19-MCH-01

Committee: Maternal and Child Health

Title: Neonatal Abstinence Syndrome Standardized Case Definition

☐Check this box if this position statement is an update to an existing standardized surveillance case definition and include the most recent position statement number here: _____.

Synopsis: This position statement creates standardized case definitions for Neonatal Abstinence Syndrome (NAS) to be used when NAS is ascertained from 1) clinical records or 2) administrative data (e.g., hospital discharge, Medicaid, or all payer claims data).

I. Statement of the Problem

Neonatal abstinence syndrome (NAS) is a constellation of signs of withdrawal in newborns (neonates less than 28 days) following *in utero* exposure to medications or illicit drugs, most commonly opioids (including opioid agonists used for treatment of opioid use disorder), benzodiazepines, and barbiturates.(1) Other substances, such as alcohol, nicotine, medications and other drugs may influence the severity and timing of withdrawal.(1) Although other substances are potentially implicated in NAS, these would be included as suspect cases until further evidence arises.

Nationally, administrative data from 2014 showed NAS affected about 8/1,000 live births overall, and about 1.4% (14.4/1,000) of all births covered by Medicaid.(2) Current reporting indicates there is considerable variation in case definition. This variation limits the interpretation of the wide range of reported NAS incidence from 0.7 to 33.4 per 1,000 hospital births in 2013.(3) Some counties in the U.S. reported approximately 10% of all live births were newborns with NAS.(4)

Newborns diagnosed with NAS may experience longer hospital stays and have higher medical costs than infants without NAS. Infants diagnosed with NAS also may be more likely to meet eligibility for special education services compared to infants without NAS, although few studies have assessed long-term follow up of these infants.(5) Not all exposed infants experience NAS, and their risk for long-term health issues has not been studied.

This position statement advances a standardized case definition for NAS to be used in provider reporting with clinical record documentation, as well as administrative claims-based data. Currently, use and application of diagnostic criteria and diagnosis codes varies from state to state, hospital to hospital, and provider to provider. A standardized case definition needs to be established to better understand NAS incidence. In addition, a standardized case definition could contribute to a better understanding of polysubstance exposures, burden of disease, and health impact of *in utero* exposures, and would facilitate resource planning to support mothers and babies with optimal care.

II. Background and Justification

The current opioid crisis has led to substantial increases in overdose deaths, hospitalizations, and opioid use disorder among the U.S. population. Of particular concern is opioid use disorder among women of reproductive age, particularly during pregnancy.(6) Chronic opioid use during pregnancy, including medication-assisted therapy with opioid agonists, and the use of benzodiazepines and barbiturates can result in withdrawal signs in newborns, known as NAS. NAS involves a constellation of central and autonomic nervous system, respiratory, and gastrointestinal dysregulation signs in the newborn. These signs worsen as the newborn's body stores of the drug decrease. In contrast, newborns with toxic effects due to other drugs which do not produce withdrawal tend to improve as body stores of the drugs

decrease.(1) Not all substance exposed infants show signs of withdrawal. Furthermore, polysubstance exposures are common, and it is difficult to attribute withdrawal signs to specific exposures.

Identification, treatment, and prevention of NAS involves complex considerations for women, newborns, and families.(7) Emerging best practices suggest caring for women and their newborns together after delivery results in improved outcomes, and may reduce adverse societal impacts and generational trauma.(8-11) These efforts require valid and reliable measures of NAS. The NAS Definition Environmental Scan conducted by the CSTE NAS Workgroup revealed diagnosis and reporting variation across geographic areas, delivery facilities, and providers.(12) Standardized surveillance measures of NAS are needed to better understand incidence and burden of disease, to assess the impact of newborn treatments, and to monitor long term effects. NAS is one component in assessing the needs of the mother infant dyad.(11) Monitoring NAS should not detract from efforts to promote family health through the provision of care for women before, during and after pregnancy. This surveillance information should be used by public health for public health purposes.

This position statement describes two tiers for NAS surveillance: (1) real time case reporting based on public health legal authority, and (2) case reporting based on claims-based administrative data.

Tier 1 case reporting to public health legal authorities describes disease surveillance based on case identification using clinical records. Reporting is from providers (i.e., clinicians, healthcare settings) and laboratories.

Tier 2 case reporting based on administrative data (e.g., identified from Medicaid, all payer claims, hospital discharge) describes disease surveillance based on case identification using International Statistical Classification of Diseases 10th revision, Clinical Modification (ICD-10-CM) diagnosis codes.

Large variability in clinical practice, diagnosis, coding and billing in hospital-based systems reflect the lack of a standardized case definition, and contribute to the variability observed in administrative claims-based data. A tiered surveillance approach with standardized definitions will help improve clinical reporting, and, in turn, improve discharge-based data. The tiered approach allows states to report NAS based on their resources and needs. Some states have made NAS a reportable condition, and will use the Tier 1 definition. The majority of states have not made NAS reportable, but they have access to one or more sources of administrative data for reporting using the Tier 2 definition.

III. Statement of the desired action(s) to be taken

CSTE recommends the following actions:

1. Implement a standardized surveillance case definition for Neonatal Abstinence Syndrome
    A. Utilize standard sources (e.g., reporting*) for case ascertainment for Neonatal Abstinence Syndrome. Surveillance for Neonatal Abstinence Syndrome should use the recommended sources of data to the extent of coverage presented in Section V.

    B. Utilize standardized criteria for case ascertainment for Neonatal Abstinence Syndrome presented in Section VI and Table VI in Technical Supplement.

    C. Utilize standardized criteria for case classification for Neonatal Abstinence Syndrome presented in Sections VII and Table VII in Technical Supplement.

    Note: Adoption of a standardized surveillance case definition does NOT add Neonatal Abstinence Syndrome to the *Nationally Notifiable Condition List*. Jurisdictions (e.g., States and Territories) conducting surveillance according to these methods may voluntarily submit case information to CDC, if requested and in a mutually agreed upon format.

*Reporting: process of a healthcare provider or other entity submitting a report (case information) of a condition under public health surveillance TO local, state, or territorial public health. Note: notification is addressed in a Nationally Notifiable Conditions Recommendation Statement and is the process of a local, state, or territorial public health authority submitting a report (case information) of a condition on the *Nationally Notifiable Conditions List* TO CDC.

IV. Goals of Surveillance

Neonatal Abstinence Syndrome (NAS) surveillance goals include:

- Estimating the incidence of NAS using standard surveillance case definitions
- Tracking trends in NAS and making meaningful comparisons between geographic regions in order to plan prevention and treatment efforts for women and infants.
- Evaluating the effectiveness of treatment and intervention strategies
- Monitoring for long term health and developmental effects of *in utero* exposure to opioids
- Identifying women with chronic opioid use and linking them to treatment
- Allocating public health and clinical resources to provide services to affected families
- Connecting families with health and social services to promote optimal child development and family well-being

V. Methods for Surveillance: Surveillance for Neonatal Abstinence Syndrome (NAS) should use the recommended sources of data and the extent of coverage listed in Table V.

No single data source completely captures all neonatal abstinence syndrome (NAS) cases. Although the vast majority of NAS cases could be ascertained from hospital records, case classification should be performed using available data from multiple data sources and include deduplication and combining across data sources.

Data sources: (See Appendix 1 for more information)

- **Healthcare records (includes hospital emergency department, inpatient, outpatient, hospital discharge, and electronic medical records):** Includes multiple diagnosis codes (ICD-10-CM, chief complaint and physician or triage notes. Reporting mechanism may include administrative/discharge records, or case reports including electronic case reporting (eCR). A patient's emergency department discharge disposition may be useful to determine maternal and possibly newborn status.
- **Clinician reporting:** Case reporting including eCR
- **Laboratory reporting:** Includes maternal and neonate clinical specimen testing performed at hospitals, commercial, state and federal labs.
- **Pediatric Residential Recovery Centers:** Includes multiple diagnosis codes (ICD-10-CM), chief complaint and physician or triage notes for the neonate. May include administrative/discharge records.

Table V. Recommended sources of data and extent of coverage for ascertainment of cases of Neonatal Abstinence Syndrome (NAS).

Source of data for case ascertainment	Coverage	
	Population-wide	Sentinel sites
Clinician reporting	X	
Laboratory reporting	X	
Reporting by: Hospitals (emergency departments and inpatient)	X	
Death certificates		
Hospital discharge or outpatient records	X	

Data from electronic medical records	X	
Telephone survey		
School-based survey		
Other, specify: • Birth Defects Registries • Claims data (e.g., Medicaid, private insurers, All Payer Claims Database Reporting to support case ascertainment should be coordinated as time and effort allow as these data sources are important but likely to identify fewer *new*, previously unrecognized cases: • Residential Pediatric Recovery Centers	X	
		2019 Template

VI. Criteria for case ascertainment

A. Narrative: A description of suggested criteria for case ascertainment of a specific condition.

Report a newborn to public health authorities that meets the following criteria:

A1. Clinical Criteria for Reporting

- A hospitalized neonate (<28 days) with any clinical signs consistent with Neonatal Abstinence Syndrome/ NAS not explained by another etiology (e.g., sepsis, intracranial hemorrhage, hypocalcemia). Signs may include:
    - CNS hyperirritability (continuous, excessive, or high-pitched cry; hypertonia; exaggerated tremors; myoclonus; hyperactive Moro reflex; poor sleep; poor feeding; seizures)
    - Autonomic over-reactivity (sneezing; nasal congestion; frequent yawning; fever; cutaneous mottling)
    - Gastrointestinal hypermotility (excessive regurgitation and/or vomiting; loose or watery stools)
    - Respiratory (tachypnea; respiratory distress)
- A hospitalized neonate (<28 days) whose healthcare record contains information about suspected Neonatal Abstinence Syndrome/NAS not explained by another etiology.
    - Healthcare records including hospital emergency department, inpatient, hospital discharge and other claims-based datasets (See Appendix 4: Case Ascertainment of Neonatal Abstinence Syndrome (NAS) using ICD-10-CM Code List)
        - Report a neonate whose health care record includes mention of Neonatal Abstinence Syndrome/NAS either a diagnosis, chief complaint, or discharge code
- A neonate (<28 days) admitted to a residential pediatric recovery center whose healthcare record contains information about suspected Neonatal Abstinence Syndrome/NAS not explained by another etiology.
    - Healthcare records including inpatient records and discharge datasets (See Appendix 4: Case Ascertainment of Neonatal Abstinence Syndrome (NAS) using ICD-10-CM Code List)
        - Report a neonate whose health care record includes mention of Neonatal Abstinence Syndrome/NAS either a diagnosis, chief complaint, or discharge code
- A neonate (< 28 days) whose healthcare record contains information about *in utero* exposure to opioids, benzodiazepines or barbiturates.

