

Supplemental Information

Appendix A. Kernicterus Nomenclature

The term kernicterus refers to the permanent disabling neurologic condition characterized by some or all of the following: choreoathetoid cerebral palsy, upward gaze paresis, enamel dysplasia of deciduous teeth, sensorineural hearing loss or auditory neuropathy or dyssynchrony spectrum disorder, and characteristic findings on brain magnetic resonance imaging.¹

The term “kernicterus spectrum disorder” (KSD) has been proposed to provide a broader conceptualization of kernicterus. KSD encompasses all the neurologic sequelae of bilirubin neurotoxicity including classic, motor-predominant, and auditory-predominant subtypes of the continuum.^{2,3} This term also suggests a possible association between subtle adverse neurodevelopmental findings and bilirubin concentrations well below those linked to classical kernicterus. However, the literature linking subtle abnormalities with bilirubin is conflicting, and there is no evidence that treating infants at these lower bilirubin concentrations prevents these outcomes.^{4–13}

“Bilirubin-induced neurologic dysfunction” is a term that has been variously used to designate both subtle neurodevelopmental findings and all neurologic conditions associated with exposure to hazardous hyperbilirubinemia, as well as a scoring system that quantitatively describes the progression and severity of acute bilirubin encephalopathy (ABE).^{5,11} Bilirubin-induced neurologic dysfunction should be used as originally intended as a score to

quantify the severity of ABE and risk of an infant with ABE subsequently developing kernicterus or KSD^{14,15}; its use for entities for which a causal effect of bilirubin has not been demonstrated should be avoided.

References for Kernicterus Nomenclature

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Appendix B. Key Action Statement Evidence Tables

The following tables summarize the

KAS 1 If the maternal antibody screen is positive or unknown because the mother did not have prenatal antibody screening, the infant should have a direct antiglobulin test (DAT) and the infant's blood type should be determined as soon as possible using either cord or peripheral blood. (Aggregate Evidence Quality Grade B, Recommendation)

Aggregate Evidence Quality	B
Benefits	Early DAT testing identifies newborn infants at risk for immune-mediated hemolytic disease and early hyperbilirubinemia born to mothers who carry anti-erythrocyte antibodies.
Risk, harm, and cost	Early DAT testing could involve an extra blood draw from newborn infants. There is a small risk of false-negative and false-positive DAT test results.
Benefit-harm assessment	Isoimmunization is the most common cause of severe hemolysis, and hyperbilirubinemia can progress rapidly. The alternative to early DAT testing is to wait and only test if jaundice develops, which could miss the opportunity for early intervention in some newborn infants with severe hemolysis. The benefit of knowing the risk for severe hemolysis through early DAT testing likely exceeds the harm of a potential extra blood draw and the risk of a false-negative or false-positive DAT in infants born to mothers with positive or unknown antibody screen results.
Intentional vagueness	None
Role of patient preferences	Minimal to none
Exclusions	None
Strength	Recommendation
Key references	1

KAS 2 Oral supplementation with water or dextrose water should not be provided to prevent hyperbilirubinemia or decrease bilirubin concentrations. (Aggregate Evidence Quality Grade B, Strong Recommendation)

Aggregate Evidence Quality	B
Benefits (from not treating)	Avoiding supplementation may help promote breastfeeding because supplementation has been associated with reduced maternal confidence in breastfeeding and breastfeeding duration. One study found no difference in peak serum bilirubin concentrations or the need for phototherapy among term breastfed newborn infants with physiologic jaundice by whether they were fed supplemental water. Another study of breastfed term infants whose weight was appropriate for gestational age found that supplementation with water or dextrose water was associated with higher bilirubin concentrations on day 6 after birth.
Risk, harm, and cost	There are no clear risks, harms, or costs associated with not routinely supplementing infants with water or dextrose water who are not receiving phototherapy.
Benefit-harm assessment	There is no evidence of the benefit of routinely providing water or dextrose water supplementation and there are possible harms, including interference with breastfeeding, hyponatremia, and water intoxication.
Intentional vagueness	None
Role of patient preferences	Minimal to none
Exclusions	None
Strength	Strong Recommendation
Key references	2–6

KAS 3 Use TSB as the definitive diagnostic test to guide phototherapy and escalation-of-care decisions, including exchange transfusion. (Aggregate Evidence Quality Grade X, Recommendation)

Aggregate Evidence Quality	X
Benefits	Virtually all treatment studies are based on TSB concentrations.
Risk, harm, and cost	There is some laboratory variation.
Benefit-harm assessment	Using TSB can lead to timely treatment and may help reduce overtreatment in infants in whom TcB overestimates TSB. However, there are no direct comparisons between TSB and TcB as a diagnostic test to distinguish between babies in whom the benefits of treatment do and do not exceed the risks and costs and such studies are unlikely to be performed.
Intentional vagueness	None
Role of patient preferences	Minimal to none
Exclusions	None
Strength	Recommendation
Key references	7–11

KAS 4 All infants should be visually assessed for jaundice at least every 12 hours following delivery until discharge. TSB or TcB should be measured as soon as possible for infants noted to be jaundiced <24 hours after birth. (Aggregate Evidence Quality Grade X, Strong Recommendation)

Aggregate Evidence Quality	X
Benefits	Onset of jaundice within 24 h of birth is more likely to be caused by hemolysis and to need treatment. Early identification of hyperbilirubinemia requiring treatment can lead to earlier initiation of phototherapy and reduce the risk of needing to perform an exchange transfusion. Identification of jaundice with onset after 24 h can inform decisions about measuring TcB or TSB and has the potential benefit of allowing parents to learn to recognize jaundice.
Risk, harm, and cost	Assessing for the onset of jaundice may require turning lights on in a previously dark room, which can interfere with sleep and disturb the infant and other family members. This harm can be minimized if the examination is conducted at the same time as other routine newborn care and by covering the infant's eyes or using focused lighting away from the infant's eyes.
Benefit-harm assessment	The benefits are likely to exceed harms, especially in the first 24 h.
Intentional vagueness	None
Role of patient preferences	Parents may have preferences regarding the frequency or timing of these examinations that can be considered as long as they occur at least every 12 h.
Exclusions	None
Strength	Strong Recommendation
Key references	12

KAS 5 The TcB or TSB should be measured between 24 and 48 hours after birth or prior to discharge if that occurs earlier. (Aggregate Evidence Quality Grade C, Recommendation)

Aggregate Evidence Quality	C
Benefits	Routine TcB or TSB screening can identify significant but undetected hyperbilirubinemia. This benefit will be greater among infants whose jaundice is harder to recognize. The TcB or TSB value can be used to plan for postdischarge follow-up and the need for subsequent measures of TcB or TSB. This planning can help increase the timely identification of subsequent hyperbilirubinemia and also avoid unnecessary follow-up care or treatment.
Risk, harm, and cost	TSB measurements can cause discomfort, which could be minimized by using TcB measures or obtaining additional blood at the same time as the collection of the dried blood spot for newborn screening. In some newborn infants, TcB measurements might lead to TSB measurements that would otherwise not have been performed and are not high enough to affect management. This may be more likely in infants with greater skin melanin concentration when JM TcB instruments are used. ^{8,15} There is a risk that hyperbilirubinemia could be detected that would have resolved without treatment had it not been identified. It is possible that the follow-up based on the TcB or TSB measure could be more or less than what the infant needs. There is the possibility of a false sense of security based on having a low TcB or TSB in infants with hyperbilirubinemia that presents later, such as from G6PD deficiency. There are additional costs related to measuring TcB or TSB.
Benefit-harm assessment	Evidence from large health care systems that implemented universal bilirubin screening suggest a decrease in the already low incidence of infants who reach a TSB ≥ 25 mg/dL, with a number needed to screen in the range of 1000 to 6000. The number needed to screen to prevent one infant from reaching a TSB ≥ 30 mg/dL is approximately 15000. The screening test alone does not directly lead to the benefit, but instead relies on follow-up care including subsequent TSB measurements and treatment with phototherapy. The effect on health disparities is uncertain but probably small: an increase in sensitivity at identifying significantly jaundiced babies, which may disproportionately benefit babies with greater skin melanin concentration, but possible increase in unnecessary TSB testing in this group. There are no randomized trials of bilirubin screening.
Intentional vagueness	None
Role of patient preferences	Parents may prefer strategies to minimize the number of heel pricks or venipunctures and, therefore, prefer TcB compared with TSB.
Exclusions	None
Strength	Recommendation
Key references	13–22

KAS 6 TSB should be measured if the TcB exceeds or is within 3 mg/dL of the phototherapy treatment threshold or if the TcB is ≥ 15 mg/dL. (Aggregate Evidence Quality Grade C, Recommendation)

Aggregate Evidence Quality	C
Benefits	The TcB is a good screening test but is not accurate enough to determine treatment decisions. TSB provides a better guide for treatment decisions than the TcB because studies of hyperbilirubinemia risk prediction and studies of treatment have been based on the TSB. As the TcB approaches the phototherapy treatment thresholds, the likelihood that the TSB will change management increases.
Risk, harm, and cost	There is a risk of an unnecessary blood test when the TSB might not change management. Infants whose skin has greater melanin concentration tend to have higher TcB measurements with JM instruments, ^{8,13,22} increasing the risk of unnecessary blood tests, whereas infants with greater skin melanin concentration and higher TSB levels may have slightly lower TcB with Spectrix instruments. However, these differences are relatively small.
Benefit-harm assessment	The benefit of having a more accurate measure to guide treatment decisions outweighs the discomfort associated with measuring the TSB.
Intentional vagueness	None
Role of patient preferences	In borderline cases, especially if one or more TcB measurements has been greater than a contemporaneous TSB level, parents may prefer to rely on the TcB.
Exclusions	None
Strength	Recommendation
Key references	8, 23, 24

KAS 7 If more than 1 TcB or TSB measure is available, the rate of increase may be used to identify higher risk of subsequent hyperbilirubinemia. A rapid rate of increase (≥ 0.3 mg/dL per hour in the first 24 hours or ≥ 0.2 mg/dL per hour thereafter) is exceptional and suggests hemolysis. In this case, obtain a DAT if not previously done. (Aggregate Evidence Quality Grade D, Option)

