Neonatal NAS Initiative Webinar

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August 13, 2019
2:00-3:00pm

EFFECTS OF IN-UTERO EXPOSURE TO OPIOIDS/DRUGS OF ABUSE

August 13th, 2019

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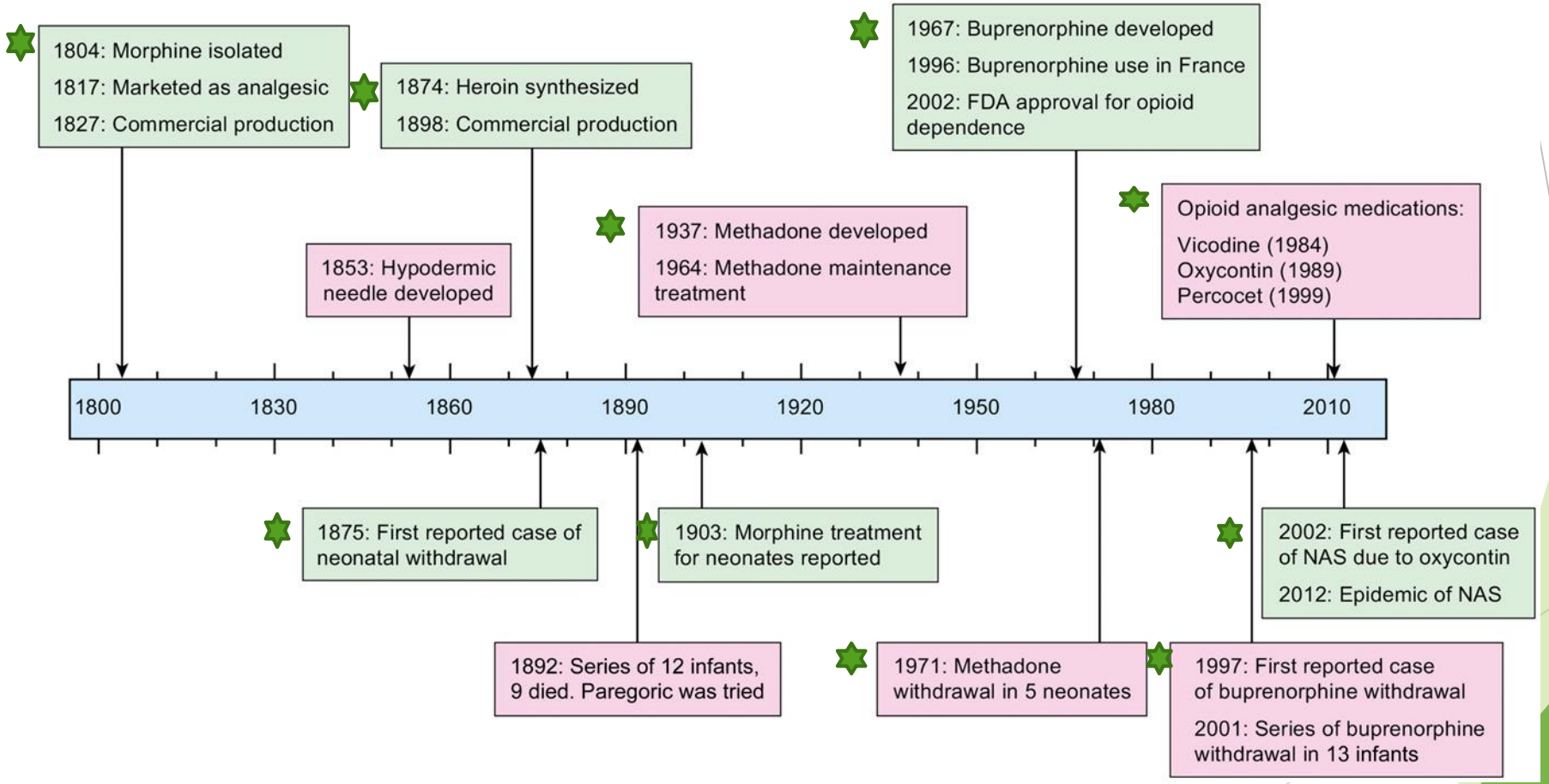
Timeline of Neonatal Abstinence Syndrome (NAS)



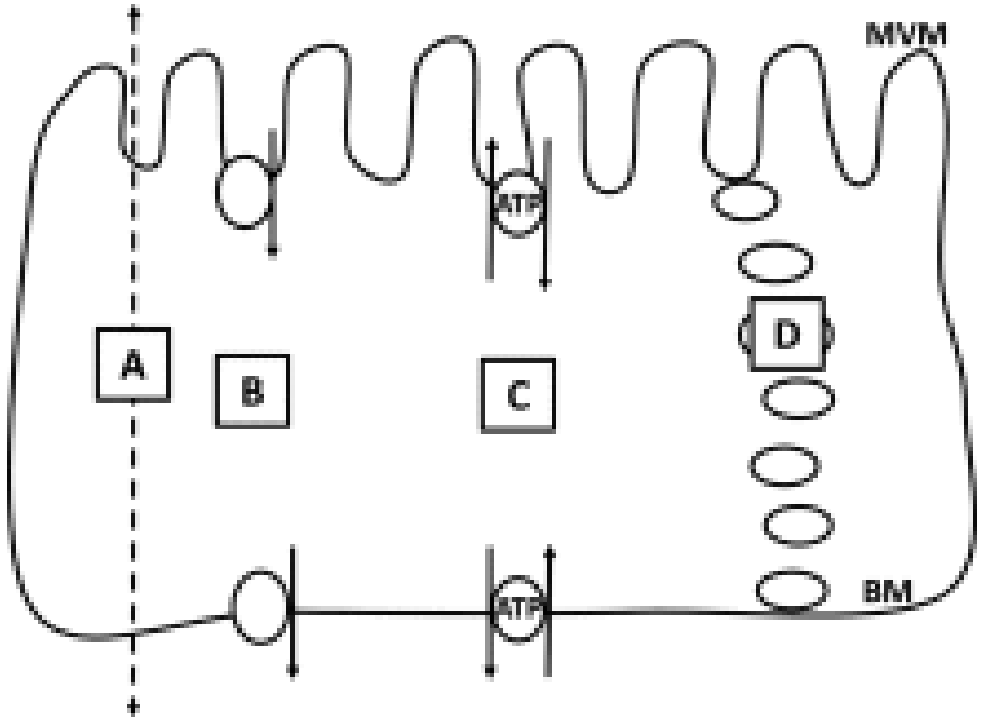
Drug Withdrawal Spectrum Over Time

- Before 1970 – Secondary to morphine or heroin
- Today - Morphine, heroin, methadone, buprenorphine, prescription opioid analgesics, antidepressants, anxiolytics, and/or other substances
- Also contributing - Medication-Assisted Therapy with methadone, buprenorphine
- More common and complex - Increased use of opioids, simultaneous use of multiple opioids, concurrent use of multiple other licit and illicit substances.
- Additional social, economic, and health care costs on society

