

**APPENDICES**

Responsive feeding for preterm or low birth weight infants: a systematic review and meta-analysis

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18Feb2022

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## Appendix 1. Search strategy for each electronic database

Database	Search Strategy
MEDLINE	<p>1 (((preterms or "pre terms" or premies or premie or preemie or preemies or premature or prematurity or preterm or "pre term" or "near term") and (infant* or newborn or "new born" or baby or babies or neonate* or neonatal)) or (low adj3 ("birth weight*" or birthweight* or "birth-weight*")) or Low-Birth-Weight or VLBW or LBW or ELBW or (SGA adj4 infant*) or "small for gestational age").ti,ab.</p> <p>2 exp infant, premature/ or exp infant, low birth weight/</p> <p>3 1 or 2</p> <p>4 ((responsive or on-demand or demand or semi-demand or semidemand or "ad libitum" or "ad lib" or adlib or self-regulatory or cue-based or infant-driven or infant-guided or infant-led or co-regulated or coregulated) adj2 (feed or feeds or feeding* or breastfeed* or method or methods)).ti,ab.</p> <p>5 (feeding\$ cue\$ or hunger cue\$).ti,ab.</p> <p>6 cues/ or exp satiation/ or exp hunger/</p> <p>7 4 or 5 or 6</p> <p>8 3 and 7</p> <p>9 exp animals/ not humans.sh.</p> <p>10 8 not 9</p>
SCOPUS	<p>( TITLE-ABS-KEY ( ( ( preterms OR "pre terms" OR premies OR premie OR preemie OR preemies OR premature OR prematurity OR preterm OR "pre term" OR "near term" ) AND ( infant* OR newborn OR "new born" OR baby OR babies OR neonate* OR neonatal ) ) OR ( low W/3 ( "birth weight*" OR birthweight* OR "birth-weight*" ) ) OR low-birth-weight OR vlbw OR lbw OR elbw OR ( sga W/4 infant* ) OR "small for gestational age" ) ) AND ( ( TITLE-ABS-KEY ( ( feed OR feeds OR feeding* OR breastfeed* OR method ) W/4 ( responsive OR on-demand OR demand OR semi-demand OR semidemand OR "ad libitum" OR "ad lib" OR adlib OR self-regulat* OR cue-based OR infant-driven OR infant-guided OR infant-led OR co-regulated OR coregulated ) ) ) OR ( TITLE-ABS-KEY ( feeding* AND cue* OR hunger AND cue* ) ) OR ( KEY ( cues OR satiation ) ) )</p>
CINAHL	<p>TI(((preterms or "pre terms" or premies or premie or preemie or preemies or premature or prematurity or preterm or "pre term" or "near term") and (infant* or newborn or "new born" or baby or babies or neonate* or neonatal)) or (low N3 ("birth weight*" or birthweight* or "birth-weight*")) or Low-Birth-Weight or VLBW or LBW or ELBW or (SGA N4 infant*) or "small for gestational age") OR AB (((preterms or "pre terms" or premies or premie or preemie or preemies or premature or prematurity or preterm or "pre term" or "near term") and (infant* or newborn or "new born" or baby or babies or neonate* or neonatal)) or (low N3 ("birth weight*" or birthweight* or "birth-weight*")) or Low-Birth-Weight or VLBW or LBW or ELBW or (SGA N4 infant*) or "small for gestational age") OR (MH "Infant, Low Birth Weight+") OR (MH "Infant, Premature")</p> <p>TI((responsive or on-demand or demand or semi-demand or semidemand or "ad libitum" or "ad lib" or adlib or self-regulatory or cue-based or infant-driven or infant-guided or infant-led or co-regulated or coregulated) N2 (feed or feeds or feeding* or breastfeed* or method or methods)) OR AB ((responsive or on-demand or demand or semi-demand or semidemand or "ad libitum" or "ad lib" or adlib or self-regulatory or cue-based or infant-driven or infant-guided or infant-led or co-regulated or coregulated) N2 (feed or feeds or feeding* or breastfeed* or method or methods))</p> <p>TI(feeding cue# or hunger cue#) OR AB(feeding cue# or hunger cue#)</p> <p>(MH "Cues") OR (MH "Satiation") OR (MH "Hunger")</p> <p>S2 OR S3 OR S4</p> <p>S1 AND S5</p>
Global Index Medicus	<p>(((preterms OR "pre terms" OR premies OR premie OR preemie OR preemies OR premature OR prematurity OR preterm OR "pre term" OR "near term") AND (infant* OR newborn OR "new born" OR baby OR babies OR neonate* OR neonatal)) OR (low AND ("birth weight" OR "birth weights" OR birthweight* OR "birth-weight" OR "birth-weights")) OR low-birth-weight OR vlbw OR lbw OR elbw OR (sga AND infant*) OR "small for gestational age") OR ( mh:("Infant, Low Birth Weight")) OR (mh:("Infant, Small for Gestational Age")) OR (mh:("Infant, Very Low Birth Weight")) OR (mh:("Infant, Premature")) OR (mh:("Infant, Extremely Premature"))))</p> <p>(  tw:((preterms OR "pre terms" OR premies OR premie OR preemie OR preemies OR premature OR prematurity OR preterm OR "pre term" OR "near term") AND (infant* OR newborn OR "new born" OR baby OR babies OR neonate* OR neonatal)))</p>

