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Newborn Transcutaneous Bilirubin Screening: A 2022 Update

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Summary of Abstracts

CADTH

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Key Messages

- One health technology assessment and 6 non-randomized studies were identified regarding the diagnostic test accuracy of transcutaneous bilirubin screening compared with serum bilirubin testing for well newborns in hospital.
- One health technology assessment and 1 randomized controlled trial were identified regarding the clinical effectiveness of transcutaneous bilirubin for well newborns in hospital.
- One health technology assessment and 1 economic evaluation were identified regarding the cost-effectiveness of transcutaneous bilirubin screening for well newborns in hospital.
- One evidence-based guideline was identified regarding transcutaneous bilirubin screening for well newborns in hospital.

Research Questions

1. What is the diagnostic test accuracy of transcutaneous bilirubin (TcB) screening compared with serum bilirubin testing for well newborns in hospital?
2. What is the clinical effectiveness of TcB screening for well newborns in hospital?
3. What is the cost-effectiveness of TcB screening for well newborns in hospital?
4. What are the evidence-based guidelines regarding TcB screening for well newborns in hospital?

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, the Cochrane Database of Systematic Reviews, the International HTA Database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were transcutaneous bilirubin AND screening tests. The search was based on a previous CADTH report. No filters were applied to limit the retrieval by study type. The search was also limited to English-language documents published between January 1, 2016, and January 17, 2022.

Selection Criteria and Summary Methods

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. The Overall Summary of Findings was based on information available in the abstracts of selected publications. Open-access full-text versions of evidence-based guidelines were reviewed when available, and relevant recommendations were summarized.

Table 1: Selection Criteria

Criteria	Description
Population	Q1 to Q4: Well newborns (i.e., < 10 days of age), in hospital
Index test or intervention	Q1 to Q4: Transcutaneous screening test(s) (e.g., Philips BiliChek, Minolta Jaundice Meter, Dräger Jaunice Meter JM-103, BiliStick, Dräger Jaundice Meter JM-105, transcutaneous Jaundice Detector JH20-1C [Ningbo David, China], novel icterometers such as smart phone camera apps, and other point-of-care, transcutaneous interventions) for measuring bilirubin in newborns
Reference standard	Q1: Serum bilirubin measurement
Comparator	Q1 to Q3: Any other transcutaneous bilirubin screening test device(s), method, approach Q4: Not applicable
Outcomes	Q1: Diagnostic test accuracy (e.g., sensitivity, specificity, positive predictive value, negative predictive value) Q2: Clinical effectiveness (e.g., benefits and harms to newborn patients and/or families, including time to treatment, impact on quality of life, feasibility of screening test, adverse events from the screening, incidental findings) Q3: Cost-effectiveness (e.g., QALYs, costs per unit of health benefit) Q4: Evidence-based recommendations and/or guidance (e.g., which screening test method is optimal; guidance as to which intervention is preferable in particular patient populations, settings, contexts; clinical and other considerations when using one screening method vs. another)
Study designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, economic evaluations, evidence-based guidelines

QALY = quality-adjusted life-year; vs. = versus.

Results

Ten relevant references were identified for this report.[1-10]

One health technology assessment (HTA)[1] and 6 non-randomized studies[3-8] were identified regarding the diagnostic test accuracy of TcB screening compared with serum bilirubin testing for well newborns in hospital. One HTA[1] and 1 randomized controlled trial[2] were identified regarding the clinical effectiveness of TcB screening for well newborns in hospital. One HTA[1] and 1 economic evaluation[9] were identified regarding the cost-effectiveness of TcB screening for well newborns in hospital. One evidence-based guideline was identified regarding TcB screening for well newborns in hospital.[10]

Additional references of potential interest that did not meet the inclusion criteria are provided in Appendix 1.

