

Neonatal Abstinence Syndrome

How We Got Here and Where We Are Going

Kathryn Ziegler, DO, FAAP

Newborn Special Care Associates

Abington Jefferson Health

Disclosures

- I have no financial disclosures
- We will discuss the use of morphine in infants which is an off label use

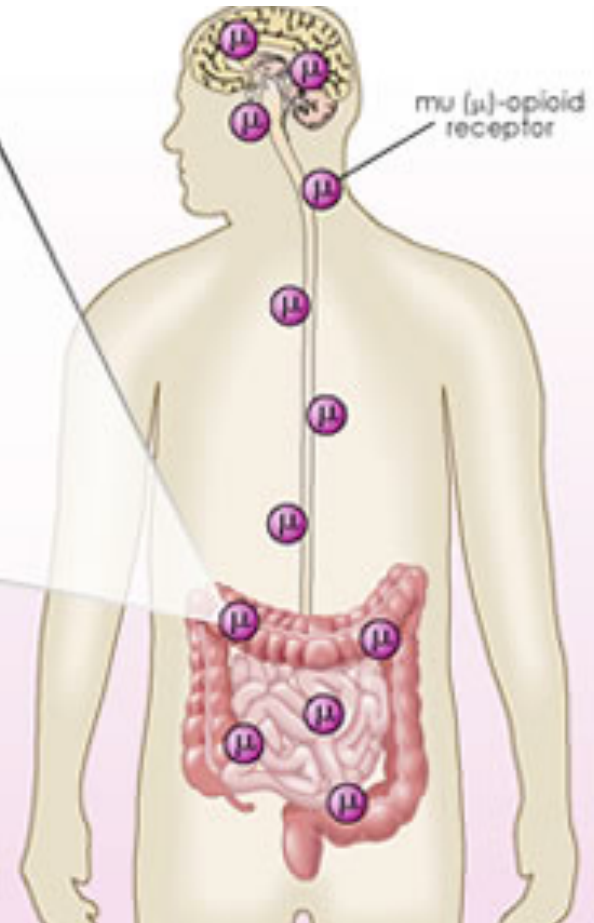
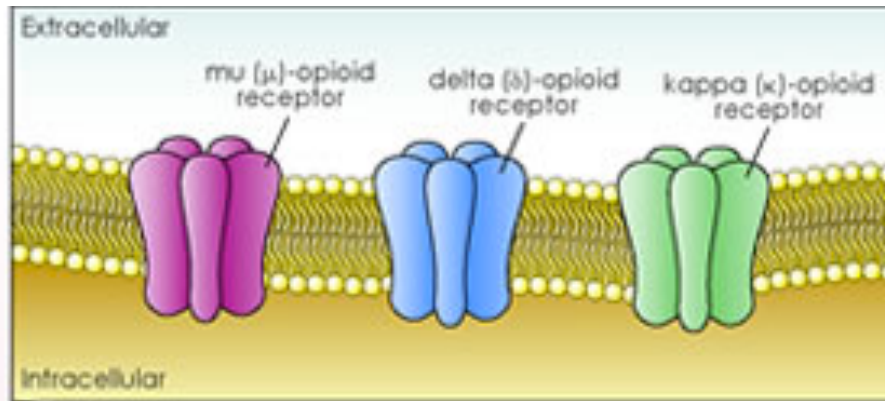
Objectives

- Discuss the incidence/epidemiology of opioid use
- Discuss the incidence/epidemiology of Neonatal Abstinence Syndrome
- Discuss treatment strategies for Neonatal Abstinence Syndrome
- Discuss Quality Improvement Efforts for Neonatal Abstinence Syndrome

Opioids

- Natural, endogenous and synthetic
- Bind μ receptors in CNS
 - Supraspinal analgesia
 - Sedation, euphoria, miosis, respiratory depression and decreased GI motility
 - Prolonged use causes physical and psychological dependence

Opioid Receptors



Opioids

- Natural
 - Morphine (extracted from opium)
- Synthetic
 - Codeine, heroin, hydromorphone, fentanyl, methadone
- Endogenous
 - Enkephalins, endorphins, endomorphins

