

Infant Mortality, Substance Use and Abuse in Pregnancy

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Disclosures

- none

Key points

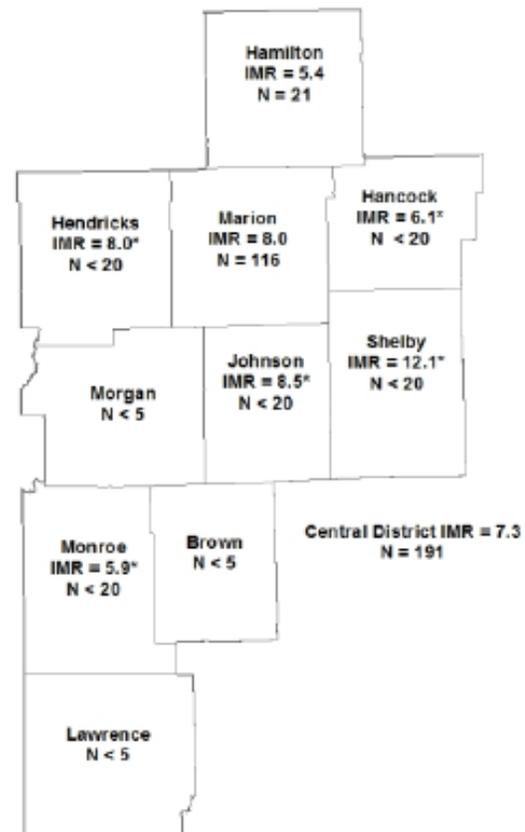
Indiana has significant problem with infant mortality and substance use and abuse during pregnancy contributes to major causes of fetal and infant deaths

Maternal substance use contributes to the 50% of infant mortality perinatal risks that are largely preventable

Substance use and abuse identified during pregnancy is a window of opportunity to educate and change lives of women and families

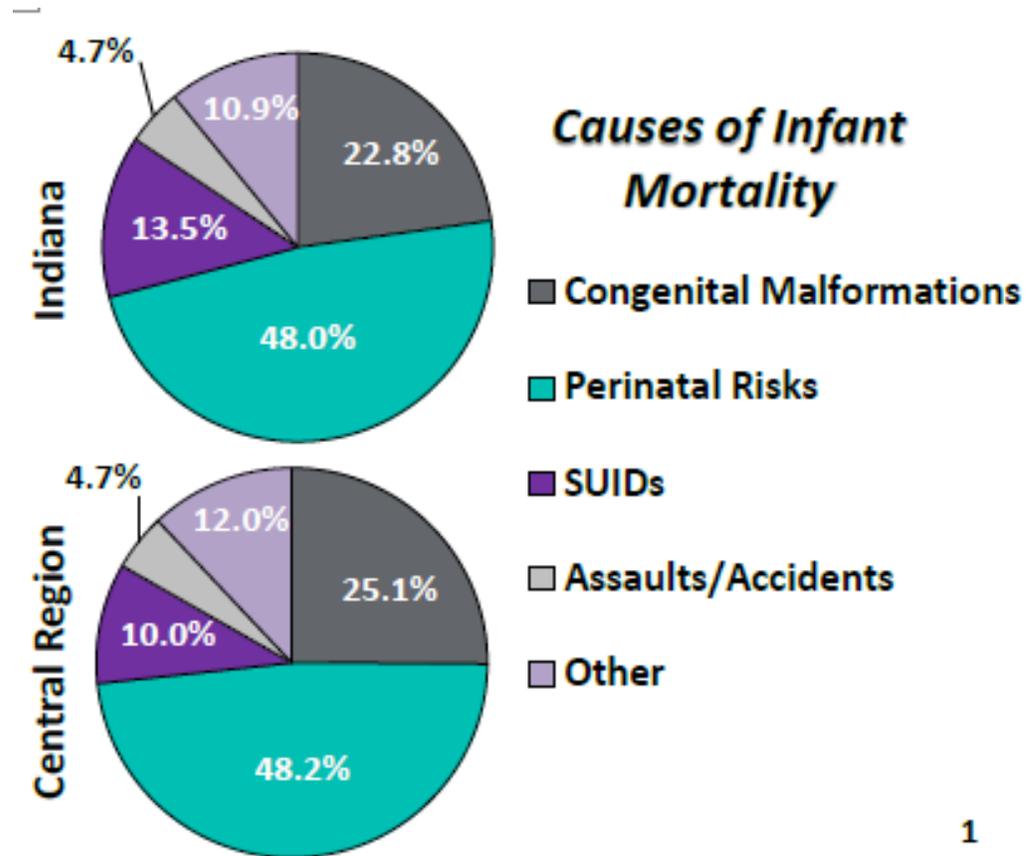
Substance abuse is a chronic disease similar to hypertension and obesity which requires ongoing treatment and management for the rest of the a patient's life.

