BREASTFEEDING MEDICINE
Volume 12, Number 5, 2017

DOI: 10.1089/bfm.2017.29042.vjf

ABM Clinical Protocol #22: Guidelines for Management of Jaundice in the Breastfeeding Infant 35 Weeks or More of Gestation—Revised 2017

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A central goal of The Academy of Breastfeeding Medicine is the development of clinical protocols free from commercial interest or influence for managing common medical problems that may impact breastfeeding success. These protocols serve only as guidelines for the care of breastfeeding mothers and infants and do not delineate an exclusive course of treatment or serve as standards of medical care. Variations in treatment may be appropriate according to the needs of an individual patient.

Purpose

1. To provide guidance in determining whether and how breastfeeding may or may not be contributing to infant jaundice.
2. To review evidence-based strategies for ameliorating jaundice in the breastfeeding infant.
3. To provide protocols for supporting breastfeeding while infants are being evaluated and/or treated for jaundice.

Biologic Basis for Jaundice in the Newborn and Its Relationship to Breastfeeding

Some comprehensive reviews of bilirubin metabolism and jaundice in the newborn are listed in the references for a more complete discussion of the biology and pathobiology of jaundice in the newborn and its relationship to breastfeeding.[1–3] Although the management of breastfeeding and jaundice varies in different countries,[4] the following principles and recommendations should apply universally.

Hyperbilirubinemia of the newborn

Virtually all newborns have some elevation of their total serum bilirubin (TSB) (>90% of which is unconjugated or indirect reacting) relative to normal adult values, which are ≤17 μmol/L (≤1.0 mg/dL).[5] The catabolism of heme by heme oxygenase (HO) produces biliverdin. Biliverdin is reduced by biliverdin reductase to unconjugated bilirubin, which is conjugated in the liver and excreted through the gut. Newborns have higher TSB levels because of a combination of three factors: increased production of bilirubin due to postnatal heme degradation; decreased uptake and conjugation of bilirubin due to developmental hepatic immaturity; and increased intestinal reabsorption of bilirubin. In the first week of life, more than 80% of newborns appear jaundiced[6,7] and, depending on the racial and sociocultural population mix, about 75% have a transcutaneous bilirubin (TcB) of >100–150 μmol/L (>6–9 mg/dL) by 96 hours.[8–10] Bilirubin is antioxidant and may protect infants from the relatively hyperoxygenic environment after birth. The term physiologic jaundice is often used to describe newborns with a TSB well above normal adult levels, but not attributable to a specific cause such as hemolytic disease; however, such terminology may be inappropriate because having an unknown etiology does not necessarily mean that a condition is physiologic.[11]

Breastfeeding and jaundice

Although some early studies[12,13] reported no differences in TSB concentrations between breastfed and formula-fed infants, subsequent studies using larger sample sizes and more robust research design demonstrated a strong association between hyperbilirubinemia and breastfeeding compared with formula feeding, especially when breastfeeding was exclusive.[14–22] Nonetheless, in comparison with previous data,[23] Buiter et al.'s[24] study of the relationship between stool production and jaundice in healthy breastfed or formula-fed newborns found significantly less stool production in formula-fed infants and no difference in stool production or TcB concentrations in the first 4 days between breastfed and formula-fed infants. Based on this body of evidence, two broad categories of the association between breastfeeding and jaundice have been described. Jaundice, which occurs in the first week in association with ongoing weight loss, has been termed breastfeeding jaundice, breastfeeding-associated jaundice, breast-nonfeeding jaundice, or starvation jaundice.[25] However, as this jaundice is almost always associated with low enteral intake rather than breastfeeding per se, in this protocol, it will be called suboptimal intake jaundice. Jaundice that persists past the onset of robust weight gain is known as breast

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milk jaundice or the breast milk jaundice syndrome. Although this protocol focuses on breastfeeding and jaundice, it is important to note that early onset jaundice occurring within 24–48 hours of birth is unlikely to be related to breastfeeding and should be assessed and treated promptly without interruption of breastfeeding.

Suboptimal intake jaundice of the newborn

During the first days after birth, it is normal for colostrum volumes to be small; appropriate for the infant's stomach size and physiologic need. In the first 24 hours of life, exclusively breastfed infants may receive no more than 1–5 mL of milk per feeding[26–29] or 5–37 mL in total.[30,31] Encouraging breastfeeding within the first hour of birth and frequently thereafter maximizes caloric and fluid intake and stimulates breast milk production.

