Optimizing Neonatal Abstinence Syndrome Management

A Tennessee Initiative for Perinatal Quality Care Collaborative Inter-institutional Improvement Project

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The TIPQC NAS Tool Kit is a compilation of suggestions & potentially better practices for consideration in NICU quality improvement projects aimed at optimizing the management of neonatal abstinence syndrome in the NICU. The contents of the toolkit should not be taken as medical advice, nor as a standard of care, but are rather a common starting point for hospital based Quality Improvement teams who are participating in the TIPQC NAS project. Local teams are responsible for local implementation decisions, and for ensuring that their QI work has appropriate local medical and administrative oversight and is in compliance with local guidelines, policy and regulations.

**Toolkit Version**
This document, Version 7/1/14, is a revision of the original TIPQC NAS toolkit Version 11/14/12. New references have been added and selected portions have been revised to reflect lessons learned by participating teams in the course of project implementation. Both the executive summary and the forward remain unchanged from the 2012 version, reflecting the situation at an earlier stage of what is now clearly an epidemic of NAS in Eastern TN. TIPQC is grateful to Tamara Wallace, DNP APRN NNP-BC for her work as editor of this revised toolkit.

**Development Team Leader Disclosures:**
Karen D’Apolito has disclosed she is a shareholder in NeoAdvances LLC, and receives speaker fees from NeoAdvances for educational presentations on Finnegan scoring and the management of Neonatal Abstinence Syndrome.

The remaining Development Team Leaders reported no financial relationships to disclose.
<table>
<thead>
<tr>
<th>Contents</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pilot Team Members</td>
<td>4</td>
</tr>
<tr>
<td>Executive Summary</td>
<td>5</td>
</tr>
<tr>
<td>Foreword: Impact of Prenatal Opiates in the NICU</td>
<td>6</td>
</tr>
<tr>
<td>Evidence Synopsis</td>
<td>8</td>
</tr>
<tr>
<td>Toolkit</td>
<td>9</td>
</tr>
<tr>
<td>Potentially Better Practices</td>
<td>17</td>
</tr>
</tbody>
</table>

Appendices
- Evidence Review                                      | 43   |
- References                                            | 52   |
- Example IRB or QI Oversight Summary                   |      |
- TIPQC Project Application                             |      |
- TIPQC Data Agreement (In Project Application)        |      |
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Executive Summary: Neonatal Abstinence Syndrome Management

Much attention has recently been focused on the epidemic increase in narcotic usage in the general population with particular attention being focused on narcotic seeking behavior of patients who are addicted to prescription opiates. Only beginning to be fully appreciated is the hidden burden of neonatal abstinence syndrome, the narcotic withdraw faced by infants of mothers who are exposed to narcotics and other substances while still in the womb. Though not addicted in the sense that these infants cannot engage in drug seeking behavior, they never the less go through withdraw symptoms- inconsolable crying, extreme irritability, diarrhea, and difficulty maintaining normal infant sleep-wake cycles, unless their abstinence syndrome is optimally managed. Critically, the evidence base for NAS management is robust as highlighted in recent Cochrane reviews as well as ACOG and AAP policy statement. However neonatologists, pediatric pharmacists, NICU staff, and hospitals have little systematic data to guide optimizing the effective and efficient implementation of the available evidence. Moreover, the recent epidemic increase in narcotic use in the general population has created micro-epidemics of infants with severe NAS who require lengthy and often resource intensive hospitalizations to safely wean off narcotics.

While addressing and alleviating the many “upstream” contributors to the NAS epidemic is beyond the scope of this project, optimizing management of these challenging infants and families is clearly possible. This TIPQC toolkit is designed to facilitate the local development and spread of effective and efficient data-driven strategies for managing NAS using the available evidence.

The experienced nursery provider and Quality Improvement Professional will see little that is new in this toolkit- all of the interventions are well described, and the improvement strategies have a proven track record. However, a number of points warrant highlighting:

- Disciplined execution of QI methodology with careful attention to data-driven audits of key processes is essential for successful improvement
- Reflective analysis of outliers should provide a rich source of data to refine the interaction of our system and our patient population
- Successful efforts uniformly require high-level unit and hospital support

Without question, this is a team effort, and we need your participation. Substantial improvements in the management of infants with NAS are possible, especially when we share what works. The members of TIPQC look forward to adding your center’s energy, enthusiasm and expertise to this important statewide effort to improve outcomes for infants in Tennessee.

Peter H. Grubb, M.D.
Medical Director
Tennessee Initiative for Perinatal Quality Care
From November 2012 version of TIPQC NAS Toolkit
Foreword: Optimizing NAS, Addressing the Impact of Increased Maternal Opiate Use in the NICU

Substance abuse, including both prescription and illicit drugs, is widespread in our society and represents a significant public health problem. The National Institute on Drug Abuse website estimates $600 billion is spent annually on costs associated with substance abuse in the United States (NIDA 2011). The Centers for Disease Control and Prevention calls the problem “epidemic” and reports that 12 million Americans aged 12 and older reported non-medical use of prescription painkillers in 2010 and 15,000 people die each year from prescription painkiller overdose (CDC 2011). The Tennessee Controlled Substance Database reported 13.7 million prescriptions (2 prescriptions per capita) in 2010 with the top drug hydrocodone accounting for 275 million tablets—enough to supply each Tennessee citizen with 46 hydrocodone tablets (Cost 2011). The National Survey on Drug Use and Health for 2008 reported that 5.1% of pregnant women aged 15 to 44 reported using illicit drugs in the past month (SAMHSA 2011).

Substance abuse among women of childbearing age places newborn infants at risk of developing neonatal abstinence syndrome (NAS), a cluster of symptoms that occurs after a baby is born to a mother who has used opioids during the pregnancy. NAS is sometimes referred to as neonatal withdrawal syndrome and is a result of the abrupt discontinuation of the substances that the fetus was receiving in utero. The management of NAS includes supportive, non-pharmacological interventions like minimizing stimulation and swaddling. The pharmacological treatment is to provide opioids, most commonly methadone or morphine, in order to gain control of the withdrawal symptoms and then wean the infant from pharmacotherapy (Osborne 2010). Occasionally the baby will require adjunctive pharmacotherapy with sedatives such as phenobarbital and/or clonidine (Osborne 2010).

East Tennessee Children’s Hospital (ETCH) is experiencing an increasing number of admitted babies who require pharmacotherapy to control withdrawal symptoms: 35 babies in 2008, 60 in 2010, 135 in 2011, and at our current rate of admissions for NAS the 2012 projection is 260.

In October 2010 the neonatologists decided to stop discharging infants to complete weaning as an outpatient because of inherent risks including: a deficit of appropriate monitoring of therapy by the caregiver, decreased capacity of caregiver to understand or adhere to therapy, and the potential of drug diversion. Pharmacy was consulted to help develop a plan that would 1) identify infants at risk for NAS, 2) consistently evaluate the presence and severity of NAS, 3) standardize and simplify the opioid weaning plan, 4) safely minimize the length of stay, and 5) discharge the infant completely weaned from pharmacotherapy.

A pharmacist, in cooperation with a nurse practitioner, identified a plan to utilize a symptom-based morphine algorithm that would be used in concert with the Finnegan Scoring system to quickly gain control of the withdrawal symptoms and wean the infant from morphine while providing good control of the symptoms. After approval by the medical staff, a multidisciplinary team was formed to create an implementation plan. In addition to the pharmacist and neonatal nurse practitioner the team included: neonatologists, physiatry, administrator, staff nurses (RN and LPN), social work, speech and occupational therapists, child-life specialists, physiatry, perinatal nurse practitioner,
volunteer services, primary care nursing, physical therapy, and consultation with outpatient methadone clinic.

Training of the NICU staff included live inservice presentations and the use of video lectures to describe the Finnegan Scoring system and the morphine algorithm. The team worked through barriers such as consistency in scoring the symptoms, adherence to the dosing algorithm, and logistical concerns with repackaging and stocking the morphine unit dose cups.

In the nineteen months since the project began ETCH has admitted 299 infants for treatment of NAS and has completely weaned 269 infants prior to discharge with an average length of stay (LOS) of 38 days. Infants with ≤ 40 days LOS (n=179, 66.5%) had an average LOS of 24 days, and infants with > 40 days LOS (n=90, 33.5%) had an average LOS of 65 days. The previous treatment plan in which the infants were discharged to wean at home had an average LOS of 30 days.

This project has engendered widespread interest in our state with the Tennessee Initiative for Perinatal Quality Care adoption as a statewide project under our direction. The project has been presented to the Tennessee Hospital Association Tennessee Center for Patient Safety Regional Networking Meeting. There is a growing interest among community organizations, healthcare professionals and lay persons, and we believe that this project will continue to expand beyond the initial scope of acute, inpatient care in the NICU to a larger mission to educate the public and advocate for a reduced incidence of prenatal substance exposure.

Certainly, and sadly, the problem of substance abuse is significant and the number of babies who innocently suffer the consequences is growing. The ETCH NAS team believes that together we can identify and prioritize meaningful actions and then work diligently to make a difference for the infants, and families, in our care. Thanks for your interest in this important work and remember to “Shoot for the moon. Even if you miss, you’ll land among the stars”.

Terry King, PharmD, BCPS
Informatics Support Pharmacist
East Tennessee Children’s Hospital

From November 2012 version of TIPQC NAS Toolkit
Evidence Synopsis

Neonatal Abstinence Syndrome is a particularly challenging topic for evidence developing research. Even so, a substantial body of evidence and published experience in this challenging population is available for the change team seeking to systematically improve care for these families.

The development team noted several areas worth highlighting briefly as a starting point for teams beginning a quality improvement effort focused on optimizing NAS management.

First, the team should broadly consider the pathways and processes by which infants with NAS are identified in the local setting. Careful attention should be directed not only to maintaining an appropriately broad differential diagnosis, but also to understanding local practice with respect to obtaining a history of fetal-maternal substance exposure, as well as the limitations of biochemical screening and confirmation strategies. Wide variation was noted between centers and providers with respect to detection strategies, and without question, understanding the strengths and limitations of your local approach to detection is foundational in this effort.

Second, once an infant at risk for or manifesting signs of NAS is identified, successful management strategies are best based on validated scoring systems that are implemented with a rigorous program to minimize inter-observer variation in the local setting. Until a high reliability scoring system with minimal inter-observer variation is in place, effective, efficient management of NAS is difficult if not impossible to achieve.

Once a highly reliable scoring system is in place, a standard local management approach can be implemented. Typically effective approaches begin with non-pharmacological behavioral and environmental interventions coupled with unambiguous scoring thresholds to initiate and then titrate pharmacological intervention. Once control of NAS signs has been achieved, high reliability scoring and score-based clinical response processes support rapid, yet appropriate weaning of pharmacological treatment, and thereby minimize length of stay for cases with straight-forward, non-complicated Neonatal Abstinence Syndrome.

Third, optimizing NAS management in a QI paradigm provides opportunities to address related processes and pathologies in a systematic fashion. The change team will want to be sure to consider not only infant specific confounding morbidities, but also the critical role of nutrition and the challenging controversies presented by the breastfeeding mother of an infant with NAS. Broader systems challenges arising with this population should also be kept in mind to include staffing ratios, staff stress and the risk of burn out, management of maternal dependence, as well as opportunities for “upstream” and “downstream” education.
and advocacy. Many of these issues are covered in greater depth, not only in the tool kit that follows, but also in the Evidence Review prepared by Karen D’Apolito for the development team that is included in the Appendices of this toolkit.

For teams wishing to further review the current state of the evidence, a number of reviews have been published on the management of neonatal abstinence syndrome (NAS.) (Jansson 2009, Cleary 2010, Bio 2011, Jansson 2012, Hamdan, 2012, Grim, 2013) Additionally, two updates of Cochrane reviews have been released (Osborn 2010, Osborn 2010b) and both the American College of Obstetrics and Gynecology and the Society of Obstetricians and Gynecologists of Canada have updated guidelines on maternal substance use (ACOG 2012, Wong 2011.) The American Academy of Pediatrics has also updated its guideline on the management of neonatal abstinence in 2012 (AAP COFN 2012.)

