

Supplemental Information

METHODS

Supplemental Tables 4 through 7 were developed by conducting a systematic literature review over the past decade of exclusive breastfeeding and potential adverse outcomes related to failure of lactogenesis, weight loss, dehydration, hypoglycemia, and hyperbilirubinemia by using the following PubMed search terms: (((“Infant, Newborn”[Mesh] OR infant OR infants OR baby OR babies OR newborn OR newborns)) AND (“Breast Feeding/adverse effects”[Mesh] OR “Breast Feeding/epidemiology”[Mesh] OR “Breast Feeding/physiology”[Mesh] OR “breast feeding” OR “breastfeeding” OR “breast fed” OR “breastfed”))) AND (“Term Birth”[Mesh] OR “term birth”) and (“Infant, Newborn”[Mesh] AND (“Breast Feeding/adverse effects”[Mesh] OR “Breast Feeding/epidemiology”[Mesh] OR “Breast Feeding/physiology”[Mesh])) AND (“2009/02/13”[PDat]: “2019/02/10”[PDat] AND “humans”[MeSH Terms] AND English[lang]).

Primary evidence included clinical trials, observational studies, systematic reviews, and primary evidence identified by additional reviews. Studies older than 10 years were included if more recent studies were unavailable. All authors reviewed the literature for inclusion or exclusion.

SUPPLEMENTAL TABLE 4 Milk Production and Transfer

Reference, Location	N	Study Objective	Method	Main Findings
Becker et al, ²⁷ Italy (trials in 14 countries)	41 trials involving 2293 participants	To assess methods of milk expression regarding acceptability, effectiveness, safety, effect on milk composition, contamination, and cost	Cochrane systematic review of randomized and quasi-randomized trials to compare methods at any time after birth	Milk expression may depend on the time since birth, the purpose of expression, and the individual mother and infant. Mothers using pumps had varying degrees of nipple pain, whereas mothers using hand expression has little or no pain. Low-cost interventions, including early initiation when not feeding at the breast, relaxation techniques, massaging and warming of the breasts, hand expression, and lower-cost pumps, may be as effective as or more effective than large electric pumps for some outcomes.
de Jersey et al, ²¹ Australia	715	To determine the influence of maternal prepregnancy wt status on infant feeding intentions during pregnancy and to assess whether high intentions to exclusively breastfeed measured during pregnancy predicted feeding mode at discharge in women with healthy wt (BMI < 25) and overweight (BMI > 25)	Prospective longitudinal cohort study from prenatal period to 4 mo post partum	Women with overweight were less likely to be exclusively breastfeeding at hospital discharge (aOR [95% CI]: 0.57 [0.33 to 0.98]), independent of intent.
Dennis et al, ⁴⁰ Latvia, Iran, and Canada	656	To assess effects of interventions in the resolution of nipple pain and the impact on nipple trauma, nipple infections, breast mastitis, breastfeeding duration, breastfeeding exclusivity, and maternal satisfaction	Meta-analysis	Applying nothing or expressed breast milk may be equally or more beneficial in the short-term experience of nipple pain than the application of an ointment such as lanolin. Regardless of the treatment used, for most women, nipple pain reduced to mild levels ~7–10 d after giving birth.
Dewey et al, ²⁰ United States	328	To determine the incidence of and risk factors for SIBB, delayed onset of lactation, and excess neonatal wt loss in a population with high educational levels and motivation to breastfeed	Prospective cohort study using the Infant Breastfeeding Assessment Tool to measure SIBB	Delayed onset of lactation (>72 h) occurred in 22% of women and was associated with primiparity, cesarean delivery, stage II labor >1 h, maternal BMI > 27, flat or inverted nipples, and birth wt >3600 g (in primiparas). Excess wt loss occurred in 12% of infants and was associated with primiparity, long duration of labor, use of labor medications (in multiparas), and infant status at birth. The risk of excess infant wt loss was 7.1 times greater if the mother had delayed onset of lactation and 2.6 times greater if the infant had SIBB on the first day after birth.
Evans et al, ¹⁶ South Australia	185 (88 vaginal births, 97 cesarean deliveries)	To determine the effect of cesarean delivery on breast milk transfer by using pre-post	Prospective cohort	The volume of milk transferred to infants born by cesarean delivery was significantly less

