Consensus Guidelines for Management of Neonatal Opioid Withdrawal Syndrome (NOWS) & Drug-Exposed Infants:

UCSF Northern California Neonatal Consortium

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UCSF Benioff Children's Hospitals

Consensus Clinical Guidelines for Management of Neonatal Opioid Withdrawal Syndrome (NOWS) & Drug-Exposed Infants:

UCSF Northern California Neonatal Consortium (NCNC)

Disclaimer

These clinical practice guidelines are based upon the latest evidence and expert consensus opinions of consortium members affiliated with UCSF Benioff Children's Hospitals. They are intended to guide pediatric/neonatal providers, but do not substitute for individual clinical judgment. Evaluation and treatment of specific patients should be adapted based upon the unique conditions of each patient, family and clinical environment.

CONSENSUS CLINICAL GUIDELINES

This guideline has a focus on best practices for identification and treatment of newborns at risk for withdrawal due to opioids, i.e., Neonatal Opioid Withdrawal Syndrome (NOWS). It will also provide some basic recommendations on management of other common prenatal drug exposures.

Inclusion criteria: Infants ≥34 weeks gestational age who have or are suspected to have Neonatal Opioid Withdrawal Syndrome.

Exclusion criteria: < 34 weeks gestational age - consult your institution's guideline for lower gestational ages (i.e., Finnegan scoring)

Definitions

Child and Family Services (CFS) - Name of child abuse reporting agency in certain counties

Child Protective Services (CPS) - Name of child abuse reporting agency in certain counties

Neonatal Abstinence Syndrome (NAS) - a group of conditions that can occur when newborns withdraw from certain substances (including opioids) that they were exposed to before birth. General term for neonatal withdrawal that may include nonopioid exposures (e.g., benzodiazepines).

Neonatal Opioid Withdrawal Syndrome (NOWS) - neonatal withdrawal syndrome specific to opioid use in pregnancy. Previously incorporated in the definition of Neonatal Abstinence Syndrome; many groups are now using the more specific term of Neonatal Opioid Withdrawal Syndrome to refer to newborns withdrawing specifically from opioids.

Social Services – in-hospital social work and hospital support services

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Background

Newborns exposed prenatally to certain birth parent medications and illicit drugs including opioids have a high risk of developing withdrawal symptoms referred to as Neonatal Abstinence Syndrome. Newer terminology focuses on withdrawal specifically from opioids and uses the term NOWS (Neonatal Opioid Withdrawal Syndrome). As the opioid crisis in the US continues, there has been an increase in Opioid Use Disorder (OUD) in pregnancy and subsequently an increase in Neonatal Abstinence Syndrome (NAS)/Neonatal Opioid Withdrawal Syndrome (NOWS). Per the National Institute of Drug Abuse there has been a 5-fold increase in the number of infants experiencing NOWS from 2004 to 2014 with an estimated 32,000 infants born with NAS/NOWS in 2014. More recent data shows a nationwide increase of NAS from 4.0 cases per 1000 birth hospitalizations to 7.3 cases between 2010-2017.

This guideline will use the term NOWS and focus on the management of opioid withdrawal in the neonate. The onset of withdrawal from opioids is dependent on many factors including the last dose of opioid taken by the birthing parent and the gestational age of the newborn. Symptoms usually occur within the first 72 hours after birth but may be later in some infants. Treatment of NOWS in infants is intended to prevent adverse consequences related to the effect on the central nervous system (high pitch crying, decreased sleep, tremors, increased muscle tone, hyperactive Moro, seizures) the gastrointestinal system (feeding difficulties, vomiting, loose or watery stools), and the autonomic system (sweating, fever, frequent yawn/sneezing, increased respiratory rate, nasal stuffiness and flaring). Generalized seizures, weight loss, and dehydration can occur if withdrawal is not adequately treated.

The Finnegan Neonatal Abstinence Scoring System (FNASS) has historically been the most common way opioid exposure infants were evaluated for signs of withdrawal. Management is dictated by the Finnegan scores with pharmacotherapy recommended at certain scores. Recently, several studies have shown that using FNASS may lead to unnecessary initiation of pharmacotherapy to treat withdrawal symptoms resulting in longer length of hospital stays. New research and studies have shown a functional scoring system, like the Eat-Sleep-Console Approach, that looks at the ability for a newborn to eat, sleep and console, is effective in managing withdrawal symptoms and can lead to decreased length of hospital stay and decreased use of medications (such as opiates) for treatment of withdrawal.

SECTION 1: COLLABORATIVE PRACTICE WITH OBSTETRICIANS

- **Birth Parent Screening**
    - Universal birth parent screening for drug use prenatally at time of entry to prenatal care with a validated verbal tool (e.g., NIDA, 4Ps) is the gold standard, though implementation is variable and site specific.
    - Using a tool can identify women who may need more resources. A positive screen should trigger a further needs assessment.
        - Example of screening tools:
            - The 4 Ps:
                - Have you ever used drugs or alcohol during this Pregnancy?
                - Have you had a problem with drugs or alcohol in the Past?
                - Does your Partner have a problem with drugs or alcohol?
                - Do you consider one of your Parents to be an addict or alcoholic?

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        - More detailed list of available screening tools is available
            - in the Mother & Baby Substance Exposure Toolkit (MBSE Toolkit) found here: https://nastoolkit.org/
            - at the National Institute on Drug Abuse (NIDA) Screening Tools and Prevention website found here: https://nida.nih.gov/nidamed-medical-health-professionals/screening-tools-resources/chart-screening-tools
    - If there is a positive birth parent screen, request documentation re: specifics of birth parent substance use in birth parent's chart (e.g., drug, dose, duration of use, prescribing MD, drug treatment program, etc.)
    - Develop a communication workflow with OB colleagues to understand their screening workflows and know where this information is being documented in the birthing parent 's chart.
        - Example of areas where information could be documented:
            - Birth parent's l problem list, HPI, Social History Sections, etc.
        - Be aware of the CURES rule of the 21 Century Cures Act that went into effect April 2021. This requires patients be provided electronic access to health information in their electronic medical records (including progress notes). By proxy this allows both parents electronic access to health information in their child's electronic medical records including progress notes. Consider where you put sensitive birth parent history and information in a newborn's chart to avoid unintentional sharing of sensitive birth parent information with the other parent of a child.
            - Learn more here: https://www.healthit.gov/curesrule/overview/about-oncs-cures-act-final-rule

- **Known opioid using birth parents**
    - Prenatally, Obstetrics (OB) team should review goals of management of neonates exposed to opioids in-utero including recommendation and encouragement of parental participation in nonpharmacologic management of NOWS and potential need for pharmacologic treatment of withdrawal symptoms.
        - **Consider pediatrician/neonatologist consult to review expectation of newborn needs with parents**

- **Identification of high-risk birth parents during labor**:
    - Factors
        - Recent history of substance use disorder (SUD) or use during pregnancy
        - No/limited prenatal care
            - Be aware of biases. There are many factors besides substance use that affect the ability of women to access prenatal care; all of these factors affect low-income women and women of color more frequently. Other factors that limit health care access include - lack of insurance, inability to take time off work and lack of access to culturally competent care.
        - Birth parent characteristics associated with substance abuse
            - Acute mental status changes, changed level of consciousness not otherwise explained

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- Unexplained disorientation, psychosis, manic symptoms, ataxia, hallucinations, internal preoccupation, severe psychomotor agitation, confusion, and or somnolence where toxicology test would dictate medical management

- When a high-risk birth parent is identified there should be discussion and education with parents by OB providers (MD, NP, Midwife), Medical Social Worker (MSW), and neonatologist/pediatric providers regarding what to expect for neonate after birth.
  - Consider involvement of psychiatry in select cases
  - Information should be shared at multidisciplinary huddles.