- Healthcare records including hospital emergency department, inpatient, hospital discharge and claims-based datasets (See Appendix 4: Case Ascertainment of Neonatal Abstinence Syndrome using ICD-CM Code List)
  - Report a neonate whose healthcare record includes mention of *in utero* exposure to opioids, benzodiazepines, or barbiturates either a diagnosis, chief complaint, or discharge code

A2. Laboratory Criteria for Reporting

- Laboratories testing neonatal specimens collected in the emergency department, hospital, or residential pediatric recovery center during the neonatal period: Any detected or positive results for opioids, benzodiazepines, or barbiturates, or their metabolites in a clinical specimen by any laboratory test.
- Laboratories testing maternal specimens (as part of routine care) collected in the emergency department or hospital, or laboratory reports from prenatal clinic or Medication Assisted Therapy clinic included in the maternal delivery record up to 4 weeks prior to delivery: Any detected or positive results for opioids, benzodiazepines, or barbiturates, or their metabolites in blood or urine by any laboratory test.

A3. Epidemiologic Linkage Criteria for Reporting

There are no epidemiologic linkage criteria for reporting Neonatal Abstinence Syndrome (NAS).

B. Disease-specific data elements to be included in the initial report

Specific data elements to be included in the initial report:

Tier 1

- Birth mother name and date of birth
- Birth mother delivery facility and medical record number (if different facility from infant)
- History of maternal (birth mother) substance use
- History of maternal (birth mother) treatment for substance use disorder during the current pregnancy
- Type of suspected opioids, benzodiazepines or barbiturates involved and how this information was obtained (source of information and laboratory results if available)
- Other *in utero* substance exposure, if known, and laboratory results if available
- Type of neonate scoring tool used to assess signs of withdrawal, scores and specific symptoms
- Gestational age
- Length of stay
- Pharmacologic treatment of neonate

Tier 2

- Length of stay
- All infant diagnoses from healthcare databases
- Relevant pharmacy records for pharmacologic treatment of neonate

VII. Case Definition for Case Classification

A. Narrative: Description of criteria to determine how a case should be classified.

A1. Clinical Criteria

Clinical evidence in a neonate of less than 28 days of age

- A diagnosis of Neonatal Abstinence Syndrome/NAS, OR
- A chief complaint mentions Neonatal Abstinence Syndrome/NAS, OR
- A clinically compatible presentation:
  Clinical effects of neonatal withdrawal manifest as central nervous, autonomic, gastrointestinal and respiratory system disturbances in the neonate, including the following signs (for more information see Appendix 2):
  - CNS hyperirritability (continuous, excessive, or high-pitched cry; hypertonia; exaggerated tremors; myoclonus; hyperactive Moro reflex; poor sleep; poor feeding; seizures)
  - Autonomic over-reactivity (sneezing; nasal congestion; frequent yawning; fever; cutaneous mottling)
  - Gastrointestinal hypermotility (excessive regurgitation and/or vomiting; loose or watery stools)
  - Respiratory (tachypnea; respiratory distress)

AND

Clinical signs are not explained by another etiology (e.g., sepsis, intracranial hemorrhage, hypocalcemia)

Clinical evidence in the birth mother includes:

- Maternal history of chronic opioid use (including Medication Assisted Therapy, illicit use, or pain medication), benzodiazepine, or barbiturate use in the four weeks prior to delivery,

  OR

- Maternal history of chronic drug use in the four weeks prior to delivery of unknown drug type, OR of known non-opioid, non-benzodiazepine, non-barbiturate drug.

A2. Laboratory Criteria

Confirmatory laboratory evidence:

- **Neonate:**
  Detection of opioids (any level) including natural (e.g., morphine, codeine), semi-synthetic (e.g., heroin), and synthetic (e.g., fentanyl, or fentanyl analogs), or opioid metabolites (e.g., 6-monoacetylmorphine), benzodiazepines (e.g., diazepam, alprazolam), or barbiturates (e.g., phenobarbital) in any clinical specimen from a screening or other laboratory test (for supplemental information see Appendix 3 laboratory criteria). This would include positive immunoassay results as well as confirmatory testing based on liquid or gas chromatography-mass spectrometry.

Presumptive laboratory evidence:

- **Maternal:**
  Detection of opioids (any level) including natural (e.g., morphine, codeine), semi-synthetic (e.g., heroin), and synthetic (e.g., fentanyl, or fentanyl analogs), or opioid metabolites (e.g., 6-monoacetylmorphine), benzodiazepines (e.g., diazepam,

alprazolam), or barbiturates (e.g., phenobarbital) in blood or urine from a screening or other laboratory test in the four weeks prior to delivery (for supplemental information see Appendix 3 laboratory criteria). This would include positive immunoassay results as well as confirmatory testing based on liquid or gas chromatography- mass spectrometry.

Supportive laboratory evidence:

- **Maternal:**
  Detection of a non-opioid, non-benzodiazepine, or non-barbiturate drug of abuse, including cocaine, methamphetamine, amphetamine, or cannabinoid in blood or urine from a screening or other laboratory test in the four weeks prior to delivery (for supplemental information see Appendix 3 laboratory criteria). This would include positive immunoassay results as well as confirmatory testing based on liquid or gas chromatography- mass spectrometry.

A3. Epidemiologic Linkage

None

A4. Case Classifications

We report below on two Tiers for case classification of Neonatal Abstinence Syndrome to be used for surveillance. Tier 1 includes case reporting based on public health legal authorities and establishes criteria that reflect greater sensitivity and specificity in reporting, as well as more real time data than current administrative databases. Tier 2 includes case reporting based on administrative claims based data and reflects a broad spectrum of clinical and laboratory features due to the variability in diagnostic criteria and facility billing rules currently in place across the country. States will select to use Tier 1 or Tier 2 criteria for reporting depending on their needs and resources. This is critical as newborns could be categorized differently depending on the Tier used, due to the lack of specificity in ICD-10-CM codes. Any comparative analysis should be conducted within Tiers.

Tier 1:

For a hospitalized neonate (<28 days) OR a neonate (<28 days) admitted to a residential pediatric recovery center

Confirmed:

Report or identification *in the absence of* another known cause/diagnosis of:

- A diagnosis of Neonatal Abstinence Syndrome/NAS with confirmatory NEONATAL laboratory evidence, OR
- A chief complaint mentions Neonatal Abstinence Syndrome/NAS with confirmatory NEONATAL laboratory evidence, OR
- A clinically compatible presentation with THREE or more signs of NEONATAL withdrawal AND with confirmatory NEONATAL laboratory evidence

Probable:

We identify two types of probable cases.

Report or identification *in the absence of* another known cause/diagnosis of:

Type 1:

- A diagnosis of Neonatal Abstinence Syndrome/NAS with MATERNAL history of chronic opioid use (including Medication Assisted Therapy, illicit use, or pain medication), or benzodiazepine, or barbiturate use in the 4 weeks prior to delivery, OR
- A chief complaint mentions Neonatal Abstinence Syndrome/NAS with MATERNAL history of chronic opioid use (including Medication Assisted Therapy, illicit use, or pain medication), or benzodiazepine, or barbiturate use in the 4 weeks prior to delivery OR
- A clinically compatible presentation with THREE or more signs of NEONATAL withdrawal AND with MATERNAL history of chronic opioid use (including Medication Assisted Therapy, illicit use, or pain medication), or benzodiazepine, or barbiturate use in the 4 weeks prior to delivery

AND no or unknown laboratory evidence in the NEONATE

OR

Type 2:

- A diagnosis of Neonatal Abstinence Syndrome/NAS with confirmatory MATERNAL laboratory evidence in the 4 weeks prior to delivery, OR
- A chief complaint mentions Neonatal Abstinence Syndrome/NAS with confirmatory MATERNAL laboratory evidence in the 4 weeks prior to delivery, OR
- A clinically compatible presentation with THREE or more signs of NEONATAL withdrawal AND with confirmatory MATERNAL laboratory evidence in the 4 weeks prior to delivery

AND no or unknown laboratory results in the NEONATE.

Suspect:

We identify five types of suspect cases.

Report or identification *in the absence of* another known cause/diagnosis of:

Type 1

- A diagnosis of Neonatal Abstinence Syndrome/NAS with MATERNAL history of chronic drug use of a non-opioid, non-benzodiazepine, non-barbiturate drug in the 4 weeks prior to delivery, OR
- A chief complaint mentions Neonatal Abstinence Syndrome/NAS with MATERNAL history of chronic drug use of a non-opioid, non-benzodiazepine, non-barbiturate drug in the 4 weeks prior to delivery, OR
- A clinically compatible presentation with THREE or more signs of NEONATAL withdrawal AND with MATERNAL history of chronic drug use of a non-opioid, non-benzodiazepine, non-barbiturate drug in the 4 weeks prior to delivery

AND no or unknown laboratory results in the NEONATE
AND no or unknown MATERNAL laboratory results.

