Neonatal Opioid Withdrawal Syndrome Inpatient Management Quality Improvement Toolkit Massachusetts PNQIN

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OVERVIEW

The purpose of this toolkit is to provide a practical guide for optimal inpatient management of substance-exposed newborns (SENs) at risk for neonatal opioid withdrawal syndrome (NOWS) / neonatal abstinence syndrome (NAS), leading to standardization of care for all birthing hospitals in Massachusetts to improve outcomes. The toolkit is meant to be a summary of best practices for the assessment and management of infants with prenatal opioid exposure. It aims to provide inpatient teams with sample guidelines and protocols, as well as links to references and websites on each topic for additional information. The practices promoted in this toolkit are based on an extensive literature review, and consultation with lead NOWS centers in the area. It applies to infants who have an underlying prenatal opioid exposure, with or without additional psychoactive medication exposures, at risk for NOWS.

PRENATAL EDUCATION / CONSULTATION

We recommend that all pregnant individuals with known opioid use receive prenatal counselling as early on as feasible after the pregnancy has been diagnosed, providing the birthing person an opportunity to decrease adverse pregnancy outcomes and improve neonatal outcomes. This consultation should be performed by both the Obstetric as well as Pediatric teams to address both birthing person as well as neonatal care provisions. The goals of the consultation are:

1) To prepare the family for a healthy pregnancy resulting in a term birth.
    a. Discuss the need for continued sobriety for the best outcomes for the infant and be able to safely breastfeed their infant
    b. Discuss the impact of poly substance exposure including tobacco, cannabis, as well prescribed psychiatric medications on infants
    c. Help create a Family Care Plan / Plan of Safe Care (POSC) with core care providers identified early in pregnancy for provision of consistent education and care
    d. Discuss what goals they need to achieve to successfully transition their infants from hospital to home with support of DCF
2) To discuss clinical signs and symptoms of NOWS
3) To prepare the family for the hospitalization of infant for NOWS monitoring.
    a. Discuss length of inpatient monitoring for 4-7 days for opioid-exposed infants
    b. Discuss location of care
    c. If baby requires pharmacologic treatment, anticipated length of hospitalization
    d. Making arrangements to be present during the hospitalization including speaking to residential treatment programs, methadone guest dosing near the hospital, childcare preparations, and transportation considerations
    e. Getting a support person to assist the mother during the hospitalization
4) To discuss non-pharmacologic and pharmacologic management of NOWS
    a. Non-pharmacologic care as first-line treatment
    b. What % of infants receive medication, which medications are used at your institution, and how will medication choice decisions be made
5) To discuss breastfeeding in the setting of birthing person substance use disorder
    a. Review hospital guidelines, eligibility criteria and resources available
6) To discuss the process of toxicology testing and possible 51A / DCF reporting depending on hospital policy

A sample prenatal consultation note template is provided as ***Appendix A.*** A parent handbook and/or handouts summarizing the above information are helpful. Examples are provided in ***Appendix B.***

INPATIENT MONITORING

The American Academy of Pediatrics recommends inpatient monitoring for **4-7 days** for SENs for signs of NOWS.[1] Approximately 30-50%% of SENs receive pharmacologic treatment for NOWS despite optimal non-pharmacologic first-line treatment. Most SENs will exhibit signs and symptoms within 48-72 hours of birth after in-utero opioid exposure. Recent data from Boston Medical Center (BMC) over a 5-year period (n=550 infants) indicated that 95% of infants who required pharmacotherapy were identified by day 4, and >99% by day 7. A 2014 meta-analysis indicated a lower risk for NOWS requiring pharmacotherapy (RR=0.90) and shorter hospitalizations by 7 days in buprenorphine versus methadone exposed infants, however there is significant confounding by indication as pregnant individuals treated with buprenorphine may potentially have less severe OUD than those treated with methadone.[2] Infants exposed to short-acting opioids such as oxycodone have a reported lower risk for NOWS requiring pharmacotherapy.[3] We recommend that infants exposed to short acting opioids be observed for a minimum of 3-5 days for signs of withdrawal.[1]