SECTION 2: IDENTIFICATION OF INFANTS AT HIGH RISK OF NOWS

- **Birth Parent Screening**
  - See Section 1 above
- **Birth Parent Testing (i.e., urine toxicology)**
  - not automatically indicated if a positive verbal screen
    i. OB should obtain thorough documentation of birth parent substance use via patient centered discussion with birth parent and assessment of overall risk factors
  - consider if birth parent has characteristics associated with substance use or acute intoxication
    i. Acute mental status changes or changed level of consciousness not otherwise explained
    ii. Unexplained disorientation, psychosis, manic symptoms, ataxia, hallucinations, internal preoccupation, severe psychomotor agitation, confusion, and or somnolence where toxicology test would dictate medical management
  - consider if a newborn exhibits symptoms consistent with intoxication (irritability, somnolence, depressed respiratory and/or cardiovascular status) or withdrawal (inconsolability, poor sleeping, and/or poor feeding) that are otherwise unexplained.
- **Neonatal Toxicology Testing Considerations**
  - Obtaining toxicology on a newborn is controversial. There should be thoughtful consideration of what indications are present and toxicology should only be obtained if it will affect the medical management of the infant.
    i. **See Appendix 2: Overview of Management**
  - Universal standing orders for urine toxicology should be avoided
  - If indicated, ideal would be to obtain urine toxicology on birth parent if possible
  - If obtaining a urine toxicology on the infant, consider also obtaining a comprehensive toxicology test to best interpret what substances the infant has been exposed to
    i. Pros- Can help distinguish drugs given during labor
    ii. Cons- results can take longer and test can cost more
    iii. Consider in select cases
  - Parental consent is not necessary when obtaining a toxicology test on an infant, but best practice is to inform parents and review why a toxicology test is being obtained.
  - Newborn testing criteria:
    i. If newborn exhibits symptoms consistent with intoxication (irritability, somnolence, depressed respiratory and/or cardiovascular status) or withdrawal (inconsolability, poor sleeping, and/or poor feeding) that are otherwise unexplained and birth parent declines to provide urine toxicology

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- The newborn should be evaluated for hypoglycemia, electrolyte abnormalities, sepsis and/or any underlying neurologic issues
- Birth parent medication history including SSRIs, antipsychotics, therapeutic benzodiazepines/anxiolytics, and smoking should be reviewed with the birthing parent and their primary providers
- If other medical causes have been excluded, obtain a urine toxicology test on the newborn. The symptoms prompting a request for urine toxicology test should be discussed by a multidisciplinary team of providers (bedside nurse, physicians)
- Obtain infant toxicology screening as soon as possible by available method because sensitivity of urine toxicology decreases with time

ii. If urine toxicology on birth parent is indicated (see ***Birth Parent Testing*** above) but birth parent declines, consider toxicology on newborn

- Other considerations
  i. A urine toxicology is more sensitive and specific the closer to delivery that it is obtained
  ii. A negative toxicology test on an infant does not rule out prior in-utero exposure to a substance, the infant could still be at risk of withdrawal
  iii. An unexpected positive result should have confirmatory testing
    - There are many birth parent medications that can cause a false positive result on toxicology testing
  iv. Toxicology does not quantify exposure

- **Infant Toxicology Methods:**
  - Testing method should be based on availability and timeliness of results to impact care. Availability of different methods may differ between institutions. Be familiar with your site's testing abilities and testing characteristics.
    i. Urine Tox screen (most commonly used – mother & infant):
    (-) Need to wait for first infant void
    (-) Poor sensitivity
    (-) difficult to collect (bag specimen)
    (-) Opioid confirmatory testing may be a send out, long turnaround time
    - Meconium screening:
      (-) Long length of time to collect, long turn-around time
    - Umbilical cord screening (may have limited availability at some centers):
      (-) long turn-around time
      (+) Easy to collect,
      (+) Confirmatory opioid testing not needed

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SECTION 3: MANAGEMENT OF NEONATAL OPIOID WITHDRAWAL SYNDROME

- **Overview**
    - Minimum neonatal observation: 3-5 days without symptoms / scores suggesting potential need for pharmacologic treatment depending on substance half life
        - Rooming-in is strongly encouraged in order to maximize non-pharmacologic interventions and encourage informed parental participation in scoring – this may be accomplished differently at different institutions
        - Once pharmacotherapy is initiated, infant should have cardiorespiratory and pulse oximetry monitoring
            - If needed, transfer to unit where monitoring is possible- nursery, ICN/NICU or other unit depending on institution

- **Scoring / Evaluation Tools**
    - New studies have shown assessment of function vs symptoms can help decrease the need for pharmacotherapy and shorten length of hospital stay. We recommend the use of a functional scoring system like Eat-Sleep-Console.
    - Scoring tool: Eat-Sleep-Console Scoring
        - Standard scoring tool: Eat-Sleep-Console Metric
            - If infant is able to eat well, sleep >1 hour, and console within 10 minutes, the infant is considered "well-managed"
                - Eating well refers to a baby's ability to breastfeed with sustained latch >10min or eats age-appropriate* volume per feed:
                    - 0-24 hours = 2-10ml
                    - 24-48 hours = 5-15ml
                    - 48-72 hours = 15-30ml
                    - 72-96 hours = 30-60ml
                - * age-appropriate ability to "eat" should be correlated with gestational age and hour of life -may include gavage feeding or other methods of feeding
        - Suggestions:
            - Maintain consistency of care providers (RN, MD, NP, parents, etc.) when possible, to maximize reliability / consistency of assessment. Ideally, parents are the primary scorer if available
    - Scoring frequency:
        - Infant should be evaluated continuously for E-S-C symptoms
        - Score is documented Q3-4 hrs
        - Continue scoring x 48hrs after pharmacologic treatment discontinued (extend to 72hr of observation after 5d of methadone)
    - Thresholds for pharmacologic treatment:
        - Inability to eat, sleep, console and unresponsive to non-pharmacologic interventions
            - See **Table 1**: Signs and Symptoms of withdrawal and appropriate non-pharmacologic intervention
            - Ensure nonpharmacologic supports are maximized and those providing supports are optimized (is parent available, have another nurse try)

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        - Team huddle to determine if pharmacotherapy should be started – team consists of bedside nurse, MD, and infant's primary caregiver
            - See ***Pharmacologic Treatment*** section below.

- **Non-Pharmacologic Therapies - the mainstay of initial NOWS treatment**
    - See **Table 1**: Signs and Symptoms of withdrawal and appropriate non-pharmacologic intervention
        - Decrease environmental stimuli when possible
    - Staff (RN, MD, NP, etc.) **and PARENTS** require training in supportive care
    - Educate families re: NOWS symptoms and strategies to help care for infant
        - Observe birth parent's interaction with infant for risks due to birth parent somnolence or altered behaviors
    - Continuous parental presence is optimal
        - If parent not available other options including cuddler/volunteer or family member if available
            - can consider adjusting nursing ratio to allow nursing to provide supportive care if no other options available
    - Maintain consistency of care providers with infant as much as possible
        - This facilitates reliability/consistency of assessment
    - Rooming in:
        - Strongly encouraged in order to maximize non-pharmacologic interventions and encourage informed parental participation in scoring
        - *Rooming in is ideal for E-S-C*; exceptions to this are based on unit policy and within parameters established by MSW, CPS/CFS, and medical team (case-by-case basis)
        - Criteria for rooming- in:
            - Medically stable infant not on standing medications
    - **Table 1: Signs and Symptoms of withdrawal and appropriate non-pharmacologic intervention** = Suggested non-pharmacologic interventions for symptoms (collected from current institutional protocols):

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Table 1: Signs and Symptoms of withdrawal and appropriate non-pharmacologic intervention

Signs and Symptoms	Intervention
Excessive or high-pitched crying	Decrease environmental stimuli (dim lights, reduce noise levels). Partially cover bassinet or incubator. Swaddle and hold infant firmly and close to body. Gentle rocking, talking, singing, humming.
Sleeplessness	Decrease environmental stimuli (dim lights, reduce noise levels). Swaddle infant. Minimize handling. Encourage skin-to-skin contact with parent. May use rocker bed or swing if available.
Myoclonic jerks, tremors, jitteriness, irritability	Prepare everything for infant care prior to disturbing infant to minimize handling. Cluster care. Decrease environmental stimuli (dim lights, reduce noise levels). Soft music, relaxing baths.
Excoriation (chin, knees, elbow, toes, nose)	Apply barrier creams to affected areas. Apply duoderm or mepilex to knees to protect skin if needed.
Sweating	Clean skin regularly. Ensure dry, clean clothing and bedding.
Hyperthermia – temperature > 37.5ºC	Ensure adequate hydration and reduce environmental temperature. Avoid heavy bedding. Dress or swaddle in loose, light fabrics. Skin-to-skin contact with parent.
Nasal flaring / tachypnea	If concerned, avoid swaddling so that respiration can be observed.
Nasal stuffiness / excessive nasal secretions	Use gentle suction if nasal secretions cause obstruction to ensure adequate respiratory function. Positioning.
Excessive sucking – fists, fingers, thumbs	Keep hands clean and monitor for skin damage. Consult with parent about use of pacifier for non-nutritive sucking to provide comfort.
Poor feeding (infrequent/uncoordinated suck)	Feed on demand but avoid over-feeding in response to frequent crying. Decrease environmental stimuli during feeding (minimize talking, eye contact). Frequent small feeds with rest between sucking. Weigh and assess hydration daily. Assess coordination of suck/swallow reflex – support cheeks and jaw during feeds if necessary.
Regurgitation / vomiting	Burp when infant stops sucking and at end of feed.
Loose stools / diarrhea	Frequent diaper changes using barrier creams. Occasional skin exposure to allow buttocks to dry.

