<td>35.71</td>
<td>37</td>
<td>35.24</td>
<td>3.45</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Seven to Ten</td>
<td>53</td>
<td>54.08</td>
<td>7</td>
<td>6.67</td>
<td>6.27</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>
Brothers Separated at Birth

Pete, is that you???
FASD

- **Total Dx**
  - 5 - 7
    - RR = 1.71
  - 8 - 14
    - RR = 5.27

- **R = Correlation**
- **RR = Relative Risk**

- **ACE**
  - 7 - 10
    - RR = 8.17
  - 2 - 6
    - RR = 2.06

- **Care**
  - Foster Residential
    - RR = 5.61
  - Residential
    - RR = 6.79

R = 0.737
R = 0.399
R = 0.390
Parenting

• If you have what it takes- It will take all you’ve got!
Emergency Departments screen pregnant women for substance use disorders only 25% as frequently as non-pregnant women.

Moyer et al., West J Em Med (2018)
43% of juveniles in corrections with FASD had given at least one false confession, two-thirds of which resulted in charges

McLachlan and collaborator Ron Roesch
Costs of FASD

Annual Costs  $22,810 to $24,308

26% higher than autism
87% higher than asthma
13% higher than diabetes
56% higher than epilepsy
Detection of Prenatal Exposures and Risk of FASD

The 5 Trimesters

1. 3 Months Prior to Pregnancy: Early Detection prevents exposure. Smoking increases risks of FASD and increases severity.

2. Detection at 10 weeks
   (Friday and Saturday Drinking 4 drinks per night and 4 cigarettes every day)
   Exposure = 80 drinks & 240 cigarettes

3. Exposure Prevented = 320 drinks + 840 cigarettes

4. 3 Months Post Delivery
   Don’t Give Up the Quit: Alcohol Smoking Other Drug Use

Never Too Late to Quit or Cut Down