OR

Type 2

- A diagnosis of Neonatal Abstinence Syndrome/NAS with MATERNAL history of chronic drug use of unknown type in the 4 weeks prior to delivery, OR
- A chief complaint mentions Neonatal Abstinence Syndrome/NAS with MATERNAL history of chronic drug use of unknown type in the 4 weeks prior to delivery, OR
- A clinically compatible presentation with THREE or more signs of NEONATAL withdrawal AND with MATERNAL history of chronic drug use of unknown type in the 4 weeks prior to delivery

AND no or unknown laboratory results in the NEONATE
AND no or unknown MATERNAL laboratory results.

OR

Type 3

- A diagnosis of Neonatal Abstinence Syndrome/NAS with positive MATERNAL laboratory results of chronic drug use of a non-opioid, non-benzodiazepine, non-barbiturate drug of abuse in the 4 weeks prior to delivery OR
- A chief complaint mentions Neonatal Abstinence Syndrome/NAS with positive MATERNAL laboratory results of chronic drug use of a non-opioid, non-benzodiazepine, non-barbiturate drug of abuse in the 4 weeks prior to delivery OR
- A clinically compatible presentation with THREE or more signs of NEONATAL withdrawal AND with positive MATERNAL laboratory results of chronic drug use of a non-opioid, non-benzodiazepine, non-barbiturate drug of abuse in the 4 weeks prior to delivery

AND no or unknown laboratory results in the NEONATE

OR

Type 4

- A clinical presentation with ONE, or TWO signs of NEONATAL withdrawal AND with MATERNAL history of chronic opioid use (including Medication Assisted Therapy, illicit use, or pain medication), benzodiazepine, or barbiturate use in the 4 weeks prior to delivery

AND no or unknown laboratory results in the NEONATE
AND no or unknown MATERNAL laboratory results.

OR

Type 5

- A clinical presentation with ONE, or TWO signs of NEONATAL withdrawal AND with positive MATERNAL laboratory results of chronic opioid use (including Medication Assisted Therapy, illicit use, or pain medication), benzodiazepine, or barbiturate use in the 4 weeks prior to delivery.

AND no or unknown laboratory results in the NEONATE

Notes:
Positive maternal (birth mother) history is considered stronger evidence of chronic *in utero* substance exposure than laboratory findings due to variability in who is tested, when testing occurs with respect to delivery, and the sensitivity and specificity immunoassay screening tests. Immunoassay tests are commonly used in hospitals without confirmatory testing due to costs, and the length of time to receive confirmatory results.

Laboratory evidence is supportive.

It is not the intention of this case classification to include infants experiencing iatrogenic NAS due to withdrawal from opioids, benzodiazepines or barbiturates prescribed for a condition post-natally. Although other substances are potentially implicated in NAS, these would be included as suspect cases until further evidence arises.

These case classifications are for surveillance purposes and should not direct clinical care of the newborn.

Jurisdictions conducting surveillance may, through case finding, identify (1) newborns who have a clinical presentation of a well newborn with no (zero) signs of neonatal withdrawal and with maternal history of chronic opioid use (including Medication Assisted Therapy, illicit use, or pain medication), benzodiazepine, or barbiturate use in the 4 weeks prior to delivery and no or unknown laboratory results in the neonate and no or unknown maternal laboratory results; or (2) newborns who have a clinical presentation of a well newborn with no (zero) signs of neonatal withdrawal and with positive maternal laboratory results of chronic opioid use (including Medication Assisted Therapy, illicit use, or pain medication), benzodiazepine, or barbiturate use in the 4 weeks prior to delivery and no or unknown laboratory evidence in the neonate. While these newborns do not fit the criteria for NAS or withdrawal syndrome, they may be eligible for services now or in the future due to an *in utero* exposure to opioids, benzodiazepines, or barbiturates. These newborns may merit identification and placement in a separate surveillance group of substance-exposed newborns. See appendices 4 and 5 for further guidance.

Appendix 6 includes information helpful for interpretation of NAS rates.

Tier 2:

Case Classification using administrative data

Confirmed:

- A neonate whose healthcare record contains any diagnosis of neonatal drug withdrawal symptoms within the birth hospitalization or a hospitalization (or similar clinic admission See Appendix 1) before 28 days of age.

Suspect:

- A neonate whose healthcare record does not contain any diagnosis of neonatal drug withdrawal AND contains any diagnosis noting maternal use of opiates, sedative-hypnotics or anxiolytics within the birth hospitalization or a hospitalization (or similar clinic admission See Appendix 1) before 28 days of age.

Table VII.A. Recommended ICD-10-CM Code for Neonatal Abstinence Syndrome for Tier 2 Case Definition

Confirmed Case
P96.1 Neonatal withdrawal symptoms from maternal use of drugs of addiction
Suspect Case
P04.14 Newborn affected by maternal use of opiates
P04.17 Newborn affected by maternal use of sedative hypnotics
P04.1A Newborn affected by maternal use of anxiolytics

Notes
Current ICD-10-CM codes are not specific enough to capture withdrawal signs solely due to opioids, benzodiazepines, or barbiturates. For this reason, Type 1, Type 2 and Type 3 suspect cases identified under Tier 1, will be categorized as confirmed cases under Tier 2. Appendix 5 provides guidance on coding to promote consistency across clinical providers and settings. It also explains where additional codes would be helpful. Appendix 6 includes information that is helpful for interpretation of NAS rates.

B. Criteria to distinguish a new case of this disease or condition from reports or notifications which should not be enumerated as a new case for surveillance

Tier 1 cases should be reported within 14 days of diagnosis or discharge of a well newborn or as soon thereafter as possible. Neonates who initially develop signs of withdrawal after initial hospital discharge but before 28 days of age should be reported as a new case. Tier 2 cases should be de-duplicated, if possible, using names, dates of birth, facility, and residential address information to ensure that neonates are only counted once. Where identifying information is unavailable, cases should be limited to those ascertained from birth hospitalizations. This will exclude cases initially diagnosed on transfer, rehospitalization, or hospitalization following an out of hospital birth, and will underascertain total cases.

VIII. Period of Surveillance

Surveillance is expected to be on-going.

IX. Data sharing/release and print criteria

1. CSTE recommends the following case statuses* be included in the 'case' count released outside of the public health agency:
   - ☒Confirmed
   - ☒Probable
   - ☐Suspect
   - ☐Unknown

   * Which case statuses are included in the case counts constitute the "print criteria."

2. Jurisdictions (e.g., States and Territories) conducting surveillance under this case definition can voluntarily submit de-identified case information to CDC, if requested and in a mutually agreed upon format.

   Production of national data summaries and national data re-release for non-NNCs:
   - Prior to release of national data summaries CDC should follow the CDC/ATSDR Policy on Releasing & Sharing Data, issued on April 16, 2003 and referenced in 11-SI-01 and custodians of such data should consult the CDC-CSTE Intergovernmental Data Release Guidelines Working Group report

(http://www.cste2.org/webpdfs/drgwgreport.pdf) which contains data release guidelines and procedures for CDC programs re-releasing state, local, or territorial-provided data.

- CDC programs have a responsibility, in collaboration with states, localities, and territories, to ensure that CDC program-specific data re-release procedures meet the needs of those responsible for protecting data in the states and territories.

Cases will be counted by jurisdiction based on case's place of residence or 'usual residence', regardless of where exposure occurred as defined in PS 11-SI-04. The guidelines are modeled after provisions developed for the U.S. Census. Since case data are often combined with population data, case notification guidelines based on census residence rules will contribute toward greater consistency in the numerator and denominator data used in rates. The overarching aim is that all cases should be counted, but no case should be counted by multiple jurisdictions. It is important to note that following these guidelines may result in cases being counted by a jurisdiction other than where the exposure occurred.

X. Revision History

N/A. This is the initial definition for Neonatal Abstinence Syndrome (NAS).

XI. References

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Table VI. Table of criteria to determine whether a case should be reported to public health authorities.

Criterion	Neonatal Abstinence Syndrome Tier 1 Clinical Records	Neonatal Abstinence Syndrome Tier 2 Administrative Data
Clinical Criteria for Reporting		
A hospitalized neonate (<28 days) with clinical signs consistent with Neonatal Abstinence Syndrome/NAS (Appendix 2) not explained by another etiology	S	
A hospitalized neonate (<28 days) whose healthcare record contains information (diagnosis, chief complaint or discharge code) about suspected Neonatal Abstinence Syndrome/NAS not explained by another etiology	S	S
A neonate (<28 days) admitted to a residential pediatric recovery center whose healthcare record contains information (diagnosis, chief complaint or discharge code) about suspected Neonatal Abstinence Syndrome/NAS not explained by another etiology	S	S
A neonate (<28 days) whose healthcare record contains information about *in utero* exposure to opioids, benzodiazepines, or barbiturates (diagnosis, chief complaint or discharge code)	S	S
Laboratory Criteria for Reporting		
Any detected or positive NEONATAL laboratory results for opioids, benzodiazepines, or barbiturates, or their metabolites in any clinical specimen by any laboratory test.	S	
Any detected or positive MATERNAL laboratory results for opioids, benzodiazepines, or barbiturates, or their metabolites in blood or urine by any laboratory test collected up to 4 weeks prior to delivery.	S	

Notes:
S = This criterion alone is SUFFICIENT to report a case.

Table VII. Classification Table: Criteria for defining a case of Neonatal Abstinence Syndrome/NAS.