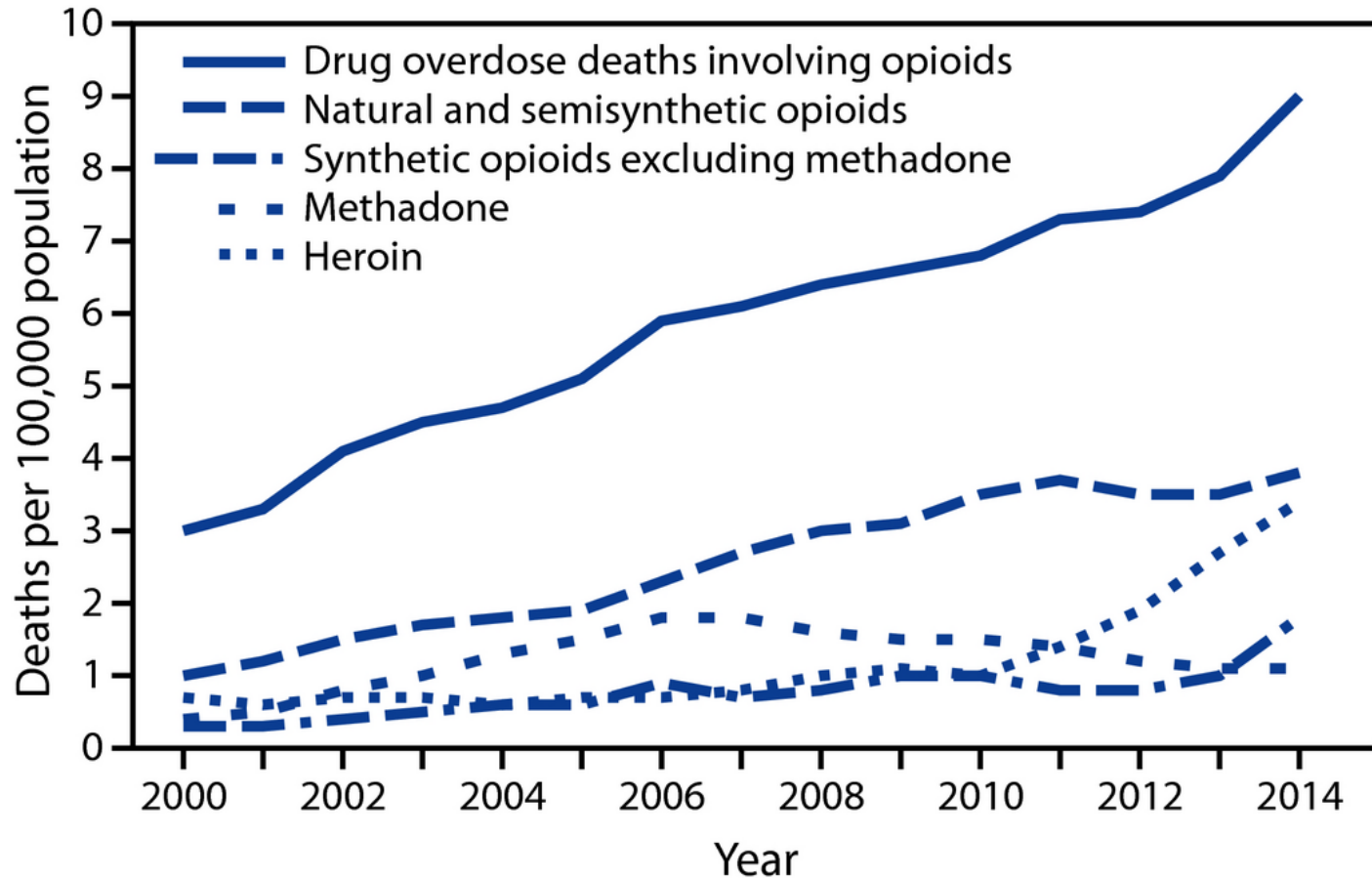
The Problem

- Overdose death rate increased by 137% since 2000
 - 200% increased in death from opioid overdose
- Americans consume 80% of global opioid supply
 - 99% of hydrocodone supply
- Heroin overdoses have tripled in last 4 years
 - Past misuse of prescription opioids clearly linked

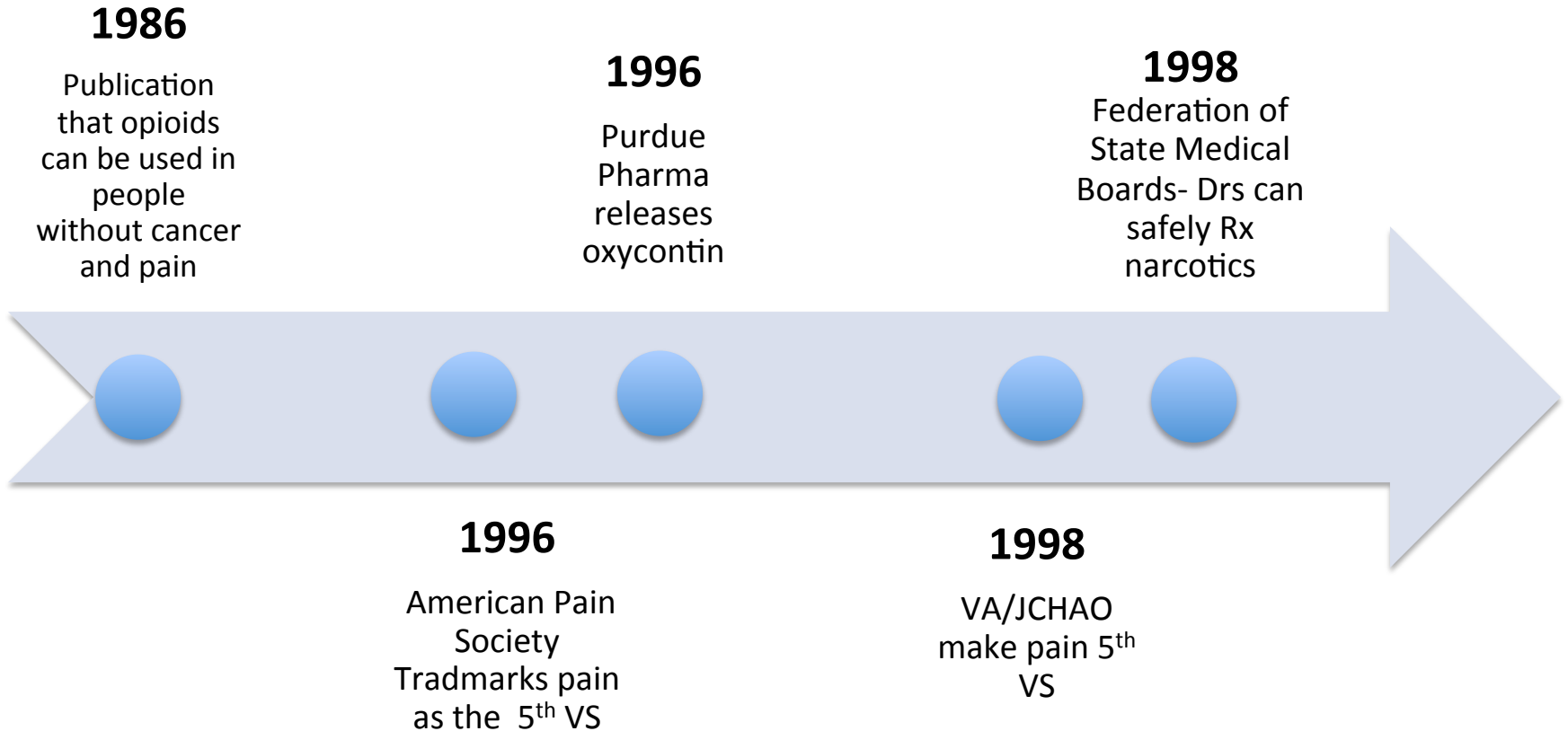
Increasing Death from Opioids

- Sex:
 - Males (7.6%)
 - Females (4.7%)
- Age
 - 25-34 year olds (10.5%)
 - 35-44 year olds (8.7%)
 - 55-64 year olds (5.7%)
 - ≥ 65 year olds (7.7%)
- Race
 - White, non hispanic (8%)
 - Black, non hispanic (8.2%)
- Geography
 - Northeast (8.8%)
 - Midwest (9.6%)
 - South (6.9%)

Increases in Drug and Opioid Overdose Deaths—United States, 2000–2014



The Problem



The Problem

2001

JCHAO issues standards urging hospitals to regularly ask patients about pain

2007

Purdue Pharma pleads guilty to misbranding of oxycontin

2013

Opioid deaths surpass car accidents as leading cause of accidental death

2001

JCHAO publishes guide to address physician concerns about addiction and tolerance

2012

259 million opioid Rx written \$9 billion

The Problem

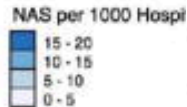
- Pregnant women do not escape the reach of opioid addiction
 - 4.5% of pregnant women report using illicit drugs
- Infants born to women on opioids are at risk of Neonatal Abstinence Syndrome (NAS)
- 300% increase in NAS (2000-2013)
 - 1.5 → 6 cases/1000 hospital births

The Problem

Neonatal Abstinence Syndrome per 1000 Hospital Births by US Census Division, 2012



US Census Division	NAS Rate per 1000 Births (95% CI)
New England	13.7 (12.5-14.5)
Middle Atlantic	6.8 (5.9-7.6)
East North Central	6.9 (6.0-7.8)
West North Central	3.4 (3.0-3.8)
South Atlantic	6.9 (6.3-7.4)
East South Central	16.2 (12.4-18.9)
West South Central	2.6 (2.3-2.9)
Mountain	5.1