	<p>OR (tw: (low AND ("birth weight" OR "birth weights" OR birthweight* OR "birth-weight" OR "birth-weights")))  OR (tw:(low-birth-weight OR vlbw OR lbw OR elbw OR (sga AND infant*) OR "small for gestational age"))  OR ( mh:("Infant, Low Birth Weight")) OR (mh:("Infant, Small for Gestational Age")) OR (mh:("Infant, Very Low Birth Weight")) OR (mh: ("Infant, Premature")) OR (mh:("Infant, Extremely Premature"))  )  AND  (  (tw: ((responsive OR on-demand OR demand OR semi-demand OR semidemand OR "ad libitum" OR "ad lib" OR adlib OR self-regulatory OR cue-based OR infant-driven OR infant-guided OR infant-led OR co-regulated OR coregulated) AND (feed OR feeds OR feeding* OR breastfeed* OR method OR methods)))  OR (tw: (feeding cue* OR hunger cue*))  OR  (mh:("cues")) OR (mh:("satiation")) OR (mh:("Satiety Response")) OR (mh:("hunger"))  )    tw:((( tw:((preterms OR "pre terms" OR premies OR premie OR preemie OR preemies OR premature OR prematurity OR preterm OR "pre term" OR "near term") AND (infant* OR newborn OR "new born" OR baby OR babies OR neonate* OR neonatal))) OR (tw: (low AND ("birth weight" OR "birth weights" OR birthweight* OR "birth-weight" OR "birth-weights")) OR (tw:(low-birth-weight OR vlbw OR lbw OR elbw OR (sga AND infant*) OR "small for gestational age")) OR ( mh:("Infant, Low Birth Weight")) OR (mh:("Infant, Small for Gestational Age")) OR (mh:("Infant, Very Low Birth Weight")) OR (mh: ("Infant, Premature")) OR (mh:("Infant, Extremely Premature")) ))) AND (tw:((( tw: ((responsive OR on-demand OR demand OR semi-demand OR semidemand OR "ad libitum" OR "ad lib" OR adlib OR self-regulatory OR cue-based OR infant-driven OR infant-guided OR infant-led OR co-regulated OR coregulated) AND (feed OR feeds OR feeding* OR breastfeed* OR method OR methods))) OR (tw: (feeding cue* OR hunger cue*)) OR (mh:("cues")) OR (mh:("satiation")) OR (mh:("Satiety Response")) OR (mh:("hunger")) )))))</p>
Web of Science	<p>*All Databases*</p> <p>TS=((preterms or "pre terms" or premies or premie or preemie or preemies or premature or prematurity or preterm or "pre term" or "near term") and (infant* or newborn or "new born" or baby or babies or neonate* or neonatal)) or (low NEAR/3 ("birth weight*" or birthweight* or "birth-weight*")) or Low-Birth-Weight or VLBW or LBW or ELBW or (SGA NEAR/4 infant*) or "small for gestational age")</p> <p>TS=((responsive or on-demand or demand or semi-demand or semidemand or "ad libitum" or "ad lib" or adlib or self-regulatory or cue-based or infant-driven or infant-guided or infant-led or co-regulated or coregulated) NEAR/2 (feed or feeds or feeding* or breastfeed* or method or methods))</p> <p>TS=(feeding cue* or hunger cue*)</p> <p>#2 OR #3</p> <p>#1 AND #4</p>

## Appendix 2. Outcome Definitions

The primary outcomes include mortality, morbidity, and growth at 28 days chronological age and at latest follow up. Standardized neurodevelopmental outcomes will be assessed at 12 months chronological age and latest follow up. Adverse events, as defined by the study, will be assessed at any time.

