QUALITY IMPROVEMENT ARTICLE



Quality improvement initiative to improve inpatient outcomes for Neonatal Abstinence Syndrome

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Abstract

Objectives To improve Neonatal Abstinence Syndrome (NAS) inpatient outcomes through a comprehensive quality improvement (QI) program.

Design Inclusion criteria were opioid-exposed infants \geq 36 weeks. QI methodology including stakeholder interviews and plan-do-study-act (PDSA) cycles were utilized. We compared pre- and post-intervention NAS outcomes after a QI initiative that included: A non-pharmacologic care bundle, function-based assessments consisting of symptom prioritization and then the "Eat, Sleep, Console" (ESC) Tool; and a switch to methadone for pharmacologic treatment.

Results Pharmacologic treatment decreased from 87.1 to 40.0%; adjunctive agent use from 33.6 to 2.4%; hospitalization length from a mean 17.4 to 11.3 days, and opioid treatment days from 16.2 to 12.7 (p < 0.001 for all). Total hospital charges decreased from \$31,825 to \$20,668 per infant. Parental presence increased from 55.6 to 75.8% (p < 0.0001). No adverse events were noted.

Conclusions A comprehensive QI program focused on non-pharmacologic care, function-based assessments, and methadone resulted in significant sustained improvements in NAS outcomes. These findings have important implications for establishing potentially better practices for opioid-exposed newborns.

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Introduction

Neonatal Abstinence Syndrome (NAS) secondary to inutero opioid exposure increased fivefold in the United States (U.S.) from 2000 to 2012, and has continued to rise with recent rates reported as high as 20 per 1000 live births [1–4]. A majority of infants with NAS are treated with replacement opioids if scores from one of the many symptom assessment tools are elevated [5–7]. Infants pharmacologically treated for NAS are often cared for in neonatal intensive care units (NICUs) and at some centers, account for about half of NICU patient days [8]. These infants have an average hospital length of stay (LOS) of 23 days, mean hospital charges of \$93,400 per hospitalization, and account for \$1.2 billion of Medicaid costs [2].

The majority of U.S. hospitals use the Finnegan Scale as an assessment tool for NAS [9–11]. This scale, developed in 1974, contains a catalog of the most common neonatal opioid withdrawal symptoms with points assigned for each item based on its perceived severity [12]. The validity of the Finnegan Scale has recently been called into question due to its poor psychometric properties [13]. Newer quality improvement (QI) work suggests that function-based assessments can reduce the number of infants who receive pharmacologic treatment [14-16]. One function-based approach is to prioritize certain items such as poor sleep and feeding on the Finnegan scale ("symptom prioritization"), which was piloted by one institution in the context of a non-pharmacologic care QI bundle with a demonstrated decrease in pharmacologic treatment rates [16]. In another study, Grossman et al. focused exclusively on how well the infant was eating, sleeping, and consoling ("ESC") in combination with a comprehensive non-pharmacologic care bundle, demonstrating a 50% reduction in medication treatment and LOS with use of this novel method [14, 15]. However, no standardized ESC nursing assessment or treatment approach was created as part of that study.

Compelling evidence exists that use of nonpharmacologic interventions as first-line treatment can result in markedly improved NAS outcomes including a 30-68% reduction in pharmacologic treatment and hospital LOS, as well as significant reductions in hospitalization costs [14–19]. These interventions include the promotion of breastfeeding, rooming-in, and parental presence at the bedside [14–19]. At our institution, the baseline pharmacologic treatment rate for opioid-exposed infants was 82%, with 35% of infants receiving a second pharmacologic agent. Despite a model of care that encouraged rooming-in, parental presence at the bedside was low at 54% and we did not adequately emphasize non-pharmacologic care as firstline treatment. The study team aimed to decrease pharmacologic treatment and LOS by 40% in 1 year through a comprehensive QI program focused on optimizing nonpharmacologic care, increasing parental presence and engagement in care, and modifications in both NAS assessment and pharmacologic treatment protocols.

