



# A narrative review of electronic clinical decision support tools for hyperbilirubinemia management

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**Background and Objective:** The objective of this narrative review is to provide an overview of common electronic clinical decision support (CDS) tools available to help clinicians manage neonatal hyperbilirubinemia. We focus on the guidelines behind their recommendations, their differences, manner of implementation, and future potential. Hyperbilirubinemia assessment is recommended in all preterm and term infants. Various guidelines for the management of hyperbilirubinemia exist, and many guidelines have corresponding electronic CDS tools. The increasingly widespread adoption of electronic health records provides an opportunity for both enhanced integration of CDS tools into daily workflow and automated data collection.

**Methods:** Based on our collective experience in pediatrics, neonatology, and clinical informatics, we identified commonly used CDS tools for neonatal hyperbilirubinemia management. We performed manual searches on the Apple App Store and Google Play Store to identify mobile applications that follow published guidelines for neonatal hyperbilirubinemia management.

**Key Content and Findings:** CDS tools have the potential to improve patient care through increased adherence to guidelines, and to improve the provider experience through workflow integration.

**Conclusions:** In addition, the electronic health record integration of hyperbilirubinemia management tools allows for the collection of data that can be used to refine recommendations over time and inform the development of future guidelines.

**Keywords:** Clinical decision support (CDS); BiliTool; Premie BiliRecs; hyperbilirubinemia

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## Introduction

### *Rationale/background*

Jaundice occurs in most newborn infants, the vast majority of whom have some degree of hyperbilirubinemia (1,2). Thankfully, the incidence of severe hyperbilirubinemia leading to kernicterus remains low (3). Nevertheless, due to the adoption of universal newborn bilirubin screening, almost all infants are assessed for hyperbilirubinemia.

Commonly referenced treatment guidelines include the American Academy of Pediatrics (AAP) (1) and the Northern California Neonatal Consortium (NCNC) guidelines (4) for infants greater than 35 weeks gestation, and the Maisels expert consensus guidelines (5) for moderately preterm infants.

Because the need for assessment of jaundice is ubiquitous, and because electronic clinical decision support (CDS) tools have the potential to improve adherence to

practice recommendations (6), many electronic tools exist for the management of neonatal hyperbilirubinemia. In general, these tools are based upon the treatment guidelines referenced above; commonly used examples include BiliTool (7) (AAP guidelines), phototherapyguidelines.com (8) (NCNC guidelines), and Premie BiliRecs (9) (Maisels guidelines). Electronic health record (EHR) vendors have also begun to incorporate EHR-embedded tools based upon existing guidelines into their commercial systems. It is also important to note that electronic clinical decision tools support tools are just that—tools to support medical decision-making, and are not a substitute for clinical judgement.

### Objective

In this article, we review several of the most common electronic CDS tools for the management of hyperbilirubinemia in term and premature newborns. We discuss the guidelines upon which they are based, the manner in which they are implemented, how they differ, and—where it exists—evidence for their efficacy. We also look ahead to ongoing research and upcoming guidelines, including the importance of making them amenable to conversion into electronic tools. We present the following article in accordance with the Narrative Review reporting checklist (available at <https://pm.amegroups.com/article/view/10.21037/pm-21-12/rc>).

### Methods

In this narrative review we discuss the most commonly used CDS tools based on over 20 years of collective clinical experience in pediatrics, neonatology, and clinical informatics amongst the authors. The mobile applications discussed were found using manual searches of the Apple App Store and Google Play Store, with a focus on applications that follow published phototherapy guidelines.

### Discussion and summary

#### *Narrative: CDS tools*

#### **BiliTool—American Academy of Pediatrics Clinical Practice Guideline**

In 2004, the AAP published guidelines on hyperbilirubinemia management for newborns greater than 35 weeks gestational age (GA) at birth (1). The guidelines recommend that all newborns be assessed for their risk of developing hyperbilirubinemia prior to discharge, and provide hour-

specific nomograms for risk assessment and phototherapy treatment thresholds. BiliTool ([www.bilitool.org](http://www.bilitool.org)), the first electronic CDS tool for hyperbilirubinemia management, was created shortly thereafter to automate the implementation of the AAP recommendations (10).

BiliTool requires as inputs a patient's total bilirubin (TB) result and their age in hours at the time of the result. The data entry screen allows for either direct input of hours of life, or for the entry of a patient's birth date and time and TB lab date and time, from which hours of life is calculated. The BiliTool results page displays the infant's age in hours, TB value, and risk zone based on the hour-specific nomogram. It also includes tables for recommended follow-up and TB thresholds for phototherapy initiation. For reference, hyperbilirubinemia risk factors and neurotoxicity risk factors are listed, and a link to the exchange transfusion nomogram is included.

Another important feature of BiliTool is its application programming interface (API) for integration of the web tool with electronic health records (EHRs). This integration automates the calculation of hours of life and passes a TB result directly to the tool, eliminating the need for manual data entry by the provider. Recently, commercial EHR vendors have incorporated electronic tools automating the AAP guidelines directly into their software as native functionality.

Several mobile applications have been created for use on Apple and Android devices to aid in decision support for hyperbilirubinemia management. Other apps that automate the 2004 AAP guidelines include BiliCalc and BiliRisk (11,12). There are also several apps that automate the 2010 U.K. National Institute for Health and Care Excellence (NICE) Guidelines (13), including Biliguru (14), BiliApp (15), and BiliChecker (16). The creation and utilization of mobile apps to aid in hyperbilirubinemia management has been shown to improve adherence to phototherapy guidelines (17).