### Primary

- Mortality at 28 days\* chronological age and latest follow up
- Morbidity at 28 days\* chronological age and latest follow up
  - Necrotizing Enterocolitis (NEC)  $\geq$  Bell's Stage II OR any grade requiring surgery
  - Infection including: omphalitis / umbilical cord infection; diarrhea / dysentery; acute respiratory illness (ARI) / Acute lower respiratory infection (ALRI) tract infections / influenza / pneumonia; Sepsis; other as defined by study.
  - Hospitalization or duration of hospitalization
  - Feed intolerance with cessation in enteral or oral feeding
- Growth / Anthropometry at 28\* days chronological age and latest follow up
  - Time to regain birth weight
  - Weight, length/height, head circumference gain -measured in g/day or cm/week
  - Wasting or stunting or underweight defined as weight for length or length for age or weight for age z scores  $<2$  SD or  $<10^{\text{th}}$  centile
- Development at 12 months\*\* chronological age and latest follow up
  - Neurodevelopmental disability: developmental delay more than two SDs below population mean on a standardized or validated test of development, cognitive outcome, educational attainment, behavior (including attachment, interaction, responsiveness) or mental health (Bayley 1993; Bayley 2005; Griffiths 1954; Griffiths 1970)
  - Standardized score (z-score) on a standardized or validated test of cognitive, motor, language, or socioemotional outcomes.
- Adverse events as defined by the study, which may include allergic reactions, hyperglycemia, electrolyte balance problems.