SUPPLEMENTAL TABLE 4 Continued

Reference, Location	N	Study Objective	Method	Main Findings
		weighing of the term infant over the first week of life		than that transferred to infants born by normal vaginal delivery on d 2–5 ($P < .05$), but by d 6, there was no difference between the 2 groups ($P = .08$). Notably, volumes were small (rising gradually from 4–6 mL/kg per d on d 1 to 13–25 mL/kg per d on d 2 and from 44–66 mL/kg per d on d 3 to 129–138 mL/kg per d on d 6).
Flaherman et al, ²⁸ United States	68	To compare bilateral electric breast pumping with hand expression among mothers of healthy term infants feeding poorly at 12–36 h after birth	RCT	The median volume of expressed milk (range) was 0.5 (0–5) mL for hand-expressing mothers and 1 (0–40) mL for pumping mothers ($P = .07$). At 2 mo, mothers assigned to hand expression were more likely to be breastfeeding (96.1%) than mothers assigned to breast pumping (72.7%) ($P = .02$).
Haase et al, ¹² United States	24 pairs	To identify variables that impact test wt and to develop an accurate test-weighing technique for preterm and high-risk infants who are hospitalized	Cross sectional, repeated measures	Of the 24 pairs of wt obtained on 12 infants with leads (1 pair: either the 2 preweights or the 2 postweights), 20 pairs were identical, 3 pairs differed by 2 g, and 1 pair differed by 4 g. Test weighing was clinically accurate at ± 5 g.
Kent et al, ³⁷ Australia	1177	To determine the frequency of nipple pain as a reason for consultation, most common attributed etiologies, and the effectiveness of the advice and treatment given	Cross-sectional audit	Nipple pain was responsible for 36% of lactation consultations. The most common attributed cause of nipple pain was incorrect positioning and attachment, followed by tongue-tie, infection, palatal anomaly, flat or inverted nipples, mastitis, and vasospasm.
Lai et al, ¹⁸ Australia	65	To compare measurements of sodium and potassium in human milk by using inductively coupled plasma optical emission spectrometry with small portable ion-selective electrode probes for sodium and potassium	Cross sectional	The ion-selective electrode is accurate and able to detect changes in concentrations of sodium and potassium in human milk associated with secretory activation and inflammation in the mammary gland. Inflammatory states result in higher milk sodium levels.
Matias et al, ²² Peru	171	To determine the incidence and risk factors for early lactation problems (SIBB, delayed OL, and excessive neonatal wt loss) among mother-infant pairs in Lima, Peru	Prospective cohort study over first 3 d after birth	Delayed OL II incidence was 17% and was associated with an infant Apgar score < 8 . Excessive neonatal wt loss occurred in 10% of neonates and was associated with maternal overweight and cesarean delivery. Both OL II and excessive wt loss percentages are similar to those in the Dewey et al ²⁰ study in the United States. Early lactation problems

