

Supplementary Online Content

MacMillan KDL, Rendon CP, Verma K, Riblet N, Washer DB, Holmes AV. Association of rooming-in with outcomes for neonatal abstinence syndrome: a systematic review and meta-analysis. *JAMA Pediatr*. Published online February 5, 2018. doi:10.1001/jamapediatrics.2017.5195

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Supplemental Methods

Inclusion Criteria & Outcomes of Interest

Category	Inclusion Criteria	Justification	Order
Study Design	Any of the following study types: Randomized Control Trials, Prospective and Retrospective Cohort Studies, Quasi-experimental designs, Before-After Quality Improvement Studies	Both because of the complex nature of the condition and intervention of interest, and limited available funding, and rapidly increasing incidence, we expect much of the work to be done as observational studies and QI initiatives	1
Population	Infants with intrauterine opioid exposure	This is the population at risk for Neonatal Abstinence Syndrome ^{1,2} . Infants with known substance use exposure are included, exposure to the following is considered but not limited to: heroin, prescription opioids, non-prescription opiates, opiate-replacement therapy, and poly-substance abuse that include at least one opioid.	2
Condition of Interest	Infants identified as needing observation or undergoing treatment for Neonatal Abstinence Syndrome	This is the condition that results in needing monitoring of NAS symptoms and treatment of NAS if necessary ^{1,2} .	3
Intervention	Rooming In: During newborn admission, infant and mother are allowed to stay together 24 hours a day unless separation is indicated for justifiable medical needs other than NAS symptoms. There may be other co-interventions, such as increased skin-to-skin, swaddling, soothing, breastfeeding support.	This is a family-centered environmental intervention where rooming in is the term applied to this approach to care as defined by the Baby-Friendly Hospital Initiative ³ . Co-interventions listed may be considered non-pharmacologic management of NAS symptoms will be allowable because given that the intervention of rooming-in for NAS is fairly recent, it may be impossible to find sufficient studies if excluded ^{2,4} . Additionally, allowing greater parental involvement in soothing and other nonpharmacologic treatments forms the primary plausible	4

		<p>mechanism for the efficacy of rooming-in.</p> <p>NAS scores are not an outcome of interest as different centers use different scoring methods; however, scoring should be consistent within each hospital.</p>	
Comparison group	<p>Newborns who received usual care but did not share a room with families. May or may not include other non-pharmacologic-interventions such as soothing, swaddling, breastfeeding promotion, keeping room quiet and avoiding bright lights.</p>	<p>These are infants in the same population with the condition of interest that did not receive the intervention, but were instead in a monitored nursery where parents “visit”. Co-interventions listed would be difficult and perhaps unethical to withhold</p>	5
Outcome	<p>One of the following - Reduction of any use of pharmacotherapy, breastfeeding, reduction of NAS symptom scores, length of stay, cost of stay, patient-family satisfaction scores</p>	<p>These include our primary and secondary positive outcomes of interest which might be expected to be impacted by the intervention of rooming-in^{1,2}. We plan to include studies that address any of these outcomes to avoid an overly narrow search in a relatively small field.</p>	6

Search strategies

Electronic bibliographic database searches

Queries in PubMed		
Search	Query	Items found
#1	Search "Neonatal Abstinence Syndrome"[Mesh] or "neonatal abstinence syndrome"[TIAB] or "neonatal passive addiction"[TIAB] or maternal opioid[TIAB] or maternal substance[TIAB] or opioid dependent mothers[TIAB] or in utero substance exposure[TIAB] or prenatal substance exposure [TIAB]	1,989
#2	Search (((("Rooming-in Care"[Mesh]) OR "Breast Feeding"[Mesh]) OR "Infant Care"[Mesh]) OR "Postnatal Care"[Mesh]) OR "Patients' Rooms"[Mesh] or room*[TIAB] or breast feeding[TIAB] or breastfeeding[TIAB] or patient centered care[TIAB] or family centered care[TIAB] or nonpharmacologic[TIAB] or non pharmacologic[TIAB]	203,375
#3	Search #1 and #2	216

Queries in Cochrane Library		
Search	Query	Items found
#1	"Neonatal abstinence syndrome"	124
#2	"Rooming in or rooming in care or infant care or postnatal care or patients room or room* or breastfeed* or breast feed* or patient centered care or family centered care or nonpharmacologic care or non pharmacologic"	28827
#3	Search #1 and #2	42

Queries in CINAHL		
Search	Query	Items found
#1	"neonatal abstinence syndrome"	543
#2	"Rooming in or rooming in care or infant care or postnatal care or patients room or room* or breastfeed* or breast feed* or patient centered care or family centered care or nonpharmacologic care or non pharmacologic"	105,732
#3	Search #1 and #2	224

Electronic trial registry database search

Queries in Clinicaltrials.gov		
Search	Query	Items found
#1	Search Condition: "Neonatal Abstinence Syndrome"	36
#2	Search Intervention: "Rooming-in"	2
#3	Search #1 and #2	0

Author contact with NAS expertise

Expert	Dr. Alison Holmes, MD, MPH, MS
Title/Affiliation	Pediatric Hospitalist, Associate Professor of Pediatrics at Geisel School of Medicine at Dartmouth
Date of contact	8/31/16
Results	Alerted us to pre-publication study and put in contact with Primary Investigator, Dr. Matthew Grossman, MD.