**Toolkit**

This toolkit is a collection of evidence-based practices based on the literature and experiences derived from NAS QI work at the TIPQC pilot centers and the other members of the development team

As with all TIPQC toolkits, this project begins with a review of the available evidence. When this toolkit was developed in 2011-12, no other large-scale collaborative QI toolkits were available. Accordingly, the project development team conducted a literature review including recent subspecialty society guidelines and consensus statements as well as the recent Cochrane Review on NAS.

Following completion of the evidence review, the development team created this toolkit, data collection forms and report generation system to support a state-wide quality improvement effort. In the process, they’ve gained substantial hands-on experience with how the toolkit works, and have added to their experience managing this challenging population. All 3 centers stand ready to assist your unit in implementing this toolkit, asking only that you in turn agree to share your experience with other units who are likewise working to improve their portion of our statewide perinatal healthcare delivery system.

This toolkit is intended for application in conjunction with a series of statewide learning sessions at TIPQC regional meetings and webinars. Though it could be used in isolation, it is really only a starting point and common reference for a collaborative multi-center improvement effort that through the course of the project will substantially build on and add to the material contained in this document.
We recognize our members have a range of needs and resources dedicated to optimizing NAS management in their NICU. Accordingly, this toolkit is presented as a menu of potential better practices; changes for participating nurseries to consider in the context of their local needs, culture, and resources. The toolkit contains elements that are appropriate for nurseries of all sizes as newborns may present with neonatal abstinence syndrome in any neonatal care delivery setting. Much of the material in the toolkit is applicable for any nursery setting, however there are elements that would only be appropriate in the intensive care setting. Each center will need to carefully select from the menu of potentially better practices in the context of their population and current practice.

Additionally, each nurseries strategy for implementation may vary. The toolkit can be implemented as a bundle where interventions in each potentially better practice subheading are undertaken simultaneously. Alternatively, many units are already implementing a substantial number of these interventions, and may find a selective menu approach to be more appropriate. The TIPQC office is available to discuss local implementation strategy with project leaders/champions as needed.

This project provides web-based data entry and Quality Improvement Statistical Process Control Analysis through REDCap. REDCap is an on-line data collection developed under an NIH CTSA grant and is currently used in clinical trials and registries worldwide. TIPQC’s implementation of REDCap provides HIPAA compliant data management for private health information, and facilitates the generation of real-time SPC reports based on local center level data within the constraints defined by the project data use agreement. The importance of the on-demand reports cannot be underestimated, as these reports provide the basis to guide the team’s PDSA cycles by providing tools to answer the critical question of whether a given change was really an improvement. Additionally, as all centers participate, real-time statewide aggregation of data provides a statewide view of the magnitude of this challenging problem and progress to date. We recognize that balancing the cost vs. value of data collection in a QI effort is challenging. Accordingly, the development team has striven to minimize the data burden, and the TIPQC office is available for consultation to assist project leaders and improvement teams with developing reliable data entry processes.

**Neonatal Abstinence Syndrome Management Optimization Project**

**Aim:** The aim of this project is to improve the health of infants admitted to the NICU for management of Neonatal Abstinence Syndrome in Tennessee. Clearly many of the social and upstream contributors to NAS length of stay are beyond the span of control of the hospital nurseries. However, substantial opportunities for optimizing in-patient management, and thereby minimizing impact to the infant, the family, and society are possible. Thus, we seek to optimize our
management by attaining high reliability (>90%) processes for NAS scoring, NAS treatment initiation and weaning, and post-NAS discharge preparation by December 2013.

**Charter:** Without question, available evidence supports the efficacy of rapid identification and treatment of NAS in affected infants in order to minimize adverse impacts on the infant and family. Equally clear, Tennessee has seen a marked increase in both indicated and addiction related narcotic use in the general population in recent years, and this trend has resulted in a growing number of infants who require hospital care for management of severe NAS following in-utero substance exposure. Accordingly, stakeholders represented at the March 2011 TIPQC State Meeting voted to develop a data-driven toolkit to support a statewide perinatal quality improvement project aimed at optimizing NAS management in Tennessee.

**Definitions** agreed to by the pilot centers 14 September 2011:

- **NAS:** neonatal abstinence syndrome can occur following sustained exposure to CNS active substances before or after birth. This project will focus primarily on NAS after in-utero exposure, however centers can opt to concurrently use this toolkit and data stream to optimize management of post-natal NAS as well.
- **Drug exposure screening test:** a screening test that requires a confirmatory laboratory test to ensure validity of the result
- **Drug exposure confirmation test:** the definitive test confirming in-utero exposure to a substance
- **Clinical NAS:** infant with clinical signs that are consistent with NAS in the context of a maternal history of exposure in the absence of laboratory confirmation.
- **Laboratory confirmed NAS:** infant with clinical signs consistent with NAS with a positive drug exposure confirmation test
- **Poly-substance NAS:** infant with clinical signs consistent with NAS with positive drug exposure to two or more substances
- **NAS Score:** formal, validated score for NAS severity (e.g. Finnegan, modified Finnegan, or other validated score)
- **NAS Rx:** NAS treatment plan, can include both behavioral/environmental and/or pharmacological components

**Target population:** Infants admitted to the newborn nursery or NICU for management of NAS

**Demographic measures (paper record fields maintained only at entering hospital*)**

- Name*
- MRN*
- TIPQC patient ID (Generated by REDCap)
- Date of Birth (Optional- required for stratification)
NAS Management Optimization: A TIPQC Inter-institutional QI Project

- Date of Admission
- Date of Discharge
- Estimated Gestational Age at birth (Optional - required for stratification)

**Outcome Measures:**
- Length of Stay for NAS Rx (calculated from:)
  - Date Start NAS Rx
  - Date Stop NAS Rx
- Length of Stay (calculated from:)
  - Date of Admission
  - Date of Discharge

**Process Measures:**
- Basis of NAS Diagnosis (Select all that apply)
  - Maternal History
  - Clinical Signs (Clinical NAS - see definitions above)
  - Screening Test
  - Confirmatory Test (Laboratory NAS - see definitions above)
- Source of substance (Select all that apply)
  - Maternal
    - Supervised Prescribed Replacement Therapy (MR)
    - Supervised Prescribed Pain Therapy (MP)
    - Prescribed for Psychiatric or Neurological Condition (PN)
    - Prescription substance obtained without Prescription (wo)
    - Non-prescription substance (non)
  - Infant
    - Prescribed after delivery for infant (neo)
- NAS Management (Select all that apply)
  - Not indicated
  - Behavioral and Environmental
  - Pharmacological
- Completion of standardized outlier review
- Review audits for reliability of implementation of PBPs (Potentially Better Practices)

**Balancing Measures:**
- Non-NAS Length of Stay (Days between end of NAS Rx and discharge)
- Readmissions

**Stratifying Measures: (Optional Measures - see data form)**
- Maternal Disposition
- Infant Disposition
• EGA adjusted estimate of LOS attributable to prematurity for infants less than 37 weeks EGA at birth (LOS(EGA) = LOS – (37 weeks – EGA))
• Diagnoses with potential for state dysregulation independent of perinatal substance exposure
  o Seizure disorder documented on EEG
  o Stroke or intracranial hemorrhage
  o Major CNS malformation
• Diagnoses or procedures requiring protracted sedation and/or analgesia
  o Total days prescribed sedation and/or analgesia
• Gastroschisis

Outlier Review:
After sufficient baseline data is accumulated, individual REDCap records with outlying lengths of stay will be identified using statistical process control charts. This will be an optional activity for participating units, however as variation in length of stay improves, outliers are expected to become relatively rare, and as such, are particularly valuable for systematic review and reflection by change team who seek to further refine the efficiency and effectiveness of their system of care. Given the wide variety of participating units, with different patient populations and volumes, three populations are envisioned to develop SPC based thresholds: 1) the local population, 2) a statewide aggregate of gestational age corrected lengths of stay, and 3) the statewide aggregate length of stay. For cases meeting criteria, change teams will be provided an outlier form to guide their reflection on the specific case. Initial data items for consideration and aggregation include:
  • Optional: Classes of substances identified during screening (Pick all that apply from maternal history, and all testing)
  • Optional: Total number of discrete substances identified by confirmatory testing
  • Optional: NAS management courses
  • Optional: Total number of prn doses of NAS agents
Additional queries will be added as participating centers reflect on and learn from complex NAS cases.

Note: Modification of current definitions and measure set may change as the collaborative learning community identifies additional change opportunities and more efficient or higher value data points. Modifications will be discussed, formulated and announced through webinar, face to face meetings and REDCap.
TIPQC NAS Toolkit: Getting Started

The TIPQC NAS toolkit follows our previous approach of presenting a menu of potentially better practices for consideration for implementation as part of a data-driven quality improvement process. The lead center ETCH, started a unit based QI project to optimize NAS management in 2009. The results of their project were presented at the 2011 TIPQC statewide meeting where the membership voted to develop this TIPQC toolkit. This TIPQC toolkit combines elements from the evidence review as well as experience garnered by the pilot teams in the course of developing and pilot testing the tool kit. The toolkit that follows is provided as a guide for centers seeking to optimize NAS management in their NICU.

The first step is formation of the primary improvement team. Typically an optimal team will consist of 5-7 end-users and multi-disciplinary stakeholders who join the project champion and team leader. Success depends on the vigorous support of administrative leadership, usually an administrative champion, who takes oversight responsibility for successful implementation, and who can provide resources and require accountability for project progress. Teams are encouraged to consider the potential benefit of including a family member with first-hand experience with NAS on the team. Though challenging, input from thoughtful, experienced family members can provide new insights that both enrich and energize the effort. Many teams report that family input provides the key perspective that leads to optimal, sustainable processes. With this foundation, a team is ready to begin work. To help guide the first time improvement team, these team elements are integrated in the material requested as part of the project application.

The second step after assembling the team and completing the project application is for the team to meet and review both the toolkit and their current practice. A simple review of current practice and comparison with material in the toolkit will provide a minimum foundation for successful participation in the kickoff meeting. Prior to the statewide kickoff, an evidence review webinar will be presented. Team participation is encouraged for this and all project related events, as the webinars, in conjunction with the face-to-face meetings provide teams additional structure for change teams to plan, execute and succeed in their effort to effectively and efficiently implement the evidence-based approaches outlined in the toolkit.

The Role of Data in Quality Improvement
Successful projects require the team to gather data on current processes and outcomes. Without data, we have no way of knowing whether the changes we attempt are actually implemented, and when reliably implemented, whether the change is actually an improvement.
Starting a data-driven improvement project requires collection of baseline data, however many are surprised by how little data is required to generate an adequate initial baseline. Additionally, many centers will find that the data required may already be available. If the minimum data to create a pre-project baseline is not available, the team will need to collect baseline data to establish a baseline before changes are implemented. Either way, baseline data collection is readily supported using the data tools in the REDCap system, and can be accomplished in parallel with a review of current policy and practice. Once existing process performance and outcomes are quantified and a baseline is established, the team is prepared to make a data-driven decision on which change to implement first.

It is expected that many units will already incorporate a subset of items from the menu of potentially better practices. Often, baseline data reveals substantial variation in the implementation of existing practices and the first PDSA (Plan-Do-Study-Act) cycle may only seek to improve the consistency of current practices before implementing new practices. In this case the goal of the first cycle is to reduce process variation with existing practice prior to implementation of new potentially better practices. Process reliability audits may be especially helpful to understand whether existing guidelines are implemented as written/intended. Similarly, when changes are introduced, reliability audits are essential tools for refining process implementation, and often provide the key to understanding why evidence-based interventions fail to deliver the intended improvement on initial implementation.