SUPPLEMENTAL TABLE 4 Continued

Reference, Location	N	Study Objective	Method	Main Findings
McClellan et al, ³⁶ Australia	50 dyads	To analyze the nipple shape and movement of the tongue of infants of mothers with and without nipple pain during the feed by using ultrasound	Case control	may be influenced by modifiable factors such as delivery mode and breastfeeding frequency. During nutritive sucking, tongue movements of infants of mothers with nipple pain resulted in a smaller intraoral space ($P = .040$) and restricted nipple expansion compared with controls ($P < .012$). Infants of mothers with nipple pain had stronger baseline and peak vacuums compared with controls ($P = .002$).
Munblit et al, ¹⁷ United Kingdom, Russia, and Italy	398	Relationships between levels of immune mediators in colostrum and mature milk and infant outcomes in the first year of life	Prospective cohort	IL-13 had protective effects for eczema, food allergy, and sensitization. Increased TGF- β 2 levels in HM were associated with a higher incidence of reported eczema. HGF revealed some protective effects on common cold incidence at 1 y of age.
Murase et al, ⁵⁰ United States	196	To determine if an elevated breast milk sodium/potassium ratio at d 7 is significantly more prevalent in mothers reporting a milk supply concern in the context of exclusive breastfeeding	Prospective cohort	An elevated d 7 milk sodium/potassium ratio occurred in 42% of mothers with a d 7 milk supply concern, compared with 21% of mothers without a d 7 milk supply concern (unadjusted relative risk, 2.0; $P = .008$), among mothers with a milk supply concern, with adjustment for maternal ethnicity (aOR of an elevated sodium/potassium ratio was 3.4 [95% CI 1.5 to 7.9]; $P = .003$).
Niazi et al ⁴¹	1801	To evaluate prevention and treatment of nipple fissures and pain	Systematic review	Menthol and a warm-water compress, as well as teaching the correct breastfeeding methods, are effective treatments to prevent and treat nipple pain and fissures. Applying herbal medicine may be beneficial as well.
Odom et al, ³⁵ United States	1177	To describe the prevalence and factors associated with not meeting desired breastfeeding duration	Prospective cohort	Approximately 60% of mothers who stopped breastfeeding did so earlier than desired. Early termination was positively associated with mothers' concerns regarding (1) difficulties with lactation, (2) infant nutrition and wt, (3) illness or the need to take medicine, and (4) the effort associated with pumping milk.
O'Shea et al, ³⁹ United Kingdom, United States, and Israel	302	To determine if frenotomy is safe and effective in improving the ability to feed orally among infants younger than 3 mo of age with tongue-tie (and problems feeding)	Meta-analysis	Frenotomy reduced breastfeeding mothers' nipple pain in the short-term. Because of a small number of trials, along with methodologic shortcomings, further RCTs of high

SUPPLEMENTAL TABLE 4 Continued

Reference, Location	N	Study Objective	Method	Main Findings
Puapornpong et al, ³⁸ Thailand	1649	To explore the incidence of nipple pain, associated predisposing factors, time for recovery after management, and the impact on exclusive breastfeeding rates	Prospective cohort study	methodologic quality are necessary to determine the effects of frenotomy. The incidence of nipple pain was 9.6% by d 7. A predisposing factor was primiparity. Reasons for nipple pain were inappropriate positioning and latching (72%), tongue-tie (23%), and oversupply (4%). The recovery period after care management was 1–2 wk. There was no significant difference of exclusive breastfeeding rates between the mothers who had early care management and the mothers without nipple pain.
Witt et al, ³⁵ United States	73	To explore if education delivered in the outpatient postpartum setting changed mothers' home management of engorgement and if they found these techniques helpful	Prospective descriptive cohort study	Among mothers with engorgement, 96% reported that the instruction on hand expression and massage was helpful to resolve symptoms. Significantly more mothers used massaging toward the axillae (25% vs 1%; $P \leq .001$), reverse pressure softening (18% vs 3%; $P = .001$), and feeding more frequently (32% vs 16%; $P = .04$). Sixty-one percent would not have used massage if they had not been educated.

HGF, human milk hepatocyte growth factor; HM, human milk; IL-13, interleukin 13; OL, onset of lactogenesis; SIBB, suboptimal infant breastfeeding behavior; TGF- β 2, transforming growth factor- β 2.