In normal adults, the absence of caloric intake, even for as brief a period as 24 hours and with good hydration, results in a small increase in unconjugated hyperbilirubinemia of about 17–34 μmol/L (1–2 mg/dL),[32–34] an effect due to an increase in the enterohepatic circulation of bilirubin.[35] Similarly, in newborns, breastfeeding difficulties or a delay in the onset of secretory activation (lactogenesis ll)[36] may result in lower caloric intake, which may lead to an increase in enterohepatic circulation[35] and the development of hyperbilirubinemia. In addition, the mechanism for an increase in TSB is likely to include other developmental limitations in bilirubin metabolism and transport in the newborn.[37–39] Because formula-fed infants are typically given volumes of milk much greater than physiologically normal (27 mL formula per feeding or about 150 mL/day), during that same period,[40] it is uncommon for them to become jaundiced. Oral intake equalizes for the groups once maternal secretory activation occurs around 2–5 days of age, and copious milk production begins.

The interaction between low enteral intake and other factors related to neonatal hyperbilirubinemia is the subject of recent investigation.[18,24,41,42] Sato et al. found that the hyperbilirubinemia associated with the G71R mutation of UDP glucuronosyltransferase family 1 member A1 (*UGT1A1*) gene could be prevented by adequate enteral intake.[41,42] People with Gilbert's syndrome have lower activity of UDP-glucuronosyltransferase and develop significantly higher TSB with fasting than the normal population.

Breast milk jaundice (prolonged jaundice associated with breast milk feeding)

Many breastfed infants have unconjugated hyperbilirubinemia that extends into the second and third week, but can continue for as long as 2–3 months.[43,44] At 28 days, 21% of predominantly breastfed infants were still visibly jaundiced and 34% had a TcB ≥85 μmol/L (≥5 mg/dL).[43] Prolonged jaundice beyond the second to third week in healthy breastfeeding newborns has been called breast milk jaundice to distinguish it from suboptimal intake jaundice, which should resolve by 1–2 weeks.[45]

The precise mechanism of breast milk jaundice remains unknown despite much investigation. Multiple factors appear to contribute to whether bilirubin is eliminated together with fecal fat[46] or reabsorbed into the blood stream (the enterohepatic circulation). The development of breast milk jaundice has been attributed to numerous processes involved in bilirubin excretion, including enhanced intestinal reabsorption of unconjugated bilirubin[43]; increased concentrations of cytokines (including IL-1, IL-10, and TNF-) in human milk[47]; low total antioxidant capacity in human milk[48]; variations in the HO-1 gene promoter[49]; variations in the UGT1A1 gene[18,41,42,50,51]; lower serum and milk levels of epidermal growth factor[52]; higher serum alpha-fetoprotein levels[53]; higher cholesterol levels[54]; and lower abundance of *Bifidobacterium adolescentis*, *Bifidobacterium longum* and *Bifidobacterium bifidum*[55] in human milk and stool. The relative contribution of each of these factors, their potential interaction, and their precise mechanism of action remain unknown. Over time, the jaundice and elevated TSB decline at varying rates to normal adult values even while breastfeeding continues. Features that may distinguish suboptimal intake jaundice from breast milk jaundice are summarized in Table 1.

Whenever jaundice in a breastfed newborn is prolonged beyond the third week, it is important to rule out cholestasis by measuring the direct or conjugated bilirubin level and to evaluate for other causes of prolonged indirect hyperbilirubinemia such as congenital hypothyroidism. For indirect hyperbilirubinemia that extends beyond 2 months, conditions such as ongoing undiagnosed hemolysis, Gilbert's syndrome, or the very rare Crigler–Najjar syndrome (with an incidence of 1 per million births) should be considered.[56]

Interaction of suboptimal intake jaundice and breast milk jaundice

Strong evidence suggests that increased serum bilirubin in the first few days is highly correlated with suboptimal enteral intake; serum bilirubin concentrations are highly associated with greater weight loss in breastfed infants.[41,42,57–62] Ineffective suckling with inadequate caloric intake during the first days of life increases TSB levels because of relative starvation.[32,35,37,38]

