Bilirubin Measurement and Phototherapy Use After the AAP 2022 Newborn Hyperbilirubinemia Guideline

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abstract

BACKGROUND AND OBJECTIVES: Guidelines for the management of neonatal hyperbilirubinemia have helped to reduce rates of significant hyperbilirubinemia. However, recent evidence suggesting overtreatment and potential harms of phototherapy have informed the American Academy of Pediatrics clinical practice guideline revision and the accompanying increase in phototherapy thresholds. These changes are predicted to safely reduce overuse; however, to date, the exact effect of these guidelines has not been established.

METHODS: We conducted a retrospective study of newborns born at ≥35 weeks' gestation across a network of 8 hospitals between January 2022 and June 2023. Outcomes included rates of phototherapy and total serum bilirubin (TSB) measurements before and after guideline publication, as well as clinical outcomes, including length of stay, readmissions, and duration of phototherapy.

RESULTS: In our cohort of >22 000 newborns, we observed a 47% decrease in phototherapy utilization, from 3.9% to 2.1% ($P < .001$). TSB measurements were reduced by 23%, from 712 to 551 measurements per 1000 newborns ($P < .001$), without an increase in outpatient TSB measurements. We did not observe an increase in readmissions receiving phototherapy, and length of stay increased by only 1 hour ($P < .001$).

CONCLUSIONS: Our study reveals that the publication of the updated American Academy of Pediatrics 2022 hyperbilirubinemia guidelines has likely yielded a significant reduction in phototherapy use and serum bilirubin measurement. Dedicated quality improvement initiatives may help determine which implementation strategies are most effective. Further population-level studies are needed to confirm safety with ongoing guideline uptake.

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WHAT'S KNOWN ON THIS SUBJECT: The 2022 American Academy of Pediatrics clinical practice guideline revision for the management of neonatal hyperbilirubinemia included increased phototherapy thresholds, which was predicted to yield a reduction in overtreatment. However, the impact of these guidelines has not yet been established.

WHAT THIS STUDY ADDS: This study reveals that the publication of the new guideline has likely yielded a significant reduction in phototherapy use and serum bilirubin measurement without increasing hospital length of stay or readmissions for phototherapy.

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Neonatal hyperbilirubinemia is a condition affecting up to 80% of newborns,[1] which if inappropriately managed, can result in permanent neurologic disability.[2,3] Observing that kernicterus, although rare, was still occurring, the 2004 Clinical Practice Guideline on the Management of Neonatal Hyperbilirubinemia in Infants of 35 or more Weeks Gestation introduced the recommendation for routine monitoring for jaundice and performing a systematic assessment on all infants for the risk of developing severe hyperbilirubinemia.[4] The implementation of this universal screening approach has been associated with better recognition and reduced rates of significant hyperbilirubinemia.[5,6]

Nonetheless, over the past 2 decades, much evidence has emerged suggesting overtreatment with phototherapy,[7,8] the potential harms of this intervention,[9,10] and the occurrence of bilirubin neurotoxicity at much higher levels than previously thought.[11–14] Previous regional updates to the 2004 management guidelines[15] and other analyses to identify predictors of severe and post-discharge hyperbilirubinemia[16,17] suggest that phototherapy can safely be initiated at significantly higher levels than those recommended by the original nomograms. Incorporating this body of evidence, the American Academy of Pediatrics (AAP) clinical practice guideline revision on the management of neonatal hyperbilirubinemia[18] includes a significant increase in thresholds for phototherapy and exchange transfusion, among other key recommendations.

Although these new guidelines have been viewed as an opportunity to safely reduce overuse in newborn medicine,[19] to date, there are no studies evaluating the clinical outcomes of the new AAP guideline, and some maintain concern that the increase in thresholds could lead to an increase in readmissions and undesirable clinical consequences. As such, we conducted a retrospective study to measure the rates of clinical interventions and unintended adverse outcomes before and after guideline publication.