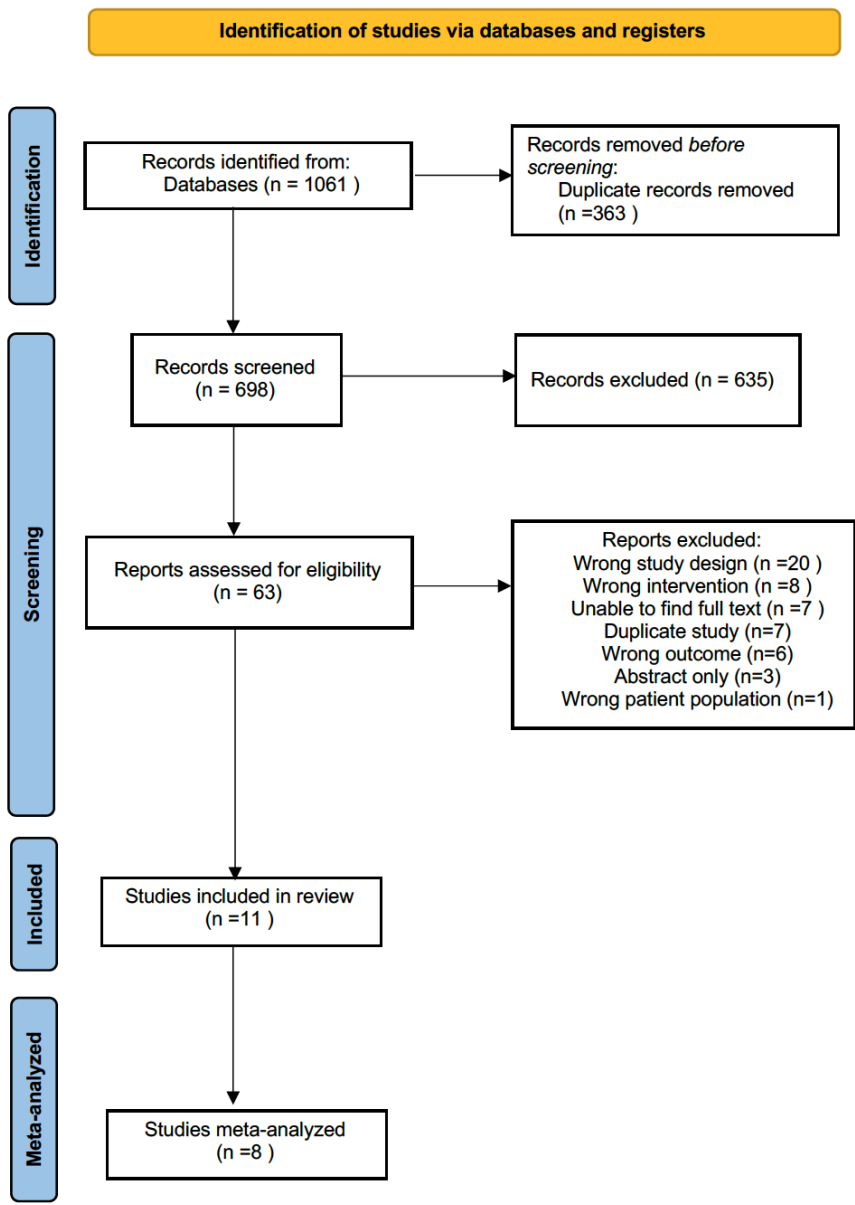
### Secondary

- Costs: including resource use; costs or cost-effectiveness data; incremental effect
- Feasibility
- Values
- Resources
- Equity
- Acceptability

\*If 28 days chronological age outcomes are not available, outcomes at hospital discharge will be used.

\*\*If 12 months chronological age outcomes are available, we will include the measurement obtained at the age closest to 12 months

Appendix 3. PRISMA flow diagram

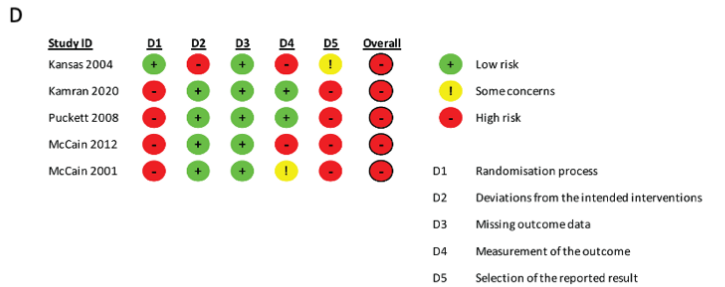
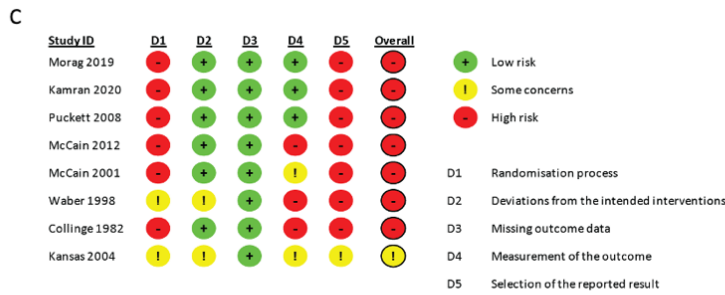
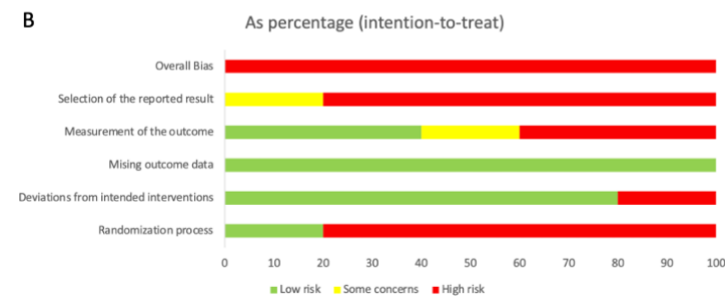
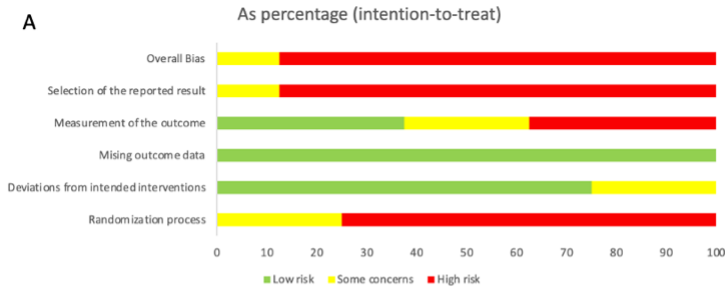