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- **Pharmacologic Treatment**
  - ***Morphine***
    - Currently the most common first line pharmacotherapy for NOWS
    - Pros:
      - readily available, familiarity with use
    - Cons:
      - frequent dosing
    - Initiation dose:
      - 0.05mg/kg
    - Route
      - PO dosing preferred
      - Consult with pediatric pharmacy if considering IV dosing
    - Dosing frequency:
      - Q 3 hr or Q3 hr PRN
    - Monitoring
      - if PRN dosing
        - Short term monitoring (at minimum continuous pulse oximetry) is recommended for a minimum of 4 hours after PRN dose.
          - Monitoring can be done in the birth parents' room if the room is appropriately equipped and there is appropriate nurse staffing and training. If not, transfer to unit/facility that can provide appropriate monitoring
      - if on scheduled medication
        - continuous cardiorespiratory + pulse ox monitoring is indicated. Transfer to ICN/nursery or another appropriate unit as indicated.
    - See **Appendix 3: NCNC ESC Algorithm – Morphine** for flowchart of treatment progression
    - *Starting morphine: PRN Phase*
      - Consider starting PRN morphine after a team huddle if infant is unable to E-S-C *despite* optimizing non-pharmacologic care
      - Team huddle consists of bedside nurse, MD, and infant's primary caregiver
      - Additional doses may be given q3 hours PRN for continued failure to E-S-C due to NOWS despite optimal non-pharmacologic care. A team huddle should occur around each PRN dose
    - *Initiating and Titrating Standing Morphine*
      - Infants who are not improving with PRN dosing and who have received **>3 PRN doses in 24 hours** should have a huddle to consider Around-the-Clock morphine
      - See Morphine Dosing below

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Morphine Dosing

Phase	Step
As-needed	Initiate 0.05 mg/kg x1 PO orders as needed to E-S-C. Do not dose more frequently than q 3 hours.
Around-the-Clock	If more than 3 PRN doses are required in 24 hours, initiate morphine 0.05 mg/kg PO q 3 hours scheduled with feeds.
Titration	If infant continues to be unable to E-S-C after 2 doses of morphine at each step, increase morphine by 0.01 mg/kg/dose.
Maximum Dose	Max dose is 0.12 mg/kg/dose PO. Consider adjunctive medication at this point.
Wean	Start wean once infant is on a stable dose with consistent ability to E-S-C for 24 hours. Wean by 10% of the maximum stabilizing dose as tolerated. May wean 1-2x/24 hours.
Discontinuation	Discontinue morphine when the dose is weaned to ≤ 0.01 mg/kg/dose PO.

- Wean: wean by 10% of the maximum stabilizing dose
  Example: Infant GA 38 weeks stabilized on 0.07 mg/kg x 3.2 kg = 0.224 mg
  0.07 mg/kg x 10% = 0.007 mg/kg = weaning increment, 3.2 kg = dosing weight
  Step 1: 0.063 mg/kg
  Step 2: 0.056 mg/kg
  Step 3: 0.049 mg/kg
  … Step 7: 0.021 mg/kg
  Step 8: 0.014 mg/kg discontinue
- Monitor for 24-48 hours after discontinuing morphine prior to discharge

- ***Methadone***
  - An option for pharmacotherapy in institutions where feasible
  - Pros
    - Longer half-life. Studies have shown use of a long-acting opioid can decrease length of stay
  - Methadone Dilution:
    - Standard 1 mg/mL oral methadone solution
  - Initiation dose:
    - 0.07 mg/kg PO
  - Route
    - PO
    - Consult with pediatric pharmacy if considering IV dosing
  - Dosing frequency:
    - Q 8 hr or Q8 hr PRN
  - Monitoring
    - Monitoring (at minimum continuous pulse ox) should be started if starting pharmacotherapy with methadone. Monitoring can be done in the birth parent's room if the room is appropriately equipped and there is appropriate nurse staffing and training. If not, transfer to unit/facility that can provide appropriate monitoring

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- See **Appendix 4: NCNC ESC Algorithm – Methadone** for flowchart of treatment progression
- *Starting methadone: PRN Phase*
  - Consider starting PRN Neonatal Methadone 1mg/ml oral solution 0.07mg/kg/dose q8 hours PRN after a team huddle if infant is unable to E-S-C *despite* optimizing non-pharmacologic care
  - Team huddle consists of bedside nurse, MD, and infant's primary caregiver
  - **Four** additional doses may be given q8 hours PRN for continued failure to E-S-C due to NOWS despite optimal non-pharm care. A team huddle should occur around each PRN dose
- *Initiating and Titrating Standing Methadone*
  - Infants who are not improving with PRN dosing who have received **>4 doses** of PRN should have a huddle to consider standing Level 1 methadone
  - Increase oral methadone dose to next level if infant continues to be unable to E-S-C due to NOWS
  - **Methadone can be increased 1 time per day (q24 hours)**

Level	Daily Dose of Standing Methadone
1	**0.2 mg/kg/day** PO divided q8 hours = 0.07 mg/kg/dose
2	**0.4 mg/kg/day** PO divided q8 hours = 0.13 mg/kg/dose
3	**0.6 mg/kg/day** PO divided q8 hours = 0.2 mg/kg/dose
4	**0.8 mg/kg/day** PO divided q8 hours = 0.27 mg/kg/dose

- *Weaning for Infants who needed to start Standing Methadone:*
  - Start wean after stable dose with consistent ability to E-S-C for 24 hours
  - Wean by 10% of maximum dose in mg/kg/day once daily as tolerated if infant is consistently able to E-S-C.
  - Monitor for 48 hours after discontinuing methadone before discharge
    - Consider extending to 72hr of observation after ≥5 days of methadone

- **Adjunctive Pharmacologic Treatment**
  - Indications / Uses:
    - Persistent severe symptoms at maximum dose of opioid therapy or inability to wean opioid therapy due to persistent symptoms
    - Use as supplemental treatment in addition to opioid
    - Consider consultation with UCSF specialist/neonatologist if requiring adjunctive treatment
  - Pharmacologic Options:
    - 1st line adjunct: clonidine
      - May affect BP
      - Monitor HR q3 hours and BP every 12 hours

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- 2nd line adjunct: phenobarbital
    - Monitor RR, HR, BP
    - Disadvantages
        - Ineffective for gastrointestinal manifestations of the syndrome
        - Results in CNS depression and impairment of the sucking reflex
        - Concerns for neuroapoptosis and potential long-term effects on neurodevelopmental outcomes
        - May need to discharge the patient home on the medication

Medication	Phase	Dose
Clonidine 10 mcg/mL compounded oral solution	Initiate	1 mcg/kg PO q 6 hours with feeds
	Titrate	May increase by 0.5 mcg/kg/dose q 6 hours
	Maximum	2 mcg/kg PO q 6 hours
	Wean*	Wean by 0.5 mcg/kg/dose as tolerated until the dose is 0.5 mcg/kg q 6 hours, then space to q 8 hours, then discontinue.
Phenobarbital	Initiate	Load: 15 mg/kg PO x1 Maintenance: 2.5 mg/kg PO q 12 hours, starting 12 hours after the loading dose
	Titrate	May increase dose by 10% every 24 hours
	Wean*	Wean by 20% of the highest dose every 48 hours

** Clonidine/phenobarbital may be weaned when the patient is off morphine/methadone for 24-48 hours*

- **Complication of NOWS**
    - Seizures
        - Rule out other acute, treatable causes (glucose, electrolytes, etc.)
        - If concerned for seizure due to opioid withdrawal, consider initiating empiric NOWS pharmacologic treatment
        - To work up further – confirm electrographic seizure events by EEG. If not available, arrange for neonatal transport to a higher level of care for further evaluation and management.
            - In case of clinical seizures without EEG correlate – initiate standard NOWS pharmacologic treatment or titrate up pharmacotherapy
            - In case of EEG confirmed seizures (this will be a small minority of patients)
                - consider the differential diagnosis/etiology
                - investigate as appropriate - i.e., MRI, LP, etc.
                - offer precision treatment (phenobarbital for acute brain injury, infection, etc.)
        - Treatment of Opioid Withdrawal Seizure causing hemodynamic instability
            - Morphine = first-line drug of choice at all institutions
                - 0.1 – 0.2 mg/kg IV or IM

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- Increase maintenance PO morphine/methadone dose once seizure controlled

- **Discharge**
  - After completing the appropriate monitoring period AND meets other discharge criteria.
    - Many infants with NOWS struggle with weight gain, and an adequate growth pattern should be established prior to discharge.
  - Ensure Plan of Safe Care (POSC); involve social services early, referral to early intervention services if qualifies- see Section 6.
  - Establish follow up with a pediatrician within 2 days.