- **3 days minimum observation for short-acting / immediate-release opioids** *(e.g., codeine, dihydrocodeine, hydrocodone, tramadol)*
- **4-day (96 hour) minimum for buprenorphine and sustained-release opioids** (e.g., fentanyl, hydromorphone, morphine, oxycodone, oxymorphone)
- **5-day (120 hour) minimum for methadone**

Co-exposures to nicotine and psychiatric medications increase the risk for NOWS requiring pharmacotherapy due to an overlap of withdrawal symptoms from these medications with opioid withdrawal, and drug interactions.[4–6] Careful consideration of the symptom profile (primary neurologic symptoms) and timing of symptoms (< 24 hours of life) can help to distinguish between opioid and co-exposure withdrawal.

TOXICOLOGY TESTING

Verbal screening for substance use in pregnancy and use of toxicology testing should be based on your individual hospital's policies. The choice of type of infant toxicology screening will be per hospital policy; general guidelines are provided below. Some general recommendations for toxicology testing consideration include:

1) Known or suspected substance use disorder during the current pregnancy, including individuals on MOUD
2) Infants with signs/symptoms of drug withdrawal
3) Unexplained neonatal seizures or apnea in a term infant

Birthing Person Screening and Urine Toxicology Testing: ACOG recommends universal verbal screening by a validated screening questionnaire, ideally with informed written consent.[7-8] Birthing person urine toxicology testing should be per hospital policy, should inform clinical management, and be unbiased.[9-10] Urine toxicology testing on Labor and Delivery will in general detect substances that have been taken within the previous 48-72 hours. Of note, THC may be present in the urine for one month following cannabis use.[10] At minimum, a basic urine panel test containing cocaine, amphetamines, benzodiazepines, fentanyl, and opiates should be sent if testing is indicated. If available and indicated, an expanded opioid panel should be sent from the urine, which will specify methadone, buprenorphine, oxycodone, opiate, and/or fentanyl exposure. Qualitative urine screening should be verified with confirmatory quantitative screening due to risk of false positives. Of note, fentanyl is commonly prescribed in labor and can remain positive in the birthing person's urine for weeks after last use, making quantitative testing critical to accurately interpreting toxicology results.[11] A sample hospital guideline for toxicology testing is included as ***Appendix C.***

Infant Urine Toxicology: Urine toxicology testing in the infant should be sent if it would change clinical management of the infant and is indicated per hospital guidelines. Attempt to collect the infant's first void for testing as this will have the highest concentration of substances. Infant urine toxicology results reflect exposure in the preceding 3 days, however cocaine metabolites may be present for 4-5 days. THC may be detected in

the urine for weeks after last birthing person use; hospitals should consider the utility of urine cannabis testing.[10] Qualitative urine testing should be validated with confirmatory quantitative screening due to risk of false positives.[12]

Meconium Toxicology: Includes enzyme-linked immunosorbent assay (ELISA) testing typically for amphetamines, barbiturates, cannabinoids, cocaine/metabolites, opioids, and PCP. Meconium testing in term infants reflects exposure during the second half of gestation. Meconium has a high sensitivity for testing for opiates and cocaine.[13] Given the long turn-around time for results, the utility of meconium testing in influencing clinical management of the infant should be considered.

Umbilical cord Toxicology Testing: Umbilical cord segment testing at the time of birth for toxicology has a more rapid turn-around time than meconium and has been shown to be >90% sensitive and specific for most drugs of abuse including opiates and cocaine, similar to meconium. Cord testing detects more prolonged period of in-utero exposure similar to meconium testing.[13-14]

Consent: Verbal and/or written consent for birthing person and infant toxicology test is recommended.