## Appendix 3. Characteristics of included studies (n=11)

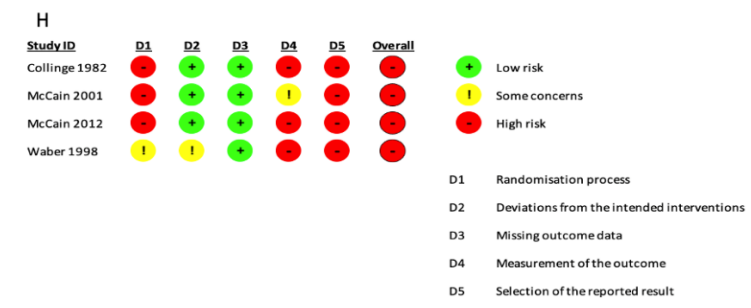
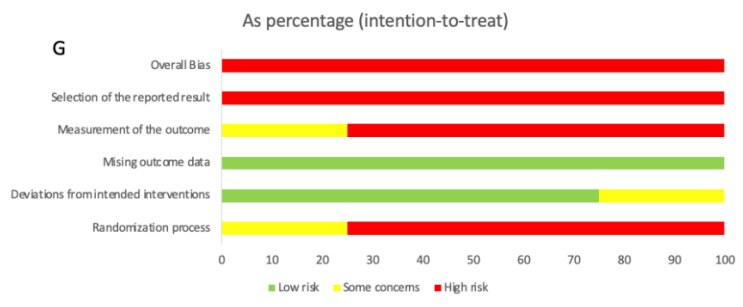
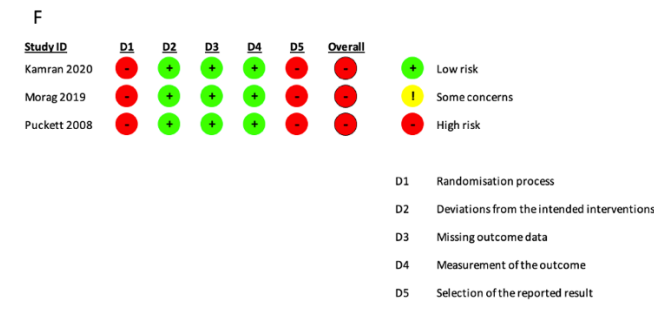
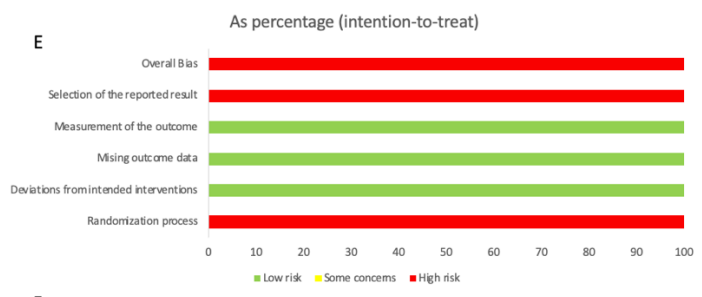
Author	Gestational age of Infants	Country	Description of intervention	Duration of Intervention	Schedule in comparator group	Type of oral feeding (breastfed, cup or bottle fed)
Collinge 1982	<37 weeks gestational age	Canada	Initiation in response to hunger cues (crying, sucking, rooting, 'unsettled'), feeds ceased in response to any infant satiation cues (unspecified)	Three days	3-4 hourly	Bottle fed or breastfed
Kamran 2020	<34 weeks gestational age	Iran	Initiation in response to hunger cues (crying, sucking, rooting, 'unsettled'), feeds ceased in response to any infant satiation cues (unspecified)	32 days	Scheduled interval feeding but frequency not stated	Bottle fed or breastfed
Kansas 2004	<33 weeks gestational age	USA	Initiation in response to hunger cues (crying, sucking, rooting, 'unsettled'), feeds ceased in response to any infant satiation cues (unspecified)	Not stated	Scheduled interval feeding but frequency not stated	Unknown
McCain 2001	<34 weeks gestational age	USA	Initiation in response to hunger cues (crying, sucking, rooting, 'unsettled'), feeds ceased in response to any infant satiation cues (unspecified)	32 days	3 hourly	Gavage and breastfed
McCain 2012	<34 weeks gestational age	USA	Initiation in response to hunger cues (crying, sucking, rooting, 'unsettled'), feeds ceased in response to any infant satiation cues (unspecified)	111 days	Scheduled interval feeding but frequency not stated	Gavage and breastfed
Morag 2019	<32 weeks gestational age	Israel	Initiation in response to hunger cues (crying, sucking, rooting, 'unsettled'), feeds ceased in response to any infant satiation cues (unspecified)	37 days	Scheduled interval feeding but frequency not stated	Gavage, bottle fed, and breastfed
Pridham 1999	<35 weeks gestational age	USA	Initiation in response to hunger cues (crying, sucking, rooting, 'unsettled'), feeds ceased in response to any infant satiation cues (unspecified)	Five days	4 hourly	Bottle fed and breastfed
Pridham 2001	<35 weeks gestational age	USA	Initiation in response to hunger cues (crying, sucking,	Five days	3 hourly	Bottle fed and breastfed

