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11-2019

Gastric residuals: Summary

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Office of Evidence Based Practice (EBP) – Critically Appraised Topic (CAT): Gastric Residuals

Specific Care Question:

In neonatal patients, does not checking gastric residuals versus checking gastric residuals, increase the incidence of necrotizing enterocolitis (NEC)?

Recommendations Based on Current Literature (Best Evidence) Only

A conditional recommendation is made against routine checking of gastric residuals, based on the Summary of Findings Table^d. The overall certainty in the evidence is low^d. See Summary by Outcome for substantiation of recommendations.

Literature Summary

Background. Routine monitoring of gastric residual volume and color in preterm infants on gavage feeds is a common practice to guide the initiation and advancement of feeds (Abiramalatha, Thanigainathan, & Ninan, 2019). Routine monitoring of gastric residual may lead to delays in the initiation, advancement of feeds, and delay in reaching full enteral feeds (Abiramalatha et al., 2019). The delay, in turn, may increase the duration of parenteral nutrition and its increased risk of associated complications (Barr, Mally, & Caprio, 2019). Delays in achieving full enteral feeds increase the risk of extrauterine growth restriction and neurodevelopmental impairment (Abiramalatha et al., 2019). Although, in the presence of abdominal distension or vomiting, measurement of gastric residuals may still be useful as part of the assessment of an individual infant with symptoms of feeding intolerance (Barr et al., 2019). This review will summarize identified literature to answer the specific care question.

Study characteristics. The search for suitable studies was completed on June 5, 2019. S. Olsen, MD reviewed the 35 titles and/or abstracts found in the search and identified one guideline and 18 single studies believed to answer the question. The guideline (Dutta et al., 2015) was assessed with the AGREE II^a instrument to assist the team in determining the appropriateness to adopt as the governing guideline for this CAT. The overall AGREE II score was 60% and it was determined to exclude the guideline for this CAT (see Table 1). After an in-depth review of the remaining articles, five studies answered the question (Kaur et al., 2015; L. A. Parker et al., 2019; Singh et al., 2018; Thomas et al., 2018; Torrazza et al., 2015). Only randomized control trials were selected for the review of this question (see Figure 1).

Summary by Outcome

NEC. Five studies (Kaur et al., 2015; Parker et al., 2019; Singh et al., 2018; Thomas et al., 2018; Torrazza et al., 2015) compared no routine monitoring of gastric residuals versus routine monitoring of gastric residuals with the outcome of NEC, ($N = 421$). There was no significant difference for the incidence of NEC, between no routine monitoring of gastric residuals versus routine monitoring of gastric residuals, $OR = 0.76$, 95 CI [0.32, 1.80] (see Figure 3 & Table 2). The reported OR and CI indicated the intervention (no routine monitoring) was not different from the comparator (routine monitoring). The heterogeneity of the studies was low, $I^2 = 5\%$.

Certainty of the evidence for NEC. The certainty of the body of evidence was low based on four factors: within-study risk of bias, directness of evidence, precision of effect estimates, and consistency among studies. The body of evidence was assessed to have very serious imprecision. Imprecision was judged as very serious due to the low number of participants and event rate.

Time to Full Feeds. Five studies (Kaur et al., 2015; L. A. Parker et al., 2019; Singh et al., 2018; Thomas et al., 2018; Torrazza et al., 2015) compared no routine monitoring of gastric residuals versus routine monitoring of gastric residuals with the outcome of time to full feeds ($N = 421$), and four (Kaur et al., 2015; L. A. Parker et al., 2019; Singh et al., 2018; Torrazza et al., 2015) are included in the meta-analysis, ($N = 371$). Thomas et al. (2018) ($n = 50$) reported time to full feeds in median and interquartile range (IQR) and was not included in the meta-analysis. Time to full feeds was significantly faster for no routine monitoring of gastric residuals compared to routine monitoring of gastric residuals, $MD = -2.84$ days, 95% CI [-4.14, 1.51] (see Figure 4 & *SOF*). The intervention of no routine monitoring of gastric residuals resulted in full feeds 1.5 to 4.1 days sooner than the comparator. The heterogeneity of the studies was low, $I^2 = 23\%$. Thomas et al. (2018) compared checking abdominal girth (AG) versus routine monitoring of gastric residuals. Time to full feeds was significantly shorter in the AG group compared to the routine monitoring of gastric residuals, Mdn (IQR) = 6 days (5, 7.5) versus 9.5 days (6.75, 13.0), respectively, $p < .0001$.

Certainty of the evidence for full feeds. The certainty of the body of evidence was very low based on four factors: within-study risk of bias, directness of evidence, precision of effect estimates and consistency among studies. The body of evidence was assessed to have serious risk of bias

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and serious imprecision. Risk of bias was judged as serious due to all studies were unblinded and could have affected the outcome. Imprecision was judged as very serious due to the low number of participants.

Identification of Studies

Search Strategy and Results (see Figure 1)

PubMed ("gastric residuals"[tw] OR GRV[tiab] OR "Gastric Emptying"[mh] OR "Gastrointestinal Contents"[mh]) AND ("Enterocolitis, Necrotizing"[mh] OR NEC[tiab] OR "necrotizing enterocolitis"[tiab] OR "Infant Nutritional Physiological Phenomena"[mh] OR "feeding advancement"[tiab] OR Enteral Nutrition[mh] OR "enteral nutrition"[tiab]) AND (Infant[mh] OR Infan*[tiab] OR Neonat*[tiab] OR Newborn*[tiab] OR "Intensive Care, Neonatal"[mh]) AND English[la] AND 2009/06:2019[dp] NOT (case reports[pt] OR comment[pt] OR letter[pt] OR news[pt] OR editorial[pt]) ("gastric residuals"[tw] OR GRV[tiab] OR "Gastric Emptying"[mh] OR "Gastrointestinal Contents"[mh]) AND (Infant[mh] OR Infan*[tiab] OR Neonat*[tiab] OR Newborn*[tiab] OR "Intensive Care, Neonatal"[mh]) AND English[la] AND 2009/06:2019[dp] NOT (case reports[pt] OR comment[pt] OR letter[pt] OR news[pt] OR editorial[pt])