Methods

Context

From May to December 2016, we conducted a QI project in a large tertiary urban academic medical center with approximately 3000 births per year and a comprehensive integrated prenatal program for women with opioid use disorders (OUD). Pregnant women with OUD are referred to this regional referral center for prenatal and postnatal care. The Pediatrics Inpatient Service cares for 120–130 opioid-exposed newborns annually. Given that mothers receive their care at our center, infants with in-utero opioid exposure are identified at birth after review of maternal records upon admission to Labor and Delivery. Mothers receive routine urine toxicology screens throughout pregnancy and upon admission, and infants have urine and meconium toxicology testing shortly after birth to confirm in-utero exposures. Infants are cared for in their mother's room until maternal discharge unless they are started on pharmacologic treatment; these infants are transferred to the newborn nursery to be placed on cardiac monitors while receiving opioids. Once the mother is discharged, all infants are transferred to the Pediatrics Inpatient Unit where there is a bed in each patient room for one parent to stay overnight. In the majority of cases, infants who are in the custody of the Department of Children and Families (DCF) are permitted to continue to room-in with their parents during the hospitalization.

Pre-intervention

Between April 2015 and April 2016 (pre-intervention period), our institution used the Finnegan tool to assess withdrawal signs and guide NAS treatment decisions, with demonstrated high inter-rater reliability. We initiated a morphine protocol for infants that received two Finnegan scores ≥ 8 or one score ≥ 12 [20, 21]. Although nonpharmacologic interventions (i.e. rooming-in) were encouraged, parental presence of only 54% served as a proxy for poor adherence [18]. Additionally, infants whose symptoms met Finnegan score treatment criteria were quickly started on medication without consideration of additional non-pharmacologic measures first.

In 2013, a multi-disciplinary QI team was formed consisting of physicians, nurses, social workers, pharmacists, lactation consultants, a peer counselor, nursing quality and safety leaders, public health and medical students, from our prenatal treatment program, Labor & Delivery, Mother-Baby Unit, Newborn Intensive Care Unit (NICU), and Inpatient Pediatrics Unit. Between 2013 and April 2016, the QI team focused on Finnegan score standardization and standardization of the pharmacologic treatment regimen. Starting in May 2016, the team began meeting monthly to focus on instituting new QI interventions. First, 24 stakeholders including physicians, nurses, and parents were interviewed regarding causes for maternal-infant separation and performed a root cause analysis to identify two key themes: (1) Infants were often started on medication in the first 48 h of life due to elevated Finnegan scores and were temporarily removed from their mother's room to be placed on a monitor in the nursery until the infant could be transferred to Inpatient Pediatrics-hindering the ability for full rooming-in, and (2) Mothers faced multiple barriers to being at the bedside once discharged, including residential treatment program requirements, daily methadone treatment, transportation, and childcare issues.

 Table 1
 Intervention timeline

Date	PDSA cycle	Intervention
May 2016	Cycle 1	Non-pharmacologic care bundle Change in prenatal / parental messaging Finnegan symptom prioritization
June 2016	Cycle 2	Staff QI project education Switch to methadone with no treatment in the first 24 h of life
Dec 2016	Cycle 3	Switch to ESC function-based assessments Cuddler program

Interventions

Using plan-do-study-act (PDSA) cycle methodology [22], the QI team developed and implemented the following interventions (Table 1).

PDSA CYCLE 1

Non-pharmacologic care bundle We implemented a nonpharmacologic bundle as the first-line treatment for infants with NAS. The bundle included parental presence, skin-toskin contact, holding, breastfeeding, and creating a calm, low stimulation environment. Infants were assessed in the mother's room and kept skin-to-skin when possible for NAS scoring.

When infant's withdrawal symptoms increased, efforts were made first to optimize non-pharmacologic care before considering medication treatment. All physicians and nurses involved in the care of opioid-exposed infants were educated on the new initiative through in-person trainings and an online nursing educational module. Rotating resident physicians received monthly education in-person at the start of their rotations on the three inpatient pediatric services (NICU, Nursery, and Inpatient Pediatrics) throughout the entire intervention and post-intervention periods.

Prenatal/parental messaging Staff at the integrated prenatal treatment program met with mothers and reviewed prenatally that the mothers would be the primary NAS treatment for the infant and that all efforts should be made to be at the bedside as much as possible. Staff emphasized how vital the mother's and parents' participation was to the infant's NAS care. We made arrangements to temporarily allow mothers to receive their methadone at a clinic near the hospital if their primary methadone clinic was from the hospital. We also worked with residential treatment programs to allow mothers to stay overnight in the hospital when appropriate. Parents were encouraged to identify support people who could assist during their newborn's hospital stay if they were not able to be present. Nursing and physician staff provided a non-pharmacologic care handout upon admission to the Mother-Baby Unit.

