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ORIGINAL ARTICLE

Extreme hyperbilirubinemia and rescue exchange transfusion in California from 2007 to 2012

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OBJECTIVE: To evaluate the impact of statewide learning collaboratives that used national guidelines to manage jaundice on the serial prevalence of extreme hyperbilirubinemia (EHB, total bilirubin $\geqslant 25$ mg dl^{-1}) and exchange transfusions introduced in California Perinatal Quality Care Collaborative (CPQCC) hospitals in 2007.

STUDY DESIGN: Adverse outcomes were retrieved from statewide databases on re-admissions for live births $\geqslant 35$ weeks' gestation (2007 to 2012) in diverse CPQCC hospitals. Individual and cumulative select perinatal risk factors and frequencies were the outcomes measures.

RESULTS: For 3 172 762 babies (2007 to 2012), 92.5% were $\geqslant 35$ weeks' gestation. Statewide EHB and exchange rates decreased from 28.2 to 15.3 and 3.6 to 1.9 per 100 000 live births, respectively. From 2007 to 2012, the trends for TB > 25 mg dl^{-1} rates were -0.92 per 100 000 live births per year (95% CI: -3.71 to 1.87, $P = 0.41$ and $R^2 = 0.17$).

CONCLUSION: National guidelines complemented by statewide learning collaboratives can decrease or modify outcomes among all birth facilities and impact clinical practice behavior.

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INTRODUCTION

Newborn jaundice continues to have important public health and economic consequences for health care in the United States.[1–3] Previous evidence-based studies identifying deficiencies in education and practice led to a systems approach that could reduce risks of neurological injury from extreme hyperbilirubinemia (EHB; total serum/plasma bilirubin (TB) $\geqslant 25$ mg dl^{-1} (428 μmol l^{-1}, at an age beyond 48 h) in otherwise healthy infants after discharge.[4–6] Better identification of infants at risk who may need 'rescue' intervention, such as a hazardous double blood volume exchange transfusion, was thought to minimize public health risk due to bilirubin-related injury.[7,8] This manuscript aims to explore the clinical impact of the most updated guideline (2004)[1] and subsequent changes to clinical practices on risks of EHB in California from 2007 to 2012 (ref. 3) and to reassess the performance of clinical risk factors and modification by awareness and practice.

Exploration of relationships between evidence-based practice guidelines and their national clinical impact is not new. Brooks *et al.*[9] accessed the Center for Disease Control and Prevention's Wide-Ranging Online Data for Epidemiologic Research and provided data on infant mortality from kernicterus in the United States. They reported a crude mortality rate of 0.39 per 1 000 000 live births from 1979 to 1985 (10 per 25.5 million) that was before the publication of The National Institute of Child Health and Development (NICHD) Phototherapy trial.[10] Following the NICHD trial, we recalculated the crude mortality rate of 0.08 per 1 000 000 live births (3 per 39.6 million) from 1986 to 1993 that was before the 1994 American Academy of Pediatrics (AAP) Practice Guideline.[3] Following this success, it was presumed that continued practices would suffice, but an unanticipated increase to 0.41 per 1 000 000 live births (16 per 39.4 million) was observed before the publication of the 2004 AAP Practice Guideline.[9] Now, policy makers need to know whether implementation of the 2004 AAP systems-approach guideline has improved outcomes.

MATERIALS AND METHODS

To assess the effects of the 2004 AAP guideline and its subsequent implementation via California-wide 'hyperbilirubinemia prevention initiatives', we used data from the California Perinatal Quality Care Collaborative (CPQCC), a collective of diverse 132-member birthing hospitals that represents over 90% of the state's neonatal intensive care unit (NICU) admission population. This neonatal clinical database is based on an expanded version of the Vermont Oxford Network data set,[11] and is subject to rigorous logic checks and audits with the intent to maximize data quality and minimize missing data. It was reasonable to assume that infants admitted to a CPQCC NICU with TB $\geqslant 25$ mg dl^{-1} (428 μmol l^{-1}) or who had an exchange transfusion would be represented in the CPQCC data set as these conditions are part of the CPQCC eligibility criteria for infants readmitted during the first 28 days of life.

