Why emphasize prenatal alcohol exposure?
Prenatal alcohol exposure often occurs with other substance abuse and is often not detected. Of all the substances of abuse (including cocaine, heroin, and marijuana), alcohol produces by far the most serious adverse effects for the fetus.

<table>
<thead>
<tr>
<th>Effect</th>
<th>Alcohol</th>
<th>Marijuana</th>
<th>Cocaine</th>
<th>Heroin</th>
<th>Tobacco</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Birth Weight</td>
<td></td>
<td></td>
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<tr>
<td>Impaired Growth</td>
<td></td>
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<tr>
<td>Facial Malformation</td>
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<tr>
<td>Small Head Size</td>
<td></td>
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<tr>
<td>Intellectual and Development Delays</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Hyperactivity, Inattention</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Sleeping Problems</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor Feeding</td>
<td></td>
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<tr>
<td>Excessive Crying</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Higher Risk for Sudden Infant Death Syndrome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Organ Damage, Birth Defects</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory Problems</td>
<td></td>
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</tr>
</tbody>
</table>


Prevalence of Prenatal Alcohol Exposure
Two recent studies demonstrate the magnitude of prenatal alcohol exposure in the United States. This data is similar to rates obtained from four sites in North Dakota over the past 30 years.
Prenatal Alcohol Exposure is Increased in Women With Current or a History of Alcohol Dependence.

This data demonstrates the need for a systematic approach to screening for prenatal alcohol exposure during prenatal care, after delivery, and during well child care.

North Dakota had 3,400 women using alcohol during pregnancy in 2017

Heavy users who drink all 40 weeks of pregnancy = 162
After birth, relapse is common.
Many women who quit drinking, smoking, or using drugs during pregnancy begin again right after the birth of the baby. The importance of screening during well child care is demonstrated by the following data. Early detection provides an opportunity to prevent exposure in a subsequent pregnancy by use of office based interventions.

Drinking while breastfeeding.
Among women who drank and breastfed (71%), alcohol use was associated with increased rates of neurobehavioral impairments and growth deficits. Drinking while breastfeeding is not recommended (May et al., 2016).

Prenatal substance exposure increases the risk for adverse outcomes for the fetus by three fold.
(Lamy et al., 2016).
Mechanisms of Exposure Differ by Gestational Age.
Pathways of ethanol entry and removal from the fetal compartment and amniotic fluid change as pregnancy progresses.

Importantly, exposure is multigenerational.
When a pregnant woman drinks she exposes herself, the fetus and the fetal germline.
The physiology of fetal alcohol exposure changes across gestation.
Early in pregnancy placental, fetal, and amniotic fluid concentrations of alcohol exposure are equivalent. Beginning in mid-pregnancy, the maturing fetal epidermis adds keratins which decrease permeability resulting in development of a barrier between fetal circulation and the amniotic fluid. By 30 gestational weeks, development of barrier function alters the pathophysiology of ethanol dispersion between the fetus and amniotic fluid. Firstly, increases in the effectiveness of barrier function decreases the rate of diffusion of alcohol from fetal circulation across fetal skin into the amniotic fluid. This reduces the volume of alcohol entering the amniotic fluid. Secondly, fetal barrier function increases the duration of fetal exposure by decreasing the rate of alcohol diffusion from amniotic fluid back into fetal circulation (Longhurst et al., 2016). Ethanol is then transported into maternal circulation for metabolism or elimination. This increases the duration of exposure from each episode of drinking.
FASD: What about the men?

- **Prenatal Alcohol Exposure**
- Increased risk of impotence 8%¹
- Lack of sexual desire increased 31% to 58%²
- Double the risk of erectile dysfunction³
- Decreased sperm (volume, motility, and abnormal sperm)⁴,⁵
- Increase in risk of miscarriage 2-15 times⁶
- Women drink with partner over 75% of the time⁷
- Drinking is initiated by man over 40% of the time⁷
- Increased risk of fetal death⁶,⁸
- Decreased birth weight⁹
- Late start to prenatal care¹⁰
- Fewer prenatal visits¹⁰


**Polysubstance Abuse Increases Risks.**

In substance abuse additional risks produce multiplicative risk enhancement especially for polysubstance abuse. This demonstrates the potential effect of risk reduction by reducing the multiplicative effects from each risk marker.
Exposure is often generational and familial.
In North Dakota sequela of prenatal alcohol exposure increases over generations and within sib ships.