Finnegan symptom prioritization In the initial phase of the intervention, staff changed from starting medication if an infant's Finnegan scores were ≥8 twice or ≥12 once to performing a team huddle instead. The huddle included a minimum of the resident physician, nurse, and parent (when present), but could also include the nurse practitioner or attending physician. The team would review the infant's withdrawal signs and would only intervene if there was a predominance of poor feeding, excessive vomiting, diarrhea, poor consolability, and/or poor sleep in the Finnegan symptom profile. The first intervention would be to increase non-pharmacologic care. If the infant did not respond to these efforts, then pharmacologic treatment was initiated. Physician (attending and resident) and nursing staff received in-person education on Finnegan prioritization prior to the start of this intervention.

PDSA CYCLE 2

Staff QI project education One month into the intervention, the NAS QI group hosted a multi-disciplinary newborn/pediatric staff conference where two regional NAS QI leaders from collaborating institutions presented their individual institutions' published QI work on non-pharmacologic, parent-led, rooming-in care, symptom prioritization, and function-based ESC care [14–16]. These collaborating team leaders outlined how their institutions' NAS QI teams systematically implemented QI changes with significant improvements in NAS outcomes without adverse events.

Transition to methadone We implemented two changes in our hospital's NAS pharmacologic treatment protocol. First, we educated staff to withhold pharmacologic treatment in the first 24 h of life if symptoms were felt to be related to co-exposures such as nicotine or anti-depressant medication rather than due to opioid withdrawal due to the nature of timing of maternal opioid administration [23–25]. Second, we changed the first-line pharmacologic agent from morphine to methadone [7]. Methadone dosing was initiated at 0.2 mg/kg/day divided every 8 h and increased by 0.2 mg/kg/day as often as every other dose to a maximum of 0.8 mg/kg/day for persistent Finnegan scores >8 with use of

symptom prioritization as described in PDSA CYCLE 1. Methadone was weaned by 10% once every 24 h for stable symptoms (Finnegan scores <8) and discontinued at 20% of the maximum dose [7, 21, 26]. Infants were monitored for 24-48 h after methadone was discontinued prior to discharge home.

PDSA CYCLE 3

Function-based ESC assessments In the last phase of the intervention, Finnegan scoring was discontinued in place of function-based ESC assessments as described by Grossman et al. [15, 16]. The hospital team developed, along with representatives of collaborating institutions, and implemented a standardized ESC nursing flowsheet documenting the infant's ability to effectively eat, sleep, and console with item definitions provided. Nurses (n = 200), resident physicians (n = 140), attending physicians and nurse practitioners (n = 43) across the three pediatric care units received standardized education on the ESC flowsheet and treatment protocol. Nurses documented ESC assessments every 3–4 h, after feedings, and notified the provider and initiated a team huddle if the infant demonstrated difficulties in eating, sleeping, or consoling due to NAS. Staff first evaluated non-pharmacologic interventions and optimized them if possible. If symptoms persisted, methadone was given, and titrated and weaned according to the same protocol as outlined in the prior intervention, with use of ESC assessments in place of Finnegan scores (Supplemental Fig. 1).

Cuddler program BMC launched the CALM (Cuddling Assists in Lowering Maternal and Infant Stress) program towards the end of PDSA CYCLE 3. The CALM coordinators trained 150 volunteers including hospital employees, medical students, and community volunteers using a standardized curriculum on NAS, addiction in pregnancy, and infant non-pharmacologic care techniques. Volunteers signed up for 1–2 h shifts between 0800 –0000 hours daily, holding infants when other caregivers were not present at the bedside. Staff documented cuddler presence in the electronic health record on the ESC nursing flowsheet.

Data collection

We collected data on all opioid-exposed infants born >36 weeks gestational age in the study period including infant and maternal baseline demographics, prenatal drug exposures, delivery history, NICU admission, feeding method, parental presence, NAS pharmacologic treatment, and discharge disposition.