Criterion	Tier 1																				Tier 2			
	Suspect											Probable						Confirmed			Suspect			Confirmed
Clinical Evidence																								
Absence of another known cause or diagnosis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
NEONATE																								
Diagnosis of Neonatal Abstinence Syndrome/NAS	N			N			N					N			N			N						
Chief complaint of Neonatal Abstinence Syndrome/NAS		N			N			N					N			N			N					
Clinically compatible presentation of neonatal withdrawal with THREE or more of the following signs: - High pitched cry - Hypertonia - Tremors - Myoclonus - Hyperactive Moro reflex - Poor sleep - Poor feeding - Seizures - Yawning - Sneezing - Nasal congestion - Fever - Cutaneous mottling - Vomiting - Vomiting - Tachypnea - Respiratory distress			N			N			N					N			N			N					
Clinically compatible presentation of neonatal withdrawal with ONE or TWO of the following signs: - High pitched cry - Hypertonia - Tremors										N	N													

- Myoclonus - Hyperactive Moro reflex - Poor sleep - Poor feeding - Seizures - Yawning - Sneezing - Nasal congestion - Fever - Cutaneous mottling - Vomiting - Vomiting - Tachypnea - Respiratory distress																								
MATERNAL																								
Maternal history of chronic opioid, benzodiazepine or barbiturate use in 4 weeks prior to delivery.										N		N	N	N										
Maternal history of chronic use of a non-opioid, non-benzodiazepine and non-barbiturate drug in 4 weeks prior to delivery.	N	N	N																					
Maternal history of chronic drug use of unknown drug type in 4 weeks prior to delivery.				N	N	N																		
Laboratory Evidence																								
NEONATE																								
Detection of opioids (any level) including natural (e.g., morphine, codeine), semi-synthetic (e.g. heroin), and synthetic (e.g. fentanyl, or fentanyl analogs), or opioid metabolites (e.g., 6-monoacetylmorphine), benzodiazepines (e.g., diazepam, alprazolam) or barbiturates (e.g., phenobarbital) in any clinical specimen from a screening or laboratory test)																	N	N	N					
Absence of or unknown laboratory results in neonate	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N							
MATERNAL																								
Detection of opioids (any level) including natural (e.g., morphine, codeine), semi-synthetic (e.g. heroin), and synthetic (e.g. fentanyl, or fentanyl analogs), or opioid metabolites (e.g., 6-monoacetylmorphine),											N				N	N	N							

benzodiazepines (e.g., diazepam, alprazolam) or barbiturates (e.g., phenobarbital) in blood or urine from a screening or laboratory test in the four weeks prior to delivery.																								
Detection of non-opioid, non-benzodiazepine, non-barbiturate drugs of abuse (any level) in blood or urine in any clinical specimen from a screening or laboratory test in four weeks prior to delivery							N	N	N															
Absence of or unknown maternal laboratory results	N	N	N	N	N	N				N														
*Administrative Claims Based ICD-10-CM Coding of the **NEONATE***																								
Confirmatory diagnostic code																								
ICD-10-CM = P96.1 in any diagnosis code																								N
Suspect diagnostic code																								
ICD-10-CM = P04.14 in any diagnosis code																				N				
ICD-10-CM = P04.17 in any diagnosis code																					N			
ICD-10-CM = P04.1A in any diagnosis code																						N		

Notes:
N = All “N” criteria in the same column are NECESSARY to classify a case. A number following an “N” indicates that this criterion is only required for a specific disease/condition subtype (see below). If the absence of a criterion (i.e., criterion NOT present) is required for the case to meet the classification criteria, list the absence of criterion as a necessary component.

Appendix 1. Neonatal Abstinence Syndrome (NAS) Data Sources.

This appendix describes the core data sources available for use in the surveillance of neonatal abstinence syndrome (NAS). Data sources - as a tool for surveillance of opioid, benzodiazepine, and barbiturate exposures and NAS - come from a variety of sources. Each source provides specific data elements that, collectively, offer a multi-dimensional view of the burden of NAS, and can provide stakeholders with an ongoing understanding of the scope and burden of this condition. A summary of these sources is provided below with detailed information, including populations covered, data collected, and limitations.

Clinician Reporting	
Description	Clinician reporting directly to public health authorities would be used for Tier 1 case reports and would include reports outside of those made using hospitalization or emergency department data. Information from patient records would likely include chief complaint and physician or triage notes. Reporting of case reports could include electronic case reporting (eCR)). Patient records could include both maternal and newborn records and could be used for case ascertainment and case classification.
Strengths	Reporting from patient records has the most comprehensive information, including demographic information, clinical impression, physician or triage notes, laboratory test results, medical treatments and procedures, medical history, and comorbidity. Ideally, both maternal and newborn medical records would be used to gather information for case classification.
Limitations	Maternal and infant visit records may not be equally accessible, and identification of maternal/infant pairs may be difficult and could result in duplicate cases. Outpatient records will normally only be inclusive of maternal data.

Laboratory reporting systems	
Description	Laboratory data are useful for Tier 1 case classification as described in Appendix 3. Required clinical laboratory reporting is mandated by states for selected reportable conditions. Data elements include: laboratory test results (and the lab reference range), the patient contact information, and the health care provider who ordered the lab test. There is variability in reporting of personal identifiers. These reports are used to determine morbidity, exposure and take public health actions.
Strengths	Maternal and neonate clinical specimen testing performed at hospitals, commercial, state and federal labs. Provides valuable information on *in utero* exposures when sensitive and specific tests are conducted close to the time of delivery. Some information is provided to national databases through the Electronic Laboratory Reporting System (ELR).
Limitations	Laboratory testing of both pregnant women and neonates can be highly variable, especially when testing may result in punitive action. Patient identifiers are not standardized to the medical records. Diverse systems of data aggregation.

Hospital Inpatient Discharge data (state and national)	
Description	Most states have access to their hospitals' inpatient discharge data, which contain case-specific discharge data including utilization data, clinical data, and demographic data for patients admitted to acute care hospitals. Some states obtain patient identifiers and others do not. These databases also contain utilization, revenue, expense, and payer data. Hospital discharge data may be used for Tier 2 ascertainment and classification of cases.

Strengths	Hospitals provide their records to a data intermediary for processing. Formatting varies from state to state. Data elements include: dates of admission and discharge, nature of admission (e.g., emergency), residence, sex, age, race, date of birth, diagnosis and procedure codes (ICD-10-CM), expected principal source of payment (including workers compensation), and charges.
Limitations	State data sets are records of all hospitalizations and duplication may exist. Most states do not include federal and non-acute care facilities. There may be a lag in data availability.

Nationwide Emergency Department Data (state and national)	
Description	Approximately 36 states have emergency department data on all ED visits, including demographic, diagnosis and procedure information. Data elements can include: birth date, hospital and physician information, sex, race (includes Hispanic), type of visit, source of payment, diagnosis and procedure codes (ICD-10-CM), reason for visit, mode of transport, medical record number. Hospitals are required to report certain data for each outpatient ED visit, by law or regulation, in selected states. The purposes of the data are to accurately quantify and track the number and type of ED visits and to provide case-mix information to hospitals and communities. ED data may be used for ascertainment and classification of Tier 1 and/or Tier 2 cases.
Strengths	Important for estimating burden of conditions in the population that does not get hospitalized, and for more real-time reporting of conditions that result in hospitalization. A patient's emergency department discharge disposition may be useful to determine maternal and possibly newborn status.
Limitations	Each state has its own procedures. Data with identifiers are not available to all States. Care should be taken to ensure duplicate records do not occur. Not available in all states, but complete visit counts in those states that have mandatory systems, and can be used for patient follow-back when patient identifiers are included.

Birth Defects Registries	
Description	Birth defects registries aligned with the National Birth Defects Prevention Network (NBDPN) are statewide, population-based surveillance systems that have identified birth defects in children born in each state. Birth defects registries may be used for ascertainment and classification of Tier 1 cases.
Strengths	May include the counts, incidence and prevalence of infants diagnosed with Neonatal Abstinence Syndrome (NAS) as well as comorbidities.
Limitations	Case definitions vary and include ascertainment throughout the first year of life with an inherent data availability delay.

Publicly Funded Health Care: Medicaid Claims Data	
Description	Medicaid is one of several publicly funded healthcare organizations serving state citizens. Medicaid is the state and federal partnership that provides health coverage for selected populations of low income and/or medical need. Medicaid claims data may be used for ascertainment and classification of Tier 2 cases.
Strengths	Includes demographic characteristics, diagnosis and procedure codes (ICD-10-CM, CPT, HCPCS), therapies, all covered services, prescriptions, costs, multiple sources of payment. Healthcare claims data, including pharmacy data can provide crucial information relating to medications, prescribed treatments, charges, and physician visits not available from other sources.
Limitations	Program coverage and funding of programs vary state by state. There may be a lag in data availability.

All Payer Claims Data	
Description	All Payer Claims Data (APCD) is available in several states and includes both publicly and privately funded healthcare information on medically-related claims from emergency department and in-patient, out-patient and skilled nursing facilities. All Payer Claims Data could be used for Tier 2 ascertainment and classification.
Strengths	Includes demographic characteristics, diagnosis and procedure codes (ICD-10-CM, CPT, HCPCS), therapies, all covered services, prescriptions, costs, sources of payment.
Limitations	Covered populations may vary by state depending on participation by federal and self-funded health care plans. There may be a lag in data availability.

Private Insurers: Health Management Plan Data	
Description	Private insurers / managed care plans keep records of all of the claims they process. Data sharing agreements can potentially be established with these entities to gather specific information on treatment, medication, etc. Private insurer data could be used for Tier 2 ascertainment and classification.
Strengths	Medical record level data with more specific information on treatment, medication, and follow-up.
Limitations	Difficult / time consuming to obtain agreements with data owners. Population varies depending on the size of the population served by each care organization. Some insurers may redact records containing information on substance use disorders. There may be a lag in data availability.

Electronic Medical Records	
Description	Electronic medical records (EMRs) are digital versions of the paper charts in clinician offices, clinics, and hospitals. EMRs contain notes and information collected by and for the clinicians in that office, clinic, or hospital and are mostly used by providers for diagnosis and treatment. Data may include diagnoses, medications, immunizations, family medical histories, and diagnostic screening results. EMRs could be used for ascertainment and classification of Tier 1 cases.
Strengths	Records are inclusive of a broader view of a patient's care including specialists and laboratory specimens. Visits from providers over time may be included including preventive treatments and tests, screenings, patient monitoring and other data not normally collected in administrative datasets.
Limitations	Database structure is based on visits and duplication may exist. Differentiating implicated drugs can be difficult using these data.