(stomach[mh] OR stomach[tiab] OR gastric[tiab] OR intestines[mh] OR colon*[tiab] OR intestin*[tiab]) AND (residual*[tiab] OR content*[tiab] OR emptying[tiab] OR GRV[tiab]) AND (feeding[tiab] OR nutrition[tiab] OR advancement[tiab] OR "Enterocolitis, Necrotizing"[mh] OR NEC[tiab] OR "necrotizing enterocolitis"[tiab] OR "Infant Nutritional Physiological Phenomena"[mh]) AND (Infant[mh] OR Infan*[tiab] OR Neonat*[tiab] OR Newborn*[tiab] OR "Intensive Care, Neonatal"[mh]) AND English[la] AND 2009/06:2019[dp] NOT (case reports[pt] OR comment[pt] OR letter[pt] OR news[pt] OR editorial[pt] OR (animals[mh] NOT humans[mh]))

CINAHL S1 (gastric N2 residual*) OR GRV OR ((stomach OR gastric OR gastrointestinal) N3 (content* OR emptying)) S2 MH "Infant Feeding" OR feeding* OR MH "Infant Nutritional Physiology" OR MH "Enterocolitis, Necrotizing" OR "Necrotizing Enterocolitis" OR NEC S3 MH "infant+" OR AE "All Infant" OR infan* OR neonat* OR newborn* S4 S1 AND S2 AND S3 AND LA English AND RV Y AND PT Journal Article AND EM 200906-

EMBASE #1 'gastric residual'/exp OR 'gastric residual volume'/exp OR (gastric NEXT/2 residual*) OR GRV:ti,ab,kw OR ((stomach OR gastric OR gastrointestinal) NEAR/3 (content* OR emptying)) #2 'infant nutrition'/exp OR 'feeding'/de OR feeding*:ti,ab,kw OR 'necrotizing enterocolitis'/exp OR 'necrotizing enterocolitis':ti,ab,kw OR NEC:ti,ab,kw #3 'infant'/exp OR infan*:ti,ab,kw OR neonat*:ti,ab,kw OR newborn*:ti,ab,kw #4 #1 AND #2 AND #3 AND English:la AND (article/it OR 'article in press'/it OR review/it) AND [01-06-2009]/sd

Cochrane Library #1 (gastric NEAR/2 residual*) OR GRV:ti,ab,kw OR ((stomach OR gastric OR gastrointestinal) NEAR/3 (content* OR emptying)) #2 [mh "Enterocolitis, Necrotizing"] OR NEC:ti,ab,kw OR "necrotizing enterocolitis":ti,ab,kw OR [mh "Infant Nutritional Physiological Phenomena"] OR feeding*:ti,ab,kw #3 [mh infant] OR infan*:ti,ab,kw OR neonat*:ti,ab,kw OR newborn*:ti,ab,kw #4 #1 AND #2 AND #3 With Publication Year from 2009 to 2019; in Trials

Records identified through database searching $n = 35$

Additional records identified through other sources $n = 1$

Studies Included in this Review

Citation	Study Type
Kaur et al. (2015)	RCT
L. A. Parker et al. (2019)	RCT
Singh et al. (2018)	RCT
Thomas et al. (2018)	RCT
Torrazza et al. (2015)	RCT

Studies Not Included in this Review with Exclusion Rationale

Citation	Reason for exclusion
T. Abiramalatha et al. (2018)	Protocol
Barr et al. (2019)	Cohort
Bertino et al. (2009)	Case-Control
Cobb et al. (2004)	Case-Control

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Dutta et al. (2015)	Guideline with low AGREE II score
Fanaro (2013)	Review Article
Kumar et al. (2017)	Review Article
Lucchini et al. (2011)	Review Article
Mihatsch et al. (2002)	Cohort
Morton et al. (2018)	Qualitative Study
L. Parker et al. (2015)	Review Article
Riskin et al. (2017)	Cohort
Shulman et al. (2011)	Cohort
Li et al. (2014)	Review Article

Methods Used for Appraisal and Synthesis

^aThe Appraisal of Guidelines Research and Evaluation II (AGREE II) is an international instrument used to assess the quality and reporting of clinical practice guidelines for this analysis (Brouwers et al. 2010).

^bRayyan is a web-based software used for the initial screening of titles and / or abstracts for this analysis (Ouzzani, Hammady, Fedorowicz & Elmagarmid, 2017).

^cReview Manager (Higgins & Green, 2011) is a Cochrane Collaborative computer program used to assess the study characteristics as well as the risk of bias and create the forest plots found in this analysis.

^d[The GRADEpro Guideline Development Tool \(GDT\)](#) is the tool used to create the Summary of Findings table(s) for this analysis (see Tables **XX**).

^eThe Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram depicts the process in which literature is searched, screened, and eligibility criteria is applied (Moher, Liberati, Tetzlaff, & Altman, 2009).

^aBrouwers, M.C. et al. for the AGREE Next Steps Consortium. (2010) AGREE II: Advancing guideline development, reporting and evaluation in healthcare. *Canadian Medical Association Journal*, 182, E839-842. Retrieved from <https://www.agreetrust.org/wp-content/uploads/2017/12/AGREE-II-Users-Manual-and-23-item-Instrument-2009-Update-2017.pdf>

^bOuzzani, M., Hammady, H., Fedorowicz, Z., & Elmagarmid, A. (2016). Rayyan-a web and mobile app for systematic reviews. *Systematic Reviews*, 5(1), 210. doi:10.1186/s13643-016-0384-4

^cHiggins, J. P. T., & Green, S. e. (2011). *Cochrane Handbook for Systematic Reviews of Interventions [updated March 2011]* (Version 5.1.0 ed.): The Cochrane Collaboration, 2011.

^dGRADEpro GDT: GRADEpro Guideline Development Tool (2015). McMaster University, (developed by Evidence Prime, Inc.). [Software]. Available from grade.org.