Central Region 2015 Infant Mortality



* Numerator less than 20, the rate is unstable. We do not recommend comparing unstable rates.
Note: Rates have been suppressed if numerator is less than 5, including zero.

Infant Mortality Central Region 2015



Perinatal Risk Factors

Smoking

Substance Use
and Abuse

Preterm birth
Low Birth
Weight

No prenatal care
or lack of early
prenatal care

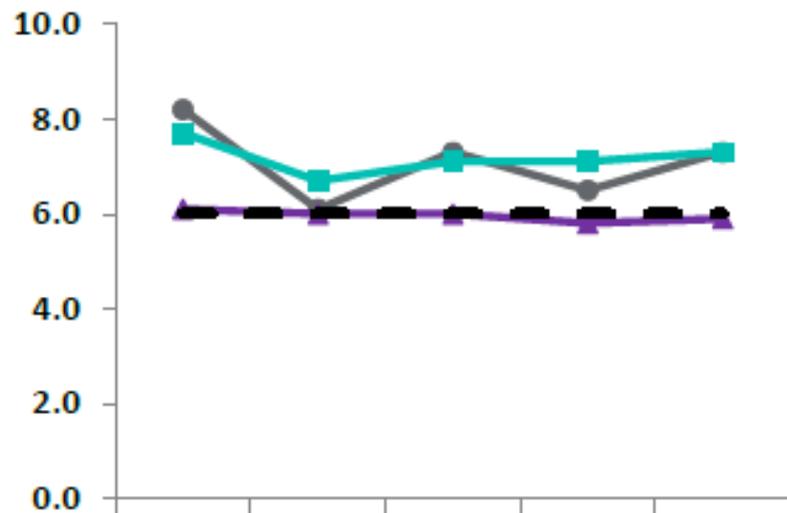
Uncontrolled
HTN, diabetes

Not
breastfeeding

Infant Mortality Rates

2011 - 2015

Rate per 1,000 live births

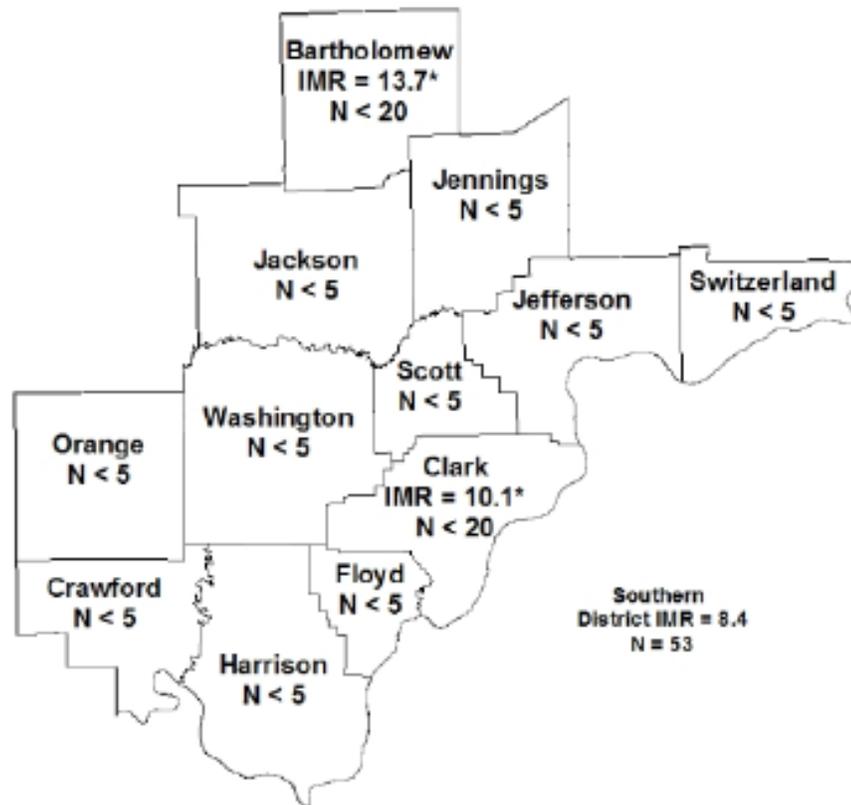


	2011	2012	2013	2014	2015
Central Region	8.2	6.1	7.3	6.5	7.3
Indiana	7.7	6.7	7.1	7.1	7.3
U.S.	6.1	6.0	6.0	5.8	5.9
HP 2020 Goal	6.0	6.0	6.0	6.0	6.0