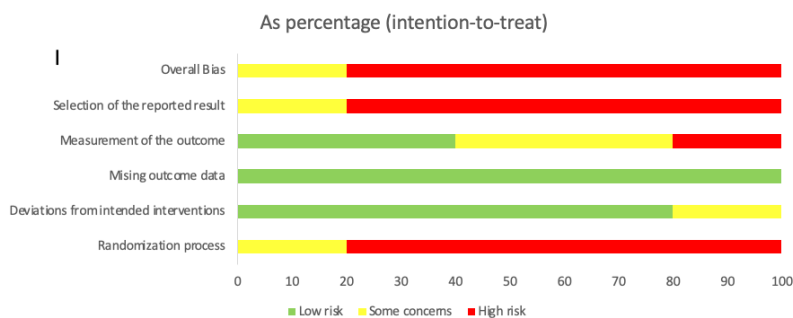
			rooting, 'unsettled'), feeds ceased in response to any infant satiation cues (unspecified)			
Puckett 2008	<36 weeks gestational age	Canada	Initiation in response to hunger cues (crying, sucking, rooting, 'unsettled'), feeds ceased in response to any infant satiation cues (unspecified)	12 days	Scheduled interval feeding but frequency not stated	Bottle fed and breastfed
Saunders 1991	<37 weeks gestational age	USA	Initiation in response to hunger cues (crying, sucking, rooting, 'unsettled'), feeds ceased in response to any infant satiation cues (unspecified)	Three to six days	3 hourly	Gavage and bottle fed
Waber 1998	<36 weeks gestational age	USA	Initiation in response to hunger cues (crying, sucking, rooting, 'unsettled'), feeds ceased in response to any infant satiation cues (unspecified)	32 days	3-4 hourly	Gavage or breastfed

Appendix 4. Risk of bias for included studies that reported weight gain (A) and length of hospitalization (B) and traffic light risk of bias for weight gain (C) length of hospitalization (D) final infant weight (E) traffic light of risk of bias for final infant weight (F) weight gain velocity in (g/day) (G) traffic light of risk of bias for weight gain velocity (g/day) (H) weight gain velocity by body weight (g/kg/day) (I) and traffic light risk of bias for weight gain velocity by body weight (g/kg/day) (J).









J

Study ID	D1	D2	D3	D4	D5	Overall
Kansas 2004	!	!	+	!	!	!
McCain 2001	-	+	+	!	-	-
McCain 2012	-	+	+	-	-	-
Morag 2019	-	+	+	+	-	-
Puckett 2008	-	+	+	+	-	-

+ Low risk  
 ! Some concerns  
 - High risk

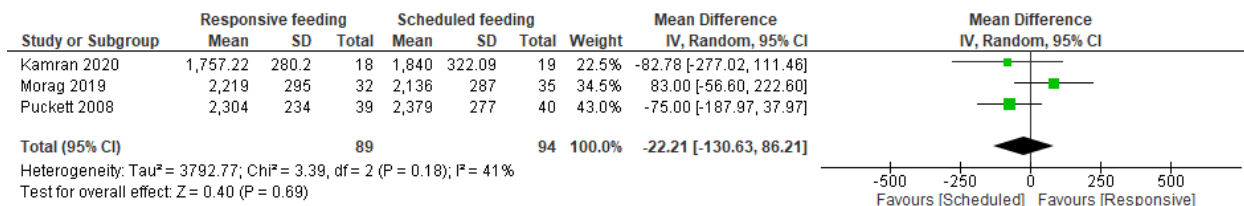
D1 Randomisation process  
 D2 Deviations from the intended interventions  
 D3 Missing outcome data  
 D4 Measurement of the outcome  
 D5 Selection of the reported result