Our study population comprised of infants $\geqslant 35$ weeks' gestational age (GA) born from 1 January 2007 to 31 December 2012, who were discharged home from any birthing facility and readmitted to a CPQCC NICU. All CPQCC member hospitals are required to report any hyperbilirubinemia-related re-admissions within 28 days of birth with a TB $\geqslant 25$ mg dl^{-1} (428 μmol l^{-1}) or an exchange transfusion regardless of their NICU admission TB level. Infants were also stratified by the level of accreditation of their birthing hospital facility regardless of their admitting NICU facility.

The background statewide activity that coincided with our observational study was an ongoing quality improvement (QI) initiative following the publication of the 2004 AAP Practice Guideline[1] and a more recent expert clarification.[3] CPQCC developed a learning collaborative through user-driven development of a variety of toolkits that were both clinician- and family-centered in 2005 and 2006.[12] These were widely publicized through local, regional and professional meetings and made accessible through the CPQCC website: 'Severe Neonatal Hyperbilirubinemia Toolkit'.[11] This

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Table 1. Observed and estimated capture rate of data from NICU readmissions for jaundice during the first 4 weeks after birth in California, 2007 to 2012

Year	*Live births*[a]	*NICU readmits*[b]	*Adverse outcomes*	*Events*	*Estimated prevalence of EHB per 10 000 live births (⩾35 weeks' GA) assuming capture rate of:*	
	⩾35 weeks	*High acuity*	*EHB*	*Number*	*100%*	*90%*
2007	519 600	534	TB ⩾ 25 mg dl^{-1}	91	17.51	19.46
			TB ⩾ 30 mg dl^{-1}	17	3.27	3.64
			All exchanges	19	3.66	4.06
2008	509 324	526	TB ⩾ 25 mg dl^{-1}	104	20.42	22.69
			TB ⩾ 30 mg dl^{-1}	25	4.91	5.45
			All exchanges	19	3.73	4.14
2009	488 795	458	TB ⩾ 25 mg dl^{-1}	119	24.35	27.05
			TB ⩾ 30 mg dl^{-1}	26	5.32	5.91
			All exchanges	16	3.27	3.64
2010	475 509	487	TB ⩾ 25 mg dl^{-1}	97	20.40	22.67
			TB ⩾ 30 mg dl^{-1}	18	3.79	4.21
			All exchanges	10	2.10	2.34
2011	469 763	454	TB ⩾ 25 mg dl^{-1}	91	19.37	21.52
			TB ⩾ 30 mg dl^{-1}	18	3.83	4.26
			All exchanges	17	3.62	4.02
2012	472 683	485	TB ⩾ 25 mg dl^{-1}	62	13.12	14.57
			TB ⩾ 30 mg dl^{-1}	9	1.90	2.12
			All Exchanges	8	1.69	1.88
2007–12	2 935 674	2944	TB ⩾ 25 mg dl^{-1}	564	19.21	21.35
			TB ⩾ 30 mg dl^{-1}	113	3.85	4.28
			All exchanges	89	3.03	3.37

Abbreviations: EHB, extreme hyperbilirubinemia; GA, gestational age; NICU, neonatal intensive care unit. [a]Source: Vital Statistics Birth Data, California Department of Public Health. [b]NICU readmission includes infant readmitted at age < 28 days to a CPQCC NICU for a variety of neonatal conditions that included neonatal hyperbilirubinemia. Source: California Perinatal Quality Care Collaborative (CPQCC). Based on inpatient admissions of infants < 28 days of age. Source: California Office of Statewide Health Planning and Development (OSHPD) inpatient discharge data. Using prior data reported to OSHPD, the exchange transfusion rates in 2005, 2006 were 3.98 and 3.67 per 100 000 live births, respectively.

statewide initiative was complemented by the inclusion of EHB on the CPQCC hospital level reports. In addition, clinicians had direct free access to the online BiliTool for pre-discharge risk-assessment.[13] The CPQCC Perinatal QI Panel made the toolkits available to all members, and conducted workshops and open webcasts to all member hospitals and clinicians. In view of the multiple high-profile national, regional and local dissemination processes, all member hospitals were considered to have initiated an individualized QI process sometime during the 4-year period commencing from October 2006 to 2009. To investigate the effects of the diverse levels of neonatal care at the birthing hospital, we used the classification of levels of care as defined by the AAP.[12]