Placental Drug Transfer

Mechanisms of placental drug transfer -
A: Simple diffusion
B: Facilitated diffusion using a carrier
C: active transport using ATP
D: Pinocytosis

Factors affecting drug transfer across the placenta-
Physical
Pharmacological



BM, basal membrane of the syncytiotrophoblast; MVM, microvillous membrane of the syncytiotrophoblast) (adapted from a diagram in Desforges and Sibley4 with kind permission from the International Journal of Developmental Biology)

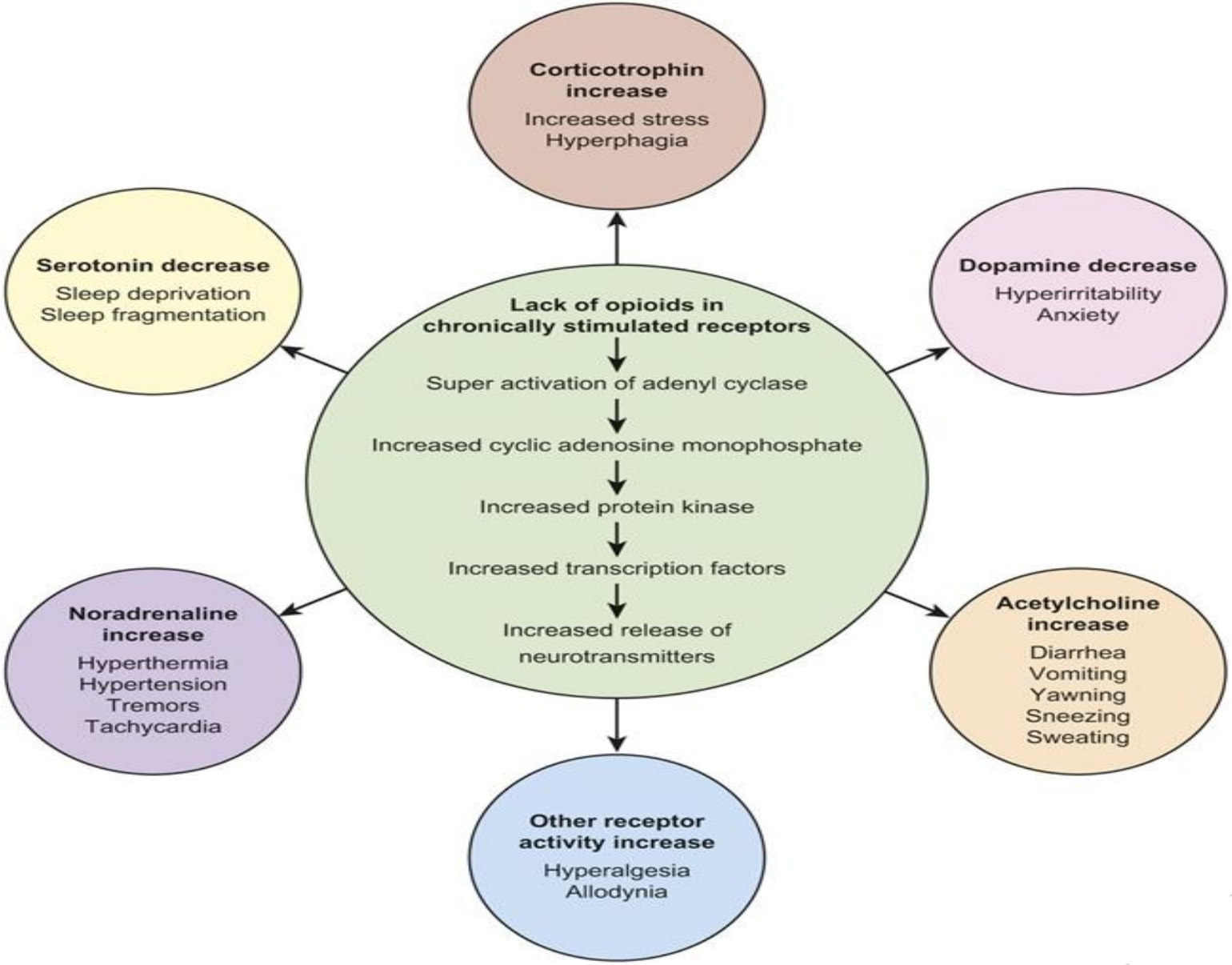
Opiates and Placental Transfer

- Low molecular weight, water soluble, lipophilic - Easily transfer across the placenta to the fetus
- Transmission increases as gestation increases
- Synthetic opiates cross more easily than semisynthetic
- Combination of cocaine or heroin with methadone - further increases permeability of methadone
- Ease of transfer across the bloodbrain barrier of the fetus + prolonged half-life in the fetus – worsens withdrawal in infants
- Sudden discontinuation of prolonged fetal exposure to opioids- Neonatal abstinence syndrome (NAS)/ Neonatal Opioid Withdrawal Syndrome (NOWS)

NAS/(NOWS)- Pathophysiology(1)

- More complex in neonates - immature neurologic development, impaired neurologic processing, and complex materno-feto-placental pharmacokinetics
- Opioids act through opioid receptors (G protein–coupled receptors, m, k, and d)- extensively distributed across the CNS
- Also located within the PNS, GI system, and various other systems.
- The density and affinity of m-receptors in neonates are as good as those in adults
- Opioid receptors in chronically stimulated state + lack of opioids - increases activity in the opioid receptors
- Leads to increased adenyl cyclase activity and cellular ionic imbalance - causes production and release of various neurotransmitters

NAS/NOWS - Pathophysiology(2)



NAS/NOWS – Clinical Signs/Symptoms

- Tremors, irritability, excessive crying, and diarrhea at presentation; sometimes seizures
- CNS signs – first irritability, jitteriness, tremors, and excessive crying
- Hallmark Hyperirritability - can lead to agitation, difficulty sleeping, and inconsolable crying
- High-pitched, uncontrollable excessive crying - requires immediate attention
- Tremors, exaggerated Moro reflex, hypertonia, and myoclonic jerks - commoner with methadone
- Can mimic seizures – may need EEG for confirmation
- Seizures in 2% to 11% - serious, should be treated immediately
- Dysregulation/instability of ANS – Impaired physiologic responses to stimuli, abnormalities of heart rate, respiratory rate, muscle tone; temperature instability, sweating, sneezing, mottling
- May persist for months, or even longer, especially with maternal buprenorphine

NAS/NOWS – Clinical Signs/Symptoms (cont.)