^eMoher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med* 6(7): e1000097. doi:10.1371/journal.pmed1000097 **For more information, visit www.prisma-statement.org.**

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Acronyms Used in this Document

Acronym	Explanation
AC	Abdominal circumference
CAT	Critically appraised topic
CI	Confidence interval
EBP	Evidence Based Practice
GR	Gastric residual
GRV	Gastric residual volume
IQR	Interquartile range
NEC	Necrotizing enterocolitis
NICU	Neonatal intensive care unit
NPO	nil per os
MD	Mean difference
Mdn	Median
OR	Odds ratio
RCT	Randomized control trial
SD	Standard deviation
SOF	Summary of findings

Date Developed

October 2019

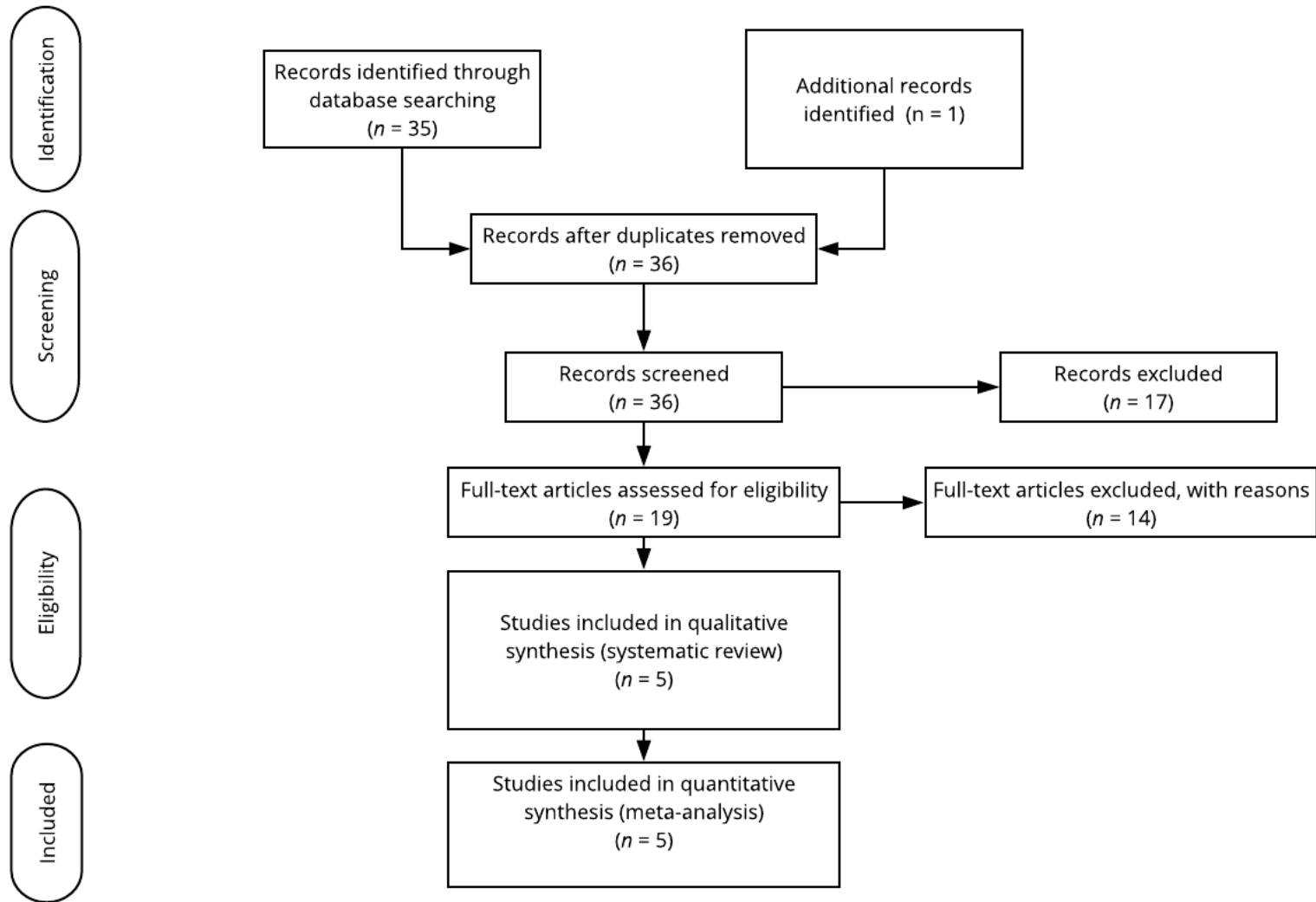


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)^e

Table 1



If you have questions regarding this Specific Care Question – please contact jmichael@cmh.edu

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AGREE II^a Summary for the Dutta et al. (2015)

Domain	Percent Agreement
Scope and purpose	83%
Stakeholder involvement	40%
Rigor of development	32%
Clarity and presentation	86%
Applicability	23%
Editorial independence	44%
Overall guideline assessment	60%
Team's recommendation for guideline use	No

Note: Four EBP Scholars completed the AGREE II for this guideline.

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	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Kaur 2015	+	+	-	?	+	+	+
Parker 2019	+	+	?	+	?	+	+
Singh 2018	+	+	-	?	+	+	+
Thomas 2018	+	+	-	?	+	+	+
Torrazza 2015	+	+	-	?	+	+	+

Figure 2. Risk of Bias Summary

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Table 2

Certainty assessment							Summary of findings				
Nº of participant s (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With routine monitoring of gastric residuals	With No routine monitoring of gastric residuals		Risk with routing monitoring of gastric residuals	Risk difference with No routine monitoring of gastric residuals
NEC stage 2 or 3 (RCTs)											
421 (5 RCTs)	Not serious	not serious	not serious	Very serious ^b	none	⊕⊕○○ LOW	11/210 (5.2%)	8/211 (3.8%)	OR 0.76 (0.32 to 1.80)	52 per 1,000	12 fewer per 1,000 (from 35 fewer to 38 more)
Time to Full Feeds (120-150ml/kg/d)											
371 (4 RCTs)	serious ^a	not serious	not serious	Very serious ^c	none	⊕⊕○○ VERY LOW				The mean full Feeds (120-150ml/kg/d) was 0	MD 2.84 lower (4.17 lower to 1.51 lower)