Residential Pediatric Recovery Centers	
Description	Health care services provided to infants in residential pediatric recovery centers. Includes multiple diagnosis codes (ICD-10-CM), chief complaint and physician or triage notes for the neonate. May include administrative/discharge records. Residential pediatric recovery center data could be used to ascertain and classify Tier 1 cases.
Strengths	Residential treatment centers treat multiple conditions from drug and alcohol addictions and in some states can provide concurrent maternal care.
Limitations	Program coverage, data acquisition and funding of programs vary state by state.

Appendix 2. Clinical Signs of Opioid, Benzodiazepine or Barbiturate Withdrawal in the Neonate

Signs of opioid, benzodiazepine or barbiturate withdrawal in the neonate include central nervous system, autonomic nervous system, gastrointestinal and respiratory dysregulation. These signs include**:**

- High pitched cry
- Hypertonia
- Tremors
- Myoclonus
- Hyperactive Moro reflex
- Poor sleep
- Poor feeding
- Seizures
- Yawning
- Nasal congestion
- Sneezing
- Fever
- Cutaneous mottling
- Vomiting
- Loose stools
- Tachypnea
- Respiratory distress

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Appendix 3. Considerations for Laboratory Testing in the diagnosis of Neonatal Abstinence Syndrome/NAS

Laboratory testing of maternal or infant samples can provide important supportive information when combined with clinical signs and symptoms consistent with a diagnosis of neonatal abstinence syndrome (NAS

Interpretation of positive results for drug testing should involve an in depth understanding of what testing is being done as this varies widely between institutions. Alternate explanations for positive results should be considered. A detailed record of what medications are administered during pregnancy, labor and delivery, and the timing of administration of those medications with respect to testing should be reviewed in conjunction with clinical signs and symptoms. Tests with low specificity should be considered presumptive positive (indicative) with confirmation further analysis (definitive).

PART 1

Laboratory Testing Sources, Advantages and Limitations

Different specimen types may provide insight into drug use at varying times in pregnancy. Urine and blood are the most common specimen types tested due to ease of collection and availability of validated test systems. Newborn blood spots may be an alternate non-invasive source of information assuming appropriate consent and method validation. While analysis of hair, meconium, cord blood and placenta are potentially viable specimen types, there are many challenges associated with collection and sampling that may make their use impractical. Additionally, analysis of these specimens is highly specialized and not widely available.

Drug screens are typically conducted by immunoassay due to the widespread availability, ease of performance and the relatively low cost. The specificity and sensitivity of these assays varies considerably by kit manufacturer and drug antigen cross-reactivity. Depending on the test system, there may be significant false positive test results requiring structural confirmation by mass spectrometry. The cross-reactivity of the novel synthetic opioids with commercially available immunoassays is not well understood but would likely result in false negative test results. A positive immunoassay result should be considered indicative of drug use requiring a mass spectral confirmation.

Mass spectrometry when preceded by liquid chromatography (LC-MS) or gas spectrometry (GC-MS) is a confirmatory technique, as it provides structural identification. The sensitivity and specificity of these tests is dependent upon specimen processing, instrument parameters and instrument make and model. This testing is more time consuming, requires greater expertise and is costly.

Table 1. Assay characteristics and limitations by source and matrix

Source	Assay type	Matrices	Comments	Limitations
Maternal American Society of Addiction Medicine, 2017; Musshoff et al. 2012.	Immunoassays[1] for initial screening (follow with confirmatory testing) Gas or liquid chromatography-mass spectrometry techniques (LC-MS, GC-MS)[2] for confirmatory testing.	Urine	Can detect longer range of exposure than blood.	Easy to tamper with
		Blood		Shortest window of detection Availability of testing varies by hospital. If not available on site, cost and time to get results may be increased.
		Hair	Hair grows at 1.25 cm/month. Hair closest to scalp is needed for most recent exposure—window of detection is 3 months. May be the most sensitive specimen to detect use over a longer time period during pregnancy	Can't be used to detect very recent exposure, determining timing of past exposure is inexact. Environmental contamination can cause false positives. Hair type can affect results—drug compounds are incorporated into thick or dark hair at greater concentrations. Hair treatments (dyeing, bleaching, perming, straightening) can degrade drug compounds present in the hair. results Hair is not useful for detecting marijuana/THC compared with other matrices. Limited guidance on sampling and analysis techniques.
Infant Gray and Huestis, 2007; Gray et al. 2010; Boy et al. 2008.	Immunoassays[1] for initial screening (follow with confirmatory testing). LC-MS, GC-MS for confirmatory testing.	Urine		Collection can be difficult
		Blood		Invasive (venous blood collection), collection is difficult in newborns
		Meconium	Can detect a long range of exposure; meconium starts to form early in the second trimester.	Not widely used; often can't do testing on site, results may be delayed up to 1 week. Does not detect first trimester exposure, cannot be used to determine if exposure was recent.

Source	Assay type	Matrices	Comments	Limitations
				Can be challenging to collect specimens as the timing of meconium varies (could take days to be passed), less useful if meconium passed in utero. Requires special handling and storage. Limited guidance on sampling and analysis techniques.
		Hair	Hair begins to appear on the scalp early in the third trimester.	Availability of specimen may be limited as some neonates do not have hair. Environmental contamination can cause false positives. Hair type can affect results. May not be acceptable to families. Limited guidance on sampling and analysis techniques.
		Blood spot	Already routinely collected for other purposes.	Limited data available comparing these samples to other matrices. Limited guidance on sampling and analysis techniques.
Maternal/fetal Castro et al. 2011a; Gray and Huestis, 2007.	Immunoassays[1] for initial screening (follow with confirmatory testing). LC-MS, GC-MS[2] for confirmatory testing.	Umbilical cord blood or tissue	Collected immediately after birth. Collection is non-invasive.	Limited data available comparing these samples to other matrices. Limited guidance on sampling and analysis techniques.
		Placenta	Tissue available at the time of birth in sufficient amounts.	Limited data available comparing these samples to other matrices. Limited data on drug and metabolite concentrations and window of detection. Window of detection may be similar to that of blood, although some drugs are thought to accumulate in the placenta. Limited guidance on sampling and analysis techniques.

[1]**Immunoassays** have varying sensitivity (depending on the drug), but can have high false positives. Therefore, positive results should be followed with confirmatory testing (LC-MS or GC-MS). Immunoassays are generally inexpensive and have a rapid turnaround for results. Tests are often available in hospitals and clinics.
False positives are due to cross reactivity with other medications. For example, for opioid assays, cross reactivity can occur with quinolone antibiotics, rifampin, verapamil, diphenhydramine, or doxylamine, or poppy seeds. Lactate dehydrogenase and lactate (resulting from diabetes, liver disease, toxin ingestion) can also cause false positives.
[2]**LC-MS, GC-MS** have very high sensitivity and specificity and are considered the gold standard. Used to confirm positive screens. Time consuming and less readily available than immunoassays. **Both types of tests** can produce false negatives due to abstinence before testing (see windows of detection in Table 2), use of a high cut-point (immunoassays), masking agents, dilution with water or using a detoxification kit. Urine is easiest to tamper with.

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PART 2

Laboratory Testing: Drug-Specific

The basic drugs of abuse (DOA) screen used consistently across the United States tests for five drugs or drug classes (Hoffman, Traub & Grayzel, 2019):

- Amphetamine
- Cocaine
- Marijuana (THC)
- Opioids (heroin, morphine, codeine)
- Phencyclidine (PCP)

Other drug testing available (Hoffman, Traub & Grayzel, 2019)
Additional drugs may be detected depending on what a given facility's clinical laboratory chooses to include in a DOA test panel.
There is no uniformity as to what is included in extended DOA assays, or what the cutoff values for detection should be for drugs not covered by workplace testing laws. In order to know what is detected on a particular assay, it is necessary to consult the manufacturer's literature for a given assay. In the United States, only amphetamine, cocaine, marijuana, opioids, and PCP should be expected on a DOA test, unless otherwise noted by the clinical laboratory performing the test or by the manufacturer. Examples of other drug tests that can be ordered in addition to the basic DOA screen include the following:

- All over-the-counter and prescription amphetamine derivatives and analogues, including cathinones, phenylethylamines, and piperazines
- All benzodiazepines and benzodiazepine-like drugs, including gamma hydroxybutyrate (GHB) and "z" drugs (eg, zolpidem, zopiclone)
- All barbiturates and similar sedative hypnotic drugs, such as methaqualone
- All over-the-counter and prescription opioids, as well as the natural analogue kratom
- Various hallucinogens, including dextromethorphan, DMT and other tryptamines, ketamine, LSD, mescaline, psilocybin, and others.

Interpreting results (Hoffman, Traub & Grayzel, 2019)

- Immunoassays in particular can yield false-positive results if specific cross-reacting medications or drugs are present in the sample (see table 2).
- False-negative results for DOA testing can occur for many reasons:
    - Improper specimen collection, transport, or testing procedures
    - Dilution of urine (e.g., from IV fluids).
    - Patients may use a variety of methods to subvert DOA testing of urine.

- Failure to detect a drug in the given class whose chemical structure renders it unreactive with the assay, such as synthetic opioids.
    - Example: most opioid screening tests fail to detect variations of fentanyl. Instead, a specific test to detect fentanyl or its metabolites would be needed for detection.

Rapid drug screening tools can be associated with a high frequency of false-positives and false-negatives (George & Braithwaite, 1995).
Based on a diagnostic study, five rapid detection kits were evaluated for their ability to detect drugs of abuse in clinic setting:

- System 1 - latex agglutination inhibition reaction
- System 2 - affinity displacement competitive immunoassay
- System 3 - competitive enzyme immunoassay
- System 4 - immunochromatographic assay based on antigen/antibody competition
- System 5 - updated version of system 4

Reference standards included the following:

- Capillary gas chromatography for amphetamines
- Syva ETS analyser and EMIT DAU reagents confirmed by thin layer chromatography for barbiturates and opiates
- Syva ETS analyser and EMIT DAU reagents for cannabinoid and cocaine metabolites

Table 2. Frequency of False Negatives and False Positives by Drug Type and Rapid Detection Kit (George & Braithwaite, 1995).

