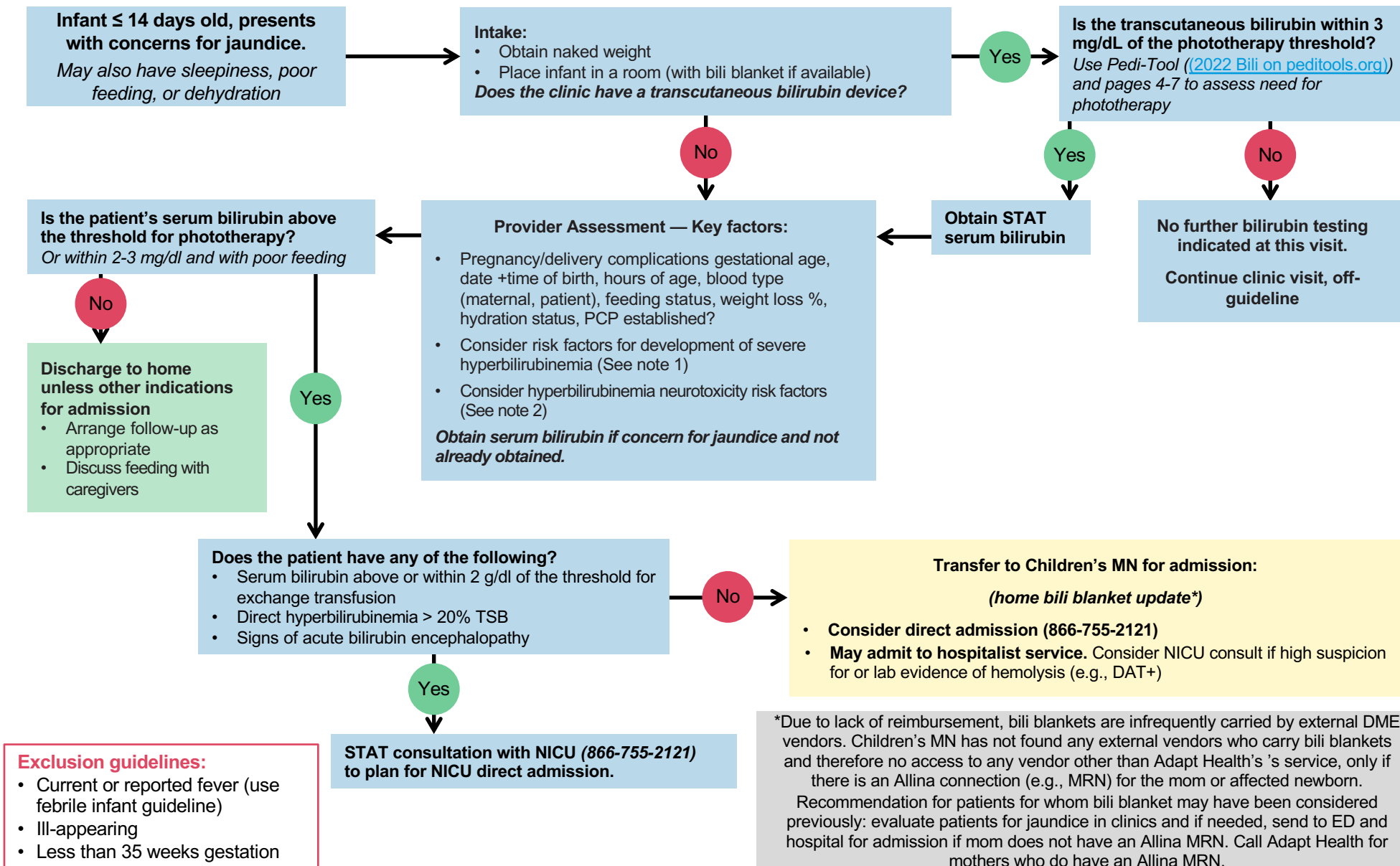