Study of the interventions

We compared outcomes during the baseline (April 2015–April 2016) and post-intervention period (January-December 2017) after the last PDSA cycle was implemented. We first compared maternal and infant demographics using independent sample t tests and chi-square test of independence during the pre- and post-intervention periods to see if changes in patient characteristics could have contributed to differences in outcomes. We then compared NAS outcomes in the preand post-intervention periods. We used statistical process control (SPC) charts and P-charts (developed using Microsoft Excel QI Macros) to evaluate the impact of our QI interventions over the time course of the project to determine if observed outcomes were due to the interventions.

Outcome measures

Our primary outcome measure was hospital LOS due to NAS (defined as 48 h after the discontinuation of NAS medication, or maximum 8 days for infants (after the recommended observation period of 5-7 days) who did not require pharmacotherapy when hospitalization was prolonged for social reasons). Total hospital LOS was also compared. Secondary measures included: (1) any pharmacologic treatment, (2) treatment with an adjunctive pharmacologic agent (phenobarbital or clonidine), (3) opioid treatment days, (4) breastfeeding initiation (any amount of breast milk consumed by the infant), and (5) hospital charges (as determined by the mean charges per day for inpatient pediatrics for a diagnosis of NAS for corresponding fiscal year). The process measure of parental presence at the infant's bedside was used to examine adherence to the non-pharmacologic care approach and impact of prenatal education about importance of parental presence in NAS care. We compared hospital re-admissions to our center within 30 days related to NAS, NICU admissions secondary to NAS complications, and seizures pre- and post-intervention as balancing measures. Three study authors reviewed data collected by research assistants for completeness and accuracy with discrepancies verified by additional chart review.

Analysis

We used independent sample t tests for continuous variables, and chi square test of independence for categorical variables to compare outcomes between the pre- and post-intervention periods and used SAS version 9.4 (SAS Institute, Inc, Cary, NC) for the analysis. We reviewed SPC charts to identify special cause variation, with use of the

 Table 2 Demographics and outcomes pre- and post-intervention

Demographic/outcome	Pre-intervention $N=101$ N (%) or Mean (95% CI)	Post-intervention <i>N</i> = 85 <i>N</i> (%) or Mean (95% CI)	p value
Maternal characteristics			
Maternal age (years)	28.9 (28.0, 29.9)	29.4 (28.4, 30.3)	0.53
White Non-Hispanic	88 (87.1%)	70 (82.4%)	0.36
Maternal opioid			
Methadone	49 (48.5%)	49 (57.7%)	0.21
Buprenorphine	52 (51.5%)	36 (42.5%)	
Illicit drugs third trimester ^a	28 (28.0%)	39 (45.9%)	0.009*
Benzodiazepines	13 (12.9%)	24 (28.2%)	0.009*
SSRIs	4 (4.0%)	11 (12.9%)	0.02*
Nicotine smoking third trimester	70 (69.3%)	63 (74.1%)	0.41
Cesarean delivery	32 (31.7%)	35 (41.2%)	0.18
Infant characteristics			
Male sex	51 (50.5%)	40 (47.1%)	0.64
Gestational age (weeks)	39.1 (38.8, 39.4)	38.7 (38.4, 39.0)	0.05
Birth weight (grams)	3090 (2989, 3192)	3025 (2925, 3126)	0.37
Breast milk ^b	49 (51.6%)	52 (61.2%)	0.20
NICU admission ^c	24 (23.7%)	18 (21.2%)	0.78
DCF custody	20 (19.8%)	24 (28.2%)	0.18
NAS outcomes			
Pharmacologic treatment	88 (87.1%)	34 (40.0%)	< 0.0001*
Adjunctive medication ^d	34 (33.6%)	2 (2.4%)	< 0.0001*
Hospital LOS—all opioid- exposed infants (days)	17.4 (15.8, 19.0)	11.3 (10.0, 12.6)	<0.0001*
Pharmacologically treated LOS (days)	19.1 (17.5, 20.7)	17.6 (16.5, 18.7)	0.11
Opioid treatment days	16.2 (14.5, 17.9)	12.7 (11.5, 13.8)	0.0007*
Caregiver presence (%)	55.6% (50.3%, 60.8%)	79.9% (74.8%, 85.1%)	< 0.0001*
Parental presence (%)	55.6% (50.3%, 60.8%)	75.8% (69.8%, 81.8%)	< 0.0001*
Cuddler presence (%)	_	4.4% (3.2%, 5.5%)	
Hospital charges (US dollars)	31,825 (28,898, 34,751)	20,668 (18,290, 23,045)	< 0.001*
Re-admission ^e	0	1 (1.2%)	_