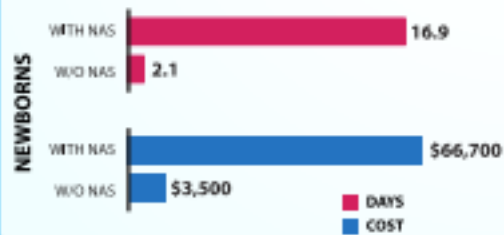


DRAMATIC INCREASES IN MATERNAL OPIOID USE AND NEONATAL ABSTINENCE SYNDROME

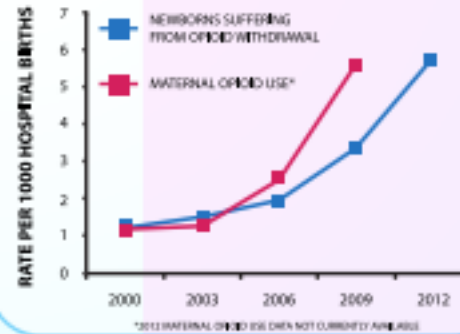


**EVERY 25 MINUTES,
A BABY IS BORN SUFFERING
FROM OPIOID WITHDRAWAL.**

AVERAGE LENGTH OR COST OF HOSPITAL STAY



NAS AND MATERNAL OPIOID USE ON THE RISE

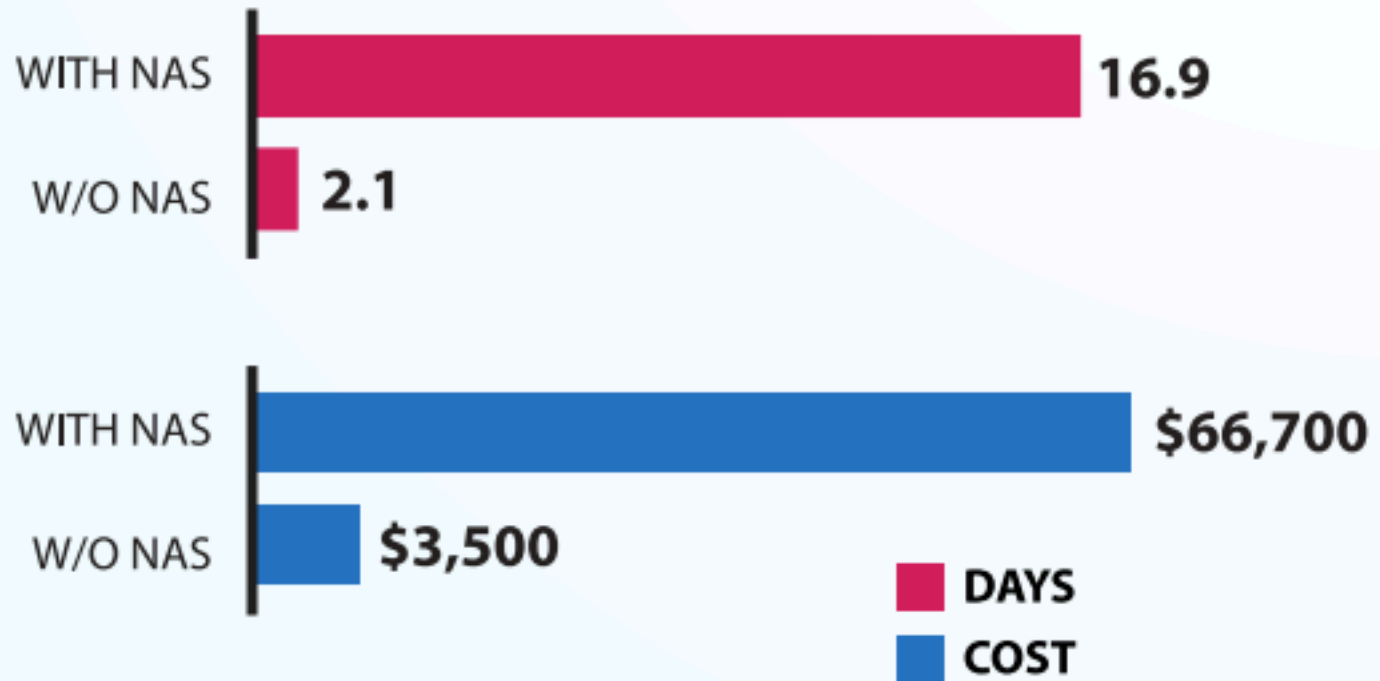


Source: [Patrick et al. JAMA 2012](#), [Patrick et al. Journal of Perinatology 2015](#)

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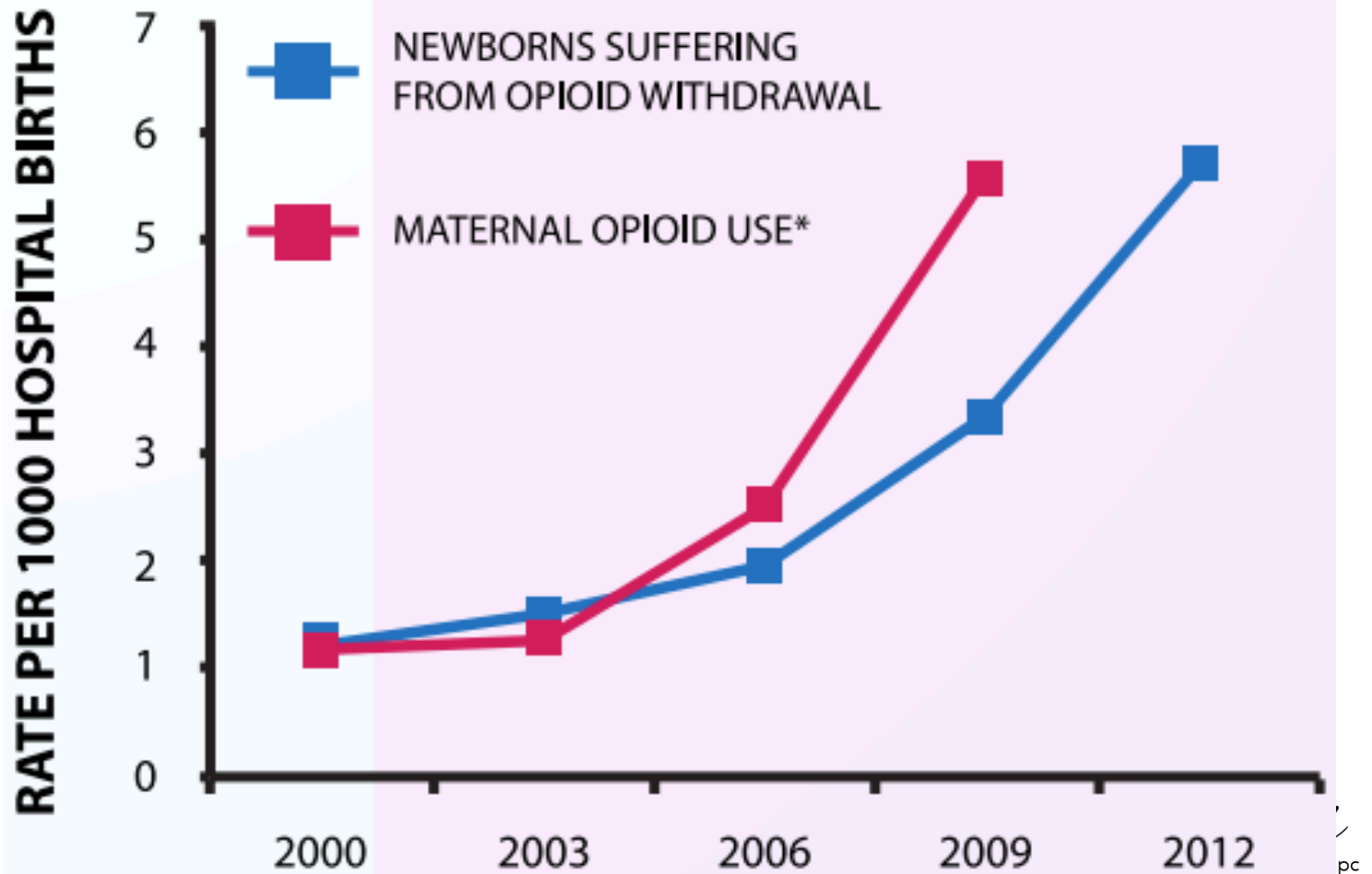
AVERAGE LENGTH OR COST OF HOSPITAL STAY