Explanations

- a. Lack of blinding
- b. Small sample size and low event rate
- c. Small sample size

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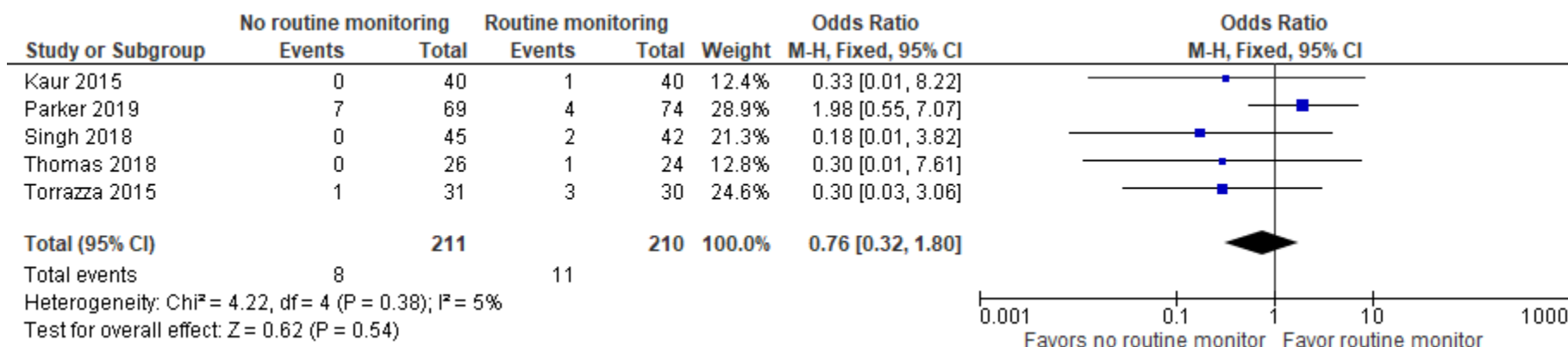


Figure 3. Comparison: No routine monitoring of GR versus routine monitoring of GR, Outcome: NEC

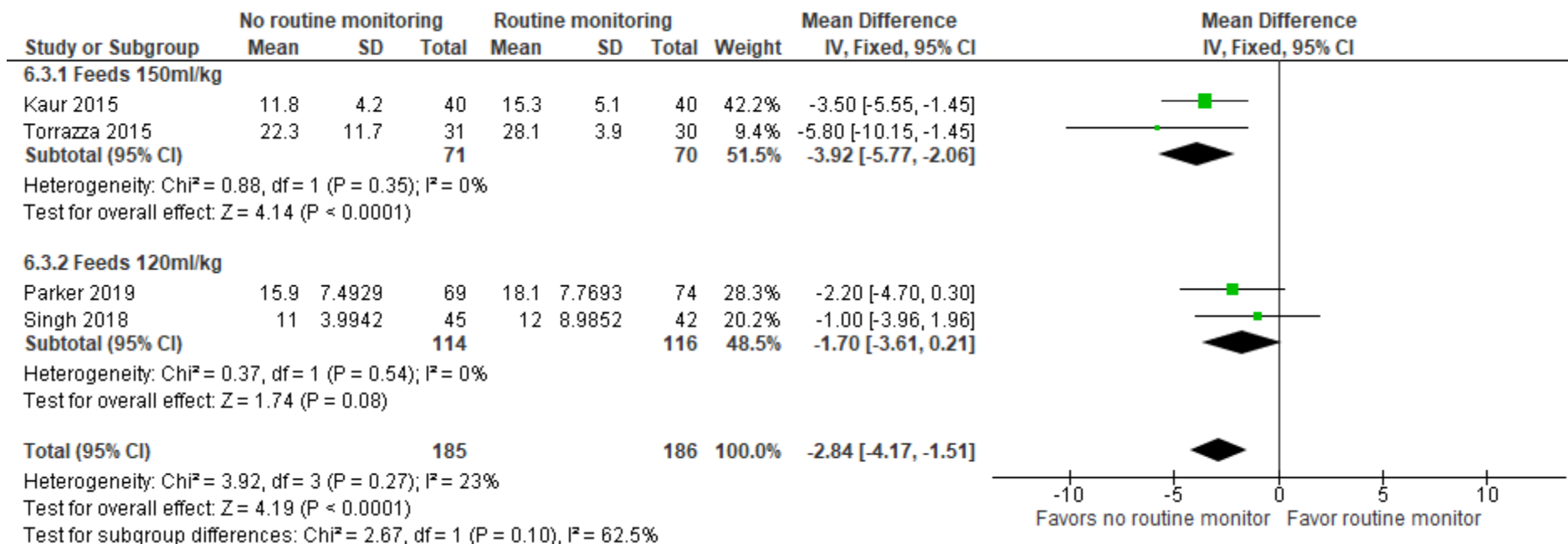


Figure 4. Comparison: No routine monitoring of GR versus routine monitoring of GR, Outcome: Time to full feeds, in days