SSRI selective serotonin re-uptake inhibitor, LOS length of hospital stay due to NAS, DCF Department of Children and Families

*denotes p < 0.05 meeting statistical significance

^aHeroin, fentanyl, oxycodone

^bAny amount of breast milk received during the hospitalization

^cNICU admission for reasons other than NAS

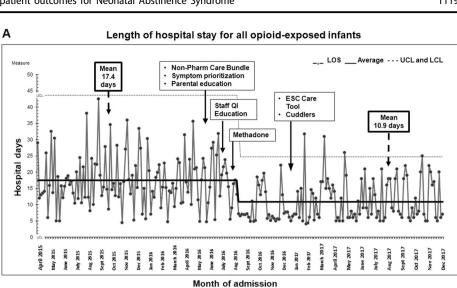
^dTreatment with a second pharmacologic agent (phenobarbital or clonidine)

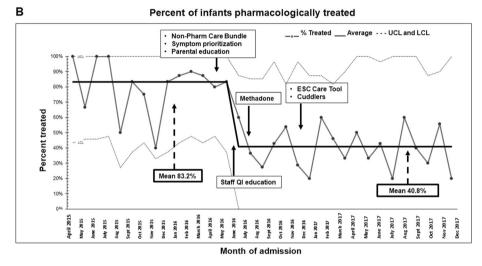
eRe-admission within 30 days for reasons related to NAS

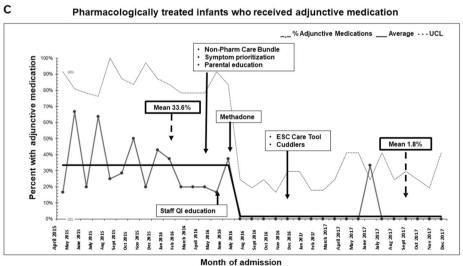
shift rule (defined as eight consecutive data points above or below the center line), and trend rule (six successive points increasing or decreasing) to identify incidences of statistical significant variability (p < 0.05) [27]. We inserted interventions by start date in the SPC and P-charts in order to infer the impact of each intervention on the outcome.

Ethical considerations

All infants born at BMC with in-utero opioid exposure meeting eligibility criteria during the study time period were eligible for the intervention including those infants with illicit drug exposure only. Our hospital's Institutional Review Board deemed our study exempt as a QI protocol. Fig. 1 NAS outcomes. a shows the LOS with each dot representing an opioid-exposed infant. b is the percentage pharmacologically treated and c adjunctive medication treatment, with each dot representing a calendar month. The centerlines shift downward in June–July 2016, corresponding to the nonpharm care bundle, parental messaging, symptom prioritization, and methadone. UCL upper confidence limit, LCL lower confidence limit







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Results

There were 275 opioid-exposed infants during the study period of April 2015–December 2017 of which 240 met inclusion criteria for analysis. We excluded 35 infants secondary to prematurity <36 weeks GA. There were no NICU admissions from the Inpatient Units for management of NAS or related complications during the study time period. There were 101 infants in the pre-intervention group (April 2015–April 2016), 54 in the intervention group (May 2016–December 2016), and 85 in the post-intervention (January–December 2017) group. Demographics comparing pre- and post-intervention groups are shown in Table 2. Infants in the post-intervention period were more likely to be co-exposed to illicit drugs and psychiatric medications.

The primary NAS outcomes are shown in Table 2. The proportion of pharmacologically treated infants decreased from 87.1 to 40.0% (p < 0.0001) with a decrease in adjunctive agent use from 33.6 to 2.4% (p < 0.0001). Mean LOS due to NAS for all opioid-exposed infants decreased from 17.4 (95% CI 15.8-19.0) to 11.3 (95% CI 10.0-12.6) days (p < 0.0001); total hospital LOS for all infants from 17.5 (95% CI 15.8-19.1) to 11.6 (95% CI 10.1, 13.1); and opioid treatment days for pharmacologically treated infants decreased from a mean of 16.2 (95% CI 14.5-17.9) to 12.7 (95% CI 11.5–13.8) days (p < 0.0001). Breastfeeding initiation rate did not differ during the two time periods. Average hospital charges decreased from \$31,825 to \$20,668 per infant during the intervention period (p <0.001). Parental presence at the bedside increased from a mean of 55.6 to 75.8% (p < 0.001). Mean cuddler presence was 4.4% in the post-intervention group, increasing total caregiver presence to 80%.