NOWS SCORING & ASSESSMENT TOOLS

All infants with in-utero opioid exposure should be assessed every 3-4 hours, timed around cares and feedings, for signs and symptoms of NOWS. Key principles of scoring include:

1) The infant should be kept in the room with the parent for scoring if possible
2) The score encompasses the entire 3-4 hour period, not one point in time
3) The infant should be scored after feeding to ensure hunger is not contributing
4) Engage parents in the scoring process, especially if rooming in

One of the most commonly used NAS/NOWS scoring tool is the **Finnegan Neonatal Abstinence Scoring Tool** (FNAST).(***Appendix D).*** The FNAST is a 21-item scoring system created in the 1970's, characterizing all possible withdrawal signs and symptoms an infant may exhibit, divided into neurologic, autonomic, gastrointestinal categories. It was demonstrated to have a high inter-rater reliability coefficient of 0.82 when first developed.[15] Typically scores $\geq$8 are used to determine the need for pharmacotherapy. Using a standardized scoring method such as that available for the FNAST through **Neoadvances** (http://neoadvances.com) in which all providers are trained has been shown to improve NOWS outcomes.[16]

A recent study found that the Finnegan had poor psychometric properties and poor internal consistency.[17] An alternative assessment method is the **Eat, Sleep, Console (ESC)** care approach, with or without use of the ESC NOWS Care Tool.[18-22] ESC is a function-based assessment method for NOWS that focuses on the infant's ability to eat expected amounts for age, sleep expected times for age, and level of support required to console the infant in order to guide management of the infant. The ESC approach incorporates non-pharmacologic care into the algorithm. The ESC Care approach has been associated with a decreased need for pharmacologic treatment and shortened length of hospitalization in center specific and statewide quality improvement initiatives. In a recent 26-centered NIH cluster-randomized clinical trial, the ESC Care approach was associated with a 6.7 day decrease in length of stay and over 30% reduction in pharmacologic treatment compared with infants with the FNASS care approach.[23] Long-term outcomes of infants assessed with the ESC approach are currently being examined. Please see the **PNQIN POP webpage** for further information and training materials on ESC.(https://pnqinma.org/perinatal-opioid-project-pop/)

NON-PHARMACOLOGIC CARE

First-line treatment for infants at risk for NOWS is non-pharmacologic care with engagement of the birthing person as the primary caretaker.[1] Proper use of non-pharmacologic care as first-line treatment has been shown to reduce the need for pharmacologic management by 30-50%.[24-27] A recent meta-analysis demonstrated a 60% reduction in need for pharmacologic treatment length of stay with rooming-in models of care.[26] Essentials of non-pharmacologic care include:

1) Rooming-in model of care: *This can include rooming-in on a postpartum ward, private room NICU, or pediatric inpatient ward.*
2) Skin-to-skin contact
3) Infant holding / gentle rocking / swaying
4) Breastfeeding
5) Clustering of infant care / allowing for uninterrupted periods of sleep
6) Swaddling
7) Pacifiers
8) Decreasing environmental stimuli to noise and light
9) Feeding on demand
10) Engagement of the parent as the primary caregiver of her infant, with active participation and presence at the bedside throughout the hospitalization. If the parent is not available, another family member or support person is strongly recommended

Additional resources on non-pharmacologic care interventions and a **Non-Pharmacologic Care Checklist** are provided in the **Eat, Sleep, Console (ESC) Care Manual** available on the PNQIN POP website. (https://pnqinma.org/perinatal-opioid-project-pop/)

Sample **NOWS symptom parent diaries** and **non-pharmacologic care handouts** are provided in ***Appendix E and F.*** All infants should also receive an **occupational / physical therapy consultation**.

BREASTFEEDING

Breastfeeding is recommended by the Academy of Breastfeeding Medicine (ABM), American Academy of Pediatrics (AAP), and the American College of Obstetrics & Gynecology (ACOG) in individuals with substance use disorders without non-prescribed drug use at the time of delivery.[28] Engagement in substance use disorder treatment programs is encouraged for those who are breastfeeding. Breastfeeding decreases the severity of NOWS and need for pharmacotherapy by 30-50%, with associated shorter hospitalizations by 1-2 weeks.[27] Timing of when to initiative breastfeeding after recent non-prescribed drug use should be based on anticipated time of clearance of the medication and follow-up care for the lactating individual.[28]

Methadone and buprenorphine are both compatible with breastfeeding regardless of maternal dose with extremely low infant plasma levels not expected to influence neonatal withdrawal severity.[29-30] Breastfeeding in the setting of oxycodone and other short-acting opioids commonly prescribed to postpartum individuals after C-section are generally safe for lactation except at higher doses due to risk for infant sedation.[28] Breastfeeding in the setting of codeine is not recommended due to the risk of ultra-rapid metabolizers with accumulation in the breastmilk and risk for infant sedation.