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Kaur et al., 2015

Characteristics of Study	
Methods	Randomized control trial comparing methods of measurement
Participants	<p>Participants: Very-low-birth-weight infants admitted to neonatal intensive care unit</p> <p>Setting: Neonatal intensive care unit of a tertiary care hospital in northern India between December 2007 and April 2009</p> <p>Randomized into study: $N = 80$</p> <ul style="list-style-type: none"> • Group 1, Abdominal circumference (AC): $n = 40$ • Group 2, Gastric residual volume (GRV): $n = 40$ <p>Completed Study: $N = 80$</p> <ul style="list-style-type: none"> • Group 1: $n = 40$ • Group 2: $n = 40$ <p>Gender, males (as defined by researchers):</p> <ul style="list-style-type: none"> • Group 1: $n = 25$ (62.5%) • Group 2: $n = 24$ (60%) <p>Race / ethnicity or nationality (as defined by researchers):</p> <ul style="list-style-type: none"> • The study occurred in India. The author did not identify race or ethnicity of the participants. <p>Gestational age at birth, mean in weeks, (SD):</p> <ul style="list-style-type: none"> • Group 1: 30.4 (1.6) • Group 2: 30.3 (1.5) <p>Birth weight, mean in grams (SD):</p> <ul style="list-style-type: none"> • Group 1: 1220 (176) • Group 2: 1210 (183) <p>Inclusion Criteria:</p> <ul style="list-style-type: none"> • Birth weight < 1500 gm admitted to neonatal intensive care unit <p>Exclusion Criteria:</p> <ul style="list-style-type: none"> • Major congenital abnormalities • Gestation < 27 or > 34 weeks • Absent or reversed end-diastolic flow • Apgar score < 3 at 5 minutes <p>Power Analysis: For an expected difference of 3 days (SD 4.1 days) in time to reach full enteral feeds, 40 subjects were required in each group, for a power of 90% and a significance level of 0.05.</p>
Interventions	<p>Both:</p> <ul style="list-style-type: none"> • Received parenteral nutrition as per unit protocol to achieve a calorie intake of 60 to 90 kcal/kg/day • Gavage feeds were initiated as intermittent boluses for 10 to 15 minutes, at 2-hourly intervals once infants were hemodynamically stable with soft abdomen and audible bowel sounds • Feed was started at 10 mL/kg in infants < 1250 gm and at 20 mL/kg in infants ≥ 1250 gm • Subsequent advancements were made by 20 mL/kg/day as tolerated to a maximum volume of 180 mL/kg/day • Expressed mother's milk was preferred; if not available, standard preterm formula with a calorie content of 80 kcal/100 mL was used • Human milk fortifier was added once the infant tolerated 100 mL/kg/day feed volume to make calorie count of 80 kcal/100 mL • PN was discontinued once 100 mL/kg/day of feeds were achieved

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	<ul style="list-style-type: none"> • Regurgitation of feeds or nonbilious vomiting were not considered as feed intolerance unless they were associated with an increase in AC of > 2 cm or large or abnormal prefeed gastric aspirates in respective groups • In infants with feed intolerance, readiness for re-initiation of feeds was assessed every 24 hours • Infants were evaluated for electrolyte imbalance, sepsis, necrotizing enterocolitis (NEC), and managed per unit guidelines • Feeds were withheld for hemodynamic instability, abnormal abdominal signs and tenderness, recurrent apnea, or persistent seizures. • Feeds restarted after 24 hours once hemodynamically stable. <p>Group 1: AC measurement</p> <ul style="list-style-type: none"> • AC measurements were performed before each feed using a standard, disposable no stretchable paper tape with minimum markings of 1 mm • The tape was positioned 1 cm above the umbilicus and was read along its bottom edge • A mark was made along the lower edge as reference for subsequent measurements • An increase in prefeed AC by ≥ 2 cm from baseline was considered as a sign of feed intolerance • In the AC group, gastric residues were not routinely performed unless the AC increased by > 2 cm • The decision for feed interruption was based on an increase in abdominal girth • Least AC measurement during the previous 24 hours was used as the baseline reference • Once AC was less than or equal to baseline, feeds were restarted at 50% of the volume being delivered at the time of feed interruption <p>Group 2: GRV measurement</p> <ul style="list-style-type: none"> • Feed intolerance was defined as presence of either 1 or more of the following features: bilious or hemorrhagic aspirates or volume of aspirates > 50% of previous feed or > 3 mL, whichever was larger • If the gastric residues were between 30% and 50% of the previous feeds, the same volume was continued without making daily increment • The gastric residues aspirated were discarded • Feeds were advanced per protocol if gastric residues were < 30% of previous feeds • Infants in both groups who experienced feed intolerance were kept nil per os (NPO) for next 24 hours and PN was continued • Once gastric aspirates were clear and < 10 mL/kg, feeds were restarted at 50% of the volume being delivered at the time of feed interruption
<p>Outcomes</p>	<p>Primary outcome:</p> <ul style="list-style-type: none"> • Time taken to achieve full feeds of 180 mL/kg/day, which were tolerated for at least 24 hours* <p>Secondary outcomes:</p> <ul style="list-style-type: none"> • Incidence of feed intolerance • Days taken to regain birth weight defined as day of life on which baby reached or crossed birth weight and maintained it for 3 days • Feed interruption days • Cumulative days on PN • NEC Bell stage ≥ 2* • Incidence of culture-positive sepsis • Duration of hospital stay • Mortality

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Notes	Results: <ul style="list-style-type: none"> • Primary outcome, time to full feeds <ul style="list-style-type: none"> ○ Reported in median days with interquartile range (IQR) ○ Group 1: 10 (9 - 13) ○ Group 2: 14 (12 - 17.5) ○ $p < .001$ • Secondary outcome, NEC, stage II or more <ul style="list-style-type: none"> ○ Group 1: 0 (0%) ○ Group 2: 1 (2.5%) ○ $p = 1.00$
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Risk of bias table

Bias	Scholar's judgment	Support for judgment
Random sequence generation (selection bias)	Low risk	A computer-generated block randomization sequence with block size of four was prepared by a person not involved in the clinical care, measurement of outcomes, or analysis of data.
Allocation concealment (selection bias)	Low risk	The randomization sequence was kept in sequentially numbered sealed opaque envelopes
Blinding of participants and personnel (performance bias)	High risk	Unblinded
Blinding of outcome assessment (detection bias)	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	No missing outcome data for outcomes of interest.
Selective reporting (reporting bias)	Low risk	All proposed outcomes were reported
Other bias	Low risk	

Parker et al., 2019

<i>Characteristics of Study</i>	
Methods	Single-center randomized control trial (RCT)
Participants	Participants: Setting: USA, urban hospital, level 4 NICU Randomized into study: $N = 146$ <ul style="list-style-type: none"> • Group 1, No gastric residual: $n = 72$ • Group 2, Gastric residual: $n = 74$ Completed Study: $N = 143$ <ul style="list-style-type: none"> • Group 1: $n = 69$ • Group 2: $n = 74$ Gender, males (as defined by researchers): <ul style="list-style-type: none"> • Group 1: $n = 36$ (52.17%)