SUPPLEMENTAL TABLE 5 Neonatal Weight and Output Assessment

Reference, Location	N	Study Objective	Method	Main Findings
Azad et al, ⁴⁵ Canada	2553	To characterized the association of breastfeeding, infant wt gain, and body composition in the first year of life and assess the impact of feeding practices during the neonatal period	Prospective birth cohort design	Compared with exclusive direct breastfeeding at 3 mo, all other feeding styles were associated with higher BMI z scores. Brief formula supplementation in the hospital did not alter these associations as long as exclusive breastfeeding was established and sustained for at least 3 mo. Formula supplementation by 6 mo was associated with higher BMI z scores, whereas supplementation with solid foods was not.
Bekkali et al, ⁵⁷ Netherlands	198	To determine if preterm infants have prolonged passage of meconium compared with term infants	Prospective cohort	Passage of meconium was associated with being born prematurely but was not associated with feeding method (breastfeeding versus formula feeding), and 76% (35–36 wk) to 83% (≥ 37 wk) passed within 48 h.
Bilgin et al, ⁵⁴ Turkey	149	To determine factors related to admission for HD among those exclusively breastfeeding	Retrospective chart review cohort design	There was positive correlation between wt loss and the serum sodium level ($P = .0001$; $r = 0.636$).
Boer et al, ⁵⁶ Netherlands and Turkey	2630 (2359 healthy, 271 with HN)	To provide evidence-based support of daily weighing to prevent HN and identify the most crucial days of weighing	Case-control study	Weighing at birth and at d 2, 4, and 7, with a -2.5 -SDS cutoff, resulted in 97.3% sensitivity, 98.5% specificity, and a PPV of 4.43%. We added explanation to the low PPV given the low population incidence.
Chantry et al, ⁴² United States	448	To describe wt loss in a multiethnic population of first-born, predominantly breastfed term infants and to identify potentially modifiable risk factors for EWL	Prospective cohort	EWL was significantly related to maternal intrapartum fluid balance, independent of delayed lactogenesis; when positive maternal fluid balance exceeded 200 mL/h, compared with <100 mL/h, the adjusted RR for EWL more than tripled. Authors suggested that diuresis from overly hydrated mothers contributed to EWL.
Chen et al, ⁴⁹ Taiwan	313	To study the influence of breastfeeding on Taiwanese neonates regarding the frequency of jaundice, BWL, and elimination of both urine and stool	Retrospective cohort	Compared with the exclusively formula feeding group, in the exclusively breastfed neonates the average BWL at 2 and 3 d after birth ($P < .001$ and $P < .001$) and the rate of BWL $\geq 10\%$ ($P < .05$) were significantly higher; the average frequency of stool passage at 2 and 3 d after birth ($P < .001$ and $P < .001$) and urination at 1, 2, and 3 d after birth ($P < .001$, $P < .001$, and $P < .001$) was significantly less. Bilirubin levels were also significantly higher (relevant in the section on bilirubin).
Feldman-Winter et al, ⁴⁴ United States	306	To examine the association between wt gain during the first week and overweight at age 2 among infants with various feeding practices and the relationship between exclusive breastfeeding in early infancy and overweight	Prospective cohort	Children who gained >100 g during the first week were 2.3 times as likely after adjustment ($P = .02$) to have overweight at age 2 compared with infants who lost wt. Exclusively breastfed infants were least likely to gain ≥ 100 g.
Ferrández-González et al, ⁵² Spain	165	To determine a valid cut point for the percentage wt loss associated with the risk of hypernatremia, taking into account risk factors	Prospective cohort	ROCs of combined variables included the following: greater wt loss, (mean 8.6% among exclusively breastfed newborns), male sex, higher education level, multiparity, and cesarean delivery, equal to 0.84 (sensitivity = 77.6%; specificity = 73.2%) to predict HN.