A lactation consultation is highly recommended for all mother-infant dyads with prenatal opioid exposure due to a higher risk for feeding difficulties secondary to NOWS including disorganized feeding. Trauma-informed support for birthing persons who may have a history of sexual trauma is recommended. Sample institutional breastfeeding guidelines are provided in ***Appendix G.*** The 2023 revised Academy of Breastfeeding Medicine (ABM) guidelines are included as ***Appendix H.***

Formula feeding and supplemental feedings:

There is no current evidence to support one formula supplement vs another for improving NOWS outcomes, or proactively starting increased calorie feedings in infants when no other medical indication is present. Babies should be fed on demand and until content. If a baby has excessive weight loss or poor weight gain, a feeding assessment should occur to ensure efficacy and sufficient frequency of feedings. Babies may require more frequent feedings or higher volumes of feeding when withdrawal symptoms are present especially symptoms likely to be associated with increased energy expenditure (e.g., undisturbed tremors, excessive crying) or increased losses (e.g., vomiting, diarrhea). We recommend use of higher calorie (24kcal/oz) breastmilk or formula when excessive weight loss or poor weight gain are present despite optimization of feeding volumes, which is supported by a recent randomized controlled trial.[31] There is no evidence to support preferential use of a low lactose formula.[32] Nasogastric feedings should be considered if the infant's suck and swallow are discoordinated and/or the infant is unable to take in the required volume of feedings felt needed (e.g., may occur in preterm infants). A feeding team / nutritional consult should be performed in the setting of feeding challenges in bottle fed infants.

Hepatitis B, Hepatitis C and breastfeeding:

Birthing persons with Hepatitis C and/or C infections can breastfeed their infants with special considerations. Babies born to persons with Hepatitis C infection should receive the Hepatitis B Immunoglobulin and Hepatitis B vaccine within 12 hours of delivery. Birthing persons with Hepatitis C infection should be advised to pay careful attention to latch and positioning to avoid nipple trauma. When nipple or surrounding skin cracking are noted, it is recommended for the birthing person to abstain from breastfeeding on the affected side until the nipple is healed. In the interim, the individual should pump and discard milk on this side due to the theoretical risk for transmission of Hepatitis C infection via the breastmilk. Of note, this recommendation comes from the American Academy of Pediatrics through the qualifier that transmission of Hepatitis C virus to infants through breastfeeding has not been documented and the risk for Hepatitis C transmission is similar in breastfed and formula-fed infants.[33] While both nipples are affected, infants should be fed with previously expressed breastmilk or an alternative milk substitute (e.g., pasteurized human donor milk, formula) until the mother is able to breastfeed again.

Cannabis and breastfeeding:

Cannabis use is estimated to impact 10-15% of pregnant individuals. There is concern for parental impairment after using cannabis while caring for her infant. Due to its lipophilic nature, THC, the active substance in marijuana, accumulates in the breast milk with potential risk for neurodevelopment impairment.[28,34-35] Long-term follow-up data on infants exposed to varying amounts of THC via the breast milk are currently lacking.

Breastfeeding recommendations should be per hospital policy. General recommendations are:

- Screen all pregnant individuals for cannabis use starting early in pregnancy and upon admission to L&D.
- Cessation or reduction in cannabis use during lactation is recommended.
- For birthing persons who continue to use cannabis and with to breastfeed, a shared decision-making process to discuss the risks and benefits is recommended.
- Further guidance on breastfeeding in the setting of cannabis use are included in the 2023 ABM guidelines ***(Appendix H)***

PHARMACOLOGIC MANAGEMENT

If using the current form of the Finnegan tool with its current recommended inter-observer reliability program, initiation of escalation of pharmacotherapy is recommended for 3 consecutive scores $\geq$8 or 2 scores $\geq$12. If using a function-based scoring system such as ESC, medication is indicated if the baby is unable to eat, sleep,

and/or console effectively despite maximization of non-pharmacologic measures for concerns felt to be related to NOWS (see ESC Care Manual).