METHODS

Study Design and Setting

This retrospective cohort study included data collected across a multihospital health care system between January 2022 and June 2023. This hospital network includes 8 birthing hospitals, including both community and university hospitals with in-hospital newborn care ranging from level 1 nursery only to level 4 neonatal intensive care.[20] All hospitals have the capacity to accept readmissions for phototherapy. Deliveries range from 121 to 6770 births per year. Level 1 nurseries are staffed by community pediatricians, newborn and pediatric hospitalists, neonatologists, and nurse practitioners. Approximately 30% of newborns discharged from our 8 hospitals are followed by outpatient pediatricians who are part of the same network. All hospitals share an electronic health record (EHR), into which the 2004 nomograms[4] were incorporated to guide phototherapy initiation; nomograms updated for the AAP 2022 guidelines became available in the shared EHR in December of 2022. The 8 hospitals otherwise function independently, including the implementation of process change after the 2022 clinical practice guideline revision for neonatal hyperbilirubinemia. Three of the sites participated in the national quality improvement project Learning and Implementing Guidelines for Hyperbilirubinemia Treatment; however, specific interventions and timing varied by institution. Although all hospitals employ a universal bilirubin screening approach, the timing of the first measurement, transcutaneous bilirubin (TCB) meter availability, and threshold for confirmatory total serum bilirubin (TSB) measurement varied by institution. All but 1 employed a stepwise approach, performing routine screening with a TCB meter with confirmatory TSB only measured if determined necessary by hospital policy or healthcare provider. After the publication of the updated AAP guidelines, including the recommendation to obtain confirmatory TSB measurement if TCB was found to be >15 mg/dL or within 3 mg/dL of the phototherapy threshold, several institutions updated their guidelines. However, the timing and threshold of this recommendation, as well as implementation and compliance, varied by institution.

Participants

Subjects of this retrospective study were newborns born at ≥ 35 completed weeks' gestation. Data from the birth hospitalization and outpatient testing in the first 28 days of life were abstracted from the EHR by query of our enterprise data warehouse. All-cause newborn readmissions to any of the 8 hospitals within 28 days of life were also abstracted, with a sub-analysis conducted on any subsequent admission during which phototherapy was administered. Infants whose birth hospitalization was >14 days were excluded.

Variables

Abstracted data included birth gestation, birth weight, sex, maternal age, gravidity, and parity, route of delivery, maternal and newborn blood type and Rhesus factor, and newborn direct Coombs, as previously described.[21] Data from the first 28 days of life included transcutaneous and TSB measurements and phototherapy start and stop times based on physician orders. Categorical predictors were represented as known to be present and included blood group A, B, or O (ABO) incompatibility as maternal blood type O and newborn blood type A or B; Rhesus factor (Rh) mismatch as maternal Rh negative and newborn Rh positive; newborn direct Coombs status; and cesarean delivery. If data were unavailable, the categorical feature

was set to not known to be present. The receipt of intravenous immunoglobulin (IVIg) for the management of hyperbilirubinemia was abstracted; IVIg given in the absence of phototherapy was not included. Birth weight z-score was calculated as previously described.[22,23]

Data Sources and Measurement

We examined the rates of birth hospitalization phototherapy before and after guideline publication, calculated as percentages, with the preguideline epoch as before August 2022, the subsequent 2 months (August and September 2022) as a discarded "washout" period to allow for provider familiarization with the new guidelines and institutional policy revisions, and the postguideline epoch as October 2022 and later. We also measured the percentages of newborns undergoing phototherapy for whom phototherapy initiation was at or above the AAP 2022 guideline threshold, as well as a more lenient definition of "near-threshold" phototherapy. We defined near-threshold phototherapy as treatment initiation for serum bilirubin level higher than 2 mg/dL below the recommended phototherapy threshold to capture potentially appropriate subthreshold phototherapy as stipulated in the AAP guidelines (eg, if the rate of rise suggested a high likelihood of exceeding phototherapy threshold after discharge or for other individual family and clinician circumstances).

Next, we examined the rates of TSB measurement during the birth hospitalization, calculating both percentages of a newborn undergoing any serum bilirubin measurement and the mean number of tests per patient. We assessed all TSB obtained within 1 hour of a TCB measurement (likely representing a confirmatory TSB) and determined if the TCB met the criteria for appropriately obtaining a confirmatory TSB (per AAP 2022 guidelines, when TCB was >15 mg/dL or within 3 points of the phototherapy threshold). We also assessed newborn outpatient TSB measurements, defined as any serum bilirubin measurement performed on a patient ≤28 days of age, after the date and time of hospital discharge, collected at any outpatient laboratory facility within our network.

