Supplemental Feeding in Healthy, Term Neonates

Evidence Summary

Date started: November 2016
Date completed: January 2017

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Objective for the Review: To critically review the evidence on supplemental feeding in healthy, term neonates.

Inclusion Criteria:
Healthy, Term Neonate:
• >/= 37 completed weeks gestation
• >/= 2500gm birth weight
• no medical morbidities or congenital abnormalities identified (e.g. hypoglycemia, significant jaundice, craniofacial anomalies, etc.)

Exclusion Criteria:
• < 37 completed weeks gestation
• < 2500gm birth weight
• infant with co-morbidities or congenital abnormalities

Definitions:
Supplementary feedings: Feedings provided in place of breastfeeding. This may include pasteurized human donor milk and/or breastmilk substitutes/formula. Any foods given prior to 4-6 months of age, the recommended duration of exclusive breastfeeding, are thus defined as supplementary.

Target Guideline Users: All clinicians caring healthy, term neonates across OHSU Partners
Review Preparation:

In healthy, term neonates,

1. what are the maternal (i.e., maternal medications, illness, delayed lactogenesis, prior best surgery, etc.) and infant indications (i.e., illness, congenital malformations, dehydration, weight loss, etc.) for supplemental feeding?
2. what is the preferred choice of supplemental feeding (i.e., human breast milk, protein hydrolysate formulas, other supplemental formulas)?
3. what is the appropriate volume of supplemental feeding based on patient condition, weight, and type of supplement?
4. what is optimal method of supplementation (i.e., cup feeding, spoon or dropper feeding, bottle feeding, syringe, etc.)?

Quality Measures:

Process-
- provider utilization of NEWT
- provider utilization of supplemental feeding assent form
- method of supplementation (e.g., bottle, cup, syringe, etc.)
- documented indication for supplementation

Outcome-
- percent of term, healthy neonates receiving supplementation prior to discharge
- percent of term, healthy neonates receiving supplemental human donor milk prior to discharge
- percent of term, healthy neonates receiving supplemental formula prior to discharge
- frequency of feeding plan and/or lactation consult prior to supplementation order
**Supplemental Feeding in Healthy, Term Neonates**

### Existing External Guidelines/Pathways/Order Sets

<table>
<thead>
<tr>
<th>Existing External Guidelines</th>
<th>Organization and Author</th>
<th>Last Update</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supplementary Feedings in the Healthy Term Breastfed Neonate</td>
<td>Academy of Breastfeeding Medicine</td>
<td>2017</td>
</tr>
<tr>
<td>Baby-Friendly USA Guidelines</td>
<td>Baby-Friendly USA</td>
<td>2016</td>
</tr>
<tr>
<td>Nutrition for Healthy Term Infants: Recommendations from 6-12 months</td>
<td>Health Canada/Canadian Paediatric Society/Dietitians of Canada/Breastfeeding Committee for Canada</td>
<td>2012</td>
</tr>
<tr>
<td>Clinical Guidelines for the Establishment of Exclusive Breastfeeding</td>
<td>International Lactation Consultant Association</td>
<td>2005</td>
</tr>
</tbody>
</table>

The four published clinical guidelines were evaluated for this review using the **University of Pennsylvania’s Center for Evidence-Based Practice Trustworthy Guideline rating scale**. The scale is based on the Institute of Medicine’s “Standards for Developing Trustworthy Clinical Practice Guidelines” (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains.

### Guideline Issuer Evaluation

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>1. Transparency</td>
<td>C</td>
<td>B</td>
<td>C</td>
<td>B</td>
</tr>
<tr>
<td>2. Conflict of interest</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>3. Development group</td>
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<td>B</td>
<td>NR</td>
<td>B</td>
</tr>
<tr>
<td>4. Systematic Review</td>
<td>B</td>
<td>B</td>
<td>B</td>
<td>B</td>
</tr>
<tr>
<td>5. Supporting evidence</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>B</td>
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<tr>
<td>6. Recommendations</td>
<td>B</td>
<td>B</td>
<td>B</td>
<td>B</td>
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<tr>
<td>7. External Review</td>
<td>A</td>
<td>A</td>
<td>NR</td>
<td>A</td>
</tr>
</tbody>
</table>
See appendix B for full description of the Trustworthy Guideline grading system.

### Guideline Evidence Evaluation Systems

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Code Criteria:</td>
<td>I Evidence obtained from at least one properly randomized study. II-1 Evidence obtained from well-organized, controlled trials without randomization. II-2 Evidence obtained from well-designed cohort or case-control analytic studies preferably from more than one center or research program. II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence. III Opinions of respected authorities, based on clinical experience, descriptive studies and case reports, or reports of expert committees.</td>
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</tr>
</tbody>
</table>

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Existing Internal Policies
## Review of Relevant Evidence: Search Strategies and Databases Reviewed

<table>
<thead>
<tr>
<th>Search Strategies</th>
<th>Document Strategies Used</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ovid MEDLINE Search Strategy</strong></td>
<td>1  (supplement* adj3 (feed* or fed or food* or nutrition* or milk or formula*) adj7 (infant* or neonat* or baby or babies)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1232)</td>
</tr>
<tr>
<td>2  Infant, Newborn/ (259237)</td>
<td>3  exp Feeding Behavior/ (90474)</td>
</tr>
<tr>
<td>4  2 and 3 (10298)</td>
<td>5  exp Infant Nutritional Physiological Phenomena/ (26109)</td>
</tr>
<tr>
<td>6  2 and 3 and 5 (9605)</td>
<td>7  limit 6 to guideline (41)</td>
</tr>
<tr>
<td>8  exp Infant Food/ (7134)</td>
<td>9  exp Milk, Human/ (8149)</td>
</tr>
<tr>
<td>10 exp Nutritional Requirements/ (8894)</td>
<td>11 Nutritional Status/ (22428)</td>
</tr>
<tr>
<td>12 exp Nutrition Surveys/ (14467)</td>
<td>13 10 or 11 or 12 (42200)</td>
</tr>
<tr>
<td>14 8 or 9 (13956)</td>
<td>15 3 or 5 (97247)</td>
</tr>
<tr>
<td>16 2 and 13 and 14 and 15 (352)</td>
<td>17 1 and 2 (528)</td>
</tr>
<tr>
<td>18 16 or 17 (863)</td>
<td>19 limit 18 to english language (808)</td>
</tr>
</tbody>
</table>

**Search Terms/Strategies Used:**

- Ovid MEDLINE
- Cochrane Database of Systematic Reviews
- National Guideline Clearinghouse

**Database Searched:**

- Ovid MEDLINE, Cochrane Database of Systematic Reviews, National Guideline Clearinghouse

**Years Searched - All Questions:**

1996-October 2016 (Included articles published in last 15 years. Older articles were included only if more recent literature was not available addressing the clinical question.)

**Language:**

- English

**Age of Subjects:**

- Infants (< 1 year)
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Evidence Found with Searches

<table>
<thead>
<tr>
<th>Check type of evidence found</th>
<th>Summary of Evidence – All Questions</th>
<th>Number of articles obtained</th>
</tr>
</thead>
<tbody>
<tr>
<td>×</td>
<td>Systematic reviews/Meta-analysis</td>
<td>8</td>
</tr>
<tr>
<td>×</td>
<td>Randomized controlled trials</td>
<td>8</td>
</tr>
<tr>
<td>×</td>
<td>Non-randomized studies</td>
<td>8</td>
</tr>
<tr>
<td>×</td>
<td>Government/State agency regulations</td>
<td>2</td>
</tr>
<tr>
<td>×</td>
<td>Professional organization guidelines/white papers, etc.</td>
<td>2</td>
</tr>
</tbody>
</table>

Evaluating the Quality of the Evidence

The GRADE criteria were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. For more detailed information, see Appendix A.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>STRONG</td>
<td>Desirable effects clearly outweigh undesirable effects or vice versa</td>
</tr>
<tr>
<td>WEAK</td>
<td>Desirable effects closely balanced with undesirable effects</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Quality</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Further research is very unlikely to change our confidence in the estimate of effect.</td>
</tr>
<tr>
<td>Moderate</td>
<td>Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.</td>
</tr>
<tr>
<td>Low</td>
<td>Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.</td>
</tr>
<tr>
<td>Very Low</td>
<td>Any estimate of effect is very uncertain.</td>
</tr>
</tbody>
</table>
Supplemental Feeding in Healthy, Term Neonates Evidence Summary

Question #1. In healthy, term neonates, what are the maternal (i.e., maternal medications, illness, delayed lactogenesis, prior best surgery, etc.) and infant indications (i.e., illness, congenital malformations, dehydration, weight loss, etc.) for supplemental feeding?