With baseline data in hand, and a clear understanding of variation in their current practice, the team is ready to make a data-driven choice about which change to implement next. More detailed discussions of the processes involved in initiating and successfully executing a data-driven QI project can be on the TIPQC website (http://www.tipqc.org/jit), and from a host of other sources. Additionally, participating centers will have access to a secure project forum on the TIPQC website where participants can discuss challenges encountered during start-up and implementation. At a minimum, we recommend that all project teams review the TIPQC toolkit, and have time and resources set-aside to fully participate in weekly team meetings and monthly TIPQC project webinars.

**Data Collection, Optional Data, and Data Collection Strategies**

The designers of the toolkit and the data collection system were keenly aware of the substantial challenge posed by additional data collection. Paradoxically, the development team also received many requests to capture substantially more data. Accordingly, the development team has created and pilot tested a minimal data set necessary to drive local improvement, and provide meaningful state level aggregate reports.

Two aspects of the data system are worth highlighting at the outset. First, the primary data form contains both required and optional data elements. Teams
can participate in this project by submitting only 7 required data elements per patient. Additional optional fields on the data form are included to better understand the sources of variation that pilot centers have encountered in analyzing the primary outcome variable, length of stay. These additional fields, in gray on the data sheet, are however optional.

Second, the data system contains both the primary data derived from patient level experience, and two additional data forms. One, an outlier analysis form is intended to assist teams in their systematic evaluation of cases with outlying lengths of stay. The outlier form will not be activated until later in the project, and will likely be used infrequently by teams. The second, is a systematized implementation audit form to guide teams in their implementation of potentially better practices. This form will be used primarily by local change team leaders, and will typically be used on a monthly basis.

All of these data tools will be run through a central data collection system called REDCap. REDCap is a secure online data entry system to support HIPPA compliant multi-center data aggregation.

As of the the 2014 revision of this toolkit, two data sets have been developed to examine NAS management from two complimentary perspectives. The first data set contains patient level data and contains minimal private health information (PHI) that must be collected through a HIPAA compliant system like REDCap. Data collected after September 23, 2013 also requires the execution of a business associates agreement (BAA) in addition to a data use agreement, or the data must be collected under a public health exemption as defined under the HIPAA/HITECH final rule. The second data set contains process measures designed to guide implementation of the potentially better practices listed in the toolkit. No patient level data or PHI is contained in the process measure data set. Data in the second set is collected and analyzed under the terms of the data use agreement. Both the data use agreement and the BAA are included in the project application which is available from the TIPQC office.

Training on data entry, standardized definitions and integration of the data collection system will be provided by TIPQC during the project Kick-off and subsequent Learning Sessions. Individual teams will need to decide who will be responsible for the collection of which data, as well as who will have access to daily reports and collaborative project reports. For this project, the in-patient pharmacy may already be collecting much of the required data and may therefore be in a unique position to report many of the primary measures for this project. Other more traditional approaches include data entry by bedside end-users, project leaders, or designated project data entry personnel.

Some centers already have robust existing clinical data or EMR systems that make their performance on project measures readily accessible, and these centers may consider uploading data from these systems directly into REDCap.
The TIPQC team is available to discuss the pros and cons of this approach for the project and can provide database specifications for uploading data. Individual centers will be responsible for creating and maintaining any software required to upload data to TIPQC, and just as with individual case-by-case data entry, security and validity of bulk data retrieval for upload is the responsibility of the individual participating center.

Teams may well find that additional data, especially process data may need to be collected on the local level in order to address change opportunities identified in key drivers and to ensure high-reliability implementation and sustainment. Minimal process data is included in the required and optional data sets. Additional process data can be obtained using the monthly potentially better practice implementation audit form. Teams may find further process data is needed on a limited basis to address specific local challenges and barriers to implementation.

**Practice Analysis and Potential Change Targets**

While data is essential for quantitative quality improvement, data collection by itself is not an improvement! To improve, we have to study our local system, and then test alternatives to determine which potentially better practice, when reliably implemented, delivers measureable improvement in the local system. This is the core of the Shewart Cycle or Model for Improvement that will be covered in the kick-off and subsequent learning events. ([http://www.tipqc.org/qi](http://www.tipqc.org/qi))

The breadth of options and approaches that might be considered by a change team contemplating improvements in the management of NAS is dauntingly large. Accordingly the remainder of this toolkit is offered as a guide to participating change teams as they search for “where to begin.” The following outline is not intended to be exhaustive, but is rather a shared starting point to help participants identify potential high-value change targets in their system (so-called “low-hanging fruit”) and then rapidly move on to resources that will assist in designing local change initiatives.

The development team has organized these practices with the assumption that participating centers have some minimal system, formal or informal, in place for the management of NAS. Accordingly the first section in the menu focuses on review and assessment of your existing infrastructure to support NAS management, while the next sections focuses on specific interventions that an NAS management program might include, and the 3rd section focuses on the critical clinical NAS scoring process. This approach should allow centers with robust, highly protocolized practices a ready means to systematically review and improve their practice. For centers starting with minimal formal infrastructure, this organization provides guidance to create the minimal system required to implement the specific interventions.
Menu of Potentially Better Practices Overview

1. Review and assess current NAS management approach in your unit
2. Establish/refine a standardized NAS management approach
   a. detection/screening
   b. non-pharmacological management
      i. behavioral
      ii. environmental
   c. pharmacological management (list of potential meds)
   d. scoring system
   e. transition to outpatient follow-up (discharge on meds)
3. Monitor evidence implementation
   a. outcome and QI measures
   b. consistent scoring system- inter-observer reliability and frequency
   c. consistent responses to scores
4. Engage upstream and downstream stakeholders
5. Monitor environment, caregivers, and families

The following topics represent specific areas in quality improvement methodology that are likely to be helpful in the execution of any QI project. Some of this material will be covered during NAS learning sessions; however, centers may wish to review these topics by referring to the “Just In Time” training modules on the TIPQC website (http://www.tipqc.org/jit). New TIPQC participants may want to review the video of the QI 101 session from the March 2011 TIPQC meeting.

Project Implementation Topics
- Care and Feeding of the Project Team
- Unit Education
- Create a Culture of Safety
- Transparency
- Audit processes
- Focus groups
- Empower Parents
- Celebrate Success

Finally, the process of review and reflection on your center’s data is not intended to be limited to project start-up. Indeed, this activity should be integrated into each PDSA cycle as successive iterative improvements are implemented and refined or rejected. Successful teams typically will find that after studying and acting on their data, they are brought full circle back to the 3 central question in the IHI model for improvement: 1) What are we trying to accomplish? 2) How will we know that a change is an improvement? 3) What change can we make that will result in improvement? (http://www.tipqc.qi) Reflection on these three questions leads the successful team back to their aim, their measures, and a consideration of their practices and alternative potentially better practices listed below or elsewhere in the literature.
NAS Management
Potentially Better Practices

Potentially Better Practice #1: Review and Assess current NAS management practices in the NICU

**Rationale:** To define current management and outcomes

**Strategies:**
- Evaluate current multidisciplinary interest and involvement
  - Should include care providers as well as social services, pharmacy, case management, and hospital administration officials
- Survey Care Providers regarding attitudes, knowledge, and skill related to NAS management
  - Should include neonatologists, obstetricians, other physicians, nurses, nurse practitioners, social workers, case managers and dietitians
  - Can be done in group meetings or one-on-one using written or verbal feedback
- Evaluate current policies and procedures for NAS management (see AAP guidelines)
- Evaluate current policies and practices for measuring NAS signs
- Evaluate current environmental management approaches, thresholds for implementation
- Evaluate current pharmacological management approaches, thresholds for implementation, dose adjustment, and weaning
- Evaluate reliability and consistency of measurement, response to threshold values; choice of primary pharmacological agent; indication for and choice of adjuvant pharmacological agents

**Measures:**
- How many babies have been treated for NAS in the past year (total number and percent of admissions)
- How many babies have been admitted for NAS only
- Mean, median and range of length of stay
- Mean, median and range of pharmacologic treatment (end at day of discharge if sent home on meds)
- Maximum opiate dose
- Adjunctive pharmacologic treatment (eg, phenobarbital, clonidine)
- Specific non-pharmacologic strategies
Pharmacologic treatments at discharge and strategies for discontinuation

Possible Challenges:
• Physician or staff pre-conceived opinions and biases may hinder development of a successful NAS approach
• Lack of support from family and community
• Lack of administrative support may hinder development of supportive NAS management infrastructure needed for consistent approach
• Systematic scoring and collection will increase workload of nursing and/or pharmacy staff
• Optimized management will require increased involvement of primary care system after discharge which may not have education, infrastructure or reimbursement model needed for transition to outpatient follow-up.

Potentially Better Practice #2: Establish/refine a standardized NAS management approach

Rationale: Formulating an evidence-based practice for NAS management in the nursery will provide caregivers with a consistent, reliable plan for managing infant with in-utero exposure. Practically, an NAS management paradigm can be divided into 5 complementary and interdependent components.

a. detection/screening
b. non-pharmacological management
   i. behavioral
   ii. environmental
c. pharmacological management (list of potential meds)
d. scoring system
e. transition to outpatient follow-up (discharge on meds)

PBP 2a Detection of and Screening for Neonatal Abstinence

Rationale: Optimal management requires reliable detection of neonatal abstinence syndrome. Once NAS is identified in a given patient, management can be divided into non-pharmacological and pharmacological (see PBP #2c) strategies- both of which are best driven by the high-reliability implementation of a validated withdrawal scoring system. (see PBP #2d).

Strategies: Detection of neonatal abstinence requires both attention to maternal history and risk factors as well as vigilance for the emergence of symptoms in infants where maternal history is non-informative. Specific tools, strategies and opportunities to consider include:

1) Evaluate current detection “system”- how are infants with NAS currently identified, by whom, and how- by history, by laboratory screening, or by clinical diagnosis of NA? Identify gaps in your detection “system,” and
seek interested stakeholders to work with the team to improve early systematic detection.

2) Discuss and review with maternal providers current maternal screening paradigm with careful attention to communication gaps between maternal and infant healthcare teams.

3) Review of maternal drug screening guidelines- who is screened, what are the triggers for screening, when are mothers screened, what testing is used, and what are the mechanisms for differentiating and appropriately communicating screening versus confirmed positive results. (see Evidence Review- Urine drug screening)

4) Review infant care (NICU, normal nursery, ward, ED) screening paradigm with careful attention to communication gaps between infant and maternal healthcare teams.

5) Devise and implement a unified screening approach that consistently identifies neonatal abstinence syndrome across the perinatal care spectrum in your facility.

Measures:
- Percent completion of Basis of NAS Diagnosis
- Percent completion of Source of substance
- Local review of readmissions with a potentially NAS attributable diagnosis
- Reliability audit of detection and screening guideline implementation

Possible Challenges:
- Communication with multiple obstetric providers in widely separated areas
- Fear of alienating mothers who do not use drugs.
- Fear of reducing maternal compliance receiving indicated therapy

PBP 2b Non-Pharmacologic Treatment of Neonatal Abstinence

Rational: Once neonatal abstinence syndrome is identified (see PBP# 2a) in a given patient, management can be divided into non-pharmacological and pharmacological (see PBP #2c) strategies- both of which are best driven by the high-reliability implementation of a validated withdraw scoring system. (see PBP #2d).

Strategies:

There are several non-pharmacologic treatments that can be used to support infants experiencing neonatal abstinence. These treatments should be implemented whether the infant requires pharmacologic management or not.

1) Assess for signs of withdrawal using an objective and a standardized neonatal abstinence assessment tool (American Academy of Pediatrics, 1998; Hamdan, 2008). The Finnegan Scoring Tool measures the severity of specific withdrawal behaviors, and can be used to set decision
thresholds for escalation of NAS management. When non-pharmacologic measures (below) have been optimally applied, consider starting pharmacologic management if the cumulative score is 8 or greater (Torrence & Horns, 1989; Finnegan, et al, 1975; Merker, et al., 1985).