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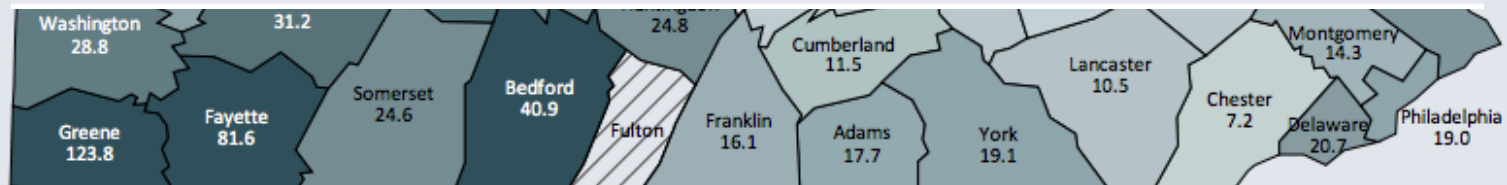
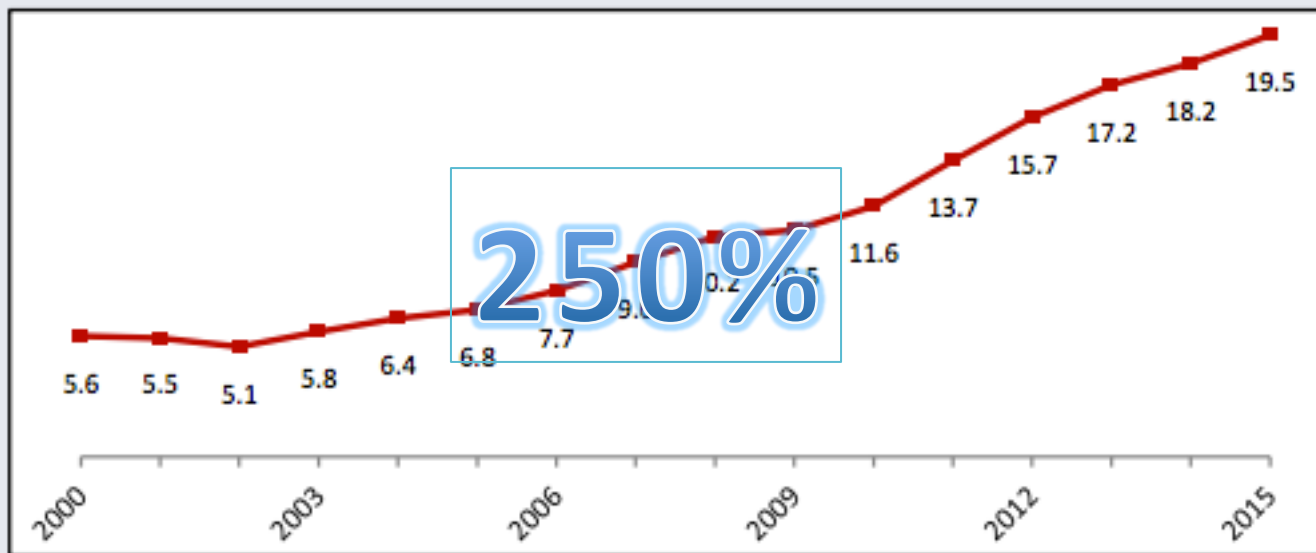
NAS AND MATERNAL OPIOID USE ON THE RISE



Pennsylvania Data

Substance-related Rate per 1,000 Neonatal Stays in FFY 2015

Substance-related Rate per 1,000 Neonatal Stays



Source: Pennsylvania Healthcare Cost Containment Council

Pennsylvania Data

	Substance-related Stays	All Other Stays
Low birth weight	15.3%	6.6%
Respiratory distress	20.7%	9.9%
Difficulty feeding	12.3%	3.4%
Prematurity	16.4%	8.4%

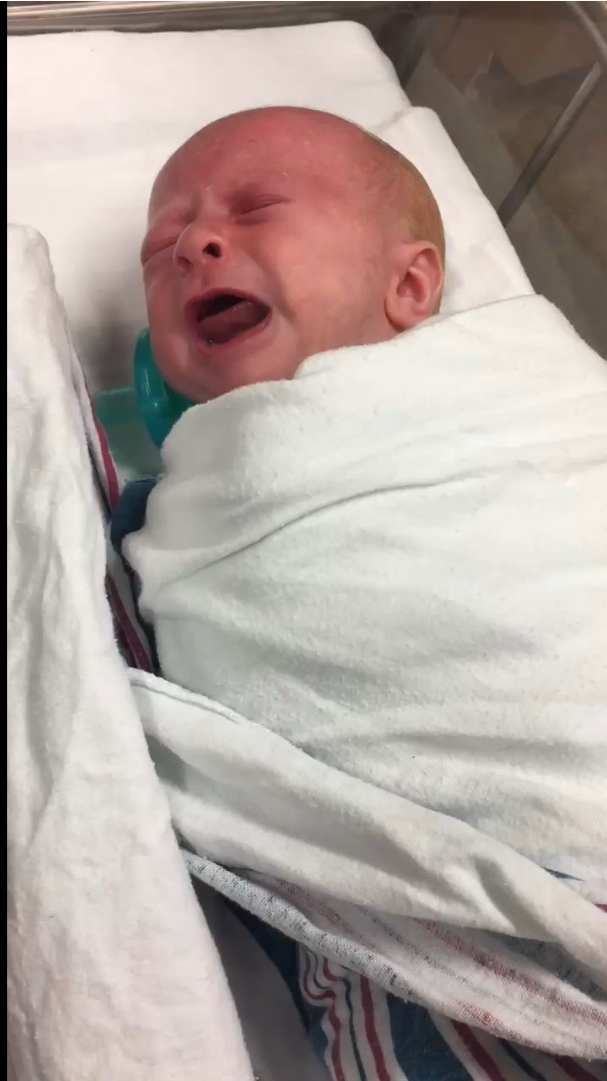
	Substance-related Stays	All Other Stays
Average length of stay	14.1 days	3.8 days
Average Medicaid payment ¹	\$17,855	\$10,316