Finally, we examined several clinical outcomes, including average length of stay, rate of inpatient readmissions during the first 28 days after birth, rate of newborns readmitted who also received phototherapy, newborns receiving IVIg, and bilirubin values exceeding phototherapy, escalation-of-care, and exchange transfusion thresholds according to the AAP 2022 guidelines.[18]

For all analyses of bilirubin levels relative to specific thresholds (ie, for phototherapy initiation, escalation of care, and exchange transfusion), we used the AAP 2022 guideline thresholds for both the pre and postguideline release epochs to allow for meaningful comparisons of bilirubin levels (rather than a comparison of AAP 2004 vs AAP 2022 guideline adherence, which was not the purpose of this study) and to improve confidence that changes observed were reflective of the incorporation of new thresholds into clinical practice.

Statistical Methods

Comparisons of outcomes between the aggregate pre and post AAP 2022 guideline release populations were performed using a *t* test (either paired or unpaired), analysis of variance, Wilcoxon rank test, Kruskal–Wallis, or Pearson's χ-squared test, as appropriate. In addition, graphical plots of monthly outcomes were generated, with center lines corresponding to the outcomes of the aggregate populations using the statistical tests described above. These plots allowed for the examination of trends over time but do not include additional statistical analysis (eg, statistical process control charts with upper and lower control limits) because they represent the combined behavior of 8 hospitals with independent clinical processes.

Human Subjects Research

This project was reviewed by our institutional review board and was determined to meet the criteria for exemption.

RESULTS

Participants and Descriptive Data

Data were abstracted on 22 455 newborns born within the network between January 2022 and June 2023 at ≥35 completed weeks' gestation. The patient cohorts during the pre and postguideline epochs were similar (Table 1), with clinically insignificant differences in birth weight, birth weight *z*-score, sex, gestational age, maternal status (age, gravidity, and parity), mode of delivery, and rate of recognition of maternal and newborn ABO or Rh mismatch, or infant direct Coombs-positive status. There were a small number of newborns for whom the method of delivery was missing from the EHR, and for ~3% of newborns, the presence or absence of ABO or Rh incompatibility was unknown. Infant direct Coombs tests were typically checked only when blood type incompatibility existed. The rate of detected direct Coombs positivity in infants did not differ significantly between the two epochs.

Rate of Phototherapy Utilization

We observed a 46.7% reduction in phototherapy utilization during the birth hospitalization, decreasing from 3.9% of all newborns in the preguideline period to 2.1% postguideline ($P < .001$; Table 2 and Fig 1). As described in the methods, we plotted monthly rates of phototherapy initiation at or above the threshold (Fig 2A) and higher than 2 mg/dL below the recommended phototherapy threshold (Fig 2B). As of June 2023, only 37.0% of phototherapy administered was initiated at or above the threshold; however,

TABLE 1 Patient Cohorts			
	Preguideline (n = 9815)	Postguideline (n = 12 640)	P
Birth weight (g, median and IQR)	3370 (3050–3684)	3350 (3027–3665)	.003[a]
Birth weight z-score (mean and 95% CI)	0.22 (0.21–0.24)	0.20 (0.19–0.22)	.053[b]
Male	4969 (50.6%)	6460 (51.1%)	.475[c]
Gestation at birth (wk, median and IQR)	39.3 (38.4–40.1)	39.3 (38.4–40.0)	.007[a]
Maternal age (y, mean and 95% CI)	33.1 (33.0–33.2)	33.2 (33.1–33.3)	.207[b]
Gravidity (median and IQR)	2 (1–3)	2 (1–3)	.430[a]
Parity (median and IQR)	2 (1–2)	2 (1–2)	.361[a]
Delivery mode			.128[c]
Vaginal	6631 (68.2%)	8444 (67.3%)	
Cesarean section	3087 (31.8%)	4108 (32.7%)	
ABO blood type mismatch	1435 (15.1%)	1752 (14.2%)	.080[c]
Rh mismatch	734 (7.8%)	861 (7.0%)	.037[c]
Infant direct Coombs positive	324 (7.4%)	385 (7.1%)	.573[c]

CI, confidence interval; IQR, interquartile range.
[a] Kruskal–Wallis rank sum test.
[b] Linear model analysis of variance.
[c] Pearson's χ-squared test.

near-threshold initiation of phototherapy had increased to 77.1%.