Detection of Prenatal Alcohol Exposure
We have well developed detection programs for prenatal alcohol exposure in North Dakota where over 90% of pregnancies have at least one systematic screen during pregnancy. We utilize the One-Question Screen.

Exposure Assessment How We Do It

Exposure

When was your last drink?

Risk Stratification

<table>
<thead>
<tr>
<th>Before</th>
<th>Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-awareness</td>
<td>Post-awareness</td>
</tr>
<tr>
<td>Unexposed</td>
<td>Exposed</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)

Dosimetry

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 _____
When a history of prenatal alcohol exposure is not available, we use the Maternal Risk Score for exposure risk stratification.

### Estimating Exposure Risk

<table>
<thead>
<tr>
<th>Maternal Risk Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age over 25 years</td>
</tr>
<tr>
<td>Unmarried, divorced, widow, living with partner</td>
</tr>
<tr>
<td>On TANF, WIC, Social Security or income &lt; $16,000 per year</td>
</tr>
<tr>
<td>Did not graduate from high school</td>
</tr>
<tr>
<td>Poor diet</td>
</tr>
<tr>
<td>Smokes more than 1/2 pack per day</td>
</tr>
<tr>
<td>Drinks, but less than 2 days/week &amp; less than 2 drinks /drinking day</td>
</tr>
<tr>
<td>Age first drunk less than 15 years</td>
</tr>
<tr>
<td>In treatment over three times</td>
</tr>
<tr>
<td>In treatment in last 12 months</td>
</tr>
<tr>
<td>Previous child died</td>
</tr>
<tr>
<td>Previous child with FASD, or developmental disability</td>
</tr>
<tr>
<td>Children out of home (foster care or adopted)</td>
</tr>
<tr>
<td>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)</td>
</tr>
<tr>
<td>Uses inhalants, sniffs or illegal drugs</td>
</tr>
</tbody>
</table>

#### Score

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>Standard prenatal care</td>
</tr>
<tr>
<td>Low</td>
<td>Standard prenatal care</td>
</tr>
<tr>
<td>Moderate</td>
<td>Standard Prenatal care and FASD education</td>
</tr>
<tr>
<td>High</td>
<td>High risk pregnancy, alcohol-drug abuse treatment</td>
</tr>
<tr>
<td>Very High</td>
<td>High risk pregnancy, alcohol-drug abuse treatment</td>
</tr>
</tbody>
</table>

We have recently added an in-office intervention strategy for prenatal care providers in North Dakota. Training across all prenatal care sites is ongoing.
Prenatal alcohol exposure predicts increase in risk for adverse outcomes.

<table>
<thead>
<tr>
<th>PAE Forecast</th>
<th>Prenatal</th>
<th>Labor and Delivery</th>
<th>Postnatal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Late and infrequent prenatal care</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inadequate nutrition</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Ideal screening opportunities are:
- Prior to pregnancy
- At the first prenatal visit
- During pregnancy
- At delivery
- During at least one well child visit

Screening for prenatal alcohol should be multi-tiered. Screeners need training to be even modestly effective.

How common is fetal alcohol spectrum disorder (FASD)?
1-5% of all live births
In North Dakota we have 11,000 births each year, So we have between 110-550 affected babies born each year. Only 5-15% will ever be diagnosed with FASD. Nearly 90% will never be treated for FASD.

A snapshot of FASD in North Dakota
New cases born each year 110-550
Annual cost for new cases (330 cases = $7.5 million)
Birth - 18 years of age cohort (1,980-9900)

As a comparison for every case of neonatal abstinence syndrome we have 7-35 cases of FASD in North Dakota

\(^1\) Greenmeyer et al 2018.
Prenatal alcohol exposure increases mortality risk. Mortality in clinical settings often occurs before a diagnosis of prenatal alcohol exposure or fetal alcohol spectrum disorder is diagnosed. Thus, mortality estimates in clinical settings are often very low. Alcohol exposure has been a cause of concern for increased mortality for over 100 years.

However, in North Dakota we have excellent estimates of mortality events in people with fetal alcohol spectrum disorder.