The Problem

- Pennsylvania by the numbers (2000-2015)
 - Neonatal stays related to substance abuse
 - ↑ 250% (6.5 → 19.6/1000 neonatal stays)
 - Neonatal abstinence syndrome
 - ↑ 870% (1.6 → 16/1000 neonatal stays)
 - Cost
 - 28,000 days
 - \$20 million



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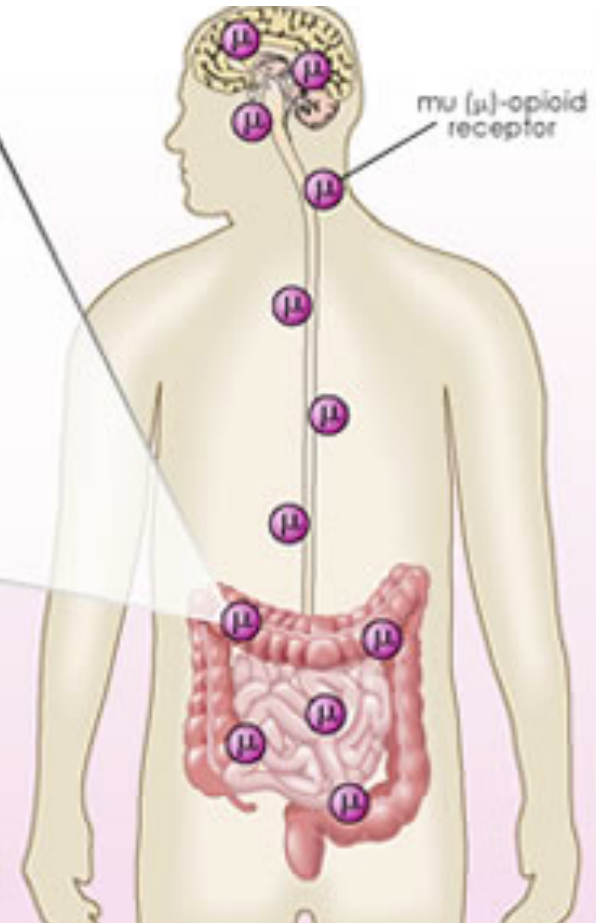
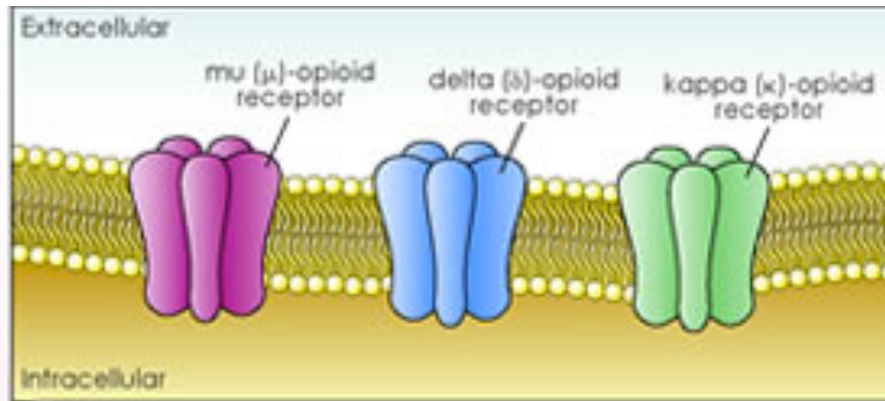
Neonatal Abstinence Syndrome

- Constellation of symptoms seen in infants who are exposed to opiates in utero
- Some variation in onset and severity of symptoms
 - Timing of most recent drug use prior to delivery
 - Maternal metabolism
 - Placental metabolism
 - Infant metabolism / excretion
 - Concomitant use of other drugs / substances

Neonatal Abstinence Syndrome

- 55-94% of infants exposed in utero exhibit symptoms
- Seldom effects infants < 34 weeks gestation

Opioid Receptors



Opioid use in Pregnancy

- Opioids are small, lipophilic, low molecular weight
 - Cross placental and blood brain barriers
- Detoxification associated with increased risk of fetal distress and loss

Neonatal Abstinence Syndrome

- CNS symptoms
 - Continuous and/or high-pitched crying
 - Difficulty sleeping
 - Hyperactive Moro Reflex
 - Tremors
 - Hypertonicity
 - Skin excoriation
 - Generalized convulsions / seizures

Neonatal Abstinence Syndrome

- Autonomic Symptoms
 - Temperature elevation
 - Sneezing / nasal stuffiness
 - Mottled skin
 - Tachypnea
 - Sweating
 - Yawning

Neonatal Abstinence Syndrome

- Gastrointestinal symptoms
 - Feeding difficulties
 - Unable to organize to feed
 - Biting nipple
 - Lack of coordination
 - Frequent watery / loose stools
 - Leads to skin breakdown
 - Regurgitation
 - Excessive sucking
 - Failure to thrive

Neonatal Abstinence Syndrome

Substance	Onset of Symptoms
Heroin	Birth – 3 days
Methadone/ buprenorphine	Birth – 7 days (subacute signs up to 6 months)
Benzodiazapene	Hours -2 weeks

Non Narcotic Substance Exposure

- Cocaine
 - No withdrawal
 - NEC, abruption, fetal distress and IUGR
- Alcohol
 - Hyperactivity, tremors, poor suck, hyperphagia
 - Sx at birth
- Caffeine
 - Jitteriness, bradycardia, vomiting, tachypnea
 - Sx at birth and for 1-7 days

Non Narcotic Substance Exposure

- Barbiturates
 - Similar to opioids
 - Sx at birth up to 14 days
- SSRI's
 - Irritability, tremors, poor suck, feeding difficulties, hypertonia, fever, hypoglycemia, seizures
 - Sx hours to days

Non Narcotic Substance Exposure

- Benzodiazapene
 - Similar to opioids
 - Hypo/hypertonia
 - Poor suck
 - Hypothermia
 - Apnea
 - Tremors
 - Vomiting
 - Tachypnea
 - Onset hours to weeks

Differential Diagnosis

- Sepsis
 - meningitis
- Electrolyte abnormality
- Hematologic irregularities
- Perinatal asphyxia
- Intracranial pathology