TSB Measurement

For the birth hospitalization, we calculated rates of both newborns undergoing any TSB measurement (Fig 3A), as well as the mean number of TSB measurements per newborn (Fig 3B). Both measures reveal a decrease in TSB measurement in the postguideline period; the percentage of newborns undergoing any TSB measurement decreased by 20.5%, from 35.1% to 27.9% ($P < .001$), and the rate of TSB measurements decreased by 22.6% from 712 to 551 per 1000 infants ($P < .001$; Table 2). In the postguideline epoch, 30.8% of TSB after TCB measurements were determined to meet the criteria for confirmatory recommendations (Fig 4). There was no statistically significant difference in outpatient TSB measurements; before guideline publication, 8.9% of newborns received any outpatient TSB in our network, compared with 8.7% after ($P = .63$). Total outpatient TSBs also remained stable, with rates of 140 measurements per 1000 infants born preguideline, and 134 measurements per 1000 infants post-guideline ($P = .61$; Table 2).

Other Clinical Outcomes

Additional pre and postguideline clinical outcomes included a comparison of length of stay, duration of phototherapy, and readmissions receiving phototherapy (Table 2). The average length of stay increased post-guideline by 1 hour ($P < .001$). The duration of phototherapy remained stable at a mean of 35 hours (95% confidence interval from 32 to 39 hours, $P = .950$). There was no significant change in the rate of overall inpatient readmissions during the first 28 days after birth (1.8% to 1.8%, $P = .86$) or readmissions receiving phototherapy (0.9% to 0.8%, $P = .15$). Of patients readmitted and receiving phototherapy, only 11.0% in the preguideline epoch and 22.1% in the postguideline epoch

TABLE 2 Clinical Outcomes			
	Preguideline (n = 9815)	Postguideline (n = 12 640)	P
Length of stay (h, median and IQR)	54.7 (43.9–74.2)	55.7 (45.2–75.3)	<.001[a]
Any TSB measurement	3445 (35.1%)	3521 (27.9%)	<.001[b]
TSB per 1000 infants (mean and 95% CI)	712 (685–738)	551 (530–573)	<.001[a]
Phototherapy received	382 (3.9%)	262 (2.1%)	<.001[b]
Phototherapy duration (h, mean and 95% CI)	35 (32–39)	35 (32–39)	.950[c]
Exceeded phototherapy threshold	75 (0.8%)	120 (0.9%)	.138[b]
Any outpatient TSB measurement	874 (8.9%)	1102 (8.7%)	.625[a]
Outpatient TSB per 1000 infants (mean and 95% CI)	140 (129–151)	134 (125–143)	.605[b]
Readmissions, any cause	181 (1.8%)	229 (1.8%)	.857[a]
Readmissions, phototherapy received	91 (0.9%)	95 (0.8%)	.150[a]
Exceeded phototherapy threshold, readmission	10 (11.0%)	21 (22.1%)	.042[a]
Exceeded 2mg/dL below phototherapy threshold, readmission	30 (33.0%)	48 (50.5%)	.015[a]

[a] Kruskal–Wallis rank sum test.
[b] Pearson's χ-squared test.
[c] Linear model analysis of variance.