	% LBW (< 2,500 G)	% PRETERM (< 37 WKS GESTATION)	% NO EARLY PNC (1 ST TRIMESTER)	% SMOKING	% NOT BREASTFEEDING	% MOTHER ON MEDICAID
BROWN	6.7*	5.8*	33.3	21.7	15.8	44.2
HAMILTON	6.6	9.0	14.8 ^S	2.0 ^S	5.7 ^S	12.6 ^S
HANCOCK	7.8	10.3	15.3 ^S	10.1	11.9 ^S	24.8 ^S
HENDRICKS	6.0	9.3	21.5 ^S	7.6 ^S	12.8 ^S	20.3 ^S
JOHNSON	7.8	9.2	23.0 ^S	13.7	17.1	32.9 ^S
LAWRENCE	7.4	9.1	20.7 ^S	30.4 ^S	24.7	48.5
MARION	9.2 ^S	11.1 ^S	33.1 ^S	10.9 ^S	22.1 ^S	57.8 ^S
MONROE	6.1	8.6	19.3 ^S	14.9	11.5 ^S	29.6 ^S
MORGAN	8.8	9.3	28.0	25.8 ^S	22.8	46.1
SHELBY	7.7	7.3	28.3	21.4 ^S	25.2	48.1
CENTRAL REGION	8.2	10.2	27.1	10.8	17.9	43.4
INDIANA	8.0	9.6	30.7	14.3	19.5	43.0

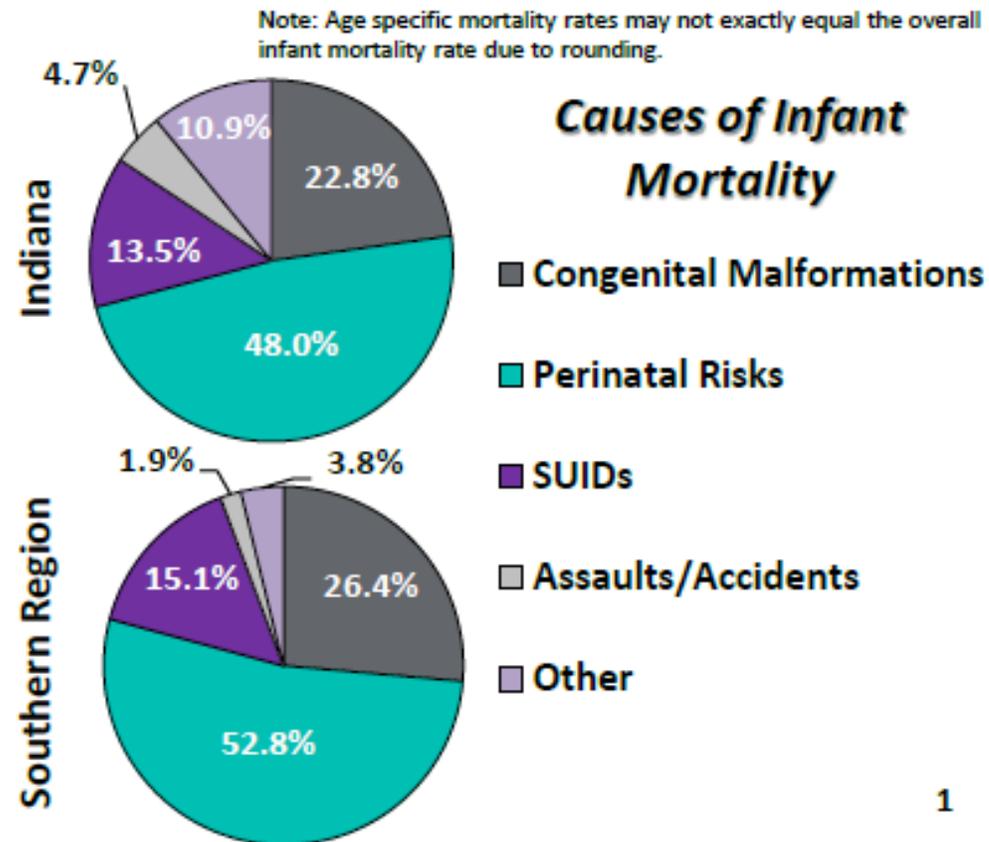
* = Unstable rate due to fewer than 20 birth outcomes.
S = Significantly different from state.

Southern Region 2015 Infant Mortality



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Note: Rates have been suppressed if numerator is less than 5, including zero.