Aggregate Evidence Quality	D
Benefits	Identification of a rapid rate of increase could lead to the identification of unrecognized hemolysis.
Risk, harm, and cost	Insufficient evidence is available to assess the test accuracy of different thresholds for the rate of rise or to recommend routinely obtaining more than 1 TcB or TSB measure.
Benefit-harm assessment	Although the balance of benefit and harm cannot be determined, evaluating the rate of rise could help detect unrecognized hemolysis.
Intentional vagueness	None
Role of patient preferences	Because this is an option, a parental preference to avoid monitoring might lead to having only 1 TcB or TSB measure available. In that case, the rate of rise cannot be calculated. However, once a rapid rate of rise is identified, a DAT should be obtained if not previously even if parents prefer to avoid additional testing because of the importance of DAT in making treatment decisions.
Exclusions	None
Strength	Option
Key references	25, 26

KAS 8 If appropriate follow-up cannot be arranged for an infant recommended to have an outpatient follow-up bilirubin measure, discharge may be delayed. (Aggregate Evidence Quality Grade D, Option)

Aggregate Evidence Quality	D
Benefits	Follow-up after discharge for some families can be challenging and potentially contribute to missing the opportunity for timely treatment of hyperbilirubinemia.
Risk, harm, and cost	Delay in discharge can be difficult for families and increase nursery-related expenses.
Benefit-harm assessment	The balance of benefit and harm depend on the risk of hyperbilirubinemia and the challenge of follow-up. Extending access for newborn follow-up can reduce the need to delay discharge.
Intentional vagueness	None
Role of patient preferences	Shared decision making can help inform the benefit-harm assessment.
Exclusions	None
Strength	Option
Key references	27

KAS 9 For breastfed infants who are still jaundiced at 3 to 4 weeks of age, and for formula-fed infants who are still jaundiced at 2 weeks of age, the total and direct-reacting (or conjugated) bilirubin concentrations should be measured to identify possible pathologic cholestasis. (Aggregate Evidence Quality Grade X, Recommendation)

Aggregate Evidence Quality	X
Benefits	Although cholestasis is uncommon, early detection of pathologic causes of cholestasis, such as biliary atresia or certain metabolic diseases, can lead to improved health outcomes.
Risk, harm, and cost	The harm is an additional blood test and the pain associated with any additional evaluation based on the laboratory findings. The additional costs are those associated with the blood test and additional evaluation.
Benefit-harm assessment	The benefit of early identification and treatment of pathologic causes of cholestasis outweighs the harm of the testing and subsequent evaluation among infants who are still jaundiced at 2 wk of age.
Intentional vagueness	None
Role of patient preferences	Parents may prefer to measure TSB at the 2-wk visit rather than returning for a TSB level at 4 wk.
Exclusions	None
Strength	Exceptional situation
Key references	28–30

KAS 10 Intensive phototherapy is recommended at the total serum bilirubin thresholds in Fig 2 (Supplemental Table 1 and Supplemental Fig 1) or Fig 3 (Supplemental Table 2 and Supplemental Figure 2) on the basis of gestational age, hyperbilirubinemia neurotoxicity risk factors, and age of the infant in hours. (Aggregate Evidence Quality Grade X, Recommendation)

Aggregate Evidence Quality	X
Benefits	Intensive phototherapy can reduce TSB levels and decrease the need for escalation of care, including the need for exchange transfusion, to prevent kernicterus. The phototherapy treatment thresholds are higher than those in the 2004 guideline but still leave a wide margin of safety. Compared with the 2004 guideline, overtreatment will be decreased.
Risk, harm, and cost	Phototherapy may lead to separation of mother and baby, maternal anxiety, and reduce breastfeeding. Phototherapy can lead to oxidative stress and DNA damage, although these risks appear to be lower with LED-based phototherapy. Two observational studies found a small increased risk of epilepsy in males treated with phototherapy. If the findings are causal, for approximately each 100 to 250 males treated with phototherapy, 1 will be diagnosed with epilepsy by 10 years of age. Hospitalization for phototherapy can increase costs because of a prolonged initial hospital stay or the need for readmission. See the technical report appendix for a review of other risks of phototherapy.
Benefit-harm assessment	Benefits are believed to exceed potential harms at the phototherapy treatment thresholds in this guideline. A weakness of the evidence linking specific TSB levels to adverse neurologic outcomes is that studies are typically based on maximum TSB levels, which are not known when decisions to initiate phototherapy are made. Even at the treatment thresholds in this guideline, the number needed to treat to prevent 1 infant from receiving an exchange transfusion may be in the hundreds or thousands, and the number needed to treat to prevent 1 case of kernicterus is considerably higher. The more the TSB exceeds the phototherapy threshold, the lower the number that will be needed to treat to prevent the need for an exchange transfusion or prevent kernicterus.
Intentional vagueness	None
Role of patient preferences	The phototherapy treatment thresholds are based on expert opinion. Some families might choose to accept a higher probability of unnecessary treatment and begin phototherapy below recommended thresholds to reduce the risk of a rehospitalization and its accompanying costs and inconvenience. Other families, with infants with TSB levels at or <2 mg/dL above thresholds, may prefer only blanket phototherapy (in the hospital or at home) or withholding phototherapy and very close follow-up of TSB concentrations.
Exclusions	None
Strength	The evidence is strong that phototherapy reduces TSB concentrations and the need for exchange transfusion. The evidence is weak regarding the specific phototherapy treatment threshold at which benefits exceeds harms. This is a recommendation because the guideline thresholds were set to reduce overtreatment while not missing the potential benefit for reducing the risk of exchange transfusion or kernicterus.
Key references	31–38

KAS 11 For newborn infants who have already been discharged and then develop a TSB above the phototherapy threshold, treatment with a home LED-based phototherapy device rather than readmission to the hospital is an option for infants who meet the following criteria: gestational age ≥ 38 weeks, ≥ 48 hours old, clinically well with adequate feeding, no known hyperbilirubinemia neurotoxicity risk factors (Table 2), no previous phototherapy, TSB concentration no more than 1 mg/dL above the phototherapy treatment threshold (Fig 2, Supplemental Table 1, Supplemental Fig 1), an LED-based phototherapy device will be available in the home without delay, and TSB can be measured daily. (Aggregate Evidence Quality Grade D, Option)

Aggregate Evidence Quality	D
Benefits	Home phototherapy for infants already discharged can help avoid readmission.
Risk, harm, and cost	Home phototherapy might not prevent significant hyperbilirubinemia if it is not used correctly and there is not close clinical follow-up. Infants with any risk factor are more likely to develop worsening hyperbilirubinemia even with appropriate home therapy use.
Benefit-harm assessment	The balance of benefit and harm depend on the risk of worsening hyperbilirubinemia.
Intentional vagueness	None
Role of patient preferences	Shared decision making can help inform the benefit-harm assessment. As with inpatient phototherapy, beginning home phototherapy at a somewhat lower threshold could reduce the readmission risk. Some families may prefer inpatient treatment, especially if lactation support is more available for inpatients than outpatients.
Exclusions	None
Strength	Option
Key references	39, 40

KAS 12 For hospitalized infants, TSB should be measured within 12 hours after starting phototherapy. The timing of the initial TSB measure after starting phototherapy and the frequency of TSB monitoring during phototherapy should be guided by the age of the child, the presence of hyperbilirubinemia neurotoxicity risk factors, the TSB concentration, and the TSB trajectory. (Aggregate Evidence Quality Grade X, Recommendation)

Aggregate Evidence Quality	X
Benefits	Early identification of infants without adequate response to phototherapy can lead to earlier escalation of care, potentially averting the need for an exchange transfusion and possibly preventing kernicterus. Early identification of infants whose TSB has decreased will facilitate timely discontinuation of phototherapy.
Risk, harm, and cost	There is a small risk that some infants would receive escalation of care who would have responded to phototherapy without additional interventions. There are costs associated with the additional testing.
Benefit-harm assessment	Although most infants treated with phototherapy will not require escalation of care, missing an infant could lead to significant harm. More frequent TSB measurements might allow earlier discontinuation of phototherapy, which might reduce the risk of adverse effects associated with phototherapy and would reduce costs.
Intentional vagueness	None
Role of patient preferences	For some families, the benefit of finding out sooner that phototherapy can be discontinued might lead to a preference for more frequent blood tests.
Exclusions	None
Strength	Exceptional situation
Key references	41–43

KAS 13 For infants receiving home phototherapy, the TSB should be measured daily. Infants should be admitted for inpatient phototherapy if the TSB increases and the difference between the TSB and the phototherapy threshold narrows or the TSB is ≥ 1 mg/dL above the phototherapy threshold. (Aggregate Evidence Quality Grade X, Recommendation)

Aggregate Evidence Quality	X
Benefits	TSB measurement is the only way to document whether there has been a response to phototherapy and to determine when phototherapy can be discontinued.
Risk, harm, and cost	TSB measurement is associated with discomfort and for those infants who have been discharged, there will often be the need to travel to a clinic or laboratory. For some families, travel can be difficult, and some infants might require an emergency department visit for TSB testing. TSB measurement increases cost.
Benefit-harm assessment	The overall benefit of assessing response to phototherapy outweighs the harms and additional expense of daily TSB testing for infants receiving home phototherapy.
Intentional vagueness	None
Role of patient preferences	Families might prefer a slightly higher or lower frequency of TSB monitoring. Factors that could influence this include the values of the previous TSB concentrations.
Exclusions	None
Strength	Recommendation
Key references	39, 44, 45

KAS 14 For infants requiring phototherapy, measure the hemoglobin concentration, hematocrit, or complete blood count to assess for the presence of anemia and to provide a baseline in case subsequent anemia develops. Evaluate the underlying cause or causes of hyperbilirubinemia in infants who require phototherapy by obtaining a DAT in infants whose mother had a positive antibody screen or whose mother is blood group O regardless of Rh(D) status or whose mother is Rh(D)—. G6PD activity should be measured in any infant with jaundice of unknown cause whose TSB increases despite intensive phototherapy, whose TSB increases suddenly or increases after an initial decline, or who requires escalation of care. (Aggregate Evidence Quality Grade X, Recommendation)

Aggregate Evidence Quality	X
Benefits	Identifying the cause of hyperbilirubinemia might identify a previously unrecognized diagnosis that leads to the need for additional care.
Risk, harm, and cost	Additional laboratory tests and related costs.
Benefit-harm assessment	The estimated overall benefit of providing potentially useful information is expected to outweigh the potential harms.
Intentional vagueness	None
Role of patient preferences	Some families might place added value in knowing the cause of the hyperbilirubinemia, especially if it could inform the care of future pregnancies.
Exclusions	None
Strength	Recommendation
Key references	46–54

