Universal Bilirubin Screening and Health Care Utilization

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KEY WORDS
hyperbilirubinemia, jaundice, practice guideline, health services, phototherapy, length of stay, patient readmission

ABBREVIATIONS
CPS—Canadian Paediatric Society
DAD—Discharge Abstract Database
ED—emergency department
GEE—generalized estimating equation
GP—general practitioner
LOS—length of stay
RR—relative risk
SES—socioeconomic status

Ms Darling conceptualized and designed the study, carried out the data analyses, and drafted the initial manuscript; Dr Ramsay contributed to the study design, provided advice about statistical analyses and interpretation, and critically reviewed the manuscript; Drs Sprague and Walker contributed to the study design and interpretation of data and critically reviewed the manuscript; Dr Guttmann contributed to the study design, supervised the data analyses and interpretation, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

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WHAT’S KNOWN ON THIS SUBJECT: Evidence from cohort studies has consistently found that universal bilirubin screening is associated with reductions in rates of severe hyperbilirubinemia but has shown variation in other outcomes such as phototherapy use, length of stay, emergency department visits, and readmission rates.

WHAT THIS STUDY ADDS: Universal bilirubin screening may not increase neonatal length of stay or postdischarge hospital use. Preexisting trends in health care utilization have an impact on observed effects of universal bilirubin screening.

OBJECTIVE: To evaluate the impact of the implementation of universal bilirubin screening on neonatal health care use in the context of a large jurisdiction with universal health insurance.

METHODS: We conducted a population-based retrospective cohort study of all newborns discharged after birth between April 2003 and February 2011 from 42 hospitals that implemented universal bilirubin screening between July 2007 and June 2010 in Ontario, Canada. We surveyed hospitals to determine their screening implementation date. We used multiple linked administrative health data sets to measure phototherapy use, length of stay (LOS), jaundice-related emergency department visits, and jaundice-related readmissions. We modeled the relationship between universal bilirubin screening and outcomes using generalized estimating equations to account for clustering by hospital, underlying temporal trends, and important covariates.

RESULTS: Screening was associated with an increase in phototherapy during hospitalization at birth (relative risk, 1.32; 95% confidence interval, 1.09–1.59) and a decrease in jaundice-related emergency department visits (relative risk, 0.79; 95% confidence interval, 0.64–0.96) but no statistically significant difference in phototherapy after discharge, LOS, or jaundice-related readmissions after accounting for preexisting temporal trends in health care service use and other patient sociodemographic and hospital characteristics.

CONCLUSIONS: Universal bilirubin screening may not be associated with increased neonatal LOS or increased subsequent hospital use. Our findings are relevant for determining the resource implications of universal bilirubin screening in Ontario. They highlight the limitations in generalizability of previous research on health care utilization associated with similar programs and underline the importance of context-specific local evaluation of guideline implementation. Pediatrics 2014;134:e1017–e1024

(Continued on last page)
Evidence from 4 large North American cohort studies suggests that universal bilirubin screening of infants reduces the risk of severe hyperbilirubinemia; however, there remains debate about the balance of costs, harms, and benefits associated with universal bilirubin screening to prevent acute bilirubin encephalopathy. Consequently, some organizations have not recommended universal screening. One challenge in determining the balance of costs, harms, and benefits is the variation in the reported impact of universal bilirubin screening on resource utilization. Despite this lack of definitive evidence, in 2007 the Canadian Paediatric Society (CPS) recommended universal bilirubin screening. The CPS hyperbilirubinemia guidelines include recommendations for follow-up and treatment but are not prescriptive with respect to the system of services that provide the recommended care. In previous work describing implementation, we have shown that in Ontario (Canada’s largest province, population 13 million) it occurred gradually, on a hospital-by-hospital basis. By 2012 the majority of hospitals had implemented some form of the guideline. Because Ontario does not have a system of universal public health home visits after birth, implementation of the CPS guidelines in Ontario included primarily hospital-based follow-up for infants who are at higher risk for severe hyperbilirubinemia. To date, there has been no evaluation of the impact of this implementation on health services use and outcomes.

Our objective was to evaluate the association of the implementation of universal bilirubin screening with neonatal health care use in the context of this large, uncoordinated natural experiment in Ontario. We examined 5 key outcomes: phototherapy use during birth hospitalization, phototherapy after hospital discharge, length of stay (LOS), jaundice-related emergency department (ED) visits, and jaundice-related readmissions. We hypothesized that the implementation of universal bilirubin screening would be associated with increases in all of these outcomes.