OHSU Partners Clinical Practice Recommendation(s):

Supplementation NOT necessary in:
- The healthy, term, appropriate for gestational age infant when the infant is feeding well, urinating and stooling adequately, weight loss is in the expected range, and bilirubin levels are not of concern
  - Ten percent weight loss is not an automatic marker for the need for supplementation, but is an indicator for infant evaluation
- The infant who is fussy at night or constantly feeding for several hours
  - Cluster feeding (several short feeds close together) is normal newborn behavior, but should warrant a feeding assessment to observe the infant’s behavior at the breast and the comfort of the mother to ensure that the infant is latched effectively
  - Some fussy infants are in pain that should be addressed
- The tired or sleeping mother
  - Some fatigue is normal for new mothers. However, rooming out for maternal fatigue does not improve mothers’ sleep time and has been shown to reduce breastfeeding exclusivity. Extreme fatigue should be evaluated for the safety of mother and baby to avoid falls and suffocation
  - Breastfeeding management that optimizes the infant feeding at the breast may make for a more satisfied infant AND allow the mother to get more rest
- Consensus Statement

Medical contraindications to breastfeeding and medical indications for supplementation:
There are few neonatal and maternal medical contraindications to breastfeeding, which are outlined in OHSU Healthcare and Tuality Healthcare policies. In addition, there are some situations (e.g., neonatal hypoglycemia, significant jaundice, late preterm delivery) where supplemental feedings may be clinically indicated.
- Consensus Statement

Weight loss indications for supplementation with continued breastfeeding and careful monitoring:
Consider feeding assessment and supplementation for weight loss greater than 75th percentile for age and mode of delivery as identified through use of the NEWT
- Strong Recommendation; Moderate Quality Evidence

Guideline Recommendations:
The 2016 Baby-Friendly USA guideline states that the facility should develop a protocol/procedure that describes the current, evidence-based medical indications for supplementation.
Level of Evidence for recommendation not provided

A 2012 joint statement of Health Canada, Canadian Paediatric Society, Dieticians of Canada and Breastfeeding Committee for Canada states the following:
Galactosemia is one of only a few rare instances when an infant cannot tolerate breastmilk.

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There are also very few situations when a mother cannot, or should not, breastfeed. These include when the mother:

- is HIV-infected
- has herpes lesions on both breasts
- has untreated, infectious tuberculosis
- has a severe illness that prevents her from caring for her infant

A mother's use of certain drugs or treatments represents a situation when stopping or interrupting breastfeeding may be indicated.

Level of Evidence for recommendations not provided

The Academy of Breastfeeding Medicine’s 2017 guideline states there are common clinical situations where evaluation and breastfeeding management may be necessary, but supplementation is NOT INDICATED, including:

1. The healthy, term, appropriate for gestational age infant when the infant is feeding well, urinating and stooling adequately, weight loss is in the expected range, and bilirubin levels are not of concern (depending on gestational age, time since birth, and any risk factors).
   - Newborns are normally sleepy after an initial alert period after birth (~2 hours). They then have variable sleep-wake cycles, with additional one or two wakeful periods in the next 10 hours whether fed or not
   - Careful attention to an infant’s early feeding cues, keeping the infant safely skin-to-skin with mother when she is awake, gently rousing the infant to attempt frequent breastfeeds, and teaching the mother hand expression of drops of colostrum
   - Increased skin-on-skin time can encourage more frequent feeding
   - Ten percent weight loss is not an automatic marker for the need for supplementation, but is an indicator for infant evaluation.

2. The infant who is fussy at night or constantly feeding for several hours
   - Cluster feeding (several short feeds close together) is normal newborn behavior, but should warrant a feeding evaluation to observe the infant’s behavior at the breast and the comfort of the mother to ensure that the infant is latched deeply and effectively
   - Some fussy infants are in pain that should be addressed.

3. The tired or sleeping mother
   - Some fatigue is normal for new mothers. However, rooming out for maternal fatigue does not improve mothers’ sleep time and has been shown to reduce breastfeeding exclusivity. Extreme fatigue should be evaluated for the safety of mother and baby to avoid falls and suffocation.
   - Breastfeeding management that optimizes the infant feeding at the breast may make for a more satisfied infant AND allow the mother to get more rest.

The guideline states infant indications for supplemental feeding include:

a. Asymptomatic hypoglycemia, documented by laboratory blood glucose measurement (not bedside screening methods) that is unresponsive to appropriate frequent breastfeeding. Note that 40% dextrose gel applied to the side of the infant’s cheek is effective in increasing blood glucose levels in this scenario and improves the rate of exclusive breastfeeding after discharge with no evidence of adverse effects. Symptomatic infants or infants with glucose <1.4 mmol/L (<25 mg/dL) in the first 4 hours or <2.0 mmol/L (<35 mg/dL) after 4 hours should be treated with intravenous glucose. Breastfeeding should continue during intravenous glucose therapy.

b. Signs or symptoms that may indicate inadequate milk intake:

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i. Clinical or laboratory evidence of significant dehydration (e.g., high sodium, poor feeding, lethargy, etc.) that is not improved after skilled assessment and proper management of breastfeeding.

ii. Weight loss of ≥ 8–10% (day 5 [120 hours] or later), or weight loss greater than 75th percentile for age.
   1. Although weight loss in the range of 8–10% may be within normal limits if all else is going well and the physical examination is normal, it is an indication for careful assessment and possible breastfeeding assistance. Weight loss in excess of this may be an indication of inadequate milk transfer or low milk production, but a thorough evaluation is required before automatically ordering supplementation.
   2. Weight loss nomograms for healthy newborns by hour of age can be found at: www.newbornweight.org

iii. Delayed bowel movements, fewer than four stools on day 4 of life, or continued meconium stools on day 5 (120 hours).
   1. Elimination patterns for newborns for urine and stool should be tracked at least through to the onset of secretory activation. Even though there is a wide variation between infants, the patterns may be useful in determining adequacy of breastfeeding. Newborns with more bowel movements during the first 5 days following birth have less initial weight loss, earlier the transition to yellow stools, and earlier return to birth weight.

   c. Hyperbilirubinemia
      i. Suboptimal intake jaundice of the newborn associated with poor breast milk intake despite appropriate intervention. This characteristically begins at 2–5 days and is marked by ongoing weight loss, limited stooling and voiding with uric acid crystals.
      ii. Breast milk jaundice when levels reach 340–425 lmol/L (20–25 mg/dL) in an otherwise thriving infant and where a diagnostic and/or therapeutic interruption of breastfeeding may be under consideration. First line diagnostic management should include laboratory evaluation, instead of interruption of breastfeeding.

   d. Macronutrient supplementation is indicated, such as for the rare infant with inborn errors of metabolism.

The guideline states maternal indications for supplemental feeding include:
   a. Delayed secretory activation (day 3–5 or later [72–120 hours] and inadequate intake by the infant).
   b. Primary glandular insufficiency (less than 5% of women—primary lactation failure), as evidenced by abnormal breast shape, poor breast growth during pregnancy, or minimal indications of secretory activation.
   c. Breast pathology or prior breast surgery resulting in poor milk production.
   d. Temporary cessation of breastfeeding due to certain medications (e.g., chemotherapy) or temporary separation of mother and baby without expressed breast milk available.
   e. Intolerable pain during feedings unrelieved by interventions.

Level of Evidence for recommendations not provided

The International Lactation Consultant’s Association’s 2005 guideline states the following as maternal contraindications for breastfeeding:
- HIV seropositivity
- HTLV-1 seropositivity
- substance abuse
- chemotherapy
- radioactive isotope therapy (interrupt breastfeeding only until the isotope has been eliminated from the mother’s body)
- active tuberculosis
- active varicella
- active herpes lesion(s) on breast

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- Chagas’ disease caused by a South American parasite

Infant contraindications include: galactosemia

**Level of Evidence: II-2 – III**

**References:**


doi:10.1089/bfm.2017.29038.ajk


**Internal Policy Recommendations**

The Tuality Healthcare 2016 Unit-Level Nursing Policy states the following infant contraindications for breastfeeding:

- Galactosemia

The Tuality Healthcare 2016 Unit-Level Nursing Policy states the following infant contraindications for breastfeeding depending on the circumstance:

- Phenylketonuria (may be able to alternate breastfeeding with special modified formula, provided appropriate blood monitoring is available)

The Tuality Healthcare 2016 Unit-Level Nursing Policy states the following maternal contraindications for breastfeeding:

- Maternal drug exposure to Primaquine/Quinine- if either infant or mother has Glucose-6-phosphate dehydrogenase deficiency

- Cancer chemotherapy agents (i.e. antimetabolites that interfere with DNA replication)

- HIV positive

- HTLV-1 or 2

- CMV seropositive (depending on circumstance) no recent converters is newborn is term, the value of breast milk outweighs risk of clinical disease in preterm and full term newborn.