First-line Pharmacotherapy Options:

Morphine and Methadone:

Both morphine and methadone are approved by the AAP as appropriate choices for first-line pharmacologic agents.[1,27] Morphine is the most commonly used medication, chosen by 50-70% of nurseries in the U.S. Morphine is typically dosed every 3−4 hours with dose ranges of 0.3−1.0 mg/kg/day and most commonly weaned in the inpatient setting. Methadone is used by 20−25% of hospitals with dose ranges of 0.2−0.9 mg/kg, typically with less frequent dosing every 6−12 hours, with recent pharmacokinetic data suggesting every 6 hour dosing may be optimal during the "capture" phase, with subsequent spacing to q12 hour dosing.[36] A single center randomized control trial of 31 methadone or buprenorphine exposed infants found that methadone had the advantage with 7 fewer days of opioid treatment in comparison with morphine.[37] A multi-centered randomized control trial of 117 infants found that methadone was associated with a shorter median length of stay by 4 days compared with morphine.[38] One benefit of morphine is its short half-life, with frequent dosing making tailoring of dose to symptoms potentially easier. The advantages of methadone are that is can be dosed less frequently with a longer half-life which may be better for cases of more severe withdrawal. Regardless of choice of primary agent, a standardized weaning protocol has been associated with improved outcomes.[39] Typically opioids are weaned by 10% daily until reaching 10-20% of the maximum dose then discontinued. ***See appendix I*** for sample protocols.

PRN Dosing:

Alternatively, using **symptom-triggered or "PRN" dosing** for opioids is currently under investigation with preliminary studies indicating significantly shorter length of treatment without adverse events. Both PRN morphine and PRN methadone have been examined in these single-center QI studies, with infants requiring on average 2 doses of medication.[20,40] A recent PNQIN multi-centered analysis showed no differences in hospitalization outcomes when PRN morphine versus methadone were used.[41] A NIH funded multi-centered trial of PRN dosing compared with the standard opioid taper is currently underway. Please see ***Appendix I*** for sample PRN dosing protocols.

Buprenorphine: Sublingual buprenorphine is also being trialed as a first line agent with promising results from studies to date.[27] Dosing used in prior studies are 13-39 micrograms per kg per day in 3 divided doses.[41] Prior randomized trials comparing buprenorphine to neonatal opium solution, morphine, or methadone indicated shorter duration of treatment in the buprenorphine on the range of 4-15 days.[42-43] Buprenorphine may be more beneficial for buprenorphine exposed infants.

Adjunctive Therapy Options:

Phenobarbital: Phenobarbital is the most commonly used second-line agent.[1] Typically phenobarbital is started as a rescue agent at daily dosing of 5-8mg/kg/day in 1-2 divided doses after an initial load after infants have been maximized in their opioid dosing. Phenobarbital requires the monitoring of serum levels, with a goal level of 20-30 for NOWS. There is no standard recommendation for phenobarbital weaning. We recommend starting the phenobarbital wean 48-72 hours after the infant has completed the wean off of their primary opioid medication (e.g., morphine, methadone). Phenobarbital can be weaned as an outpatient by 20% every 3-5 days. Phenobarbital may be better for polypharmacy exposed infants, and those with severe neurologic symptoms.[44] There is concern that prolonged use of phenobarbital in neonates may put infants at risk for future neurodevelopmental delays based on the seizure literature.[45] Sample phenobarbital protocols are provided in ***Appendix I.***