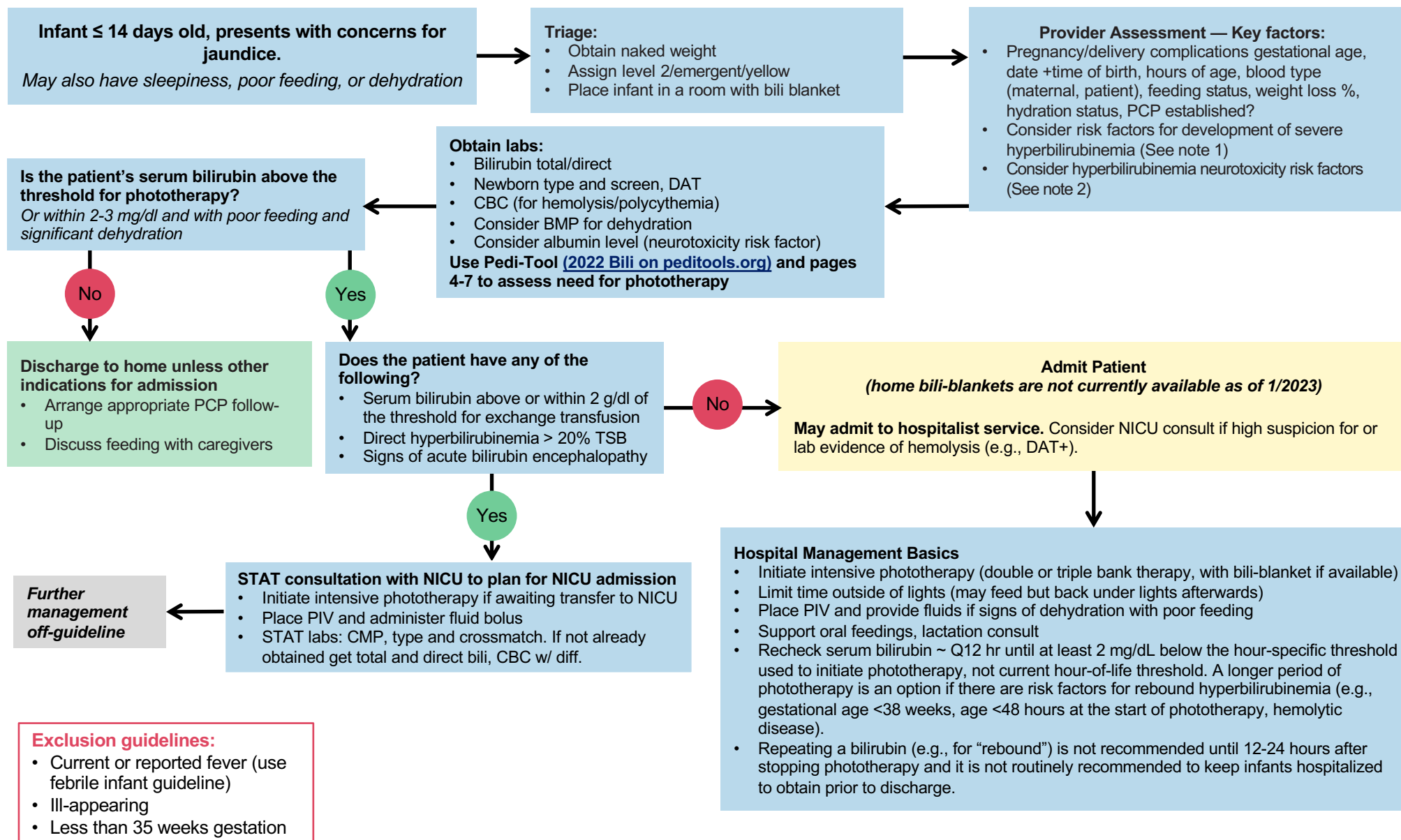