- Exposure to chemotherapy agents (depending on circumstance)

- radioactive isotope therapy (interrupt breastfeeding only until the isotope has been eliminated from the mother’s body)

- active untreated tuberculosis (may breastfeed two weeks after initiation of treatment)

- brucellosis-untreated

- active herpes lesions on both breasts, if on one breast, cover with opsite and breastfeed on unaffected breast

- drugs of abuse (cocaine, PCP, methamphetamine)

- non prescribed controlled substances (depending on circumstance) unless enrolled in supervised methadone maintenance program and tests negative for street drugs and HIV negative

- high dose Metronidazole (discontinue breastfeeding until 12-24 hours after medication administration)

- Sulfa Drug- possible problems with newborn hyperbilirubinemia, G6PD, premature, or stressed

The Tuality Healthcare 2016 Unit-Level Nursing Policy on Supplemental Nutrition state the following infant indications for supplementation:

- Physical anomaly (example: cleft lip)

- Neurological anomaly (example: Down’s syndrome)

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- Asymptomatic hypoglycemia documented by laboratory glucose conformation and is unresponsive to frequent breastfeeding
- Hyperbilirubinemia (elevated bilirubin associated with poor breastmilk intake despite lactation intervention and bilirubin >20-25mg/dL in otherwise thriving infant)
- Neonatal care provider orders supplementation

The Tuality Healthcare 2016 Unit-Level Nursing Policy on Supplemental Nutrition state the following maternal indications for supplementation:
- Breast tissue (breast surgery or trauma, anatomical breast abnormalities, primary breast insufficiency)
- Adoption (breastfeeding possible but may not result in adequate milk supply)
- Delayed lactogenesis (example: retained placenta)
- Maternal request for formula (after breastfeeding education and informed consent)

The Tuality Healthcare 2016 Unit-Level Nursing Policy on Supplemental Nutrition state the following are NOT indications for supplementation:
- Sleepy baby (no signs of illness and fewer than 8 feedings in 24-48 hours and less than 7% weight loss)
- Bilirubin levels < 20 mg/dL 72 hours old, breastfeeding and stooling well
- Fussy baby
- Frequent cluster feeding
- Fatigued mother
- Mother receiving antibiotics for infection
- Weight loss >7%, associated with perinatal bolus IV therapy

The OHSU 2017 Breastfeeding Policy states that the following are infant indications for supplementation with formula only:
- Galactosemia, a special galactose-free formula is needed
- Maple syrup urine disease, a special formula free of leucine, isoleucine and valine is needed
- Phenylketonuria, a special phenylalnine-free formula is needed (some breastfeeding is possible with careful monitoring)

The OHSU 2017 Breastfeeding Policy states that the following are infant indications for supplementation with continued breastfeeding:
- Very low birth weight (less than 1500g)
- Infants who are at risk of hypoglycemia by virtue of impaired metabolic adaptation or increased glucose demand (small for gestational age, who have experienced significant intrapartum hypoxic/ischemic stress, those who are ill and those whose mothers are diabetic if their blood sugar fails to respond to optimal breastfeeding or breast milk feeding)

Statements and guidelines from breastfeeding-friendly authorities regarding appropriate weight losses and weight gains by newborn infants:

<table>
<thead>
<tr>
<th>Organization and Reference</th>
<th>Statement on weight loss and weight gain</th>
</tr>
</thead>
</table>
| **American Academy of Pediatrics**  
Breastfeeding Support Tools for Clinicians | Nutritional guidelines and expectations:  
- Normalcy of weight loss (average of 7%, not to exceed 10% in term newborns)  
- Normal timing to regain birth weight (by day 10) |

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### Primary Literature:

**PICO Question #1:** In healthy, term neonates, what are the maternal (i.e., maternal medications, illness, delayed lactogenesis, prior best surgery, etc.) and infant indications (i.e., illness, congenital malformations, dehydration, weight loss, etc.) for supplemental feeding?

<table>
<thead>
<tr>
<th>Author/Date</th>
<th>Purpose of Study</th>
<th>Study Design</th>
<th>Sample</th>
<th>Outcomes</th>
<th>Design Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chang et al., 2011, <em>Pediatrics and Neonatology</em></td>
<td>To analyze the association between weight loss percentage and hyperbilirubinemia and investigate the best weight loss percentage cut-off value for the</td>
<td>Retrospective chart review analyzed the association between weight loss percentage</td>
<td>874 exclusively breastfed healthy neonates with a gestational age &gt;/= 35 weeks and birth body weight (BBW) &gt; 2500 g</td>
<td>219 infants (25.1%) presented significant hyperbilirubinemia after 72 hours of age</td>
<td>Study Limitations = None</td>
</tr>
</tbody>
</table>

#### Evidence Evaluation for Weight Loss Indications:

- **Lower Quality Rating if:**
  - Studies inconsistent
  - When there are differences in the direction of the effect, populations, interventions or...

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<table>
<thead>
<tr>
<th>Study</th>
<th>Objective</th>
<th>Design</th>
<th>Population</th>
<th>Limitations</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flaherman et al., 2015, Pediatrics</td>
<td>To develop an hour-by-hour newborn weight loss nomogram to assist in early identification of those on a trajectory for adverse outcomes</td>
<td>Retrospective observational study</td>
<td>161,471 term, singleton neonates born at ≥36 weeks gestation at Northern California Kaiser Permanente hospitals in 2009–2013, data were extracted from the birth hospitalization</td>
<td>None</td>
<td>Almost 5% of vaginally delivered newborns and 10% of those delivered by cesarean had lost ≥10% of their birth weight 48 hours after delivery. By 72 hours, &gt;25% of newborns delivered by cesarean had lost ≥10% of their birth weight Study Limitations = None Non-Experimental/Observational Studies (case-control, cohort, cross sectional, longitudinal, descriptive, epidemiologic, case study/series, QI, survey) Insufficient sample size Sample not representative of patients in the population as a whole Variables (confounders, exposures, predictors) were not described Outcome criteria not objective or were not applied in blind fashion Insufficient follow-up, if applicable For diagnostic study, sample not defined at common point in course of disease/condition For diagnostic study, gold standard not applied to all patients For diagnostic study, no independent, blind comparison between index test and gold standard Publication Bias (e.g. pharmaceutical company sponsors study on effectiveness of drug) Increase Quality Rating if: Large Effect Level of evidence for studies as a whole: High Moderate Low</td>
</tr>
</tbody>
</table>
### Supplemental Feeding in Healthy, Term Neonates Evidence Summary

<table>
<thead>
<tr>
<th>Study Authors</th>
<th>Purpose</th>
<th>Study Type</th>
<th>Participants</th>
<th>Intervention</th>
<th>Outcomes</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hren et al., 2009, <em>Pediatrics</em></td>
<td>To assess whether formula supplementation of infants with failure to thrive can improve underweight without jeopardizing breastfeeding</td>
<td>Prospective intervention study</td>
<td>31 term exclusively breast-fed infants admitted to hospital at an age of 28-99 days with failure to thrive (&lt;%= 40% expected weight gain for age and/or body weight &lt;%= 10th percentile for age) without underlying disease</td>
<td>Infant formula was offered ad libitum after each breastfeeding, while continued breastfeeding was supported.</td>
<td>Energy intake per day increased from 352 ± 111 kJ/kg (mean ± SD) at study start to 387 ± 115 kJ/kg (P &lt; 0.001, days 1 – 3 of supplementation) and 501 ± 99 kJ/kg (days 29 – 31; P &lt; 0.001 vs study entry). Twenty-five infants continued to be partially (n= 21) or fully (n = 4) breast-fed. Human milk intake decreased from 476 ± 163 g/day (study days 1 – 3) to 349 ± 285 g/day (study days 29 – 31; P &lt; 0.01). The contribution of breast milk to total milk intake decreased from 100% to 42 ± 35% (P &lt; 0.001). Supplementation over 31 days led to increased weight (0.98 [0.70], standard deviation scores [SDS]), length (+0.40 [0.41] SDS) and head circumference (+0.59 [0.93] SDS). One month of formula supplementation successfully improved growth in 72% of infants with failure to thrive on human milk feeding. Breastfeeding was maintained in 81% of infants.</td>
<td>None</td>
</tr>
<tr>
<td>Isolauri et al., 1999, <em>Pediatrics</em></td>
<td>To evaluate whether allergic infants should continue breastfeeding</td>
<td>Prospective intervention study</td>
<td>100 infants who had atopic eczema during exclusive breastfeeding</td>
<td>The extent and severity of the eczema, allergic sensitization, and the patients’ growth and</td>
<td>The mean body length SD score decreased at the onset of allergic disease, and an association was seen between the duration of symptoms and poor growth (r = –.23, P = .04). Some improvement could be achieved by strict elimination diet by the mothers. The atopic eczema improved significantly after breastfeeding was</td>
<td>None</td>
</tr>
</tbody>
</table>

**Study Limitations:**
- For diagnostic study, no independent, blind comparison between index test and gold standard
- Very Low Evidence Evaluation for Condition-Specific Indications:
  - Lower Quality Rating if:
    - Studies inconsistent (When there are differences in the direction of the effect, populations, interventions or outcomes between studies)
    - Studies are indirect (Your PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)
    - Studies are imprecise (When studies include few patients and few events and thus have wide confidence intervals and the results are uncertain)
- Publication Bias (e.g. pharmaceutical company sponsors)
### Supplemental Feeding in Healthy, Term Neonates Evidence Summary