Diagnosis

- History, history, history
 - Maternal medical, family and social history
 - Pregnancy history
 - Birth history
- Labs
 - Cbc, bmp, +/- blood culture (if ill appearing)
 - Urine/meconium drug screens
- Risk/benefit evaluation
 - Rarely LP if history c/w NAS

Drug testing

- Ideally UDS from mother on admission
- Infant UDS (preferably first void)
- Infant Meconium drug screen
 - Reflects exposure from 20 weeks GA
 - Collect first two samples
- Infant hair
- Umbilical cord tissue

Maternal Urine Toxicology

Drug Detection Times (since last use):

Drug or Class	Detection Time
Alcohol	6 - 12 hours
Amphetamine or methamphetamine	48 hours
Barbiturates, short acting	24 hours
Barbiturates, long acting	3 weeks
Benzodiazepines, short acting	3 days
Benzodiazepines, long acting	30 days
Cocaine	2 - 4 days
Marijuana, single use	3 days
Marijuana, daily use	2 weeks
Codeine	48 hours
Heroin	2 - 4 days
Hydromorphone	2 - 4 days
Methadone	3 days
Morphine	2 - 3 days
Oxycodone	2 - 4 days

Source: PEDIATRICS Volume 129, Number 2, February 2012

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Potential False Positives

Drug or Class	Drugs which Potentially Cause False Positive Readings on Screening Tests
Amphetamines	Amantadine, chlorpromazine, desipramine, ephedrine, fluoxetine, labetalol, phentermine, phenylephrine, ranitidine, trazodone
Barbiturates	Ibuprofen, naproxen
Benzodiazepines	Sertraline
Cannabinoids	Dronabinol, NSAIDS (ibuprofen, ketoprofen, naproxen, piroxicam, sulindac, tolmetin), promethazine, PPIs
Cocaine	Amoxicillin, coca leaf teas, tonic water
Methadone	Chlorpromazine, diphenhydramine, ibuprofen, verapamil
Opiates	Dextromethorphan, diphenhydramine, poppy seeds, rifampin, quinine
Phencyclidine	Dextroamphetamine, dextromethorphan, diphenhydramine, ibuprofen, imipramine, tramadol, venlafaxine

Source: Partnership Health Plan of California, 2015

Physical Exam

- Hypertonicity
 - Global vs. extremities
 - Head lag
 - Ventral suspension



Physical Exam

- Skin
 - Mottling
 - Diaper area
 - Excoriation

NEONATAL ABSTINENCE SCORING SYSTEM

SYSTEM	SIGNS AND SYMPTOMS	SCORE	Day				Night				COMMENTS		
CENTRAL NERVOUS SYSTEM DISTURBANCES	Continuous High Pitched (or other) Cry	2											Daily Weight:
	Continuous High Pitched (or other) Cry	3											
	Sleeps <1 Hour After Feeding	3											
	Sleeps <2 Hours After Feeding	2											
	Sleeps <3 Hours After Feeding	1											
	Hyperactive Moro Reflex	2											
	Markedly Hyperactive Moro Reflex	3											
	Mild Tremors Disturbed	1											
	Moderate-Severe Tremors Disturbed	2											
	Mild Tremors Undisturbed	3											
	Moderate-Severe Tremors Undisturbed	4											
	Increased Muscle Tone	2											
	Exoriation (Specific Area)	1											
Myoclonic Jerks	3												
Generalized Convulsions	5												
METABOLIC/VASOMOTOR/RESPIRATORY DISTURBANCES	Sweating	1											
	Fever 100.4°-101°F (38°-38.3°C)	1											
	Fever > 101°F (38.3°C)	2											
	Frequent Yawning (>3-4 times/interval)	1											
	Mottling	1											
	Nasal Stuffiness	1											
	Sneezing (>3-4 times/interval)	1											
	Nasal Flaring	2											
	Respiratory Rate >60/min	1											
	Respiratory Rate > 60/min with Retractions	2											
GASTROINTESTINAL DISTURBANCES	Excessive Sucking	1											
	Poor Feeding	2											
	Regurgitation	2											
	Projectile Vomiting	3											
	Loose Stools	2											
	Watery Stools	3											
TOTAL SCORE													
INITIALS OF SCORER													

FIGURE 1

Modified Finnegan's Neonatal Abstinence Scoring Tool. Adapted from ref 101.

Using the Finnegan Score

- Begin scoring when infants show signs of withdrawal
 - Score q3-4 hours, after feeds when infant at best
- Start “treatment” when 3 scores ≥ 24 or 2 scores ≥ 24 or one score of ≥ 14

Treatment

- Nonpharmacologic
 - Swaddling
 - Holding, rocking, swaying
 - Quiet, dark, non stimulating environment
 - Encourage rooming in
 - Extended family

Breastfeeding and NAS?

- YES!!!
 - If mother is in a treatment program
 - UDS is positive only for methadone/
buprenorphine
- Associated with less severe NAS that presents later and is less severe
- Less frequently requires pharmacologic intervention

Breastfeeding and NAS

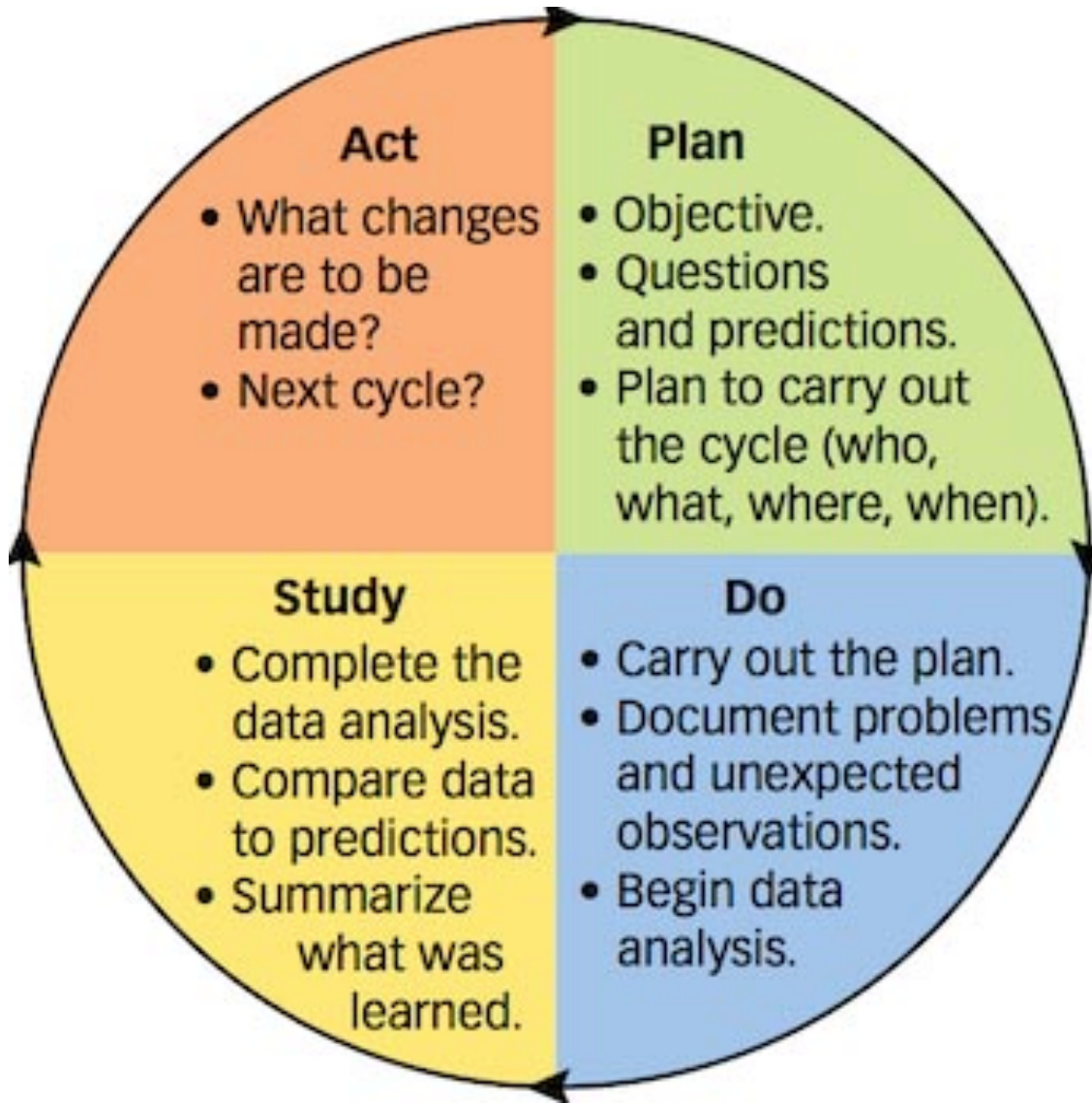
- Small amounts methadone/buprenorphine secreted into breast milk
- Long term neurodevelopmental information not available
- Not enough data to discourage breastfeeding
- Frank discussion with mother about slow weaning