Aim: Facilitate evaluation and management of hyperbilirubinemia in newborns.



Aim: Facilitate evaluation and management of hyperbilirubinemia in newborns.



**Note 1. Major risk factors for development of severe hyperbilirubinemia (per AAP 2021 guideline):**

- Lower gestational age (ie, risk increases with each additional week less than 40 wk)
- Jaundice in the first 24 h after birth
- Pre-discharge (birth hospitalization) transcutaneous bilirubin (TcB) or total serum bilirubin (TSB) concentration close to the phototherapy threshold
- Hemolysis from any cause, if known or suspected based on a rapid rate of increase in the TSB or TcB of  $>0.3$  mg/dL per hour in the first 24 h or  $>0.2$  mg/dL per hour thereafter.
- Phototherapy before discharge from birth hospitalization
- Parent or sibling requiring phototherapy or exchange transfusion
- Family history or genetic ancestry suggestive of inherited red blood cell disorders, including glucose-6-phosphate dehydrogenase (G6PD) deficiency
- Exclusive breastfeeding with suboptimal intake
- Scalp hematoma or significant bruising
- Trisomy 21
- Macrosomic infant of a diabetic mother

**Note 2. Hyperbilirubinemia neurotoxicity risk factors**

- Gestational age  $<38$  wk and this risk increases with the degree of prematurity
- Albumin  $<3.0$  g/dL
- Isoimmune hemolytic disease (ie, positive direct antiglobulin test), G6PD deficiency, or other hemolytic conditions
- Sepsis
- Significant clinical instability in the previous 24 h