**March 2017**

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Population</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Konetzny et al., 2009, <em>Eur J Pediatr</em></td>
<td>Prospective cohort study</td>
<td>2,788 breastfed healthy term newborns at hospital in Switzerland</td>
<td>Sixty-seven (2.4%) newborns had a weight loss ≥10% of birth weight; 24 (36%) of these had moderate and 18 (27%) severe hypernatraemia</td>
<td>None</td>
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<tr>
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<td>All newborns regained weight 24 h after additional fluids</td>
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<td>Study Limitations = None</td>
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<td></td>
<td>Non-Experimental/Observational Studies (case-control, cohort, cross sectional, longitudinal, descriptive, epidemiologic, case study/series, QI, survey)</td>
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<td></td>
<td></td>
<td></td>
<td>Insufficient sample size</td>
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<td>Sample not representative of patients in the population as a whole</td>
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<td>Variables (confounders, exposures, predictors) were not described</td>
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<td>Outcome criteria not objective or were not applied in blind fashion</td>
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<td>Insufficient follow-up, if applicable</td>
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<td></td>
<td>For diagnostic study, sample not defined at common point in course of disease/condition</td>
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<td>For diagnostic study, gold standard not applied to all patients</td>
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</tr>
<tr>
<td>Miller et al., 2015, <em>Hosp Pediatrics</em></td>
<td>Retrospective observational study</td>
<td>Newborns whose first feeding formula was from a cohort of 161,471 healthy, term, singleton neonates born at ≥36 weeks’ gestation between 2009 and 2013 were identified (n=7075)</td>
<td>The median weight loss was 2.9% at 48 hours after vaginal delivery; weight loss &gt;7% was rare. For cesarean-delivered neonates, median weight losses at 48 and 72 hours were 3.7%</td>
<td>None</td>
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<td>Study Limitations = None</td>
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<tr>
<td>Study</td>
<td>Objective</td>
<td>Design</td>
<td>Description</td>
<td>Findings</td>
</tr>
<tr>
<td>-------</td>
<td>-----------</td>
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<td>-------------</td>
<td>----------</td>
</tr>
<tr>
<td>Paul et al., 2016, <em>Pediatrics</em></td>
<td>To determine the distribution of weight loss and subsequent regain in neonates during the first month, the proportion not surpassing birth weight by 14 and 21 days, and whether findings differed by delivery mode</td>
<td>Retrospective observational study</td>
<td>143,889 singleton neonates delivered at ≥36 weeks’ gestation at Kaiser Permanente Northern California Medical Centers between 2009 and 2013 and weighing 2000 to 5000 g at birth</td>
<td>50% of newborns were at or above birth weight at 9 and 10 days after vaginal and cesarean delivery, respectively. Among those delivered vaginally, 14% and 5% were not back to birth weight by 14 and 21 days, respectively. For those delivered by cesarean, 24% and 8% were not back to birth weight by 14 and 21 days, respectively.</td>
</tr>
</tbody>
</table>

**Supplemental Feeding in Healthy, Term Neonates Evidence Summary**

Newborns who are exclusively formula fed and 3.5%, respectively; weight loss>8% was rare. Epidemiologic, case study/series, QI, survey

- Insufficient sample size
- Sample not representative of patients in the population as a whole
- Variables (confounders, exposures, predictors) were not described
- Outcome criteria not objective or were not applied in blind fashion
- Insufficient follow-up, if applicable
- For prognostic study, sample not defined at common point in course of disease/condition

Study Limitations = None.
### Supplemental Feeding in Healthy, Term Neonates Evidence Summary

<table>
<thead>
<tr>
<th>Study Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
</tr>
</tbody>
</table>

#### References:


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**Preer et al., 2012, *Journal of Human Lactation***

To determine average weight loss in a cohort of exclusively breastfed infants delivered by cesarean birth and to identify correlates of greater than expected weight loss

- **Retrospective chart review**
- **200 exclusively breastfed infants delivered via cesarean birth at a Baby-Friendly hospital between 2005 and 2007**

**Average weight loss during the hospital stay in our cohort of 200 infants was 7.2% ± 2.1% of birth weight, slightly greater than the American Academy of Pediatrics guideline of 7%. Absence of labor prior to delivery was significantly associated with a greater percentage of weight loss (P = .0004), as were lower gestational age (P = .0004) and higher birth weight (P < .0001).**

**Study Limitations**
- Non-Experimental/Observational Studies (case-control, cohort, cross sectional, longitudinal, descriptive, epidemiologic, case study/series, QI, survey)
- Insufficient sample size
- Sample not representative of patients in the population as a whole
- Variables (confounders, exposures, predictors) were not described
- Outcome criteria not objective or were not applied in blind fashion
- Insufficient follow-up, if applicable
- For prognostic study, sample not defined at common point in course of disease/condition
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- For diagnostic study, no independent, blind comparison between index test and gold standard

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**March 2017**
Supplemental Feeding in Healthy, Term Neonates Evidence Summary


Question #2. In healthy, term neonates, what is the preferred choice of supplemental feeding (i.e., human breast milk, protein hydrolysate formulas, other supplemental formulas)?

OHSU Partners Clinical Practice Recommendation(s):

Neonates should not be given food or drink other than their mother’s breast milk, unless medically indicated. A medical provider’s order is required when supplements are medically indicated, and an informed, documented decision from the parent is required when supplements are not medically indicated. It is the responsibility of the healthcare provider to fully inform parents of the benefits and risks of supplementation, document parental decisions, and support the parents after they have made a decision.

-Consensus Statement

Guideline Recommendations:

A 2012 joint statement of Health Canada, Canadian Paediatric Society, Dieticians of Canada and Breastfeeding Committee for Canada states the following: When feeding at the breast is not possible, the first choice is to feed expressed breastmilk from the infant’s own mother. For infants who cannot or should not be fed their mother’s breastmilk, pasteurised human milk from appropriately screened donors and commercial infant formula are suitable alternatives. These options depend on individual circumstances.

Commercial infant formula may be the most feasible alternative if it is not possible for an infant to be exclusively fed their mother’s breastmilk. The commercial infant formula chosen must be appropriate for the infant, and prepared and stored safely to reduce the risk of illness from bacterial growth.

- Recommend cow milk-based, commercial infant formula for an infant who is not exclusively fed breastmilk. Soy-based infant formula is indicated only for those infants who have galactosemia or who cannot consume dairy-based products for cultural or religious reasons.
- Recommend infant formulas for special medical purposes only when you detect or suspect that the formula-fed infant has the indicated condition.
- Discourage the use of home-made, evaporated milk formula. Cow milk, goat milk, soy beverage, rice beverage or any other beverages should not be given to young infants.

Level of Evidence for recommendations not provided

The Academy of Breastfeeding Medicine’s 2017-guideline states:

1. Expressed breast milk from the infant’s mother is the first choice for extra feeding for the breastfed infant. (III) Hand expression may elicit larger volumes than a breast pump in the first few days following birth and may increase overall milk supply. Breast massage and/or compression along with expressing with a mechanical pump may also increase available milk. (II-3)
2. If the volume of the mother’s own colostrum/milk does not meet her infant’s feeding requirements and supplementation is required, donor human milk is preferable to other supplements.

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3. When donor human milk is not available or appropriate, protein hydrolysate formulas may be preferable to standard infant formula as they avoid exposure to intact cow’s milk proteins and reduce bilirubin levels more rapidly, (II-2) although recent data are less supportive of its role in preventing allergic disease. (I) The use of this type of formula may also convey the psychological message that the supplement is a temporary therapy, not a permanent inclusion of artificial feedings.

4. Supplementation with glucose water is not appropriate because it does not provide sufficient nutrition, does not reduce serum bilirubin, and might cause hyponatremia.

5. The potential risks and benefits of other supplemental fluids, such as cow’s milk formulas, soy formulas, or protein hydrolysate formulas, must be considered along with the available resources of the family, the infant’s age, the amounts needed, and the potential impact on the establishment of breastfeeding.

Level of Evidence for recommendations not provided

The International Lactation Consultant’s Association’s 2005 guideline states the following: If medically indicated, provide additional nutrition using a method of supplementation that is least likely to compromise the transition to exclusive breastfeeding.

Guidelines for supplementation:
- use mother’s own milk first
- pasteurize the mother’s milk if she is HIV positive
- pasteurized donor milk is the next best alternative to the mother’s own milk
- human milk substitute (formula) is the last choice
- the selection of a human milk substitute should take into account any family history of allergic disease

Level of Evidence: I – III

References:

Internal Policy Recommendations

The Tuality Healthcare 2016 Unit-Level Nursing Policy on Supplemental Nutrition states that fresh Expressed Breast Milk (EBM) is the best supplemental source followed by refrigerated EBM, Donor Milk (if available) and then Breast Milk Substitution (not preferred).

The OHSU 2017 Breastfeeding Policy states that newborns should not be given food or drink other than breast milk, unless medically indicated. Supplemental human donor milk will not be given unless indicated and specifically ordered by the LIP. Formula will not be given unless indicated and ordered by the LIP or by the parent’s documented and informed request.

Primary Literature:
### PICO Question #2: In term, healthy neonates, what is the preferred choice of supplemental feeding (i.e., human breast milk, protein hydrolysate formulas, other supplemental formulas)?