In addition to the CPQCC data, the California Office of Statewide Health Planning and Development (OSHPD) inpatient discharge data and the California Department of Public Health (CDPH) Vital Statistics birth date data helped inform conservative estimates of the prevalence of EHB in California. Administrative data from the OSHPD was used to track the readmission of infants with diagnoses related to newborn jaundice/hyperbilirubinemia (for example, ICD-9 codes 243, 277.4, 773, 773.1, 773.4, 774, 774.2, 774.3, 774.31, 774.39, 774.4, 774.5, 774.6, 774.7, 782.4, 775.5, 779.3 and 783.3). For our birth weight subgroups, we obtained denominator data from the CDPH administrative data set.

Patient characteristics in this study included maternal demographics: age, race, ethnicity, prenatal care; obstetrical risk factors: fetal distress, hypertension, chorioamnionitis and mode of delivery. Neonatal demographics included: gender, birth weight, GA at birth and calendar year of birth. GA was the best estimate available, with the following hierarchy: (i) obstetric measures, based on last menstrual period, obstetrical parameters or prenatal ultrasonography as recorded in the maternal chart; and (ii) pediatric provider's estimate based on physical or neurologic examination, combined with physical and GA examinations (using Ballard/Dubowitz examinations).

The primary outcome of this study was to identify the specific high-risk population that required NICU admission within 28 days of birth for EHB or the use of exchange transfusion in the context of a recommended universal pre-discharge systems approach. Our second concurrent objective was to evaluate the impact of a multipronged statewide learning collaborative on high-risk adverse outcomes. EHB-related relative risk (RR) was estimated for all live births ⩾35 weeks' GA ($n = 2\,935\,674$) and for each of the three main 'adverse events': TB ⩾ 25 mg dl^{-1} (428 μmol l^{-1}), TB ⩾ 30 mg dl^{-1} (513 μmol l^{-1}) and use of exchange transfusion. Linear regressions were performed to analyze for trends and all other analyses were performed using SAS 9.4 (SAS, Cary, NC, USA). Stanford University Institutional Review Board approved this study.

RESULTS

Study population

A total of 3 172 762 babies were born in California from 2007 to 2012 and 2 935 674 (92.5%) were ⩾35 weeks' GA (study population). A total 2944 (0.1% of the study population) were readmitted before 28 days of life to a CPQCC NICU for various high acuity conditions. The total frequencies of the three main 'adverse events' recorded by CPQCC in this subcohort were: 564 with TB ⩾ 25 mg dl^{-1} (19.2 per 100 000 live births); a subset of 113 with TB ⩾ 30 mg dl^{-1} (3.8 per 100 000 live births) and 89 that underwent exchange transfusion (3.0 per 100 000 live births). Assuming a 90% capture rate (used for all subsequent data in this manuscript), the estimated frequencies are 21.3, 4.2 and 3.3 per 100 000 live births, respectively, over the period of 2007 to 2012 (Table 1). For comparison, we provided the prevalence of exchange transfusion rates in Table 2 with rates based on the California Linked Vital Statistics/Inpatient Discharge Data.

Baseline characteristics of the infants readmitted to NICU. The risk of TB ⩾ 25 mg dl^{-1} (428 μmol l^{-1}) or exchange transfusion was higher among males (RR = 1.88; 95% CI = 1.60 to 2.21) and lower among infants delivered by C-section (RR = 0.21;