Southern Region 2015 Infant Mortality



LBW = Low Birthweight PNC = Prenatal Care IMR = Infant Mortality Rate

	% LBW (< 2,500 G)	% PRETERM (< 37 WKS GESTATION)	% NO EARLY PNC (1 ST TRIMESTER)	% SMOKING	% NOT BREASTFEEDING	% MOTHER ON MEDICAID
BARTHOLOMEW	8.4	8.4	32.6	16.2	14.7 ^s	34.8 ^s
CLARK	7.7	9.2	28.5	13.2	20.6	21.0 ^s
CRAWFORD	6.8*	14.4*	23.7	26.3 ^s	24.6	44.9
FLOYD	7.2	9.1	21.0 ^s	15.2	21.1	27.5 ^s
HARRISON	7.3	11.9	21.9 ^s	20.6 ^s	23.5	35.2
JACKSON	5.9	8.2	24.1	17.7	26.6 ^s	37.7
JEFFERSON	8.9	9.2	23.7	31.3 ^s	32.6 ^s	47.7
JENNINGS	7.0	8.3	29.9	27.1 ^s	27.1	50.0
ORANGE	6.3*	7.1*	29.2	27.5 ^s	23.7	47.9
SCOTT	6.7	10.7	33.3	28.0 ^s	34.7 ^s	53.7 ^s
SWITZERLAND	11.1*	11.1*	37.3	28.6 ^s	31.7	36.5
WASHINGTON	7.8	6.6	35.2	17.2	22.9	36.7
SOUTHERN REGION	7.5	9.1	27.8	18.7	22.6	34.0
INDIANA	8.0	9.6	30.7	14.3	19.5	43.0

*= Unstable rate due to fewer than 20 birth outcomes.
 S = Significantly different from state.

Executive Summary

At the direction of Governor Mike Pence, reducing infant mortality became the top priority of the Indiana State Department of Health (ISDH) in January 2013. Indiana falls at the bottom 20% of all states for this frontline measure of health [1]. In 2011, Indiana's infant mortality rate was 7.7 deaths per 1,000 live births, well below the Healthy People 2010 goal of 6.0 deaths per 1,000 live births and the subsequent Healthy People 2020 goal of 4.5 deaths per 1,000 live births [2]. While the nationwide infant mortality rate declined 12% from 2005 through 2011, Indiana was among the states the Centers for Disease Control & Prevention classified as showing "no significant change" during that time [1].

To address this situation, the state of Indiana commissioned a data-driven analysis centered on infant mortality that unified information from previously unlinked sources across state agencies. The KSM Consulting (KSMC) team utilized sophisticated machine learning techniques on the available data to identify highly granular at-risk subpopulations and provide actionable insights for stakeholders and policy makers.

Findings from this analysis included:

- Infant mortality risk in the state of Indiana is not randomly distributed, but exhibits statistically significant patterns that could be used for targeted investment of resources to improve outcomes.
- Inadequate prenatal care, Medicaid enrollment, and young maternal age were shown to be the strongest predictors for adverse birth outcomes.
- While the identified high-risk subpopulations account for only 1.6% of all births in Indiana, they account for nearly 50% of infant deaths, suggesting that the identified subpopulations are not only significant, but could be used as the basis for targeted interventions.

Key points:

Indiana has significant problem with infant mortality and substance use and abuse during pregnancy contributes to major causes of fetal and infant deaths.

Maternal substance use contributes to the 50% of infant mortality perinatal risks that are largely preventable.

Substance use and abuse identified during pregnancy is a window of opportunity to educate and change lives of women and families

Substance abuse is a chronic disease similar to hypertension and obesity which requires ongoing treatment and management for the rest of the a patient's life.

Illicit Substance Use in Pregnancy

2010 National Survey on drug use and health, 4.4% of pregnant women were current illicit drug users within the past 30 days

Another study showed 0.1% used heroin and 1% reported nonmedical use of opioid pain meds

Random UDS showed 2.6% positive for opiates in urban teaching hospital

Opioid use in pregnancy is associated with many adverse pregnancy outcomes including preterm birth, low birth weight, fetal and infant demise, growth restriction, placental abruption and Neonatal Abstinence syndrome (NAS).

Women with substance use in pregnancy have increased risk of high-risk behaviors to support drug use such as prostitution, theft and violence.

Opioids Rising:
The Wide and
Tragic Reach of
Indiana's
Growing
Addiction
Epidemic
(Fairbanks
Foundation
2014)

Some 5.3 percent of Indiana's residents—or 286,000 Hoosiers—report having engaged in non-medical use of opioid pain relievers.

657 infants (IN) were born with NAS in 2014. However, a lack of data and our limited understanding of the effects of NAS make it likely that the true number of cases was higher.

Cost of treating Neonatal Abstinence Syndrome is \$97,555 per newborn (IN).

In 2014, hospitalization of Indiana babies with NAS cost more than \$64 million.