Table 1. Characteristics Distinguishing Suboptimal Intake Jaundice from Breast Milk Jaundice

	Typical time frame	*Weight*	*Stool output*	*Urine output*	*Clinical findings*
Suboptimal intake jaundice	Onset 2–5 days of age and usually resolved by 2 weeks	Ongoing weight loss	<5/day with color black, brown, or green	<5/day with uric acid crystals (brick color)	Commonly <38 weeks and rarely ≥40 weeks gestation. May be fussy and difficult to settle between feedings or sleepy and difficult to wake for feeding
Breast milk jaundice	Onset 2–5 days and may last up to 3 months	Gaining ≥30 g/day[107]	≥8/day with yellow color	≥8/day with yellow or clear color	Waking to feed 8–12×/day

If jaundice continues beyond the second and third weeks, despite adequate milk intake and weight gain, it is likely that one or more of the factors listed above are contributing to the hyperbilirubinemia. Early optimizing of breastfeeding and consideration of additional enteral intake when there is clinical or laboratory evidence that breastfeeding is compromised might mitigate the development of subsequent hyperbilirubinemia. Options for additional enteral intake are discussed below.

Kernicterus and bilirubin encephalopathy

The most recent studies in high-resource countries suggest that in the absence of significant comorbidities such as sepsis or Rh hemolytic disease, kernicterus or chronic bilirubin encephalopathy occurs in about 1 in 200,000 live births and only when TSB levels exceeded 600 μmol/L (35 mg/dL).[63–65] In lower resource countries, bilirubin encephalopathy and comorbidities are much more common so that kernicterus can and does occur more frequently and at lower bilirubin levels.[66] Even in high-resource countries, extreme hyperbilirubinemia in apparently healthy breastfeeding infants can cause kernicterus.[67,68] In the U.S. Kernicterus Registry, a database of 125 cases of kernicterus in infants discharged as healthy newborns, 98% of these infants were fully or partially breastfed, highlighting the importance of appropriate breastfeeding support and follow-up from the prenatal period through to the early postpartum months. Whether hyperbilirubinemia, in the absence of the classic symptoms of bilirubin toxicity, produces subtle neurologic deficits is a controversial topic beyond the scope of this protocol. Recent studies suggest, however, if severe hyperbilirubinemia does cause subtle neurologic deficits, it is a rare occurrence.[63–65]

Evidence-Based Strategies for Preventing or Ameliorating Jaundice in the Breastfeeding Infant

Management of jaundice once treatment thresholds for TSB are reached is discussed in the next section. The following measures are recommended to maintain TSB levels below those proposed for treatment while supporting the successful establishment of breastfeeding:

1. Initiate early breastfeeding.
   a. Initiate breastfeeding as early as possible, preferably in the first hour after birth[69–72] (I) (quality of evidence [levels of evidence IA, IB, IIA, IIB, III, and IV] is based on levels of evidence used for the National Guidelines Clearing House[73] and is noted in parentheses) even for infants delivered by cesarean section. In the vast majority of births, breastfeeding should be initiated in the first hour.
2. Encourage frequent exclusive breastfeeding.
   a. Frequent breastfeeding (8–12 times or more in 24 hours) is crucial both to increase infant enteral intake and to maximize breast emptying, which is essential for the establishment of milk supply. Feeding anything before the onset of breastfeeding delays the establishment of good breastfeeding practices and may hinder milk production, increasing the risk of reduced enteral intake and exaggerated hyperbilirubinemia. There is a positive association between the number of breastfeeds a day and lower TSB.[74] (III) It is unnecessary to give glucose water to test the infant's ability to swallow or avoid aspiration.
   b. Hand expression or pumping of colostrum or breast milk can provide extra milk to support intake in some infants at risk for suboptimal intake jaundice and exaggerated hyperbilirubinemia and assist in establishing a good milk supply. Although pumping is commonly used, it is noteworthy that hand expression may be better tolerated by mothers in the immediate postpartum period. Randomized trials have shown that the initiation of pumping may reduce milk transfer and eventual breastfeeding duration for some populations of infants.[26,27] (IB)
3. Optimize early breastfeeding management.
   a. Ensure comfortable positioning (that avoids nipple compression or rubbing), effective latch, and adequate milk transfer (swallowing) from the outset by having a healthcare provider trained in breastfeeding management (e.g., nurse, lactation consultant, midwife, or physician) and evaluate position and latch, providing recommendations as necessary.
   b. Support skin-to-skin contact for all mothers and infants (in a safe manner when the mother is awake and alert), but particularly for those breastfeeding, starting immediately after birth and throughout the postpartum period as it helps with milk supply and makes mother's milk easily available to the infant in the first days and weeks of life.[72] (I)
4. Provide education on early feeding cues.
   a. Teach the mother to respond to the earliest cues of infant hunger, such as moving about or restlessness, lip smacking, hand movements toward the mouth, and vocalizing. Most newborns need to be fed every 2 ½ to 3 hours. Infants should be put to the breast before the onset of crying as crying is a late sign of hunger and often results in a poor start to the breastfeeding episode. Attention should also be paid to infants who are sleepy or do not show signs of hunger.
5. Identify mothers and infants at risk for hyperbilirubinemia.
   a. Some maternal factors (e.g., diabetes, Rh sensitization, and past family history of jaundiced infants) increase the risk of hyperbilirubinemia in the newborn. Primiparous mothers are at risk for delayed secretory activation as are those who give birth through cesarean section or have a maternal body–mass index over 27 kg/m^2. Infants of these mothers are therefore at risk for suboptimal intake.[75] (III)
   b. With the exception of infants with pathologic conditions such as Rh or ABO hemolytic disease and glucose-6-phosphate dehydrogenase (G6PD) deficiency, the single most important clinical risk factor for hyperbilirubinemia in newborns is decreasing gestational age. For each week of gestation below 40 weeks, the odds of developing a TSB ≥428 μmol/L (25 mg/dL) increase by a factor of 1.7 (95% CI 1.4–2.5).[19] Management of 34–37-week late preterm and early term infants who are not breastfeeding well can be found in the relevant ABM Clinical Protocol.[76] (IV)
   c. Significant bruising or cephalohematoma can increase the risk of hyperbilirubinemia due to the

increased breakdown of heme. East Asian newborns also have a higher risk of jaundice, perhaps related to their ethnic or genetic background.[59] (III)

d. The above factors can be additive with suboptimal intake jaundice and/or breast milk jaundice and produce even higher bilirubin levels than would otherwise be seen. When risk factors are identified, it is prudent to seek assistance with breastfeeding in the early hours after birth to ensure optimal breastfeeding management. Mothers may benefit from early instruction about milk expression by hand or pump to protect the milk supply.

6. Do not supplement infants with anything other than mother's own expressed milk in the absence of a specific clinical indication. Indications for supplementation are discussed briefly below. Full details on indications for supplementation, choice of supplement, and methods of supplementation are available in ABM Clinical Protocol #3: Supplementary Feedings in the Healthy Term Breastfed Neonate, Revised 2017.[77] (IV)
7. While management of newborns varies from country to country, most infants discharged before 72 hours of age should be seen by a healthcare provider within 2 days of discharge from birth hospitalization. This is especially important for exclusively breastfed infants. Close follow-up of the breastfeeding newborn both facilitates prevention of excess weight loss that may contribute to hyperbilirubinemia[17,20,57–60] (III) and ensures that elevated bilirubin concentrations are promptly treated.[21] (IV) Individual clinical judgment regarding follow-up can be used, such as in the case of an experienced multiparous mother who has breastfed previous infants and is going home with an infant who has no hyperbilirubinemia risk factors.[21] Protocols for monitoring bilirubin vary from country to country and within countries. While the U.K. guidelines do not recommend measuring bilirubin levels at follow-up unless the infant is visibly jaundiced, frequent monitoring using a TcB meter is recommended by the Japanese Society for Neonatal Health and Development.