2) Reduce ambient light exposure (Hamdan, 2008; Lauridsen-Hoegh, 1991; Finnegan & Kaltenbach, 1992; Torrence & Horns, 1989; Gosse, 1992; D’Apolito & Hepworth, 2001). Consider covering the bassinet with a receiving blanket to shield the baby’s eyes from the ambient light (Lauridsen-Hoegh, 1991; Gosse, 1992).

3) Minimize excessive noise (Lauridsen-Hoegh, 1991; Finnegan & Kaltenbach, 1992; Torrence & Horns, 1989; Hamdan, 2008). Place the infant in a quiet environment. This may help reduce sleep disturbances. Limit talking near the infant’s bed. It is also helpful to place the infant’s bed in a quiet section of the nursery if possible (Lauridsen-Hoegh, 1991; D’Apolito & Hepworth, 2001).

4) Swaddle the infant in a blanket to provide containment (Hamdan, 2008; Finnegan & Kaltenbach, 1992; American Academy of Pediatrics, 1998; D’Apolito & Hepworth, 2001). Swaddling will assist the infant in their ability to control tremors or a hyperactive Moro reflex (D’Apolito & Hepworth, 2001). Swaddling also stops the infant from thrashing about when the central nervous system is disorganized. It is helpful to position the infant’s knees and hips in flexion when swaddled and the ankles dorsiflexed. Flexion counteracts the high extensor tone and the tendency of the baby to arch his/her back (common in this population)( Lauridsen-Hoegh, 1991).

5) The role of breastfeeding in the setting of neonatal abstinence syndrome is controversial. For mothers on a stable maintenance methadone regimen, breastfeeding may reduce length of stay, though care must be taken in weaning from mother’s own milk. (Dryden 2009, Isemann 2011.) Outpatient follow-up and likelihood of sustaining breastfeeding in the outpatient setting need to be considered carefully as Isemann’s group noted a 5% readmission rate in this population due to rebound NAS following abrupt reductions in breast milk intake. Even in centers with notably high rates of successful breastfeeding initiation and sustainment, initiation rates are low, and sustainment beyond the first week of life is exceedingly challenging among dyads where the mother is on opiate substitution therapy (Wachmann 2010.)

6) Consider small frequent feedings of a hypercaloric (24 cal/oz) formula for proper growth of an infant experiencing significant withdrawal. Caloric intake should be calculated daily to provide 150-250 cal/kg/day as necessary (Hamdan, 2008; Velez & Jansson, 2008; Lauridsen-Hoegh, 1991; Jorgenson, 1992; Torrence & Horns, 1989; Wilson, 1975; Hill &
Desmond, 1963). It is important not to over-feed infants who exhibit excessive sucking or increased irritability. Sometimes excessive sucking in interpreted at hunger and over feeding may result in regurgitation or vomiting. Maintain the infant on the appropriate number of calories/kg/day to maintain growth (D’Apolito & Hepworth, 2001). Many drug-exposed infants may have a disorganized suck when feeding despite excessive non-nutritive sucking. Gavage feeding may be necessary if infants are unable to take the necessary amounts of nutrition by breast or bottle (Jorgenson, 1992).

7) Offer the infant a pacifier (Weiner & Finnegan, 2006; Hamdan, 2008). Providing sucking with a pacifier will assist the infant with excessive sucking needs (D’Apolito & Hepworth, 2001).

8) Avoid unnecessary handling and abrupt changes in the infant’s environment (Hamdan, 2008). Gentle awakening of the infant prior to performing procedures, moving the infant slowly and containing the infant’s extremities while undressing may help to diminish tremors and/or a hyperactive Moro reflex. These interventions may also decrease the infant’s respiratory rate by decreasing startles from unexpected activity (D’Apolito & Hepworth, 2001; Harrison, 1997).

9) Keep the infant dressed in a shirt, diaper, swaddled in a blanket and place another blanket over the infant while in the crib. This will help to distinguish between a fever due to withdrawal or over dressing (D’Apolito & Hepworth, 2001).

10) Aspirate nasal secretions with a bulb syringe when needed (Weiner & Finnegan, 2006).

11) Provide boundaries around the infant when in the bed (Jorgensen, 1992).

12) Allow the infant hand-to-mouth opportunities. This can be accomplished by allowing the infant’s hands near their face when swaddled in a blanket. This will assist the infant in self-regulatory behaviors that may decrease energy expenditure (Jorgensen, 1992; Frank & Vilardi, 1995; Lauridsen-Hoegh, 1991; D’Apolito & Hepworth, 2001).

13) Weigh the infant daily (Lauridsen-Hoegh, 1991.)

14) Avoid overstimulation. Consider doing one thing at a time with the infant since even simple procedures can startle the infant (Gosse, 1992; Velez, & Jansson, 2008).

15) Consider applying clear transparent dressings over reddened or excoriated areas on the elbows, knees, heels (Weiner & Finnegan, 2006).
16) A plan should be in place for the transition to current safe sleep guidelines. Caregiver education and modeling of current safe sleep guidelines should be undertaken. Avoid the use of soft sleeping surfaces in the bed and prone positioning because of the risk of sudden infant death syndrome in this population (Kandall, 1999; Franck & Vilardi, 1995; American Academy of Pediatrics, 2011).

**Measures:**
- Serial review of local guideline for non-pharmacological management of NAS
- Reliability audit of implementation of non-pharmacological management guideline
- Change in LOS over time
- Proportion of Infants Failing non-pharmacological measures
- Change in Readmissions (Balancing)

**Possible Challenges:**
- Patience to see if non-pharmacologic treatment is effective.

**PBP 2c Pharmacological Management of Neonatal Abstinence**

**Rational:** Once neonatal abstinence syndrome is identified (see PBP# 2a) in a given patient, management can be divided into non-pharmacological (see PBP #2b) and pharmacological strategies - both of which are best driven by the high-reliability implementation of a validated withdraw scoring system. (see PBP #2d).

**Strategies:** A variety of agents and specific strategies have been proposed and implemented. Four strategies, demonstrating a variety of approaches are outlined below. Change teams are encouraged to review their current practice, and in consultation with local hospital pharmacy devise a local consensus strategy with input from physicians attending in your unit. While detailed consensus is challenging to achieve, inter-provider variation in agent and approach will make systematic, data-driven improvement difficult if not impossible to achieve. Direct leadership of this effort by the medical director of the unit is strongly advised, and oversight of this activity by the medical director is essential.

**GENERAL CONSIDERATIONS:**
1) It is likely that infants exposed to multiple illicit or licit drugs in utero may benefit from the use of more than one treatment drug. Polydrug withdrawal is typically treated with opioids alone. If control of withdrawal signs cannot be achieved adding a drug such as Phenobarbital or Clonidine may be helpful (Johnson, 2005; Sarkar & Donn, 2006; Zahorodny et al, 1998).
2) An opiate such as morphine or dilute tincture of opium should be used as initial treatment for infant withdrawal signs due to maternal opioid use in pregnancy (Osborn, S., Jeffery, H., & Cole, M., 2005).


4) When treating infants for NAS the dosing interval should not be more than 4 hours because longer dosing intervals are associated with longer hospital stays (Jones, 1999).

5) Opioids are the drugs used most often by neonatologists. Methadone is used 20% of the time and opioids other than methadone are used 63% of the time (Sarkar & Dunn, 2006). Many hospitals today use alcohol free oral morphine sulfate (0.4 mg/ml). Other drugs that contain the same morphine equivalent as oral morphine include dilated tincture of opium and paregoric. Paregoric is no longer used because it contains toxins such as benzoic acid, camphor and alcohol (45%). Methadone has a long half-life (up to 62 hours in infants) and is hard to wean because of this (Berde, et al, 1987). Diazepam is no longer used to treat NAS because it may cause late-onset seizures and excretion of the drug is prolonged in the neonatal period (American Academy of Pediatrics, 1998).

6) Normal sucking is restored when infants in withdrawal were treated with an opioid rather than phenobarbital (Finnegan, et al, 1975; Kron, Litt & Finnegan, 1975 & 1976).

7) Treatment with an opioid is more effective in preventing seizures associated with neonatal abstinence than treatment with diazepam or phenobarbital (Herzlinger, et al., 1977 & Pacifico, et al., 1989).

8) Opioids were found to be more effective in controlling signs of NAS than combined treatment with sedatives (Kaltenbach & Finnegan, 1986). The American Academy of Pediatrics recommends oral morphine or methadone should be used when pharmacologic treatment is indicated (AAP, 2012).

9) There is not enough evidence to identify the drug that should be used to treat NAS from polydrug exposure (AAP, 2012). Phenobarbital in conjunction with an opiate has been shown to decrease signs of withdrawal more effectively than single agent management of NAS in infants with polydrug exposure (Finnegan, et al, 1984; AAP, 1998; Colye, et al, 2002, NSW Department of Health, 2006; Osborn, Jeffery & Cole, 2005).
EXAMPLE TREATMENT PROTOCOLS:


Infant: Oral Morphine Treatment
Treatment Protocol with Oral Morphine Sulfate Solution 0.40 mg/ml solution.
Optimal Morphine dosing is Q3-4 hr. Do not exceed 4 hours between morphine dosing.
Initial Dose: Score the baby before a feeding before starting treatment.

<table>
<thead>
<tr>
<th>Score</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-8</td>
<td>0.0</td>
</tr>
<tr>
<td>9-12</td>
<td>0.1cc (0.04mg) X1 (requires re-scoring before treating). Base treatment on the highest score</td>
</tr>
<tr>
<td>13-16</td>
<td>0.2cc (0.08mg) X 1 (does not require re-scoring to treat. Treat Immediately).</td>
</tr>
<tr>
<td>17-20</td>
<td>0.3cc (0.12 mg) X1 (Does not require re-scoring. Treat Immediately).</td>
</tr>
<tr>
<td>21-24</td>
<td>0.4cc (0.16 mg) X1 (Does not require re-scoring. Treat Immediately).</td>
</tr>
<tr>
<td>&gt;25</td>
<td>0.5cc (0.20mg) X1 (Does not require re-scoring. Treat Immediately).</td>
</tr>
</tbody>
</table>

Morphine Maintenance (Escalate Treatment):
Prior to increasing the dose repeat scoring at the end of the feeding to determine need to escalate treatment.

<table>
<thead>
<tr>
<th>Score Remains:</th>
<th>Increase dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>9-12</td>
<td>0.05cc (0.02 mg) – add 0.05cc to initial dose</td>
</tr>
<tr>
<td>13-16</td>
<td>0.10cc (0.04mg) – add 0.10cc to initial dose</td>
</tr>
<tr>
<td>17-20</td>
<td>0.15cc (0.06mg) – add 0.15 to initial dose</td>
</tr>
</tbody>
</table>

Continue to increase using these doses Q3-4hr while the withdrawal score is still between the indicated score range.

Weaning Instructions:
Maintain on dose 48 hours before starting weaning:

<table>
<thead>
<tr>
<th>Score</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-8</td>
<td>0.05cc (0.02mg) oral morphine/day</td>
</tr>
<tr>
<td></td>
<td>Wean infant in this fashion until off morphine for 24 hours prior to discharge.</td>
</tr>
<tr>
<td></td>
<td>Defer wean for score of 9-12</td>
</tr>
</tbody>
</table>
Re-Escalation (prior to increasing the dose at any time, re-score after feeding and increase dose based on the feeding):

<table>
<thead>
<tr>
<th>Score</th>
<th>Increase Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>9-12 for 2 consecutive scores</td>
<td>0.025cc (0.01mg) Q4hr</td>
</tr>
<tr>
<td>13-16 for 2 consecutive scores</td>
<td>0.05cc (0.02mg) Q4 hr</td>
</tr>
<tr>
<td>17-20 for 2 consecutive scores</td>
<td>0.1cc (0.04mg) Q4hr</td>
</tr>
</tbody>
</table>

Consecutive scores include one score before a feeding and another score after a feeding.

