JAMA Pediatrics | Original Investigation

Association of Rooming-in With Outcomes for Neonatal Abstinence Syndrome
A Systematic Review and Meta-analysis

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IMPORTANCE Rising incidence of neonatal abstinence syndrome (NAS) is straining perinatal care systems. Newborns with NAS traditionally receive care in neonatal intensive care units (NICUs), but rooming-in with mother and family has been proposed to reduce the use of pharmacotherapy, length of stay (LOS), and cost.

OBJECTIVE To systematically review and meta-analyze if rooming-in is associated with improved outcomes for newborns with NAS.

DATA SOURCES MEDLINE, CINAHL, The Cochrane Library, and clinicaltrials.gov were searched from inception through June 25, 2017.

STUDY SELECTION This investigation included randomized clinical trials, cohort studies, quasi-experimental studies, and before-and-after quality improvement investigations comparing rooming-in vs standard NICU care for newborns with NAS.

DATA EXTRACTION AND SYNTHESIS Two independent investigators reviewed studies for inclusion. A random-effects model was used to pool dichotomous outcomes using risk ratio (RR) and 95% CI. The study evaluated continuous outcomes using weighted mean difference (WMD) and 95% CI.

MAIN OUTCOMES AND MEASURES The primary outcome was newborn treatment with pharmacotherapy. Secondary outcomes included LOS, inpatient cost, and harms from treatment, including in-hospital adverse events and readmission rates.

RESULTS Of 413 publications, 6 studies (n = 549 [number of patients]) met inclusion criteria. In meta-analysis of 6 studies, there was consistent evidence that rooming-in is preferable to NICU care for reducing both the use of pharmacotherapy (RR, 0.37; 95% CI, 0.19-0.71; I^2 = 85%) and LOS (WMD, −10.41 days; 95% CI, −16.84 to −3.98 days; I^2 = 91%). Sensitivity analysis resolved the heterogeneity for the use of pharmacotherapy, significantly favoring rooming-in (RR, 0.32; 95% CI, 0.18-0.57; I^2 = 13%). Three studies reported that inpatient costs were lower with rooming-in; however, significant heterogeneity precluded quantitative analysis. Qualitative analysis favored rooming-in over NICU care for increasing breastfeeding rates and discharge home in familial custody, but few studies reported on these outcomes. Rooming-in was not associated with higher rates of readmission or in-hospital adverse events.

CONCLUSIONS AND RELEVANCE Opioid-exposed newborns rooming-in with mother or other family members appear to be significantly less likely to be treated with pharmacotherapy and have substantial reductions in LOS compared with those cared for in NICUs. Rooming-in should be recommended as a preferred inpatient care model for NAS.

JAMA Pediatr. 2018;172(4):345-351. doi:10.1001/jamapediatrics.2017.5195
Published online February 5, 2018.

Supplemental content

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Neonatal abstinence syndrome (NAS) is a collection of signs and symptoms of newborn opioid withdrawal after intrauterine exposure.[1] Other descriptions of the syndrome include neonatal opioid withdrawal syndrome and neonatal withdrawal syndrome.[2] Neonatal abstinence syndrome manifests 24 to 96 hours after delivery with increased muscle tone, tremors, sweating, vomiting, diarrhea, and other symptoms. Between 1999 and 2013, the incidence of NAS in the United States increased from 1.5 to 6.0 cases per 1000 births,[3] with a mean cost in 2012 of $93 400 per newborn stay.[4]

While standardized approaches to pharmacologic treatment of NAS improve outcomes, the role of nonpharmacologic or "environmental" interventions in managing NAS is less clear.[5] Opioid-exposed newborns are typically cared for in neonatal intensive care units (NICUs), and standardized scoring systems, such as the modified Finnegan system, are used to quantify NAS symptoms and to adjust medications used in treatment.[6] Paradoxically, studies[6,7] have found that opioid-exposed newborns in NICUs experience more severe withdrawal, longer length of stay (LOS), and increased pharmacotherapy compared with newborns who room in. In rooming-in care, infant and mother remain together 24 hours a day unless separation is indicated for medical reasons or safety concerns.[8] More maternal time at the infant bedside improves NAS outcomes but is harder to accomplish in a typical NICU.[9] Neonatal intensive care units may be poor settings for newborns with NAS because of increased sensitivity to high clinical activity levels.[10] In settings where separation from mothers is inherent in a NICU admission, it can interfere with bonding and may contribute to maternal perceptions of guilt and stigma.[9-11] While rooming-in may be effective for NAS, potential risks include unintentional suffocation, falling from an adult bed, or undertreated NAS after hospital discharge.[10-12]

The benefits and harms of rooming-in for NAS have to date only been evaluated by single-center studies. We conducted a systematic review and meta-analysis to evaluate the benefits and harms of rooming-in compared with standard NICU care for management of NAS.