SECTION 4: MANAGEMENT OF OTHER DRUG EXPOSURES

- **Overview**
  - Treatment of other recent/current nonopioid drug exposures is mainly supportive nonpharmacologic interventions
    - See above- Table 1: Signs and Symptoms of withdrawal and appropriate non-pharmacologic intervention

- **Benzodiazepines:**
  - **Scoring**? – No
  - **Can baby remain with birth parent**? – Yes, if no other indication for monitoring in nursery and birth parent has capacity to care for baby
  - **Potential symptoms** – delayed symptom onset, fever, tremors, sleep disturbance, vomiting, diarrhea, sneezing, muscle twitching, yawning, excessive crying, grimacing, Jitteriness, seizures, hypotonia, irritability
  - **Reported complications** - low birth weight, preterm delivery
  - **Treatment** - Supportive care/comfort measures - see Table 1.
  - **Referrals** - involve social services early, referral to early intervention services if qualifies - see Section 6.
  - **Discharge** - recommend monitoring for 24-48 hrs. Develop a plan for safe discharge and discharge based on standard discharge criteria and appropriate follow-up plan.
  - **Breastfeeding** – Supported if no other contraindications. If mom desires to breastfeed, consider maternal consult with a pharmacist about safest dose & type of benzo for ongoing use. See Section 5: Breastfeeding Guidance for more details.

- **Buprenorphine/Suboxone:**
  - **Scoring?** – Yes, can use NOWS Scoring (i.e., E-S-C)
  - **Can baby remain with birth parent?** – Yes, can room-in if parents can do the E-S-C monitoring
  - **Potential symptoms** – Same as opioid withdrawal (NOWS)
  - **Treatment** – non-pharmacologic & pharmacologic treatments per above NOWS guidelines
    - NOTE: these medications may provoke less withdrawal in infants leading to shorter hospital stay, less need for pharmacologic treatment; literature not as robust compared to opioids

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- **Referrals** – involve social services early, referral to early intervention services if qualifies - see Section 6.
- **Discharge** – per E-S-C guidance
- **Breastfeeding**- Supported if no other contraindications. See Section 5: Breastfeeding Guidance for more details

- **Cannabis:**
  - **Scoring?** – No
  - **Can baby remain with birth parent?** – Yes, if no other indication for monitoring in nursery and birth parent has capacity to care for baby
  - **Potential symptoms** – irritability, hyperactive Moro, excessive suck, increased startles and tremors
  - **Reported Complications** – low birth weight, shorter gestation. Later on - prolonged sleep disturbances, visual development issues, cognition and memory issues
  - **Treatment** – None
    - Counsel family re: risks to infant (I.e., passage in breastmilk, parental altered state when using, second hand smoke exposure)
  - **Referrals** - involve social services early, smoking cessation resources
  - **Discharge** - no minimum length of monitoring required for this drug exposure. Develop a plan for safe discharge and discharge based on standard discharge criteria and appropriate follow-up plan.
  - **Breastfeeding** - supported, but should encourage cessation or reduction of cannabis usage. See Section 5: Breastfeeding Guidance for more details

- **Cocaine:**
  - **Scoring?** – No
  - **Can baby remain with parent?** – Yes, if no other indication for monitoring in nursery and birth parent has capacity to care for baby.
  - **Potential symptoms** – fever, tremors, sleep disturbances, vomiting, diarrhea, sneezing, feeding difficulty, failure to thrive, excessive suck, Jitteriness, hypertonia / hyperreflexia, irritability
    - Infant may exhibit behavioral changes caused by CNS stimulation & peripheral sympathomimetic effects which can mimic opioids withdrawal.
  - **Reported complications** – poor fetal growth, prolonged growth restriction, stroke risk. Later on - developmental delay, learning disabilities, lower IQ
  - **Treatment** – Supportive care/comfort measures - see Table 1.
  - **Referrals** - involve social services early, referral to early intervention services if qualifies - see Section 6.
  - **Discharge** - no minimum length of monitoring required for this drug exposure. Develop a plan for safe discharge and discharge based on standard discharge criteria and appropriate follow-up plan.
  - **Breastfeeding** – Prohibited until birth parent urine toxicology is negative and birth parent discharging into Substance Use Disorder (SUD) treatment. See Section 5: Breastfeeding Guidance for more details.
    - If desires to breastfeed, can encourage expression of breastmilk, i.e., pump and discard, until conditions allow safe breastfeeding (e.g., negative birth parent urine toxicology and discharging into Substance Use Disorder (SUD) treatment).

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- **ETOH:**
  - **Scoring?** – No
  - **Can baby remain with birth parent?** – Yes, if no other indication for monitoring in nursery and birth parent has capacity to care for baby
  - **Potential symptoms** – Symptomatic hypoglycemia
  - **Reported complications** - at risk for fetal alcohol spectrum disorders which includes a spectrum of facial anomalies, poor growth and neurobehavioral impairment including development delays and cognitive deficits
  - **Treatment** – Monitor & treat hypoglycemia as needed
    - Counsel family re: risks to infant (I.e., passage in breastmilk, parental altered state when using)
  - **Referrals**- involve social services early, referral to early intervention services if qualifies (i.e., fetal alcohol syndrome)- see Section 6.
  - **Discharge** - no minimum length of monitoring required for this drug exposure. Develop a plan for safe discharge and discharge based on standard discharge criteria and appropriate follow-up plan.
  - **Breastfeeding** - supported, but should encourage cessation or reduction. See Section 5: Breastfeeding Guidance for more details

- **Methamphetamine:**
  - **Scoring?** – No
  - **Can baby remain with birth parent?** – Yes, if no other indication for monitoring in nursery and birth parent has capacity to care for baby
  - **Potential symptoms** – fever, tremors, excoriations, vomiting, loose stools, sneezing, Jitteriness, hypertonia / hyperreflexia, irritability
  - **Reported complications** – low birth weight, premature birth. Later on - long term adverse effects on behavior, cognitive skills and physical dexterity
  - **Treatment** – Supportive care/comfort measures - see Table 1.
  - **Referrals** – involve social services early, referral to early intervention services if qualifies - see Section 6.
  - **Discharge** - no minimum length of monitoring required for this drug exposure. Develop a plan for safe discharge and discharge based on standard discharge criteria and appropriate follow-up plan.
  - **Breastfeeding?** – Prohibited until birth parent urine toxicology is negative and birth parent discharging into Substance Use Disorder (SUD) treatment. See Section 5: Breastfeeding Guidance for more details.
    - If desires to breastfeed, can encourage expression of breastmilk, i.e., pump and discard, until conditions allow safe breastfeeding (e.g., negative birth parent urine toxicology and discharging into Substance Use Disorder (SUD) treatment).

- **Nicotine**
  - **Scoring?** - No
  - **Can baby remain with birth parent?** Yes, if no other indication for monitoring in nursery and birth parent has capacity to care for baby

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- **Potential symptoms**- greater need for handling, poor self- regulation, irritability, hypertonia; can cause exaggerated withdrawal symptoms if also opioid exposed
- **Reported complications** – low birth weight, intrauterine growth restriction. Later on – inattention and externalizing behavior, poor language development
- **Treatment** – none
  - Counsel family re: risks to infant (I.e., passage in breastmilk, parental altered state when using, second hand smoke exposure)
- **Referrals** - involve social services early, smoking cessation resources
- **Discharge** - no minimum length of monitoring required for this drug exposure. Develop a plan for safe discharge and discharge based on standard discharge criteria and appropriate follow-up plan.
- **Breastfeeding** - supported, but should encourage cessation or reduction of nicotine usage

- **SSRIs:**
  - **Scoring?** – No
  - **Can baby remain with birth parent?** – Yes, if no other indication for monitoring in nursery and birth parent has capacity to care for baby
  - **Potential symptoms** – irritability, seizure, agitation, tremors, hypertonia, increased respiratory rate, nasal congestion, vomiting diarrhea, fever, hypoglycemia, jitteriness, poor feeding
  - **Reported complications** – PPHN (rare); Later on-effects on motor development and motor control
  - **Treatment** – Supportive care/comfort measures - see Table 1.
    - If symptomatic, evaluate based on symptoms and continue observation until symptoms consistently decreasing
  - **Referrals** – involve social services early, referral to early intervention services if qualifies - see Section 6
  - **Discharge** – recommend monitoring for 24-48 hrs. Develop a plan for safe discharge and discharge based on standard discharge criteria and appropriate follow-up plan.
  - **Breastfeeding** – Supported. If birth parent desires to breastfeed, consider consult with a pharmacist about safest dose & type of SSRI for ongoing use. See Section 5: Breastfeeding Guidance for more details

- **Poly-Substance Exposure:**
  - **Scoring** – use NOWS Scoring if exposure includes opioids or concerns for opioid exposure
  - **Can baby remain with birth parent?** Yes, if no other indication for monitoring in nursery and birth parent has capacity to care for baby
  - **Potential symptoms** - Varied
  - **Treatment** –
    - If known/concerns for opioid exposure, treat per NOWS guidelines
    - If no opioid exposure, then per other drug exposure; supportive care/comfort measures - see Table 1.
  - **Referrals** - involve social services early, referral to early intervention services if qualifies - see Section 6.
  - **Discharge-** if +opioid use, per E-S-C guidelines,

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        - If other exposures, develop a plan for safe discharge and discharge based on standard discharge criteria and appropriate follow-up plan.
    - **Breastfeeding** - Prohibited until birth parent urine toxicology is negative and birth parent discharging into Substance Use Disorder (SUD) treatment. See Section 5: Breastfeeding Guidance for more details.
        - If desires to breastfeed, can encourage expression of breastmilk, i.e., pump and discard, until conditions allow safe breastfeeding (e.g., negative birth parent urine toxicology and discharging into Substance Use Disorder (SUD) treatment).