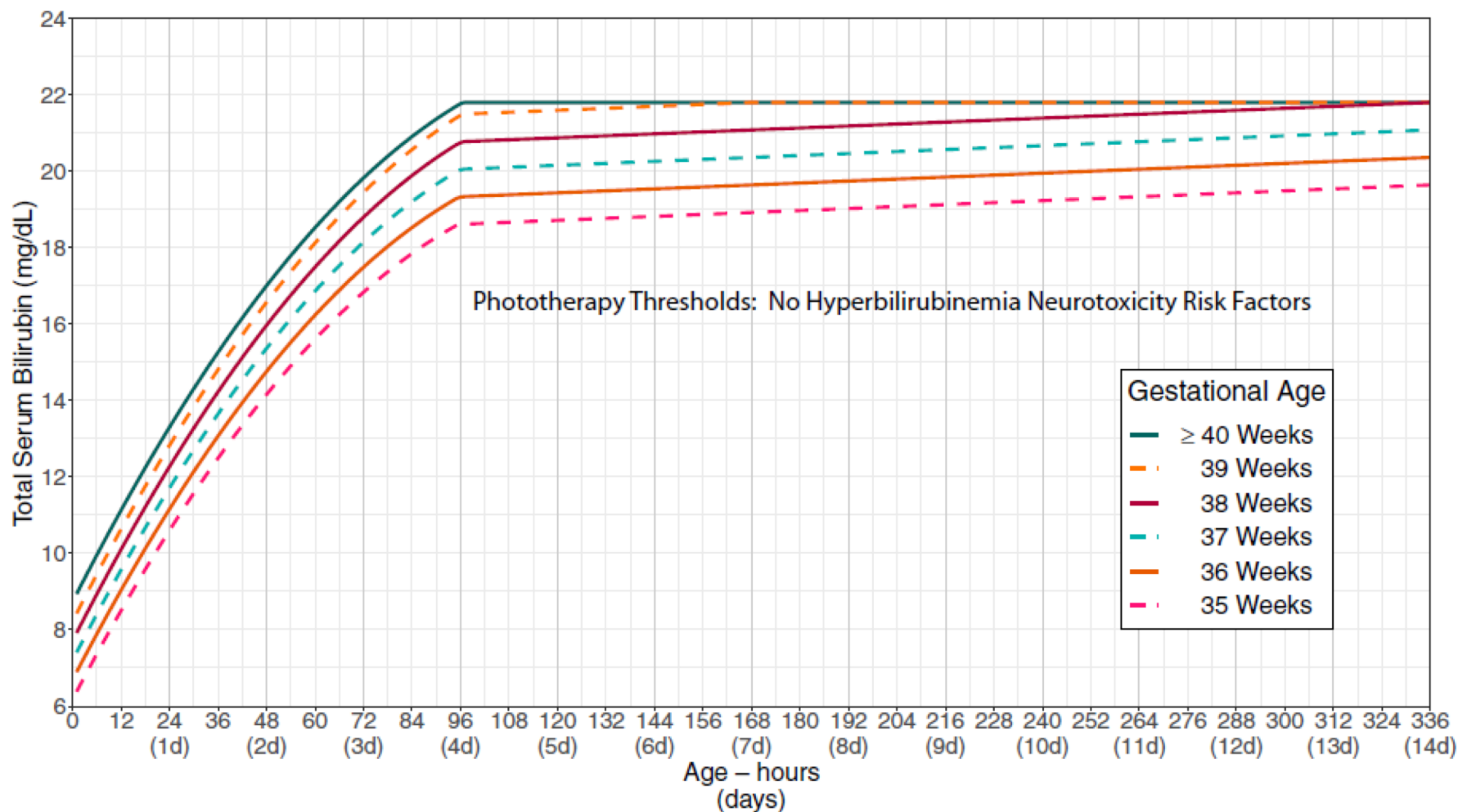
**Note 3. G-6-PD information**

- Glucose-6-phosphate dehydrogenase (G6PD) deficiency, an X-linked recessive enzymopathy that decreases protection against oxidative stress, is one of the most important causes of hyperbilirubinemia leading to kernicterus in the US and across the globe.
- Most affected infants will not have a positive family history.
- Even after what appears to be an acute hemolytic event, there may be little or no laboratory evidence of hemolysis
  - If G6PD deficiency is strongly suspected but the measurement of G6PD activity is normal or close to normal, the G6PD activity should be measured at least 3 months later.
- There are clinical events that should raise suspicion about the presence of G6PD deficiency.
  - Newborn infants with G6PD deficiency are more likely to receive phototherapy before hospital discharge probably because of both increased bilirubin production and decreased conjugation and have a greater risk of readmission and retreatment.
  - Severe hyperbilirubinemia or atypical development of hyperbilirubinemia, such as elevated TSB in a formula-fed infant or late-onset jaundice, should raise the possibility of G6PD deficiency.