Clonidine: Clonidine is an α2-adrenergic receptor agonist which has been used to treat opioid withdrawal in older children and adults, and is being used increasingly in neonates with NOWS.[46-48] Clonidine has been used

primarily as an adjunctive agent, either started at the same time as the opioid or as rescue therapy, though has also been trialed as a primary agent.[44,46-48] Typically dosing of clonidine is 6 micrograms per kg per day divided every 4-6 hours. Blood pressure and heart rate monitoring is necessary during clonidine treatment and weaning due to potential adverse effects including arrhythmias and rebound hypertension. Though an RCT demonstrated no increased risk for these when weaning is done in a stepwise manner.[47] Clonidine is typically weaned in the inpatient setting after the opioid has been discontinued by decreasing the dose in a stepwise manner, such as by increasing the interval between dosing. See sample clonidine protocol in ***Appendix I.***

In a single center randomized study phenobarbital versus clonidine were evaluated as an adjunctive therapy with morphine sulfate as the primary agent and found that though the phenobarbital group had lower number of inpatient days of treatment, they had a much higher outpatient treatment profile.[47] Another recent randomized trial found that adjunctive phenobarbital was associated with shorter morphine treatment days compared with clonidine.[49]

Gabapentin: Co-prescription of gabapentin with opioids is common and it is used to potentiate the effects of opioids and other CNS depressants.[50-51] Neonates born after co-exposure to opioids and gabapentin appear to have more severe NOWS. A recent case series of 19 co-exposed neonates described a specific pattern of withdrawal including tongue thrusting, back arching, wandering eye movements, and continuous movements of the extremities. Treatment with gabapentin and subsequent tapering improved signs of withdrawal, in cases with treatment failure with the standard pharmacologic regimens.[52]

Department of Children and Families (DCF)

A copy of the Massachusetts DCF guidelines for perinatal substance use is provided in ***Appendix J.*** Key recommendations are:

- Physicians, nurses and social workers are all mandated reporters for any concerns related to abuse or neglect of children.
- Hospitals should have a written policy for reporting protective concerns to DCF.
- A mandated reporter should consider filing a 51A report with DCF for all infants with neonatal drug withdrawal or prenatal substance exposure AND when protective concerns are present.
- A social work consultation should be obtained shortly after delivery to facilitate 51A filing and DCF evaluation.
- A DCF decision must be obtained before the infant is discharged home if a report was filed.
- DCF will ask if a Plan of Safe Care (POSC) has been established and may request that the POSC be communicated to their agency prior to the newborn's discharge.

DCF website: http://www.mass.gov/eohhs/gov/departments/dcf/
51A filing website: http://www.mass.gov/eopss/docs/msp/missing/51a.pdf

Plan of Safe Care (POSC)

For all substance exposed newborns, federal requirements are that a Plan of Safe Care (POSC), also referred to as a Family Care Plan (FCP) be developed for the family (CAPTA 106) before the newborn is discharged from the hospital.[53] The POSC should be a family comprehensive plan that addresses the parents' behavioral and physical health needs (including substance use and mental health supports) and family or child-focused services and developmental needs (Ex: Early Intervention services, prenatal and pediatric care, other family and community support services). In addition to listing key services for the infant and family, the POSC will include a parenting preparation plan, safety and prevention plan, and contingency planning for any return to non-prescribed use.

The POSC document should be created jointly by the pregnant or parenting person and their provider. Ideally, this document would be started prenatally with updates throughout the pregnancy and around the time of delivery. The POSC document can be started by the postpartum team if one was not started prenatally.

Who Might Coordinate a POSC?

A POSC coordinator is the person who works with the birthing person / caregiver on creating and maintaining a plan and identifying and accessing desired resources. Any provider working with perinatal clients (including recovery coaches, case managers, home visitors, doulas, Early Intervention staff, treatment providers, medical providers, etc.) can serve as a POSC coordinator, provided they have the availability to meet regularly for a period of time with the client/patient and are equipped to make warm referrals to needed services.