*If baby requires greater than 0.5cc (0.20mg) Q3-4hr of oral morphine or infant appears somnolent or difficult to rouse notify treating nurse practitioner or physician immediately.*

Important Note: If baby has a score between 0-8 and 4 hours later a score > 8, use re-escalation dosing and continue using this scale for the remainder of the time.

<table>
<thead>
<tr>
<th>Score</th>
<th>Morphine daily dose (administer in four divided doses)</th>
<th>Morphine single dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-10</td>
<td>0.32 mg/kg/day</td>
<td>0.08 mg/kg</td>
</tr>
<tr>
<td>11-13</td>
<td>0.48 mg/kg/day</td>
<td>0.12 mg/kg</td>
</tr>
<tr>
<td>14-16</td>
<td>0.64 mg/kg/day</td>
<td>0.16 mg/kg</td>
</tr>
<tr>
<td>17+</td>
<td>0.8</td>
<td>0.2 mg/kg</td>
</tr>
</tbody>
</table>
3) Enteral Morphine Protocol for NAS, Developed by Jon Wispe and Jackie Schneider, Nationwide Children’s Hospital (McClead, Franklin TN, 2012)

Enteral Morphine Protocol for
Neonatal Abstinence Syndrome (NAS)

Protocol should be initiated if an infant has 2 consecutive scores ≥ 8 or 1 scores ≥ 12 within a 24 hour period (just as was done previously with the methadone taper).
Concentration of Enteral Morphine to be used for ALL doses: 0.2 mg/ml

Starting Dose:
- Enteral: 0.05 mg/kg/dose po q3hr
- IV: 0.02 mg/kg/dose (IV morphine and enteral morphine doses are not equivalent)

Titration:
- Enteral: Increase by 0.025-0.04 mg/kg every 3 hrs until controlled (NAS < 8)
- IV: increase by 0.01 mg/kg every 3 hrs until controlled (NAS < 8)

*Rescue Dose*: If infant has 1 score of ≥ 12, double the previous dose given (enteral or IV) x 1 and then adjust accordingly:
- If NAS score now < 12: make the scheduled maintenance dose (MD) the same as the rescue dose that was just administered. The first higher MD should be given at the next scheduled care/feed.
- If NAS score still ≥ 12: increase next dose by 50%. Continue to do so until score is < 12. Once < 12, then follow guideline listed above.
Enteral Morphine Protocol for
Neonatal Abstinence Syndrome (NAS)

**Wean:** Once stabilized on a dose for 72-96 hours, use this dose as the starting point of the wean *(please note this dose on infant’s card).* Begin weaning the dose by 10% (of the original dose when the first wean was started) every 24-48 hours. Drug may be discontinued when a single dose is < 0.02 mg/kg/dose. Please see below for example.

*Ad lib infants*: Given the shorter duration of action of enteral morphine, it is best suited to be dosed on a q3hr schedule. Infants should be allowed to ad lib feed volumes but kept on a q3hr schedule.

*Backslide*: If infant’s NAS scores become consistently elevated (ex: 2 consecutive ≥ 8) during the weaning process, assure that nonpharmacological measures are optimized (ie: swaddling, holding, decreased stimuli, etc) before going back to previous dose at which patient was stable. If infant’s scores continue to be elevated (even after physical exam to ensure nothing else is wrong/bothering the infant), adjust medication and/or continue to back up in a stepwise fashion until patient’s scores are <8. Once stabilized on new dose for minimum 48 hrs, resume 10% wean but consider weaning at longer intervals.

**Discharge:** Observe in-house x 48-72 hours off of medication before discharge.
4) Enteral Morphine Protocol for NAS, Developed by Gary Snyder, MD, and the Pediatrix Medical Group of Central Ohio (2011)

Phase 1: To treat, or not to treat.

**NAS Management Algorithm**

**Phase #1 To Treat or Not:**

Employ comfort measures and rescore 1 hour later

- Scores ≥9
  - Next score is <9
    - Admit to NICU and Start Morphine

- Scores <9
  - Resume original q3h Scoring Schedule (next score on the 3h mark) until first 72h of scoring is complete

**Qualifies for NAS scoring (q3h):**

Scores done for minimum of 72h from the first score.

**General Scoring Rules Through the Entire Algorithm:**

1. Scoring Interval "Clock" should be in sync with q3h cares/feeds and carried all the way through until dic.
2. Anytime a score ≥9 follows a lower score, Non-Pharm Measures are employed followed by another score 1 hour later. The very next score should be done back on the original q3 interval "clock."
3. Anytime scores are ≥9 twice in a row, Pharm action is called for and the new dose/drug given ASAP w/ scoring resumed on the current q3h "clock."
4. Anytime a change in drug or dose is made, the 24h scoring countdown begins w/ the next rounding period after the drug is given.
5. Anytime criteria are met to extend scoring another 24h, the countdown begins ("zeros") in sync with rounds. For example, if a backside occurs at noon, zero-time for 24h weaning occurs during the next rounding period. AIM the next day.

**Hold discharge and continue q3h Scoring**

- Last 2 scores are increasing.
  - Last 2 scores < 9 & not increasing.
    - Go to NAS Stabilization Phase #2

- Last 2 scores < 9 & not increasing.
  - Home with NCH F/u within a week.

*Starting Morphine Doses:
  - IV @ 0.02mg/kg/dose
  - Ent @ 0.05mg/kg/dose
**Phase 2: Stabilization on Morphine**

**NAS Management Algorithm**

**Phase #2 Stabilization:**

- Baby is now on Morphine.

Continue q3h scoring

- No consecutive scores $\geq$ 8
- Scores 9-12 x2 in a row
- Scores $> 12$ x2 in a row

**No change in dose**

- No dose changes for the 48h before rounds

**Increase Morphine dose by 0.02mg/kg ent or 0.01mg/kg IV**

- No dose changes for the 48h before rounds

**Increase Morphine dose by 0.04mg/kg ent or 0.02mg/kg IV**

- No dose changes for the 48h before rounds

Go to Weaning Phase

*MAX of 0.2mg/kg/dose ent
MAX of 0.1mg/kg/dose IV

If max dosing of morphine does not lead to the Weaning Phase start on Phenobarbital Load with 10mg/kg
Maintain on 4mg/kg/d
Phase 3: Weaning Morphine

**NAS Management Algorithm**

When entering Phase 3, start by weaning the Morphine dose after rounds.

Determine amount to wean by:

For the weaning increment, use the higher dose between:
- 0.01 mg/kg/dose enterally
- 0.005 mg/kg/dose IV
or
10% of the stabilization dose

Then continue q3h scoring.

Scores ≥ 9 twice in a row

Follow Backslide Mgt.

Scores ≥ 9 twice in a row

Follow Backslide Mgt.

No consecutive scores ≥ 9 for 24h

In the second 12h:
- has a score of ≥9
  - or
- shows a rising trend in last 3 scores.

Repeal wean q24h until dose is @ or below:
- 0.01 mg/kg/dose enterally
- 0.005 mg/kg/dose IV
Then stop the morphine.

Then continue q3h scoring.

In the last 12h:
- has a score of ≥9
  - or
- shows a rising trend in last 3 scores.

No dose change and score another 24h

In the last 12h:
- has a score of ≥9
  - or
- shows a rising trend in last 3 scores.

No dose change and score another 24h

Home w/ NCH I/f/u within the week.
Phase 3: Backsliding

NAS Management Algorithm

Backslide = Two consecutive scores of \( \geq 9 \) During the Weaning Phase

Scores < 9 for 24h and not climbing

In the second 12 hours, Scores \( \geq 9 \) or are Climbing

Stay at Step One & score another 24h.

Return to Weaning

Backslide Mgt Step One:
Resume previous dose where patient was stable.

In the second 12 hours, Scores \( \geq 9 \) or are Climbing

Stay at Step One & score another 24h.

Return to Weaning

Backslide Mgt Step Two:
Go Back up Dosing Ladder* until scores are \( < 9 \) for 24h

MAX of 0.2 mg/kg/dose ent MAX of 0.1 mg/kg/dose IV

Scores < 9 for 24h and not climbing

In the second 12 hours, Scores \( \geq 9 \) or are Climbing

Stay at Step Two & score another 24h.

Return to Weaning

Backslide Mgt Step Three:
Add phenobarbital (if not already on it)

In the second 12 hours, Scores \( \geq 9 \) or are Climbing

Stay at Step Three & score another 24h.

Return to Weaning
4) Western Australian Centre for Evidence Based Nursing & Midwifery, 2007

Guidelines for the Pharmacologic Management of NAS

**Oral Morphine Regime**

<table>
<thead>
<tr>
<th>NAS score (every 4 hours)</th>
<th>Dose/Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score average &gt; 8 for 3 scores</td>
<td>Morphine 0.5mg/kg/day in 4 divided oral doses</td>
</tr>
<tr>
<td>If score persists &gt;8 despite morphine 0.5 mg/kg/day</td>
<td>Morphine 0.7 mg/kg/day in 4 divided oral doses</td>
</tr>
<tr>
<td>If score persists &gt;8 despite morphine 0.7 mg/kg/day</td>
<td>Morphine 0.9 mg/kg/day in 4 divided doses</td>
</tr>
<tr>
<td>When infants are on 0.9 mg/kg/day</td>
<td>Monitor cardio-respiratory function</td>
</tr>
</tbody>
</table>

**Weaning Infants from Morphine**

1) There is little evidence on how to wean infants from morphine. When scores fall below treatment level (< 8) for 48 hours, reduce the dose by 0.05 mg/dose every 4 days or longer, depending on the scores.
2) Given the half-life of morphine it is more appropriate to reduce the dose rather than the frequency.
3) The usual length of morphine treatment ranges from 1 to several months (Osborn, 2007).

**Management of the Vomiting Baby**

1) Administer morphine before a feeding
2) Give small feedings frequently
3) Ensure the infant is not being overfed
4) Posture the infant appropriately during and after a feeding
5) If the infant has a large vomit after being given morphine:
   a) If vomiting within 10 minutes of dose, re-dose
   b) If vomiting after 10 minutes of dose, give ¼ dose
   c) If vomiting occurs after feed, do not give further morphine

**Pharmacologic Management of Non-Opioid Induced NAS**

<table>
<thead>
<tr>
<th>NAS score (every 4 hours)</th>
<th>Dose/Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score average &gt; 8 for 3 scores</td>
<td>Phenobarbital 15 mg/kg oral or IM stat (loading dose) then 6 mg/kg/day in 2 divided doses orally (maintenance dose)</td>
</tr>
<tr>
<td>If score persists &gt;8 despite phenobarbital 6 mg/kg/day</td>
<td>Phenobarbital 8 mg/kg/day in 2 divided doses orally</td>
</tr>
<tr>
<td>If score persists &gt;8 despite phenobarbital 8 mg/kg/day</td>
<td>Phenobarbital 10 mg/kg/day in 2 divided doses orally</td>
</tr>
<tr>
<td>When infants are on 10 mg/kg/day</td>
<td>Monitor cardio-respiratory function</td>
</tr>
</tbody>
</table>
Barbiturate Withdrawal:
When scores fall below treatment level (≤ 8) for 48 hrs reduce the dose by 2 mg/dose every 4th day or longer depending on scores (Osborn, 2007).

Non-Barbiturate Withdrawal (e.g. benzodiazepines):
The dose may be reduced more rapidly after withdrawal symptoms settle (Osborn, 2007).