KAS 15 Discontinuing phototherapy is an option when the TSB has decreased by at least 2 mg/dL below the hour-specific threshold at the initiation of phototherapy. A longer period of phototherapy is an option if there are risk factors for rebound hyperbilirubinemia (eg, gestational age <38 weeks, age <48 hours at the start of phototherapy, hemolytic disease). (Aggregate Evidence Quality Grade C, Option)

Aggregate Evidence Quality	C
Benefits	Discontinuing phototherapy as soon as it is safe reduces unnecessary exposure to phototherapy while minimizing the risk of rebound hyperbilirubinemia.
Risk, harm, and cost	Stopping phototherapy too soon increases the risk that it will need to be restarted again. The cost and inconvenience of restarting phototherapy is greater when it would require readmission to the hospital. Continuing phototherapy longer than necessary increases costs and might increase the risk of adverse effects.
Benefit-harm assessment	Suggested levels for discontinuing phototherapy reflect an attempt to minimize both the duration of phototherapy and need to initiate it again. Different families and clinicians may have different values for these conflicting goals; estimation of the risk of significant rebound hyperbilirubinemia can facilitate joint decision making.
Intentional vagueness	None
Role of patient preferences	Parents wanting to end phototherapy sooner may be willing to accept a higher risk of rebound; those who want to reduce even a small risk of readmission may wish to continue the phototherapy until the TSB is lower.
Exclusions	None
Strength	Recommendation
Key references	55, 56

KAS 16 Follow-up bilirubin measurement after phototherapy is based on the risk of rebound hyperbilirubinemia. Infants who exceeded the phototherapy threshold during the birth hospitalization and (1) received phototherapy before 48 hours of age; (2) had a positive DAT; or (3) had known or suspected hemolytic disease, should have TSB measured 6 to 12 hours after phototherapy discontinuation and a repeat bilirubin measured on the day after phototherapy discontinuation. All other infants who exceeded the phototherapy threshold during the birth hospitalization should have bilirubin measured the day after phototherapy discontinuation. Infants who received phototherapy during the birth hospitalization and who were later readmitted for exceeding the phototherapy threshold should have bilirubin measured the day after phototherapy discontinuation. Infants readmitted because they exceeded the phototherapy threshold following discharge but who did not receive phototherapy during the birth hospitalization and infants treated with home phototherapy who exceeded the phototherapy threshold should have bilirubin measured in 1 to 2 days after phototherapy discontinuation or clinical follow-up 1 to 2 days after phototherapy to determine whether to obtain a bilirubin measurement. Risk factors for rebound hyperbilirubinemia to consider in this determination include the TSB at the time of phototherapy discontinuation in relationship to the phototherapy threshold, gestational age <38 weeks, the adequacy of feeding and weight gain, and other hyperbilirubinemia and hyperbilirubinemia neurotoxicity risk factors. It is an option to measure TcB instead of TSB if it has been at least 24 hours since phototherapy was stopped. (Aggregate Evidence Quality Grade X, Recommendation)

Aggregate Evidence Quality	X
Benefits	Following up closely with infants discharged early or with hyperbilirubinemia risk factors can lead to more timely identification of those who need treatment. Infants who required phototherapy should be followed closely because of the risk of rebound hyperbilirubinemia. TcB is reliable after 24 h of phototherapy and can, therefore, be used instead of TSB.
Risk, harm, and cost	Some infants might receive additional TSB or TcB testing or have clinic follow-up that might not be necessary.
Benefit-harm assessment	The benefits of identifying infants with hyperbilirubinemia that develops after discharge or infants with rebound hyperbilirubinemia exceeds the associated follow-up risks.
Intentional vagueness	None
Role of patient preferences	Parents wanting to avoid additional testing or clinic follow-up might accept a higher risk of delayed detection of hyperbilirubinemia. However, other parents might want closer follow-up to avoid this risk.
Exclusions	None
Strength	Recommendation
Key references	55–58

KAS 17 Care should be escalated when an infant's TSB reaches or exceeds the escalation-of-care threshold, defined as 2 mg/dL below the exchange transfusion threshold, as detailed in Fig 5 (infants with no known hyperbilirubinemia neurotoxicity risk factors; Supplemental Table 3 and Supplemental Fig 3) or Fig 6 (infants whose TSB is increasing despite phototherapy and or infants with at least one recognized hyperbilirubinemia neurotoxicity risk factor; Supplemental Table 4 and Supplemental Fig 4). (Aggregate Evidence Quality Grade X, Recommendation)

Aggregate Evidence Quality	X
Benefits	Escalation of care below the exchange transfusion threshold may prevent the need for an exchange transfusion or allow for a timelier exchange transfusion if it is necessary, which could help prevent kernicterus.
Risk, harm, and cost	Some infants for whom care is escalated may have experienced a leveling off or decrease in TSB without this additional care. Escalation of care can lead to separation of mother and baby and greater costs if transfer to another hospital is required.
Benefit-harm assessment	The overall benefit of escalation of care to potentially avoid the need for an exchange transfusion and to be prepared to provide an exchange transfusion in as safe a manner as possible is believed to outweigh the potential harms at about the TSB concentrations at which escalation of care is recommended. The TSB concentration or trajectory at which the benefits of escalation of care exceed the risks and costs is not known, and will vary with individual circumstances, such as the proximity of a NICU.
Intentional vagueness	None
Role of patient preferences	Decisions regarding NICU transfer can be difficult, especially if this would require transfer to another hospital or separation from the mother. Parent preferences should be considered in in borderline cases.
Exclusions	None
Strength	Recommendation
Key references	37, 59

KAS 18 For infants requiring escalation of care, blood should be sent STAT for total and direct-reacting serum bilirubin, a complete blood count, serum albumin, serum chemistries, and type and crossmatch. (Aggregate Evidence Quality Grade X, Recommendation)

Aggregate Evidence Quality	X
Benefits	Avoiding delays for infants who require exchange transfusion can improve outcomes. Knowledge of the albumin level and complete blood count results can inform exchange transfusion decisions and the differential diagnosis of the hyperbilirubinemia.
Risk, harm, and cost	Some infants might receive additional testing that might not be necessary.
Benefit-harm assessment	The benefits of being prepared for an exchange transfusion outweigh the harm of additional testing.
Intentional vagueness	None
Role of patient preferences	None
Exclusions	None
Strength	Recommendation
Key references	Expert opinion

KAS 19 Infants requiring escalation of care should receive intravenous hydration and emergent intensive phototherapy. A neonatologist should be consulted for transfer to a neonatal intensive care unit that can perform an exchange transfusion. (Aggregate Evidence Quality Grade C, Recommendation)

Aggregate Evidence Quality	C
Benefits	Emergent intensive phototherapy and intravenous (IV) hydration can increase the rate of decline in TSB and may prevent the need for an exchange transfusion.
Risk, harm, and cost	The risks and costs of short-term intensive phototherapy and IV hydration are small and minimal compared with the possibility of an exchange transfusion.
Benefit-harm assessment	The possible benefit of preventing an exchange transfusion outweighs the potential harm.
Intentional vagueness	None
Role of patient preferences	Parents might choose to defer IV hydration if obtaining vascular access is difficult and the TSB is stabilizing.
Exclusions	None
Strength	Recommendation
Key references	60–65

KAS 20 TSB should be measured at least every 2 hours from the start of the escalation-of-care period until the escalation-of-care period ends. Once the TSB is lower than the escalation-of-care threshold, management should proceed according to the section “C. Monitoring Infants Receiving Phototherapy.” (Aggregate Evidence Quality Grade X, Recommendation)

Aggregate Evidence Quality	X
Benefits	Frequent measurement of TSB provides timely guidance regarding the efficacy of phototherapy and the possible need for an exchange transfusion.
Risk, harm, and cost	Frequent TSB monitoring requires repeated blood sampling and laboratory testing.
Benefit-harm assessment	Infants who require escalation of care benefit from frequent monitoring to identify if or when they qualify for an exchange transfusion. The benefit of identifying those who exceed exchange thresholds as soon as possible outweighs the possible harms from the risks and costs of frequent blood sampling and laboratory testing.
Intentional vagueness	None
Role of patient preferences	Minimal to none
Exclusions	None
Strength	Recommendation
Key references	Expert opinion

KAS 21 Intravenous immune globulin (IVIG; 0.5–1 g/kg) over 2 hours may be provided to infants with isoimmune hemolytic disease (ie, positive DAT) whose TSB reaches or exceeds escalation of care threshold. The dose can be repeated in 12 hours. (Aggregate Evidence Quality Grade C, Option)

Aggregate Evidence Quality	C
Benefits	Use of IVIG during escalation of care may reduce hemolysis and thereby stabilize or reduce TSB concentrations, preventing the need for exchange transfusion.
Risk, harm, and cost	The effect of IVIG for immune-mediated hemolytic disease has been understudied with conflicting evidence supporting a reduction in exchange transfusions. Recent investigations using routine single early dose prophylactic IVIG do not demonstrate benefit in reducing the need for exchange transfusion and the routine use of prophylactic IVIG in DAT+ neonates should be discouraged. However, targeted dosing may be more effective. Although observational studies suggest that IVIG may be associated with necrotizing enterocolitis, the risk of necrotizing enterocolitis with exchange transfusion is well documented so the benefits of IVIG may outweigh this potential harm when exchange thresholds are approached.
Benefit-harm assessment	The benefits of IVIG are not clear, and there is a small risk of harm. Treatment with IVIG may be more strongly considered if there is a poor response to phototherapy and there is difficulty in obtaining an exchange transfusion.
Intentional vagueness	None
Role of patient preferences	Some families may want to avoid IVIG treatment given limited evidence for its effectiveness, especially for Rh+ infants and the potential risk of necrotizing enterocolitis.
Exclusions	None
Strength	Option
Key references	Technical report and 66–75

KAS 22 An urgent exchange transfusion should be performed for infants with signs of intermediate or advanced stages of intermediate or advanced stages of acute bilirubin encephalopathy (eg, hypertonia, arching, retrocollis, opisthotonos, high-pitched cry, or recurrent apnea). (Aggregate Evidence Quality Grade C, Recommendation)