- Chemical odor - neonates born to mothers who abuse inhalants
- Tachypnea, nasal flaring, and nasal stuffiness - misinterpreted as respiratory distress
- Hyperthermia, although rarely higher than 102°F - misdiagnosis as sepsis
- Poor feeding, excessive motor activity, regurgitation, vomiting, and diarrhea - poor weight gain
- Severe diarrhea, leading to dehydration and electrolyte imbalance – especially for heroin
- Non-CNS causes of increased irritability and agitation - perianal skin excoriation secondary to excessive loose stools; unattended skin excoriation over the face and body, secondary to excessive motor movements
- Hyperphagia widely recognized - may require intake of more than 150 calories per kilogram per day

Preterm Infant

- Incidence and severity of withdrawal less extensive in preterm neonates
- Various factors :

  Decreased cumulative exposure

  Decreased transmission across the placenta during early gestation

  Decreased morphine clearance

  Decreased excretion because of immaturity of the kidneys and liver

  Decreased fatty tissues in preterm infants (methadone is accumulated in fatty tissue)

  Decreased receptor development

  Decreased receptor sensitivity

Onset, Duration and Frequency

TABLE 1 Onset, Duration, and Frequency of NAS Caused by Various Substances

Drug	Onset, h	Frequency, %	Duration, d
Opioids			
Heroin	24–48	40–80[27]	8–10
Methadone	48–72	13–94[37]	Up to 30 or more
Buprenorphine	36–60	22–67[46,48]	Up to 28 or more
Prescription opioid medications	36–72	5–20[56,60]	10–30
Nonopioids			
SSRIs	24–48	20–30[64]	2–6
TCAs	24–48	20–50[64]	2–6
Methamphetamines	24	2–49[101]	7–10
Inhalants	24–48	48[70]	2–7

Withdrawal presentation differs by exposure, so monitoring of infants for signs and symptoms of withdrawal should be commensurate (e.x. a methadone exposed infant may need a longer period of monitoring)

Course – Severity and Intensity

TABLE 2 Risk Factors for Increasing Severity and/or Intensity of NAS

Definite	Probable
Term[97,98,108]	Male gender[112,113]
Good birth weight[97,109]	Methadone[45,46]
Polydrug abuse[106,107, 110]	Smoking[97,109,114]
Combination with benzodiazepines[97,111]	Combination with SSRIs[97,100,115]
μ-opioid receptor (OPRM1 118 AA) positive[105]	
Catechol-O-methyltransferase (COMT 158 AA) positive[105]	

- **Initial phase - short but intense, with tremors, seizures, irritability, feeding problems, vomiting, diarrhea, hyperthermia, and other systemic signs lasting for 1 to 2 weeks**
- **Long chronic and relapsing course - hyperirritability, sleep disturbances, hyperphagia, and other neurologic and autonomic signs, lasting for a few weeks to a few months**

Non-Opiate Withdrawal

- SSRI intake by mothers - withdrawal symptoms from excess serotonin and noradrenaline.
- Tricyclic antidepressants – withdrawal is cholinergic rebound phenomenon
- Benzodiazepines – withdrawal from increased release of g-amino butyric acid
- Methamphetamine - withdrawal from decrease in dopamine, serotonin, and other monoamines
- Inhalant - withdrawal through dopamine, glutamate, and g-amino butyric acid pathways

Effects of Fetal Exposures to Various Substances

- Decreased growth
- Deficits in attention
- Increased impulsivity
- Long-term deficits in executive function
- Depression diagnosis
- Future substance use

- Neonatal abstinence syndrome
- Preterm birth and obstetric complications
- Attenuated myelination in infants
- Respiratory insufficiency
- Heart defects
- Reduced growth
- Deficits in cognitive and motor ability
- Attention deficit hyperactivity disorder
- Lower IQ
- Behavioral problems

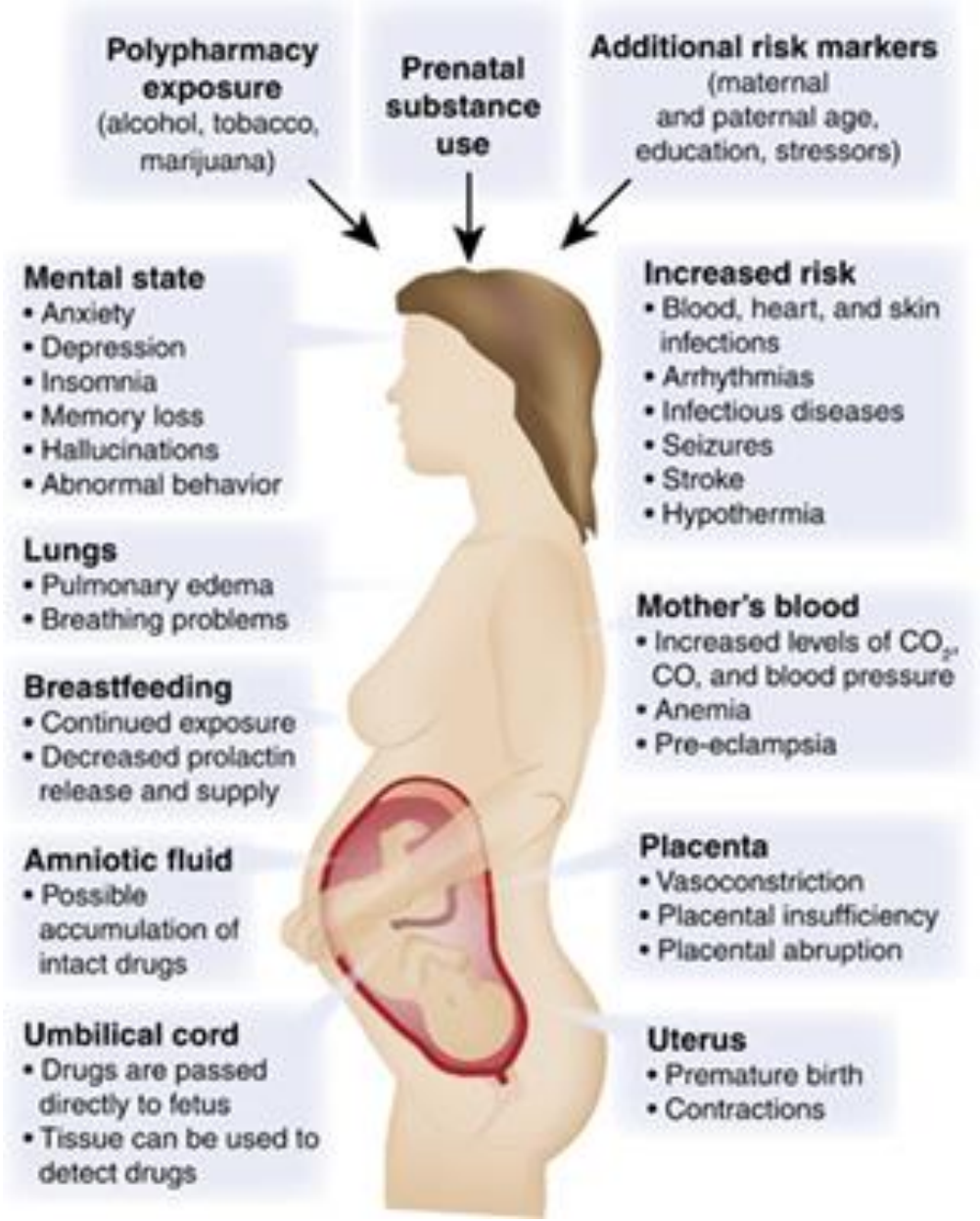
- Increased risk of growth restriction and prematurity (at high levels)
- Possible decrease in executive function at school age