<table>
<thead>
<tr>
<th>Population</th>
<th>Rate</th>
<th>Surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>FASD</td>
<td>5.4%</td>
<td>15 years</td>
</tr>
<tr>
<td>Maternal</td>
<td>4.5%</td>
<td>15 years</td>
</tr>
<tr>
<td>Sibling</td>
<td>11.4% / 2.0% / 530%</td>
<td>14 years</td>
</tr>
</tbody>
</table>

◆ Infectious OR 13.7
◆ SIDS OR 10.2

Burd et al., 2004
Mortality Publications


Maternal mortality is hugely increased in mothers of children who have been diagnosed with a fetal alcohol spectrum disorder.

Fetal alcohol spectrum disorders (FASD) are associated with an increase in risk for mortality for people with an FASD and their siblings. In this study we examine mortality rates of birth mothers of children with FASD, using a retrospective case control methodology. We utilized the North Dakota FASD Registry to locate birth certificates for children with FASD which we used to identify birth mothers. We then searched for mothers’ death certificates. We then compared the mortality rates of the birth mothers with an age matched control group comprised of all North Dakota women who were born and died in the same year as the birth mother. The birth mothers of children with FASD had a mortality rate of 15/304 = 4.93%; (95% CI 2.44-7.43%). The mortality rate for control mothers born in same years as the FASD mothers was 126/114,714 = 0.11% (95% CI 0.09-0.13%). Mothers of children with an FASD had a 44.82 fold increase in mortality risk and 87% of the deaths occurred in women under the age of 50. Three causes of death (cancer, injuries, and alcohol related disease) accounted for 67% of the deaths in the mothers of children with FASD. A diagnosis of FASD is an important risk marker for premature death in the mothers of children diagnosed with an FASD. These women should be encouraged to enter substance abuse treatment (Li et al., 2012).
Summary of the North Dakota 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: 15%
Cerebral Palsy: 6%
Intellectual Disability: 20%
ADHD: 75%
Out of Home: 85%
Head Injury: 15%
If FASD Diagnosis:
1 dead sibling (9%)
2 dead siblings (2%)
3 dead siblings (5%)

Mortality Rate
FASD: 5.4%
FASD Sibling: 11.4%
Sibling Controls: 2.0%
RR: 530%
Infection OR: 13.7
SID 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
50% died by age 41.5
87% died by age 50
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 ↑

Prevalence of fetal alcohol spectrum disorder in North Dakota

<table>
<thead>
<tr>
<th>FASD in North Dakota</th>
</tr>
</thead>
<tbody>
<tr>
<td>◆ 1% of live births</td>
</tr>
<tr>
<td>◆ 20% recurrence risk</td>
</tr>
<tr>
<td>◆ More severe in younger siblings</td>
</tr>
<tr>
<td>◆ 5% ever diagnosed</td>
</tr>
<tr>
<td>◆ Increasing rates of neuropsychiatric disorders</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Fetal Alcohol Spectrum Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>North Dakota, 2013</td>
</tr>
<tr>
<td>Deliveries</td>
</tr>
<tr>
<td>FASD (1%)</td>
</tr>
<tr>
<td>Children birth-18</td>
</tr>
<tr>
<td>FASD recurrent (20%)</td>
</tr>
<tr>
<td>North Dakota Diagnosed</td>
</tr>
</tbody>
</table>

FASD is more prevalent than Down Syndrome, muscular dystrophy, or autism spectrum disorder.

**What does FASD cost?**

On average we hit the million dollar cost of care for FASD at age 43 years.\(^1\)

The annual cost for FASD worldwide is $22,810/year for children. Thus each year we spend an extra $22,810/child with FASD. By 21 years of age we have spent $479,010. For adults the annual cost is $24,308, so by age 40 we will have spent another $461,852.