**OTHER DOSING CONSIDERATIONS:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Dose</th>
<th>Increment</th>
<th>Maximum Dose</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral morphine</td>
<td>0.04mg/kg Q3-4 hr</td>
<td>0.04mg/kg/dose</td>
<td>0.2mg/kg/dose</td>
<td>Khoo, 1996; Jackson et al, 2004; Langenfeld, et al, 2005; Agthe et al, 2009</td>
</tr>
<tr>
<td>Oral methadone</td>
<td>0.05-0.1 kg/kg Q 6 hr</td>
<td>0.05 mg/kg/dose</td>
<td>To effect</td>
<td>Lainwala et al, 2005</td>
</tr>
<tr>
<td>Oral clonidine</td>
<td>0.5-1ug/kg Q3-6hr</td>
<td>Not studied</td>
<td>1 ug/kg Q3hr</td>
<td>Hoder, et al, 1984; Agthe et al, 2009; Leikin, et al, 2009; Esmaeili, et al, 2010</td>
</tr>
<tr>
<td>Sublingual Buprenorphine</td>
<td>13.2-39.0 ug/kg/day in 3 divided doses</td>
<td>Not yet known</td>
<td>Not yet known</td>
<td>Kraft, et al, 2008</td>
</tr>
<tr>
<td>Sublingual Buprenorphine</td>
<td>15.9 ug/kg/day in 3 divided doses</td>
<td>25% for NAS scores ≥ 24 total on 3 measures or a single score of ≥ 12. Rescue doses of 50% previous dose if not controlled, subsequent dose increased by 25%</td>
<td>60 ug/kg/day. Phenobarbital was added 20mg/kg load followed by 2.5 mg/kg 2X/day for 2 days. Phenobarbital was discontinued before reduction of the buprenorphine</td>
<td>Kraft et al, 2011</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>15-30mg/kg loading dose. 30mg/kg dose was divided into 3 oral doses Q 12 hrs</td>
<td>Maintenance: 5-10 mg/kg/day in 2 divided doses and titrated against scores. Decrease dose to 3 mg/kg/day. Discontinue when serum level &lt; 15 mcg/ml</td>
<td>10mg/kg/day</td>
<td>Khoo, 1995; Finnegan, 1984 Coyle, 2002; Weiner &amp; Finnegan, 2006</td>
</tr>
</tbody>
</table>
5) Pilot Center Protocols

Each of the pilot centers has developed local protocols for management based on review of the literature and local experience that are somewhat specific to the local patient population and resource options. These protocols have been added to the project forum that is available to project participants after completing the project application. The pilot centers have shared these “works in progress” in hopes that they will be helpful to you, and that your team will, in-turn, share your protocol on the forum.

Measures:

• Serial review of local guideline for pharmacological management of NAS
• Reliability audit of implementation of pharmacological management guideline
• Change in LOS over time
• Change in Readmissions (Balancing)

Possible Challenges:

• Scoring systems have not been formally evaluated or optimized for poly-substance NAS
• Evidence to guide management of poly-substance NAS is limited, and achieving a consensus based approach to care may be difficult

PBP 2d Implement and Ensure High-Reliability Sustainment of a Validated Neonatal Abstinence Clinical Scoring System

Rationale: Once neonatal abstinence syndrome is identified (see PBP# 2a) in a given patient, management can be divided into non-pharmacological (see PBP #2b) and pharmacological (see PBP #2c) strategies- both of which are best driven by the high-reliability implementation of a validated withdraw scoring system.

Strategies: Local change teams may adopt a number of approaches depending on local challenges and resources. As outlined in the evidence review a number of scoring systems are available. These vary with respect to validation and with cost vs. benefit for implementation. Change teams should consider carefully the amount of time a scoring system takes to execute, the validity of the score in the local context and patient population, and the degree to which different scores may or may not provide reliable, validated clinical decision making thresholds for management.

Measures:
NAS Management Optimization: A TIPQC Inter-institutional QI Project

• Serial review of local guideline for standardized scoring of NAS and response to NAS scores
• Reliability audit of implementation of standardized scoring system including inter-operator reliability of frequency of scoring, scoring, and response to score
• Change in LOS over time
• Change in Readmissions (Balancing)
• Statewide Centers completed validation training/Centers participating in project
• Graphic fraction of centers completing over time
• Stratified analysis of results of centers completers vs. non-completers

Possible Challenges:
• Should you intensively train all nurses, or just a core group that will do all the scoring? The latter would be more consistent but likely cause scheduling problems.

PBP #2e Transition to Outpatient Follow-up with Neonatal Abstinence

Rational: Patients benefit from a post-discharge follow-up "safety net" upon discharge from the NICU. These infants can be very challenging. It is beneficial for the NICU to insure that the parents have scheduled a follow-up appointment with a pediatrician and any other follow-up services that are considered to be beneficial.

Strategies: These strategies may include, but are not limited to:

1. Educate Biological parents proactively in anticipation of the DCS reunification efforts

2. Educate potential foster parents regarding the challenges associated with taking on the care of a NAS infant (ETCH is developing a class with DCS for this)

3. Educate health department regarding the challenges associated with taking on the care of a NAS infant

4. Referral to local health departments (e.g., Helping Us Grow/HUG in TN) and early intervention programs (e.g., TN Early Intervention System/TEIS),

5. Follow-up developmental screening via Pediatric Physiatry,

6. Home health referrals for nursing, social work, and therapy (if needed)
7. Educate DCS regarding the medical and long term follow-up needs
8. Educate primary care physician offices regarding follow-up recommendations

Measures:
- Tracking of post-discharge hospital re-admissions
- Tracking post-discharge physiatry follow up compliance if utilizing an outpatient follow up paradigm
- Partner with Fetal Infant Fatality Review Teams in the state to determine the number of infant deaths potentially attributable to substance abuse or impaired caregiver
- Establishing relationship with Home Health Agencies to monitor and enhance compliance with follow-up recommendation

Possible Challenges:
1. Though possible (Backes 2011), transition of pharmacological management to an outpatient setting may by problematic for multiple reasons:
   a. Difficulty obtaining medication via community retail pharmacies in order to continue weaning process post-discharge,
   b. Difficulty locating medical follow-up providers willing to manage post-discharge weaning process,
   c. Inconsistent weaning approaches among follow-up providers,
   d. Caregiver non-compliance with medication administration and follow-up with follow-up care providers, apparently due to multiple factors (e.g., diversion of medication and denial of need for medication and follow-up), and
   e. Caregiver requests for duplicate prescriptions from follow-up providers.
2. Limitations of caregivers
3. Inconsistent reinforcement by follow-up providers
4. Post-discharge placement changes
5. Social stigma
6. Lack of knowledge regarding disease process
7. Lack of research regarding long term outcomes
8. Financial limitations

Potentially Better Practice #3: Monitoring Implementation of Evidence-Based Practice

Rationale: One of the fundamental questions in quality improvement methodology is “how will you know if a change is an improvement?” Without measurement, the simple answer is you will not know. Without measurement,
we don’t know if we are actually implementing current practice, and we certainly can’t know whether a change in practice is an improvement, or just more noise in our system. Accordingly, this toolkit seeks to link a menu of evidence based options with a turn-key data system that will facilitate rigorous, quantitative quality improvement.

**Strategies:** Many of the issues around data collection, data entry, report generation, and review of on-demand SPC analyses are covered in the data sections that precede this menu of potentially better practices. A few specific team strategies are listed below:

- Many teams find that simply sitting down to answer the questions who, what, when, where, and how often will form the backbone of a data entry plan. Answering why often facilitates reliability, and helps minimize the infamous “garbage in, garbage out” phenomenon.
- REDCap Data forms are organized to facilitate data entry by different personnel who may have better access to specific pieces of data. For example admission data could be entered by a unit receptionist or ward clerks, pharmacy data could be entered from the hospital pharmacy, and clinical data may be best entered by bedside nurses.
- Some centers choose to have very few data entry personnel in order to ensure maximal consistency. Other centers choose to distribute data entry widely to maximize involvement and encourage ownership of the clinical processes and outcomes that the data seeks to measure.
- Daily review of the daily rounding report generated in REDCap will not only facilitate execution of tests of change, but also provide an opportunity to rapidly detect and correct data entry errors and misguided project processes.
- Review of data quality and data timeliness is essential to producing meaningful analytic results that will guide improvement over time. Highly successful teams will perform occasional periodic audits of their own REDCap data to ensure the data entered into REDCap matches clinical reality as closely as possible.
- Designating a project data champion to review your center’s data processes and watch for potential problems in data collection and report review can be essential for long term success.
- Engage unit and hospital leadership; ask for assistance with the data workload; *and ask to be held accountable* with at least monthly reporting of cases entered, current data lag, and progress to date.

**Measures:** The following measures appear in your REDCap report and may be helpful in optimizing data collection, review of analyses, and implementation of tests of change.

- Data lag- a measure of time since your team’s last REDCap session, often shared in a “box-and-whiskers” plot at regional and state meetings.
• Data checks- broad series of data checks developed from experience that helps identify most common data entry errors. Appears on the daily rounding report.

Possible Challenges:
• You will be working to improve your clinical practice based on the results of your individual SPC analyses. The analyses are only as good as the data your team enters into REDCap. Your opportunity for measurable improvements for your patients is limited by the quality of the data you enter.
• Single data “czars” are great for consistency, but can create real challenges if they become ill or move to another position or institution.
• Broad distribution of data entry is great for project engagement by staff, but can create real challenges for consistent application of definitions during data entry.
• Data lag happens much faster than expected.
• Data entry errors can create very interesting if not outright misleading analyses. Correct errors early. Consult with the TIPQC office when reports look strange or don’t appear to reflect clinical reality.
• Data entry is resource intensive, and resources may be limited.

Potentially Better Practice #4: Engage Upstream and Downstream Stakeholders

Rationale: In order to decrease the number of infants affected by NAS, upstream stakeholders should be engaged in provider and community education efforts intended to decrease drug use in women of child-bearing age. Downstream stakeholders should be involved in order to facilitate the process of arranging appropriate follow-up for infants with NAS.

Strategies: Both upstream and downstream stakeholders may be engaged by invitation/ involvement in hospital-organized task forces. Such task forces may facilitate the process of stakeholder communication and coordination of limited community resources. Written materials may be supplied by the hospital to support community education and prevention efforts.

Upstream may include, but are not limited to:
1) Primary care providers for women of child-bearing age, including obstetricians and perinatologists,
2) Health departments,
3) Community agencies serving the homeless population,
4) Substance abuse prevention agencies, and
5) Pain clinics and drug rehabilitation programs.
Downstream providers may include, but are not limited to:
1) Primary care providers for drug-exposed infants,
2) Developmental follow-up providers for infants (e.g., NICU developmental follow-up programs/Physiatry, state early intervention programs),
3) School systems and other agencies serving youth, particularly those of middle school age,
4) Criminal justice systems, and
5) Third party payors.

**Measures:** The local change team may consider both quantitative and qualitative measurement techniques. Qualitative measures may be little more than making initial contact with upstream and downstream stakeholders who are “missing” from the local network needed to identify, treat, and follow infants with NAS. Progressively more quantitative approaches might include the frequency of meeting with other stakeholder groups, audits of frequency of referral to specific services where specified by local guidelines, or even formal exchange of data with follow up clinics (e.g. fraction presenting to follow-up after referral at discharge, interval growth, neurodevelopment outcome.)

• Serial review of local opportunities for stakeholder engagement
• Reliability audit of implementation of local strategy and goals for stakeholder engagement

**Challenges:** Upstream providers may face limitations in their education and prevention efforts due to limited funding. There may be inconsistency in follow-up recommendations for infants with NAS, leading to potential obstacles in obtaining funding for these follow-up services.

**Potentially Better Practice #5: Monitor Families, Caregivers, and Environment**

**Rationale:** NAS patients may evoke a wide range of responses from their biological families, foster families, and NICU staff caregivers. Long-term outcome for the infant as well as long-term sustainment of the caregiver role may be facilitated by ongoing reflective evaluation of key relationships required for the patient’s care. Long term improvement in outcomes may be facilitated with appropriate environmental adaptation and additional NAS education for biological families, foster families, and NICU staff caregivers.

**Strategies:** Strategies may be broadly divided in focus between family and nursery staff, though clearly significant overlap may exist, especially for nursery staff who care for these patients on a recurrent basis.