**METHODS**

**Overall Design**

This was a population-based retrospective cohort study of all newborns discharged after birth between April 1, 2003 and February 28, 2011 from 42 Ontario hospitals. We surveyed all 100 hospitals providing maternal–newborn services in Ontario to determine guideline implementation date. Of the 97 responding hospitals, 42 implemented the CPS hyperbilirubinemia guidelines between July 1, 2007 and June 30, 2010. Full details of the hospital survey have been published. We linked the survey data to multiple administrative health data sets available at the Institute for Clinical Evaluative Sciences. Scrambled health insurance numbers were used to link individual records. Research ethics approval was obtained from the Ottawa Hospital Research Ethics Board.

**Cohort Creation**

We extracted records from the Institute for Clinical Evaluative Sciences–derived MOMBABY data set, which links maternal and infant hospital records (Discharge Abstract Database [DAD]). We included only infants born to Ontario residents. The cohort was limited to infants born at ≥35 weeks’ gestation, with an LOS of no more than a week, who were discharged from the hospital, so as to mirror the target population for the CPS hyperbilirubinemia guidelines. We excluded higher-order multiples, and to avoid potentially correlated outcomes within twin pairs we randomly selected 1 twin to include in the cohort if both twins were eligible. We excluded births that occurred at hospitals that did not provide maternity services as of the end of the study period (this included both emergency births that occurred at a hospital with no maternity services and births that occurred at a hospital that stopped providing maternity services before February 28, 2011). To create the final analytical cohort, we excluded infants born at hospitals that had not implemented universal bilirubin screening between July 2007 and June 2010 or without a known date of implementation.

**Bilirubin Screening**

Infants with a date of discharge before the date of bilirubin screening implementation were categorized as not being screened. Infants with a discharge date in the same month and year as bilirubin screening was implemented or later were categorized as being screened. This was the main exposure of interest.

**Outcomes**

Our outcomes included phototherapy and LOS of the initial birth hospitalization as well as the following outcomes that occurred within 14 days after the initial discharge after birth: jaundice-related ED visits, jaundice-related readmissions, and phototherapy after initial discharge. We used admission dates and registration dates, respectively, to identify records from the DAD and the National Ambulatory Care Reporting System of any hospital admissions or ED visits within the 2-week time frame. We calculated LOS in hours by using the date and time of the infant’s discharge from hospital to the infant’s record in MOMBABY and the delivery time from the mother’s record in the DAD. Newborn admissions, readmissions, and ED visit records within 2 weeks of discharge with a Canadian Classification of Intervention procedure code of 1YZ12JADQ were classified as having received phototherapy. Two authors (E.K.D., a midwife, and A.G., a pediatrician) established by consensus a priori diagnostic codes to define ED visits and readmissions as “jaundice-related” (Table 1).
Covariates

We adjusted for covariates known to be associated with the study outcomes or risk of jaundice. These included gestational age (35–38 weeks versus ≥39 weeks), mode of birth (spontaneous vaginal, assisted vaginal, cesarean), maternal parity (multiparous versus primiparous), age category at discharge (LOS ≤24 hours, 24 < LOS ≤72 hours, LOS >72 hours), midwifery care, and maternal prenatal care from a general practitioner (GP). Infants under midwifery care in Ontario are much more likely to have early discharge from the hospital (within a few hours of birth), which results in different service utilization patterns. We used prenatal care from a GP as a marker of access to primary care for the infant, which has been shown to reduce ED use.12 We adjusted for the level of neonatal services offered by the hospital where the birth occurred (based on provincially recognized designations).11 We also used maternal postal code to derive 4 area-level variables related to rurality and socioeconomic status (SES). We classified infants as rural or urban by using the Rurality Index of Ontario (2008), which is based on census subdivision-level data on population density and travel time from referral centers.13 We adjusted for SES because even in settings with universal health insurance, SES is associated with health system utilization patterns.14,15 We assigned 3 SES variables based on census data at the level of dissemination area (the smallest geographic census unit in Canada, which has a population of 400–700): material deprivation quintile, social deprivation quintile,16 and income quintile.