Figure 1a-c shows the process control charts for NAS outcomes across the study period. Special cause variation for LOS (Fig. 1a) first occurred in July 2016, coinciding with PDSA 1 and 2. For the percentage of infants pharmacologically treated (Fig. 1b) special cause variation occurred in June 2016, corresponding with implementation of the non-pharmacologic care bundle, symptom prioritization, and change in parental messaging (PDSA 1). Special cause variation occurred for adjunctive medication treatment (Fig. 1c) in July 2016, after the nonpharmacologic care bundle, symptom prioritization, change in parental messaging, staff education, and change to methadone (PDSA 1 and 2). There was not a significant shift in outcomes between PDSA 2 and 3. The process measure of parental presence at the bedside shifted upward in July 2016, coinciding with the non-pharmacologic care bundle and change in parental messaging.(Supplemental Figure 2).

There were no 30-day re-admissions for NAS in the preintervention period. There was one re-admission during the intervention period during PDSA 2. An infant that had been treated with methadone and discharged home 24 h after stopping therapy was re-admitted 24 h after discharge, re-started on methadone and was subsequently discharged after 5 days. We subsequently amended the methadone protocol to ensure 48 h of inpatient monitoring prior to discharge due to the longer half-life of methadone. There were no NICU admissions for management of NAS or its complications, and no seizures reported during the study period.

Discussion

This comprehensive QI program using a multi-disciplinary team approach focusing on non-pharmacologic care with parents as primary NAS treatment, symptom and functionbased assessments and treatment decisions, and transition to methadone as primary pharmacologic treatment, was associated with increased parental presence, decreased need for pharmacological treatment, elimination of adjunctive agent use, shorter LOS and opioid treatment days, and lower hospital charges. The results were sustained over the 12month post-intervention period and represented a significant culture shift in the institution.

This study is consistent with prior studies that have examined the impact of non-pharmacologic care bundles that include rooming-in and breastfeeding to improve NAS outcomes [14–19]. A recent meta-analysis by MacMillan including six studies of rooming-in showed a risk ratio for pharmacologic treatment of 0.37 with a rooming-in model of care [19]. Future QI efforts at our institution will focus on expansion of our cuddler program, measuring skin-to-skin contact, and intermittent cardiac monitoring for infants who require pharmacologic treatment while on the postpartum unit to further improve non-pharmacologic care especially continuous parental presence at the bedside.

This study has several strengths. First, this study demonstrated the ability to institute major changes in care practices in a relatively brief period at a large academic medical center with a large volume of substance-exposed infants through a rigorous multi-disciplinary QI approach. Infants with NAS in our institution are cared for in three separate inpatient units with a large staff who all received education on our practice change. In addition, we needed to educate 50 inpatient pharmacists on the new methadone protocol. To sustain our interventions, we instituted regular in-services and educational updates for all staff, including monthly in-person education for resident physicians and online educational updates for nursing. Second, the study demonstrates for the first time the impact of positive messaging on parental presence at the bedside as the infant's primary treatment [18]. This highlights that it is not only the physical space allowing for rooming-in that's important, but also parental engagement as a key component of the QI bundle to improved outcomes. Third, the team developed an innovative, standardized nursing flowsheet, ESC item definitions, and standardized treatment algorithm based on the novel "Eat, Sleep, Console" approach developed by Grossman et al. [14, 15]. While the Grossman studies made decisions about medication treatment based on the infant's ability to eat, sleep, and console, no formal ESC assessment tool or treatment protocol was used. Of note, we did not see any significant change in outcomes after switching from a Finnegan symptom prioritization method (PDSA 1) to a formal ESC approach (PSDA 3), suggesting that the benefits of this approach may have been primarily related to the non-pharmacologic care bundle and Finnegan symptom prioritization. Though the ESC care approach appears to be safe and effective, its psychometric properties have not yet been assessed. The ESC care tool used in the current study has been further developed into a formal ESC Care Tool with a standardized training program and now includes expanded case definitions to decrease subjectivity and formal promotion of non-pharmacologic care interventions. (Supplemental Figure 3). It is currently being independently evaluated for inter-rater reliability and validity in an Northern New England regional collaborative.