Pharmacologic Treatment

- 83% of clinicians in the United States use an opioid as the drug of first choice
 - Morphine or Methadone
- Phenobarbital is most typical second-line drug if opiate does not control symptoms
- Clonidine as adjunctive therapy also an option
- Also consider using methadone

Quality Improvement

- Recently multiple studies have surfaced looking at the care of NAS
- Focus on decreased LOS
 - Decreased cost
- Standardization of treatments
- NAS Education
- Rooming In



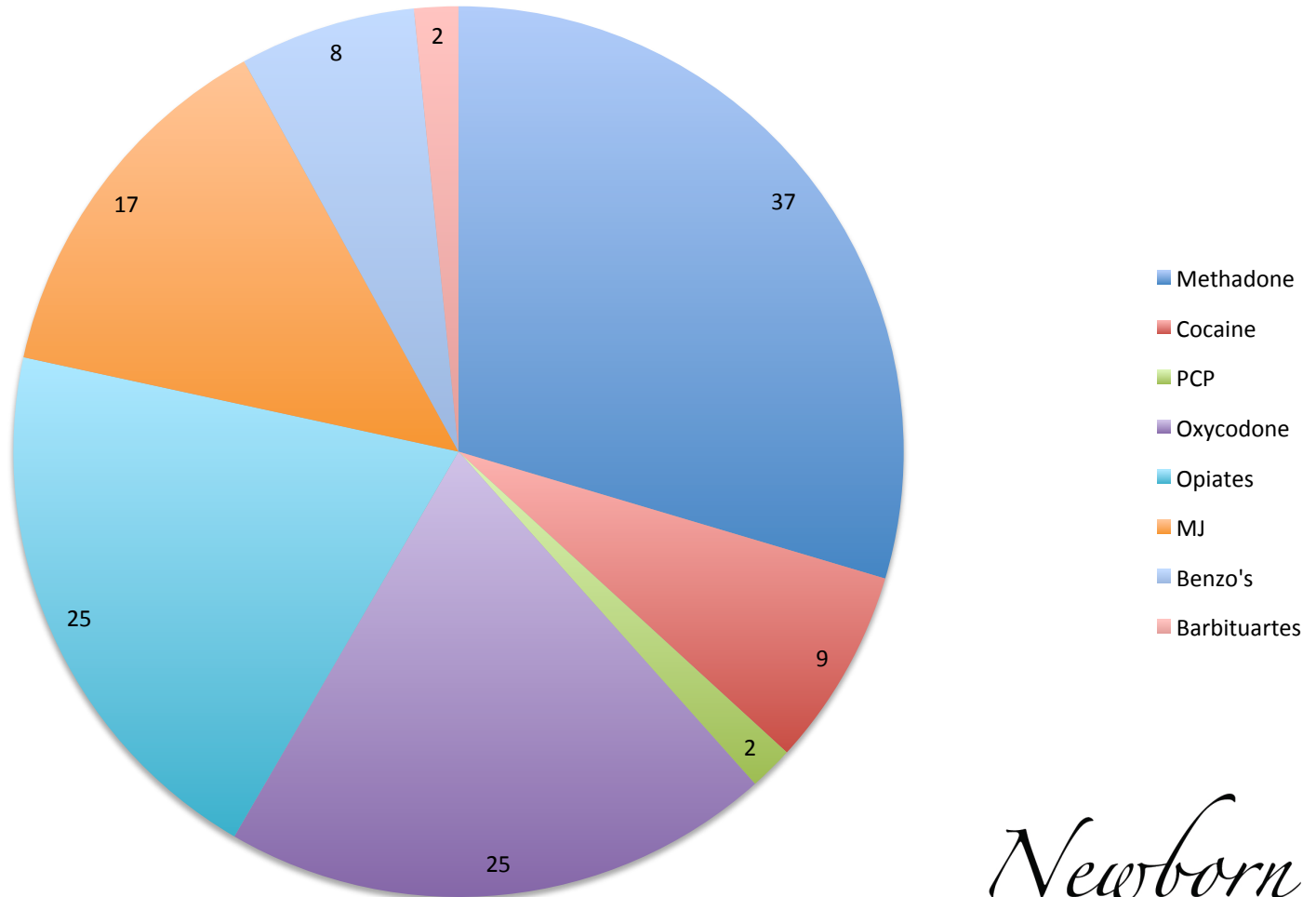
NAS at Abington Hospital

- Abington Hospital
 - 8 miles north of Philadelphia
 - Approximately 5000 deliveries/year
 - 34 bed; Level 3b NICU
- Increasing opioid exposed infants
- NAS task force formed in 2014