Analyses

We graphed the basic trend in outcomes over the study period by using quarterly rates for categorical outcomes and mean values for LOS. We used generalized estimating equations (GEEs) to model the relationship between universal bilirubin screening and outcomes, by using a class variable for hospital to account for clustering by hospital. We included a linear quarterly time variable in each model to account for underlying temporal trends. We used log binomial GEE to estimate relative risk (RR) for categorical outcomes and normal GEE to estimate the change in LOS in hours. Using a predefined list of potential covariates for each model, we conducted univariate analyses of covariates and selected variables with a P value for the χ² statistic <.10 to include in the initial model. We then used backward elimination to eliminate variables based on the highest P value until all covariates had P < .05. Because of the colinearity between social deprivation, material deprivation, and income deprivation, we held these 3 variables out of the models until non-significant variables had been eliminated. We then included each socioeconomic variable in the model individually and selected the best model based on the quasi-likelihood under the independence model criterion goodness-of-fit statistic.17 We also conducted post hoc analyses removing the quarterly time variable from the model to assess the impact of the time trend variable. All analyses

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**TABLE 1** International Classification of Diseases, 10th Revision Codes Used to Define Jaundice-Related ED Visits and Readmissions

<table>
<thead>
<tr>
<th>Diagnostic Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>P57, P58, and P59</td>
<td>Pediatric kernicterus or neonatal jaundice codes</td>
</tr>
<tr>
<td>E806, E807, and R17</td>
<td>Nonpediatric codes for disorders of bilirubin metabolism or jaundice</td>
</tr>
<tr>
<td>P550, P551, P558, P559, and D589</td>
<td>Pediatric codes for hemolytic diseases</td>
</tr>
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**FIGURE 1** Flowchart detailing exclusion criteria applied to identify the study cohort.

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1,060,081 records of live births in MOMBABY2010 that met the following criteria were extracted:
- Baby was discharged between April 1, 2003 and February 28, 2011
- Baby’s health record is linked to a single maternal health record
- Baby’s health record has a valid Ontario Health Insurance Plan number

87,363 babies were excluded (8.24%)

<table>
<thead>
<tr>
<th>Reason for exclusion</th>
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<tbody>
<tr>
<td>34,146 (3.22%) Gestational age at birth was &lt;35 weeks or missing</td>
</tr>
<tr>
<td>13,733 (1.30%) Baby was not discharged from the hospital (includes babies transferred to another facility or discharged to social services)</td>
</tr>
<tr>
<td>1209 (0.11%) Baby’s mother was not a resident of Ontario or her postal code was unknown</td>
</tr>
<tr>
<td>418 (0.04%) Baby died before discharge or on the day of discharge</td>
</tr>
<tr>
<td>12,461 (1.18%) Were triplets or quadruplets, or randomly selected twin from twin sibling pairs</td>
</tr>
<tr>
<td>3080 (0.29%) Were born at a hospital that did not provide maternity services, or that closed maternity services before March 2011</td>
</tr>
<tr>
<td>4577 (0.43%) Were born at a hospital (n = 3) that did not respond to the survey</td>
</tr>
<tr>
<td>271 (0.03%) Were missing information about length of stay (LOS) or had an LOS less than 0 hours</td>
</tr>
<tr>
<td>17,468 (1.65%) Had a length of stay &gt;1 week (168 hours)</td>
</tr>
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</table>

Of the remaining 972,718 babies:
- 438,615 (41.38%) were born at a hospital that did not implement bilirubin screening between July 2007 and June 2010
- 534,103 (50.38%) were born at a hospital that implemented bilirubin screening between July 2007 and June 2010
were conducted by using SAS 9.3 (SAS Institute, Inc, Cary, NC).

RESULTS

The analytical cohort contained 534,103 infants, or roughly half of all infants born in Ontario during the study window (Fig 1). When compared with the 438,615 eligible infants who were not born at a hospital that implemented universal bilirubin screening between July 2007 and June 2010, infants in the analytical cohort were more likely to be born at a hospital with the highest level (level 3) of neonatal services (22.0% vs 10.4%) and more likely to reside in an urban area (92.2% vs 86.9%) but were otherwise similar with respect to clinical and socioeconomic characteristics (data not shown). Within the analytical cohort, characteristics of infants born before and after implementation of screening were similar (Table 2). Statistical testing was not conducted, given our large sample, because it would invariably lead to statistical significance even for very small absolute differences.

Unadjusted rates of each outcome over time in the analytical cohort are shown in Fig 2. Each graph contains a vertical line at the second quarter of 2007 to indicate the release of the CPS hyperbilirubinemia guidelines. The graphs illustrate increases in the crude rates of phototherapy and jaundice-related readmissions over the 8-year time period, a much more subtle increase in the crude rate of jaundice-related ED visits, and a decrease in the crude mean LOS.