95% CI = 0.16 to 0.28). The RR data for maternal race/ethnicity compared with infants born to White (non-Hispanic) women are shown in Table 3. Infants born to Asian mothers were not found to be at a higher risk of adverse outcomes (RR = 1.07; 95% CI = 0.88 to 1.30) while infants born to Hispanic mothers experienced half the risk of EHB or exchange transfusion (RR = 0.51; 95% CI = 0.44 to 0.60). Infants born to African-American mothers had a significantly lower risk for TB ⩾ 25 mg dl^{-1} ((428 μmol dl^{-1}) RR = 0.25; 95% CI = 0.16 to 0.42), but not for TB ⩾ 30 mg dl^{-1} ((513 μmol dl^{-1}) RR = 0.51; 95% CI = 0.23 to 1.14) or exchange transfusion (RR = 0.62; 95% CI = 0.28 to 1.39). Native-American infants were not found to have significantly different risks for EHB than Whites. The risk for hyperbilirubinemia was found to be elevated in infants born to women less than 20 years of age (RR = 1.21; 95% CI = 0.93 to 1.56) and women greater than 35 years of age (RR = 1.16; 95% CI = 0.94 to 1.43) when compared with infants born to 20- to 35-year-old women, but results were not statistically significant. Infants assigned Apgar score values of 0 to 3, as compared with those with scores of 8 or more at age 5 min were at high risk for all categories of adverse outcomes.

Outcomes

Adverse outcomes over time. Figure 1 shows the estimated prevalence rates of EHB and use of exchange transfusion regardless of the TB level. CPQCC data shows that with the exception of a steady rate from 2007 to 2008 (implementation phase) and higher rate in 2011, rates for exchange transfusion have been steadily declining over the entire study period. From 2007 to 2012, linear regression analyses yielded trends of -0.92 per 100 000 live births/year (95% CI = − 3.71 to 1.87, $P = 0.41$ and $R^2 = 0.17$) for TB > 25 mg dl^{-1} (428 μmol dl^{-1}) rates, − 0.37 per 100 000 live births per year (95% CI = − 1.23 to 0.49, $P = 0.30$ and $R^2 = 0.26$) for TB > 30 mg dl^{-1} (513 μmol dl^{-1}) rates, and − 0.36 per 100 000 live births per year (95% CI = − 0.89 to 0.17, $P = 0.14$ and $R^2 = 0.47$) for exchange transfusion rates. For consecutive years from 2009 to 2012 (post-implementation phase), a statistically significant decrease in TB > 25 mg dl^{-1} (428 μmol dl^{-1}) rates was observed (−3.86 per 100 000 live births per year, 95% CI = − 7.12 to − 0.60, $P = 0.04$ and $R^2 = 0.93$), but not for TB > 30 mg dl^{-1} (513 μmol dl^{-1}) rates (−1.13, 95% CI = − 2.37 to 0.09, $P = 0.06$ and $R^2 = 0.89$) nor exchange transfusion rates (−0.36, 95% CI = − 2.51 to 1.79, $P = 0.55$ and $R^2 = 0.21$).

Adverse outcomes related to birthing hospital. The RRs by birth hospital for infants who were subsequently admitted with bilirubin-related adverse outcomes compared with infants born and cared for at hospitals with a California Children's Services (CCS) designated Community NICU are shown in Table 4. Infants born at Primary Care Hospitals with level I care were found to have almost twice the risk of TB > 30 mg dl^{-1} (513 μmol dl^{-1}) compared with infants born at a hospital with a community NICU with Level III A/B care (RR = 1.75; 95% CI = 1.19 to 2.58). Risks of TB > 25 mg dl^{-1} (428 μmol dl^{-1}) and of exchanges transfusion, however, were similar in infants born at Primary Care Hospitals versus infants born at hospitals with a NICU. For all other outcomes studied, there were no significant differences in the rates of TB ⩾ 25 mg dl^{-1}, (428 μmol dl^{-1}) ⩾ 30 mg dl^{-1} (513 μmol dl^{-1})

Table 2. Exchange transfusion rate per 100 000 live births ⩾ 35 weeks GA based on California linked VS birth and inpatient discharge (IP) data and CPQCC

Year	*Exchange transfusion rate based on VS/IP*	*Exchange transfusion rate based on CPQCC assuming 90% capture rate*
2007	4.0	4.1
2008	2.9	4.1
2009	1.8	3.6
2010	2.3	2.3
2011	1.9	4.0
2012	1.7	1.9
All years	2.5	3.4

Abbreviations: CPQCC, California Perinatal Quality Care Collaborative; GA, gestational age; VS, vital statistics.