Key Points

Question Does rooming-in with family reduce the use of medications, length of stay, and costs in the inpatient treatment of neonatal abstinence syndrome?

Findings In this systematic review and meta-analysis of 6 studies comprising 549 patients, rooming-in was associated with a reduction in the need for pharmacologic treatment and a shorter hospital stay when rooming-in was compared with standard neonatal intensive care unit admission for neonatal abstinence syndrome.

Meaning Rooming-in should be considered as the preferred inpatient care model for all opioid-exposed newborns, including those with neonatal abstinence syndrome.

Methods

Review Protocol

We used Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines for reporting of methods and findings (**Figure 1**).[13] We included randomized clinical trials, cohort studies, quasi-experimental studies, and before-and-after quality improvement (QI) investigations of rooming-in as an intervention for opioid-exposed newborns. Prenatal opioid exposure comprised maternal use of heroin, prescription opioids, and nonprescription opioids, as well as prescribed or illicit opioid replacement therapy. Polysubstance users were not excluded. We defined rooming-in as infant and mother remaining together 24 hours per day throughout the postpartum hospital stay unless separation was indicated for medical needs other than NAS symptoms. We included studies reporting on other cointerventions, such as increased skin-to-skin contact, swaddling, soothing, and breastfeeding support, because greater parental involvement in infant soothing is the primary plausible mechanism for rooming-in efficacy.[14,15] We required reporting on at least the primary outcome of interest. Our systematic review protocol and search methods are available in the eMethods in the Supplement.

Outcome Measures

The primary outcome was the proportion of infants requiring pharmacologic treatment. Current treatment guidelines call for the use of oral morphine sulfate or methadone hydrochloride to relieve moderate or severe NAS symptoms.[5] Therefore, the proportion of pharmacologically treated newborns was used as an adequate proxy for those with significant NAS.[5] As secondary outcomes, we assessed the cumulative dose of opioid medication, duration of opioid treatment course, LOS, total cost of hospitalization, family satisfaction, breastfeeding incidence, and the proportion of infants discharged home in familial custody. To evaluate potential harms of rooming-in, we examined reports of adverse events and readmission rates.[16]

Search Strategy, Study Selection, and Data Collection

We searched MEDLINE (1946 to June 25, 2017), CINAHL (1981-2016), and The Cochrane Library using keywords and Medical Subject Headings to generate sets for the themes of NAS and rooming-in. We used the Boolean term "AND" to find intersections. No limits were applied. In addition, we searched clinicaltrials.gov, reviewed references of included studies meeting inclusion criteria, and used the expertise of one of us (A.V.H.) in the field of NAS to identify any unpublished studies not identified by our principal electronic database search strategy. Complete search strategies for each database are included in the eMethods in the Supplement. Two of us (K.D.L.M. and C.P.R.) independently screened titles and abstracts. After the initial screening, these 2 authors independently assessed selected full texts to determine appropriateness for inclusion. They then independently used a standardized, piloted data collection form to extract data on key study components, including methods, participant characteristics, outcomes, and assessment techniques. Two independent reviewers (2 of us, K.V. and D.B.W.) then applied the Risk of Bias in Non-randomised Studies of Interventions (ROBINS-I) tool[17] to each study. Studies were defined as having low risk of bias if the 2 independent reviewers rated the study as such across

all categories. The results of our quality assessment were incorporated into the described sensitivity analysis. Discrepancies at each stage were resolved by consensus.

Statistical Analysis

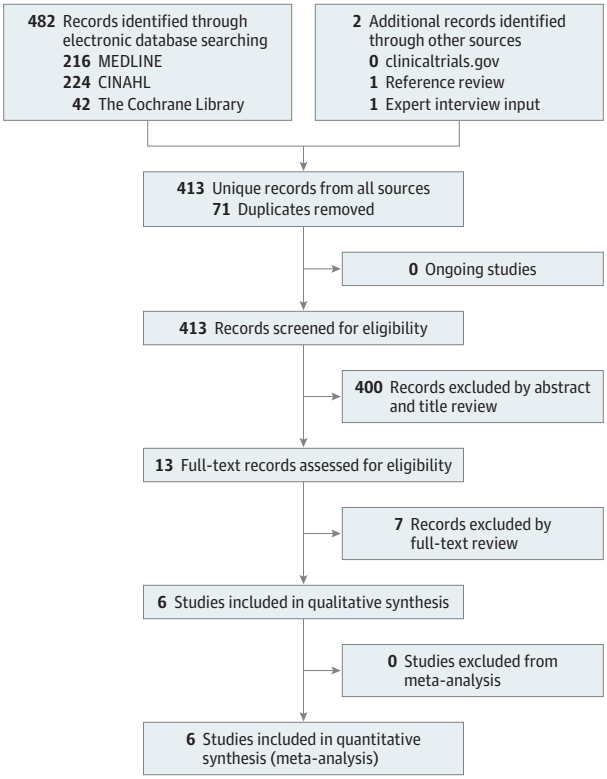
To summarize the treatment effect, we measured risk ratio (RR) and 95% CI for dichotomous outcomes and weighted mean difference (WMD) and 95% CI for continuous outcomes. Some secondary outcomes were not amenable to quantitative analysis because either studies measured them in disparate manners that could not be mathematically resolved or too few studies reported on the primary outcome of interest. Therefore, we provided a qualitative summary for this subset of outcomes across studies.