SUPPLEMENTAL TABLE 5 Continued

Reference, Location	N	Study Objective	Method	Main Findings
Flaherman et al, ⁴⁶ United States	108 907	To develop an hour-by-hour newborn wt loss nomogram to assist in early identification of those on a trajectory for adverse outcomes	Retrospective cohort from CA	Almost 5% of vaginally delivered newborns and >10% of those delivered by cesarean delivery had lost $\geq 10\%$ of their birth wt 48 h after delivery. By 72 h, >25% of newborns delivered by cesarean delivery had lost $\geq 10\%$ of their birth wt. Data contributed to the development of NEWT curves, which were externally validated in a population in PA.
Grossman et al, ⁴⁵ United States	121	To investigate normal newborn wt loss among infants born in a US Baby-Friendly hospital by weighing infants daily for the first week of life	Prospective cohort	Mean wt loss was 4.9% (range = 0.0%–9.9%); 19.8% (24 of 121) of infants lost >7% of their birth wt; no infant lost >10%. The maximum percentage wt loss was significantly associated with feeding type: exclusively and mainly breastfed infants lost 5.5%, mainly formula-fed infants lost 2.7%, and exclusively formula-fed infants lost 1.2% ($P < .001$). More than one-third reached nadir after leaving the hospital.
Lavagno et al, ⁵⁵ Switzerland	115 articles; 1485 patients	To describe the clinical features of HN dehydration among breastfed newborns and to identify risk factors for it	Systematic review	Breastfeeding-associated neonatal hypernatremia was recognized in infants who were ≤ 21 d of age and had $\geq 10\%$ wt loss of birth wt. Cesarean delivery, primiparity, breast anomalies or breastfeeding problems, excessive prepregnancy maternal wt, delayed first breastfeeding, lack of previous breastfeeding experience, and low maternal education level were significantly ⁵⁵ associated with breastfeeding-associated hypernatremia. In addition to excessive wt loss ($\geq 10\%$), the following clinical findings were observed: poor feeding, poor hydration state, jaundice, excessive body temperature, irritability or lethargy, decreased urine output, and epileptic seizures.
Manganaro et al, ⁵¹ Italy	686	To determine the incidence of HN dehydration in term, exclusively breastfed infants and identify possible maternal and/or infant factors that interfere with successful breastfeeding	Prospective cohort	Fifty-three (7.7%) neonates had a wt loss $\geq 10\%$ of the birth wt, and 19 (2.8%) also had hypernatremia. These 53 neonates had a significantly higher incidence of cesarean delivery and lower maternal education than neonates with a wt loss <10%.
Nommsen-Rivers et al, ⁴⁸ United States	242	To determine the sensitivity and specificity at 72–96 h after birth of wet and soiled output, in addition to the timing of onset of lactation, in identifying cases of breastfeeding inadequacy (defined as neonatal wt loss $\geq 10\%$ of birth wt)	Prospective cohort	Wet diapers were not predictive. The most efficient d 4 predictor of breastfeeding inadequacy was soiled diaper output ≤ 3 (sensitivity = 0.75; specificity = 0.66). Sensitivity improved when used in parallel with delayed onset of lactation (≥ 72 h); sensitivity = 0.86 (95% CI 0.73 to 0.99) and specificity = 0.59 (0.55 to 0.63), but low specificity will result in many false-positives.

SUPPLEMENTAL TABLE 5 Continued

Reference, Location	<i>N</i>	Study Objective	Method	Main Findings
Oddie et al, ⁵⁵ United Kingdom	62	To describe incidence, presentation, treatment, and short-term outcomes of severe neonatal hypernatremia (sodium level \geq 160 mmol/L)	Prospective population-based study	Among the 62 patients, 12 had jaundice and 57 had wt loss as a presenting feature; 58 presented with wt loss \geq 15%; 25 infants had not stoolled in the 24 h before admission. Authors stressed the importance of monitoring for wt loss.
van Dommelen et al, ⁴⁷ Netherlands	2359	To construct charts for wt loss among exclusively breastfed newborns	Case-control study	Patients with (or who will develop) HD (84%; +1 SDS line) fell below the -1-SDS line at d 3, the -2-SDS line at d 4, and the -2.5-SDS line at d 5 in the chart of the healthy breastfed newborns. Such charts are helpful in identifying newborns at risk for HN dehydration.

BWL, body weight loss; CA, California; EWL, excess weight loss; HN, hypernatremic; PA, Pennsylvania; ROC, receiver operating characteristic; RR, relative risk; SDS, standard deviation score.