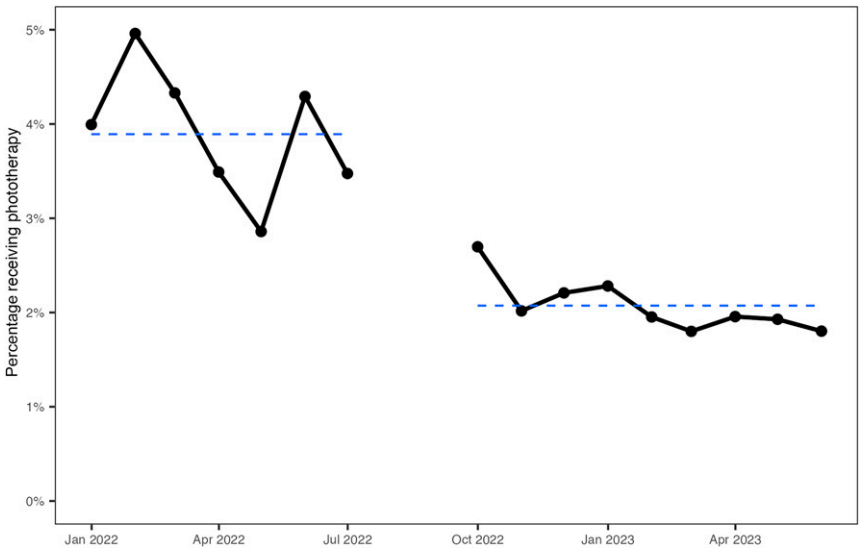

FIGURE 1

Rate of phototherapy utilization. Monthly rates of phototherapy utilization during the birth hospitalization of all infants born at ≥35 weeks' gestation. The dashed line represents the mean rates across all infants in each of the pre and postguideline epochs.

had a bilirubin measurement exceeding the threshold (P = .04), and only 33.0% and 50.5% exceeded 2 mg/dL below the threshold in the pre and postguideline epochs (P = .02), respectively.

Rare Outcomes

We observed slight increases pre to postguideline in newborns with bilirubin values exceeding the escalation-of-care threshold (n = 4 vs 6, P = .81) and newborns who received IVIg in the setting of hyperbilirubinemia (n = 1 vs 5, P = .18) during the birth hospitalization (Table 3). Similar changes were observed in newborns readmitted for phototherapy; in the post-guideline epoch, 3 had bilirubin levels exceeding the escalation-of-care threshold and 1 received IVIg, compared with 0 in the preguideline epoch (P = .087 and .326, respectively). Additionally,