Management of Breastfeeding in the Newborn with Jaundice

Consensus-based guidelines for the management of hyperbilirubinemia, including monitoring procedures, recommended treatment, and thresholds for treatment, have been developed in the United States, Canada, Norway, the United Kingdom, and some 14 other countries.[1,21,78,79] (IV) For monitoring, guidelines from the United States,[21] Canada,[80] and several other countries recommend a measurement of the TSB or TcB in every infant before discharge from the birth hospitalization, although this is not specifically recommended in the U.K. guidelines. Universal TcB measurement is also standard practice in Japan. Combining the TcB measurement with the infant's gestational age and plotting on an appropriate graph provide a prediction of the risk of hyperbilirubinemia that is as accurate as the combination of all other nonpathologic risk factors. When TSB levels rise above the thresholds stated in guidelines, despite adequate lactation support, phototherapy is recommended as the most effective treatment. Other therapeutic options, which may be used either alone or in combination with phototherapy, depending on clinical circumstance, include (1) temporary additional feedings with expressed breast milk; (2) temporary supplementation with donor human milk if available; (3) temporary supplementation with infant formula; or (4) very rarely, temporary interruption of breastfeeding and replacement feeding with infant formula. These options are described in more detail below.

When discussing any treatment options with parents, healthcare providers should emphasize that all treatments are compatible with continuation of breastfeeding. Because parents may associate breastfeeding with the development of jaundice requiring special treatment or hospitalization, they may be reluctant to continue breastfeeding, particularly if infant formula supplementation or interrupting breastfeeding is suggested as treatment. Healthcare providers should offer special assistance to these mothers to ensure that they understand the importance of continuing to breastfeed and know how to maintain their milk supply if temporary interruption is necessary. Special care should be taken to address and discuss any guilt parents have about their feeding decisions, both because such guilt can be counterproductive to continued breastfeeding[81–84] (III) and because many factors contribute to jaundice and the relative contribution of each factor is often unknown.[85–88] (III, IV)

Treatment options

1. Phototherapy. Phototherapy is the most frequently used treatment option when TSB concentrations exceed treatment thresholds, especially when levels are rising rapidly. Phototherapy can be used while continuing full breastfeeding or it can be combined with supplementation of expressed breast milk or infant formula if maternal supply is insufficient. Only in extenuating circumstances is temporary interruption of breastfeeding with replacement feeding necessary.[1,21,89] (IV) Phototherapy can be done in the hospital or at home. Home phototherapy is acceptable for low-risk infants provided TSB levels are monitored.[90] (IV) In the hospital, it is best done in the mother's room or a hospital room where the mother can also reside to minimize mother–infant separation and so that breastfeeding can be continued. Interruption of phototherapy for durations of up to 30 minutes or longer to permit breastfeeding without eye patches does not alter the effectiveness of the treatment.[91–93] (III, IB) Although phototherapy increases insensible water loss to some degree, infants under phototherapy do not routinely require extra oral or intravenous fluids.[90] (IV) However, if newborns receiving phototherapy are too sleepy to breastfeed vigorously, or if breastfeeding appears ineffective, mothers should express milk to feed by syringe, bottle, or gavage until newborns are vigorous enough to transfer milk effectively. The routine provision of intravenous fluids is discouraged because they may inhibit thirst and diminish oral intake. However, they may be indicated in cases of infant dehydration, hypernatremia, or inability to ingest adequate milk.
2. In settings where phototherapy is not readily available, results in significant mother–infant separation, or has other potential negative consequences, physicians may consider recommending supplementary feedings at

levels of bilirubin approaching those recommended for initiating phototherapy. Such decisions should be individualized with the goal of keeping mother and infant together as well as preserving and optimizing breastfeeding while effectively preventing or treating the hyperbilirubinemia.

a. First and best supplement is expressed own mother's milk. It can be hand expressed into a small cup or spoon and directly fed to the infant with help from staff who are knowledgeable in this technique. In this way, breastfeeding is best supported.
b. If own mother's milk is not available, supplementing with donor human milk will increase enteral intake. Breastfeeding infants supplemented only with donor milk meet the World Health Organization definition of exclusive breastfeeding. The specific effect of donor milk supplementation on bilirubin levels has not been studied.
c. It may be necessary to supplement with infant formula if neither own mothers' milk nor donor human milk is available. The impact of introducing formula to an exclusively breastfed infant must be considered. The effect of supplementation with donor human milk versus infant formula is not well studied.
d. Supplementation with water or glucose water is contraindicated because it does not reduce serum bilirubin,[94,95] (IIA, III) interferes with breastfeeding, and might cause hyponatremia.
e. Supplementation of breastfeeding should preferably be undertaken using a cup, spoon, syringe, or supplemental nursing system (if infant is latching) simultaneously with or immediately following each breastfeed. Nipples/teats and bottles should be avoided where possible. However, there is no evidence that any of these methods are unsafe or that one is necessarily better than the other.[77,96] (IA)