- Decreased birthweight
- Altered response to stimuli
- Poorer academic achievement
- Poorer cognition
- Attention deficits and hyperactivity
- Adolescent aggression
- Oppositional defiance issues

- Preterm labor
- Short- and long-term growth defecits
- Cardiac and cardiovascular anomalies
- Cranial and brain abnormalities
- Behavior problems
- Emotional and social effects
- Deficits in attention, memory and motivation
- Anxious/depressed behaviors and symptoms
- Aggression and delinquent behavior

- Prematurity and spontaneous abortion
- Limb and facial development
- Reduced growth
- Cognitive delays and impairments
- Reduced brain volumes
- Abnormalities in the corpus callosum
- Deficits in attention, memory, verbal fluency, executive functioning, reaction times, and motor learning

Indirect Effects of Fetal Drug Exposure



VON Day Audit

GaPQC Results

VON Day Audit Participation

- 38 hospitals participated
  - 80% of the Collaborative
- 16 hospitals audited 34 infants

Policies and Guidelines

	Georgia (GaPQC)		
	Yes	Centers	(%)
Our hospital has a policy or guideline that defines indications and procedures for screening for maternal substance abuse.	30	38	(78.9)
Our hospital has a policy or guideline for the evaluation and comprehensive treatment of infants at risk for or showing signs of withdrawal.	27	38	(71.1)
Our hospital routinely uses a scoring system to evaluate signs and symptoms of drug withdrawal.	35	38	(92.1)
The following scoring tools are used at your hospital to evaluate signs and symptoms of drug withdrawal:			
Finnegan	17	35	(48.6)
Modified Finnegan	20	35	(57.1)
Lipsitz	1	35	(2.9)
Fir Square checklist	0	35	(0.0)
Locally Developed Instrument	0	35	(0.0)
Other	0	35	(0.0)
Our hospital has guidelines or policies addressing the use of the Eat, Sleep, Console (ESC) assessment in the management of opiod exposed infants.	3	38	(7.9)
Our hospital has a formal education program that promotes standardization of NAS scoring among caregivers.	9	38	(23.7)
Our hospital has a policy or guideline for the non-pharmacological treatment of neonatal abstinence syndrome.	21	38	(55.3)
Our hospital has a policy or guideline for the pharmacological treatment of neonatal abstinence syndrome	17	38	(44.7)
Our hospital has a policy or guideline that encourages breastfeeding or the provision of expressed human milk in substance exposed infants.	17	38	(44.7)

Demographics

	Georgia (GaPQC)		
	Cases	N	(%)
Birth weight			
<1501g	0	34	(0.0)
1501 to 2500g	5	34	(14.7)
>2500g	29	34	(85.3)
Gestational age			
<35 weeks	3	34	(8.8)
35 to 37 weeks	14	34	(41.2)
>37 weeks	17	34	(50.0)
Inborn	28	34	(82.4)
Was toxicological screening (including urine, meconium, hair, or cord) obtained on the infant to document substance exposure?	29	34	(85.3)
Was the infant scored for NAS at any time during hospitalization?	34	34	(100.0)

Non-Pharmacologic Care

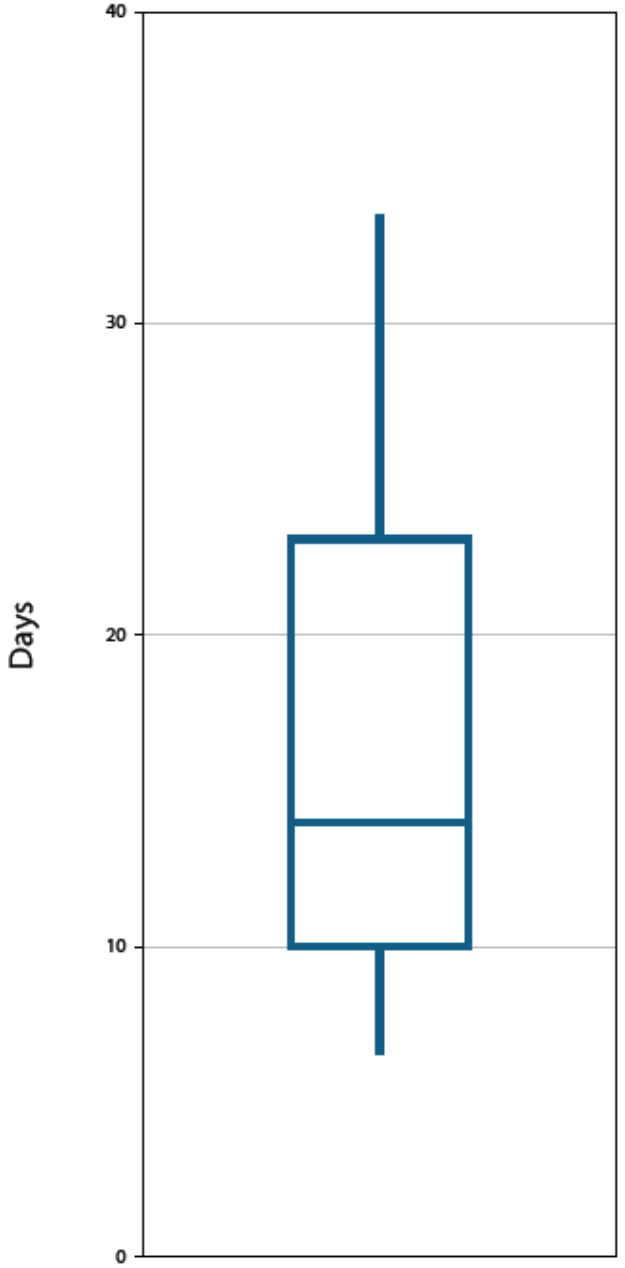
	Georgia (GaPQC)		
	Cases	N	(%)
Was the infant assessed using the Eat, Sleep, Console (ESC) assessment at any time prior to initiating pharmacologic treatment for NAS?	1	34	(2.9)
In the 24 hours preceding discharge from your hospital, did the infant receive any of his/her mother's own milk?	5	34	(14.7)
Where was the infant discharged to:			
Home	24	34	(70.6)
Home with a guardian or foster parent	7	34	(20.6)
Transferred to another hospital	1	34	(2.9)

Pharmacologic Agents

	Georgia (GaPQC)					
	In Hospital			At Discharge		
	Cases	N	(%)	Cases	N	(%)
Pharmacologic agents administered for the treatment of NAS						
Morphine	26	34	(76.5)	1	2	(50.0)
Methadone	9	34	(26.5)	1	2	(50.0)
Buprenorphine	0	34	(0.0)	0	2	(0.0)
Clonidine	3	34	(8.8)	0	2	(0.0)
Phenobarbital	6	34	(17.6)	0	2	(0.0)
Paregoric	0	34	(0.0)	0	2	(0.0)
Deodorized Diluted Tincture of Opium	0	34	(0.0)	0	2	(0.0)