Aggregate Evidence Quality	C
Benefits	There are some case reports and case series that suggest an immediate exchange transfusion may prevent kernicterus in some infants already showing signs of intermediate to advanced stages of bilirubin encephalopathy, and reduction of the time the brain is exposed to high TSB concentration may also reduce the severity of chronic bilirubin encephalopathy if it develops.
Risk, harm, and cost	The risks of exchange transfusion include death, necrotizing enterocolitis, apnea, hypocalcemia and other electrolyte abnormalities, and thrombocytopenia. The infectious risks from donor blood products are low. The costs of an exchange transfusion are incompletely described but at least thousands of dollars.
Benefit-harm assessment	The benefit of avoiding kernicterus or reducing its severity among newborns already showing signs of intermediate or advanced acute bilirubin encephalopathy probably exceed the risks and costs of exchange transfusion.
Intentional vagueness	None
Role of patient preferences	Some parents have a strong preference to avoid blood products.
Exclusions	None
Strength	Recommendation
Key references	59, 64, 65, 76–82

KAS 23 An urgent exchange transfusion should be performed for infants if the TSB is at or above the exchange transfusion threshold. If, while preparing for the exchange transfusion but before starting the exchange transfusion, a TSB concentration is below the exchange transfusion threshold and the infant does not show signs of intermediate or advanced stages of acute bilirubin encephalopathy, then the exchange transfusion may be deferred while continuing intensive phototherapy and following the TSB every 2 hours until the TSB is below the escalation of care threshold. (Aggregate Evidence Quality Grade C, Recommendation)

Aggregate Evidence Quality	C
Benefits	Treatment at these levels may prevent kernicterus.
Risk, harm, and cost	The risks of exchange transfusion include death, necrotizing enterocolitis, apnea, hypocalcemia and other electrolyte abnormalities, and thrombocytopenia. The infectious risks from donor blood products are low. The costs of an exchange transfusion are incompletely described but at least thousands of dollars.
Benefit-harm assessment	Studies are not sufficient to set a definite TSB concentration or duration of time with TSB above exchange thresholds at which the kernicterus-preventing benefits of exchange transfusion exceed the risks and costs. These thresholds may differ in low- and middle-income countries, where the risk of kernicterus may be substantially higher. The potential benefits of exchange transfusions are unlikely to exceed risks at the exchange thresholds in the AAP 2004 guideline. Whether benefits exceed risk at these levels is not known. The exchange transfusion thresholds were raised in this guideline to decrease the likelihood of harm while still recommending treatment of infants most likely to benefit.
Intentional vagueness	None
Role of patient preferences	Given uncertainty about what the exchange transfusion thresholds should be, parent preferences may be considered.
Exclusions	None
Strength	Recommendation
Key references	35, 59, 83–86

KAS 24 Beginning at least 12 hours after birth, if discharge is being considered, the difference between the bilirubin concentration measured closest to discharge and the phototherapy threshold at the time of the bilirubin measurement should be calculated and used to guide follow-up, as detailed in Fig 7. (Aggregate Evidence Quality Grade C, Recommendation)

Aggregate Evidence Quality	C
Benefits	These recommendations for timing of follow-up after discharge seek to improve follow-up of those at highest risk of developing jaundice that will benefit from treatment while minimizing unnecessary visits and laboratory testing.
Risk, harm, and cost	These guidelines for follow-up may lead to some infants with significant hyperbilirubinemia being detected late or missed and others receiving more visits or earlier visits than were needed to detect and manage their hyperbilirubinemia.
Benefit-harm assessment	These thresholds for bilirubin testing and follow-up seek to balance benefit and harm, but necessarily depend on value judgements. Depending on the level of concern about jaundice and the difficulty of outpatient follow-up and bilirubin testing, clinicians and families can jointly decide on more or less aggressive follow-up, especially with TSB concentrations close to the cutoffs suggested here.
Intentional vagueness	None
Role of patient preferences	Parent preferences around the specific timing of TcB or TSB monitoring can be considered given the gaps in evidence.
Exclusions	None
Strength	Recommendation
Key references	20, 87–91

KAS 25 Before discharge, all families should receive written and verbal education about neonatal jaundice. Parents should be provided written information to facilitate postdischarge care, including the date, time, and place of the follow-up appointment and, when necessary, a prescription and appointment for a follow-up TcB or TSB. Birth hospitalization information, including the last TcB or TSB and the age at which it was measured, and DAT results (if any) should be transmitted to the primary care provider who will see the infant at follow-up. If there is uncertainty about who will provide the follow-up care, this information should also be provided to families. (Aggregate Evidence Quality Grade X, Strong Recommendation)

Aggregate Evidence Quality	X
Benefits	Educating families and providing explicit instructions for follow-up can decrease the risk of missed cases of hyperbilirubinemia or other problems requiring treatment.
Risk, harm, and cost	There is a small risk of causing anxiety. The costs of providing the information and appropriate education are minimal.
Benefit-harm assessment	The benefits far exceed the potential harms.
Intentional vagueness	None
Role of patient preferences	Parents value complete information about their newborn infants.
Exclusions	None
Strength	Strong recommendation
Key references	92

evidence for each key statement according to the AAP evidence review process.

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APPENDIX C. PHOTOTHERAPY AND EXCHANGE TRANSFUSION THRESHOLDS

The 2004 AAP guideline did not make specific recommendations for

phototherapy or exchange transfusion by week of gestational age.¹ Rather, gestational age dichotomized at 38 weeks was an important, separate hyperbilirubinemia neurotoxicity risk factor that led to more aggressive treatment. In the current guideline, the new phototherapy threshold for infants born at 40 weeks' gestational age and no recognized hyperbilirubinemia neurotoxicity risk factors was set at 2 mg/dL higher than the previous guideline's recommendations for infants at lower risk (≥ 38 weeks' gestation with no hyperbilirubinemia neurotoxicity risk factors). For infants born at 35 weeks' gestational age with no recognized hyperbilirubinemia neurotoxicity risk factors, the new threshold was set at 1 mg/dL higher than "medium-risk" infants in the 2004 guideline (either gestational age 35 to <38 weeks or presence of hyperbilirubinemia neurotoxicity risk factors but not both). The new thresholds for infants born at 36 to

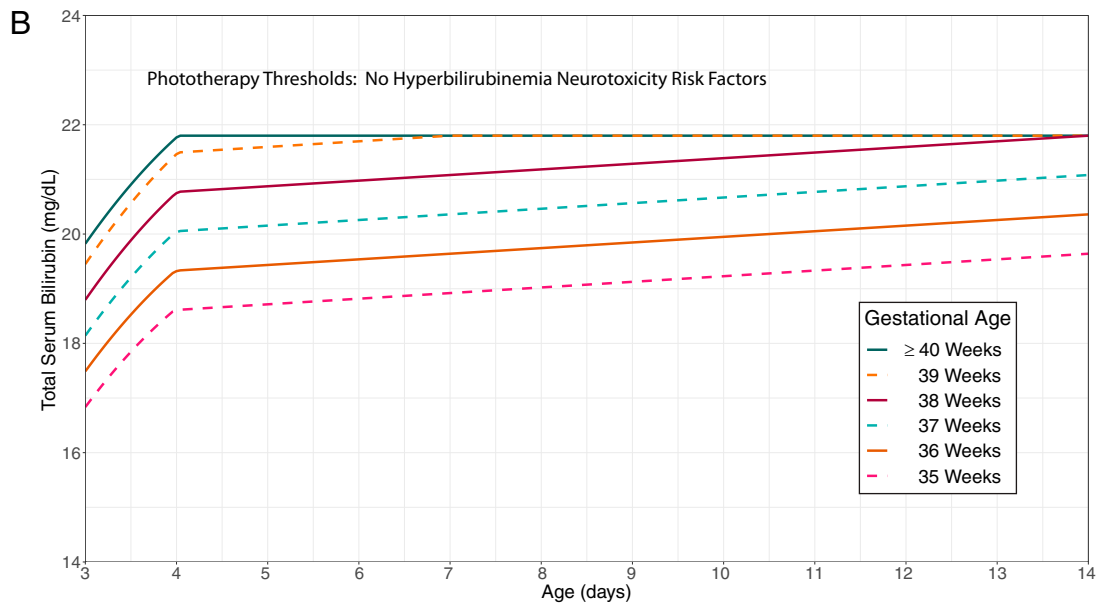
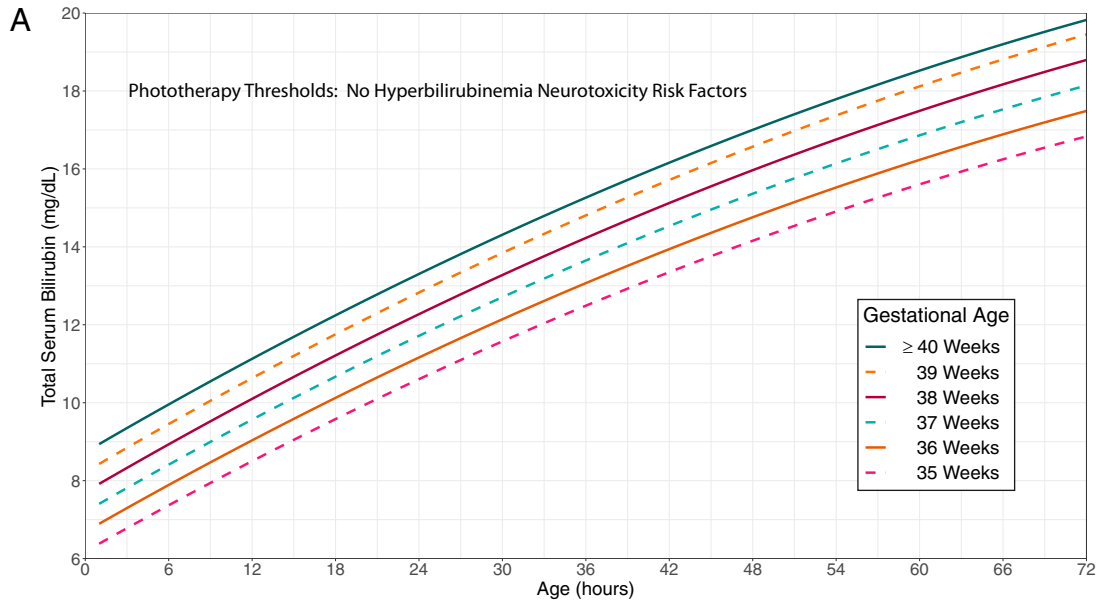
39 weeks' gestational age with no hyperbilirubinemia neurotoxicity risk factors were evenly spaced between the thresholds for infants with gestational ages of 35 weeks and 40 weeks.