Frequency of False Negatives					
	System 1	System 2	System 3	System 4	System 5
Amphetamine/methamphetamine	0%	N/A	N/A	0%	0%
Barbiturates	3%	N/A	N/A	N/A	0%
Cannabinoids/THC	20%	N/A	N/A	43%	3%-26%
Cocaine	0%	N/A	N/A	N/A	0%
Morphine/opiates	N/A	33%	28%	N/A	0%
Frequency of False Positives					
	System 1	System 2	System 3	System 4	System 5
Amphetamine/methamphetamine	0%	N/A	N/A	43%	0%-33%
Barbiturates	0%	N/A	N/A	N/A	3%-6%
Cannabinoids/THC	0%	N/A	N/A	0%	3%-10%
Cocaine	0%	N/A	N/A	0%	0%-6%
Morphine/opiates	3%	0%	0%	14%	0%-9%

Abbreviations: N/A, not available; THC, tetrahydrocannabinol

Window of detection depends on the following: (SAMHSA, 2012)

- Chemical properties of the substances for which the test is being performed;
- Individual metabolism rates and excretion routes;
- Route of administration, frequency of use, and amount of the substance ingested;
- Sensitivity and specificity of the test;
- Selected cutoff concentration;
- The individual's health, diet, weight, gender, fluid intake, and pharmacogenomic profile; and
- The biological specimen tested.

Table 3. Characteristics of drug testing by matrix (American Society of Addiction Medicine, 2017).

	Matrix					
	Blood	Breath	Saliva	Urine	Hair	Meconium
Detection period	1-48 hours	~ 1 hour/drink	1-48 hours	1-4 days	7-90 days	Months

POCT/onsite immunoassays available?	Yes	For alcohol	Yes	Yes	No	No
Detects	Parent drug compound	Parent drug compound, blood alcohol concentration	Parent drug compound	Drug metabolite	Parent drug compound	?
Ease of collection	Requires phlebotomist	Easily collected	Easily collected	Easily collected	Easily collected	Requires access to first meconium, special processing

	Matrix					
	Blood	Breath	Saliva	Urine	Hair	Meconium
Detection period	1-48 hours	~ 1 hour/drink	1-48 hours	1-4 days	7-90 days	Months
POCT/onsite immunoassays available?	Yes	For alcohol	Yes	Yes	No	No
Detects	Parent drug compound	Parent drug compound, blood alcohol concentration	Parent drug compound	Drug metabolite	Parent drug compound	?
Ease of collection	Requires phlebotomist	Easily collected	Easily collected	Easily collected	Easily collected	Requires access to first meconium, special processing

Table 4. Drug-specific information when testing for opioids, benzodiazepines, and barbiturates. (The length of detection of drugs of abuse in urine varies widely depending on the individual's metabolism, physical condition, fluid intake, and frequency/quantity of ingestion, as well as the method of detection used. The following periods of detection should only be considered rough estimates.)

Drug	Half-life in Adults (general information based on no renal or hepatic impairment) (Lexi-Drugs, 2019)	Window of Detection (time after last dose)			Examples of cross-reacting substances that may cause false-positive results	Notes
		Urine	Hair	Saliva		
Opioids (this row applies to all opioids)					Poppy seed ingestion (Hoffman, Traub & Grayzel, 2019) (DynaMed Plus, 2018) Fluoroquinolones (e.g., ciprofloxacin, levofloxacin, norfloxacin) (Lexi-Drugs, 2019) Dextromethorphan (DynaMed Plus, 2018)	Standard screening assays are designed to detect morphine, a major metabolite of non-synthetic opioids (Hoffman, Traub & Grayzel, 2019)

Drug	Half-life in Adults (general information based on no renal or hepatic impairment) (Lexi-Drugs, 2019)	Window of Detection (time after last dose)			Examples of cross-reacting substances that may cause false-positive results	Notes
		Urine	Hair	Saliva		
					Doxylamine Enoxacin Quinine Ranitidine Rifampin, Rifampicin Tolmetin (IBM Micromedex, 2017)	
Morphine	2-4 hours	1-5 days (Hadland & Levy, 2016) (DynaMed Plus, 2018) 2-14 days (IBM Micromedex, 2010)	90 days (Hadland & Levy, 2016)	1-36 hours (Hadland & Levy, 2016)	Codeine (major metabolite includes morphine) (IBM Micromedex, 2017)	
Codeine AND major metabolites	~3 hours	1-4 days (Hadland & Levy, 2016) (DynaMed Plus, 2018) 2-6 days[9]	90 days (Hadland & Levy, 2016)	1-36 hours (Hadland & Levy, 2016)		Major metabolites include morphine, which may cause false positive for use of morphine
Semisynthetic opioids (e.g., oxycodone, hydrocodone, hydromorphone, oxymorphone)	Hydrocodone and oxycodoone IR: ~4 hours Oxymorphone: 7-10 hours Hydrocodone ER: 8-12 hours (depending on the brand) Oxycodone ER: ~4-6 hours	3 days (American Addiction Centers, 2017)	*	*		Requires specific screening assays (Hoffman, Traub & Grayzel, 2019)

Drug	Half-life in Adults (general information based on no renal or hepatic impairment) (Lexi-Drugs, 2019)	Window of Detection (time after last dose)			Examples of cross-reacting substances that may cause false-positive results	Notes
		Urine	Hair	Saliva		
Buprenorphine	IV: 2.2-3 hours Buccal film: 27.6 -/+ 11.2 hours SL tab: ~37 hours Patch: ~26 hours	3-4 days (IBM Micromedex, 2010)	*	*	Amisulpiride Codeine Dihydrocodeine Methadone Morphine Sulpiride Tramadol (IBM Micromedex, 2017)	Requires specific screening assays (Hoffman, Traub & Grayzel, 2019)
Synthetic opioids (e.g., fentanyl, meperidine, pentazocine, propoxyphene, tramadol)	<u>Fentanyl</u> **IV**: 2-4 hours **Patch**: 20-27 hours **Transmucosal**: 3-14 hours (dose dependent) **Intranasal**: 15-25 hours **Buccal film**: ~14 hours **Buccal tablet**: 100-200 mcg: 3-4 hours; 400-800 mcg: 11-12 hours Meperidine: 2.5-4 hours Normeperidine (metabolite): 8-16 hours Tramadol IR: 5-8 hours Tramadol ER: 8-11 hours Pentazocine: 2-5 hours	3 days (American Addiction Centers, 2017)	*	*		Requires specific screening assays (Hoffman, Traub & Grayzel, 2019)

Drug	Half-life in Adults (general information based on no renal or hepatic impairment) (Lexi-Drugs, 2019)	Window of Detection (time after last dose)			Examples of cross-reacting substances that may cause false-positive results	Notes
		Urine	Hair	Saliva		
Methadone	8-59 hours (may be prolonged with alkaline pH)	3 days (American Addiction Centers, 2017; (IBM Micromedex, 2010) 1-7 days (DynaMed Plus, 2018)	*	*	Chlorpromazine Clomipramine Creatinine Diphenhydramine Doxylamine Quetiapine Tapentadol Thioridazine Verapamil (IBM Micromedex, 2017)	Requires specific screening assays (Hoffman, Traub & Grayzel, 2019) Half-life is dose dependent (Lexi-Drugs, 2019)
Heroin (metabolite: 6-monoacetylemorphine (6MAM))	15-30 minutes (Habal & Taylor, 2018)	1-3 days (Hadland & Levy, 2019) (DynaMed Plus, 2018) 2-4 days (IBM Micromedex, 2010)	90 days (Hadland & Levy, 2016)	1-36 hours (Hadland & Levy, 2016)		Only heroin is metabolized to 6-MAM – can test for this metabolite to confirm definite heroin use (Habal & Taylor, 2018)
Benzodiazepines (this row applies to all benzodiazepines)		1-6 weeks (Hadland & Levy, 2016) (DynaMed Plus, 2018) Short term use: 3 days Extended use (>1 year): 4-6 weeks (IBM Micromedex, 2010)	90 days (Hadland & Levy, 2016)	N/A (Hadland & Levy, 2016)	Efavirenz NSAIDs Oxaprozin Sertraline Tolmetin (IBM Micromedex, 2017)	Generally good specificity but variable sensitivity for particular benzos; the National Academy of Clinical Biochemists in the U.S. does not recommend screening in ED due to low sensitivity Standard screening assays are designed to detect oxazepam, a major metabolite of most benzodiazepines Chronic abuse of benzodiazepines may result

Drug	Half-life in Adults (general information based on no renal or hepatic impairment) (Lexi-Drugs, 2019)	Window of Detection (time after last dose)			Examples of cross-reacting substances that may cause false-positive results	Notes
		Urine	Hair	Saliva		
						in up to 30 days of detection after last dose (SAMHSA, 2012)
Alprazolam	IR: 6.3-26.9 hours ER: 10.7-15.8 hours ODT: 7.9-19.2 hours	7 days (American Addiction Centers, 2017)	*	*		Requires specific screening assays (Hoffman, Traub & Grayzel, 2019)
Clonazepam	17-60 hours	7 days (American Addiction Centers, 2017)	*	*		Requires specific screening assays (Hoffman, Traub & Grayzel, 2019)
Lorazepam	~12-18 hours (depending on route of administration)	7 days (American Addiction Centers, 2017)	*	*		Requires specific screening assays (Hoffman, Traub & Grayzel, 2019)
Flurazepam (major metabolite: N-desalkylflurazepam)	2.3 hours N-desalkylflurazepam (metabolite): 74-90 hours; multiple doses: 111-113 hours	*	*	*		Requires specific screening assays (Hoffman, Traub & Grayzel, 2019)
Midazolam	1.8-6.8 hours	*	*	*		Requires specific screening assays (Hoffman, Traub & Grayzel, 2019)
Triazolam, estazolam, alorazepam	1.5-5.5 hours	*	*	*		Requires specific screening assays (Hoffman, Traub & Grayzel, 2019)
Temazepam	3.5-18.4 hours	7 days (American Addiction Centers, 2017)	*	*		
Chlordiazepoxide (major metabolite: demoxepam)	24-48 hours Demoxepam: 14-95 hours	30 days (IBM Micromedex, 2010)	*	*		
Diazepam (major metabolite: desmethyldiazepam)	IM: ~60-72 hours Desmethyldiazepam: ~152-174 hours	14 days (American Addiction Centers, 2017)	*	*		Half-life is dose dependent