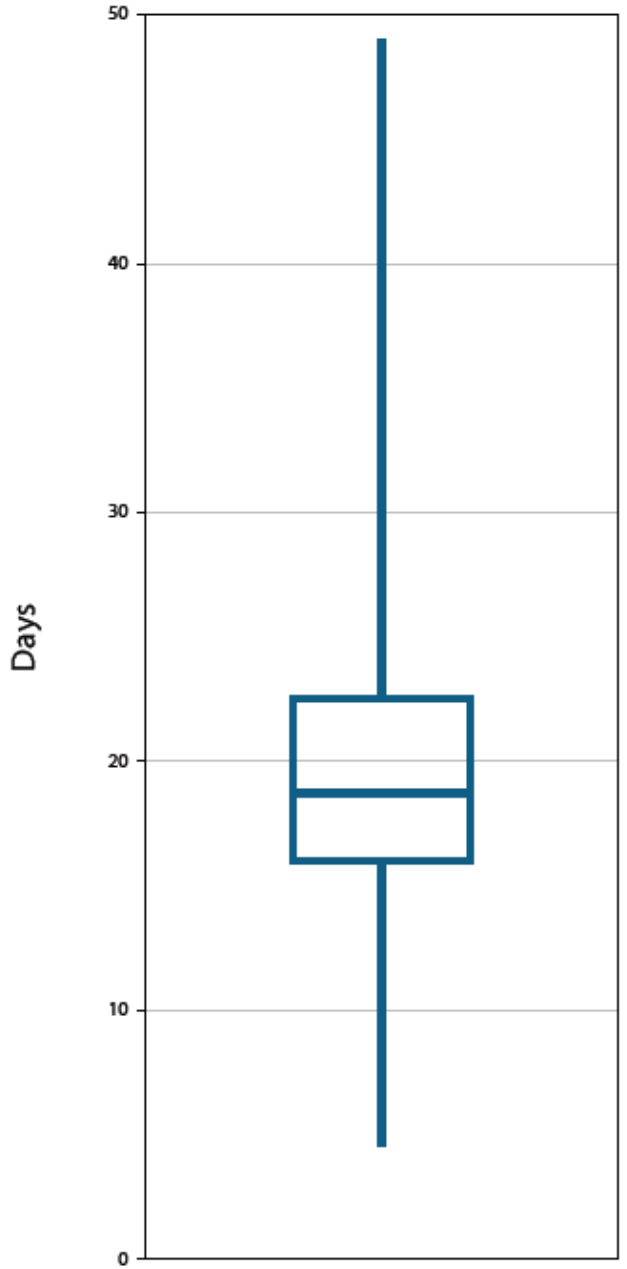
Total Duration of Pharmacologic Treatment

- Max: 75
- Q3: 23
- Median: 13
- Q1: 9
- Min: 2



Total Length of NICU Stay

- Max: 77
- Q3: 24
- Median: 18
- Q1: 10
- Min: 2



Total Length of Hospital Stay

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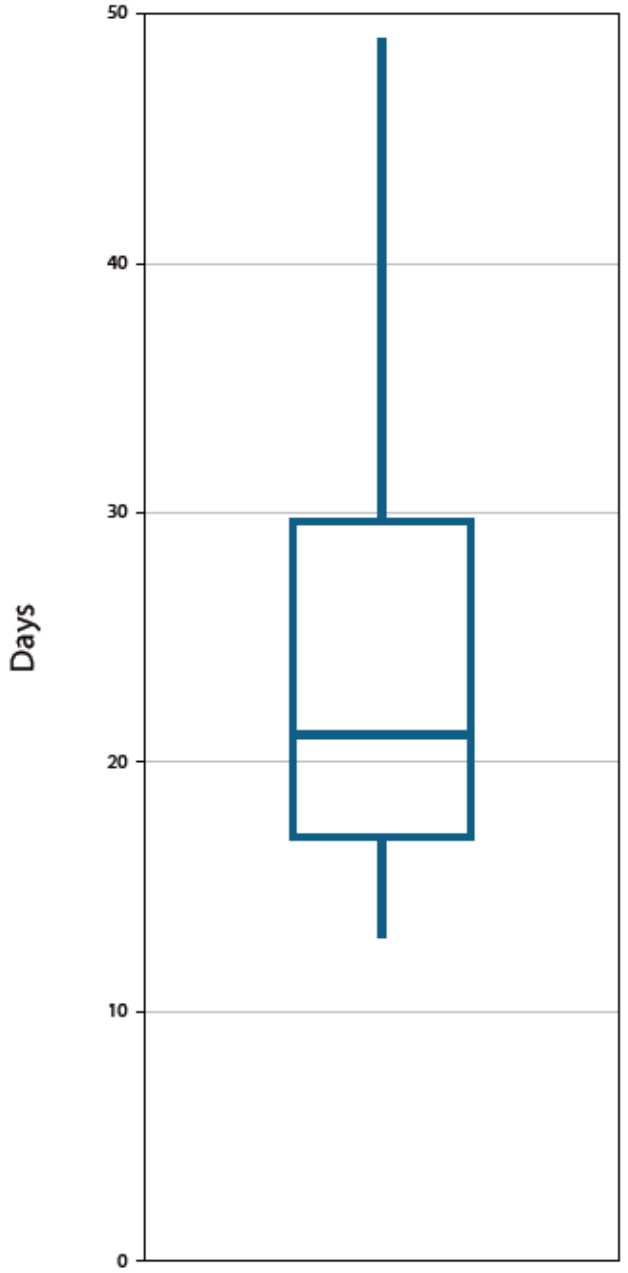

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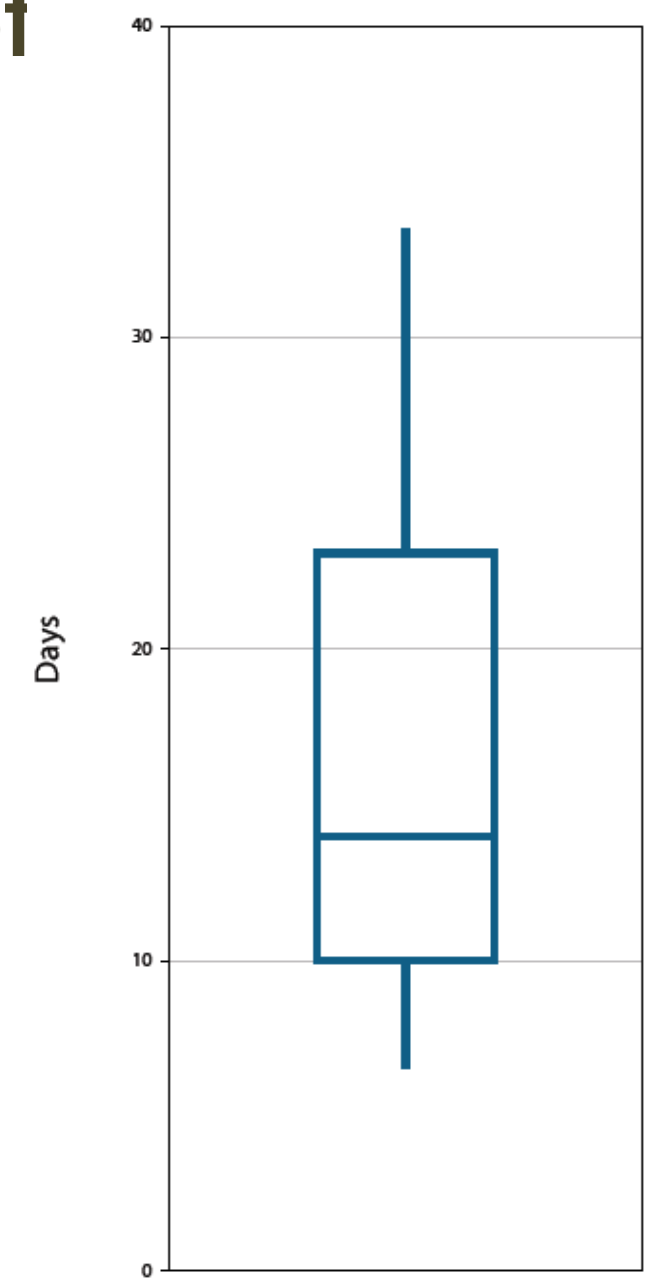