Self Reporting Surveys Inadequate

- In a national survey, 2.9% of patients admitted using marijuana in pregnancy*
- Surveys in Indiana indicate:
 - 29% tested positive for THC on the first prenatal visit in a major Southwestern Indiana Hospital (2006)
 - 40% positive for THC in a similar Indianapolis survey (2005)
 - In both surveys, all patients were detected by a urine drug screen at the first prenatal visit.
- Self-reporting underestimates prevalence!

* NIDA's National Pregnancy and Health Survey (1992/1993)

Prevalence of Maternal Drug Use By Meconium Analysis in Newborn

- Every other newborn tested, Nov. 1988 to Sep. 1989
- 3010 subjects studied
- 1333 (44%) were positive for cocaine, morphine, or cannabinoid;
 - 31% were positive for cocaine,
 - 21% for morphine, and
 - 12% for cannabinoid.
- In contrast, only 335 (11%) mothers admitted to illicit drug use:
 - 52% of their newborns had a positive urine drug screen and
 - 88% had a positive meconium drug screen.

- Ostrea EM, Jr., Brady M, Gause S, Raymundo AL, Stevens M. Drug screening of newborns by meconium analysis: a large-scale, prospective, epidemiologic study. *Pediatrics* 1992 Jan;89(1):107-13.

Estimates of Substance Use In Pregnancy in Indiana

- Approximately 80,000 deliveries annually in Indiana
- At least 25% use tobacco (20,000)
- Estimates vary from a low of 10% to a high of 20% using alcohol, illegal or illicit drugs in pregnancy in pregnancy.
- The estimate is that approximately 15% of pregnancies in IN may be affected by alcohol or opiate drug use (12,000)

The ACOG and AMA Recognize an Ethical Duty to Screen Because **Treatment Works**

- Treatment Works: over 80% of pregnant patients can be “clean” at delivery
- **Early intervention can reduce the effects of tobacco and cocaine.**
- Pregnancy enhances long term recovery: up to 65% are still abstinent after one year.
- **Brief physician advice has been shown to be as effective as conventional treatment for substance abuse.**

Why Universal Screening?

Pregnancy Enhances Recovery

- Pregnancy makes a difference in long-term recovery.
- After one year of treatment:
 - 65.7% of women who entered treatment while pregnant used no drugs, while
 - Only 27.7% of non-pregnant women remained drug free. (p<0.0005)
- Peles E, Adelson M. Gender Differences and Pregnant Women in a Methadone Maintenance Treatment (MMT) Clinic. *J Addictive Diseases* 2006; 25: 39-45.

Why Universal Screening?

To Identify the Patient!

- Once identified, if the patient is simply told to stop using alcohol, tobacco or drugs:
 - About 50% will be “clean” at delivery
 - If urine testing done at each subsequent visit
- Using a brief intervention, most patients will stop using alcohol, tobacco or other drugs:
 - About 85% of mothers will be clean at delivery
 - Urine testing at each visit is a critical adjunct
- **Treatment Works**

Universal Screening Is Highly Cost Effective

- **When identified and treated:**

- Rate of abstinence increases,
- Maternal and fetal complications decrease.
- Less Preterm labor
- Less Growth restriction
- Less abruption

- **Reducing preterm labor and low birth weight account for the largest savings.**

- Hubbard RL, French MT. New perspectives on the benefit-cost and cost-effectiveness of drug abuse treatment. NIDA Res Monogram 1991;113:94-113.

Treatment Cost Effective

Reducing Preterm Delivery

- About 80,000 deliveries in Indiana
- 50% funded by Medicaid – 40,000
- 15% substance use - 6,000
- 95% are undetected – 5,700
- 20% Preterm delivery – 1,140
- Mean nursery cost per preterm \$75,000
- Total cost just for the nursery stay
 - **\$85,500,000**

Resistance to Screening

Myth

- Don't know how
- Too much time:
- Won't make a difference.
- Lack of referral resources
- Affects inner-city poor on crack cocaine and rural women on crystal meth.

Reality

- Easy to master
- Takes less than 5 min.
- Up to 85% will “clean up”
- Referral resources are somewhat available
- It is just as common in middle and upper class women living in the suburbs.