A similar process was used for the phototherapy thresholds for infants with at least 1 hyperbilirubinemia neurotoxicity risk factor. In this case, the new phototherapy threshold for infants with a gestational age of 35 weeks was set to 1 mg/dL above the 2004 threshold for infants at higher risk (both gestational age <38 weeks and hyperbilirubinemia neurotoxicity risk factors), and for infants born at gestational age of ≥ 38 weeks with at least 1 hyperbilirubinemia neurotoxicity risk factor, the new threshold was set to 1 mg/dL above the threshold for infants at medium risk (defined above), and infants born at gestational age of 36 or 37 weeks were evenly spaced out between these 2 curves.

In addition to the change above, the new guideline takes into account the chronologic (ie, postmenstrual) age of the infant by increasing the phototherapy threshold. For example, by 7 days after birth, the phototherapy threshold for infants born at 39 weeks' gestation far reaches that for infants born at 40 weeks' gestation.

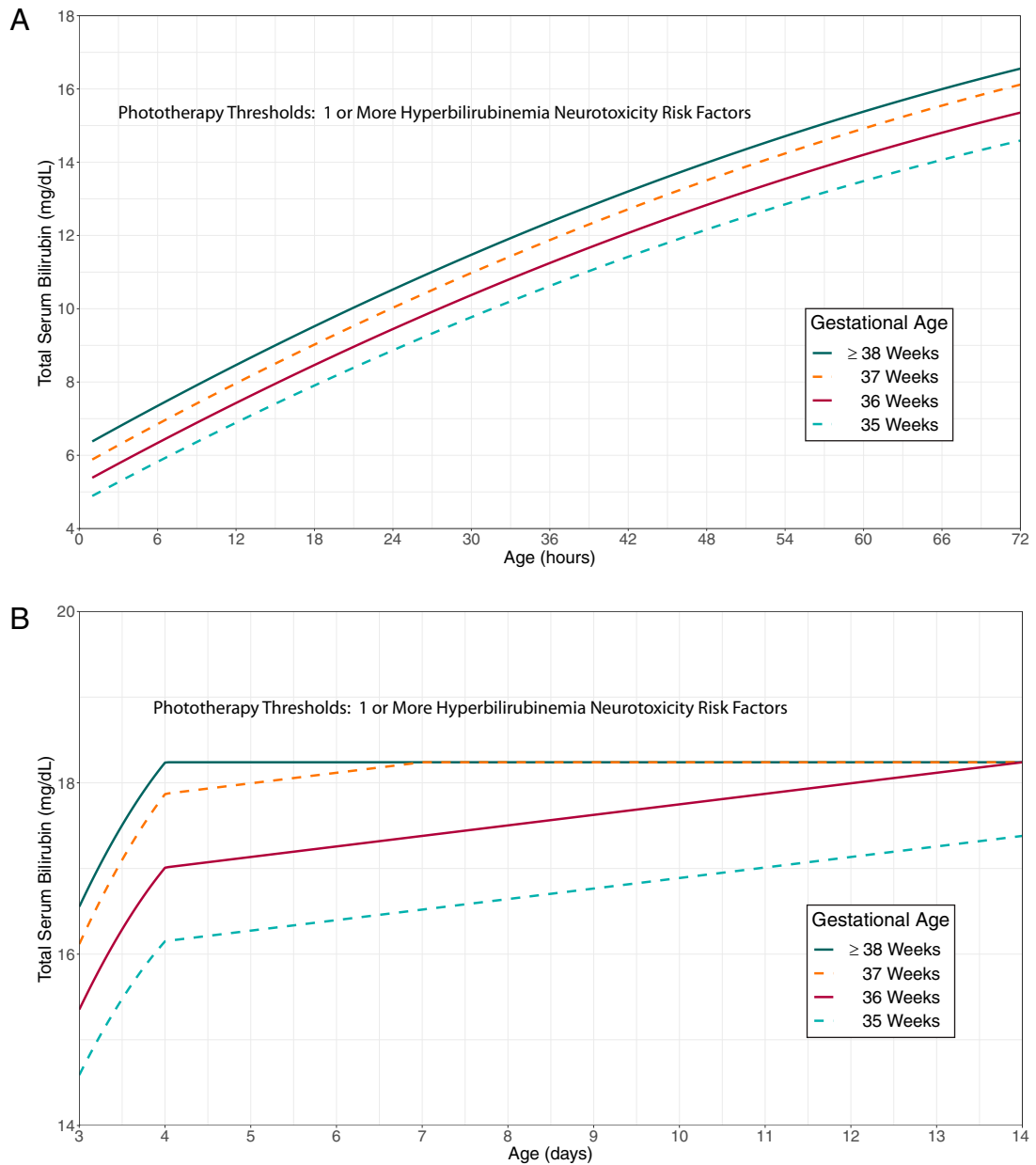
The exchange transfusion thresholds were developed by determining the difference between the exchange transfusion and phototherapy threshold for each group from the 2004 guideline and adding that difference to the new phototherapy thresholds in the current guideline.

The following tables list the specific thresholds for phototherapy and exchange transfusion shown in Figs 2, 3, 6, and 7. Each set of tables is followed by figures that illustrate the thresholds from birth to 72 hours and then from 72 hours (ie, 3 days) to 336 hours (ie, 14 days).



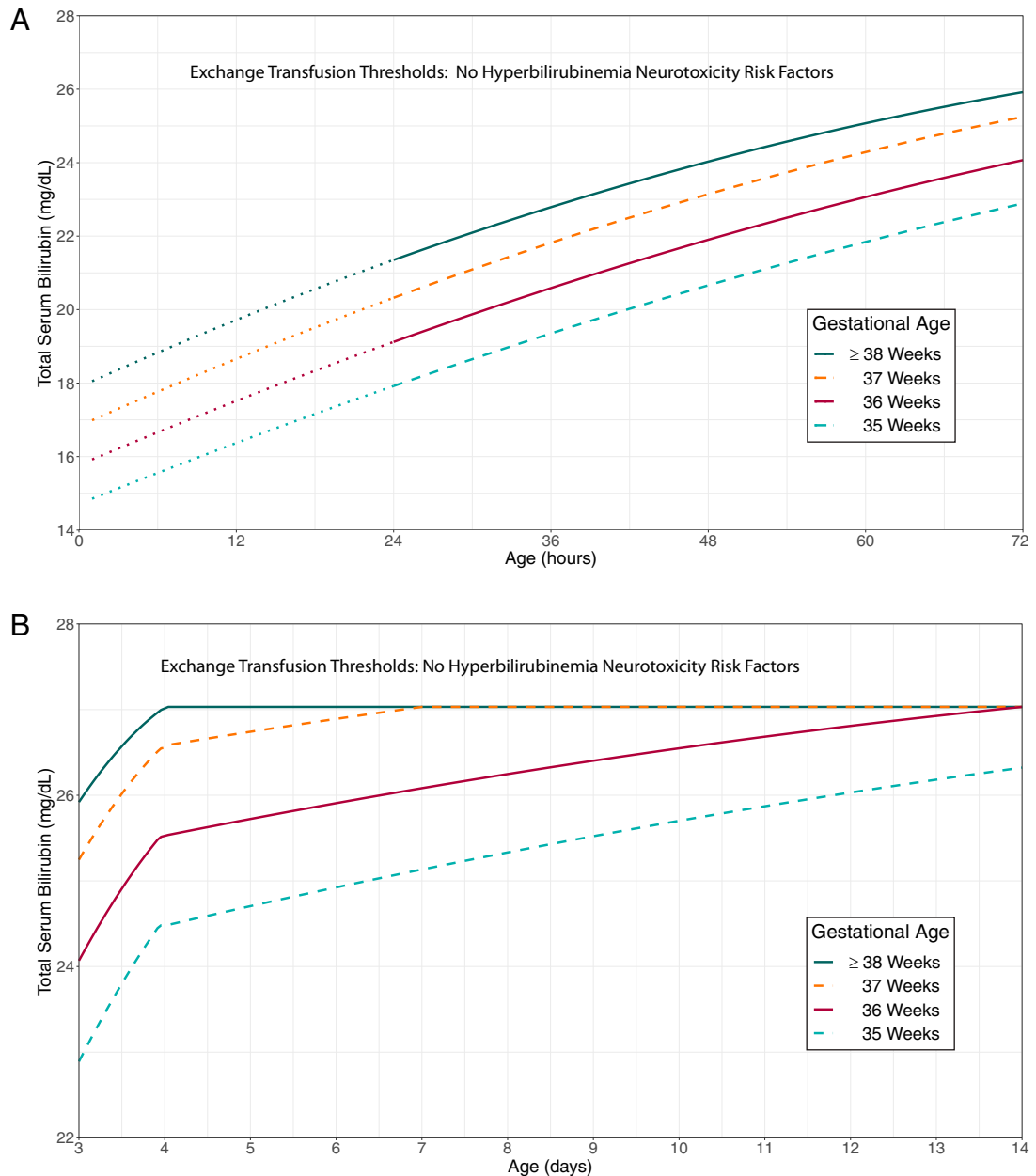
SUPPLEMENTAL FIGURE 1

A, Phototherapy thresholds by gestational age and age in hours for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age from birth to 72 hours (ie, 3 days). B, Phototherapy thresholds by gestational age and age in hours for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age from 3 to 14 days. This is an enlarged version of Fig 2. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of phototherapy exceed its potential harms. Use total serum bilirubin concentrations; do not subtract direct-reacting or conjugated bilirubin from the total serum bilirubin. In rare cases of severe hyperbilirubinemia in which the direct-reacting or conjugated bilirubin exceeds 50% of the TSB, consult an expert. Note that infants <24 hours old with a TSB at or above the phototherapy threshold are likely to have a hemolytic process and should be evaluated for hemolytic disease as described in recommendation 14. Hyperbilirubinemia neurotoxicity risk factors include gestational age <38 weeks; albumin <3.0 g/dL; isoimmune hemolytic disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, or other hemolytic conditions; sepsis; or any significant clinical instability in the previous 24 hours.