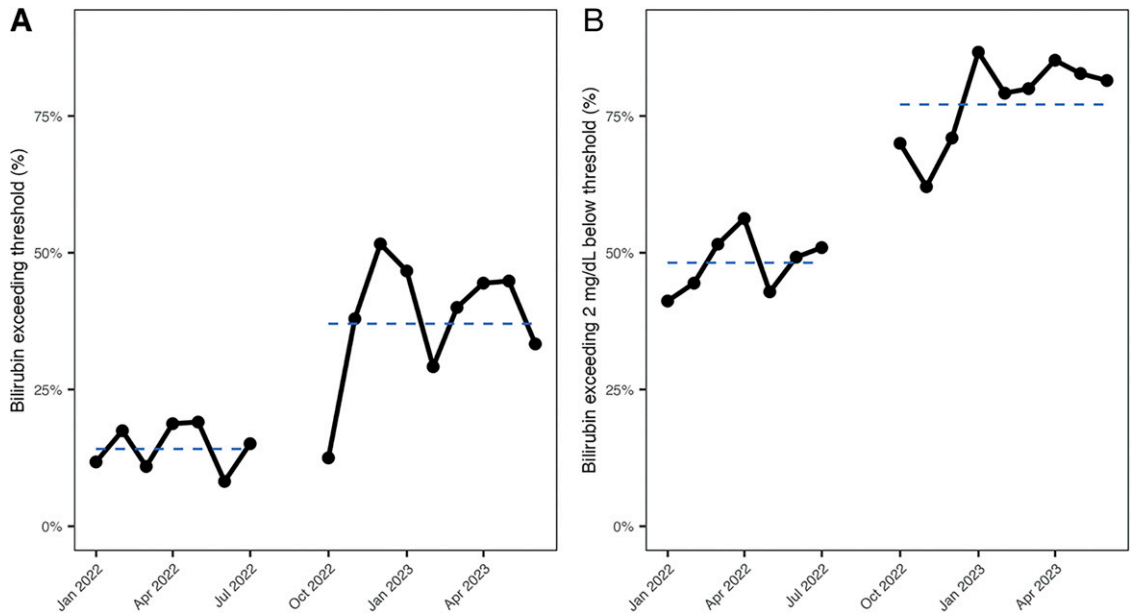

FIGURE 2

Phototherapy initiation relative to AAP 2022 guideline thresholds. Points reflect the monthly percentage of phototherapy initiated with highest bilirubin level (A) at or above the threshold or (B) at or above 2 mg/dL below the threshold. The dashed line represents mean rates across all infants in each of the pre and postguideline epochs.

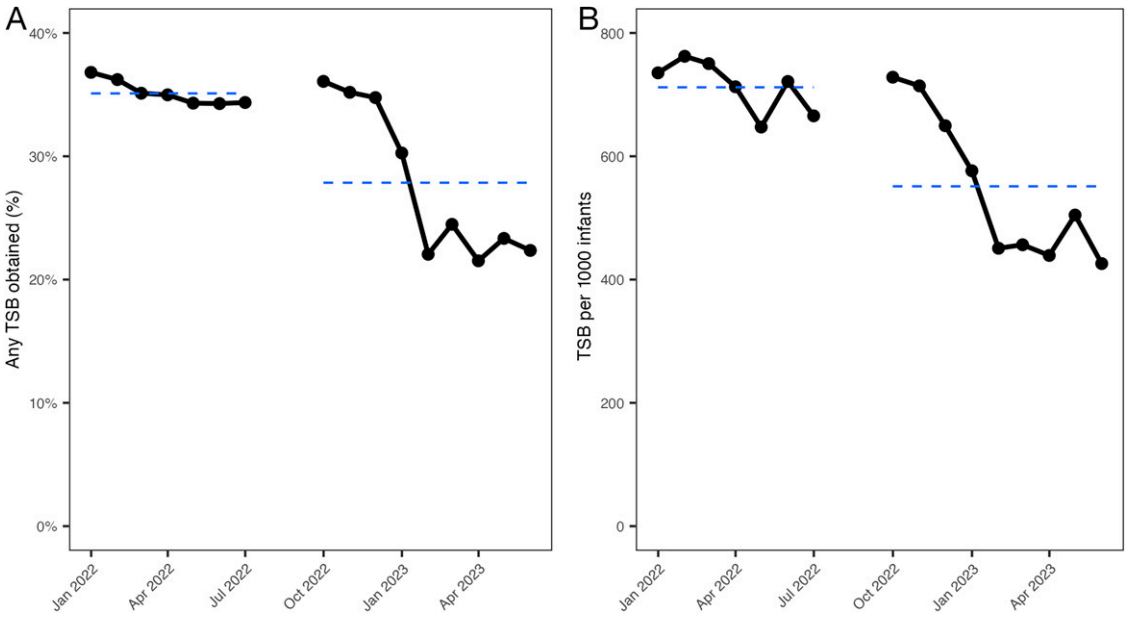

FIGURE 3

TSB measurements: (A) monthly rates of newborns undergoing any TSB measurement during the birth hospitalization and (B) mean number of TSB measurements per 1000 infants. The dashed line represents the mean rates across all infants in each of the pre and postguideline epochs.

there were 2 newborns in the postguideline epoch whose bilirubin level exceeded exchange transfusion thresholds ($n = 0$ vs 2, $P = .21$); of note, both of these newborns were identified during the birth hospitalization, and none of the patients readmitted for phototherapy had values exceeding exchange transfusion thresholds.