Universal Screening Summary

- Traditional H&P is inadequate.
- Substance use is common.
- It is easy to screen.
- When detected, patients abstain.
- Preterm labor and low birth weight decreases.
- **Treatment is simple and effective as the best way to identify and treat substance use in pregnancy**
- **It is healthy and COST EFFECTIVE**

Universal Screening Strategies

- All pregnant patients are asked about their use of alcohol, drugs and prescription opioids in a non judgmental, confidential and empathetic fashion
- Inform that ALL patients are asked regarding drug use to ensure they receive adequate care for themselves and their fetus
- 2 tools endorsed by ACOG: 4 P's and CRAFFT (age <26 years)

Four P's Screening (modified Plus)

- PARENTS: Did either of your **PARENTS** have a problem with alcohol or drugs?
 - PARTNER: Does your **PARTNER** have a problem with alcohol or drugs?
 - PAST: Have you ever drunk beer, wine or liquor in the **PAST?**
 - PRESENT:(Modified) Have you smoked any cigarettes, used any alcohol or any drug at any time in the past month (or during this **PREGNANCY**)?
-
- Morse B, Gehshan S, Hutchins E. Screening for substance abuse during pregnancy: improving care, improving health. Washington, DC: National Center for Education in Maternal and Child Health; 1977.
 - Chasnoff, et al. The four P's plus screen for substance use in pregnancy: clinical application and outcomes. J Perinat 2005;25:368-374.

Four P's Plus Results

- A “yes” answer to any question was considered positive.
- The modified 4 P's Plus screen adds a question about the current pregnancy and a positive answer identifies 34% of drug and alcohol users.
- With a positive answer about “partner,” 65% were found to need drug treatment.
- Chasnoff IJ, Hung WC. *The 4 P's Plus*. Chicago, IL: NTI Publishing; 1999.

When the Screen is positive:

- Patient is **at risk** for substance use
- Does not mean she is using.
- **Urine Drug screen indicated.**
- Brief Intervention is indicated.
- Re-evaluate in two weeks.
- If no change in behavior, refer to specific treatment program.

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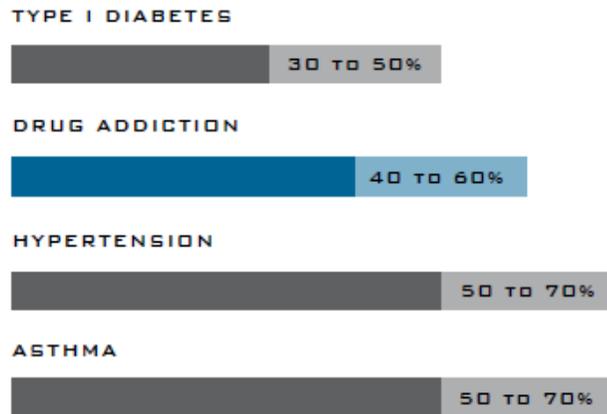
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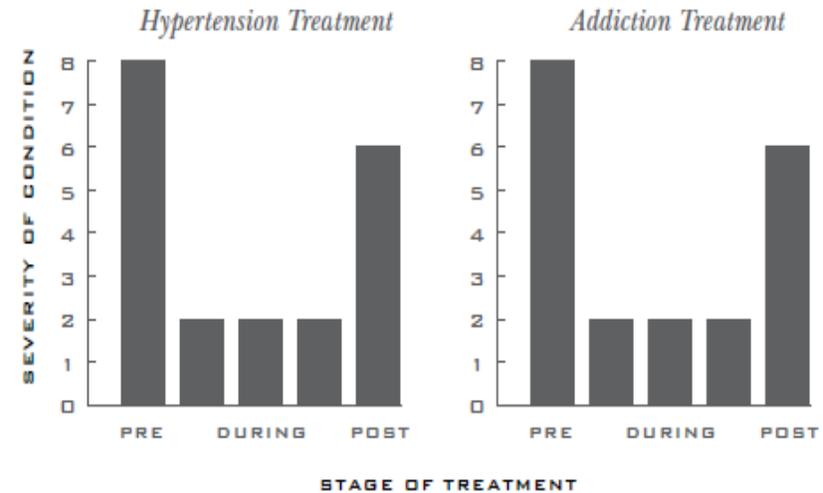
Addiction is a chronic relapsing condition

COMPARISON OF RELAPSE RATES BETWEEN DRUG ADDICTION AND OTHER CHRONIC ILLNESSES

Percentage of Patients Who Relapse



WHY IS ADDICTION TREATMENT EVALUATED DIFFERENTLY? BOTH REQUIRE ONGOING CARE



Take Home Message

- Addiction is a Chronic Relapsing Disease of the Adult Brain
- Successful treatment is comparable to, or better than, compliance with treatment plans for hypertension or diabetes.

- McLellen AT, Lewis DC, O'Brien CP, Kleber HD. Drug dependence, a chronic medical illness: implications for treatment, insurance and outcomes evaluation. *JAMA* 2000;284:1689-1695.

Maintenance vs detox therapy: History

Initially in 1960's Methadone taper was used to get women off heroin. Associate with high relapse rates, less prenatal care and worse outcomes.