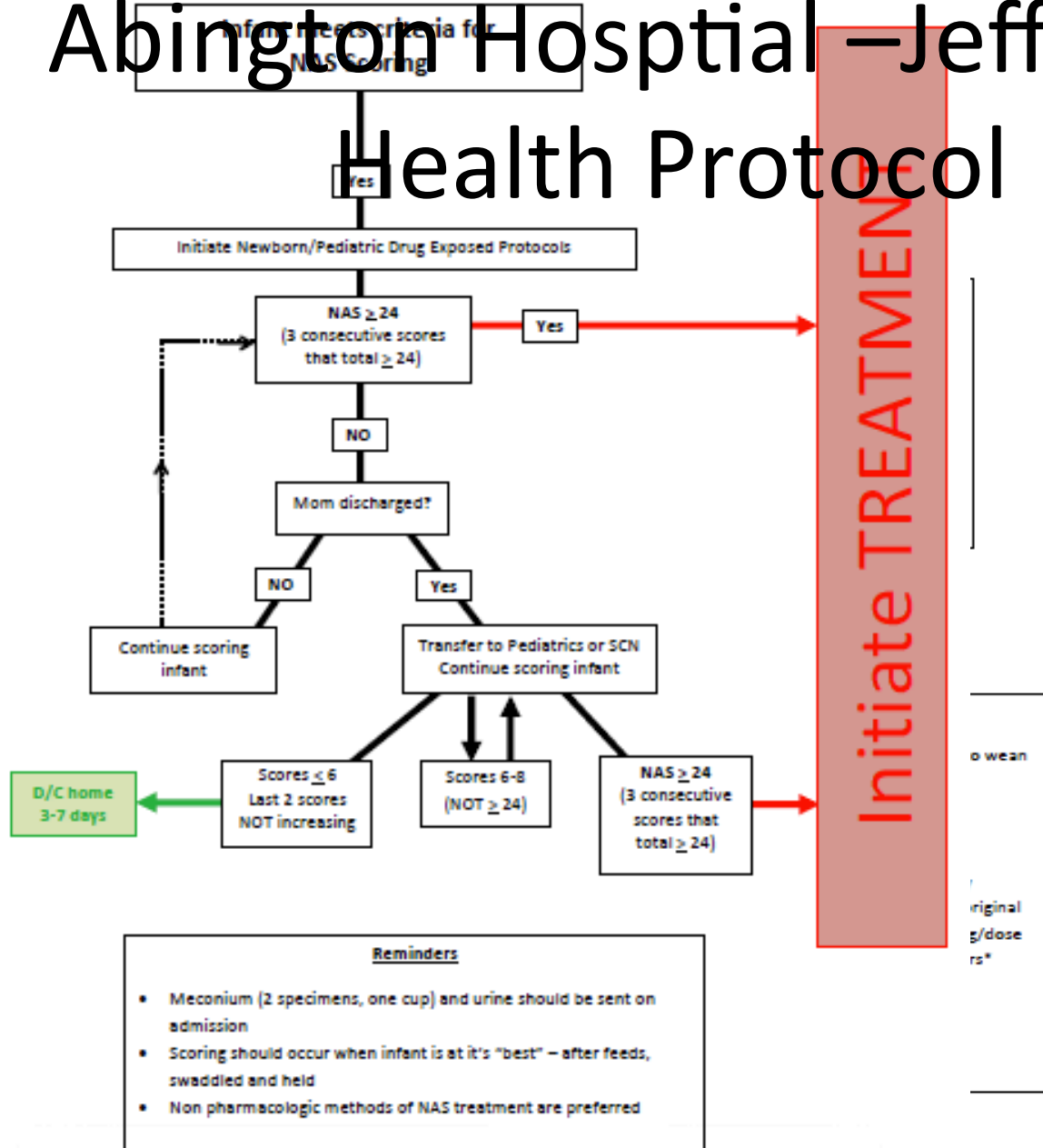
NAS at Abington Hospital

- Pre Data
 - June 2013- June 2015
 - 101 infants with positive UDS/MDS
 - 36 infants required treatment with morphine
 - LOS with NAS 22.4 days
 - LOS without NAS 4.1 days

Abington Hospital- Positive Drug Screen



Abington Hospital – Jefferson Health Protocol



Post Data

- July 2015-May 2016
 - 38 babies opioid exposed
 - 18 babies treated for NAS
 - LOS 16.8 days

PEDIATRICS

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ARTICLES

Trends in Use of Prescription Opioids

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Trends in PSM Diagnosis and Management for VSDs

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Stability in Group Management and Follow-up

A. Cyr et al 21

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TEACHING POINTS

Standardization of nonpharmacologic care

Matthew R. Grossman, A Matthew J. Bizzarro

FAMILY PARTNERSHIPS

Parental education

Matthew R. Grossman, A Matthew J. Bizzarro

MENTAL FEATURE

Novel Assessment Approach

Matthew R. Grossman, A Matthew J. Bizzarro

COMMUNITIES

Morphine prn

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Bypassing the NICU

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Standardization of nonpharmacologic care

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Neonatal Abstinence

erman, Eugene D. Shapiro,

An Initiative to In Syndrome

Matthew R. Grossman, A Matthew J. Bizzarro

- Yale New Haven Children's Hospital
 - Standardization of nonpharmacologic care
 - Parental education
 - Novel Assessment Approach
 - Morphine prn
 - Bypassing the NICU

An Initiative to Improve the Quality of Care of Infants With Neonatal Abstinence Syndrome

Matthew R. Grossman, Adam K. Berkwitt, Rachel R. Osborn, Yaqing Xu, Denise A. Esserman, Eugene D. Shapiro, Matthew J. Bizzarro

- Novel Approach to NAS
 - Functional Assessment
 - Ability to eat
 - BF effectively or take >1oz/feed
 - Ability to sleep
 - Undisturbed > 1 hour
 - Ability to be consoled
 - Within 10 minutes

An Initiative to Improve the Quality of Care of Infants With Neonatal Abstinence Syndrome

Matthew R. Grossman, Adam K. Berkwitt, Rachel R. Osborn, Yaqing Xu, Denise A. Esserman, Eugene D. Shapiro, Matthew J. Bizzarro

- Novel approach to Treatment
 - If on scheduled morphine
 - 10% wean TID
- After maximum nonpharmacologic interventions
 - 1 dose of morphine given (0.05mg/kg)
 - Reassessed 3 hours later
 - Eating, sleeping and consoling well
 - No further doses

An Initiative to Improve the Quality of Care of Infants With Neonatal Abstinence Syndrome

Matthew R. Grossman, Adam K. Berkwitt, Rachel R. Osborn, Yaqing Xu, Denise A. Esserman, Eugene D. Shapiro, Matthew J. Bizzarro

- 55 infants pre implementation
- 44 infants post implementation
 - LOS: 22.4 → 5.9 days
 - Pharmacologic Tx: 98% → 14%
 - Costs: \$44,000 → \$10,000
 - No readmissions, no adverse events

Summary

- Opioid addiction is currently an epidemic
- Pregnant women can be addicted
- Neonatal Abstinence Syndrome – treatment has been stable through the years
- Breast feed when able
- Assessment change has no ADRs
- Nonpharmacologic treatment is feasible

Acknowledgements

- NAS Task Force at Abington Hospital Jefferson Health
- Moira Winstanley, NNP- BC
- Andrew Loh, MD

Thank you!



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