SECTION 5: BREASTFEEDING GUIDANCE

- **General Guidance**
    - There should be a timely multidisciplinary discussion to review proposed patient counseling for breastfeeding in the setting of illicit or polysubstance drug use to ensure consistent messaging to birth parent and ensure infant safety.
    - Additional resources for most up to date recommendations and if additional questions about safety of birth parent medication/drug use and lactation:
        - Consult pharmacist or lactation specialist if available
        - CDC website found online - https://www.cdc.gov/breastfeeding/index.htm
        - Hale's Medications & Mothers' Milk –
            - Check if you institution has in library or online access
                - May be available via UCSF library resources for those with access.
            - Available to purchase as printed text or online subscription - https://www.halesmeds.com/
        - LactMed database found online - https://www.ncbi.nlm.nih.gov/books/NBK501922/
- **Opioids:**
    - Contraindications to breastfeeding: birth parent actively using heroin / illegal opioids
    - No contraindication IF:
        - birth parent on stable methadone/buprenorphine dosing + established treatment program, regardless of methadone dose
        - opioid use is prescribed by physician at a stable, dose and periodicity (if dose and periodicity are variable, consult with pharmacist
        - educate birth parent re: risk of infant withdrawal if sudden cessation of breastfeeding

- **Benzodiazepine:**
    - No contraindication to breastfeeding.
    - Counseling – small amounts may be passed in breastmilk. There is a potential for sedation, irritability, and impaired suckling in the infant. Monitor breastfed infants for drowsiness.
    - There is variability in safety and effects with different benzos. Consult with a pharmacist or lactation reference to review safest drugs within this class.

- **Buprenorphine/Suboxone:**
    - See opioid guidelines above

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- **Cannabis:**
    - Is it safe to breastfeed and use? – current data are insufficient to say yes or no.
        - Reference CDC.gov website on breastfeeding or other lactation reference for most up to date counseling and guidance
    - No contraindication to breastfeeding but provide counseling re: risks to infant - i.e., passage in breastmilk, parental altered state when using, second-hand smoke exposure.
    - Counseling – THC is stored in body fat and slowly released over time so amount infant is exposed to can be unknown and last an unknown amount of time. Risk to infants is not completely understood at this time but there is concern about the effects on the infant's growing brain. Safest not to use while breastfeeding. Encourage reduction or cessation. If smoking, same counseling as tobacco re: reducing second hand smoke exposure – smoke away from infant, ideally outside, wash hands and change clothes before handling infant.

- **Cocaine:**
    - Contraindications to breastfeeding: birth parent actively using by verbal screen or has + urine toxicology at delivery.
    - Do not allow breastfeeding until birth parent urine toxicology is negative and birth parent discharging into Substance Use Disorder (SUD) treatment.
        - If desires to breastfeed, can encourage expression of breastmilk, i.e., pump and discard, until conditions allow safe breastfeeding (e.g., negative birth parent urine toxicology and discharging into Substance Use Disorder (SUD) treatment).
    - Counseling- should not breastfeed if actively using or has recurrence of use

- **ETOH**
    - No contraindications to breastfeeding depending on usage.
        - The alcohol level in breast milk is basically the same as the alcohol level in the birth parent's bloodstream. Breastmilk continues to contain alcohol as long as alcohol is still in the birth parent's bloodstream.
        - It is recommended to wait at least 2 hours after moderate drinking prior to feeding or feed by an alternative method
        - Generally, moderate alcohol consumption (up to 1 standard drink per day) is not harmful to the infant, especially if the birth parent waits at least 2 hours after a single drink before nursing.
        - It is not recommended to breastfeed if consuming more than 1 drink per day. Safest is not to drink alcohol while breastfeeding.
    - Counseling –exposure to alcohol through breastmilk above the moderate level could be damaging to an infant's development, growth and sleep patterns. Safest is to not drink while breastfeeding. If drinking more than a moderate amount, should feed via an alternative method (prior expressed breastmilk or formula) or pump and discard. Higher than moderate levels of alcohol consumption can impair a person's judgment and ability to safely care for an infant.

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- **Methamphetamine:**
  - Contraindications to breastfeeding: birth parent actively using by verbal screen, or has + urine toxicology at delivery.
  - Do not allow breastfeeding until birth parent urine toxicology is negative and birth parent discharging into Substance Use Disorder (SUD) treatment.
    - If desires to breastfeed, can encourage expression of breastmilk, i.e., pump and discard, until conditions allow safe breastfeeding (e.g., negative birth parent urine toxicology and discharging into Substance Use Disorder (SUD) treatment).
  - Counseling- should not breastfeed if actively using or has recurrence of use. Can provide education materials to birth parent.

- **Nicotine:**
  - No contraindication to breastfeeding but provide counseling re: risks to infant (e.g., second hand smoke exposure, increased risks of SIDs, respiratory and ear infections and can affect lung function
  - Counseling –breastfeeding while using can allow harmful chemicals to pass to infant via breastmilk and via second-hand smoke exposure. Safest not to use while breastfeeding. Encourage reduction or cessation. If smoking, educate on reducing second-hand smoke exposure – smoke away from infant, ideally outside, wash hands and change clothes before handling infant.

- **SSRIs:**
  - No contraindication to breastfeeding
  - Counseling - There is a potential for sedation, irritability, and impaired suckling in the infant. Monitor breastfed infants for drowsiness.
  - There is variability in safety and effects with different SSRIs. Consult with pharmacist or lactation reference to review safest drugs within this class.

- **Poly-Substance:**
  - Breastfeeding is contraindicated.
  - Do not allow breastfeeding until birth parent urine toxicology is negative and birth parent discharging into Substance Use Disorder (SUD) treatment.
    - If desires to breastfeed, can encourage expression of breastmilk, i.e., pump and discard, until conditions allow safe breastfeeding (e.g., negative birth parent urine toxicology and discharging into Substance Use Disorder (SUD) treatment).

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SECTION 6: ADJUNCTIVE CARE

- **Social Services**
    - Engage hospital social services with family early in L&D or nursery course to support family and help create safe discharge plan
    - Criteria for engagement of social services (if not already engaged)
        - need for further needs assessment
            - especially if suboptimal prenatal care, no or limited prenatal care; late to prenatal care
        - Documented birth parent h/o drug use during current pregnancy (reported or +tox screen)
        - **Concerns about birth parent capacity to care for self or infant**
        - Birth parent characteristics associated with active substance abuse
            - Acute mental status changes or changed level of consciousness not otherwise explained
            - Unexplained disorientation, psychosis, manic symptoms, ataxia, hallucinations, internal preoccupation, severe psychomotor agitation, confusion, and
    - Referral to CFS/CPS
        - Should involve multidisciplinary discussion to review indications for referral.
            - Should include providers who know the birth parent the best.
        - Birth parent +tox screen at time of delivery or infant +tox screen (if obtained) alone is not an indication to refer to CFS/CPS.
            - California law does not require a toxicology test be administered, leaving the decision to clinicians managing the care of the dyad. CFS/CPS hotline workers will ask if a toxicology test was done but should not request a toxicology test be administered.
        - Criteria for referral
            - CFS/CPS referral is indicated if birth parent substance use AND unmitigated, significant risk to infant
                - Examples of risk to infant
                    - **Concerns about birth parent's protective capacity for baby**
                    - Birth parent characteristics associated with active substance abuse
                        - Acute mental status changes or changed level of consciousness not otherwise explained
                        - Unexplained disorientation, psychosis, manic symptoms, ataxia, hallucinations, internal preoccupation, severe psychomotor agitation, confusion, and or somnolence
                    - Concerns about ongoing domestic violence
                    - Psychiatric evaluation of birth parent indicating decreased capacity
                    - Open CPS case on another child
                        - May not be known to providers, can call current case worker to check
            - Prior CPS cases that are closed but risk not mitigated/risk ongoing would promote new CPS referral
            - Evidence of maternal drug use in hospital