Staff caregiver strategies may include:
• Provision of staff education regarding:
  o NAS treatment protocol (to be provided by NICU)
  o Addictive process (to be provided by NICU social workers, local addiction experts, or hospital employee assistance program); this may include provision of "scripts" to assist staff in dealing with sensitive staff/family issues.
  o Local resources (such as hospital employee assistance program) which may assist staff in coping with stress related to work with this population (i.e., drug-exposed infants and addicted parents).

• Provision of staff forums to provide opportunities for collaboration and follow-up regarding concerns relating to:
  o Protocol use,
  o Work load/staffing issues, and
  o Environmental issues (e.g., noise level, bed spacing, and equipment/supply accessibility)

• Additional hospital resources may help monitor for and prevention of morbidity among staff caregivers.
  o Employee wellness programs
  o Hospital ethics consultation
  o Clinical psychology
  o Pastoral care

Family strategies may include:
• Provision of verbal information and written materials regarding NAS, including symptoms, Finnegan scoring system, treatment, and post-discharge follow-up,
• Provision of social work services (for individuals, families, and groups, such as support groups) to promote bonding and coping with the experience of parenting an infant with NAS. Social Work involvement may include referrals to local community resources for ongoing support and rehabilitation.

Measures: Multiple formal measurement approaches may be considered on the local level.
• Serial review of local opportunities for family and provider support
• Reliability audit of implementation of family and provider support
• Time and motion studies to evaluate unit processes (e.g., evaluation of staff time needed to travel between bedside and Omni-Cell to obtain medications needed by patients on a daily basis),
• Tracking and comparison of length of stay in conjunction with implementation of treatment protocol and environmental adaptation.

Comparatively non-quantitative methods may also provide critical insight into the system of care for these challenging infants. The clinical microenvironment may also be productively defined, evaluated and improved using techniques such as experience-based co-design which are familiar in the NICU. Alternatively, teams
may consider careful modification of potentially better practices from adolescent and adult inpatient addiction treatment.

**Challenges:** Limited funds and staff may prevent implementation of necessary environmental evaluation/adaptation as well as addition of staff needed to implement other strategies.
Evidence Review:
Karen D’Apolito, PhD, APN, NNP-BC, FAAN

Neonatal Abstinence: Strategies and Challenges-
Data from a study of national discharge data between 2000 and 2009 identified a 5-fold increase in infants born to women who consume opioids during pregnancy at a cost of nearly $720 million dollars in hospital charges. This represents a $530 million increase within a 9 year period (Patrick et al, 2012). This increase in neonates who may potentially experience neonatal abstinence presents a challenge to health care providers who care for these infants. Some of these challenges include the following:

1) Differential Diagnosis – Whether a maternal history of drug use is known or not it is important to rule out conditions that may simulate neonatal abstinence syndrome. Consider performing a complete diagnostic work up for sepsis, hypoglycemia, hypocalcemia, CNS hemorrhage, respiratory disorders, hyperbilirubinemia and hypoxic-ischemic encephalopathy. If these conditions are ruled out and signs of withdrawal persist begin neonatal abstinence scoring and confirm withdrawal through neonatal drug screening. Continue scoring for neonatal abstinence until another etiology is found or neonatal abstinence in confirmed (Torrence & Horns, 1989; American Academy of Pediatrics, Committee on Drugs, 1998).

2) Reliability of Scoring - The American Academy of Pediatrics recommends that each nursery use an abstinence scoring method to assess the severity of neonatal abstinence and the need for pharmacologic treatment (Committee on Drugs, 1983). One of the challenges associated with these clinical assessment tools is assurance that the score is reliable. All neonatal abstinence scoring tools list the signs of withdrawal that require assessment. Using a list of signs is an attempt to make the assessment tool more objective (Committee on Drugs, 1983). This, however, is not the case since many of the signs can be interpreted differently by individual scorers. One strategy to improve the accuracy of scoring an infant for signs of withdrawal using these tools is to develop specific definition for each sign comprising the tool. This will help to decrease different interpretations among scorers making the tool more reliable. A program is available that specifically define the items comprising the Neonatal Abstinence Scoring Tool (Finnegan Scoring Tool) developed by Dr. Karen D’Apolito and Dr. Loretta Finnegan and provides a mechanism for staff nurses to obtain inter-observer reliability when using the tool. (D’Apolito, K, 1994; D’Apolito, K, & Finnegan, L., 2010). An inter-observer reliability test can increase the accuracy of this tool. The Finnegan Neonatal Abstinence Scoring tool has a reported inter-observer reliability of 82% (Finnegan, et al., 1975). This reliability can be increased to 90% or greater when staff nurses are trained to use the tool with
increased accuracy (Hamdan, 2008; D’Apolito & Finnegan, 2010). Item definitions have also been published for a modified version of the Finnegan Scoring Tool (Jansson, L., et, al, 2009). In this modified version of the Finnegan Scoring Tool alterations were made in some of the original items listed without reporting a scientific basis for the change. A short version of the tool has been developed and tested for validation however it is recommended this shortened form only be used for initial screening. Beyond screening, the full NASS should be used (Maguire, et al.; 2013.

3) Providing adequate nutrition – It is sometimes difficult for neonates going through active withdrawal to consume an adequate number of calories for growth. Some neonates may be able to nipple adequate calories and fluid while others may require gavage feedings to meet their caloric and fluid requirements. Torrence & Horns, 1989). Some neonates may require small frequent feedings (Jorgenson, 1999). It is essential that neonates are provided adequate calories for growth however caloric requirements can reach 150-250 kcal/kg/day when withdrawal scores are high (Wilson, 1975; Hill & Desmond, 1963; Hamdan, 2008). Neonates may also benefit from receiving a 22 or 24 calorie infant formula to increase calories and normalize electrolytes due to the slight increase in sodium in these formulas (Torrence & Horns, 1989) particularly in infants with regurgitation, vomiting and/or diarrhea.

4) Continuous crying and increased irritability – Dealing with a neonate who is continuously crying and/or irritable is challenging. Crying and irritability can be the result of pain or hypersensitivity of the central nervous system (CNS) to environmental stimuli. It is important not to settle a crying baby with overfeeding (Lauridsen-Hoegh, 1991). There are a number of other strategies that can be used to decrease crying and CNS hyperirritability:
   • Swaddle the neonate in a blanket with hands placed midline over the chest and hips and knees flexed. Placing the hands midline prior to swaddling allows the fingers to be available for sucking. Holding the neonate close to your body while being swaddled can provide comfort and reduce crying (Lauridsen-Hoegh, 1991).
   • Vertical rocking can be help to quiet a crying, fussy neonate. Hold the baby as if in a sitting position upright in the palm of one hand. Tilt the baby slightly forward and support the baby’s chest with the other hand. Then gently move the baby up and down (Lauridsen-Hoegh, 1991).
   • Offer the baby a pacifier. Non-nutritive sucking has a calming effect on infant and is commonly used as an intervention in neonatal intensive care units and newborn nurseries (Kimble, 1992). Studies suggest that non-nutritive sucking reduces crying in infants receiving painful procedures such as heel sticks, intravenous catheter insertion and intubation (Mathai, et al, 2006; South, et al, 2005; Miller & Anderson, 1993, Cochrane Data Base, 2011). Non-nutritive sucking has also been used to calm crying and irritable neonates/infants experiencing neonatal abstinence (Torrence &
Neonatal Abstinence Scoring Tools
There are several tools available to assess the severity of neonatal abstinence. These tools include the following:

1) Neonatal Abstinence Scoring System (NASS) (Finnegan, et al, 1975). The NAS is also known as the Finnegan Scoring Tool. This is a 21 item scale with each symptom numerically scored (1-5) based on symptom severity. Items comprising the tool came from a literature review and clinical observations of over 200 infants. Twenty one of the most commonly found symptoms of withdrawal comprise the tool. Symptoms are scored as single items or in several categories. Scoring is dynamic rather than static meaning all symptoms exhibited during the entire scoring interval, not just at a single point in time, should be included in the interval scoring. Scoring is done every 3 or 4 hours. Pharmacologic management is indicated if the total score for the interval is 8 or greater (Finnegan & Kaltenbach, 1992). This was the first tool that included a protocol for pharmacologic management based on scores. Inter-observer reliability was reported between 0.75-0.96 when the tool was initially developed. There is an inter-observer reliability program available to train staff in the appropriate use of this tool (D’Apolito & Finnegan, 2010). NASS has been used in research (Elliott, et al, 2004). The tool has been tested rigorously to identify infants requiring pharmacologic treatment and ongoing pharmacologic therapy (Finnegan, et al, 1975; Besunder & Blumer, 2001). This tool has been used in research in the US and internationally (Coghlan, et al, 1999; Martinez, et al, 1999; Lifshitz, 2004; Katz, 2004; Murphy-Oikonen, J., et al.,(2010); Zimmermann, et al, 2010). In two national surveys of healthcare professionals the Finnegan scoring tool is most widely used (O’Grady et al, 2009; Sarkar & Donn, 2006).

2) Lipsitz (Lipsitz,P, & Blatman, S., 1974). This is an 11 item scale with each symptom numerically scored (0-3) based on symptom severity. Infants who scored greater than 10 were given pharmacologic treatment. Scoring is subjective and no reliability has been reported for this tool. There is no pharmacologic treatment protocol associated with the use of this tool. Tool is infrequently used (Sarkar & Donn, 2006). No description of how the tool was developed. No scoring interval is recommended. Sleep disturbances not evaluated with this tool. Lipsitz tool does not include several clinically important symptoms that may increase morbidity from narcotic withdrawal such as vomiting, seizures and sleep disturbances. The Finnegan scoring tool is more detailed and has greater emphasis on symptoms more likely to correlate with morbidity and mortality therefore, it is better suited to quantify the severity of withdrawal to guide pharmacologic management (Besunder & Blumer, 2001).

3) Neonatal Withdrawal Inventory (NWI) (Zahorodny, et al, 1998). This is a 7 item scale that gives the scorer a choice of scoring a baby for tremors disturbed or
undisturbed; irritability or sweating or mottling; or frantic fist sucking or crying; or fresh excoriation of limbs; or continuous crying. It is unclear how to score the baby if all of these symptoms are present. Items are weighted numerically based on symptom severity (1-4). Has a reported inter-observer reliability of 0.89-0.98; however, no definition of items provided. Inter-rater reliability between the NWI and the NASS was 0.98 and 0.93 respectively. (Zahorondny, 1998) Pharmacologic treatment is recommended when scores are 8 or greater. Score is not dynamic. Scoring is based on observed symptoms 2 hours after a feeding. No description of how the tool was developed. Sleep disturbances are not evaluated with this tool.

4) Neonatal Narcotic Withdrawal Index (NNWI) (Green, M., 1981) – This is a 6 item tool with an “other” category that contains 12 additional signs and symptoms. The items are numerically scored (0-2). The scores assigned are not based on severity. In the “other” category a score between 0-2 is given based on the number of signs and symptoms present (0-5 or more). The tool does include seizures and vomiting but does not evaluate sleep disturbances. The signs and symptoms selected were based on those most likely to be found. Has a reported inter-observer reliability of 0.77 for each score and 90% agreement for total score given to the baby. (Green, 1981) Pharmacologic treatment is recommended when scores are 5 or greater. Score is not dynamic. Scoring is based on frequent clinical symptoms (no specific times recommended). No definition of items provided.

**Neonatal Substance Exposure Testing**

The terms sensitivity, specificity, and positive and negative predictive values are used throughout this section. The sensitivity of a test is its ability to identify positive results. The specificity is the ability to identify negative results. Positive predictive value is the proportion of positive test results that are truly positive. Negative predictive value is the proportion of negative test results that are truly negative. For all of these values, the higher the number, the better the test.