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	<ul style="list-style-type: none"> • Group 2: $n = 37$ (50%) <p>Race / ethnicity or nationality (as defined by researchers):</p> <table border="1"> <thead> <tr> <th>Race/Ethnicity</th> <th>Group 1: No Residual</th> <th>Group 2: Residual</th> </tr> </thead> <tbody> <tr> <td>White</td> <td>28 (40.58%)</td> <td>49 (66.2%)</td> </tr> <tr> <td>African American</td> <td>39 (56.5%)</td> <td>22 (29.7%)</td> </tr> <tr> <td>Asian</td> <td>1 (1.45%)</td> <td>0</td> </tr> <tr> <td>Other</td> <td>1 (1.45%)</td> <td>3 (4.1%)</td> </tr> <tr> <td>Hispanic</td> <td>6 (8.7%)</td> <td>10 (13.51%)</td> </tr> </tbody> </table> <p>Gestational Age, mean (SD), week</p> <ul style="list-style-type: none"> • Group 1: 27.0 (1.2) • Group 2: 27.1 (2.4) <p>Inclusion Criteria:</p> <ul style="list-style-type: none"> • Born at 32 or fewer weeks' gestation • Birth weight of 1250 g or less • Younger than 72 hours • Receiving some feedings by 72 hours after birth <p>Exclusion Criteria:</p> <ul style="list-style-type: none"> • Congenital or chromosomal abnormalities, including complex congenital heart disease or a gastrointestinal condition • Infants were withdrawn from study if stage II or greater NEC or spontaneous intestinal perforation occurred <p>Power Analysis: With a sample size of 104 infants there would be 80% power to detect a 50% improvement (2-sided $p = .05$). Covariates were mentioned in discussion of analysis models but researchers did not list what the covariates were.</p> <p>Trial Registration: ClinicalTrials.gov identifier: NCT01863043</p>	Race/Ethnicity	Group 1: No Residual	Group 2: Residual	White	28 (40.58%)	49 (66.2%)	African American	39 (56.5%)	22 (29.7%)	Asian	1 (1.45%)	0	Other	1 (1.45%)	3 (4.1%)	Hispanic	6 (8.7%)	10 (13.51%)
Race/Ethnicity	Group 1: No Residual	Group 2: Residual																	
White	28 (40.58%)	49 (66.2%)																	
African American	39 (56.5%)	22 (29.7%)																	
Asian	1 (1.45%)	0																	
Other	1 (1.45%)	3 (4.1%)																	
Hispanic	6 (8.7%)	10 (13.51%)																	
<p>Interventions</p>	<p>Both: All feeding decisions and clinical decisions were based on the NICU nutritional guidelines. All infants were fed only human milk.</p> <ul style="list-style-type: none"> • Group 1: <ul style="list-style-type: none"> ○ Did not receive pre-feed gastric residual evaluation ○ Combination of 2 insertion depth measurement strategies and verification of the calculated depth was used to verify feeding tube placement prior to every feeding • Group 2: Underwent pre-feed gastric residual evaluation 																		
<p>Outcomes</p>	<p>Primary outcome:</p> <ul style="list-style-type: none"> • Weekly enteral nutrition measured in mL/kg for 6 weeks after birth <p>Secondary outcomes</p> <ul style="list-style-type: none"> • *Days to full feeds (120 mL/kg/d) • Hours of PN • Hours with a central line • Evidence of PN-associated liver disease, assessed by level of direct bilirubin and of alkaline phosphatase • Growth indices (weekly weight, head circumference, and length) • Days to discharge • Evidence of feeding intolerance 																		

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	<ul style="list-style-type: none"> • Episodes of presumed or culture-proven late-onset sepsis (occurring \geq 3 days of life) • * Evidence of stage II or greater NEC • Occult fecal blood, fecal calprotectin and S100A12 levels - identified as not included in this study report • Motilin and gastrin levels - identified as not included in this study report <p>Safety outcome(s):</p> <ul style="list-style-type: none"> • Not reported <p>*Outcomes of interest to the CMH CPG or CAT development team</p>
Notes	<ul style="list-style-type: none"> • Researchers identified using "modified intent-to-treat" analysis <ul style="list-style-type: none"> ○ 146 infants were randomized but only 143 were analyzed <ul style="list-style-type: none"> ▪ 2 infants were excluded as parents withdrew consent ▪ 1 infant did not meet inclusion criteria, and this was discovered after randomization • Eighteen infants (26.1%) in the no residual group had 10 or more gastric residuals evaluated, either inadvertently or when ordered for symptoms of gastrointestinal dysfunction • Four infants (5.8%) were withdrawn for NEC <p>Trial results:</p> <ul style="list-style-type: none"> • No residual group exhibited steeper increase in enteral nutrition over time compared to residual group, without an increase in adverse health outcomes. • No residual group was discharged home 8 days earlier. • No difference found in incidents of NEC between the two groups • The study was not powered to address safety concerns, including the risk for NEC.

Risk of bias table

Bias	Scholar's judgment	Support for judgment
Random sequence generation (selection bias)	Low risk	Use of computer-generated sequence with random-length permuted blocks of sizes
Allocation concealment (selection bias)	Low risk	Randomization was concealed until intervention was assigned
Blinding of participants and personnel (performance bias)	Unclear risk	Blinding not possible due to intervention; unclear if this could affect a clinician's behavior and effect study outcome
Blinding of outcome assessment (detection bias)	Low risk	Blinding did not occur but not likely to influence the outcome measurement
Incomplete outcome data (attrition bias)	Unclear risk	Utilization of modified intent-to-treat; 3 patients excluded after randomization but prior to treatment.
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes have been reported on
Other bias	Low risk	