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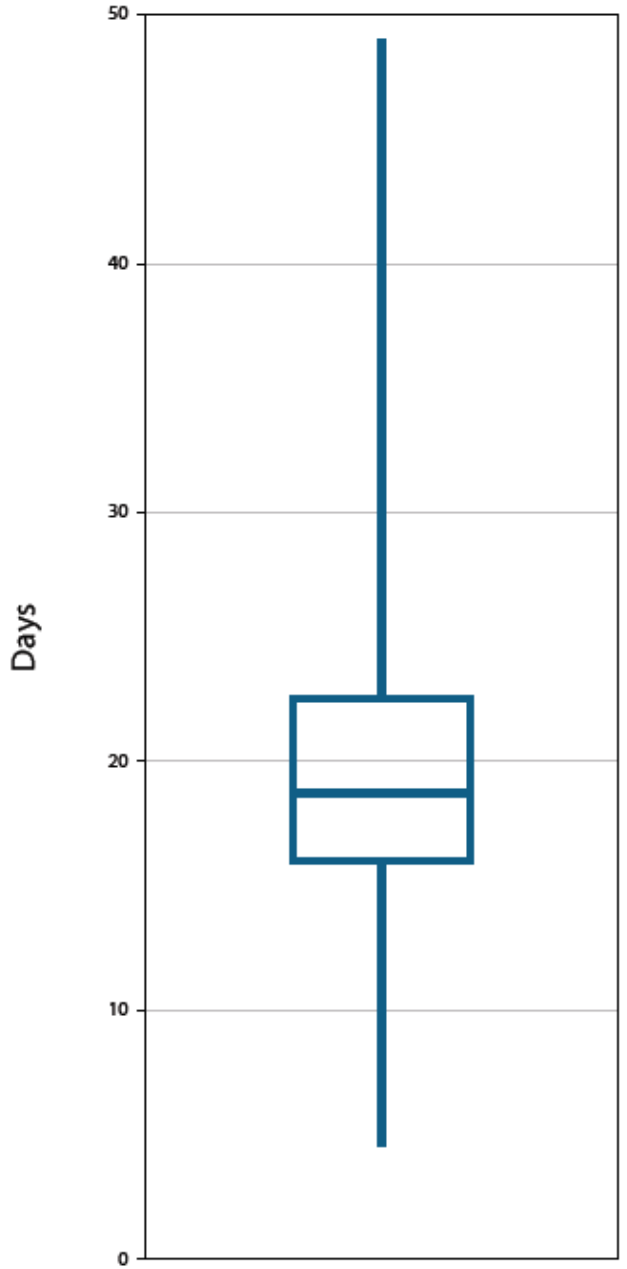

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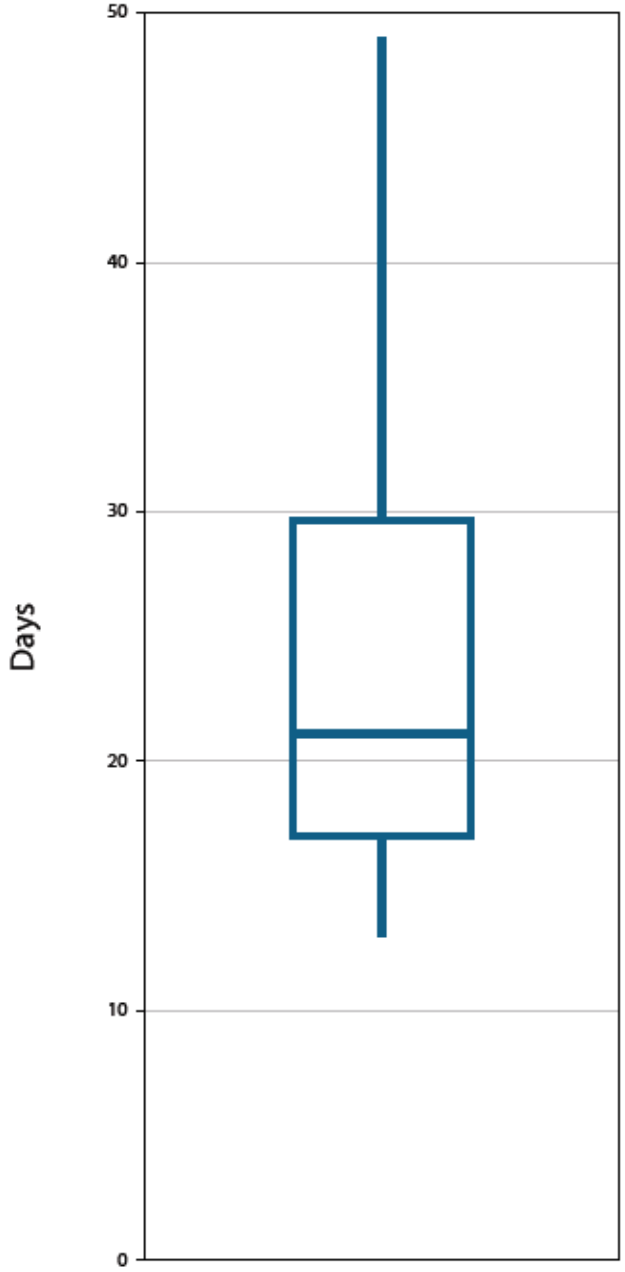