eTable 1. Risk of Bias Assessments for Included Studies

Study	Confounding	Selection of participants	Classification of interventions	Departure from intended interventions	Missing data	Measurement of outcomes	Selection of reported data	Other sources of bias
Abrahams, 2007 ⁵	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>Unclear</i>
Holmes, 2016 ⁶	<i>Unclear</i>	<i>Low</i>	<i>Low</i>	<i>High</i>	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>None</i>
Hünsleler, 2013 ⁷	<i>Low</i>	<i>High</i>	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>None</i>
Grossman, 2017 ⁸	<i>Low</i>	<i>Unclear</i>	<i>Low</i>	<i>High</i>	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>None</i>
McKnight, 2016 ⁹	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>None</i>
Saiki, 2010 ¹⁰	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>Low</i>	<i>None</i>

Low = Low risk of bias, High = High risk of bias, Unclear = Unclear risk of bias. *Based on ROBINS-I Risk of Bias assessment tool for non-randomized interventions.*¹⁶

eTable 2. Cost of Hospital Stay for Infants With NAS

Author (year)	Total sample size	RI Mean (SD)	CG Mean (SD)	Standard mean difference (95% CI)	Study arm favored (RI or CG)	Is difference statistically significant?
Grossman, 2017 ⁸	99	10,289 (5,068)	44,824 (23,726)	-1.90 (-2.38, -1.42)	RI	Yes
Holmes, 2016 ⁶	163	5,327 (3,627)	11,006 (9,628)	-0.76 (-1.16, -0.35)	RI	Yes
Hünseler, 2013 ⁷	77	14,203 (7,096)	19,166 (8,061)	-0.63 (-1.12, -0.14)	RI	Yes

Qualitative summary:

All three studies demonstrated a statistically significant reduction in cost of stay for infants with NAS. There was significant heterogeneity across the three studies ($I^2=97\%$), which precluded formal meta-analysis.

RI=Rooming-In, CG=Comparison Group; CI=confidence interval, SD=standard deviation.

eTable 3. Qualitative Assessment of Readmissions Rates for Infants With NAS

Author (year)	Total sample size	Outcome measure reported	RI Rate # (%)	CG Rate # (%)	Difference between groups RR (95% CI; p-value)	Study arm favored (RI or CG)	Is difference statistically significant?
Abrahams (2007) ⁵	106	Readmission for symptoms of NAS within 6 months	0/32 (0)	NR	NR	RI	N/A
Holmes (2016) ⁶	163	All-cause readmission within 30 days	7/109 (6.2)	2/54 (3.7)	1.7 (0.4-8.1; 0.46)	CG	No
Saiki (2010) ¹⁰	60	All-cause readmission within 2 months	0/18 (0)	0/42 (0)	0	Neither	No

Qualitative summary: None of the three studies reviewed which followed infants for hospital readmission reported a statistically significant increase in readmission for infants who roomed-in with their mothers.

RI=Rooming-In, CG=Comparison Group; RR=Risk ratio

eTable 4. Qualitative Assessment of Breastfeeding Rates for Infants With NAS

Author (year)	Total sample size	Outcome measure reported	RI Rate # (%)	CG Rate # (%)	Difference between groups RR (95% CI; p-value)	Study arm favored (RI or CG)	Is difference statistically significant?
Abrahams (2007) ⁵	106	Any breastfeeding	20/32 (62.5)	7/74 (9.5)	6.6 (3.1-14.0; <0.0001)	RI	Yes
Grossman (2017) ⁸	99	Breastfeeding at discharge	20/44 (45.5)	11/55 (20.0)	2.3 (1.2-4.2; 0.0094)	RI	Yes
McKnight (2016) ⁹	44	Any breastfeeding	14/20 (70.0)	12/24 (50.0)	1.4 (0.9-2.3; 0.18)	RI	No
Saiki (2010) ¹⁰	60	Breastfeeding with or without complementary formula feeds	8/18 (44.4)	17/42 (40.5)	1.1 (0.6-2.1; 0.77)	RI	No

Qualitative summary: One study reported a statistically significant increase in breastfeeding at discharge for infants who roomed-in with their mothers. The three remaining studies reported any breastfeeding during hospital stay, with one study demonstrating a statistically significant increase in any breastfeeding and two studies showing no statistically significant difference in breastfeeding rates between study groups.

RI=Rooming-In, CG=Comparison Group; RR=Risk ratio

eTable 5. Qualitative Assessment of Rate of Discharge Home With Mother for Infants With NAS

Author (year)	Total sample size	Outcome measure reported	RI Rate # (%)	CG Rate # (%)	Difference between groups RR (95% CI; p-value)	Study arm favored (RI or CG)	Is difference statistically significant?
Abrahams (2007) ⁵	106	Discharged in custody of mother	23/32 (71.9)	29/74 (39.2)	1.8 (1.3-2.6; 0.0009)	RI	Yes
Holmes (2016) ⁶	102	Discharged in parental care	43/48 (89.6)	50/54 (92.6)	0.97 (0.9-1.1; 0.60)	CG	No
Hünseler (2013) ⁷	77	Discharged into family	19/24 (79.2)	37/53 (69.8)	1.1 (0.9-1.5; 0.36)	RI	No
Saiki (2010) ¹⁰	60	Discharged with mother	13/18 (72.2)	25/42 (59.5)	1.2 (0.8-1.8; 0.32)	RI	No

Qualitative summary: One of the four studies reported a significant increase in proportion of infants discharged home with mother among the rooming-in group. The remaining three studies all reported relatively high rates of discharge home with family, with no statistically significant difference in rates between study groups.

RI=Rooming-In, CG=Comparison Group; RR=Risk ratio

References

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