So then taper changed to maintenance therapy, women stayed in PNC with improved maternal and fetal outcomes compared to heroin or taper

BUT: maintenance therapy led to increased NAS compared to heroin (short acting)

1970's Methadone story

- Trying to reduce NAS so tried rapid taper (over 3 days) and low dose maintenance therapy (<20 mg/day) lead to worse outcomes because women went back to heroin
- HIV epidemic 1980-1990's
 - Maternal to fetal transmission of HIV among IV drug users became common
 - Elimination of IV drug use and neonatal HIV infection became a higher priority than reduction of NAS

1997 NIH Consensus Panel became standard of care

- Methadone maintenance is recommended as the standard of care for opioid use disorder during pregnancy
- Fast forward 20 years...
- Buprenorphine approved for office based therapy in 2002
- Milder withdrawal syndrome noted in adults
- More widespread availability of prescription opioids

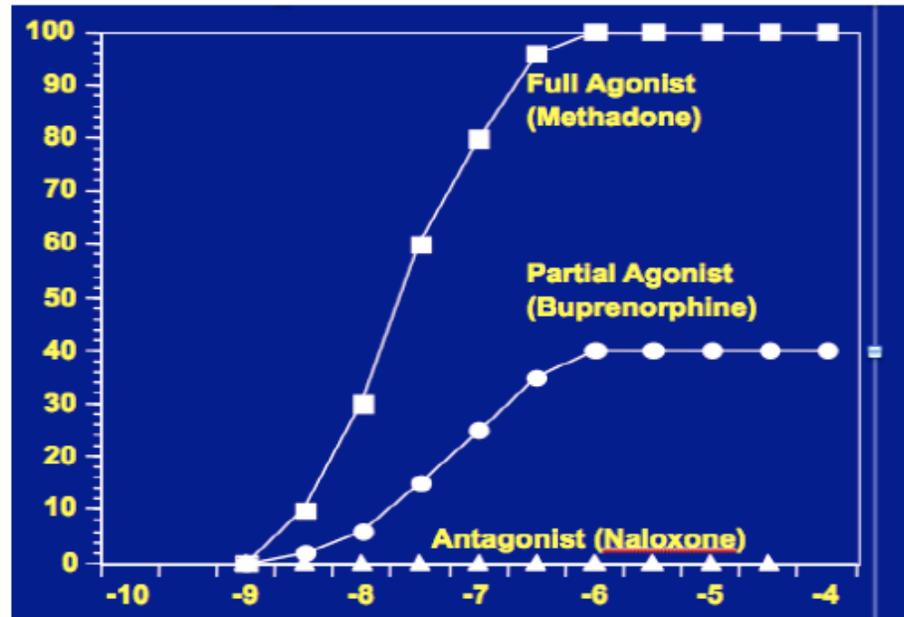
MOTHER Study (Multisite randomized controlled trial comparing Methadone vs Buprenorphine)

- Compared maternal and neonatal outcomes in opioid-addicted women treated with methadone vs buprenorphine
- Buprenorphine showed less infant need for treatment NAS and shorter hospital stays
- BUT women had much higher dropout rate in buprenorphine arm because of drug dissatisfaction than for methadone

Jones HE, Johnson RE, Jasinski DR. (2004). Buprenorphine versus methadone in the treatment of pregnant opioid-dependent patients: effects on NAS. *Drug Alcohol Depend*; 75: 253-260.

Buprenorphine is partial agonist (ceiling effect)

Buprenorphine: Partial Agonist Properties



Methadone vs. Buprenorphine Major Pregnancy Outcomes

	Bup. (25)	Meth (54)	p
Preterm Delivery	3 (12 %)	18 (33%)	NS
Low Birth Weight (<2500g)	2	19	0.04
Mean Birth Weight	3019 g	2733 g	0.005
Neonatal Abstinence (NAS)	6	48	0.001
NAS Treated	0	46	0.001
Mean Length of Stay	2.8	27	0.001

See also, Kakko J, Heilig M, Sarman I. Buprenorphine and methadone treatment of opiate dependence during pregnancy: comparison of fetal growth and neonatal outcomes in two consecutive case series. *Drug Alcohol Depend* 2008 Jul 1;96(1-2):69-78.

Buprenorphine versus methadone

- Less suppression of fetal breathing, movement and heart rate
- Fewer drug interactions
- Less QT interval prolongation
- Fewer dosing changes during pregnancy
- Fewer regulatory obstacles once get a physician that is certified to dispense

Present day....

- Many women may self refer to the opioid treatment program for methadone or to office based therapy with buprenorphine
- Some women enter treatment are asking to be “detoxed”
- Party line continues to be “Medically supervised withdrawal from opioids in opioid-dependent women is NOT recommended during pregnancy because the withdrawal is associated with a high relapse rate.” ASAM, ACOG

BUT...