Of the included publications, 3 studies[7,18,19] provided insufficient data to allow for quantitative analysis. We contacted the respective authors and received responses from 2, allowing us to analyze the need for pharmacotherapy and LOS from these 2 studies.[18,19] The third study[7] was included in the systematic review but was excluded from the portion of the analysis associated with the missing data.

We used a software program (RevMan, version 5.3; The Cochrane Collaboration[20]) to conduct the meta-analysis using a random-effects model by pooling study results for all outcomes to appropriately address expected heterogeneity. In the case of multiple comparison groups, only one group was selected for dichotomous variables.[7] We assessed groupings for the heterogeneity using the I^2 statistic. This statistic evaluates the consistency of the results across studies. A notable advantage of the I^2 statistic is that it does not depend on the number of studies included in the meta-analysis and thus can be used even when the study sample size is small.[21] We used the conventional threshold of I^2 exceeding 50% to define meaningful heterogeneity. In instances of heterogeneity, we first considered the contribution of study design or methodological flaws. We then performed sensitivity analyses to reanalyze outcomes, including the greatest possible number of homogeneous studies (I^2<50%). We performed sensitivity analyses based on each element of the ROBINS-I methodological quality assessment tool on the overall summary estimates, restricting analysis to only those studies deemed to have low risk of bias. We evaluated whether this restricted analysis affected the magnitude, direction, and statistical significance of the overall summary estimate. We also performed additional sensitivity analysis to account for the different types of study designs. First, we limited the summary estimates to the before-and-after studies.[7,18,19,22,23] Second, we removed the study by Hünseler et al[24] owing to high risk of bias in selection of participants (ie, mothers were encouraged to choose the intervention rather than systematically applying rooming-in to the entire population of interest). We then excluded 2 QI studies, by Holmes et al[18] and by Grossman et al,[19] because during the implementation phase of the rooming-in intervention there were concurrent changes in how NAS scores affected the use of pharmacotherapy.

For the outcomes not amenable to quantitative analysis, we provided a qualitative result summary, first assessing which group (rooming-in vs comparison group) was favored for each outcome and then considering potential methodological flaws influencing these results. We generated a summary assessment based on the overall trends in the results and categorized outcomes as favoring rooming-in, the comparison group, or neither group or as unclear. Statistical significance was determined using *P* values calculated by 2-sided *t* tests.

Figure 1. PRISMA Study Selection Flow Diagram



PRISMA indicates Preferred Reporting Items for Systematic Reviews and Meta-analyses.

Results

The initial search identified 482 potentially eligible studies. After removing duplicates, we screened 413 studies and excluded 400 based on title and abstract. We performed full-text review of 13 publications, and 6 studies[7,18,19,22-24] (n = 549 [number of patients]) met our inclusion criteria (Figure 1 and **Table**). The included studies were published between 2007 and 2017 and were varied in sample size, geographic location, and clinical setting. In 3 included studies,[7,19,22] all infants in the comparison group were admitted to the NICU for increased observation. In the remaining 3 studies,[18,23,24] only infants in the comparison group who needed increased observation or pharmacologic intervention were transferred to NICU-level care. The reasons for exclusion of 7 studies after full-text review included overlapping populations across studies, institutional practices that limited pharmacologic treatment during the initial 36 to 72 hours of life, or insufficient data on rooming-in.