DISCUSSION

In this study, we analyzed the effect of the new AAP 2022 guidelines for the management of hyperbilirubinemia in newborns of ≥35 weeks' gestation in a large cohort of >22 000 infants from 8 birthing hospitals. Phototherapy utilization decreased by 46.7% and the rates of TSB measurement decreased by 23% without an observed increase in outpatient TSB measurements or readmissions receiving phototherapy. Length of stay due to phototherapy receipt was minimally impacted, increasing by 1 hour; however, the duration of phototherapy did not change. These data provide early evidence that the updated neonatal hyperbilirubinemia guidelines can lead to

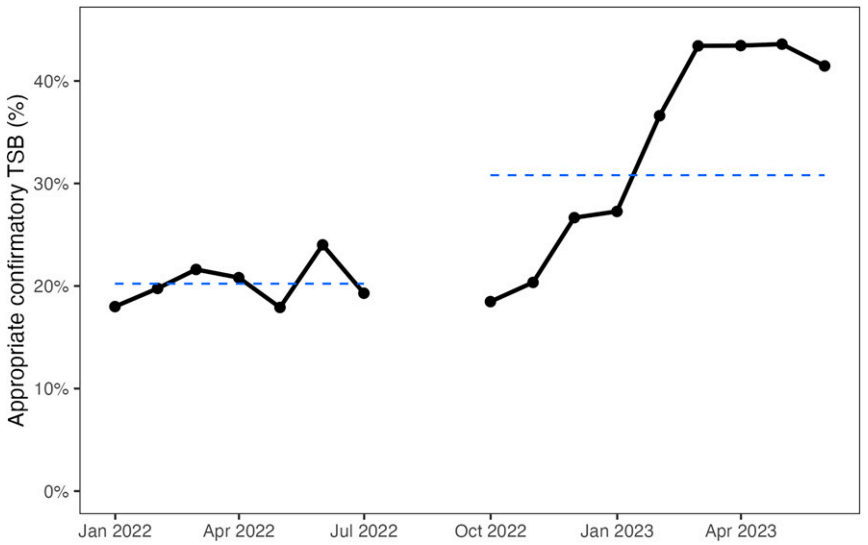

FIGURE 4

Appropriate confirmatory TSB Measurements. Of all TSB measurements obtained within 1 hour of a TCB, monthly rates of TCB being either ≥15 mg/dL or at or above 3 mg/dL below the phototherapy threshold. The dashed line represents mean rates across all infants in each of the pre and postguideline epochs.

TABLE 3 Rare Outcomes			
	Pre-guideline	Post-guideline	*P*
Birth hospitalization	(n = 9815)	(n = 12 640)	
Exceeded escalation of care threshold	4 (0.04%)	6 (0.05%)	.813[a]
Exceeded exchange transfusion threshold	0 (0.0%)	2 (0.02%)	.213[a]
Intravenous immune globulin given	1 (0.01%)	5 (0.04%)	.182[a]
Readmissions	(n = 91)	(n = 95)	
Exceeded escalation threshold	0 (0.0%)	3 (3.2%)	.087[b]
Exceeded exchange transfusion threshold	0 (0.0%)	0 (0.0%)	(undefined)
Intravenous immune globulin given	0 (0.0%)	1 (1.1%)	.326[b]

[a] Pearson's χ-squared test.
[b] Kruskal–Wallis rank sum test.

a marked reduction in unnecessary interventions for many newborns.

The reduction in potentially unnecessary newborn interventions has many short- and long-term implications. As outlined in the AAP guideline, immediate harms of phototherapy include infant–family separation, parental anxiety, and the disruption of the breastfeeding relationship. Recent evidence has also revealed increased rates of epilepsy among children who have received phototherapy.[9,10] The benefits of a reduction in serum bilirubin monitoring include fewer painful procedures for newborns resulting in an improved family experience, as well as decreased hospital resource utilization. Although the evidence is mixed, studies also suggest potential long-term harms, including increased care utilization among families of children with a history of neonatal hyperbilirubinemia.[24–26] More simply put, establishing a pattern of or expectations for overuse early in life may have implications for care utilization well into the future.[27] Our data revealing a nearly 50% reduction in phototherapy and >20% reduction in TSB measurements suggests that the implementation of the new hyperbilirubinemia guidelines may have significant consequences, not only in the neonatal period but throughout childhood.