SUPPLEMENTAL TABLE 6 Glucose Stabilization During Exclusive Breastfeeding

Reference, Location	N	Study Objective	Method	Main Findings
Forster et al, ⁷⁴ Australia	635	To determine the safety and efficacy of antenatal hand expression for women with diabetes in pregnancy	Unblinded RCT	There was no difference in NICU admission between the 2 groups. Infants in the antenatal hand expression group were more likely to be exclusively breastfed in the first 24 h of life (69% vs 60%; RR 1.15 [95% CI 1.02 to 1.28]).
Harding et al, ⁷⁰ New Zealand	2129	Study protocol for RCT to test the efficacy of dextrose gel versus a placebo for at-risk infants to prevent hypoglycemia	Multicenter, randomized, double-blinded, placebo-controlled trial	Infants at risk for hypoglycemia (preterm infants, infants of mothers with diabetes, infants who were SGA or LGA) received a 0.5-mL/kg dextrose gel or placebo. The primary outcome was admission to neonatal intensive care.
Harris et al, ⁷² New Zealand	237	To test the efficacy of dextrose gel versus a placebo in addition to feeding to treat neonatal hypoglycemia	Randomized, double-blinded, placebo-controlled trial	Among infants who received dextrose gel, 86% achieved target glucose levels, compared with 76% of infants who received a placebo ($P = .04$), and 14% were admitted to the NICU for hypoglycemia, compared with 25% of infants who received a placebo ($P = .03$).
Hay et al, ⁶¹ United States	NA	To identify major gaps in knowledge related to neonatal hypoglycemia and propose a research agenda	NICHD workshop	The workshop identified gaps in knowledge and proposed a research agenda for glucose metabolism and the brain, clinical management, and laboratory tests and glucose monitoring.
Hegarty et al, ⁷¹ New Zealand	416	To compare the efficacy of different doses and schedules of buccal dextrose gel to prevent hypoglycemia in at-risk infants	Randomized, double-blinded, placebo-controlled trial	Compared with a placebo, the authors found the lowest risk of hypoglycemia among infants randomly assigned to a single dose of 200 mg/kg of dextrose gel (RR 0.68 [95% CI 0.47 to 0.99]; $P = .04$).
LeBlanc et al, ⁶⁴ United States	478	To evaluate the impact of a QI intervention to reduce NICU admissions for infants at risk for hypoglycemia	Pre-post intervention evaluation	The intervention included SSC, including in the operating room for cesarean deliveries, and treatment of hypoglycemia with measurable amounts of maternal milk, donor milk, or formula before transfer to the NICU. NICU admission rates declined from 17% to 3% during the study period.
McKinlay et al, ⁶² New Zealand	404	To determine neurodevelopmental outcomes at 2 y of age among infants at risk for hypoglycemia who were treated to maintain glucose levels ≥ 47 mg/dL	Prospective cohort study	Neonatal hypoglycemia was not associated with any difference in neurosensory impairment or processing difficulty.
McKinlay et al, ⁶³ New Zealand	477	To determine neurodevelopmental outcomes at 4.5 y of age among infants at risk for hypoglycemia who were treated to maintain glucose levels ≥ 47 mg/dL	Prospective cohort study	Neonatal hypoglycemia was not associated with neurosensory impairment; however, it was associated with increased risk of low executive function and visual motor function. Risk was highest in infants with severe, recurrent, or clinically undetected hypoglycemia.
Moore et al ⁶⁵	144 infants, 3 studies	To quantify the effect of SSC on maternal and infant outcomes	Meta-analysis	Infants receiving SSC had higher BGLs, (MD 10.49; 95% CI 8.39 to 12.59).
Newnam and Bunch, ⁷³		To review current evidence regarding dextrose gel to treat TANH	Systematic review	Clinical protocols can be revised to include the use of buccal dextrose gel.