## Legend:

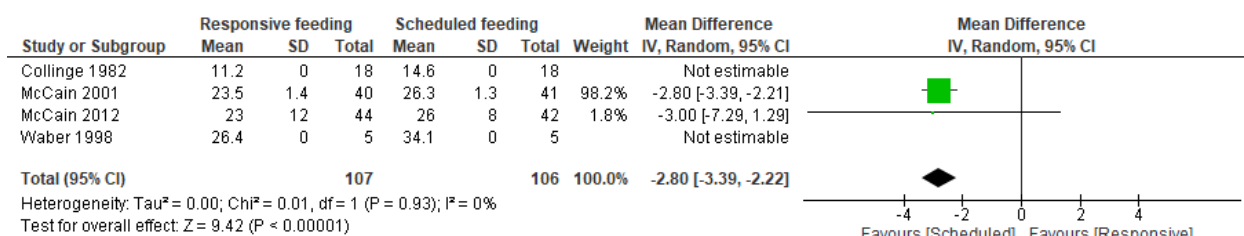
- High risk for the randomization process was indicated when blinding was impossible due to study population, intervention, and comparator and/or when randomization was based on a non-random component. Low risk for the randomization process was indicated when blinding was possible and/or when randomization was based on a random component.
- High risk for deviations from intended interventions was indicated when carers and people delivering the intervention were likely to have affected the outcome. Low risk for deviations from intended interventions was indicated when appropriate analysis was completed to estimate the effect of the intervention.
- High risk for missing outcome data was indicated when data for the outcome was not available for all or nearly all participants and if there was evidence that the result was biased based on missing data. Low risk for missing outcome data was indicated when data was available for all or nearly all participants.
- High risk for measurement of the outcome was indicated when the method of measuring the outcome was inappropriate and when measurement of the outcome could have differed between intervention groups. Low risk for measurement of the outcome was indicated when the method of measuring the outcome was appropriate.
- High risk for selection of the reported result was indicated when multiple eligible outcome measures and multiple eligible analyses of the data were available within the outcome domain. Low risk for selection of the reported result was indicated when produced data in the result was analyzed according to the pre-specified analysis plan.

## Appendix 5 – Forest plots

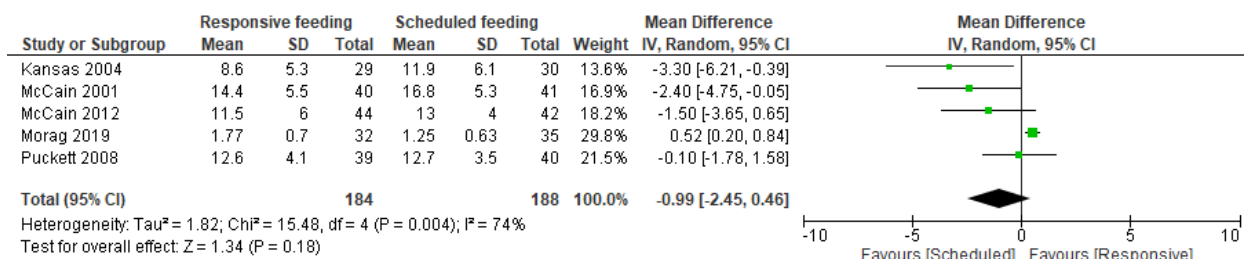
## 1. Weight in grams at discharge



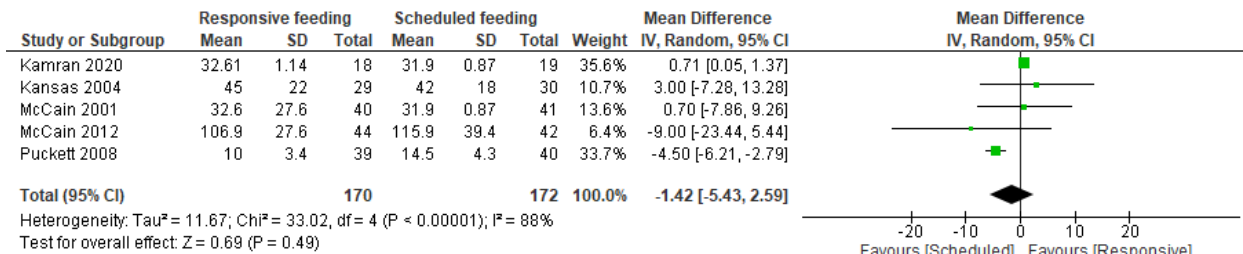
## 2. Weight gain g / day at discharge



## 3. Weight gain g / kg / d at discharge



## 4. Duration of hospitalization in days



## 5. Time to establishment of full oral feeds (after trial entry)