---

**FASD becomes more complex over time.**
(Burd, L. Fetal alcohol spectrum disorder: Complexity from comorbidity. Lancet, vol 387, March 5, 2016)

---

**FASD Forecast**
The Future of FASD: Increasing Severity of Neurobehavioral Impairments

---

**FASD is a huge risk enhancer for developmental disorders and mental illness**

---

**Figure 1. Percentage of Disorders Comorbid With FASD (1981-2015) (n=5,618)**

- ADD/ADHD
- ID/MR
- Learning Disability
- Oppositional Defiant Disorder
- Bipolar Manic-Depressive Disorder
- Anxiety Disorder
- Depression
- Conduct Disorder
- PTSD
- Autism
- Reactive Attachment Disorder
- Obsessive Compulsive Disorder

---

**Severity**

Age in Years

Birth 10 20 24

Weighted Average Prevalence
Incarceration Risk for FASD

◆ In Canada youth 12-18 years of age with FASD have a 19 fold increase risk of incarceration.

Popova L., Am J Epidemiol, 2012

Nearly all FASD is Alcohol Related Neurodevelopmental Disorder and not Fetal Alcohol Syndrome.

Behind the Face of FASD: We See

◆ ADHD
◆ Depression
◆ Cognitive Impairment
◆ Intellectual Disability
◆ Learning Disabilities
◆ Substance Abuse
◆ Judgment Deficits

Most children with FASD are in out-of-home foster care system.

Foster Care Placement in Children (Birth - 18 Years of Age)

◆ FAS: 336
◆ ARND: 1344
◆ Total FASD: 1680
◆ Years of Foster Care: 768

Several hundred hours of foster care are required every year for children with FASD in North Dakota.
FASD is a large and enduring risk enhancer for development of mental disorders and developmental disabilities.
The costs for health care, mental health are greatly increased for children with FASD.

Fetal alcohol syndrome (FASD) is a common developmental disability. FASD is thought to be 100% preventable. While this is a theoretical truth, a prevention rate of 100% appears unlikely in the near future. However, several prevention strategies are available. In this paper, we examine the potential cost savings from prevention of one case of FASD each year in the state of North Dakota. We utilized the North Dakota Health Claims Database to examine annual cost of health care for children birth through 21 years of age with FASD and controls. The mean annual cost of health care for children birth through 21 years of age with FASD was $2842 (n = 45). This is $2342 per capita more than the annual average cost of care for children in North Dakota who do not have FASD ($500 per year).

Prevention of one case of FASD per year in North Dakota would result in a cost savings of $128,810 in 10 years and $491,820 after 20 years. After 10 years of prevention, the annual savings in health care costs alone for one case of FASD would be $23,420 (Klug & Burd, 2003).

Popova et al have completed a series of cost of care estimates for FASD in Canada that are likely to be useful in North Dakota.

Popova, S., Lange, S., Burd, L., & Rehm, J. Health care burden and cost associated with fetal alcohol syndrome: Based on official Canadian data. PloS ONE, 2012, Aug. 7(8) e43024 doi:10.1371/journal.pone.0043024.t004.


Prevention strategies for prenatal alcohol exposure and FASD in North Dakota. (Always Reduce Smoking).
Prevention of fetal alcohol spectrum disorder is one of the most effective strategies for reducing the cost of health care, foster care, special education, juvenile justice, developmental disabilities, substance abuse treatment, and in the corrections system.

This table models cost of prevention by risk level using alcohol treatment as the intervention when treatment 50% effective.

<table>
<thead>
<tr>
<th>Alcohol Use &amp; Other Risk Factors</th>
<th>Risk of FASD</th>
<th>Women Treated</th>
<th>Women Quit&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Cases Prevented</th>
<th>Cost Per Case Prevented</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily alcohol use</td>
<td>0.01%</td>
<td>20,100</td>
<td>10,000</td>
<td>1</td>
<td>$100,000,000</td>
</tr>
<tr>
<td>Heavy Drinkers, middle class, non-smokers</td>
<td>.29%</td>
<td>690</td>
<td>344</td>
<td>1</td>
<td>3,450,000</td>
</tr>
<tr>
<td>Heavy drinkers, low income, smokers, poor diet</td>
<td>4.3%</td>
<td>47</td>
<td>23</td>
<td>1</td>
<td>235,000</td>
</tr>
<tr>
<td>Women who have had a previous child with FASD</td>
<td>75.0%</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>15,000</td>
</tr>
</tbody>
</table>

Additional information and more detailed modeling data are available at: [http://www.online-clinic.com](http://www.online-clinic.com) on FASD Exposure Model.

<sup>a</sup>Quit after 1 year.