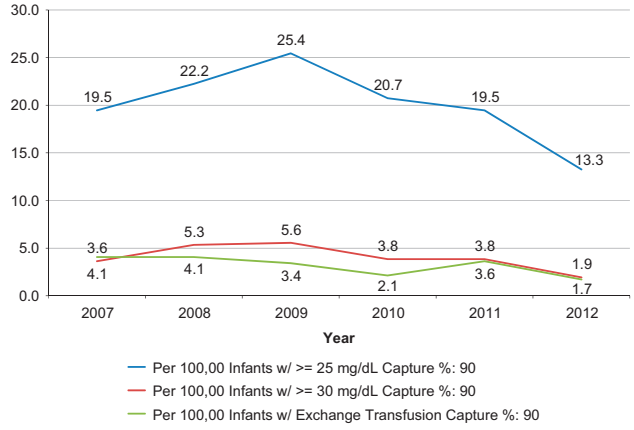

Figure 1. Estimated prevalence of extreme hyperbilirubinemia per 100,000 live births from 2007 to 2012 in California (based on California Perinatal Quality Care Collaborative (CPQCC) data and assuming a 90% capture rate).

Table 3. RRs for admission and adverse outcomes in infants ⩾ 35 weeks GA in California, 2007 to 2012

	TB ⩾ 25 mg dl^{-1} (428 μmol l^{-1})	*TB ⩾ 30 mg dl^{-1} (513 μmol l^{-1})*	*Use of exchange transfusion*	*TB ⩾ 25 mg dl^{-1} and/or use of exchange transfusion*
White (non-Hispanic) ($n = 825\,738$)		Reference comparison by race		
Asians ($n = 319\,643$)	1.13 (0.93–1.38)	1.00 (0.63–1.59)	0.88 (0.51–1.51)	1.07 (0.88–1.3)
Hispanic ($n = 1\,482\,685$)	0.53 (0.45–0.62)	0.61 (0.43–0.85)	0.40 (0.27–0.61)	0.51 (0.44–0.60)
African-American ($n = 169\,448$)	0.25 (0.16–0.42)	0.51 (0.23–1.14)	0.62 (0.28–1.39)	0.27 (0.17–0.43)
Native-American ($n = 13\,152$)	0.65 (0.22–1.92)	No cases	No cases	0.61 (0.21–1.80)
Other race ($n = 73\,940$)	0.78 (0.50–1.19)	0.59 (0.20–1.77)	0.71 (0.24–2.16)	0.76 (0.50–1.16)
No prenatal care ($n = 40\,682$)	0.40 (0.14–1.16)	1.37 (0.36–5.16)	1.65 (0.44–6.26)	0.50 (0.20–1.28)
C-section versus vaginal birth ($n = 937\,412$)	0.19 (0.14–0.26)	0.08 (0.03–0.20)	0.27 (0.14–0.50)	0.21 (0.16–0.28)
Female versus male gender ($n = 1\,436\,162$)	0.53 (0.45–0.63)	0.62 (0.43–0.89)	0.59 (0.39–0.88)	0.53 (0.45–0.63)
Apgar score 0–3 versus 8+ at age 5 min ($n = 2536$)	285 (235–345)	381 (255–566)	324 (202–519)	292 (243–351)

Abbreviations: GA, gestational age; RR, relative risk.

Table 4. RR for birth site of infants subsequently admitted with bilirubin-related adverse outcomes in California, 2007–2012

Birthing facility	*Primary care*	*Non-CCS NICUs*	*CCS[a] intermediate NICU*	*CCS community NICU*	*CCS regional NICU*
Level of care	*I*	*I*	*II*	*III A/B*	*III C*
% Births ⩾35 weeks' GA	34.9%	5.8%	7.0%	41.9%	10.5%
Births ⩾35 weeks' GA	1 023 535	168 951	205 834	1 229 566	307 788
TB⩾25 mg dl^{-1} OR exchange transfusion[b]	219	38	42	232	61
RR of TB⩾25 mg dl^{-1} [c]	1.17 (0.98–1.4)	1.2 (0.86–1.67)	1.02 (0.74–1.41)	Reference	1.06 (0.80–1.39)
RR of TB⩾30 mg dl^{-1} [c]	1.75 (1.19–2.58)[d]	0.75 (0.28–1.98)	0.86 (0.38–1.95)	Reference	0.82 (0.40–1.69)
RR for exchange transfusion[c]	1.22 (0.79–1.88)	0.59 (0.19–1.80)	0.91 (0.40–2.06)	Reference	0.65 (0.29–1.47)
RR of TB⩾25 mg dl^{-1} or exchange transfusion	1.15 (0.96–1.37)	1.19 (0.86–1.65)	1.02 (0.74–1.39)	Reference	1.05 (0.80–1.37)