Drug	Half-life in Adults (general information based on no renal or hepatic impairment) (Lexi-Drugs, 2019)	Window of Detection (time after last dose)			Examples of cross-reacting substances that may cause false-positive results	Notes
		Urine	Hair	Saliva		
	IV: 33-45 hours Desmethyldiazepam: 87 hours Oral: 44-48 hours Desmethyldiazepam: 100 hours Rectal: 45-46 hours Desmethyldiazepam: 71-99 hours					
Barbiturates (this row applies to all barbiturates)		7 days (Hadland & Levy, 2019) 2-10 days (DynaMed Plus, 2018) Short acting (e.g., secobarbital): 24 hours Long acting (e.g., phenobarbital): 2-4 weeks (IBM Micromedex, 2010)	90 days (Hadland & Levy, 2016)	N/A	Ibuprofen Naproxen Phenytoin Tolmetin (IBM Micromedex, 2017)	Half-life is dose dependent
Phenobarbital	53-118 hours	14 days (American Addiction Centers, 2017)	*	*		Requires specific screening assays (Hoffman, Traub & Grayzel, 2019)
Pentobarbital	15-50 hours	*	*	*		Requires specific screening assays (Hoffman, Traub & Grayzel, 2019)
Secobarbital	15-40 hours	3 days (American Addiction Centers, 2017)	*	*		Requires specific screening assays (Hoffman, Traub & Grayzel, 2019)

Drug	Half-life in Adults (general information based on no renal or hepatic impairment) (Lexi-Drugs, 2019)	Window of Detection (time after last dose)			Examples of cross-reacting substances that may cause false-positive results	Notes
		Urine	Hair	Saliva		
Amobarbital	16-40 hours	2-4 days (IBM Micromedex, 2010)	*	*		Requires specific screening assays (Hoffman, Traub & Grayzel, 2019)
Butalbital	~100 hours	7 days (American Addiction Centers, 2017)	*	*		Requires specific screening assays (Hoffman, Traub & Grayzel, 2019)

**Data not available for this specific drug*

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Appendix 4. ICD-10-CM Code List – Neonatal Abstinence Syndrome for Tier 2 Case Definition

Confirmed Case
P96.1 Neonatal withdrawal symptoms from maternal use of drugs of addiction
Suspect Case
P04.14 Newborn affected by maternal use of opiates
P04.17 Newborn affected by maternal use of sedative hypnotics
P04.1A Newborn affected by maternal use of anxiolytics

Appendix 5. Recommendations for use of ICD-10-CM codes to promote consistency relevant to Neonatal Abstinence Syndrome/NAS

In a hospital setting, the healthcare provider will state clinical signs and findings based on their expertise. Neonatal laboratory results, maternal laboratory results and maternal history will be used to inform clinical decision-making. In classifying cases of NAS using ICD-10-CM codes, we recommend the following guidelines to promote consistency in reporting for coding infants with neonatal abstinence syndrome and/or *in utero* exposure to opioids, benzodiazepines, or barbiturates.

Confirmed and Probable NAS:
For neonates with clinical signs of withdrawal and confirmed neonatal or maternal laboratory results or maternal history, the following ICD-10-CM hospital discharge code should be reported:

P96.1	Neonatal abstinence syndrome

At the time of this position statement, there is only one code for neonatal abstinence syndrome (P96.1), which does not allow specification of the main substance of exposure. A code specifically for neonatal opioid withdrawal syndrome and one for primarily polysubstance exposure would be useful.

Suspect NAS:
Presence of the clinical signs compatible with NAS without a history for or laboratory confirmation of maternal opioid use. For these infants, there are no ICD-10-CM codes available.

Exposed but no clinical signs of withdrawal:
When an infant has been exposed prenatally to drugs/substances that can cause withdrawal signs (known via maternal history/laboratory testing or neonatal laboratory testing), but does not show signs of withdrawal, they may be eligible for services now or in the future due to an *in utero* exposure. These newborns may merit identification and placement in a separate surveillance group of substance-exposed newborns. One or more of the following ICD-10-CM discharge codes may be reported. These ICD-10-CM codes were new in October 2018 (FFY 2019) to designate *in utero* exposure:

P04.14	Newborn affected by maternal use of opiates
P04.17	Newborn affected by maternal use of sedative-hypnotics
P04.1A	Newborn affected by maternal use of anxiolytics

Note: The category P04 is used for instances when the newborn is affected by noxious substances transmitted via the placenta or breast milk. Other specific exposure codes which may be of interest are coded as follows:

P04.0	Newborn affected by maternal anesthesia and analgesia in pregnancy, labor, and delivery
P04.1	Newborn affected by other maternal medication
P04.11	Newborn affected by maternal antineoplastic chemotherapy (new in FFY 2019)
P04.12	Newborn affected by maternal cytotoxic drugs (new in FFY 2019)
P04.13	Newborn affected by maternal use of anticonvulsants (new in FFY 2019)
P04.15	Newborn affected by maternal use of antidepressants (new in FFY 2019)
P04.16	Newborn affected by maternal use of amphetamines (new in FFY 2019)
P04.18	Newborn affected by other maternal medication (new in FFY 2019)
P04.19	Newborn affected by maternal use of unspecified medication (new in FFY 2019)
P04.2	Newborn affected by maternal use of tobacco
P04.3	Newborn affected by maternal use of alcohol
P04.40	Newborn affected by maternal use of unspecified drugs of addiction (new in FFY 2019)
P04.41	Newborn affected by maternal use of cocaine
P04.42	Newborn affected by maternal use of hallucinogens (new in 2019)
P04.49	Newborn affected by maternal use of other drugs of addiction
P04.5	Newborn affected by maternal use of nutritional chemical substances
P04.6	Newborn affected by maternal exposure to environmental chemical substances
P04.81	Newborn affected by maternal use of cannabis
P04.89	Newborn affected by other maternal noxious substances
P04.9	Newborn affected by maternal noxious substance, unspecified

Infants with any of these diagnoses who do not have a diagnosis listed in Table VII.A (and in Appendix 4 as of July 31, 2019) are not considered to experience Neonatal Abstinence Syndrome/NAS according to the case definition of the position statement 19-MCH-01.

Iatrogenic NAS:
For neonates who require opioids to prevent or to treat signs of withdrawal following prolonged use of opioids due to post-natal exposure (i.e., for neonatal medical conditions such as extracorporeal life support, treatment of pain after major surgical procedures), the following ICD-10 hospital discharge code should be reported:

P96.2	Withdrawal after therapeutic use of drugs

Infants with this diagnosis who do not have a diagnosis listed in Table VII.A (and in Appendix 4 as of July 31, 2019) are not considered to experience Neonatal Abstinence Syndrome/NAS according to the case definition of the position statement 19-MCH-01 as the case definition only includes *in utero* exposures.

Appendix 6. Information for Interpretation.

Substance use during pregnancy impacts a pregnant woman, her fetus/newborn, and her family, and neonatal abstinence syndrome/NAS is only one outcome of interest related to substance use exposures. For this reason, it is important to place NAS into this broader context, to both facilitate interpretation of data and inform decisions related to implementation of this case definition. A CSTE policy brief is being developed on the Considerations for State and Jurisdictional Analysis of Data on Neonatal Abstinence Syndrome and Opioid- and Other Substance-Exposed Newborns. Recommendations in the policy brief will be made on some of the areas of concern/challenge. This Appendix serves to identify some of these concerns for states to consider while the policy brief is under development.

Pregnant Women with Infants diagnosed with NAS

Infants diagnosed with neonatal abstinence syndrome are born to three distinct groups of women:

- women who are on long-term opioid, benzodiazepine or barbiturate therapy for a chronic disease or condition (e.g., chronic pain, anxiety disorders),
- women with opioid use disorder who are on medication assisted therapy including methadone or buprenorphine, and
- women with untreated opioid use or other substance use disorder.

Current surveillance practices do not allow us to distinguish these three groups of women who have very different treatment needs. For example, we cannot tell the extent to which recent increases in NAS are due to more women with opioid or substance use disorder in need of treatment, improvements in connecting women with opioid use disorder in pregnancy to treatment, and/or increases in women with chronic opioid, benzodiazepine, or barbiturate therapy for a disease. Such information is critical to evaluation efforts. Implementing surveillance practices that promote this distinction is a goal of this position statement, as it would enable us to better characterize disease trends, and the need for different interventions. States that are able to distinguish these three groups should report stratified data. Those not able to distinguish NAS among these three groups of women should clearly call out this inability as a surveillance limitation on all reports so it is clear to data users. Furthermore, states should recognize that it is not a goal of NAS surveillance to reduce the number of cases to zero. Indeed, an increase in NAS may result from improvements in addressing the opioid crisis if states are able to connect more pregnant women with opioid use disorder with treatment and support. We are also likely to see changes in the incidence of NAS as states start reporting using the new standardized surveillance case definition.

NAS and Substance Use in Pregnancy

Identification, treatment, and prevention of substance use in pregnancy and related outcomes, including NAS, involves complex considerations for women, newborns, and families. The professional associations for obstetricians and gynecologists, maternal-fetal medicine specialists, pediatricians, and addiction medicine specialists have all recognized this complexity and called for a public health response to substance use in pregnancy.(1-3) Such a response focuses on an ethical approach, promoting practices that benefit infant and maternal health, and considering mothers together with their infants as a dyad in providing preventive, treatment and recovery care.