<table>
<thead>
<tr>
<th>Author/Date</th>
<th>Purpose of Study</th>
<th>Study Design</th>
<th>Sample</th>
<th>Outcomes</th>
<th>Design Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boyle et al., 2016, BMJ</td>
<td>To determine whether feeding infants with hydrolysed formula reduces their risk of allergic or autoimmune disease</td>
<td>Systematic Review and meta-analysis</td>
<td>37 prospective intervention trials (n=19,000) of hydrolysed cows’ milk formula compared with another hydrolysed formula, human breast milk, or a standard cows’ milk formula,</td>
<td>Overall there was no consistent evidence that partially or extensively hydrolysed formulas reduce risk of allergic or autoimmune outcomes in infants at high pre-existing risk of these outcomes. Odds ratios for eczema at age 0-4, compared with standard cows’ milk formula, were 0.84 (95% confidence interval 0.67 to 1.07; I²=30%) for partially hydrolysed; 0.55 (0.28 to 1.09; I²=74%) for extensively hydrolysed casein based formula; and 1.12 (0.88 to 1.42; I²=0%) for extensively hydrolysed whey based formula.</td>
<td>Study Limitations = None Systematic Review Study did not address focused clinical question Search was not detailed or exhaustive Quality of the studies was not appraised or studies were of low quality Methods and/or results were inconsistent across studies</td>
</tr>
<tr>
<td>Makrides et al., 2005, Am J Clin Nutr</td>
<td>To determine the effect of supplementing infant formula with long-chain polyunsaturated fatty acids (LCPUFAs) on the growth of term infants</td>
<td>Systematic review and meta-analysis</td>
<td>14 RCTs with 1846 infants that involved LCPUFA supplementation of infant formula fed to term infants</td>
<td>no significant effect of LCPUFA supplementation on infant weight, length, or head circumference at any assessment age</td>
<td>Study Limitations = None Systematic Review Study did not address focused clinical question Search was not detailed or exhaustive Quality of the studies was not appraised or studies were of low quality Methods and/or results were inconsistent across studies</td>
</tr>
<tr>
<td>Osborne et al., 2006, Cochrane Database of</td>
<td>To determine the effect of feeding hydrolysed formulas on allergy and food intolerance in infants and children</td>
<td>Systematic Review</td>
<td>20 trials that compare the use of a hydrolysed infant formula to human milk or cow’s milk formula</td>
<td>Two trials compared early, short term hydrolysed formula to human milk feeding. No significant difference in infant allergy or childhood cow’s milk allergy (CMA) were reported. No</td>
<td>Study Limitations = None Systematic Review Study did not address focused clinical question</td>
</tr>
</tbody>
</table>
## Supplemental Feeding in Healthy, Term Neonates Evidence Summary

### Systematic Reviews

<table>
<thead>
<tr>
<th>Study</th>
<th>Objective</th>
<th>Design</th>
<th>Eligibility</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compared to adapted cow’s milk or human breast milk.</td>
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<td>No significant benefits were reported. One large quasi-random study reported a reduction in infant CMA of borderline significance in low risk infants (RR 0.62, 95% CI 0.38, 1.00).</td>
</tr>
<tr>
<td>To evaluate the efficacy and safety of prebiotic supplementation in full-term neonates</td>
<td>Systematic review and meta-analysis</td>
<td>11 trials (n=1459) comparing formula milk supplemented with or without prebiotics, commenced at or before age 28 days and continued for 2 weeks or longer.</td>
<td>Infants who received a supplement had slightly better weight gain than did controls (weighted mean difference, 1.07 g; 95% confidence interval, 0.14-1.99; 4 trials) with softer and frequent stools similar to breastfed infants. All but 1 trial reported that prebiotic supplementation was well tolerated. In that trial, diarrhea (18% vs 4%; P=.008), irritability (16% vs 4%; P=.03), and eczema (18% vs 7%; P=.046) were reported more frequently by parents of infants who received prebiotic supplements.</td>
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<tr>
<td>To examine whether supplementary feeding of cow’s milk at the maternity hospital would increase the risk of cow’s milk allergy when compared with feeding with pasteurized human milk or hydrolyzed formula</td>
<td>RCT</td>
<td>6209 unselected healthy, full-term infants, of whom 5385 (87%) required supplementary milk while in the hospital.</td>
<td>The cumulative incidence of CMA in the infants fed CM was 2.4% compared with 1.7% in the pasteurized human milk group (odds ratio [OR], 0.70; 95% confidence interval [CI], 0.44-1.12) and 1.5% in the whey hydrolysate group (OR, 0.61; 95% CI, 0.38-1.00). In the comparison group, CMA developed in 2.1% of the infants.</td>
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### Study Limitations

- None

### Level of evidence for studies as a whole:

- High
- Moderate
- Low
- Very Low
Sievers et al., 2002, *Ann Nutr Metab*

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Objective</th>
<th>Results</th>
<th>Limitations</th>
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</thead>
<tbody>
<tr>
<td>RCT</td>
<td>To evaluate the effects of different supplemental feedings on the term health neonates</td>
<td>Two groups of healthy, term newborn infants (n = 64 in each group)</td>
<td>None</td>
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<tr>
<td></td>
<td>whey hydrolysate formula (1737 infants). The comparison group (824 infants) was composed of infants who were exclusively breast-fed</td>
<td>The energy intake of group B was higher prior to the 3rd day of study (p &lt; 0.05). Afterwards a higher mean intake of human milk, a faster weight gain but a lower frequency of exclusive breastfeeding at discharge were observed in study group A. Hyperbilirubinemia was more frequent in the group B. Fifty-five percent (group A) and 52% (group B) of the participants were exclusively breast-fed at the age of 8 weeks.</td>
<td>RCT &amp; Quasi-Experimental Studies</td>
</tr>
</tbody>
</table>

Study Limitations:
- Insufficient sample size
- Lack of randomization
- Lack of blinding
- Stopped early for benefit
- Lack of allocation concealment
- Selective reporting of measures
- Large losses to F/U
### Supplemental Feeding in Healthy, Term Neonates Evidence Summary

**Singhal et al., 2010, Pediatrics**

To test the hypothesis that nucleotide supplementation of formula benefits early infant growth

<table>
<thead>
<tr>
<th>Study Design</th>
<th>To test the hypothesis that nucleotide supplementation of formula benefits early infant growth</th>
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<tbody>
<tr>
<td>RCT</td>
<td>RCT</td>
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</table>

200 healthy term infants who had already started formula feeding

| Infants fed nucleotide-supplemented formula had greater occipitofrontal head circumference at ages 8, 16, and 20 weeks than infants fed control formula (mean difference in z scores at 8 weeks: 0.4 [95% confidence interval: 0.1–0.7]; P = .006) even after adjustment for potential confounding factors (P = .002). Weight at 8 weeks and the increase in both occipitofrontal head circumference and weight from birth to 8 weeks were also greater in infants fed nucleotide-supplemented formula than in those fed control formula

<table>
<thead>
<tr>
<th>Study Limitations</th>
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<tr>
<td>None</td>
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<tr>
<td><strong>RCT &amp; Quasi-Experimental Studies</strong></td>
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<td>Large losses to F/U</td>
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</tbody>
</table>

**Table 3. Postnatal development of weight (median, range)**

<table>
<thead>
<tr>
<th>Period</th>
<th>Supplement A</th>
<th>Supplement B</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.34</td>
<td>64</td>
<td>64</td>
</tr>
<tr>
<td>0.48</td>
<td>64</td>
<td>64</td>
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<td>0.72</td>
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<td>0.96</td>
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<tr>
<td>6.00</td>
<td>18</td>
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</tbody>
</table>

March 2017
**Supplemental Feeding in Healthy, Term Neonates Evidence Summary**

<table>
<thead>
<tr>
<th>Study</th>
<th>Objective</th>
<th>Design</th>
<th>Participants</th>
<th>Outcomes</th>
<th>Study Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Szajewska et al., 2013, <em>BMC Pediatrics</em></td>
<td>to determine the effects of supplementation of infant formulae with <em>Bifidobacterium lactis</em> Bb12 (B lactis) and/or <em>Lactobacillus rhamnosus</em> GG (LGG) compared with unsupplemented formula on the growth of healthy infants</td>
<td>Systematic review and meta-analysis</td>
<td>9 RCTs of healthy, term neonates (n=100) from birth to the age of 20 weeks, and in infants who were breastfed (reference group; n=101)</td>
<td>Compared with unsupplemented controls, supplementation of infant formula with <em>B lactis</em> had no effect on weight gain (4 RCTs, n = 266, mean difference (MD) 0.96 g/day, 95% confidence interval (CI) -0.70 to 2.63), length gain (4 RCTs, n = 261, MD −0.39 mm/month, 95% CI -1.32 to 0.53), or head circumference gain (3 RCTs, n = 207, MD 0.56 mm/month, 95% CI −0.17 to 1.30). Data limited to one small (n = 105) trial suggest that infants who received standard infant formula supplemented with LGG grew significantly better. No such effect was observed in infants fed hydrolyzed formula supplemented with LGG.</td>
<td>None</td>
</tr>
<tr>
<td>Tozier et al., 2013, <em>JOGNN</em></td>
<td>To describe how a practice change facilitated breastfeeding while maintaining glucose stabilization in infants born to diabetic mothers</td>
<td>Quasi-experimental; pre-post- study</td>
<td>The convenience sample consisted of 163 infants born to mothers with type 1 or gestational diabetes, with 86 infants in the prepractice change group and 77 infants in the postpractice change group.</td>
<td>There were no significant differences between glucose values for infants given formula supplementation versus those fed colostrum. Postpractice change, admissions to the neonatal intensive care unit (NICU) for glucose stabilization decreased (18.8% (16/85) of the term infants born to diabetic mothers were transferred to the NICU for blood glucose stabilization as compared to 6.5% (5/77) postpractice</td>
<td>None</td>
</tr>
</tbody>
</table>