Abbreviations: CCS, California Children's Services; GA, gestational age; NICU, neonatal intensive care unit; RR, relative risk. [a]California Children's Services. [b]Total adverse outcomes include infants admitted with TB ⩾25 mg dl^{-1} (428 μmol l^{-1}) or for exchange transfusion. [c]Calculated using outcome count that is based on a 90% capture rate. Those infants with TB>30 mg dl^{-1} are a subset of those infants with TB>25 mg dl^{-1}. [d]Significance level $P<0.001$.

Table 5. RR associated with of GA at birth for adverse outcomes in infants ⩾35 weeks' GA, California, 2007–2012

GA *in completed weeks*	*TB⩾25 mg dl^{-1} (428 μmol l^{-1})*	*TB⩾30 mg dl^{-1} (513 μmol l^{-1})*	*Use of exchange transfusion*	*TB⩾25 mg dl^{-1}or use of exchange transfusion*
35	2.14 (1.34–3.42)	No cases	0.64 (0.10–4.2)	2.13 (1.35–3.35)
36	4.82 (3.73–6.22)	4.08 (2.24–7.45)	3.55 (1.86–6.81)	4.79 (3.73–6.13)
37	3.33 (2.67–4.16)	3.63 (2.26–5.82)	2.8 (1.65–4.75)	3.25 (2.62–4.03)
38	2.24 (1.84–2.73)	2.32 (1.51–3.56)	1.25 (0.73–2.15)	2.16 (1.78–2.62)
⩾39	Reference group			

Abbreviations: GA, gestational age; RR, relative risk.

or rates of exchange transfusion for infants born at hospitals with different levels of care.

Adverse outcomes related to infant GA. As shown in Table 5, the risk of bilirubin-related adverse outcomes (per 100 000 live births) was higher at lower GA. Infants>42 weeks' GA comprised about 2% of study cohort and showed no bilirubin-related adverse outcomes.

DISCUSSION

Infants with TB>25 mg dl^{-1} (428 μmol dl^{-1}) serve as potential and possibly the most effective surrogate for 'kernicterus'; whereas, the rate of exchange transfusion is often practitioner-dependent. Infants with TB>30 mg dl^{-1} (513 μmol dl^{-1}) may be attributed to unrecognized glucose 6-phosphate dehydrogenase deficiency. The post-2004 AAP Practice Guideline[1] multi-year (2007 to 2012) data demonstrated the positive impact of a concerted statewide effort to reduce the prevalence of infants ⩾35 weeks' GA with TB>25 mg dl^{-1}, (428 μmol dl^{-1}) regardless of their birthing facility. Our data specifically attests to the reduction of these adverse outcomes in newborns with Asian and Hispanic heritage who have been previously identified to be at higher risk after the 2009 clarification.[3] However, African-American newborns continued to demonstrate an overall lower risk; the RR appeared less, but was not significant. In contrast to prior reports, our data suggest a possible increased clinician awareness of race-related risk factors that may have led to a more rigorous follow-up and prophylactic interventions. Our study continues to highlight the persistent risk of increasing immaturity each week of GA <39 weeks, vaginal versus C-section delivery (shortened in hospital-medical supervision of the newborn), and male gender. In an area with mature regionalized perinatal care, the absence of disparity by location of a primary birthing facility versus non-CCS, NICU versus CCS intermediate, NICU versus CCS community, NICU versus CCS regional NICU attested to an effective penetration and implementation of the statewide learning collaborative.

In estimating the statewide levels, we needed to validate the accuracy of the voluntary reporting of adverse outcomes. For this specific study, we compared the rates of exchange transfusion for live births ⩾35 weeks' GA based on both California-linked vital statistics and the birth and inpatient discharge data for facilities that comprise CPQCC. The data listed in Table 2 indicate equal or higher rates for CPQCC data collected during the evaluation period. In addition, we used a sensitivity analysis based on a 90% capture rate (Table 1). This approach also allowed us to effectively track EHB prevalence rather than relying on qualitative analysis of administrative outcome data by OSHPD.