There was strong and robust consistency in the results across included studies (eTable 1 in the Supplement). The most common methodological concern was risk for confounding. In the

Table. Characteristics of Studies Evaluating the Use of Rooming-in to Reduce the Need for Pharmacotherapy to Treat Neonatal Abstinence Syndrome

Source	Study Design	Total No.	RI, No.	CG, No.	Maternal Age, Mean (SD), y		Gestational Age, Mean (SD), wk		Birth Weight, Mean (SD), g	
					RI	CG	RI	CG	RI	CG
Abrahams et al,[7] 2007	Before-and-after assessment, retrospective cohort	106	32	38,[a] 36	29.2	29.8, 26.2	NR	NR	NR	NR
Holmes et al,[18] 2016	Before-and-after assessment of QI intervention	163	48	61, 54[a]	NR	NR	39	39	2979	2979
Hünseler et al,[24] 2013	Retrospective cohort	77	24	53	28.8 (5.7)	29.9 (5.8)	38.1 (1.9)	37.9 (2.6)	2720 (570)	2620 (630)
Grossman et al,[19] 2017	Before-and-after assessment of QI study	99	44	55	29.1 (5.1)	27.5 (5.8)	38.4 (1.4)	38.9 (1.6)	3100 (600)	3100 (600)
McKnight et al,[22] 2016	Before-and-after assessment	44	24	20	30	30	39	40	3261.9 (366.0)	3314.4 (532.3)
Saiki et al,[23] 2010	Before-and-after assessment	60	18	42	29.5	31	39.5	39.1	2910	2860

Abbreviations: CG, comparison group; NR, not recorded; QI, quality improvement; RI, rooming-in.

[a] Comparison group used in meta-analysis of dichotomous variables.

2 QI studies,[18,19] clinical criteria for pharmacologic management were adjusted during implementation of the rooming-in intervention. Baseline study characteristics for the rooming-in vs control groups were not described in one study.[18] Five studies[7,19,22-24] provided data to support that there were no statistically significant differences between the rooming-in and comparison groups. Specifically, 4 studies[7,22-24] reported on maternal type of specific drug abuse, with no statistically significant difference in rates of use between intervention and comparison groups. The use of the different patient samples as controls in the before-and-after studies and the historical controls in QI studies also raised concerns that the reported change in outcomes may have been due to secular trends rather than the rooming-in intervention.[18,19,22,23] One study[7] also included an external control group. In all included studies, outcomes were reported based on the initial assignment to intervention or comparison group, which was determined before birth.

Need for Pharmacotherapy

All 6 studies found that rooming-in was associated with a lower proportion of infants requiring pharmacotherapy compared with standard NICU care (RR, 0.37; 95% CI, 0.19-0.71). However, there was significant heterogeneity among the included studies (I^2 = 85%). After removing 3 studies for simultaneously using multiple interventions[18,19] or for allowing maternal group selection,[24] the heterogeneity resolved, and rooming-in continued to be significantly favored (RR, 0.32; 95% CI, 0.18-0.57) (I^2 = 13%) (**Figure 2**).

In the first sensitivity analysis, we examined the value of using a historical internal control group (vs an external control) for the study by Abrahams et al.[7] This resulted in an unchanged RR of 0.37. In our second sensitivity analysis, we limited the investigation to 4 before-and-after studies.[18,19,22,23] This resulted in an RR of 0.28, with significant heterogeneity (I^2 = 62%). In our third sensitivity analysis, we removed the 2 QI studies.[18,19] This resulted in an RR of 0.35, with an I^2 of 81%. Finally, we removed the QI studies[18,19] and the study by Hünseler et al.[24] This resulted in an RR of 0.32, with an I^2 of 13%. All sensitivity analyses demonstrated an association between rooming-in as an intervention and limiting pharmacotherapy, with statistically significant RRs between 0.27 and 0.37.

Length of Stay

All 6 studies found that LOS was significantly shorter with rooming-in vs standard NICU care (WMD, −10.41 days; 95% CI, −16.84 to −3.98 days). However, there was again significant heterogeneity among the included studies (I^2 = 91%). After removing 3 studies[18,19,24] for the same reasons related to study design noted above (see the Need for Pharmacotherapy subsection in this Results section), the heterogeneity resolved, and rooming-in continued to be favored (WMD, −12.84 days; 95% CI, −20.02 to −5.67 days) (I^2 = 58%) (**Figure 3**).

In the first sensitivity analysis on LOS, we examined the value of using the historical internal control group (vs the external control) in the study by Abrahams et al[7] and found an unchanged LOS (WMD, −10.41 days). In the second sensitivity analysis, we limited our investigation to 4 before-and-after studies.[18,19,22,23] This resulted in a WMD of −10.84 days, with significant heterogeneity (I^2 = 95%). In the third sensitivity analysis, we removed the 2 QI studies.[18,19] This resulted in a WMD of −10.86, with significant heterogeneity (I^2 = 65%). Finally, we removed the QI studies[18,19] and the study by Hünseler et al.[24] This resulted in a WMD of −12.84 days, with an I^2 of 58%. All sensitivity analyses demonstrated a strong association between rooming-in as an intervention and shortening LOS by approximately 10 to 12 days.

Sensitivity analyses conducted based on each element of the ROBINS-I methodological quality assessment tool showed no significant association with the need for pharmacotherapy. Similar results were found for length of stay.