SUPPLEMENTAL TABLE 6 Continued

Reference, Location	N	Study Objective	Method	Main Findings
	5 articles (1 systematic review and 4 abstracts)			There is a need for rigorous long-term studies to compare treatment thresholds and neurodevelopmental outcomes among various treatment strategies for TANH.
Singh et al, ⁷⁶ India	407	To quantify incidence of hypoglycemia among high-risk infants (low birth wt, late preterm, SGA, LGA, or infants of mothers with diabetes)	Prospective cohort study	Among 407 exclusively breastfed high-risk newborns, 27% had ≥ 1 episode of hypoglycemia, defined as a BGL ≤ 46 mg/dL.
Stewart et al, ⁶⁸ United Kingdom	52	To evaluate the impact of a QI initiative for management of hypoglycemia	Pre-post intervention evaluation	After the implementation of a stakeholder-developed protocol, the No. heel sticks and the duration of glucose monitoring decreased, and rates of exclusive in-hospital breastfeeding and continued breastfeeding at 3 mo increased.
Ter et al, ⁶⁷ Australia	200	To evaluate the impact of a dextrose gel protocol for hypoglycemia	Pre-post intervention evaluation	After implementation, NICU admission rates for hypoglycemia decreased from 29% to 14% ($P = .01$), although recurrent hypoglycemia increased (31% vs 49%; $P = .02$).

BGL, blood glucose level; LGA, large for gestational age; MD, mean difference; NA, not applicable; NICHD, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development; RR, relative risk; SGA, small for gestational age; SSC, skin-to-skin care; TANH, transient asymptomatic neonatal hypoglycemia.

SUPPLEMENTAL TABLE 7 Hyperbilirubinemia

Reference, Location	N	Study Objective	Method	Main Findings
Bhutani et al, ⁸²	NA	AAP COFN review of phototherapy	Systematic review	Reviews performance characteristics of phototherapy devices and guidelines for clinical use
Chang et al, ⁸⁶ Taiwan	874	To determine the predictive value of infant wt loss for hyperbilirubinemia among exclusively breastfed infants	Retrospective cohort study	Of infants, 25.1% developed significant hyperbilirubinemia. Gestational age at birth and maximum wt loss were both associated with hyperbilirubinemia. Wt loss of <8% at 48 h had a negative predictive value of 77.7%, and wt loss of <11% at 72 h had a negative predictive value of 76.8%.
Chen et al, ⁸⁷ Taiwan	323	To determine incidence and risk factors for TcB levels ≥ 15 mg/dL at outpatient follow-up among exclusively breastfed infants	Retrospective cohort study	Of exclusively breastfed infants in this cohort, 35.3% had bilirubin levels ≥ 15.0 mg/dL. Risk factors included higher bilirubin levels at nursery discharge, greater wt loss from birth to the outpatient evaluation, and less wt gain from nursery discharge to the outpatient evaluation.
Chen et al, ⁸⁸ Taiwan	98	To determine if frequency of breastfeeding, as recorded by parents after hospital discharge, was associated with TcB levels >15 mg/dL at outpatient follow-up	Prospective cohort study, pre-post intervention evaluation	Among infants fed ≥ 8 times per d, 5.7% had hyperbilirubinemia, compared with 25.4% of those fed <8 times per d ($P < .05$). Implementation of written discharge instructions was associated with a decrease in hospitalization of breastfed infants for hyperbilirubinemia (93 of 574 [16.2%] to 57 of 703 [8.1%]; $P < .01$).
Chu et al, ⁸⁴ Taiwan	9 mothers	To explore breastfeeding experiences of mothers of infants with breastfeeding or breast milk jaundice	Qualitative descriptive design	Mothers were unaware of neonatal jaundice until medical attention was required. They experienced physical and mental distress and gradually learned to manage jaundice while breastfeeding.
Hansen et al ⁸⁰	NA	To test whether bilirubin inhibits growth of GBS bacteria	In vitro study	Increasing levels of bilirubin reduced growth of GBS isolates, suggesting that physiologic hyperbilirubinemia may confer protection against early-onset sepsis.
Hassan and Zakerihamidi, ⁸⁹ Iran	634	To measure the association between breastfeeding frequency and bilirubin levels	Case series	Among infants referred for idiopathic hyperbilirubinemia, more frequent breastfeeding was associated with lower levels of bilirubin.
Huang et al, ⁷⁸ Singapore	1034	To test the extent to which jaundice risk varies by Asian ethnicity	Retrospective cohort study	Compared with non-Chinese infants, Chinese infants had a higher risk of jaundice (32% vs 21%). Exclusive breastfeeding was associated with an increased risk among Chinese infants but not among non-Chinese infants.
Huang et al, ⁹⁰ Taiwan	771 (development), 760 (validation)		Retrospective cohort study	Gestational age at delivery, maximum wt loss, and peak