There are several limitations to this study. Our integrated prenatal program for women with OUDs in which women receive significant counseling to prepare for the hospitalization including parental presence and our rooming-in model of care may limit generalizability. However, the intervention was not limited to those mothers who were actively engaged in the prenatal care program, with benefits seen even in those with continued illicit drug use. Additionally, not all hospitals are able to modify their physical space and staffing models to promote rooming-in and parental presence. Next, there were differences in the coexposures of the mothers with more infants exposed to illicit drugs and benzodiazepines during the postintervention period. Typically co-exposure to psychiatric medications has been associated with worse NAS outcomes; however, we saw improvements even in those infants with polypharmacy exposure [23, 25]. Given that this was a QI project, no adjustment for co-variates was performed. Another limitation was the use of a more aggressive initiation of pharmacologic treatment with the use of two Finnegan scores ≥ 8 or one score ≥ 12 originally, which could have led to overtreatment during this phase. However, we did not see significant differences in pharmacologic treatment rates at our institution when previously using three scores ≥ 8 or two scores ≥ 12 [21, 28]. Lastly, given our comprehensive QI bundle, we cannot isolate the effect of methadone from other interventions on NAS outcomes. While there was only one re-admission identified as a balancing measure, the study was only able to identify admissions returning to the study hospital. It is unknown if infants returned for readmission to another hospital, or had higher utilization of primary or urgent care services. Lastly, we did not perform long-term follow-up on this cohort to evaluate the impact of the interventions on longer-term health outcomes.

This study has important implications. It provides further evidence that hospitals should implement models of care that promote parental engagement and other important nonpharmacologic care measures to improve NAS outcomes. It also suggests a need to re-evaluate standard NAS assessment tools and to consider utilizing new function-based approaches to guide management. Implementation of similar QI initiatives at other institutions could result in decreased need for pharmacologic treatment and subsequent shorter hospitalizations and significant cost savings, as well as potential long-term benefits for both the mother and the infant including improved infant attachment and maternal resilience and confidence in the care of her infant.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

- Patrick SW, Schumacher RE, Benneyworth BD, Krans EE, McAllister JM, Davis MM. Neonatal abstinence syndrome and associated healthcare expenditures—United States, 2000–2009. JAMA. 2012;307:1934–40.
- Patrick SW, Davis MM, Lehman CU, Cooper WO. Increasing incidence and geographic distribution of neonatal abstinence syndrome: United States 2009 to 2012. J Perinatol. 2015;35:667.
- Milliren CE, Gupta M, Graham DA, Melvin P, Jorina M, Ozonoff A. Hospital variation in neonatal abstinence syndrome incidence, treatment modalities, resource use, and costs across pediatric hospitals in the United States, 2013 to 2016. Hosp Pediatr. 2018;8:15–20.
- Massachusetts Department of Public Health. 2017. Data brief: an assessment of opioid-related overdoses in Massachusetts 2011 -2015 [Homepage on the Internet]. http://www.mass.gov/eohhs/ docs/dph/stop-addiction/data-brief-chapter-55-aug-2017.pdf (Accessed August 2017).