Cost

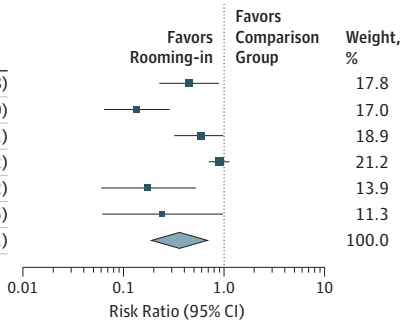
The results of the 3 studies[18,19,24] reporting inpatient costs in US dollars suggested that rooming-in is associated with lower costs (eTable 2 in the Supplement). However, there

Figure 2. Rooming-in vs Usual Care on the Need for Pharmacotherapy

A Meta-analysis

Source	Rooming-in No. of Events	Rooming-in Total No.	Comparison Group No. of Events	Comparison Group Total No.	Risk Ratio (95% CI)	Weight, %
Abrahams et al,[7] 2007	8	32	21	38	0.45 (0.23-0.88)	17.8
Grossman et al,[19] 2017	6	44	54	55	0.14 (0.07-0.29)	17.0
Holmes et al,[18] 2016	13	48	25	54	0.58 (0.34-1.01)	18.9
Hûnseler et al,[24] 2013	19	24	47	53	0.89 (0.71-1.12)	21.2
McKnight et al,[22] 2016	3	20	20	24	0.18 (0.06-0.52)	13.9
Saiki et al,[23] 2010	2	18	19	42	0.25 (0.06-0.95)	11.3
Total (95% CI)	51	186	186	266	0.37 (0.19-0.71)	100.0

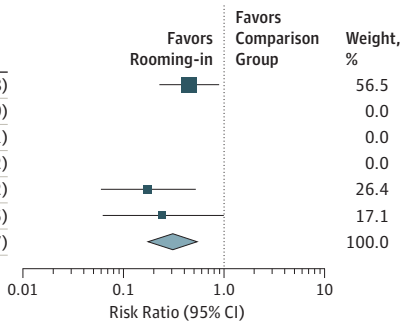
Heterogeneity: $\tau^2 = 0.51$; $I^2 = 85\%$
Test for overall effect $z = 2.99$; $P = .003$



B Sensitivity analysis

Source	Rooming-in No. of Events	Rooming-in Total No.	Comparison Group No. of Events	Comparison Group Total No.	Risk Ratio (95% CI)	Weight, %
Abrahams et al,[7] 2007	8	32	21	38	0.45 (0.23-0.88)	56.5
Grossman et al,[19] 2017	6	44	54	55	0.14 (0.07-0.29)	0.0
Holmes et al,[18] 2016	13	48	25	54	0.58 (0.34-1.01)	0.0
Hûnseler et al,[24] 2013	19	24	47	53	0.89 (0.71-1.12)	0.0
McKnight et al,[22] 2016	3	20	20	24	0.18 (0.06-0.52)	26.4
Saiki et al,[23] 2010	2	18	19	42	0.25 (0.06-0.95)	17.1
Total (95% CI)	13	70	60	104	0.32 (0.18-0.57)	100.0

Heterogeneity: $\tau^2 = 0.04$; $I^2 = 13\%$
Test for overall effect $z = 3.86$; $P < .001$



A, Meta-analysis, including 6 studies.[7,18,19,22-24] B, Sensitivity analysis, including only the before-and-after studies that were not quality improvement investigations.

was significant heterogeneity across studies (I^2 = 97%), which precluded a formal meta-analysis.

Qualitative Analysis

None of the included studies reported any adverse events with rooming-in. Three studies[7,18,23] reported on readmission rates, with no increase found (eTable 3 in the Supplement). Four studies[7,19,22,23] reported on breastfeeding, with 2 studies noting an increase in breastfeeding with rooming-in and 2 studies reporting no difference (eTable 4 in the Supplement). Four studies[7,18,23,24] reported on discharge home with mother or other family member; only one study[7] showed a larger proportion of rooming-in infants remaining in familial custody. The remaining 3 studies[18,23,24] all reported high rates of discharge with family, with no statistically significant difference in rates between study groups (eTable 5 in the Supplement).