Our findings continue to highlight the complex relationship between newborn biology, societal healthcare, racial and ethnic demographics, public policy, published clinical guidelines and individual physician practices. There are several strengths and some limitations. This is one of the first statewide neonatal population-based studies that allow the assessment of the practice or adoption of a national guideline by diverse healthcare providers through the use of web-based toolkits supported by several workshops with multiple options for local adaptations. This demonstrates beneficial outcomes that improve and are sustained over a 6-year period.

Perinatal risk factors were recently reported from the Swedish Medical Birth Register (1999 to 2012) of 1 330 421 deliveries at GA of 38 weeks, maternal obesity, primiparity and infants large or small for GA.[14] Similarly, specific positive and negative prenatal risk factors for EHB in our data included GA of 37 to 38 weeks (adjusted odds ratio [aOR] = 2.83); surrogates of neonatal bruising (failed vacuum extraction (aOR = 2.79) and vacuum extraction (aOR = 2.22)); Asian mother (aOR = 2.09); primiparous mother (aOR = 2.06); large for GA infant (aOR = 1.84); obese mother

(aOR = 1.83); and, small for GA infant (aOR = 1.66) as well as planned C-section delivery (aOR = 0.45) and complemented those observed by us for postnatal adverse outcomes in this study and prior studies.[6,14–16] Previous postnatal cohorts or regional network studies have identified similar population risk factors and outcomes.[17–22] A more recent report of 250 047 live births in Denmark (2004 to 2007) linked national registries with medical laboratory databases to identify 258 infants with TB $\geqslant$ 25 mg dl^{-1} (428 μmol dl^{-1}) during the first 21 days after birth.[23] With an incidence of 103 per 100 000 newborns inborn and readmitted, two had significant acute bilirubin encephalopathy (estimated 1 per 100 000 live births). Our study highlights several continued consequences. First, net adverse outcomes were no longer significantly higher among infants born to Asian mothers probably because of altered clinical practice behavior. We also demonstrated a lower than expected frequency in the use of risk-laden exchange transfusions, which may be associated with anticipated declining clinical skills to safely conduct exchange transfusions. These observations underscore the need to plan for urgent triage and direct readmission of infants with progressive hyperbilirubinemia to critical care units for timely interventions. That some of these risk factors are modifiable to improve outcomes provides a rationale for continued QI, monitoring and surveillance until novel interventions are available.

Because the CPQCC does not collect data on acute bilirubin encephalopathy, we are not able to provide population-based frequencies for related adverse outcomes. In addition, we were unable to report data on kernicterus as an outcome, though previous studies have reported that 1 in 7 to 16 infants with TB $\geqslant$ 30 mg dl^{-1} (513 μmol l^{-1}) are at risk for kernicterus.[5] Furthermore, we were unable to diagnose the cause of EHB. In the absence of statewide screening for glucose 6-phosphate dehydrogenase deficiency,[24,25] we could not assess the contribution of this condition other than higher EHB prevalence and use of exchange transfusions in African-American neonates. However, by allocating the adverse outcomes to the birthing facility, we were able to best judge the efficiency of their pre-discharge risk assessment capacity as encouraged by the statewide collaborative.

This report (of serial prevalence) attests to the successful impact of the 2004 AAP Practice Guideline from the time of its inception, to statewide learning and sustenance over the subsequent 4 years. There have been no such prior reports of success and our data clearly attest to the value of implementing national guidelines and lead to a slow but steady modification of clinical practice. In addition, these data are useful to inform the current and ongoing revision of the AAP Practice Guideline. Our data demonstrates that infants born in California and United States remain at continued biologic risk for EHB and undetected hemolysis. Continued reliance on institutional and statewide implementation of prenatal and post-birthing (pre-discharge) risk-assessment(s) continues to guide clinical practice behaviors for timely, targeted follow-up of at-risk infants for selective, individualized and prudent interventions that are amenable to local institutional QI processes.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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