**Study Limitations**
- Systematic Review
- Review did not address focused clinical question
- Search was not detailed or exhaustive
- Quality of the studies was not appraised or studies were of low quality
- Methods and/or results were inconsistent across studies

**RCT & Quasi-Experimental Studies**
- Insufficient sample size
- Lack of randomization
- Lack of blinding
- Stopped early for benefit
- Lack of allocation concealment
- Selective reporting of measures
- Large losses to F/U
testing, and skin-to-skin contact

change, a 68% improvement) and exclusive breastfeeding increased

Udell et al., 2005, *Lipids*

To evaluate the effect of modifying 18-carbon PUFA [18-C PUFA: α-linolenic acid (ALA, 18:3n-3) and linoleic acid (LA, 18:2n-6)] in the diets of term and preterm infants on DHA (22:6n-3) status, growth, and developmental outcomes

Systematic review and meta-analysis

8 RCTS involving formula-fed term (5 studies) and preterm infants (3 studies), in which the 18-C PUFA composition of the formula was changed and growth or developmental outcomes were measured

In term infants, ALA supplementation was associated with increased weight and length at 12 mon, which was at least 4 mon after the end of dietary intervention. Developmental indices of term infants did not differ between groups

Study Limitations = None

Systematic Review

Review did not address focused clinical question

Search was not detailed or exhaustive

Quality of the studies was not appraised or studies were of low quality

Methods and/or results were inconsistent across studies

Verner et al., 2007, *Cochrane Database of Systematic Reviews*

To assess the effect of providing supplemental taurine for enterally or parenterally fed preterm or low birth weight infants on growth and development

Systematic review and meta-analysis

9 small RCTs or quasi-randomised controlled trials that compared taurine supplementation versus no supplementation in preterm or low birth weight newborn infants

In eight of the studies, taurine was given enterally with formula milk

Taurine supplementation increased intestinal fat absorption [weighted mean difference 4.0 (95% confidence interval 1.4, 6.6) percent of intake]. However, meta-analyses did not reveal any statistically significant effects on growth parameters assessed during the neonatal period or until three to four months chronological age [rate of weight gain: weighted mean difference -0.25 (95% confidence interval -1.16, 0.66) grams/kilogram/day; change in length: weighted mean difference 0.37 (95% confidence interval -0.23, 0.98) millimetres/week; change in head circumference: weighted mean

Study Limitations = None

Systematic Review

Review did not address focused clinical question

Search was not detailed or exhaustive

Quality of the studies was not appraised or studies were of low quality

Methods and/or results were inconsistent across studies

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Supplemental Feeding in Healthy, Term Neonates Evidence Summary

There are very limited data on the effect on neonatal mortality or morbidities, and no data on long-term growth or neurological outcomes.

References:


Question #3. In healthy, term, what is the appropriate volume of supplemental feeding based on patient condition, weight, and type of supplement?

**OHSU Clinical Practice Recommendation(s):**

The amount of supplement given should reflect the normal amounts of colostrum available, and the age and size of the infant. Intake on day 2 post-birth is generally higher than day 1 in relation to infant’s demand. Suggested intakes for healthy, term infants are given below:

**Average Reported Intakes of Colostrum by Healthy, Term Breastfed Infants**

<table>
<thead>
<tr>
<th>Time (hours)</th>
<th>Intake (mL/feed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First 24</td>
<td>2–10</td>
</tr>
<tr>
<td>24–48</td>
<td>5–15</td>
</tr>
<tr>
<td>48–72</td>
<td>15–30</td>
</tr>
<tr>
<td>72–96</td>
<td>30–60</td>
</tr>
</tbody>
</table>

- **Consensus Statement**

March 2017
Supplemental Feeding in Healthy, Term Neonates Evidence Summary

**Guideline Recommendations:**

The Academy of Breastfeeding Medicine’s 2017 guideline states that:

1. Several studies give us an idea of intakes at the breast over time. In most studies, the range of intake is wide, while formula-fed infants usually take in larger volumes than breastfed infants.
2. Infants fed infant formula ad libitum commonly have much higher intakes than breastfed infants. Acknowledging that ad libitum breastfeeding emulates evolutionary feeding and considering recent data on obesity in formula-fed infants, it appears that formula-fed infants may be overfed.
3. As there is no definitive research available, the amount of supplement given should reflect the normal amounts of colostrum available, the size of the infant’s stomach (which changes over time), and the age and size of the infant. Intake on day 2 post-birth is generally higher than day 1 in relation to infant’s demand.
4. Based on the limited research available, suggested intakes for healthy, term infants are given below, although feedings should be based on infant cues.

**Average Reported Intakes of Colostrum by Healthy, Term Breastfed Infants**

<table>
<thead>
<tr>
<th>Time (hours)</th>
<th>Intake (mL/feed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First 24</td>
<td>2–10</td>
</tr>
<tr>
<td>24–48</td>
<td>5–15</td>
</tr>
<tr>
<td>48–72</td>
<td>15–30</td>
</tr>
<tr>
<td>72–96</td>
<td>30–60</td>
</tr>
</tbody>
</table>

**Level of Evidence for recommendations not provided**

**References:**


**Internal Policy Recommendations**

The OHSU 2017 Breastfeeding Policy states that infants who require medically indicated supplementation will be fed physiologically appropriate volumes based on their age.

**Primary Literature:**

No primary research studies were found that addressed this question.

**Question #4. In healthy, term neonates, what is optimal method of supplementation (i.e., cup feeding, spoon or dropper feeding, bottle feeding, syringe, etc.)?**

March 2017
OHSU Clinical Practice Recommendation(s):

Any fluid supplementation (whether medically indicated or following informed decision of the parent) should be given by tube, syringe, spoon, or cup in preference to an artificial nipple or bottle

- Strong Recommendation; Low Quality Evidence

Guideline Recommendations:

The 2016 Baby-Friendly USA guideline states that any fluid supplementation (whether medically indicated or following informed decision of the mother) should be given by tube, syringe, spoon, or cup in preference to an artificial nipple or bottle.

Level of Evidence for recommendation not provided

The Academy of Breastfeeding Medicine’s 2017 guideline states:

1. When supplementary feedings are needed, there are a number of delivery methods from which to choose: a supplemental nursing device at the breast, cup feeding, spoon or dropper feeding, finger-feeding, syringe feeding, or bottle feeding.

2. An optimal supplemental feeding device has not yet been identified, and may vary from one infant to another. No method is without potential risk or benefit.

3. When selecting an alternative feeding method, clinicians should consider several criteria:
   a. cost and availability
   b. ease of use and cleaning
   c. stress to the infant
   d. whether adequate milk volume can be fed in 20–30 minutes
   e. whether anticipated use is short- or long-term
   f. maternal preference
   g. expertise of healthcare staff
   h. whether the method enhances development of breastfeeding skills

4. There is no evidence that any of these methods are unsafe or that one is necessarily better than the other. There is some evidence that avoiding teats/artificial nipples for supplementation may help the infant return to exclusive breastfeeding; however, when hygiene is suboptimal, cup feeding is the recommended choice. Cup feeding also allows infants to control feeding pace. Cup feeding has been shown safe for both term and preterm infants and may help preserve breastfeeding duration among those who require multiple supplemental feedings.

5. If bottles are being used, pacing the feed may be beneficial, especially for preterm infants.

6. Supplemental nursing systems have the advantages of supplying a supplement while simultaneously stimulating the breast to produce more milk, reinforcing the infant’s feeding at the breast, enabling the mother to have a breastfeeding experience, and encouraging skin-to-skin. However, mothers may find the systems awkward to use, difficult to clean, relatively expensive, requiring moderately complex learning, and the infant must be able to latch effectively. A simpler version, supplementing with a dropper, syringe, or feeding tube attached to the breast while the infant is feeding at breast, may be effective.

7. Bottle feeding is the most commonly used method of supplementation in more affluent regions of the world, but concerns have been raised because of distinct differences in tongue and jaw movements, and faster flow may result in higher (and unnecessary) volumes of feeds. Some experts have recommended a teat/nipple with a wide base and slow flow to try to mimic breastfeeding and to avoid nipple confusion or preference, but little research has been done evaluating outcomes with different teats/nipples.

Level of Evidence for recommendations not provided

References:

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Supplemental Feeding in Healthy, Term Neonates Evidence Summary


Internal Policy Recommendations

The Tuality Healthcare 2016 Unit-Level Nursing Policy on Supplemental Nutrition states that the following lactation aids should be used with supplementation:
- Supplemental Nursing System (SNS) at the breast
- Cup
- Pipet with finger feed
- Feeding syringe
- Nipple and bottle (not preferred)

The OHSU 2017 Breastfeeding Policy states:
Artificial nipples, infant feeding bottles, and pacifiers are to be avoided.
Mothers requesting feeding bottles will be educated on the potential negative consequences and this will be documented.