3. When TSB levels are very high or associated with evidence of poor breast milk intake despite appropriate intervention, supplementation with infant formula can eliminate the deleterious effect of *UGT1A1* polymorphisms on serum bilirubin and is a reasonable addition if it can be done in a way that is supportive of breastfeeding.[51] (IIA) Depending on the TSB level, follow-up TSB measurements within 4–24 hours are needed. Supplementation cannot be substituted for phototherapy in the treatment of infants with hemolytic hyperbilirubinemia.

a. Supplementation of breastfeeding with infant formula. As infant formula inhibits the intestinal reabsorption of bilirubin,[97] (IV) it may sometimes be used to lower TSB in breastfeeding infants.[77] Small-volume (10–15 mL) feedings of formula immediately following a breastfeeding may be preferred to intermittent large-volume (30–60 mL) supplementation so as to maintain frequent breastfeeding and preserve maternal milk production at a high level.[98] (IA) Larger volumes may be required if the infant is not receiving sufficient milk at the breast (i.e., low milk supply or poor milk transfer).
b. Temporary interruption of breastfeeding. Temporary interruption of breastfeeding is very rarely needed, but may be considered for specific clinical scenarios in which rapid reduction in TSB is urgently needed or if phototherapy is unavailable.[99] (IIA) If urgent clinical needs necessitate the temporary interruption of breastfeeding, it is critical to maintain maternal milk production by teaching the mother to effectively and frequently express milk by hand or pump. The infant needs to return to a good supply of milk when breastfeeding resumes, or poor milk supply may result in a return of higher TSB concentrations.

Post-treatment follow-up and evaluation

Infants who have had any of the above treatments for excessive hyperbilirubinemia need to be carefully followed with repeat TSB determinations and support of breastfeeding because suboptimal breast milk intake may result in recurrence of hyperbilirubinemia.

Encouragement to continue breastfeeding is of the greatest importance since many parents will be fearful that continued breastfeeding may result in more jaundice or other problems. Parents can be reassured that almost all hyperbilirubinemia requiring treatment resolves within the first 5 days after birth. Even those infants with more prolonged breast milk jaundice who required and received treatment rarely have sufficient rise in bilirubin with continued breastfeeding to require further intervention.

Summary and Conclusions

Breastfeeding and some degree of hyperbilirubinemia are normal and expected aspects of neonatal development.[45] Managing the confluence of jaundice and breastfeeding in a physiologic and supportive manner to ensure optimal health, growth, and development of the infant is the responsibility of all healthcare providers. A complete understanding of normal and abnormal states of both bilirubin and breastfeeding is essential if optimal care is to be provided and the best outcome achieved for the child. We provide guidelines for managing this problem while recognizing the need for adjusting the guidelines to the individual needs of each infant.

Research Needs

The recommendations above are based on the most current research and clinical experience available. Identifying the components in human milk that increase total serum bilirubin and whether and to what extent these components interact with genetic variation to increase jaundice might substantially improve risk-based strategies to prevent and treat hyperbilirubinemia. Because both commercial and noncommercial sources of banked donor milk are increasingly available,[100–104] further research on the effect of supplementing breastfed infants with banked donor milk on TSB levels is urgently needed. Small volumes of L-aspartic acid, enzymatically hydrolyzed casein or whey/casein, immediately after breastfeeding show potential promise in reducing TSB without interfering with breastfeeding or milk supply, but such interventions need further evaluation before they can be recommended for use.[105] In addition, widely generalizable research is also needed to evaluate specific strategies for feeding management of the breastfed infant with hyperbilirubinemia that allow uninterrupted breastfeeding while reducing serum bilirubin concentrations to safe levels. Additional strategies to maximize maternal milk intake and

shorten the duration of phototherapy need to be further explored and considered.[106]

Acknowledgment

The authors are grateful to Heather Molnar, MD, for her review of the manuscript.

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ABM protocols expire 5 years from the date of publication.

Content of this protocol is up-to-date at the time of publication. Evidence-based revisions are made within 5 years or sooner if there are significant changes in the evidence.

The first version of this protocol was authored by Lawrence Gartner.

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