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        - Should also prompt further needs assessment
    - If birth parent is in foster care, CPS must be notified of birth
    - + Homelessness
    - Other social / safety concerns per usual institutional protocols
- **Each institution is encouraged to develop relationship/lines of communication with local CFS/CPS to discuss best practices**

- Referrals to other services
    - Public Health Nursing (if available in county)
    - Early Intervention Services
        - Refer all drug-exposed infants (Prenatal substance exposure, positive infant neonatal toxicology screen or symptomatic neonatal toxicity or withdrawal) to early intervention programs if qualifying comorbidities
            - https://www.dds.ca.gov/services/early-start/

- Establish Medical Home prior to discharge
    - Clear communication of ongoing needs of infant and family

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Appendix 1

Characteristics of Various Substances Causing Neonatal Abstinence Syndrome (NAS)

Drug	Onset, h	Frequency, %	Half life	Duration, d
Opioids				
Heroin	24–48	40–80	Short	8–10
Methadone	48–72	13–94	Long	Up to 30 or more
Buprenorphine	36–60	22–67	Long	Up to 28 or more
Other prescription opioid medications	36–72	5–20	Depends	10–30
Nonopioids				
SSRIs	24–48	20–30	Long (range 20h-4 days)	2–6
TCAs	24–48	20–50	Depends (most ~24h)	2–6
Methamphetamines	24	2–49	Short	7–10
Inhalants	24–48	48	Short	2–7

Onset, frequency and duration of withdrawal in infants exposed to various substances with addition Of general half-life of substance.

Adapted from Prabhakar Kocherlakota; Neonatal Abstinence Syndrome. Pediatrics August 2014

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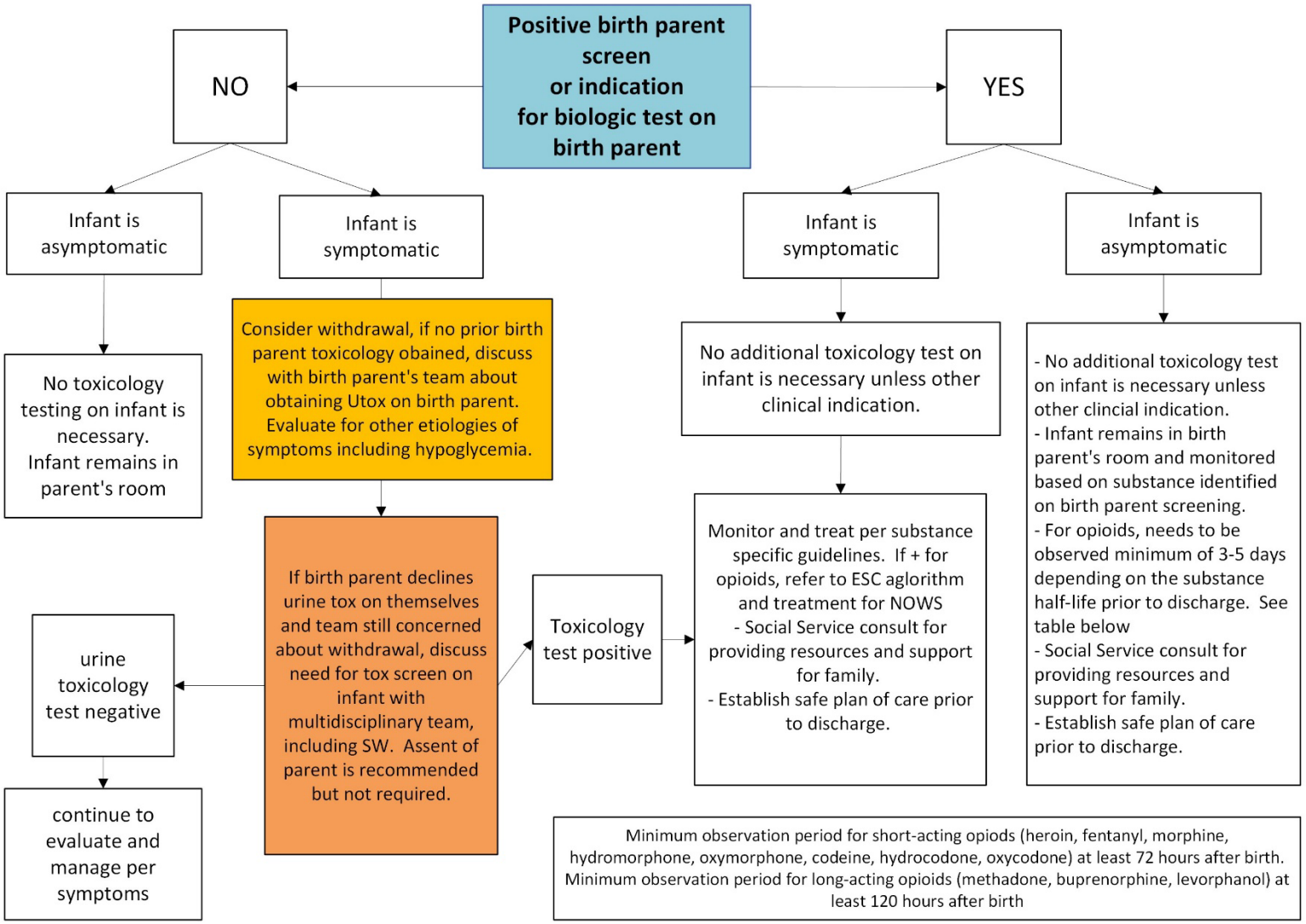
Appendix 2: Overview of Management

Management of Neonatal Opioid Withdrawal Syndrome (NOWS) & Drug- Exposed Infants



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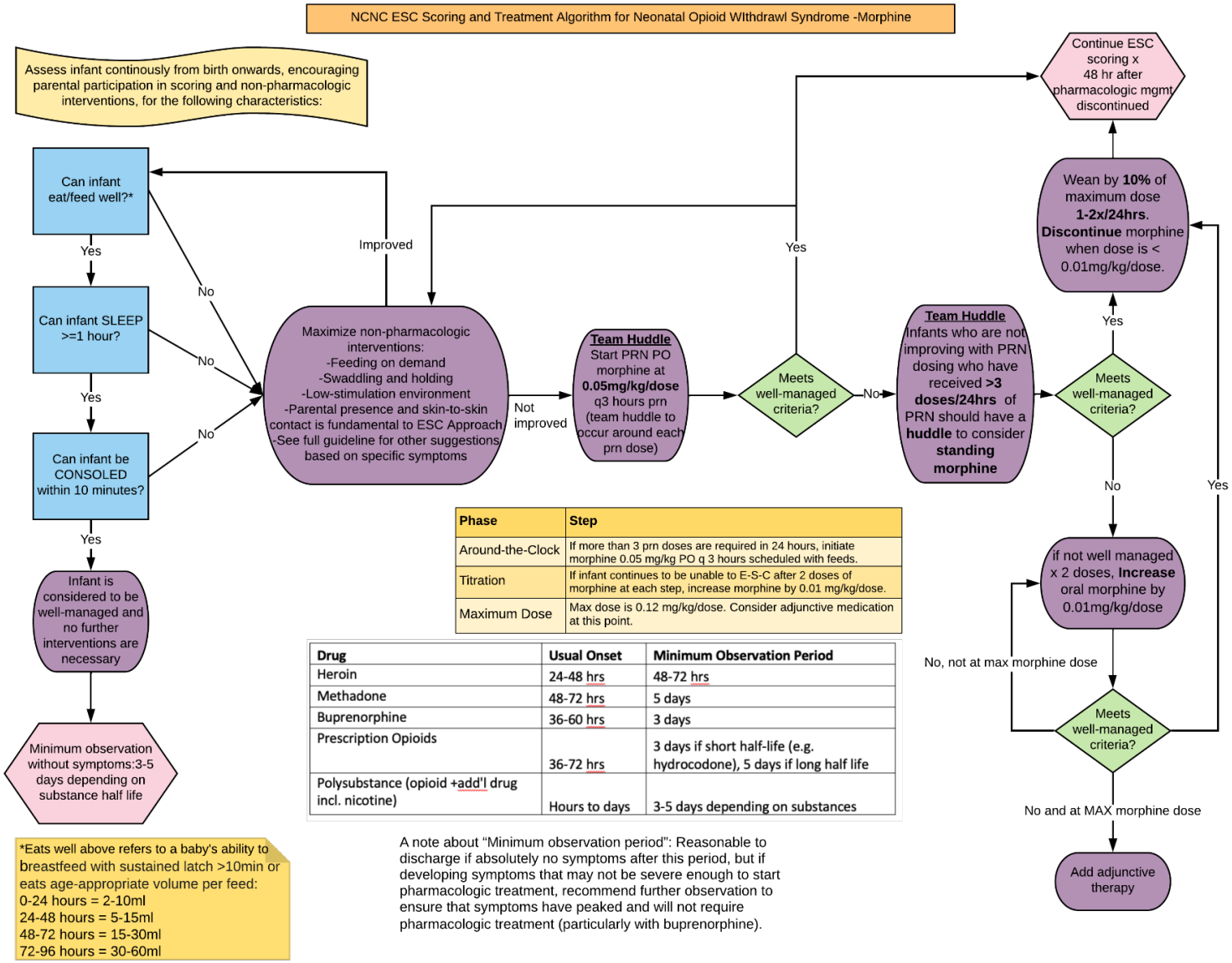
Appendix 3: NCNC ESC Algorithm – Morphine