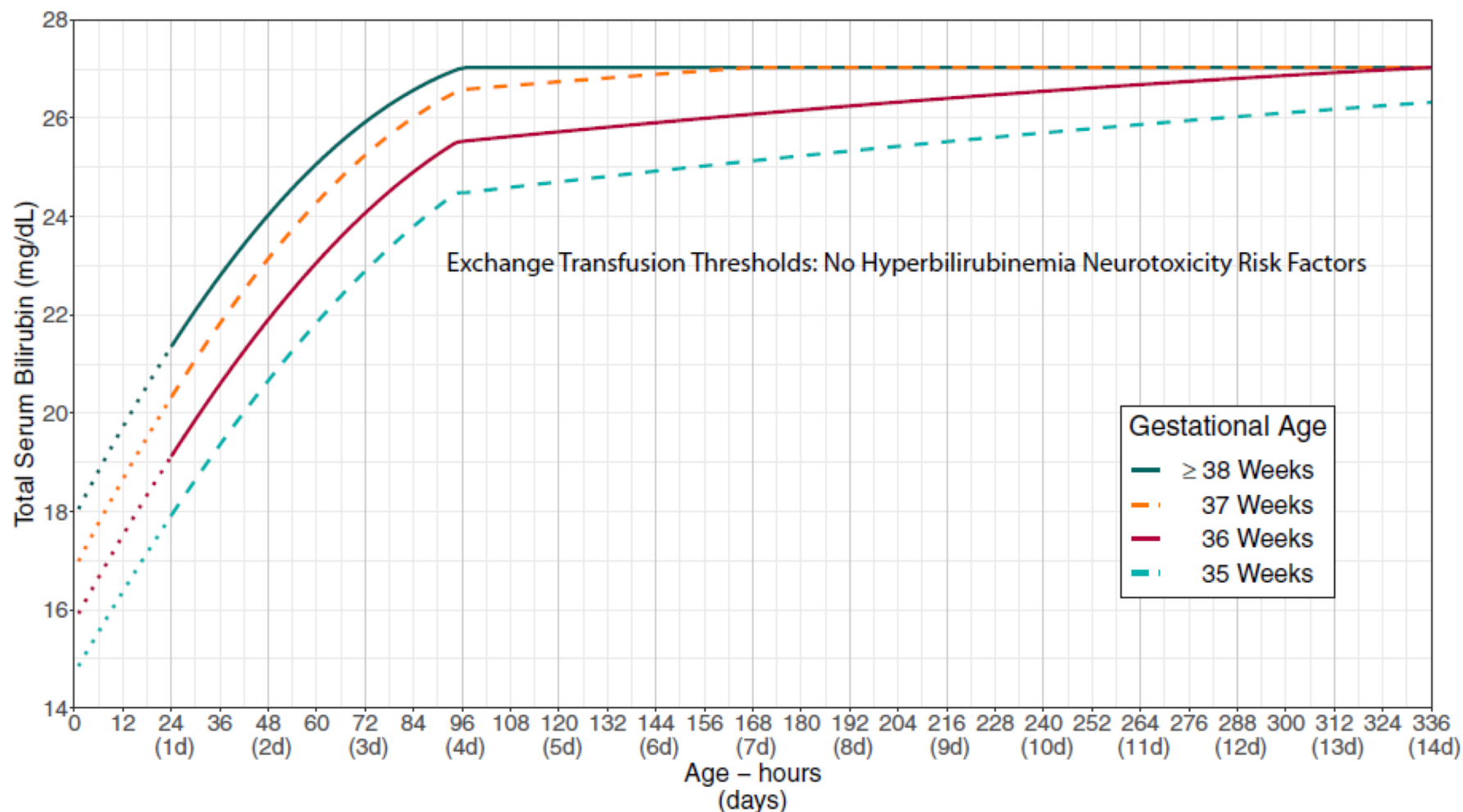
**REFERENCES**

- Kemper AR, Newman TB, Slaughter JL, Maisels MJ, Watchko JF, Downs SM, Grout RW, Bundy DG, Stark AR, Bogen DL, Holmes AV, Feldman-Winter LB, Bhutani VK, Brown SR, Maradiaga Panayotti GM, Okechukwu K, Rappo PD, Russell TL. Clinical Practice Guideline Revision: Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation. *Pediatrics*. 2022 Sep 1;150(3):e2022058859. doi: 10.1542/peds.2022-058859. PMID: 35927462.
- Slaughter JL, Kemper AR, Newman TB. Technical Report: Diagnosis and Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation. *Pediatrics*. 2022 Sep 1;150(3):e2022058865. doi: 10.1542/peds.2022-058865. PMID: 35927519.
- [\(2022\) Hyperbilirubinemia management guidelines \(peditools.org\)](https://peditools.org/)