Three studies[7,23,24] reported on the mean length of opioid medication treatment, all of which identified a decrease in the number of days receiving pharmacotherapy, proportionate to the decrease in LOS seen above (see the Length of Stay subsection herein). Only one study[18] reported on changes in the cumulative dose of opioid medication, and no included studies reported on patient satisfaction. We were unable to conduct a formal assessment for publication bias due to inclusion of only 6 studies in the meta-analysis.[25]

Discussion

This systematic review and meta-analysis demonstrates that rooming-in is associated with decreased need for pharmacologic treatment of NAS and shorter LOS. The results of several included studies[18,19,24] suggest that rooming-in is associated with reduced hospital costs, but the significant heterogeneity across studies precluded quantitative analysis. Because of variable reporting, we were unable to draw formal conclusions about the role of rooming-in on other secondary outcomes of interest. The findings of 2 studies[7,19] suggested that breastfeeding increases with rooming-in. There was no evidence that rooming-in for NAS was associated with a significant increase in hospital readmission. Reporting of adverse events was insufficient to draw any conclusions about an association between rooming-in and these outcomes. Our findings agree with prior review articles[14,26,27] of nonpharmacologic management of NAS, which also suggested that rooming-in is associated with decreased NAS severity and shorter LOS.

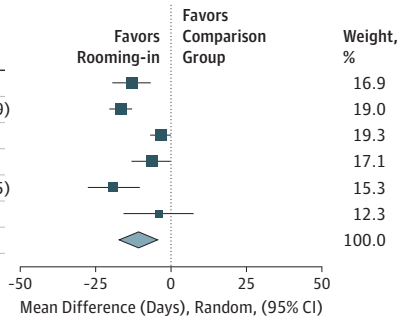
Our systematic review included studies from the United States, Canada, and Europe and covered a range of clinical settings. Therefore, rooming-in could be effective in diverse settings that manage neonates at risk for NAS. Our findings are relevant to current practice because implementing rooming-in for opioid-exposed newborns is straightforward and has

Figure 3. Rooming-in vs Usual Care on Length of Stay

A Meta-analysis

Source	Rooming-in Mean	Rooming-in SD	Rooming-in Total	Comparison Group Mean	Comparison Group SD	Comparison Group Total	Mean Difference (Days), Random, (95% CI)	Weight, %
Abrahams et al,[7] 2007	11.8	9.1	32	24.7	22.2	74	-12.90 (-18.86 to -6.94)	16.9
Grossman et al,[19] 2017	5.9	1.9	44	22.4	10.8	55	-16.50 (-19.41 to -13.59)	19.0
Holmes et al,[18] 2016	6.7	4.2	48	10	7.5	54	-3.30 (-5.63 to -0.97)	19.3
Hûnseler et al,[24] 2013	36.6	10.2	24	42.8	15.3	53	-6.20 (-12.00 to -0.40)	17.1
McKnight et al,[22] 2016	5	17.8	20	24	2.2	24	-19.00 (-26.85 to -11.15)	15.3
Saiki et al,[23] 2010	15.9	21.4	18	19.8	17.9	42	-3.90 (-15.17 to 7.37)	12.3
Total (95% CI)			186			302	-10.41 (-16.84 to -3.98)	100.0

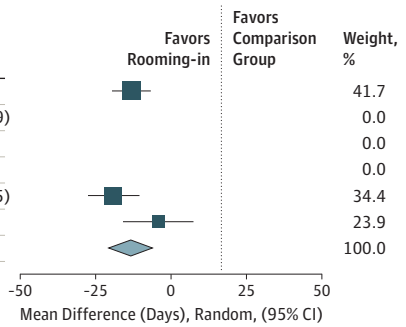
Heterogeneity: $\tau^2 = 54.31$; $I^2 = 91\%$
Test for overall effect $z = 3.17$; $P = .002$



B Sensitivity analysis

Source	Rooming-in Mean	Rooming-in SD	Rooming-in Total	Comparison Group Mean	Comparison Group SD	Comparison Group Total	Mean Difference (Days), Random, (95% CI)	Weight, %
Abrahams et al,[7] 2007	11.8	9.1	32	24.7	22.2	74	-12.90 (-18.86 to -6.94)	41.7
Grossman et al,[19] 2017	5.9	1.9	44	22.4	10.8	55	-16.50 (-19.41 to -13.59)	0.0
Holmes et al,[18] 2016	6.7	4.2	48	10	7.5	54	-3.30 (-5.63 to -0.97)	0.0
Hûnseler et al,[24] 2013	36.6	10.2	24	42.8	15.3	53	-6.20 (-12.00 to -0.40)	0.0
McKnight et al,[22] 2016	5	17.8	20	24	2.2	24	-19.00 (-26.85 to -11.15)	34.4
Saiki et al,[23] 2010	15.9	21.4	18	19.8	17.9	42	-3.90 (-15.17 to 7.37)	23.9
Total (95% CI)			70			140	-12.84 (-20.02 to -5.67)	100.0

Heterogeneity: $\tau^2 = 22.87$; $I^2 = 58\%$
Test for overall effect $z = 3.51$; $P < .001$



A, Meta-analysis, including 6 studies.[7,18,19,22-24] B, Sensitivity analysis, including only the before-and-after studies that were not quality improvement investigations.

clear benefits. It allows for greater parental involvement by increasing opportunities for families to provide nonpharmacologic treatment and permits more efficient use of institutional resources.