It is likely that further progress can be made in reducing resource utilization. Given our finding that >60% of newborns undergoing phototherapy are still below recommended thresholds (with >20% of infants receiving phototherapy >2 mg/dL below the threshold), we anticipate further reductions in interventions with further guideline implementation. Additionally, although we did not detect a change in readmissions requiring phototherapy, the fact that the majority did not have readmission inpatient bilirubin measurements over the phototherapy threshold, and only half were higher than 2 mg/dL below the threshold, highlights additional opportunities for improvement and collaboration between inpatient and outpatient providers. Finally, we found that nearly 70% of confirmatory TSB measurements after screening TCB did not meet the criteria as defined by the guideline. A quality improvement initiative conducted before the 2022 guideline publication was able to achieve a rate of 0.26 TSBs per patient day.[28] As such, it is reasonable to expect that even lower rates could be achieved after guideline publication. Visual inspection of Figs 3 and 4 indicates a downward trend in TSB and an upward trend in appropriate confirmatory TSB, suggesting that with time, increased provider comfort and experience with higher bilirubin levels may also lead to increased guideline adherence.

We observed a slight (but not statistically significant) increase in newborns with bilirubin levels exceeding escalation-of-care or exchange transfusion thresholds or receiving IVIg for hyperbilirubinemia. Although these new thresholds are still well below levels at which neurologic sequelae have been observed,[11–14] future population-level studies with adequate power to detect potentially significant changes would substantially improve our understanding of all clinical outcomes after guideline publication. We do find it reassuring that both incidences of bilirubin levels exceeding exchange transfusion thresholds occurred during birth hospitalization, suggesting that the new guidelines are effective in identifying newborns at risk for severe hyperbilirubinemia.

One major limitation of our study was the ability to analyze practices after the birth hospitalization. For example, we were unable to evaluate the number of newborns readmitted to hospitals outside of our network. However, all 8 hospitals had the capacity to readmit newborns for phototherapy, our overall rates of readmission in both the pre- and post-guideline epochs are consistent with published data,[29] and the proportion of readmitted patients receiving phototherapy also remained stable. Therefore, we estimate that the loss of readmissions to outside institutions had minimal impact on our findings. Our analysis of outpatient TSBs, however, is likely an underestimate; the majority of newborns born at our hospitals follow up with providers outside of our network, and as such, may undergo laboratory monitoring at facilities not captured by our analysis. However, the stable rates of outpatient TSB measurement in the pre and postguideline epochs still provide useful information.

Our study has several other limitations. This study was conducted across a hospital network with EHR

integration of hyperbilirubinemia nomograms. Findings may be less generalizable to institutions without this level of clinical decision support. Certain characteristics of our birthing population may limit the applicability of these findings to populations with greater proportions of newborns at risk for hyperbilirubinemia. Home phototherapy was also not available in any regions served by our hospital network. Institutions with more community resources may achieve even greater reductions in the need for in-hospital phototherapy. Finally, it is important to note that this study is meant to be descriptive, and as such, we did not specifically evaluate which interventions led to the most change in the management of neonatal hyperbilirubinemia. Future work may include dedicated quality improvement initiatives and statistical methods to better identify effective interventions and support other institutions in achieving similar or superior outcomes. Based on our observed rates of subthreshold phototherapy and unnecessary TSBs, it is likely that with dedicated quality improvement work, these metrics can be substantially improved; however, as noted, this was not the design nor the objective of our study.

CONCLUSIONS

The 2022 AAP guidelines on neonatal hyperbilirubinemia represent an opportunity to significantly reduce the overtreatment of a common newborn condition. Our study reveals that the implementation of these recommendations can yield a significant reduction in interventions. Future work studying which inventions prove most successful in guideline implementation will help achieve more widespread improvement, and further population-level work is needed to confirm safety with ongoing guideline uptake.

ABBREVIATIONS

AAP: American Academy of Pediatrics
ABO: blood group A, B, or O
EHR: electronic health record
IVIg: intravenous immunoglobulin
Rh: rhesus factor
TCB: transcutaneous bilirubin
TSB: total serum bilirubin

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CONFLICT OF INTEREST DISCLOSURES: Dr Chou is the developer of the PediTools website, which includes a bilirubin clinical decision support tool and generates revenue from advertisements served by Google Adsense. Google Adsense had no input on the content of this study or on the PediTools website. The remaining authors have indicated they have no potential conflicts of interest relevant to this article to disclose.

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