The Model for Improvement

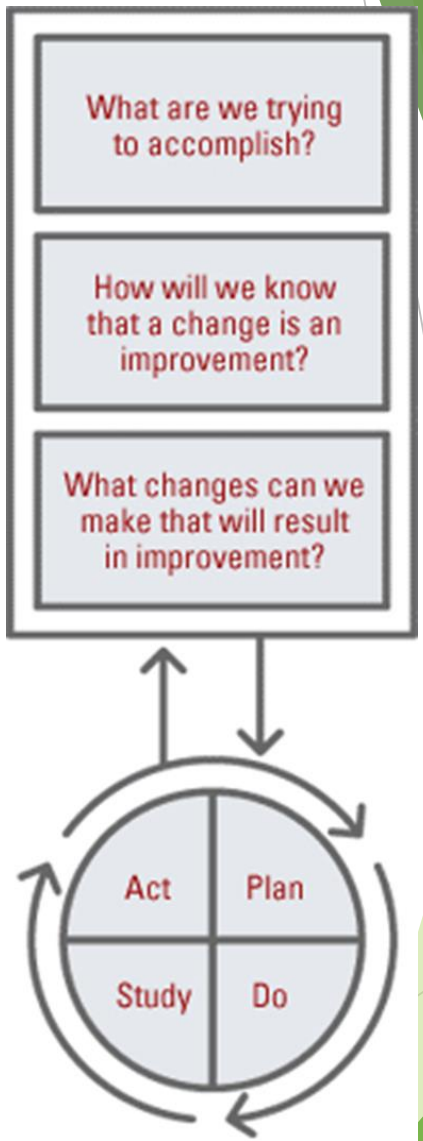
- What are we trying to accomplish?

  AIM STATEMENT
- How will we know that a change is an improvement?

  MEASURE
- What changes will result in an improvement

  PROCESS IMPROVEMENT TOOLS
- Tests of change

  Plan-Do-Study-Act (PDSA)



The Model for Improvement is recommended by the Institute for Healthcare Improvement and was originally developed by API (http://www.apiweb.org/)

SMART AIM statement template

We will increase/decrease _____ (what) among _____(population) from _X_(baseline) to _Y_ (goal) by _____ (date)

Example of a SMART AIM

We will increase the percentage of drug screens obtained on infants born to at-risk mothers from 85% to 95% by July of 2021

Specific, **M**easurable, **A**chievable

We will increase the percentage of drug screens obtained on infants born to at-risk mothers from 85% to 95% by July of 2021

Relevant - Defined population

We will increase the percentage of drug screens obtained on infants born to at-risk mothers from 85% to 95% by July of 2021

Time-specific

We will increase the percentage of drug screens obtained on infants born to at-risk mothers from 85% to 95% by July of 2021

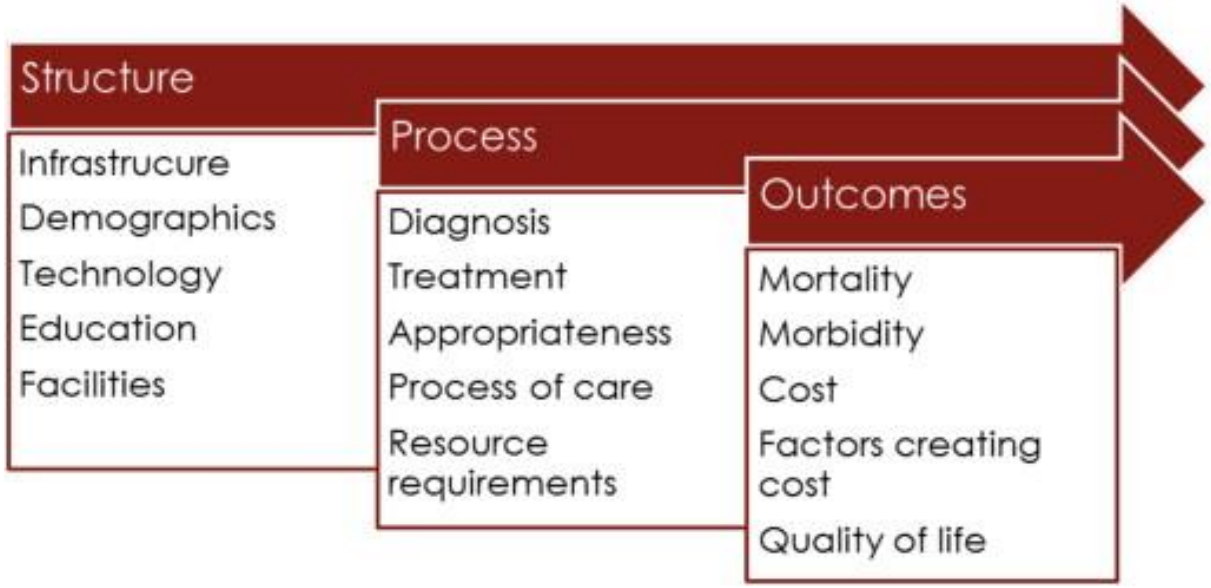
Steps – Model for Improvement

1. Form a team
2. Make an AIM statement
3. **Establish measures**
4. Identify and select changes to test using process improvement tools
5. Test changes using PDSA cycles
6. Implement changes that work
7. Spread changes to other locations

QI - Measurement in Healthcare

- Maxim - “You can't manage what you don't measure”
- Goal - Understand a process quantitatively and provide interventions to improve performance
- Apply interventions - Use a metric to determine the effect of the intervention
- Monitor the measure over time and track the performance trend

The Donabedian model



QI – IMPROVEMENT MEASURES

- Measurement strategy - Important for data to determine whether your changes are, in fact, leading to improvement
- **Types of measures**

  Structure measures : All factors that affect the context in which care is delivered – Infrastructure, demographics, technology, facilities etc.

  Process measures : Related to the processes you are working on as part of the improvement effort – Diagnosis, treatment, process of care, appropriateness etc.

  Outcome measures : Tied to the overall aim of the project- Mortality, morbidity, cost, LOS, etc. **Can take a long time**

  Balancing measures *:* Help ensure that you're not improving one part of the system at the expense of another

  Example- For reducing patients' length of stay in the hospital: Make sure readmission rates are not increasing

SMART AIM

We will increase the percentage of drug screens obtained on infants born to at-risk mothers from 85% to 95% by July of 2021

Process

Urine drug screens obtained

Outcome

Identification of newborns at risk for drug withdrawal

Balancing

False-positive/negative drug screens

Patient-family centered measure:

Infant discharged to mother's care

Measures: Process Measures

- Is the process happening as planned
- Must find a way to track and document whether process is happening as defined in your measure
- Example: Tracking UDS in at risk infants i.e born to mothers with a history and/or positive UDS

Outcome Measures

- Is the intervention having the desired effect on the target population (e.g. increased testing helping to identify at newborns at risk for withdrawal)
- Clinically relevant, concrete data is best
- Example: Length of stay

- Most QI projects should have at least one outcome measure, although for some projects this may be difficult to define

Balancing Measures

- Are there untoward consequences of your specified intervention?
- Example:
  - Process: Urine drug screens obtained
  - Outcome: Identification of newborns at risk for drug withdrawal
  - Balancing: False-positive drug screens
- Try to anticipate possible outcomes, but be open for unexpected ones

Family-centered measure

- If none of your measures capture the patient-family experience, think about if you can incorporate a measure related to this
- This is often difficult to measure, so most QI projects do not have this
- Example: mother providing skin-to-skin care/mother providing own breastmilk