Phase	Step
Around-the-Clock	If more than 3 prn doses are required in 24 hours, initiate morphine 0.05 mg/kg PO q 3 hours scheduled with feeds.
Titration	If infant continues to be unable to E-S-C after 2 doses of morphine at each step, increase morphine by 0.01 mg/kg/dose.
Maximum Dose	Max dose is 0.12 mg/kg/dose. Consider adjunctive medication at this point.

Drug	Usual Onset	Minimum Observation Period
Heroin	24-48 hrs	48-72 hrs
Methadone	48-72 hrs	5 days
Buprenorphine	36-60 hrs	3 days
Prescription Opioids	36-72 hrs	3 days if short half-life (e.g. hydrocodone), 5 days if long half life
Polysubstance (opioid +add'l drug incl. nicotine)	Hours to days	3-5 days depending on substances

A note about "Minimum observation period": Reasonable to discharge if absolutely no symptoms after this period, but if developing symptoms that may not be severe enough to start pharmacologic treatment, recommend further observation to ensure that symptoms have peaked and will not require pharmacologic treatment (particularly with buprenorphine).

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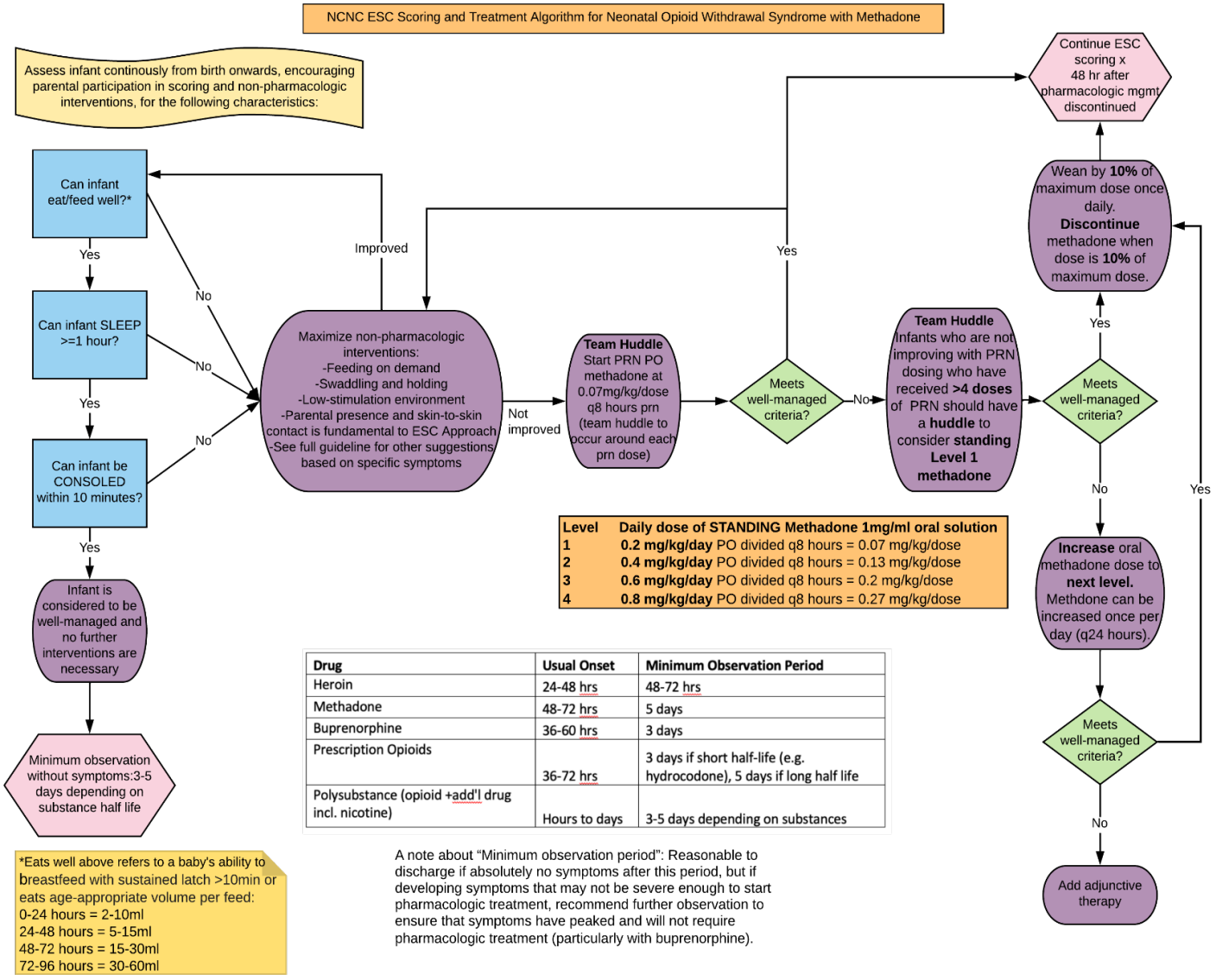
Appendix 4: NCNC ESC Algorithm – Methadone



Drug	Usual Onset	Minimum Observation Period
Heroin	24-48 hrs	48-72 hrs
Methadone	48-72 hrs	5 days
Buprenorphine	36-60 hrs	3 days
Prescription Opioids	36-72 hrs	3 days if short half-life (e.g. hydrocodone), 5 days if long half life
Polysubstance (opioid +add'l drug incl. nicotine)	Hours to days	3-5 days depending on substances

A note about "Minimum observation period": Reasonable to discharge if absolutely no symptoms after this period, but if developing symptoms that may not be severe enough to start pharmacologic treatment, recommend further observation to ensure that symptoms have peaked and will not require pharmacologic treatment (particularly with buprenorphine).

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Appendix 5: Resources

This is a list of transition-of-care resources from the CMQCC toolkit with California & national links.

https://nastoolkit.org/category/transition-of-care/audience/labor-delivery/best-practice/25

Resources

- California Budget and Policy Center Report: Home Visiting is a Valuable Investment in California's Families.
- Helping Hands: A Review of Home Visiting Programs in California.
- Nurse Family Partnership.
- Healthy Families America.
- Local First 5 Commission websites and their local programs.
- National Head Start Association.
- Early Head Start.
- California Head Start.
- CalWORKS.
- Comprehensive Perinatal Services Program.
- Healthy Start.
- Early Start.

Pre-, Peri-, and Postnatal Programs: The programs described below begin services during pregnancy and cover the mother/baby dyad. Most pre-, peri-, and postnatal programs are federally funded. In California, many of these programs are also funded by local First 5 Commissions, which use money from a state excise tax on cigarettes and other tobacco products to fund programs from birth (i.e., during pregnancy) to five years of age. In addition to the ones listed in this toolkit, other evidence-based pre-, peri-, and postnatal programs can be found in the Resources section of this Best Practice.

- California Home Visiting Program (CHVP): CHVP oversees implementation of various evidence-based home visiting programs throughout California, including the Nurse-Family Partnership (NFP) and Healthy Families America (HFA), and currently 23 California counties have these evidence-based programs. State-level agency workgroups conduct needs assessments to determine the greatest need for and potential impact from these programs based on factors such as poverty rates, rates of child abuse and neglect, and the ability to find and enroll at-risk parents in particular areas.