Table 3 shows the crude and adjusted RRs of phototherapy, jaundice-related ED visits, and jaundice-related readmissions for infants born after universal bilirubin screening was implemented. Screening was associated with an increase in the use of phototherapy during the initial hospitalization at birth and with a decrease in jaundice-related ED visits but no statistically significant difference in phototherapy after discharge or jaundice-related readmissions. There was no statistically significant difference in LOS associated with the implementation of screening after we adjusted for hospital, quarter, gestational age category, mode of birth, maternal parity, midwifery care, and social deprivation quintile. Post hoc analyses removing the quarterly time variable from the models for all outcomes demonstrated that adjusting for preexisting temporal trends accounted for most of the difference seen for each outcome between the crude and adjusted rates.
DISCUSSION

Contrary to our hypothesis, the implementation of universal bilirubin screening in Ontario, Canada was associated only with an increase in the rate of phototherapy during the initial hospitalization at birth. Rates of phototherapy after discharge and jaundice-related readmissions have risen over the 8-year study period, but this pattern predated the implementation of universal bilirubin screening. Similarly, there was an underlying temporal trend of rising rates of jaundice-related ED visits. Absolute rates of jaundice-related ED visits leveled off toward the end of the study period, and this was attributable to a decrease in the RR of jaundice-related ED visits associated with the implementation of universal bilirubin screening. This finding corresponds with results from the hospital survey, which determined that a majority of hospitals conducting universal bilirubin screening have developed processes to facilitate postdischarge follow-up for hyperbilirubinemia via locations other than the ED. Our finding of no significant difference in LOS also corresponds with the variety of responses to the hospital survey, which revealed that although some hospitals reported delays in discharge after implementation of universal bilirubin screening, others reported being able to implement processes to avoid this problem or in some cases to even shift to earlier discharge because of improved processes for postdischarge follow-up.

For all 5 outcomes, adjusting for the underlying temporal trend had a notable impact on the effect estimates. The preexisting trends suggest that heightened awareness of hyperbilirubinemia preceded release of the CPS guidelines, and they illustrate the value of being able to examine outcomes over a long time period when evaluating the impact of guideline implementation on health service utilization using a cohort design. Our findings are consistent with the hypothesis that implementation of the CPS hyperbilirubinemia guideline led to a more structured approach to screening and treatment, which minimized the impact of universal bilirubin screening on health care use. Previous studies from Utah (n = 101,272), California (n = 358, 086), the United States (n = 1,028,817), and Calgary (n = 28,908) have reported changes in crude rates of service utilization after implementation of universal bilirubin screening. The crude total phototherapy rate in our cohort at the end of the study was lower than that reported in California but higher than rates reported in Calgary or the US study. Compared with our cohort, the Calgary study observed lower rates of phototherapy at birth and higher rates of phototherapy after discharge, and contrary to our findings, universal screening

FIGURE 2

A. Frequency of phototherapy use by quarter. B. Mean LOS in hours by mode of birth by quarter.

CPS Guidelines Released

A

B

Rate of Phototherapy (%) Time

Mean LOS in Hours

CPS Guidelines Released

FIGURE 2

A. Frequency of phototherapy use by quarter. B. Mean LOS in hours by mode of birth by quarter. C. Frequency of ED visits within 2 weeks of discharge by quarter. D. Frequency of readmission within 2 weeks of discharge by quarter.
was associated with decreases in both outcomes. The crude rate of jaundice-related readmission in our cohort at the end of the study was higher than that reported in Utah but lower than those reported in California and in the U.S. study. Although both the Utah and the Calgary studies observed screening to be associated with reductions in readmissions, the California study observed the opposite. In contrast to Ontario, Calgary had a preexisting comprehensive public health nurse follow-up program and shorter LOS; the observed differences in outcomes illustrate how a pre-existing care delivery model can alter the effect on resource utilization. Previous authors have noted that comparison of outcomes between different settings may be complicated by differences in patient demographics, duration of hospital stay, and clinical practice (ie, sub-threshold treatment). Although these authors have noted that preexisting trends and changes in other elements of clinical practice may also contribute to changes in outcomes, no previous cohort studies have adjusted for underlying temporal trends. Our findings suggest that adjusting for underlying temporal trends in service utilization outcomes may notably influence the estimation of the effect of universal bilirubin screening on these outcomes. Our findings also suggest that there are limitations to previous economic analyses, given the wide variation in the impact of universal screening on resource use. One published cost-effectiveness analysis modeled anticipated costs associated with the implementation of universal bilirubin screening and systematic follow-up in Ontario. The authors assumed a higher baseline rate of predischarge phototherapy than we observed in our cohort but estimated a much lower increase in this rate than we observed. They also assumed a much lower baseline rate of jaundice-related readmission and estimated that this would decrease, whereas we saw no change in this outcome. The assumptions made with respect to ED visits were similar to what we observed. Although our findings may facilitate a more accurate analysis of the cost of universal bilirubin screening in Ontario, they also highlight the challenge in predicting the impact in other contexts.