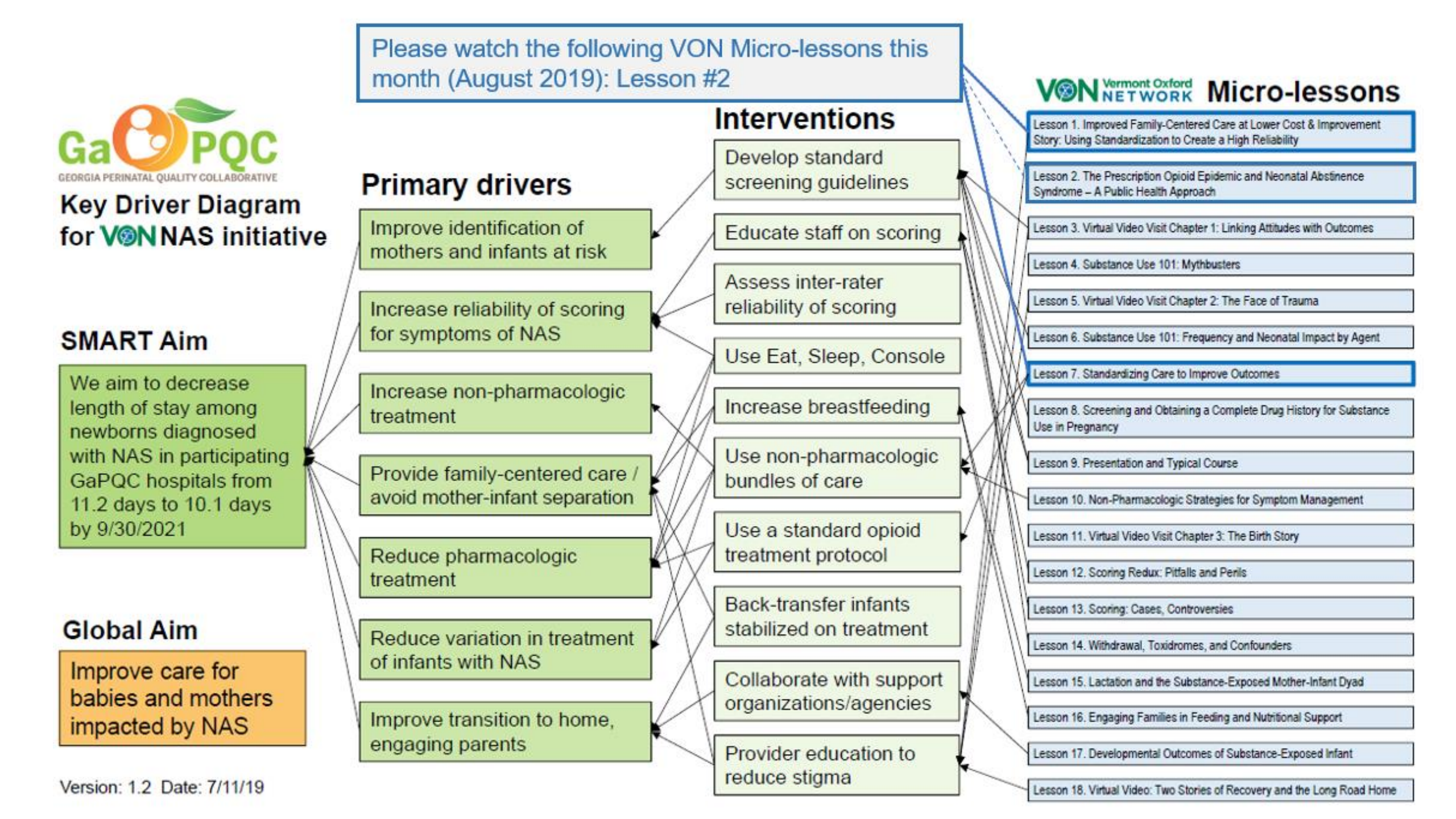
Examples of team SMART aims

- Ex 1: we aim to decrease the length of treatment time among infants diagnosed with NAS who are treated with pharmacotherapy from xxx to xx by April 2021
- *What type of measure is involved?*

- Ex 2: we will educate at least 85% of the staff taking care of newborns by having them complete the VON NAS Universal Training Program
- *What type of measure is involved?*

Housekeeping Items

- Watch VON Micro-Lesson #2 this month
- You will receive reports on your micro-lesson progress soon
- Thank you for sending in your SMART Aim!!


Please watch the following VON Micro-lessons this month (August 2019): Lesson #2
GaPQC
GEORGIA PERINATAL QUALITY COLLABORATIVE
Key Driver Diagram for VON NAS initiative
SMART Aim
We aim to decrease length of stay among newborns diagnosed with NAS in participating GaPQC hospitals from 11.2 days to 10.1 days by 9/30/2021
Global Aim
Improve care for babies and mothers impacted by NAS
Version: 1.2 Date: 7/11/19
Primary drivers
Improve identification of mothers and infants at risk
Increase reliability of scoring for symptoms of NAS
Increase non-pharmacologic treatment
Provide family-centered care / avoid mother-infant separation
Reduce pharmacologic treatment
Reduce variation in treatment of infants with NAS
Improve transition to home, engaging parents
Interventions
Develop standard screening guidelines
Educate staff on scoring
Assess inter-rater reliability of scoring
Use Eat, Sleep, Console
Increase breastfeeding
Use non-pharmacologic bundles of care
Use a standard opioid treatment protocol
Back-transfer infants stabilized on treatment
Collaborate with support organizations/agencies
Provider education to reduce stigma
VON Vermont Oxford NETWORK Micro-lessons
Lesson 1. Improved Family-Centered Care at Lower Cost & Improvement Story: Using Standardization to Create a High Reliability
Lesson 2. The Prescription Opioid Epidemic and Neonatal Abstinence Syndrome – A Public Health Approach
Lesson 3. Virtual Video Visit Chapter 1: Linking Attitudes with Outcomes
Lesson 4. Substance Use 101: Mythbusters
Lesson 5. Virtual Video Visit Chapter 2: The Face of Trauma
Lesson 6. Substance Use 101: Frequency and Neonatal Impact by Agent
Lesson 7. Standardizing Care to Improve Outcomes
Lesson 8. Screening and Obtaining a Complete Drug History for Substance Use in Pregnancy
Lesson 9. Presentation and Typical Course
Lesson 10. Non-Pharmacologic Strategies for Symptom Management
Lesson 11. Virtual Video Visit Chapter 3: The Birth Story
Lesson 12. Scoring Redux: Pitfalls and Perils
Lesson 13. Scoring: Cases, Controversies
Lesson 14. Withdrawal, Toxidromes, and Confounders
Lesson 15. Lactation and the Substance-Exposed Mother-Infant Dyad
Lesson 16. Engaging Families in Feeding and Nutritional Support
Lesson 17. Developmental Outcomes of Substance-Exposed Infant
Lesson 18. Virtual Video: Two Stories of Recovery and the Long Road Home