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    - ***NFP:*** Geared towards low income, first-time pregnant women. Care starts in pregnancy and follows the dyad until the child reaches two years of age. The mother must be referred before 28 weeks of pregnancy.
    - ***HFA*****:** Geared towards low-income, at-risk families from birth to a minimum of three years.
- Early Head Start*:* Early Head Start provides preschool and home visiting services geared towards low-income, at risk families. This is one of the few programs that can be started either during pregnancy or after delivery and follows the dyad until the child reaches three years of age.
- CalWORKS: CalWORKS offers a new three-year home visiting pilot initiative that began in January 2019. It is supported by both state General Fund and federal Temporary Assistance for Needy Families dollars. The program provides up to 24 months of home visiting for pregnant and parenting people, families, and infants born into poverty.
- Healthy Start*:* Healthy start targets communities with infant mortality rates that are at least one and a half times the U.S. national average. Women and their families can be enrolled into Healthy Start at various stages of pregnancy, including pre- inter-, and post-conception. Each family that enrolls receives a standardized, comprehensive assessment.

Postnatal Programs: These programs are primarily geared towards infants and can be implemented in the postnatal period.

- Early Start: Early Start is California's early intervention program (i.e., Part C of the Individuals with Disability Education Act), providing early intervention services to at-risk infants and children less than three years of age who meet eligibility criteria based on the presence or risk of developmental disability. Services include infant education, occupational therapy, physical therapy, and speech therapy. Referrals can be made from the NICU or newborn nursery and are often coordinated by a social worker, although anyone can make a referral, including parents, medical providers, neighbors, family members, foster parents, and day care providers.

- Home Health Visits: A number of public and commercial insurance companies offer home health visits, usually in response to a medical need. If the patient does not have insurance, or if the patient's insurance declines to cover the home health visit, the county often will provide a public health nurse. Some counties or local areas have established their own system (e.g,. Palomar Home Health Services).

County Specific Resources (Not a comprehensive list)

Alameda County

Alameda County Behavioral Health Care Services -Substance Use Continuum of Care

Main Helpline: 844-682-7215

website: https://www.acbhcs.org/substance-use-treatment

San Francisco County

Treatment Programs

- Road to Resilience through the Epiphany Center
    - Website: https://www.theepiphanycenter.org/services
- New Beginnings through the Homeless Prenatal Program
    - Phone: 415.546.6756
    - Website: http://www.homelessprenatal.org/services

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References

1. About Opioid Use During Pregnancy. Centers for Disease Control and Prevention. Updated July 20, 2021, https://www.cdc.gov/pregnancy/opioids/basics.html#:~:text=Withdrawal%20caused%20by%20opioids%20during,excessive%20or%20high%2Dpitched%20crying. Accessed May 27,2022.
2. Ayako Nishimura, Ayako Furugen, Takeshi Umazume, Seika Kitamura, Mayuko Soma, Kiwamu Noshiro, Yoh Takekuma, Mitsuru Sugawara, Ken Iseki, and Masaki Kobayashi. Benzodiazepine Concentrations in the Breast Milk and Plasma of Nursing Mothers: Estimation of Relative Infant Dose. Breastfeeding Medicine. May 2021.424-431.http://doi.org/10.1089/bfm.2020.0259
3. Breastfeeding-Alcohol. Centers for Disease Control and Prevention. Updated Feb. 9,2021 https://www.cdc.gov/breastfeeding/breastfeeding-special-circumstances/vaccinations-medications-drugs/alcohol.html. Accessed May 27,2022.
4. Breastfeeding-Hepatitis B or C Infections. Centers for Disease Control and Prevention. Updated Aug 10, 2021. https://www.cdc.gov/breastfeeding/breastfeeding-special-circumstances/maternal-or-infant-illnesses/hepatitis.html. Accessed May 27, 2022.
5. Breastfeeding- Marijuana. Centers for Disease Control and Prevention. Updated August 10,2021. https://www.cdc.gov/breastfeeding/breastfeeding-special-circumstances/vaccinations-medications-drugs/marijuana.html. Accessed May 27,2022.
6. Breastfeeding-Tobacco and E-cigarettes. Centers for Disease Control and Prevention. Updated Feb 16, 2021. https://www.cdc.gov/breastfeeding/breastfeeding-special-circumstances/vaccinations-medications-drugs/tobacco-and-e-cigarettes.html#:~:text=Can%20mothers%20who%20use%20tobacco,recommended%20food%20for%20an%20infant. Accessed May 27,2022.
7. Crew E, Chowfla A, DuPlessis H, Lee H, Main E, McCormick E, Oldini C, Smith H, Robinson R, Waller C, Wong J. Mother and Baby Substance Exposure Toolkit. Stanford, CA: California Maternal Quality Care Collaborative and California Perinatal Quality Care Collaborative. 2020. Accessed from https://nastoolkit.org/.
8. Farst KJ, Valentine JL, Hall RW. Drug testing for newborn exposure to illicit substances in pregnancy: pitfalls and pearls. Int J Pediatr. 2011;2011:951616. doi:10.1155/2011/951616
9. Grisham, L. M., Stephen, M., Coykendall, M. R., Kane, M. F., Maurer, J. A., & Bader, M. Y. (2019). Eat, Sleep, Console Approach. Advances in Neonatal Care, 19(2), 138-144.
10. Grossman, M et al. A Novel Approach to Assessing Infants With Neonatal Abstinence Syndrome. *Hosp Peds* 2018.
11. Hirai AH, Ko JY, Owens PL, Stocks C, Patrick SW. Neonatal Abstinence Syndrome and Maternal Opioid-Related Diagnoses in the US, 2010-2017. *JAMA.* 2021;325(2):146–155. doi:10.1001/jama.2020.24991
12. Hoyme HE, Kalberg WO, Elliott AJ, Blankenship J, Buckley D, Marais AS, Manning MA, Robinson LK, Adam MP, Abdul-Rahman O, Jewett T, Coles CD, Chambers C, Jones KL, Adnams CM, Shah PE, Riley EP, Charness ME, Warren KR, May PA. Updated Clinical Guidelines for Diagnosing Fetal Alcohol Spectrum Disorders. Pediatrics. 2016 Aug;138(2):e20154256. doi: 10.1542/peds.2015-4256. Epub 2016 Jul 27. PMID: 27464676; PMCID: PMC4960726.
13. Hudak ML, Tan RC; COMMITTEE ON DRUGS; COMMITTEE ON FETUS AND NEWBORN; American Academy of Pediatrics. Neonatal drug withdrawal. Pediatrics. 2012 Feb;129(2):e540-60. doi:

UCSF NCNC. Originated 12/2013. Last revised 7/2019, 9/2023
Approved by UCSF BCH San Francisco ICN Patient Safety/Joint Practice: 9/17/2019, 9/19/2023
Approved by Pediatric Medication Review Committee: 10/3/2023
Approved by UCSF BCH P&T: 10/11/2023

10.1542/peds.2011-3212. Epub 2012 Jan 30. Erratum in: Pediatrics. 2014 May;133(5):937. PMID: 22291123.
14. Karen J. Farst, Jimmie L. Valentine, R. Whit Hall, "Drug Testing for Newborn Exposure to Illicit Substances in Pregnancy: Pitfalls and Pearls", International Journal of Pediatrics, vol. 2011, Article ID 951616, 7 pages, 2011. https://doi.org/10.1155/2011/951616
15. Lester, Will; Andrews, Lacey; Nellhaus, Emma M.; Murray, Sara; Loudin, Sean; and Davies, Todd H. (2019) "Symptomology Associated with in Utero Exposures to Polysubstance in an Appalachian Population.," Marshall Journal of Medicine: Vol. 5: Iss. 2, Article 9.
16. National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services; Infographic: Dramatic Increases in Maternal Opioid Use and Neonatal Abstinence Syndrome. Jan 22, 2019; https://archives.drugabuse.gov/trends-statistics/dramatic-increases-in-maternal-opioid-use-neonatal-abstinence-syndrome
17. Neonatal Quality Improvement Collaborative of MA: http://www.neoqicma.org/sen-toolkit
18. Patrick SW, Barfield WD, Poindexter BB and COMMITTEE ON FETUS AND NEWBORN, COMMITTEE ON SUBSTANCE USE AND PREVENTION Neonatal Opioid Withdrawal Syndrome. Pediatrics; November 2020, 146 (5) e2020029074; DOI: https://doi.org/10.1542/peds.2020-029074
19. Prabhakar Kocherlakota; Neonatal Abstinence Syndrome. Pediatrics August 2014; 134 (2): e547–e561. 10.1542/peds.2013-3524
20. Wachman, Elisha et al. Boston Medical Center Methadone NAS Protocol.
21. Wachman EM, Schiff DM, Silverstein M. Neonatal Abstinence Syndrome: Advances in Diagnosis and Treatment. JAMA. 2018 Apr 3;319(13):1362-1374. doi: 10.1001/jama.2018.2640. PMID: 29614184

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Approved by UCSF BCH San Francisco ICN Patient Safety/Joint Practice: 9/17/2019, 9/19/2023
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