Primary Literature:

<table>
<thead>
<tr>
<th>Author/Date</th>
<th>Purpose of Study</th>
<th>Study Design</th>
<th>Sample</th>
<th>Outcomes</th>
<th>Design Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borucki et al., 2005, Journal of Human Lactation</td>
<td>To describe the experiences of breastfeeding mothers who used supplemental feeding tube devices to establish, re-establish or supplement breastfeeding</td>
<td>Naturalist field study</td>
<td>22 fully or partially breastfeeding mothers, all well-educated and affluent</td>
<td>Introduced at birth in 3 infants, during the first week of life for 7 infants and by the second week of life for 5 infants After using the SFTD 5 mothers stopped breastfeeding within a week; 5 of the infants were breastfed for 2 weeks-6 months, while 16 of the infants were breastfed for longer than 6 months</td>
<td>None Non-Experimental/Observational Studies (case-control, cohort, cross sectional, longitudinal, descriptive, epidemiologic, case study/series, QI, survey) ☒ Insufficient sample size ☒ Sample not representative of patients in the population as a whole ☐ Variables (confounders, exposures, predictors) were not described</td>
</tr>
</tbody>
</table>

Lower Quality Rating if:
- Studies inconsistent (When there are differences in the direction of the effect, populations, interventions or outcomes between studies)
- Studies are indirect (Your PICO question is quite different from the available evidence in regard to population, intervention,
### Supplemental Feeding in Healthy, Term Neonates Evidence Summary

<table>
<thead>
<tr>
<th>Study</th>
<th>Design/Methodology</th>
<th>Findings</th>
<th>Limitations</th>
<th>Quality Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown et al., 1999, Midwifery</td>
<td>Retrospective chart review</td>
<td>Women found SFTD to be an acceptable alternative that facilitated their breastfeeding experience.</td>
<td>Outcome criteria not objective or were not applied in blind fashion</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>63 term breast-feeding babies; 30 supplemented by cup and 33 supplemented by bottle.</td>
<td>There were no significant differences between the bottle and cup supplementation groups in relation to feeding outcome (OR 1.94 95% CI 0.61, 6.31), or in the length of time from the beginning of supplementation to leaving hospital (median difference 1.95% CI 0.0, 1.95). Babies who received supplements of expressed breast milk, as opposed to artificial milk, were more likely to be supplemented by cup (OR 4.29, 95% CI 0.9, 26.91; p=0.05), but were not more likely to be discharged from midwifery care breast feeding (OR 3.79, 95% CI 0.69, 38.36).</td>
<td>Non-Experimental/Observational Studies (case-control, cohort, cross sectional, longitudinal, descriptive, epidemiologic, case study/series, QI, survey) ☑ Insufficient sample size ☑ Sample not representative of patients in the population as a whole ☑ Variables (confounders, exposures, predictors) were not described ☑ Outcome criteria not objective or were not applied in blind fashion ☑ Insufficient follow-up, if applicable ☑ For diagnostic study, sample not defined at common point in course of disease/condition ☑ For diagnostic study, gold standard not applied to all patients ☑ For diagnostic study, no independent, blind comparison between index test and gold standard</td>
<td>None</td>
</tr>
<tr>
<td>Flint et al., 2016, Cochrane Database of</td>
<td>Systematic review and meta-analysis</td>
<td>The experimental intervention was cup feeding and the control intervention was bottle feeding in all five studies</td>
<td>Study Limitations = None</td>
<td>Systematic Review</td>
</tr>
<tr>
<td></td>
<td>5 randomised or quasi-randomised controlled trials comparing cup feeding to</td>
<td>The experimental intervention was cup feeding and the control intervention was bottle feeding in all five studies</td>
<td>Publication Bias (e.g. pharmaceutical company sponsors study on effectiveness of drug)</td>
<td></td>
</tr>
</tbody>
</table>

March 2017
### Supplemental Feeding in Healthy, Term Neonates Evidence Summary

**Systematic Reviews**

**supplemental enteral feeding on weight gain and achievement of successful breastfeeding in term and preterm infants who are unable to fully breastfeed**

**other forms of enteral feeding for the supplementation of term and preterm infants**

**included in this review. One study reported weight gain as g/kg/day and there was no statistically significant difference between the two groups (MD = 0.60, 95% CI = 3.21 to 2.01); while a second study reported weight gain in the first seven days as grams/day and also showed no statistically significant difference between the two groups (MD = 0.10, 95% CI = 0.36 to 0.16).**

There was substantial variation in results for the majority of breastfeeding outcomes, except for not breastfeeding at three months (three studies) (typical RR 0.83, 95% CI 0.71 to 0.97) which favoured cup feeding.

Where there was moderate heterogeneity meta-analysis was performed: not breastfeeding at six months (two studies) (typical RR 0.83, 95% CI 0.72 to 0.95); not fully breastfeeding at hospital discharge (four studies) (typical RR 0.61, 95% CI 0.52 to 0.71).

**Authors’ conclusion: As the majority of infants in the included studies are preterm infants, no recommendations can be made for cup feeding term infants due to the lack of evidence in this population**

- **Review did not address focused clinical question**
- **Search was not detailed or exhaustive**
- **Quality of the studies was not appraised or studies were of low quality**
- **Methods and/or results were inconsistent across studies**

---

**Howard et al., 2003, Pediatrics**

To evaluate the effects of 2 types of artificial nipple RCT randomly assigned to 1 of 4 intervention 700 breastfed newborns (36-42 weeks, birth weight >2200 g)

Supplemental feedings, regardless of method (cup or bottle), had a detrimental effect on breastfeeding duration. There were no differences in

- **Study Limitations =**
  - None
  - RCT & Quasi-Experimental Studies
  - Insufficient sample size
## Supplemental Feeding in Healthy, Term Neonates Evidence Summary

### Exposure on Breastfeeding Duration

<table>
<thead>
<tr>
<th>Study</th>
<th>Exposure Groups</th>
<th>Study Design</th>
<th>Study Population</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Howard et al., 1999, <em>Pediatrics</em></td>
<td>Groups: bottle/early pacifier (n = 169), bottle/late pacifier (n = 167), cup/early pacifier (n = 185), or cup/late pacifier (n = 179). The cup/bottle intervention was invoked for infants who received supplemental feedings: cup (n = 251), bottle (n = 230).</td>
<td>Randomized to either cup-feeding (n=58) or bottle-feeding (n=47); compared to 25 breastfed newborns</td>
<td>98 term, healthy newborns 1 to 3 days old</td>
<td>There were no significant differences in administration time, amounts ingested or overall HR, RR and oxygen saturation rates between cup and bottle groups. Breastfed babies had longer administration times and lower overall HR, RR and higher oxygen saturation as compared to cup- and bottle-fed infants. See table 2 below.</td>
</tr>
</tbody>
</table>

### Cup versus Bottle Groups for Breastfeeding Duration

Exclusive breastfeeding at 4 weeks was less likely among infants exposed to pacifiers (early pacifier group; odds ratio: 1.5; 95% confidence interval: 1.0 –2.0). Early, as compared with late, pacifier use shortened overall duration (adjusted hazard ratio: 1.22; 95% confidence interval: 1.03–1.44) but did not affect exclusive or full duration. See table 1 below.

### Study Limitations

- Lack of randomization
- Lack of blinding
- Stopped early for benefit
- Lack of allocation concealment
- Selective reporting of measures
- Large losses to F/U

### References


March 2017
Table 1. Kaplan-Meier Estimates of Breastfeeding Duration, Supplemental Feeding, and Pacifier Interventions

<table>
<thead>
<tr>
<th>Breastfeeding Duration (D)</th>
<th>Supplemental Feeding Intervention</th>
<th>Pacifier Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bottle (n = 230)</td>
<td>Cup (n = 251)</td>
</tr>
<tr>
<td></td>
<td>Median (95% CI)</td>
<td>Median (95% CI)</td>
</tr>
<tr>
<td>Full</td>
<td>37 (28–49)</td>
<td>45 (35–49)</td>
</tr>
<tr>
<td>Overall</td>
<td>140 (112–157)</td>
<td>105 (90–150)</td>
</tr>
</tbody>
</table>

P Value

- Early vs. Late
  - Exclusive: 0.29
  - Full: 0.74
  - Overall: 0.50

Table 2. Differences in Overall Physiologic Outcomes in Breastfed, Bottle-fed, and Cup-fed Infants