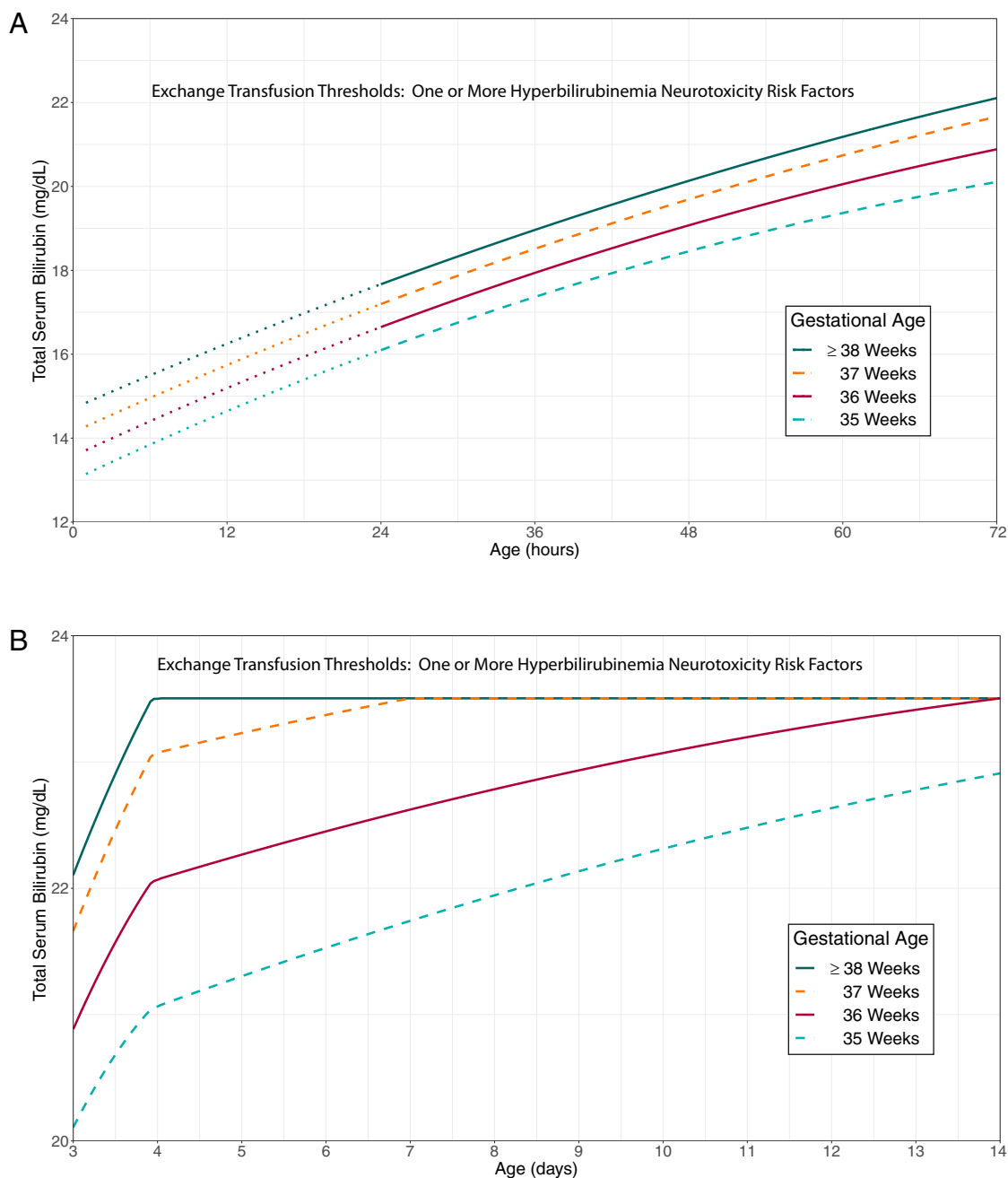
SUPPLEMENTAL FIGURE 2

A, Phototherapy thresholds by gestational age and age in hours for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age from birth to 72 hours (ie, 3 days). B, Phototherapy thresholds by gestational age and age in hours for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age from 3 to 14 days. This is an enlarged version of Fig 3. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of phototherapy exceed its potential harms. Use total serum bilirubin concentrations; do not subtract the direct-reacting or conjugated bilirubin from the total serum bilirubin. In rare cases of severe hyperbilirubinemia in which the direct-reacting or conjugated bilirubin exceeds 50% of the TSB, consult an expert. Hyperbilirubinemia neurotoxicity risk factors include gestational age <38 weeks; albumin <3.0 g/dL; isoimmune hemolytic disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, or other hemolytic conditions; sepsis; or any significant clinical instability in the previous 24 hours.



SUPPLEMENTAL FIGURE 3

A, Exchange transfusion thresholds by gestational age for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age from birth to 72 hours (ie, 3 days). B, Exchange transfusion thresholds by gestational age for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age from 3 to 14 days. This is an enlarged version of Fig 5. See Fig 4, which describes escalation of care. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of escalation of care exceed its potential harms. The stippled lines for the first 24 hours indicate uncertainty because of the wide range of clinical circumstances and responses to intensive phototherapy. Use total serum bilirubin concentrations; do not subtract direct bilirubin from the total serum bilirubin. In rare cases of severe hyperbilirubinemia in which the direct-reacting or conjugated bilirubin exceeds 50% of the TSB, consult an expert. Hyperbilirubinemia neurotoxicity risk factors include gestational age <38 weeks; albumin <3.0 g/dL; isoimmune hemolytic disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, or other hemolytic conditions; sepsis; or any significant clinical instability in the previous 24 hours.



SUPPLEMENTAL FIGURE 4

A, Exchange transfusion thresholds by gestational age for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age, from birth to 72 hours (ie, 3 days). B, Exchange transfusion thresholds by gestational age for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age from 3 to 14 days. This is an enlarged version of Fig 6. See Fig 4, which describes escalation of care. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of escalation of care exceed its potential harms. The stippled lines for the first 24 hours indicate uncertainty because of the wide range of clinical circumstances and responses to intensive phototherapy. Use total serum bilirubin concentrations; do not subtract direct bilirubin from the total serum bilirubin. In rare cases of severe hyperbilirubinemia in which the direct-reacting or conjugated bilirubin exceeds 50% of the TSB, consult an expert. Hyperbilirubinemia neurotoxicity risk factors include gestational age <38 weeks; albumin <3.0 g/dL; isoimmune hemolytic disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, or other hemolytic conditions, sepsis; or any significant clinical instability in the previous 24 hours. B, Exchange transfusion thresholds by gestational age for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age from 3 to 14 days.

SUPPLEMENTAL TABLE 1 Phototherapy thresholds by gestational age and age in hours for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. These thresholds, also provided in Fig 2, are based on expert opinion rather than strong evidence on when the potential benefits of phototherapy exceed its potential harms. Use the total serum bilirubin concentration. Do not subtract direct-reacting or conjugated bilirubin from the total serum bilirubin. Hyperbilirubinemia neurotoxicity risk factors include gestational age <38 weeks; albumin <3.0 g/dL; isoimmune hemolytic disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, or other hemolytic conditions; sepsis; or any significant clinical instability in the previous 24 hours.

Gestational age of 40 weeks or more and no hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

Day	Hour on Completed Day																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		8.9	9.1	9.3	9.6	9.8	10.0	10.2	10.4	10.5	10.7	10.9	11.1	11.3	11.5	11.7	11.9	12.1	12.2	12.4	12.6	12.8	13.0	13.1
1	13.3	13.5	13.6	13.8	14.0	14.1	14.3	14.5	14.6	14.8	15.0	15.1	15.3	15.4	15.6	15.7	15.9	16.0	16.2	16.3	16.4	16.6	16.7	16.9
2	17.0	17.1	17.3	17.4	17.5	17.7	17.8	17.9	18.0	18.2	18.3	18.4	18.5	18.6	18.8	18.9	19.0	19.1	19.2	19.3	19.4	19.6	19.7	19.7
3	19.8	19.9	20.0	20.1	20.2	20.3	20.4	20.5	20.6	20.7	20.7	20.8	20.9	21.0	21.1	21.1	21.2	21.3	21.4	21.4	21.5	21.6	21.6	21.7
4	21.8 ^a	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8

^aThe threshold ≥ 96 h (eg, 4 completed days) after birth is 21.8 mg/dL.

Gestational age of 39 weeks and no hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

Day	Hour on Completed Day																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		8.4	8.6	8.8	9.0	9.3	9.5	9.7	9.9	10.0	10.2	10.4	10.6	10.8	11.0	11.2	11.4	11.6	11.8	11.9	12.1	12.3	12.5	12.7
1	12.8	13.0	13.2	13.3	13.5	13.7	13.8	14.0	14.2	14.3	14.5	14.7	14.8	15.0	15.1	15.3	15.4	15.6	15.7	15.9	16.0	16.2	16.3	16.4
2	16.6	16.7	16.8	17.0	17.1	17.2	17.4	17.5	17.6	17.8	17.9	18.0	18.1	18.2	18.4	18.5	18.6	18.7	18.8	18.9	19.0	19.1	19.2	19.3
3	19.5	19.6	19.7	19.7	19.8	19.9	20.0	20.1	20.2	20.3	20.4	20.5	20.6	20.6	20.7	20.8	20.9	21.0	21.0	21.1	21.2	21.3	21.3	21.4
4	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6
5	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7
6	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.8 ^a	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8

^aThe threshold ≥ 157 h (eg, 6 completed days and 13 h) after birth is 21.8 mg/dL.

Gestational age of 38 weeks and no hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

Day	Hour on Completed Day																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		7.9	8.1	8.3	8.5	8.7	8.9	9.1	9.3	9.5	9.7	9.9	10.1	10.3	10.5	10.7	10.8	11.0	11.2	11.4	11.6	11.7	11.9	12.1
1	12.3	12.4	12.6	12.8	12.9	13.1	13.3	13.4	13.6	13.8	13.9	14.1	14.2	14.4	14.5	14.7	14.8	15.0	15.1	15.3	15.4	15.6	15.7	15.8
2	16.0	16.1	16.2	16.4	16.5	16.6	16.8	16.9	17.0	17.1	17.3	17.4	17.5	17.6	17.7	17.8	17.9	18.1	18.2	18.3	18.4	18.5	18.6	18.7
3	18.8	18.9	19.0	19.1	19.2	19.3	19.4	19.5	19.5	19.6	19.7	19.8	19.9	20.0	20.0	20.1	20.2	20.3	20.3	20.4	20.5	20.6	20.6	20.7
4	20.7	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.9	20.9	20.9	20.9	20.9
5	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	21.0	21.0	21.0	21.0	21.0	21.0
6	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.1	21.1	21.1	21.1	21.1	21.1
7	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.2	21.2	21.2	21.2	21.2	21.2
8	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.3	21.3	21.3	21.3	21.3	21.3
9	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4
10	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5
11	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6
12	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7
13	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.8 ^a	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8

^aThe threshold ≥ 325 h (eg, 13 completed days and 13 h) after birth is 21.8 mg/dL.