- Methadone maintenance or buprenorphine therapy is not available to all patients. Medically supervised withdrawal should only be undertaken in second trimester and under the supervision of a physician experienced in perinatal addiction therapy
- Don't make a patient wait until the second trimester if the only alternative is illicit drug use.

Maintenance vs Medically managed withdrawal

- 1997 NIH consensus was determined to be the standard of care based on experience from 1960-1970's in IV heroin using pregnant population
- Population today is largely addicted to use/misuse/addiction of prescription pain medication
- We have more advanced capability of monitoring fetuses with modern noninvasive fetal surveillance techniques readily available

Maintenance vs tapering or detoxification

- Is there a select group of pregnant women with opioid use disorder that can be safely medically managed through a withdrawal that maintain abstinence?
- Non-IV using, non-heroin using women??
- **ASAM** still reports NOT to medically withdrawal during pregnancy because the risk of relapse (and subsequent heroin use) is too great
- **ACOG** “For pregnant women with an opioid use disorder, opioid agonist pharmacotherapy is the recommended therapy and is preferable to medically supervised withdrawal because withdrawal is associated with high relapse rates, which lead to worse outcomes. More research is needed to assess the safety (particularly regarding maternal relapse), efficacy, and long-term outcomes of medically supervised withdrawal.”

Parkland Hospital Data on Medically Supervised Withdrawal (MSW) 1990-96

- Supervised in singleton, inpatient, multi-disciplinary case management program using methadone and clonidine at 24 weeks
- Maximum dose 85 mg (range 30-85 mg), median taper 12 days (range 3-39 days), decrease dosage by 20% every 1-3 days based on symptoms during inpatient hospitalization
- 34 women elected to try MSW:
 - 59% were successful and did not relapse before delivery
 - 29% resumed street opioid use before delivery
 - 12% chose to go to methadone maintenance (MMT)

No evidence fetal distress or death during MSW and no delivery before 36 weeks

The obstetrical and neonatal impact of maternal opioid detoxification in pregnancy

- Retrospective data Jan 2006-Dec 2011 in 95 inpatient pregnant women

56% were successfully detoxed (neg UDS at time of delivery)

18% did not complete MSW, left program for maintenance therapy

20% left program

3% had fetal demise, not during hospitalization

The obstetrical and neonatal impact of maternal opioid detoxification in pregnancy

- Retrospective data Jan 2006-Dec 2011 in 95 inpatient preg women

No specific demographic or social risk factors were associated with success

Successful women had a longer inpatient detoxification stays (25 vs 15 days) and were less likely to leave prior to completion than women that relapsed (9% vs 33%)

Infants of mothers that detoxed had shorter stays (3 vs 22 days), had lower NAS scores and less likely to be treated for withdrawal

The obstetrical and neonatal impact of maternal opioid detoxification in pregnancy

Conclusion:

No association of outcomes with route of illicit opioid administration, amount of daily use or years of prior use

So...inpatient medically supervised withdrawal is possible without significant risk to the fetus.
Must exclude fetuses with growth restriction, oligohydramnios, <24 weeks.

Biggest concern is :RELAPSE

Detox vs maintenance therapy

- There may be selected non-IV, non-heroin using pregnant women that may have good success with withdrawal during pregnancy
- Lesser addictive severity may have a better prognosis so further study is warranted.
 - Is inpatient medically supervised detox possible?
 - Can outpatient tapers be safe and successful?
 - Should we use demographics and drug history to influence treatment options?

Key points

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Maternal Fetal Medicine
Indiana University Health

Objectives

- Provide a in-depth overview of the Outpatient Based Opioid Treatment Program at IU Health.
- Take a look at the processes, methods, and tools that were used to develop our protocols.
- Give suggestions for how to effectively implement and utilize protocols in your organization.

Where to start

- Program development and implementation
 - Guidelines
 - Requirements
- Education
 - Multidisciplinary
- Develop specific protocols
 - Initiation
 - Relapse
 - Peripartum and postpartum management

Guidelines

- Vermont Guidelines for Medication Assisted Treatment for Pregnant Women
 - http://contentmanager.med.uvm.edu/docs/default-source/vchip-documents/vchip_4mat_guidelines.pdf?sfvrsn=2

Education

- Provide education to promote understanding of Opioid Use Disorder in pregnancy.
 - Inpatient
 - Outpatient
 - Social workers
 - Case managers

Protocols

- Buprenorphine initiation
- Methadone initiation
- Relapse
- Peripartum pain management
- Postpartum pain management

References

The Treatment of Opioid Dependence in Pregnancy: Vermont Guidelines.

http://contentmanager.med.uvm.edu/docs/default-source/vchip-documents/vchip_4mat_guidelines.pdf?sfvrsn=2