**Workgroup:** Hester, Street, Chawla, George, Bloomquist, Palmer, Shutak, Smeltzer, Sicoli, Therien



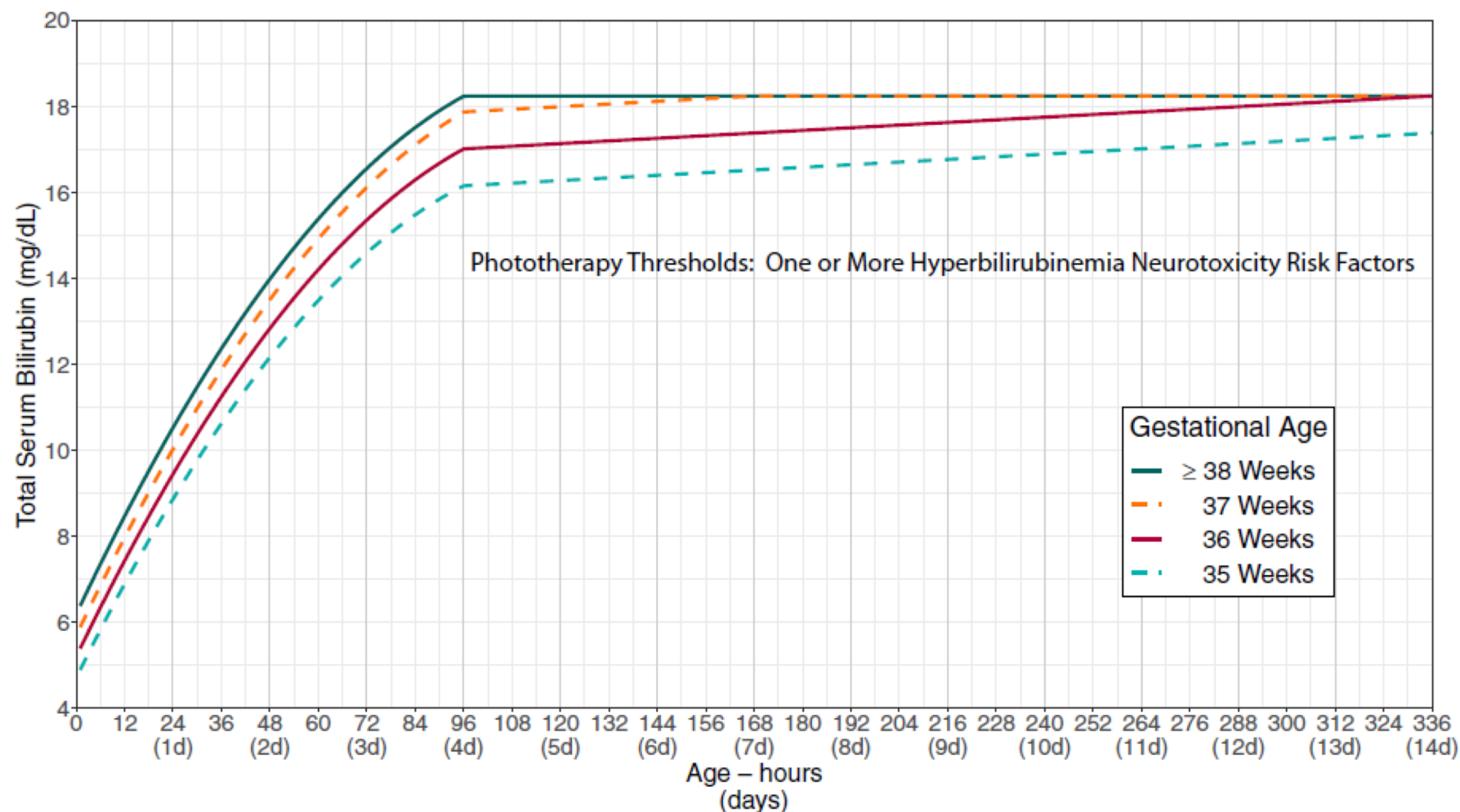
Per AAP 2021 Guideline: Phototherapy thresholds by gestational age and age in hours for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of phototherapy 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.



Per AAP 2021 Guideline: Exchange transfusion thresholds by gestational age for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age.