Singh et al., 2018

Characteristics of Study

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Methods	Single Center, Randomized Control Trial
Interventions	<p>Both:</p> <ul style="list-style-type: none"> • Feedings started on day 1 or later once infant was hemodynamically stable • Feedings started at 3 mL every 3 hours and increased by 3 mL every 9 hours in infants with a BW of 1500-1750 g • Feedings started at 6 mL every 3 hours and increased by 3 mL every 6 hours in infants with a BW of 1751-2000 g • Infants fed breast milk if available and preterm formula when breast milk not available (after obtaining parental consent) • Feedings fortified when enteral feeds of 150 mL/kg per day were achieved • Algorithms with instructions for advancing or holding feeds were utilized and based on clinical assessment, gastric residual volume and color <p>Group 1:</p> <ul style="list-style-type: none"> ○ Maximum of 0.5 mL of gastric contents was aspirated before feedings with purpose to confirm tube placement and evaluate for hemorrhagic residuals ○ Feedings were withheld until assessment was done by physician if repeated bilious aspirates, vomiting, gastric aspirates containing frank blood or abnormal abdominal examinations occurred. Feedings were then continued or withheld or further diagnostic procedures were ordered and documented based on the assessment. <p>Group 2:</p> <ul style="list-style-type: none"> ○ Per unit policy, gastric residual volume was aspirated before each feed. ○ Feeding advancement was done using a comprehensive algorithm. ○ Intravenous access was discontinued when feeds reached 120 mL/kg per day unless needed for another purpose such as giving antibiotics.
Outcomes	<p>Primary outcome(s):</p> <ul style="list-style-type: none"> • Time to reach full enteral feedings (120 mL/kg per day) based on BW or actual weight if above BW * <p>Secondary outcome(s):</p> <ul style="list-style-type: none"> • Time to regain BW • Time to regain 120% of BW • Incidence of late-onset culture-proven sepsis (≥ 72 hours) • NEC (Bell stage of ≥ 2) * • Number of occasions feedings were either discontinued for > 24 hours or not increased for > 24 hours <p>Safety outcome(s): Not reported</p> <p>*Outcomes of interest to the CMH CPG or CAT development team</p>
Notes	<ul style="list-style-type: none"> • The intervention was discontinued if infants transferred to another hospital before completion of study intervention and infant data were censored at that time. If infants were transferred after completion of the intervention but before completion of the relevant outcome data, the data collection forms were provided to parents. The forms were then completed by the new care providers (physicians or nurses) and parents mailed the completed forms back to the study personnel. Results could have been impacted due to subjectivity of individual clinical judgment to initiate feeds. • More infants in the study group received mainly breast milk as compared with the control group. The authors stated this may affect the time to reach full feeds due to breast milk being better tolerated. • Analysis of the data was done using an intention-to-treat model.

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Risk of bias table		
Bias	Scholar's judgment	Support for judgment
Random sequence generation (selection bias)	Low risk	The randomization sequence was computer generated and permuted, even-numbered; randomly varying block sizes were generated with a 1:1 allocation ratio
Allocation concealment (selection bias)	Low risk	The allocation sequence was concealed using serially numbered opaque sealed envelopes
Blinding of participants and personnel (performance bias)	High risk	Unmasked trial
Blinding of outcome assessment (detection bias)	Unclear risk	Assessors were not blinded; however, authors state the outcome assessment was objective
Incomplete outcome data (attrition bias)	Low risk	All 87 randomized infants were included in the analysis
Selective reporting (reporting bias)	Low risk	The study protocol had been published. All proposed outcomes were reported
Other bias	Low risk	

Thomas et al., 2018

Characteristics of Study	
Methods	Randomized Control Study
Participants	<p>Participants: Infants between 26 and 37 weeks of gestation with a birth weight of more than 750g and less than 2000 g and likely to require gavage feeds for at least</p> <p>Setting: The Neonatal Intensive Care Unit (NICU) of St. John's Medical College Hospital in Bangalore India.</p> <p>Randomized into study: $N = 52$</p> <ul style="list-style-type: none"> • Group 1, routine prefeed aspiration for gastric residual volume (GRV): $n = 26$ • Group 2, prefeed abdominal girth (AG) measurement: $n = 26$ <p>Completed Study: $N = 50$</p> <ul style="list-style-type: none"> • Group 1: $n = 24$ • Group 2: $n = 26$ <p>Gender, males:</p> <ul style="list-style-type: none"> • Group 1: $n = 16$ (61.5%) • Group 2: $n = 15$ (62.5%) <p>Race / ethnicity or nationality:</p> <ul style="list-style-type: none"> • The study occurred in India. The author did not identify race or ethnicity of the participants. <p>Gestational Age, Weeks (mean \pm SD)</p> <ul style="list-style-type: none"> • Group 1: 30 ± 1.5 • Group 2: 31.0 ± 1.4 <p>Inclusion Criteria:</p> <ul style="list-style-type: none"> • Infants between 26- and 37-weeks gestation