Gestational age of 37 weeks and no hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

Day	Hour on Completed Day																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		7.4	7.6	7.8	8.0	8.2	8.4	8.6	8.8	9.0	9.2	9.4	9.6	9.8	9.9	10.1	10.3	10.5	10.7	10.8	11.0	11.2	11.4	11.5
1	11.7	11.9	12.1	12.2	12.4	12.5	12.7	12.9	13.0	13.2	13.3	13.5	13.6	13.8	13.9	14.1	14.2	14.4	14.5	14.7	14.8	15.0	15.1	15.2
2	15.4	15.5	15.6	15.8	15.9	16.0	16.1	16.3	16.4	16.5	16.6	16.7	16.9	17.0	17.1	17.2	17.3	17.4	17.5	17.6	17.7	17.8	17.9	18.0
3	18.1	18.2	18.3	18.4	18.5	18.6	18.7	18.8	18.9	19.0	19.0	19.1	19.2	19.3	19.4	19.4	19.5	19.6	19.7	19.7	19.8	19.9	19.9	20.0
4	20.0	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1
5	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.3
6	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.4	20.4
7	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.5	20.5	20.5
8	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.6	20.6	20.6
9	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.7	20.7	20.7
10	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.8	20.8	20.8	20.8	20.8
11	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.9	20.9	20.9	20.9	20.9
12	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	21.0	21.0	21.0	21.0	21.0	21.0
13	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.1	21.1	21.1	21.1	21.1	21.1
14	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1

Gestational age of 36 weeks and no hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

Day	Hour on Completed Day																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		6.9	7.1	7.3	7.5	7.7	7.9	8.1	8.3	8.5	8.7	8.8	9.0	9.2	9.4	9.6	9.8	9.9	10.1	10.3	10.5	10.6	10.8	11.0
1	11.2	11.3	11.5	11.7	11.8	12.0	12.1	12.3	12.5	12.6	12.8	12.9	13.1	13.2	13.4	13.5	13.7	13.8	13.9	14.1	14.2	14.4	14.5	14.6
2	14.8	14.9	15.0	15.1	15.3	15.4	15.5	15.6	15.8	15.9	16.0	16.1	16.2	16.3	16.5	16.6	16.7	16.8	16.9	17.0	17.1	17.2	17.3	17.4
3	17.5	17.6	17.7	17.8	17.9	17.9	18.0	18.1	18.2	18.3	18.4	18.4	18.5	18.6	18.7	18.8	18.8	18.9	19.0	19.0	19.1	19.2	19.2	19.3
4	19.3	19.3	19.3	19.3	19.3	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4
5	19.4	19.4	19.4	19.4	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5
6	19.5	19.5	19.5	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6
7	19.6	19.6	19.6	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7
8	19.7	19.7	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8
9	19.8	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9
10	19.9	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0
11	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1
12	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2
13	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.4	20.4
14	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4

Gestational age of 35 weeks and no hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

Day	Hour on Completed Day																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		6.4	6.6	6.8	7.0	7.2	7.4	7.6	7.8	7.9	8.1	8.3	8.5	8.7	8.9	9.0	9.2	9.4	9.6	9.8	9.9	10.1	10.3	10.4
1	10.6	10.8	10.9	11.1	11.3	11.4	11.6	11.7	11.9	12.0	12.2	12.3	12.5	12.6	12.8	12.9	13.1	13.2	13.4	13.5	13.6	13.8	13.9	14.0
2	14.2	14.3	14.4	14.5	14.7	14.8	14.9	15.0	15.1	15.3	15.4	15.5	15.6	15.7	15.8	15.9	16.0	16.1	16.2	16.3	16.4	16.5	16.6	16.7
3	16.8	16.9	17.0	17.1	17.2	17.3	17.4	17.5	17.6	17.7	17.8	17.8	17.9	18.0	18.1	18.1	18.2	18.3	18.3	18.4	18.5	18.5	18.6	18.6
4	18.6	18.6	18.6	18.6	18.6	18.6	18.6	18.6	18.6	18.6	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7
5	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8
6	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9
7	18.9	18.9	18.9	18.9	18.9	18.9	18.9	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0
8	19.0	19.0	19.0	19.0	19.0	19.0	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1
9	19.1	19.1	19.1	19.1	19.1	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2
10	19.2	19.2	19.2	19.2	19.2	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3
11	19.3	19.3	19.3	19.3	19.3	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4
12	19.4	19.4	19.4	19.4	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5
13	19.5	19.5	19.5	19.5	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6
14	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6

SUPPLEMENTAL TABLE 2 Phototherapy thresholds by gestational age and age in hours for infants with a recognized hyperbilirubinemia neurotoxicity risk factor. These thresholds, also provided in Fig 3, are based on expert opinion rather than strong evidence on when the potential benefits of phototherapy exceed its potential harms. Use the total serum bilirubin concentration. Do not subtract direct-reacting or conjugated bilirubin from the total serum bilirubin. Hyperbilirubinemia neurotoxicity risk factors include gestational age <38 weeks; albumin <3.0 g/dL; isoimmune hemolytic disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, or other hemolytic conditions; sepsis; or any significant clinical instability in the previous 24 hours.

Gestational age of 38 weeks or more and a hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

Day	Hour on Completed Day																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		6.4	6.6	6.8	7.0	7.2	7.3	7.5	7.7	7.9	8.1	8.3	8.5	8.6	8.8	9.0	9.2	9.4	9.5	9.7	9.9	10.0	10.2	10.4
1	10.5	10.7	10.8	11.0	11.2	11.3	11.5	11.6	11.8	11.9	12.1	12.2	12.4	12.5	12.7	12.8	12.9	13.1	13.2	13.3	13.5	13.6	13.7	13.9
2	14.0	14.1	14.2	14.4	14.5	14.6	14.7	14.8	14.9	15.1	15.2	15.3	15.4	15.5	15.6	15.7	15.8	15.9	16.0	16.1	16.2	16.3	16.4	16.5
3	16.6	16.6	16.7	16.8	16.9	17.0	17.1	17.1	17.2	17.3	17.4	17.4	17.5	17.6	17.6	17.7	17.8	17.8	17.9	18.0	18.0	18.1	18.1	18.2
4	18.2 ^a	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2

^aThe threshold ≥96 h (eg, 4 completed days) after birth is 18.2 mg/dL.

Gestational age of 37 and an additional hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

Day	Hour on Completed Day																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		5.9	6.1	6.3	6.5	6.7	6.9	7.0	7.2	7.4	7.6	7.8	8.0	8.1	8.3	8.5	8.7	8.9	9.0	9.2	9.4	9.5	9.7	9.9
1	10.0	10.2	10.4	10.5	10.7	10.8	11.0	11.1	11.3	11.4	11.6	11.7	11.9	12.0	12.2	12.3	12.4	12.6	12.7	12.9	13.0	13.1	13.2	13.4
2	13.5	13.6	13.8	13.9	14.0	14.1	14.2	14.4	14.5	14.6	14.7	14.8	14.9	15.0	15.1	15.2	15.3	15.4	15.5	15.6	15.7	15.8	15.9	16.0
3	16.1	16.2	16.3	16.4	16.5	16.6	16.6	16.7	16.8	16.9	17.0	17.1	17.2	17.2	17.3	17.4	17.4	17.5	17.6	17.6	17.7	17.7	17.8	17.8
4	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0
5	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1
6	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.2 ^a	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2

^aThe threshold ≥151 h (eg, 6 completed days and 7 h) after birth is 18.2 mg/dL.

Gestational age of 36 and an additional hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

Day	Hour on Completed Day																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		5.4	5.6	5.8	6.0	6.2	6.3	6.5	6.7	6.9	7.1	7.3	7.4	7.6	7.8	8.0	8.1	8.3	8.5	8.6	8.8	9.0	9.1	9.3
1	9.4	9.6	9.8	9.9	10.1	10.2	10.4	10.5	10.7	10.8	11.0	11.1	11.2	11.4	11.5	11.7	11.8	11.9	12.1	12.2	12.3	12.5	12.6	12.7
2	12.8	13.0	13.1	13.2	13.3	13.4	13.5	13.7	13.8	13.9	14.0	14.1	14.2	14.3	14.4	14.5	14.6	14.7	14.8	14.9	15.0	15.1	15.2	15.3
3	15.4	15.4	15.5	15.6	15.7	15.8	15.8	15.9	16.0	16.1	16.1	16.2	16.3	16.4	16.4	16.5	16.6	16.6	16.7	16.7	16.8	16.8	16.9	17.0
4	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1
5	17.1	17.1	17.1	17.1	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.3
6	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.4	17.4	17.4	17.4
7	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5
8	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.6	17.6	17.6	17.6	17.6	17.6	17.6	17.6	17.6	17.6	17.6	17.6	17.6	17.6
9	17.6	17.6	17.6	17.6	17.6	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7
10	17.7	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.9	17.9	17.9
11	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0
12	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1
13	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2
14	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2

Gestational age of 35 and an additional hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

Day	Hour on Completed Day																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		4.9	5.1	5.3	5.5	5.6	5.8	6.0	6.2	6.4	6.5	6.7	6.9	7.1	7.2	7.4	7.6	7.7	7.9	8.1	8.2	8.4	8.6	8.7
1	8.9	9.0	9.2	9.3	9.5	9.6	9.8	9.9	10.1	10.2	10.3	10.5	10.6	10.8	10.9	11.0	11.2	11.3	11.4	11.5	11.7	11.8	11.9	12.0
2	12.2	12.3	12.4	12.5	12.6	12.7	12.8	13.0	13.1	13.2	13.3	13.4	13.5	13.6	13.7	13.8	13.9	14.0	14.1	14.2	14.2	14.3	14.4	14.5
3	14.6	14.7	14.8	14.8	14.9	15.0	15.1	15.1	15.2	15.3	15.3	15.4	15.5	15.5	15.6	15.7	15.7	15.8	15.8	15.9	15.9	16.0	16.1	16.1
4	16.1	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.3	16.3	16.3
5	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.4	16.4	16.4	16.4	16.4	16.4	16.4	16.4	16.4
6	16.4	16.4	16.4	16.4	16.4	16.4	16.4	16.4	16.4	16.4	16.4	16.5	16.5	16.5	16.5	16.5	16.5	16.5	16.5	16.5	16.5	16.5	16.5	16.5
7	16.5	16.5	16.5	16.5	16.5	16.5	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6
8	16.6	16.6	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.8	16.8	16.8
9	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.9	16.9	16.9	16.9	16.9	16.9
10	16.9	16.9	16.9	16.9	16.9	16.9	16.9	16.9	16.9	16.9	16.9	16.9	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0
11	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1
12	17.1	17.1	17.1	17.1	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.3
13	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.4	17.4	17.4	17.4
14	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4

SUPPLEMENTAL TABLE 3 Exchange transfusion thresholds by gestational age for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. These thresholds, also provided in Fig 6, are based on expert opinion rather than strong evidence on when the potential benefits of exchange transfusion exceed its potential harms. Use the total serum bilirubin concentration. Do not subtract direct-reacting or conjugated bilirubin from the total serum bilirubin. Hyperbilirubinemia neurotoxicity risk factors include gestational age <38 weeks; albumin <3.0 g/dL; isoimmune hemolytic disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, or other hemolytic conditions; sepsis; or any significant clinical instability in the previous 24 hours.