#### **Phototherapyguidelines.com—Northern California Neonatal Consortium Guidelines**

In 2016, new phototherapy guidelines for infants greater than or equal to 35 weeks gestational age were developed and published by the Northern California Neonatal Consortium (NCNC) (4). The development of updated guidelines was pursued by the NCNC out of concern for over-treatment of hyperbilirubinemia in context of low rates of kernicterus (3), an unknown number needed to treat (NNT) to prevent kernicterus, and the

potential adverse effects of phototherapy (18,19). The NCNC used the 2004 AAP Guidelines as a foundation, increasing thresholds for most infants depending on GA and the presence of neurotoxicity risk factors. Treatment thresholds were not changed for infants 35 weeks GA with neurotoxicity risk factors.

A web-based tool that automates the NCNC guidelines is available at [www.phototherapyguidelines.com](http://www.phototherapyguidelines.com). The data entry page requires inputs of gestational age at birth, TB value, and age in hours at the time the TB level was obtained. The results display provides treatment thresholds for initiating phototherapy, and shows the 2004 AAP treatment thresholds for comparison purposes. An API exists for EHR integration. Recently, an abstract reported decreased phototherapy exposure with adoption of the NCNC guidelines, including the avoidance of phototherapy for 34% of TB values above AAP thresholds with no increase in hazardous hyperbilirubinemia (20).

#### **Premie BiliRecs—Maisels expert consensus recommendations**

Premie BiliRecs (PBR) is a web-based CDS tool for the management of hyperbilirubinemia in preterm infants from 27 through 34 weeks post-menstrual age (PMA) (9). PBR was developed to automate and standardize the phototherapy and exchange transfusion treatment thresholds for infants less than 35 weeks PMA published by Maisels *et al.* (5). These expert consensus recommendations include ranges for treatment thresholds and PMA, reflecting the clinical uncertainty in the management of hyperbilirubinemia in the preterm population—but such ranges are not amenable to automation. In order to operationalize the guidelines, the ranges were extrapolated into discrete TB thresholds for each day of PMA (21).

The PBR web tool automates the process of determining the TB thresholds for initiation of phototherapy and exchange transfusion for a given PMA. To that end, the PBR data entry page requires 2 inputs: a TB value and a corresponding PMA. The PBR results page displays the user-entered PMA and TB, a table of TB thresholds for initiation of treatment, and a visual indication if any threshold is exceeded. An API is provided for EHR integration.

The implementation of PBR in an EHR was associated with significantly improved adherence to hyperbilirubinemia management guidelines in preterm infants: less phototherapy was initiated below recommended treatment thresholds (22). Despite initiation

of phototherapy at higher TB values, the incidence of exchange transfusions and TB values exceeding exchange transfusion thresholds was not increased.

#### **Summary**

Given the ubiquitous practice of hyperbilirubinemia evaluation in newborns, several sets of management guidelines exist, including from the AAP, the NCNC, and from expert consensus. Thankfully, corresponding electronic decision support tools have been created that automate the process of hyperbilirubinemia evaluation: BiliTool for the AAP guidelines, [phototherapyguidelines.com](http://phototherapyguidelines.com) for NCNC guidelines, and Premie BiliRecs for the Maisels expert consensus guidelines. Each of these electronic tools has published an API for workflow integration with commercial EHRs, and the creators of Premie BiliRecs demonstrated significantly improved adherence to guidelines following EHR-integration of the electronic CDS tool (22). Additionally, EHR vendors have begun to incorporate bilirubin reference applications directly into their software as native functionality.

Bilirubin assessment and the management of hyperbilirubinemia is not without controversy. Among term infants, critics of universal screening and hour-specific nomograms exist (23,24). There is a paucity of data to guide the optimal management of hyperbilirubinemia in preterm infants. While the implications of non-treatment of severe hyperbilirubinemia are well recognized, there is growing evidence for both the short- and long-term consequences of phototherapy, including DNA damage (25), changes in immune system function (26), infantile cancer (27), and possibly increased mortality in preterm infants (28,29).

As such, guidelines and clinical practice related to hyperbilirubinemia continue to evolve, and new approaches such as cycled phototherapy are beginning to emerge in an attempt to decrease phototherapy exposure (30,31). Another mechanism for decreasing phototherapy exposure is to use more permissive bilirubin thresholds; implementation of the more permissive NCNC guidelines was suggested to be safe in at least one report (20). Electronic CDS tools can play a role in decreasing phototherapy exposure in various ways. Improved adherence to phototherapy guidelines by decreasing the (unnecessary?) initiation of phototherapy below recommended thresholds using a CDS tool was demonstrated by Arain *et al.* with no increase in the incidence of severe hyperbilirubinemia (22). Similarly, Electronic CDS tools also have the potential to generate

data and contribute to practice-based evidence that could inform phototherapy thresholds themselves (32). It is possible that examining these data would allow for a safe increase in phototherapy thresholds, encouraging initiation of phototherapy at higher bilirubin levels, thereby decreasing exposure to phototherapy.

As new guidelines for and approaches to the management of hyperbilirubinemia and administration of phototherapy are developed, particular attention should be paid to the importance of automating new workflows with electronic CDS tools. In the EHR era, electronic CDS tools can both contribute to guideline adherence and help generate practice-based evidence to inform future guidelines.

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