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	<ul style="list-style-type: none"> • Birth weight of more than 750 g and less than 2000 g • Likely to require gavage feeds for at least 48 hours of life • Extramural neonates who had not received any feeds <p>Exclusion Criteria:</p> <ul style="list-style-type: none"> • Infants with life-threatening congenital anomalies • Anomalies of the gastrointestinal tract <p>Power Analysis: A sample size of 24 in each group, assuming a difference in time to reach full feeds of 5 days, with a power of 80% and a .05 level of significance</p>																																
Interventions	<p>Group 1: Per hospital protocol.</p> <ul style="list-style-type: none"> • Aspiration of the infant feeding tube prior to the next feed. Feeds are given every two hours, either expressed milk from the infants' own mother or donor milk. The aspirated gastric contents are to be replaced if not altered. <p>Group 2: Checking of AG at baseline, that is before feeds were initiated and at two-hourly intervals, before the next feeds.</p>																																
Outcomes	<p>Primary Outcomes:</p> <ul style="list-style-type: none"> • Time to reach full feeds* <p>Secondary Outcomes:</p> <ul style="list-style-type: none"> • Number of episodes of feeding intolerance • Number of feeds that were withheld • Duration of hospital stay • Duration of parenteral nutrition • Incidence of late-onset sepsis • Necrotizing enterocolitis (NEC) stage 2* <p>*Outcomes of interest to the CMH CPG or CAT development team</p>																																
Results	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: left;">Outcomes</th> <th style="text-align: center;">GRV (n = 24) Median (IQR)</th> <th style="text-align: center;">AG (n = 26) Median (IQR)</th> <th style="text-align: center;">P</th> </tr> </thead> <tbody> <tr> <td>*Times to reach full feeds, d</td> <td style="text-align: center;">9.5 (6.75-13)</td> <td style="text-align: center;">6 (5-7.75)</td> <td style="text-align: center;">.042</td> </tr> <tr> <td>Episodes of feed intolerance</td> <td style="text-align: center;">0.5 (0-1)</td> <td style="text-align: center;">0 (0-1)</td> <td style="text-align: center;">.15</td> </tr> <tr> <td>Number of feeds withheld</td> <td style="text-align: center;">0 (0-15)</td> <td style="text-align: center;">0 (0-1.25)</td> <td style="text-align: center;">.12</td> </tr> <tr> <td>Duration of hospital stay, d</td> <td style="text-align: center;">30 (14.25-38.75)</td> <td style="text-align: center;">21 (13-27)</td> <td style="text-align: center;">.28</td> </tr> <tr> <td>Duration of parenteral nutrition, d</td> <td style="text-align: center;">5.5 (3-11.75)</td> <td style="text-align: center;">5 (3-7)</td> <td style="text-align: center;">.21</td> </tr> <tr> <td>Sepsis, n</td> <td style="text-align: center;">5</td> <td style="text-align: center;">4</td> <td style="text-align: center;">.61</td> </tr> <tr> <td>*NEC</td> <td style="text-align: center;">1</td> <td style="text-align: center;">0</td> <td></td> </tr> </tbody> </table>	Outcomes	GRV (n = 24) Median (IQR)	AG (n = 26) Median (IQR)	P	*Times to reach full feeds, d	9.5 (6.75-13)	6 (5-7.75)	.042	Episodes of feed intolerance	0.5 (0-1)	0 (0-1)	.15	Number of feeds withheld	0 (0-15)	0 (0-1.25)	.12	Duration of hospital stay, d	30 (14.25-38.75)	21 (13-27)	.28	Duration of parenteral nutrition, d	5.5 (3-11.75)	5 (3-7)	.21	Sepsis, n	5	4	.61	*NEC	1	0	
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Risk of bias table

Bias	Scholar's judgment	Support for judgment
Random sequence generation (selection bias)	Low risk	Randomization was completed using a computer-generated random number table in unequal block sizes ranging from four to 12 by the principal investigator.
Allocation concealment (selection bias)	Low risk	Allocation concealment was done using sequentially numbered opaque sealed envelopes. Participant enrollment was obtained by the study team. Only the primary investigator had access to the envelopes and was not part of the clinical team.

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Blinding of participants and personnel (performance bias)	High risk	Blinding during the study protocol was not possible as GRV and AG needed to be documented as part of the input and output chart. Blinding would not have affected the outcome of NEC but could have affected time to full feeds.
Blinding of outcome assessment (detection bias)	Unclear risk	Not reported by the author
Incomplete outcome data (attrition bias)	Low risk	Two patients were discharged against medical advice before full feeds but still reached power.
Selective reporting (reporting bias)	Low risk	None detected
Other bias	Low risk	

Torrazza et al. 2015

Characteristics of Studies	
Methods	Randomized Control Trial
Participants	<p>Setting: Florida</p> <p>Randomized into study: $N = 61$</p> <ul style="list-style-type: none"> • Group 1, check of gastric residuals (GR): $n = 30$ • Group 2, no check of GR: $n = 31$ <p>Completed Study: $N = 61$</p> <ul style="list-style-type: none"> • Group 1: $n = 30$ • Group 2: $n = 31$ <p>Gender, males:</p> <ul style="list-style-type: none"> • Group 1: $n = 14$ • Group 2: $n = 14$ <p>Race / ethnicity or nationality (as defined by researchers):</p> <ul style="list-style-type: none"> • The study occurred in the United States. The author did not identify race or ethnicity of the participants. <p>Age, gestational age, weeks (mean):</p> <p>Group 1: check of GR - 24.52 - 29.54 (27.03)</p> <p>Group 2: no check of GR - 25.22 - 29.42 (27.32)</p> <p>Inclusion Criteria:</p> <ul style="list-style-type: none"> • Postmenstrual age greater than 23 weeks but less than or equal to 32 weeks • Birth weight less than or equal to 1250 grams • Without congenital or chromosomal anomalies or gastrointestinal malformations • Receiving some enteral nutrition by 48 hours of age <p>Exclusion Criteria: none identified</p> <p>Power Analysis: 31 subjects per arm, at 80% power at $P = .05$ (two-sided)</p>
Interventions	<p>Both groups: were provided care based on the published institutional feeding algorithm of the NICU.</p> <p>Group 1: received routine evaluation of GRs prior to every feeding</p> <p>Group 2: did not receive routine evaluation of GRs prior to every feeding.</p>
Outcomes	Primary Outcomes:

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	<ul style="list-style-type: none"> • Enteral intake at 2 weeks • Days to reach 120 ml kg per day of enteral feedings <p>Secondary Outcomes:</p> <ul style="list-style-type: none"> • Enteral intake at 3 weeks • Days to reach 150 ml kg per day • Growth indices at 3 weeks (weight, head circumference and length) • Days requiring parenteral nutrition and central line access, • Incidence of NEC, sepsis and parental nutrition-associated liver disease
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Risk of bias table

Bias	Scholar's judgment	Support for judgment
Random sequence generation (selection bias)	Low risk	A computer-generated block randomization sequence with variable block sizes was used
Allocation concealment (selection bias)	Low risk	The randomization sequence was kept in sequentially numbered sealed opaque envelopes
Blinding of participants and personnel (performance bias)	High risk	Unblinded
Blinding of outcome assessment (detection bias)	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All primary and secondary outcomes were reported
Other bias	Low risk	

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