- Hudak ML, Tan RC. From the American Academy of Pediatrics: Neonatal drug withdrawal. Pediatrics. 2012;129: e540–560.
- Kraft WK, Adeniyi-Jones SC, Chervoneva I, Greenspan JS, Abatemarco D, Kaltenbach K, et al. Buprenorphine for the treatment of the neonatal abstinence syndrome. N Engl J Med. 2017;376:2341–8.
- Brown MS, Hayes MJ, Thornton LM. Methadone versus morphine for treatment of neonatal abstinence syndrome: a prospective randomized clinical trial. J Perinatol. 2015;35: 278–83.
- Tolia VN, Patrick SW, Bennett MM, Murthy K, Sousa J, Smith PB, et al. Increasing incidence of the neonatal abstinence syndrome in U.S. neonatal ICUs. N Engl J Med. 2015;372:2118–26.
- Sarkar S, Donn SM. Management of neonatal abstinence syndrome in neonatal intensive care units: a national survey. J Perinatol. 2006;26:15–17.
- Mehta A, Forbes KD, Kuppala VS. Neonatal abstinence syndrome management from prenatal counseling to post-discharge follow-up care: results of a national survey. Hosp Pediatr. 2013;3:317–23.
- Bogen DL, Whalen BL, Kair LR, Vining M, King BA. Wide variation found in care of opioid-exposed newborns. Acad Pediatr. 2017;17:374–80.
- Finnegan LP, Connaughton JF Jr, Kron RE, Emich JP. Neonatal abstinence syndrome: assessment and management. Addict Dis. 1975;2:141–58.
- Jones HE, Seashore C, Johnson E, Horton E, O'Grady KE, Andringa K, et al. Psychometric assessment of the Neonatal Abstinence Scoring System and the MOTHER NAS Scale. Am J Addict. 2016;25:370–3.
- 14. Grossman M, Berkwitt A, Osborn R, Xu Y, Esserman DA, Shapiro ED. et al. An initiative to improve the quality of care of infants with neonatal abstinence syndrome. Pediatrics. 2017;139: e20163360
- Grossman MR, Lipshaw MJ, Osborn RR, Berkwitt AK. A novel approach to assessing infants with neonatal abstinence syndrome. Hosp Pediatr. 2018;8:1–6.
- Holmes AV, Atwood EC, Whalen B, Beliveau J, Jarvis JD, Matulis J. et al. Rooming-in to treat neonatal abstinence syndrome: improved family-centered care at lower cost. Pediatrics. 2016;137:e20152929

- Bagley SM, Wachman EM, Holland E, Brogly SB. Review of the assessment and management of neonatal abstinence syndrome. Addict Sci Clin Pract. 2014;9:19.
- Howard MB, Schiff MD, Penwill N, Si W, Rai A, Wolfgang T, et al. Impact of parental presence at infants' bedside on neonatal abstinence syndrome. Hosp Pediatr. 2017;7:63–69.
- MacMillan KD, Rendon CP, Verma K, Riblet N, Washer DB, Holmes AV. Rooming-in for neonatal abstinence syndrome: a systematic review and meta-analysis. *JAMA Pediatrics*. Feb. 5. https://doi.org/10.1001/jamapediatrics.2017.5195 [Epub ahead of print].
- 20. Neo Advances [homepage on the Internet]. Karen D'Apilito. Available from: https://www.neoadvances.com/index.html.
- Clinical Trials.Gov: improving outcomes in neonatal abstinence syndrome [homepage on the Internet]. First posted October 2013, updated December 2017. Available from: https://clinicaltrials.gov/ ct2/show/NCT01958476.
- Taylor MJ, McNicholas C, Nicolay C, Darzi A, Bell D, Reed JE. Systematic review of the application of the plan-do-study-act method to improve quality in healthcare. BMJ Qual Saf. 2014;23:290–8.
- 23. Wachman EM, Newby PK, Vreeland J, Byun J, Bonzagni A, Bauchner H, et al. The relationship between maternal opioid agonists and psychiatric medications on length of hospitalization for neonatal abstinence syndrome. J Addict Med. 2011;5:293–9.
- Jones HE, Heil SH, Tuten M, Chisolm MS, Foster JM, O'Grady KE, et al. Cigarette smoking in opioiddependent pregnant women: neonatal and maternal outcomes. Drug Alcohol Depend. 2013;131:271–7.
- Patrick SW, Dudley J, Martin PR, Harrell FE, Warren MD, Hartmann KE, et al. Prescription opioid epidemic and infant outcomes. Pediatrics. 2015;135:842–50.
- Hall ES, Meinzen-Derr J, Wexelblatt SL. Cohort analysis of a pharmacokinetic-modeled methadone weaning optimization for neonatal abstinence syndrome. J Pediatr. 2015;167:1221–5.e1.
- Benneyan JC, Lloyd RC, Plsek PE. Statistical process control as a tool for research and healthcare improvement. BMJ Qual Saf. 2003;12:458–64.
- Saia K, Bagley SM, Wachman EM, Patel PP, Nadas MD, Brogly SB. Prenatal treatment for opioid dependency: observations from a large inner-city clinic. Addict Sci Clin Pract. 2017;12:5.