SUPPLEMENTAL TABLE 7 Continued

Reference, Location	N	Study Objective	Method	Main Findings
		To develop and validate a prediction model for jaundice among infants		bilirubin levels before 72 h were independent predictors of serum bilirubin levels ≥ 15 mg/dL during d 4–10 of life. In the validation model, the area under the ROC curve was 0.83.
Mah et al, ⁸³ United States	1 028 817 infants	To demonstrate efficacy of universal predischarge neonatal bilirubin screening in reducing potentially dangerous hyperbilirubinemia in a large diverse national population	Prospective study	With a program of universal screening, the incidence of infants with total bilirubin levels of 25.0–29.9 mg/dL declined significantly from 43 per 100 000 to 27 per 100 000, and the incidence of infants with total bilirubin levels ≥ 30.0 mg/dL dropped significantly from 9 per 100 000 to 3 per 100 000. This change was associated with a small statistically significant increase in phototherapy use.
Newman et al, ⁸⁴ United States	496 632 infants	To study the association between the risk of childhood epilepsy and phototherapy after birth	Retrospective cohort study	The adjusted 10-y excess risks per 1000 were 2.4 (95% CI 0.6 to 4.1) overall, 3.7 (95% CI 1.2 to 6.1) in boys, and 0.8 (95% CI –1.7 to 3.2) in girls.
Salas et al, ⁹¹ Bolivia	2140 live births, 137 admissions for hyperbilirubinemia, 79 otherwise healthy breastfed infants with adequate medical records	To quantify correlates of bilirubin levels ≥ 20 mg/dL among otherwise healthy breastfed infants admitted for hyperbilirubinemia	Retrospective cohort study	The population readmission rate for hyperbilirubinemia was 6.4%. Otherwise healthy, exclusively breastfed infants admitted with bilirubin levels ≥ 20 mg/dL were older (6.3 vs 4.0 d) and were more likely to have lost >7% of their birth wt (61% vs 29%; $P < .05$) than those with bilirubin levels <20 mg/dL.
Sato et al, ⁷⁹ Japan	401	To determine the extent to which fetal genotype modifies the effect of wt loss on hyperbilirubinemia	Cohort study	<i>UGT1A1</i> , <i>SLCO1B1</i> , and <i>SLCO1B3</i> polymorphisms are risk factors for hyperbilirubinemia in exclusively breastfed infants with >10% wt loss.
Sen et al, ⁹³ Massachusetts	363	To quantify use of banked donor milk in a tertiary care center over time (2013–2016)	Retrospective cohort study	Increased use of banked donor milk for healthy newborns and term newborns with hyperbilirubinemia and other indications
Szucs and Rosenman, ⁹⁵ Indiana	1	To describe family-centered phototherapy	Case report	The authors describe an institutional policy for in-room phototherapy for hyperbilirubinemia.
Wickremasinghe et al, ⁸⁵ United States	25 895 newborns	To estimate the efficacy of subthreshold phototherapy during the birth hospitalization in preventing readmissions for phototherapy and to identify predictors of readmission for phototherapy	Retrospective cohort	Among newborns with qualifying total serum bilirubin levels from 0.1 to 3.0 mg/dL below the appropriate AAP phototherapy threshold, 19.1% received subthreshold phototherapy, and 4.9% of these were readmitted for phototherapy, compared with 80.9% newborns who were untreated, of whom 12.8% got readmitted. Newborns who received formula feedings had lower adjusted odds (0.58) of

SUPPLEMENTAL TABLE 7 Continued

Reference, Location	<i>N</i>	Study Objective	Method	Main Findings
				readmission for phototherapy compared with exclusively breastfed newborns (0.24). Subthreshold phototherapy was associated with a 22-h longer length of stay (95% CI 16 to 28 h).

COFN, Committee on Fetus and Newborn; GBS, group B *Streptococcus*; NA, not applicable; ROC, receiver operating characteristic; TcB, transcutaneous bilirubin.