Gestational age of 38 weeks or more and no hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

Day	Hour on Completed Day																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		18.0	18.2	18.4	18.5	18.7	18.8	19.0	19.1	19.3	19.4	19.6	19.7	19.9	20.0	20.1	20.3	20.4	20.6	20.7	20.8	21.0	21.1	21.2
1	21.4	21.5	21.6	21.7	21.9	22.0	22.1	22.2	22.3	22.4	22.6	22.7	22.8	22.9	23.0	23.1	23.2	23.3	23.4	23.5	23.6	23.7	23.8	23.9
2	24.0	24.1	24.2	24.3	24.4	24.5	24.6	24.7	24.7	24.8	24.9	25.0	25.1	25.2	25.2	25.3	25.4	25.5	25.5	25.6	25.7	25.7	25.8	25.9
3	25.9	26.0	26.0	26.1	26.2	26.2	26.3	26.3	26.4	26.4	26.5	26.5	26.6	26.6	26.7	26.7	26.7	26.8	26.8	26.9	26.9	26.9	27.0	27.0
4	27.0 ^a	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0

^aThe threshold ≥ 96 h (eg, 4 completed days) after birth is 27 mg/dL.

Gestational age of 37 weeks and no hyperbilirubinemia neurotoxicity risk factor other than gestational age. The threshold is TSB in mg/dL.

Day	Hour on Completed Day																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		17.0	17.1	17.3	17.5	17.6	17.8	17.9	18.1	18.2	18.4	18.5	18.7	18.8	18.9	19.1	19.2	19.4	19.5	19.6	19.8	19.9	20.1	20.2
1	20.3	20.5	20.6	20.7	20.8	21.0	21.1	21.2	21.3	21.5	21.6	21.7	21.8	21.9	22.1	22.2	22.3	22.4	22.5	22.6	22.7	22.8	22.9	23.0
2	23.1	23.2	23.3	23.4	23.5	23.6	23.7	23.8	23.9	24.0	24.1	24.2	24.3	24.4	24.5	24.5	24.6	24.7	24.8	24.9	24.9	25.0	25.1	25.2
3	25.2	25.3	25.4	25.5	25.5	25.6	25.7	25.7	25.8	25.8	25.9	26.0	26.0	26.1	26.1	26.2	26.2	26.3	26.3	26.4	26.4	26.5	26.5	26.5
4	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7
5	26.7	26.7	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.9	26.9	26.9	26.9	26.9
6	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	27.0 ^a	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0

^aThe threshold ≥ 151 h (eg, 6 completed days and 10 h) after birth is 27.0 mg/dL.

Gestational age of 36 weeks and no hyperbilirubinemia neurotoxicity risk factor other than gestational age. The threshold is TSB in mg/dL.

Day	Hour on Completed Day																								
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	
0		15.9	16.1	16.2	16.4	16.5	16.7		16.8	16.9	17.1	17.2	17.4	17.5	17.7	17.8	17.9	18.1	18.2	18.3	18.5	18.6	18.7	18.9	19.0
1	19.1	19.2	19.4	19.5	19.6	19.7	19.9		20.0	20.1	20.2	20.4	20.5	20.6	20.7	20.8	20.9	21.0	21.2	21.3	21.4	21.5	21.6	21.7	21.8
2	21.9	22.0	22.1	22.2	22.3	22.4	22.5		22.6	22.7	22.8	22.9	23.0	23.1	23.2	23.2	23.3	23.4	23.5	23.6	23.7	23.8	23.9	24.0	
3	24.1	24.1	24.2	24.3	24.4	24.4	24.5		24.6	24.6	24.7	24.8	24.8	24.9	25.0	25.0	25.1	25.2	25.2	25.3	25.3	25.4	25.4	25.5	25.5
4	25.5	25.5	25.5	25.6	25.6	25.6	25.6		25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.7	25.7	25.7	25.7	25.7	25.7	25.7	25.7	25.7
5	25.7	25.7	25.7	25.7	25.8	25.8	25.8		25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.9	25.9	25.9	25.9	25.9	25.9	25.9
6	25.9	25.9	25.9	25.9	25.9	25.9	26.0		26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.1	26.1	26.1	26.1
7	26.1	26.1	26.1	26.1	26.1	26.1	26.1		26.1	26.1	26.1	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2
8	26.2	26.3	26.3	26.3	26.3	26.3	26.3		26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.4	26.4	26.4	26.4	26.4	26.4	26.4	26.4
9	26.4	26.4	26.4	26.4	26.4	26.4	26.4		26.4	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5
10	26.5	26.6	26.6	26.6	26.6	26.6	26.6		26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.7	26.7	26.7	26.7
11	26.7	26.7	26.7	26.7	26.7	26.7	26.7		26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8
12	26.8	26.8	26.8	26.8	26.8	26.8	26.8		26.8	26.8	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9
13	26.9	26.9	26.9	26.9	26.9	26.9	27.0		27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0
14	27.0	27.0	27.0	27.0	27.0	27.0	27.0		27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0

Gestational age of 35 weeks and no hyperbilirubinemia neurotoxicity risk factor other than gestational age. The threshold is TSB in mg/dL.

Day	Hour on Completed Day																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		14.9	15.0	15.1	15.3	15.4	15.6	15.7	15.8	16.0	16.1	16.2	16.4	16.5	16.6	16.8	16.9	17.0	17.2	17.3	17.4	17.5	17.7	17.8
1	17.9	18.0	18.2	18.3	18.4	18.5	18.7	18.8	18.9	19.0	19.1	19.2	19.4	19.5	19.6	19.7	19.8	19.9	20.0	20.1	20.2	20.3	20.5	20.6
2	20.7	20.8	20.9	21.0	21.1	21.2	21.3	21.4	21.5	21.6	21.7	21.7	21.8	21.9	22.0	22.1	22.2	22.3	22.4	22.5	22.6	22.6	22.7	22.8
3	22.9	23.0	23.1	23.1	23.2	23.3	23.4	23.4	23.5	23.6	23.7	23.7	23.8	23.9	23.9	24.0	24.1	24.1	24.2	24.3	24.3	24.4	24.4	24.5
4	24.5	24.5	24.5	24.5	24.5	24.5	24.5	24.5	24.6	24.6	24.6	24.6	24.6	24.6	24.6	24.6	24.6	24.6	24.6	24.6	24.7	24.7	24.7	24.7
5	24.7	24.7	24.7	24.7	24.7	24.8	24.8	24.8	24.8	24.8	24.8	24.8	24.8	24.8	24.8	24.8	24.9	24.9	24.9	24.9	24.9	24.9	24.9	24.9
6	24.9	24.9	24.9	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.1	25.1	25.1	25.1	25.1	25.1	25.1	25.1	25.1
7	25.1	25.1	25.2	25.2	25.2	25.2	25.2	25.2	25.2	25.2	25.2	25.2	25.2	25.2	25.3	25.3	25.3	25.3	25.3	25.3	25.3	25.3	25.3	25.3
8	25.3	25.3	25.3	25.4	25.4	25.4	25.4	25.4	25.4	25.4	25.4	25.4	25.4	25.4	25.4	25.5	25.5	25.5	25.5	25.5	25.5	25.5	25.5	25.5
9	25.5	25.5	25.5	25.5	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.7	25.7	25.7	25.7	25.7
10	25.7	25.7	25.7	25.7	25.7	25.7	25.7	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.9	25.9
11	25.9	25.9	25.9	25.9	25.9	25.9	25.9	25.9	25.9	25.9	25.9	25.9	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0
12	26.0	26.0	26.0	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.2	26.2	26.2	26.2
13	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3
14	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3

SUPPLEMENTAL TABLE 4 Exchange transfusion thresholds by gestational age for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. These thresholds, also provided in Fig 7, are based on expert opinion rather than strong evidence on when the potential benefits of exchange transfusion exceed its potential harms. Use the total serum bilirubin concentration. Do not subtract direct-reacting or conjugated bilirubin from the total serum bilirubin. Hyperbilirubinemia neurotoxicity risk factors include gestational age <38 weeks; albumin <3.0 g/dL; isoimmune hemolytic disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, or other hemolytic conditions, sepsis; or any significant clinical instability in the previous 24 hours.

Gestational age of 38 weeks or more and any hyperbilirubinemia neurotoxicity risk factors. The threshold is TSB in mg/dL.

Day	Hour on Completed Day																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		14.8	15.0	15.1	15.2	15.4	15.5	15.6	15.8	15.9	16.0	16.1	16.3	16.4	16.5	16.6	16.7	16.9	17.0	17.1	17.2	17.3	17.4	17.6
1	17.7	17.8	17.9	18.0	18.1	18.2	18.3	18.4	18.5	18.7	18.8	18.9	19.0	19.1	19.2	19.3	19.4	19.5	19.6	19.7	19.8	19.9	19.9	20.0
2	20.1	20.2	20.3	20.4	20.5	20.6	20.7	20.8	20.8	20.9	21.0	21.1	21.2	21.3	21.3	21.4	21.5	21.6	21.7	21.7	21.8	21.9	22.0	22.0
3	22.1	22.2	22.2	22.3	22.4	22.5	22.5	22.6	22.7	22.7	22.8	22.8	22.9	23.0	23.0	23.1	23.1	23.2	23.3	23.3	23.4	23.4	23.5	23.5
4	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
6	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
7	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
8	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
9	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
10	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
11	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
12	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
13	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
14	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5

Reference for Phototherapy and Exchange Transfusion Thresholds

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