A key strength of the study is that it was population based and included all infants born at an Ontario hospital that implemented bilirubin screening in the first 3 years after release of the CPS guidelines (with the possible exception of 3 small hospitals that did not respond to our survey). However, our study has limitations inherent in observational studies. To mitigate some of the limitations of a historical control group, we modeled our outcomes by using individual-level data and adjusted for confounding variables and underlying temporal trends. One possible limitation of our approach is that we did not have sufficient data points to include an
TABLE 3  RR of Phototherapy, Jaundice-Related ED Visits, and Jaundice-Related Readmissions Associated With Implementation of Bilirubin Guidelines

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Crude RR</th>
<th>Adjusted RR (95% CI)</th>
<th>Pr &gt; χ² (Full Model)</th>
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<tr>
<td>Phototherapy at birtha</td>
<td>1.61</td>
<td>1.32 (1.09–1.59)</td>
<td>0.004</td>
</tr>
<tr>
<td>Phototherapy after dischargeb</td>
<td>1.28</td>
<td>0.95 (0.75–1.20)</td>
<td>NS (0.65)</td>
</tr>
<tr>
<td>Jaundice-related readmissionc</td>
<td>1.21</td>
<td>0.95 (0.78–1.16)</td>
<td>NS (0.61)</td>
</tr>
<tr>
<td>Jaundice-related ED visitd</td>
<td>1.05</td>
<td>0.79 (0.64–0.96)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

CI, confidence interval; NS, not significant; Pr, probability. Variables in the model:

a Hospital, quarter, gestational age category, mode of birth, maternal parity, midwifery care.
b Hospital, quarter, gestational age category, mode of birth, maternal parity, midwifery care, material deprivation quintile.
c Hospital, quarter, gestational age category, mode of birth, maternal parity, hospital level, midwifery care, prenatal care.
d Hospital, quarter, gestational age category, mode of birth, maternal parity, age at discharge, social deprivation quintile.

autocorrelation term in our time trend analysis. The date of implementation was determined retrospectively and by survey data, which may have decreased accuracy. The data we collected on implementation date included only the month and year of implementation, and we did not include a washout period at the time of implementation. This approach might slightly underestimate the impact on outcomes if screening actually began later in the month and would potentially bias results in favor of the null hypothesis. Another limitation is that we were not able to verify adherence to the guidelines. As noted by others,2 it is possible that there was subthreshold treatment, such as use of phototherapy for infants with bilirubin levels below recommended treatment thresholds, which limits our ability to quantify the impact on resource utilization if the guidelines were followed accurately. We restricted our cohort to infants with an LOS of ≤1 week because the guidelines are aimed at the normal, healthy newborn population. This decision resulted in a slightly lower mean LOS and slightly lower rates of phototherapy at birth than if infants with a length of stay >1 week had been included (only 1.65% of infants had a LOS >168 hours, but 14.4% of them received phototherapy during their initial hospital stay).

Another limitation is that we were not able to adjust for breastfeeding status. National survey data suggest that breastfeeding initiation rates remained stable between 2003 and 2010,20 but if this was not the case in Ontario, our approach of adjusting for underlying temporal trends would have accounted for linear temporal changes in infant feeding patterns. Furthermore, we adjusted for SES, which is a predictor of breastfeeding.21 During the study period ~1.65% of infants in Ontario were born at home,22 and our findings address only infants born in the hospital. Finally, our research was limited in scope. As with many studies in this area, the rarity of kernicterus precludes its use as an outcome for modeling.

CONCLUSIONS

Although universal bilirubin screening might be seen as the linchpin of a systematic approach to preventing severe neonatal hyperbilirubinemia,2 the system of follow-up and treatment that accompanies screening is important. Our study suggests that universal screening can be implemented without increasing the need for hospital care, although pre-existing upward trends in rates of phototherapy, jaundice-related readmissions, and jaundice-related ED visits may have reflected increased bilirubin testing before guideline implementation. Our findings are relevant for determining the resource implications of universal bilirubin screening in Ontario and also highlight the potential challenges in estimating resource implications in other settings, given the limitations in generalizability of previous research, underlining the importance of context-specific local evaluation of guideline implementation.

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