DCF will ask everyone who files a 51-A report for substance exposed newborns whether a POSC has been created. The POSC itself is not required to be shared with DCF. However, POSC coordinators should encourage patients to sign releases of information (ROI) so that their POSC can be shared with DCF and their other providers, in order to help provide the best coordinate care if necessary. ROIs facilitate prompt communication with other providers and can aid DCF staff in their decision-making and planning processes.

**Please refer to http://www.healthrecovery.org/safecare/ for POSC templates and more information on the Massachusetts POSC.

DISCHARGE PLANNING

Criteria for discharge include inpatient monitoring for 4-7 days for long-acting opioid exposure and 3-5 days for short-acting opioid exposure for infants who do not meet criteria for pharmacotherapy, and 24-48 hours off of opioid replacement therapy for pharmacologically treated infants.[1] Stable weight for age and adequate oral intake should be observed prior to discharge. Essential considerations for discharge planning include development of a plan of safe care (POSC) - ensuring a safe home environment (including a safe sleep space separate from the parents' bed) and early infant follow-up.

Infants with prenatal opioid exposure are at higher risk for failure to thrive, and behavioral and developmental delays which are multifactorial in nature.[54-56] They are also at higher risk for eye abnormalities, particularly strabismus.[55,57] Lastly, they are at risk for perinatal hepatitis C virus (HCV) transmission, with 58% of birthing persons with opioid use disorders in a Boston Medical Center cohort from 2006-2015 found to be HCV-exposed, and a documented 4-8% transmission rate in HIV-negative individuals with chronic hepatitis C, although many infants do spontaneously clear the virus.[58-60]

Specific recommendations for follow-up include:

1) Safe sleep promotion
2) Written and verbal hand off with outpatient primary care provider (e.g., pediatrician, family physician) discussing relevant medical and social issues during hospital course including:
    - Birthing person substance use disorder treatment status
    - Parental responsive to infant's needs
    - Any parenting behaviors of concern, if observed prior to discharge
    - Custody status of infant
    - Documentation of phenobarbital weaning plan, if indicated
5) Primary care follow-up within 1-2 days of discharge
6) Boston area: Referral to a comprehensive care program for postpartum families with substance use disorders (Boston Medical Center SOFAR Clinic or Massachusetts General Hospital HOPE clinic) if desired
4) Visiting nurse assessment including weight check and NOWS assessment within 1-3 days of discharge if available.
5) Outpatient lactation support visits as able for continuing support

5) Early Intervention referral is recommended for all substance exposed newborns: http://www.mass.gov/eohhs/gov/departments/dph/programs/family-health/early-intervention/ The following infants are automatically eligible for EI services: 1) Prematurity < 32 weeks GA, 2) Low birth weight < 1500g, 3) Diagnosis of NOWS or substance exposed newborn diagnosis, 4) NICU stay greater than 5 days, 5) Hospital length of stay over 25 days, 6) Intrauterine growth restriction or small for gestational age, 7) central nervous system anomaly, 8) other conditions that could impact development.
6) High risk infant follow-up clinic starting at 6-8 weeks of life, as available
7) Pediatric infectious diseases outpatient appointment for Hepatitis C exposed infants: https://www.bmc.org/pediatrics-infectious-disease
   a. Recommended laboratory testing includes:[58-60]
      1. Antibody testing at 15-18 months, as maternal antibody can take up to 15-18 months to clear
      2. If a diagnosis is desired sooner for parental anxiety or clinical suspicion, RNA testing can also be done starting as early as 2-6 months (earlier is not recommended because of more frequent false positive results).
   b. Recommended Approach:
      1. If feasible, pediatric infectious diseases outpatient referral, with initial appointment at age 2-6 months for counselling and/or testing to assist with long-term retention.
      2. If preference to follow infant in primary care, send serum *quantitative* HCV RNA every 6 months, starting at age 3-6 months, along with HCV Antibody starting at 15 months of age. Two negative HCV RNAs (on separate occasions) or any negative antibody are considered sufficient to exclude chronic HCV infection. For any positive tests, refer to pediatric infectious diseases.
8) Ophthalmology follow-up at 4-6 months of age to look for refractive errors and strabismus.[55,57]

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