<table>
<thead>
<tr>
<th>Value</th>
<th>Outcome</th>
<th>(i) Treatment Group</th>
<th>(j) Treatment Group</th>
<th>Mean Difference (i–j)</th>
<th>95% CI for Difference</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>Bottle</td>
<td>Cup</td>
<td></td>
<td>3.55</td>
<td>7.95</td>
<td>.11*</td>
</tr>
<tr>
<td></td>
<td>Breast</td>
<td>Bottle</td>
<td></td>
<td>-11.81</td>
<td>-15.95</td>
<td>.000†</td>
</tr>
<tr>
<td></td>
<td>Breast</td>
<td>Cup</td>
<td></td>
<td>-6.50</td>
<td>-10.62</td>
<td>.002†</td>
</tr>
<tr>
<td>RR (breaths/min)</td>
<td>Bottle</td>
<td>Cup</td>
<td></td>
<td>.34</td>
<td>2.40</td>
<td>.74*</td>
</tr>
<tr>
<td></td>
<td>Breast</td>
<td>Bottle</td>
<td></td>
<td>-2.35</td>
<td>-4.44</td>
<td>.028†</td>
</tr>
<tr>
<td></td>
<td>Breast</td>
<td>Cup</td>
<td></td>
<td>-2.72</td>
<td>-4.78</td>
<td>.010†</td>
</tr>
<tr>
<td>O₂ saturation (percent)</td>
<td>Bottle</td>
<td>Cup</td>
<td></td>
<td>.15</td>
<td>1.22</td>
<td>.78*</td>
</tr>
<tr>
<td></td>
<td>Breast</td>
<td>Bottle</td>
<td></td>
<td>1.71</td>
<td>3.11</td>
<td>.018†</td>
</tr>
<tr>
<td></td>
<td>Breast</td>
<td>Cup</td>
<td></td>
<td>1.43</td>
<td>2.82</td>
<td>.043†</td>
</tr>
</tbody>
</table>

* Analysis conducted with repeated measures ANOVA.
† Because of significant differences in baseline measures (prefeeding values) between breastfed versus cup- and bottle-fed infants, analyses were conducted with repeated measures ANOVA with prefeeding values entered as a covariate.
Appendix A. GRADE criteria for rating a body of evidence on an intervention
Developed by the GRADE Working Group

**Grades and interpretations:**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Further research is very unlikely to change our confidence in the estimate of effect.</td>
</tr>
<tr>
<td>Moderate</td>
<td>Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.</td>
</tr>
<tr>
<td>Low</td>
<td>Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.</td>
</tr>
<tr>
<td>Very low</td>
<td>Any estimate of effect is very uncertain.</td>
</tr>
</tbody>
</table>

**Type of evidence and starting level**

<table>
<thead>
<tr>
<th>Evidence Type</th>
<th>Starting Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized trial</td>
<td>High</td>
</tr>
<tr>
<td>Observational study</td>
<td>Low</td>
</tr>
<tr>
<td>Any other evidence</td>
<td>Very low</td>
</tr>
</tbody>
</table>

**Criteria for increasing or decreasing level**

**Reductions**

- Study quality has serious (−1) or very serious (−2) problems
- Important inconsistency in evidence (−1)
- Directness is somewhat (−1) or seriously (−2) uncertain
- Sparse or imprecise data (−1)
- Reporting bias highly probable (−1)

**Increases**

- Evidence of association† strong (+1) or very strong (+2)
- Dose-response gradient evident (+1)
- All plausible confounders would reduce the effect (+1)

†Strong association defined as significant relative risk (factor of 2) based on consistent evidence from two or more studies with no plausible confounders. Very strong association defined as significant relative risk (factor of 5) based on direct evidence with no threats to validity.
Appendix B. Trustworthy Guideline rating scale

The University of Pennsylvania’s Center for Evidence-Based Practice Trustworthy Guideline rating scale is based on the Institute of Medicine’s “Standards for Developing Trustworthy Clinical Practice Guidelines” (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains.

The purpose of this scale is to focus on the weaknesses of a guideline that may reduce the trust a clinical user can have in the guideline, and distinguish weaknesses in documentation (e.g. guideline does not have a documented updating process) from weaknesses in the guidance itself (e.g. recommendations are outdated). Current quality scales like AGREE emphasize documentation. They are important checklists for developers of new guidelines, but are less useful for grading existing guidelines. These scales also are harder for clinicians and other persons who are not methodology experts to apply, and their length discourages their use outside formal technology assessment reports. This new scale is brief, balanced, and easy and consistent to apply.

We do not attempt to convert the results of this assessment into a numeric score. Instead we present a table listing the guidelines and how they are rated on each standard. This facilitates qualitative understanding by the reader, who can see for what areas the guideline base as a whole is weak or strong as well as which guidelines are weaker or stronger.

1. Transparency

| A | Guideline development methods are fully disclosed. |
| B | Guideline development methods are partially disclosed. |
| C | Guideline development methods are not disclosed. |

The grader must refer to any cited methods supplements or other supporting material when evaluating the guideline. Methods should include:
- Who wrote the initial draft
- How the committee voted on or otherwise approved recommendations
- Evidence review, external review and methods used for updating are not addressed in this standard.

2. Conflict of interest

| A | Funding of the guideline project is disclosed, disclosures are made for each individual panelist, and financial or other conflicts do not apply to key authors of the guideline or to more than 1 in 10 panel members. |
| B | Guideline states that there were no conflicts (or fewer than 1 in 10 panel members), but does not disclose funding source. |
| C | Lead author, senior author, or guideline panel members (at least 1 in 10) have conflict of interest, or guideline project was funded by industry sponsor with no assurance of independence. |
| NR | Guideline does not report on potential conflict of interests. |

March 2017
For purposes of this checklist, conflicts of interest include employment by, consulting for, or holding stock in companies doing business in fields affected by the guideline, as well as related financial conflicts. This definition should not be considered exclusive. As much as anything, this is a surrogate marker for thorough reporting, since it may be assumed that guideline projects are funded by the sponsoring organization and many authors think it unnecessary to report a non-conflict.

3. Guideline development group

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Guideline development group includes 1) methodological experts and clinicians and 2) representatives of multiple specialties.</td>
</tr>
<tr>
<td>B</td>
<td>Guideline development group includes one of the above, but not both.</td>
</tr>
<tr>
<td>C</td>
<td>Guideline developers all from one specialty or organization, and no methodologists.</td>
</tr>
<tr>
<td>NR</td>
<td>Affiliations of guideline developers not reported</td>
</tr>
</tbody>
</table>

The purpose of this standard is to ensure that supporters of competing procedures, or clinicians with no vested interest in utilization of one procedure or another, are involved in development of the guideline. Both AGREE II and IOM call for patient or public involvement: very few guideline panels have done so to date, so this is not necessary for guidelines to be rated A. Involvement of methodologists or HTA specialists in the systematic review is sufficient involvement in the guideline development group for our purposes. In the absence of any description of the guideline group, assume the named authors are the guideline group.

4. Systematic review

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Guideline includes a systematic review of the evidence or links to a current review.</td>
</tr>
<tr>
<td>B</td>
<td>Guideline is based on a review which may or may not meet systematic review criteria.</td>
</tr>
<tr>
<td>C</td>
<td>Guideline is not based on a review of the evidence.</td>
</tr>
</tbody>
</table>

In order to qualify as a systematic review, the review must do all of the following:
- Describe itself as systematic or report search strategies using multiple databases
- Define the scope of the review (including key questions and the applicable population)
- Either include quantitative or qualitative synthesis of the data or explain why it is not indicated

Note: this element does not address the quality of the systematic review: simply whether or not it exists. Concerns about quality or bias of the review will be discussed in text, where the analyst will explain whether the weaknesses of the review weaken the validity or reliability of the guideline.

Note: a guideline may be rated B on this domain even if the review on which it is based is not available to us. This potential weakness of the guideline should be discussed in text of the report.

5. Grading the supporting evidence

March 2017
Supplemental Feeding in Healthy, Term Neonates Evidence Summary

| A | Specific supporting evidence (or lack thereof) for each recommendation is cited and graded |
| B | Specific supporting evidence (or lack thereof) for each recommendation is cited but the recommendation is not graded |
| C | Recommendations are not supported by specific evidence. |

To score a B on this domain there should be specific citations to evidence tables or individual references for each relevant recommendation in the guideline, or an indication that no evidence was available. Any standardized grading system is acceptable for purposes of this rating. If a guideline reports that there is no evidence available despite a thorough literature search, it may be scored B on this domain, or even A if evidence for other recommendations is cited and graded.

6. Recommendations

| A | Considerations for each recommendation are documented (i.e. benefits and harms of a particular action, and/or strength of the evidence); and recommendations are presented in an actionable form. |
| B | Either one or the other of the above criteria is met. |
| C | Neither of the above criteria are met |

In order to be actionable, the guideline should specify the specific population to which the guideline applies, the specific intervention in question, and the circumstances under which it should be carried out (or not carried out). The language used in the recommendations should also be consistent with the strength of the recommendation (e.g. directive and active language like “should” or “should not” for strong recommendations, and passive language like “consider” for weak recommendations). A figure or algorithm is considered actionable as long as it is complete enough to incorporate all the applicable patients and interventions. Please see the forthcoming NICE manual (24) for a good discussion of actionability in guidelines.

7. External review

| A | Guideline was made available to external groups for review. |
| B | Guideline was reviewed by members of the sponsoring body only. |
| C | Guideline was not externally reviewed. |
| NR | No external review process is described. |

8. Updating and currency of guideline

| A | Guideline is current and an expiration date or update process is specified. |
| B | Guideline is current but no expiration date or update process is specified. |
| C | Guideline is outdated. |

March 2017
A guideline is considered current if it is within the developers’ stated validity period, or if no period or expiration data is stated, the guideline was published in the past three years (NOTE: the specific period may be changed at the analyst’s discretion, based on whether the technology is mature and whether there is a significant amount of recent evidence). A guideline must address new evidence when it is updated. A guideline which is simply re-endorsed by the panel without searching for new evidence must be considered outdated.