The quality of the included studies was high, and the results were consistent across them. Because most of the studies used a historical cohort, it is important to consider the observed results in light of secular trends. Studies that included a concurrent external control group also favored rooming-in and demonstrated no significant change in the findings. The risk for ascertainment bias in studies was low because the included studies used standardized definitions for rooming-in and the studied outcomes were objective (ie, the proportion treated with medications, LOS, and total cost). However, rooming-in is not an isolated intervention. In the 2 included QI studies,[18,19] a number of cointerventions occurred during the course of the investigations, including changes to scoring practices that could have explained some of the observed improvement in outcomes. While the results of all included studies could be considered confounded by factors known to lessen NAS symptoms, such as increased skin-to-skin time, more opportunities for breastfeeding, and greater parental involvement and improved soothing techniques, we believe that these covariates are not confounders but rather are mediators that contribute to the benefits of rooming-in.

Strengths and Limitations

This study has a number of strengths, including strict adherence to The Cochrane Library and PRISMA guidelines for systematic review and meta-analysis conduct and reporting. We used a comprehensive search strategy that included multiple electronic databases and additional techniques to identify unpublished studies. Because rooming-in is a recent intervention for NAS, there is limited available literature. We believe that our search strategy comprehensively synthesized the available data.

First among the limitations of this systematic review and meta-analysis is the likely publication bias favoring rooming-in because it would be unlikely for researchers to publish their results with negative or insignificant findings. This is particularly concerning for QI studies because negative QI interventions are rarely published.[25,28] We were unable to formally assess publication bias due to analyzing less than 10 studies.[25] Second, to comprehensively identify negative or insignificant outcomes, we incorporated all reported outcome measures from each study, regardless of whether the measure was the intervention target. The included studies may have lacked sufficient power to fully evaluate secondary outcomes. Third, there was variable reporting of the secondary outcomes of this systematic review and meta-analysis across the included studies, particularly regarding adverse events and readmission rates. While the included studies[7,18,23] measuring readmission demonstrated no increase among roomed-in infants, these events are rare, and it is possible that investigations lacked sufficient power to detect potential negative consequences of rooming-in. Fourth, we encountered significant heterogeneity among the included studies for the primary and secondary outcomes. This was anticipated given the varied nature of the study designs and settings and was particularly exacerbated by inclusion of 2 large QI studies[18,19] that by virtue of their methods incorporated several

staged interventions. Reassuringly, when we accounted for these methodological issues in our sensitivity analysis, we were able to resolve the heterogeneity for our primary outcome, and rooming-in continued to show a statistically significant benefit over standard NICU care. The results of this systematic review and meta-analysis should be interpreted with careful consideration of the validity of the final estimations of intervention effect size.

As rooming-in interventions are implemented across a growing number of institutions, it will be important to monitor for potential adverse events of rooming-in, such as failure to thrive, accidental suffocation, and readmission rates. It will also be necessary to determine an association between rooming-in and breastfeeding and custody arrangements at discharge. While there is emerging evidence to suggest that rooming-in may also be associated with lower hospital costs, future studies should evaluate this in a systematic and standardized manner, allowing for adequate comparison across studies. Finally, future research should explore the possible long-term implications of rooming-in for infant health and development, strength of the mother-child bond, and potential to mitigate the risk of maternal relapse into active substance abuse.

Conclusions

There is consistent evidence supporting rooming-in as an effective strategy for managing NAS by reducing the need for pharmacotherapy and decreasing LOS. This systematic review and meta-analysis of the current literature demonstrates compelling data for rooming-in as beneficial for newborns with NAS or at risk for NAS. In clinical care settings where it is safe and feasible, we recommend that rooming-in be considered as a preferred management strategy for opioid-exposed newborns and for newborns with NAS.

ARTICLE INFORMATION

Accepted for Publication: November 9, 2017.

Published Online: February 5, 2018. doi:10.1001/jamapediatrics.2017.5195

Author Contributions: Ms Verma had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: All authors.
Acquisition, analysis, or interpretation of data: MacMillan, Rendon, Verma, Washer.
Drafting of the manuscript: MacMillan, Rendon, Verma, Riblet, Washer.
Critical revision of the manuscript for important intellectual content: MacMillan, Rendon, Verma, Volpe Holmes.
Statistical analysis: MacMillan, Rendon, Verma, Washer, Volpe Holmes.
Administrative, technical, or material support: Volpe Holmes.
Study supervision: Riblet, Volpe Holmes.

Conflict of Interest Disclosures: None reported.