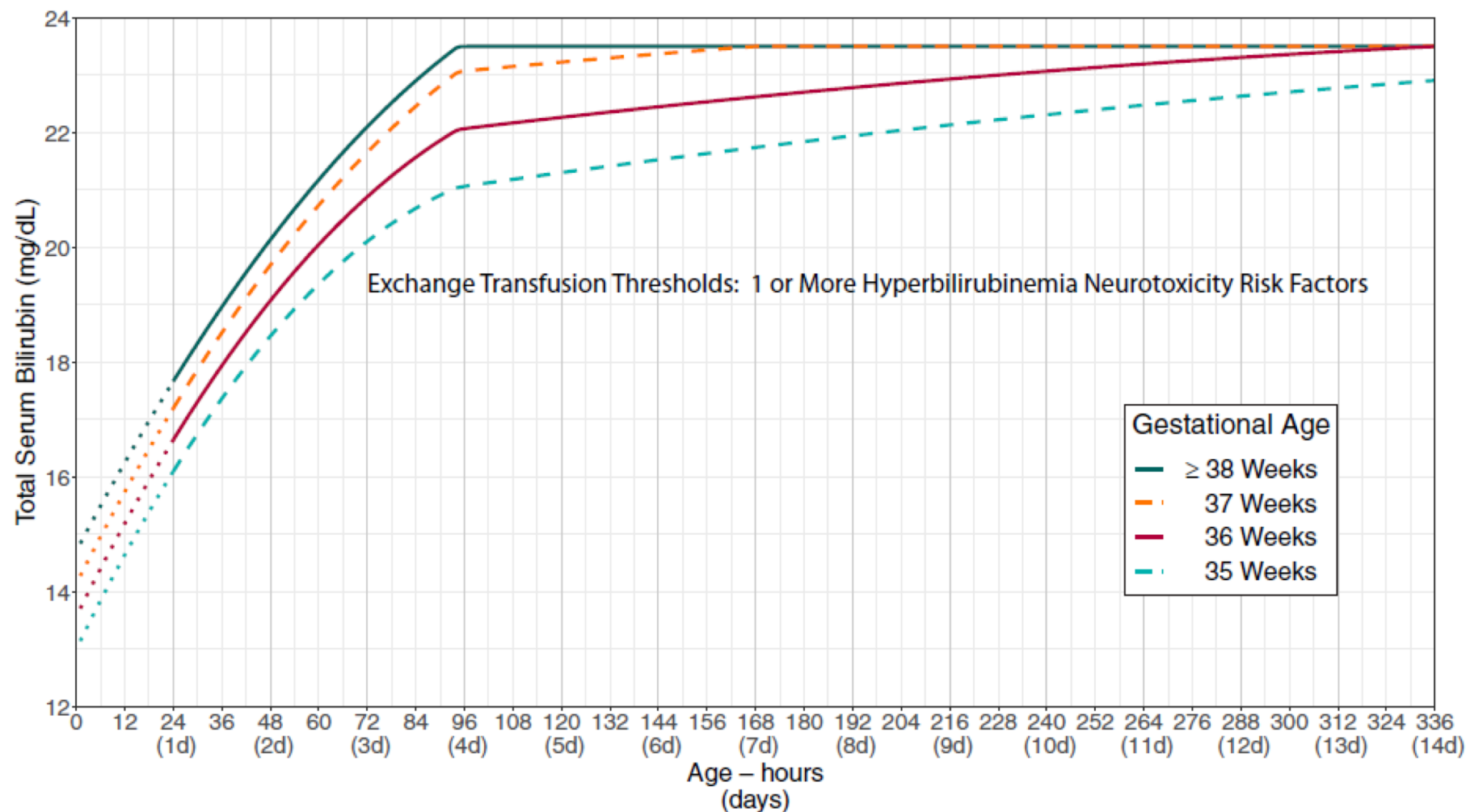
These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of escalation of care exceed its potential harms. The stippled lines for the first 24 hours indicate uncertainty because of the wide range of clinical circumstances and responses to intensive phototherapy. 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 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.

*Disclaimer: This guideline is designed for general use with most patients; each clinician should use their own independent judgment to meet the needs of each individual patient. This guideline is not a substitute for professional medical advice, diagnosis or treatment.*



Per AAP 2021 Guideline: Phototherapy thresholds by gestational age and age in hours for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. 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.





\*Per AAP 2021 Guideline: Exchange transfusion thresholds by gestational age for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. 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 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.