The life course health development framework posits health outcomes as a consequence of biologic, social, genetic and behavioral contexts that influence health and are compounded across a lifespan or even across generations.(4) Viewing substance use in pregnancy within this framework suggests that treatment and supports provided to women with opioid and substance use disorder prior to pregnancy, prenatally, during labor and delivery, immediately postpartum, and long-term will impact a woman's, her infant's and her family's long-term health and well-being. Emerging best practices suggest caring for women and their newborns together after delivery results in improved outcomes, and may reduce adverse societal impacts and generational trauma.(5-8)

Opioid- and substance use disorders are chronic health conditions. "Like other chronic diseases, addiction [substance use disorder] often involves cycles of relapse and remission."(9) Furthermore, substance use disorders are associated with behavioral co-morbidities, which may be more likely among pregnant and postpartum women.(3) Ethical practice includes screening all pregnant women for substance use as early in pregnancy as possible with appropriate drug testing after informed consent by women who screen positive. While drug testing can be an important tool for healthcare practitioners to inform treatment decisions, it is important to acknowledge that testing and diagnosis can have unanticipated health consequences in settings

where policies require their use for punitive social and legal practices. Women may be hesitant to access services, and providers may be hesitant to recommend testing, potentially delaying needed care. Such practices may also impact NAS surveillance if screening and or testing of pregnant women or newborns is biased and not conducted universally.

To the extent possible, states should consider conducting and disseminating information on NAS and substance use during pregnancy that provides a better understanding of the woman's and infant's social and behavioral context, health conditions and co-morbidities, treatment (pharmacologic and non-pharmacologic), as well as access to care prior to pregnancy, prenatally, during labor and delivery, and postpartum.

CAPTA and CARA

The Child Abuse Prevention and Treatment Act (CAPTA) was originally enacted in 1974 and is the key source of federal funding and guidance to states in support of prevention, assessment, investigation, prosecution, and treatment activities relating to child abuse and neglect. One of the most recent amendments to CAPTA was the **Comprehensive Addiction and Recovery Act (CARA). CARA was the first major federal addiction legislation in 40 years and the most comprehensive effort undertaken to address the opioid epidemic in a coordinated response—prevention, treatment, recovery, law enforcement, criminal justice reform, and overdose reversal.** These recent amendments are intended to promote better health practices for women with opioid and substance use disorders and their children, including, timely access and engagement in treatment, prenatal care, consistent and non-biased drug screening, and supportive plans of safe care (are housing and supports available, medication assisted therapy, adequate pain medication, etc.) for mothers and newborns.(10)

Epidemiologists should be aware of their state regulations stemming from the **CARA amendments to** CAPTA) that set forth the state procedures for early identification, screening, engagement and treatment of women and plans of safe care for newborns / infants with *in utero* substance exposure.(10, 11) Epidemiologists also should be aware that definitions of substance use may differ from the standardized surveillance definitions in this Position Statement and ICD-10-CM diagnosis codes and could result in conflicting reports of NAS incidence.

Substance Use Treatment during Pregnancy

Research in addiction medicine has demonstrated the benefits of treatment during pregnancy. Treatment with methadone or buprenorphine improves newborn outcomes by (2):

- stabilizing fetal levels of opioids, reducing repeated prenatal withdrawal (12);
- linking mothers to treatment for infectious diseases (e.g., HIV, HBV, HCV), reducing likelihood of transmittal to the fetus (3, 13);
- providing opportunity for better prenatal care; and
- improving long-term health outcomes for the mother and her newborn(14, 15).

Compared to untreated pregnant women with opioid use disorders, women treated with methadone or buprenorphine had newborns with:

- lower risk of NAS;
- less severe NAS;
- shorter neonate treatment time.(16)

Every effort should be made to engage women in treatment as early as possible. Pregnant women are identified as a priority population in regulations (42 CFR Part 8.12(e)(3), (f)(3), and (j)). Federal block grant programs, which provide for substance use treatment, may use these funds to assure timely, effective treatment. Although substance dependence is a chronic disease, stigma and bias among healthcare providers can result in both under-reporting of drug use and insufficient medication dosing, which often leads to delayed or ineffective treatment. In addition, at least 18 states classify maternal drug use as child abuse, and 3 other states consider it as reason for involuntary hospitalization, disincentivizing women from seeking treatment.(17-19) Women who are allowed to stay with their children during treatment are more likely to start treatment and maintain abstinence.(17)

The SAMHSA report "*Advancing the Care of Pregnant and Parenting Women with Opioid Use Disorder and Their Infants: A Foundation for Clinical Guidance*" (https://www.regulations.gov/document?D=SAMHSA-2016-0002-0001) summarizes the evidence review and rating process, and resultant clinical recommendations to optimize the outcomes for both pregnant women and their infants. SAMHSA recognizes, however, that if

programs and providers are not available in a community, being a priority population is of limited benefit.(14) Efforts to expand access to medication for opioid use disorder are underway but access may still be limited. Limiting factors include the perceived regulatory burden and the persistent lack of acceptance of substance use disorder as a chronic brain disease leading to resistance to using medication. Rejection of the evidence base supporting the use of medication may result in the exclusion of persons receiving medication from social and behavioral services available to others.

Recovery and Long-Term Support

SAMHSA also suggests that providers of medication for opioid use disorder have a special role in implementing the guidance for care of pregnant and parenting women.(14) For example, providers can provide ready access to effective substance use disorder treatment, including tobacco cessation counseling/treatment, prior to conception and during pregnancy, and to family-friendly substance use disorder treatment for parents. Providers also can support the continuation of treatment for substance use disorder from preconception through pregnancy and minimally one year postpartum and tailor medication according to parental need. To the extent possible, providers should assure that their relapse prevention and recovery support for pregnant and parenting individuals are family-friendly. Lastly, treatment providers should promote breastfeeding for women who receive opioids for pain or the treatment of opioid use disorder when not otherwise contraindicated and consistent with appropriate guidelines. Women with opioid / substance use disorders often have complex needs. Providers of medication for treatment can be critical partners in initiation, engagement, and maintenance of treatment in the continuum of care through the first year postpartum and may require innovative solutions to meet the needs of the woman and her family. The need for comprehensive strategies for assuring long-term treatment and recovery of women with substance use disorder and safe residential recovery settings is addressed in a recent National Academy for State Health Policy (NASHP) brief.(15) Residential recovery settings where women can receive treatment and keep children with them during treatment and recovery are few in number and vary in design.

Reimbursement of Costs Associated with NAS

The majority of costs associated with NAS and treatment for substance use disorders are shouldered by Medicaid and the majority of care for newborns with NAS occurs within a hospital setting.(20) Coverage for newborns and Medicaid-eligible mothers of newborns with NAS is described in the CMCS Informational Bulletin: *Neonatal Abstinence Syndrome: A Critical Role for Medicaid in the Care of Infants*.(21) Some women and newborns may have private insurance coverage that covers all of their care and others may be underinsured and have the benefit of dual coverage. In the event the mother of a newborn with NAS is not Medicaid-eligible, the newborn and, in some cases, the mother of the newborn, may be eligible for certain services under the Early Periodic Screening, Diagnostic, and Treatment (EPSDT) benefit.

NAS and Polysubstance Use

Polysubstance use is common among pregnant substance users.(22) Identification of the substances contributing to NAS is needed to better understand the impact of distinct substances, as well as to plan for appropriate treatment resources and prevention approaches. Current ICD-10-CM codes do not allow for identification of distinct drugs or drug classes associated with withdrawal. Development of specific ICD-10-CM codes that identify:

- withdrawal due to opioid use only
- withdrawal due to anxiolytic use only
- withdrawal due to sedative hypnotic use only
- withdrawal due to use of multiple controlled substances

would be helpful to states. Moreover, identifying whether the substance was prescribed—and in the case of opioids, prescribed to treat opioid use disorder—would be helpful. It would also be quite useful to provide clarification of the language used with the P04 codes to explain the intent of the phrase “newborn affected by” to indicate whether this encompasses exposure or measurable impacts.

Potential Biases

Bias may impact rates of NAS in several ways and should be considered when reporting rates. The case definition in this position statement includes neonatal testing as well as maternal history and testing as part of the case definition. Frequently, symptomatic neonates are not tested for substances, if the test results will not inform their treatment. This may be the case when the mother is in treatment and exposure is already known. Pregnant women may not be screened universally and/or tested due to provider biases, Furthermore, staff may not have access to maternal and infant records equally. Missing maternal records may limit the ability to identify a case if *in utero* exposures are not noted in the neonatal record and neonatal testing is not performed.

Benefit of Maternal/Infant Record Linkage

An approach that would facilitate improved understanding of short- and long-term impacts of substance use in pregnancy is through longitudinal linkage of mother-infant records. Linkage would allow the investigation of prenatal exposures, including treatment approaches and supports. Outcomes of interest could include maternal treatment retention, pregnancy-related comorbidity, labor and delivery characteristics, as well as neonatal outcomes, including NAS, and subsequent infant morbidity and development. Access to a broad range of longitudinal health and social service data would provide more context and potentially allow the exploration of factors associated with substance use disorder, such as history of trauma, homelessness, and/or food insecurity.

Conclusion

As this Appendix indicates, the issue of NAS cannot be considered in isolation from the complex nature of substance use in pregnancy. Differentiating the source of exposure for infants experiencing NAS is critical for evaluating prevention efforts and ensuring that pregnant and parenting women and their families have the care and support they need to thrive. Potential biases in screening and testing women for substance use disorders need to be considered, as does polysubstance use, and the availability of treatment and support for pregnant women and their families in order to better grasp the context in which NAS occurs. Such understanding will improve our interpretation and communication of NAS rates and trends.

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