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REFERENCES

1. Jones HE, Fielder A. Neonatal abstinence syndrome. *Prev Med*. 2015;80:12-17.

2. McQueen K, Murphy-Oikonen J. Neonatal abstinence syndrome. *N Engl J Med*. 2016;375(25):2468-2479.

3. Ko JY, Patrick SW, Tong VT, Patel R, Lind JN, Barfield WD. Incidence of neonatal abstinence syndrome. *MMWR Morb Mortal Wkly Rep*. 2016;65(31):799-802.

4. Patrick SW, Schumacher RE, Benneyworth BD, Krans EE, McAllister JM, Davis MM. Neonatal abstinence syndrome and associated health care expenditures: United States, 2000-2009. *JAMA*. 2012;307(18):1934-1940.

5. Hudak ML, Tan RC; Committee on Drugs; Committee on Fetus and Newborn; American Academy of Pediatrics. Neonatal drug withdrawal. *Pediatrics*. 2012;129(2):e540-e560.

6. Newman A, Davies GA, Dow K, et al. Rooming-in care for infants of opioid-dependent mothers. *Can Fam Physician*. 2015;61(12):e555-e561.

7. Abrahams RR, Kelly SA, Payne S, Thiessen PN, Mackintosh J, Janssen PA. Rooming-in compared with standard care for newborns of mothers using methadone or heroin. *Can Fam Physician*. 2007;53(10):1722-1730.

8. World Health Organization. *Baby-Friendly Hospital Initiative: Revised, Updated and Expanded for Integrated Care*. Geneva, Switzerland: WHO Press; 2009.

9. Velez M, Jansson LM. The opioid dependent mother and newborn dyad. *J Addict Med*. 2008;2(3):113-120.

10. Cleveland LM, Bonugli R. Experiences of mothers of infants with neonatal abstinence syndrome in the neonatal intensive care unit. *J Obstet Gynecol Neonatal Nurs*. 2014;43(3):318-329.

11. Cleveland LM, Gill SL. "Try not to judge": mothers of substance exposed infants. *MCN Am J Matern Child Nurs*. 2013;38(4):200-205.

12. Isemann B, Meinzen-Derr J, Akinbi H. Maternal and neonatal factors impacting response to methadone therapy in infants treated for neonatal abstinence syndrome. *J Perinatol*. 2011;31(1):25-29.

13. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-analyses. *Ann Intern Med*. 2009;151(4):264-269, W64.

14. Edwards L, Brown LF. Nonpharmacologic management of neonatal abstinence syndrome. *Neonatal Netw*. 2016;35(5):305-313.

15. Jansson LM, Dipietro JA, Elko A, Velez M. Infant autonomic functioning and neonatal abstinence syndrome. *Drug Alcohol Depend*. 2010;109(1-3):198-204.

16. Feldman-Winter L, Goldsmith JP; Committee on Fetus and Newborn; Task Force on Sudden Infant Death Syndrome. Safe sleep and skin-to-skin care in the neonatal period for healthy term newborns. *Pediatrics*. 2016;138(3):pii:e20161889.

17. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I. *BMJ*. 2016;355:i4919.

18. Holmes AV, Atwood EC, Whalen B, et al. Rooming-in to treat neonatal abstinence syndrome. *Pediatrics*. 2016;137(6):e20152929.

19. Grossman MR, Berkwitt AK, Osborn RR, et al. An initiative to improve the quality of care of infants with neonatal abstinence syndrome. *Pediatrics*. 2017;139(6):e20163360.

20. *Review Manager (RevMan)* [computer program]. Version 5.3. Copenhagen, Denmark: The Nordic Cochrane Centre, The Cochrane Collaboration; 2014.

21. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557-560.

22. McKnight S, Coo H, Davies G, et al. Rooming-in for infants at risk of neonatal abstinence syndrome. *Am J Perinatol*. 2016;33(5):495-501.

23. Saiki T, Lee S, Hannam S, Greenough A. Neonatal abstinence syndrome. *Eur J Pediatr*. 2010;169(1):95-98.

24. Hünseler C, Brückle M, Roth B, Kribs A. Neonatal opiate withdrawal and rooming-in. *Klin Padiatr*. 2013;225(5):247-251.

25. Mittman BS. Creating the evidence base for quality improvement collaboratives. *Ann Intern Med*. 2004;140(11):897-901.

26. Grossman M, Seashore C, Holmes AV. Neonatal abstinence syndrome management. *Rev Recent Clin Trials*. 2017;12(4):226-232.

27. Boucher AM. Nonopioid management of neonatal abstinence syndrome. *Adv Neonatal Care*. 2017;17(2):84-90.

28. Ralston S, Comick A, Nichols E, Parker D, Lanter P. Effectiveness of quality improvement in hospitalization for bronchiolitis. *Pediatrics*. 2014;134(3):571-581.