There are several screening methods that can be used to identify drug-exposure in the neonate. They include the following:

1) Urine – Some of the advantages of urine analysis for drug-exposure include 1) drug concentration is higher in urine than in plasma; 2) urine is easier to analyze than plasma; 3) increased volumes of urine can be collected, and 4) urine can be tested in most hospitals (American Academy of Pediatrics and Center for Advanced Health, 1988). However, there are drawbacks to testing urine in neonates. Drugs in the infant’s urine represent recent drug use by the mother and may test negatively if the mother does not use drugs frequently. Urine needs
to be collected as close to birth as possible. Collecting the sample can be difficult and uncomfortable for the infant. The incidence of false negative results can be as high as 63% (Halstead, et al, 1988; Ostrea, et al, 1989; Osterloh, J, & Bee, B., (1989).

2) Meconium – Meconium is the most reliable and comprehensive toxicology screen in the neonate. It has a high degree of precision and reproducibility. Meconium is easier to collect than urine. The sample should be collected from two diapers and combined to increase the likelihood of a positive test. The total amount needed is 0.5 to 1 gm of meconium. Once collected, the sample should be sent to the lab for evaluation. Allowing meconium to stand at room temperature for 24 hours can decrease the concentration of cocaine and marijuana by 25%. Compared to maternal and newborn testing, meconium testing has a sensitivity of 93%; specificity of 77%; positive predictive value of 82%, and negative predictive value of 91% (Ostrea et al. 1989; Maynard, E et al., 1991). A sample of meconium can be tested up to 3 postnatal days and will detect past and present drug exposure. The usual turnaround time for analysis is approximately 6 hours for single a single drug. Batch testing for more than one drug may delay turnaround time (Ostrea, E., 2000). Meconium is more reliable in detecting benzoylcegonine (cocaine metabolite) than maternal or infant urine and does not have an advantage over urine for detection of cannabinoid, codeine, morphine or methadone (Wingert, et al, 1994).

3) Hair Analysis – Hair analysis can be used to detect illicit drug exposure in the neonate; however, the hair sample may be insufficient. Since hair grows slowly (about ½ inch/month) recent drug exposure may not be detected. Additionally, neonatal hair does not begin to grow until the latter half of pregnancy; therefore drug use during pregnancy may not be found (Cone, et al., (1991; Cone et al, 1993). It has been reported that meconium is more sensitive than hair to intrauterine drug exposure (Bar-oz, et al., (2003). It has also been reported that median cocaine concentrations are 10 fold higher in maternal hair than her infant's hair (Ostrea, et al, 2001).

4) Umbilical Cord - The umbilical cord tissue can be tested for neonatal intrauterine drug exposure (de Castro 2011.) Studies have been done to compare meconium to cord samples for amphetamines, opiates, cocaine and cannabinoids. Agreements between the meconium and cord samples ranged from 90.7 to 100% with sensitivity ranging from 75-95% and specificity from 91-100% (Montgomery, et al, 2006). Umbilical cord testing for amphetamines has a reported sensitivity and specificity of 97%, positive predictive value of 72% and negative predictive value of 100%; for opiates a sensitivity of 91%, specificity of 98%, positive predictive value of 88% and negative predictive value of 98%; for cocaine 95% sensitivity, 100% specificity, positive predictive value 95% and negative predictive value of 100%, and for cannabinoids 96% sensitivity, 98% specificity; positive predictive value of 72% and negative predictive value of 100% (Montgomery, et al, 2008).
Pharmacological Management of Neonatal Abstinence Syndrome

Several drugs have been discussed in the literature for the treatment of NAS. The American Academy of Pediatrics, Committee on Neonatal Drug Withdrawal recommends that drug selection should match the type of agent causing the withdrawal. For withdrawal from opioids an opioid such as tincture of opium should be used. For signs of withdrawal from sedative-hypnotics, phenobarbital is the agent of choice (American Academy of Pediatrics, 1998). Since this publication a systematic review by the Cochrane Collaborative was conducted in 2005. This systematic review examined the efficacy of various combinations of treatments. The combination of drugs used included paregoric, morphine, and methadone vs phenobarbital (Carin, et al, 1983; Finnegan, 1984; Kaltenbach, 1983; Klandall, 1983; Madden, 1977; Jackson, 2004; Khoo, 1985) and paregoric or methadone vs diazepam (Finnegan, 1984; Kaltenbach, 1986; Madden, 1977). Methodological issues were reported for some of the studies. These issues included problems with subject randomization and treatment blinding (Osborn, Jeffery, & Cole, 2002). Results of the review suggest that treatment with opioids will decrease the time to regain birth weight, reduce the duration of supportive care, and increase duration of hospital stay. No evidence of treatment failure was reported. Opioids may also reduce seizures when compared to phenobarbital and duration of treatment was found for infants treated with morphine. It was also noted that the results of this review should be treated with caution because of methodological issues. This review could not determine which opioid to use for NAS. Paregoric was used in some of these studies; however, Paregoric is no longer recommended as a treatment option because of its high alcohol content. Paregoric also contains toxic ingredients such as camphor, anise oil and benzoic acid (American Academy of Pediatrics, 1998). The American Academy of Pediatrics has recommended that Paregoric be replaced by other opioids such as Tincture of Opium, morphine or methadone (American Academy of Pediatrics, 1998; Osborn, Jeffery & Cole, 2002; American Academy of Pediatrics, 2012). Therefore, treatment of neonatal opioid withdrawal should be treated with oral morphine, diluted tincture of opium or methadone (Osborn, et al, 2002).

Infants prenatally exposed to opioids should be monitored in the hospital to observe for signs of drug withdrawal.

- Infants born to women taking low-dose prescription drugs such as hydrocodone, which has a short half-life (about 4 hours) may be discharged from the hospital if no signs of withdrawal are present by 3 days of age (American Academy of Pediatrics, 2012).
- Infants born to women taking an opiate with a long half-life such as methadone should be observed in the hospital for signs of withdrawal for 5-7 days after birth (American Academy of Pediatrics, 2012)
Specific Evidence for Pharmacological Treatment of Neonatal Abstinence Syndrome


Seven studies were included in this review (585 infants). All of the infants had intrauterine exposure to opioids, with or without other drugs. The outcomes evaluated in these studies included treatment failure (failure of treatment to keep withdrawal score in a safe range and/or the need to add another drug therapy), incidence of seizures, survival and neurodevelopmental outcomes. Some of the studies did not address these specific outcome measures but discussed other outcomes such as duration of treatment, length of hospitalization and rate of weight gain. None of the studies reported increased mortality or adverse neurodevelopmental outcomes. Four out of the seven studies compared the use of an opioid (paregoric, oral morphine or methadone) vs phenobarbital to treat NAS (Finnegan, 1984; JCKAON, 2004; Kandall, 1983; Khoo, 1995). Meta-analysis of these studies found no significant difference in treatment failure among these drugs. One study reported that opiate treatment resulted in a significant decrease in treatment failure among infants who were only exposed to opioids in utero (Finnegan, 1984). Another study reported a significant decrease in duration of treatment and admission to the nursery for infants treated with morphine compared to phenobarbital (Jackson, 2004) while another reported a statistically significant reduction in seizures when infants were treated with an opioid (Kandall, 1983). It is important to mention that there were several methodological issues with these studies so the results should be used with caution (Osborn, Duffy & Cole, 2005).

Results of this review suggests that an opioid is the best first line treatment for NAS in infants who are exposed to an opioid, with or without other drugs, in utero.


Six studies were included in this review (305 infants). All of the infants included in the studies were born to women with an opioid dependence and either received standard treatment (another sedative or non-pharmacologic management) or treatment with phenobarbital, diazepam or chlorpromazine. One study compared phenobarbital to supportive care to control NAS. No difference in treatment failure was found but treatment with phenobarbital significantly increased the duration of therapy and hospital stay (Khoo, 1995). Another study randomly assigned infants (n=20) already being treated with diluted tincture of opium (DTO) to additionally receive phenobarbital as a second line drug for the treatment of NAS. No infants had treatment failure. Infant’s receiving both drugs has a significant reduction in hospital stay (38 vs 79 days). These infants also required a lower dose of opioid when additionally receiving phenobarbital. The problem was that those infants receiving phenobarbital along with the opioid continued to require treatment with phenobarbital for 3.5 months after the opioid was discontinued (Coyle, Ferguson, Lagasse, Oh & Lester, 2002). Two studies
compared phenobarbital with diazepam treatment. One found a significantly lower treatment failure rate in the phenobarbital group vs the diazepam group (n=107) (Finnegan, 1984). One study of phenobarbital versus chlorpromazine (n=36) did not report any differences in treatment with either of these drugs (Kahn, Neumann & Polk, 1969). There were methodological concerns with all of these studies (quasi-random allocation, sizable unexplained differences in reported numbers in several of the studies) (Osborn, Jeffery & Cole, 2005). Results of this review need to be considered in light of the review “Opiate treatment for opiate withdrawal in newborn infants.” Infants with NAS due to an opioid should be treated with an opioid. If a sedative needs to be added to help control signs of withdrawal, phenobarbital rather than diazepam should be used. There is insufficient evidence to support the use of chlorpromazine or clonidine to treat NAS in newborns (Osborn, Jeffery & Cole, 2005).

3) Summary table of other studies:

<table>
<thead>
<tr>
<th>Year</th>
<th>Drugs</th>
<th>Type of Study</th>
<th>Outcome</th>
<th>Recommendation</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>Sublingual buprenorphine (bup) vs oral morphine</td>
<td>RCT</td>
<td>Length of treatment in bup group 23 days (n=12) vs 38 days (n=12). Length of stay reduced from 42 to 32 days in bup group. Three infants in the bup group also needed phenobarbital vs one in the morphine group.</td>
<td>Sublingual buprenorphine is safe and effective.</td>
<td>Kraft, W., Dysart, K., Greenspan, J., Gibson, E., Kaltenbach, K., &amp; Ehrlich, M., (2011). Revised dose schema of sublingual buprenorphine in the treatment of the neonatal opioid abstinence syndrome. Addiction 106(3), 574-580.</td>
</tr>
<tr>
<td>2009</td>
<td>Standard treatment with DTO vs Clonidine or placebo as second line drug</td>
<td>RCT</td>
<td>Median length of hospital stay was 27% shorter in clonidine group than placebo group; higher doses of DTO were needed in placebo group; more</td>
<td>Addition of Clonidine to standard opioid therapy for detoxification of heroin or methadone.</td>
<td>Agthe, A., Kim, G., Mathias,K., Hendrix, C., et al., (2009). Clonidine as an adjunct therapy to opioids for neonatal abstinence syndrome: A randomized, controlled trial.</td>
</tr>
<tr>
<td>Year</td>
<td>Study Type</td>
<td>Design</td>
<td>Findings</td>
<td>Reference</td>
<td></td>
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<td>------</td>
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<td>--------------------------------------------------------------------------</td>
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<tr>
<td>2005</td>
<td>Methadone vs oral morphine</td>
<td>Retrospective Chart Review</td>
<td>No difference in length of hospital stay in infants treated with oral morphine or methadone. Length of stay was longer when mother was on high doses of methadone during pregnancy and when infant received higher opioid treatment doses.</td>
<td>Pediatrics 123(5), e849-e856.</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>DTO VS Oral Morphine</td>
<td>Comparison Study</td>
<td>Dose of oral morphine was higher than DTO to control signs. Duration of therapy was 5 days longer in the morphine group but weight gain was better in the morphine group (25 g/day vs 19 g/day).</td>
<td>Oral morphine is suitable to treat NAS in a similar manner as DTO but avoids the unwanted effects of alcohol and other alkaloids in DTO and allows for better weight gain in neonates. Langenfeld, S., Birkenfeld, L., Hellmich, M., &amp;Theisohn, M., (2005). Therapy of the neonatal abstinence syndrome with tincture of opium or morphine drops. Journal of Drug and Alcohol Dependence 77 (1), 31-36.</td>
<td></td>
</tr>
</tbody>
</table>
References:


Elliott, M., et al. (2004). Frequency of Newborn Behaviors Associated with Neonatal Abstinence


SAMHSA, Results from the 2008 National Survey on Drug Use and Health: National Findings.