Overall Summary of Findings

One HTA[1] and 6 non-randomized studies[3-8] were identified regarding the diagnostic test accuracy of TcB screening compared with serum bilirubin testing for well newborns in hospital. The HTA compared to total serum bilirubin (TSB) screening and found that TcB had poorer diagnostic accuracy than TSB measurements, when it is assumed that TSB has perfect diagnostic accuracy.[1] All of the non-randomized studies that examined the diagnostic test accuracy of TcB measurements compared to serum bilirubin levels found that TcB devices could be used as reliable tools to screen for hyperbilirubinemia in newborn

populations.[3-8] The specific newborn populations examined, outcomes investigated, and additional conclusions made by authors varied across studies.[3-8] A detailed summary of the identified studies relevant to research question 1 can be found in Table 2.

One HTA[1] and 1 randomized controlled trial[2] were identified regarding the clinical effectiveness of TcB screening for well newborns in hospital. The HTA examined TcB screening methods, specifically the BiliChek and Jaundice Meter JM-105 devices.[1] The authors found that after TcB implementation, there was a trend toward decreased health care resource usage, including TSB testing, phototherapy, and hospital readmissions.[1] A randomized controlled trial examined the effect of predischarge TcB screening on the rate of hospital readmission for jaundice and the incidence of severe hyperbilirubinemia.[2] The study found that predischarge screening with TcB better identified newborns at risk of severe hyperbilirubinemia compared to visual inspection.[2]

One HTA[1] and 1 economic evaluation[9] were identified regarding the cost-effectiveness of TcB screening for well newborns in hospital. The HTA performed a cost-effectiveness analysis and found that the overall differences in health outcomes (e.g., quality-adjusted life-years) between TcB, TSB, and visual assessment were small.[1] When it was assumed that patients must wait in the hospital for TSB results, the TcB devices that were evaluated tended to be less costly than TSB.[1] However, TSB was preferred when patients didn't have to wait for results in the hospital because TcB resulted in higher costs in these scenarios.[1] Among TcB devices, the Jaundice Meter JM-105 was less costly and had equivalent benefits in terms of clinical outcomes when compared to the BiliChek.[1] The Jaundice Meter JM-105 was less costly and more effective than visual assessment.[1] The economic evaluation used a cost-minimization analysis to compare a TcB-TSB screening program to a TSB-only screening program in a tertiary care centre.[9] The authors found that the TcB-TSB program reduced nurses' time to screen and provided immediate results at the point-of-care.[9] TcB reduced the need for painful heel pokes while improving access to screening and decreasing the overall program cost.[9]

One evidence-based guideline was identified regarding TcB screening for well newborns in hospital.[10] The guideline, published by the Association of Ontario Midwives, recommended that TcB screening should be offered in instances where screening for hyperbilirubinemia is requested or recommended and bilimetres are available.[10] The authors classified this as a "strong recommendation" with "very low certainty of evidence."[10]

Table 2: Summary of Included Diagnostic Test Accuracy Studies

Study citation	Study design, population	Intervention and comparator(s)	Relevant outcome(s)	Authors' conclusions
Health technology assessments				
Dowsett et al. (2017)[1]	HTA with 9 diagnostic accuracy studies included **Population**: Newborns in an acute care setting	**Intervention**: TcB measurement **Comparator**: TSB measurement	Sensitivity, specificity	Sensitivity of TcB ranged from 72% to 100%. Specificity of TcB ranged from 58% to 88%. Based on the assumption that TSB has perfect diagnostic accuracy, TcB has poorer diagnostic accuracy than TSB.

Study citation	Study design, population	Intervention and comparator(s)	Relevant outcome(s)	Authors' conclusions
Non-randomized studies				
Casnocha et al. (2021)[3]	**Study design**: NRS **Population**: Healthy term infants from Slovakia **N** = 102	**Intervention**: TcB using the JM-105 device **Comparator:** TSB screening	TcB/TSB correlation, mean difference of TcB and TSB, sensitivity, area under the curve	Transcutaneous bilirubinometry is an accurate, sensitive, and convenient screening method in term Caucasian newborns. TcB measurements showed best performance on the forehead. Confirmation of higher transcutaneous bilirubin values with a TSB measurement is necessary.
Khajehei et al. (2021)[4]	**Study design**: NRS **Population**: Ethnically diverse neonates > 35 weeks gestation, aged > 168 hours **N** = 78	**Intervention:** Two TcB devices (JM-105, MBJ-20) **Comparator:** SBR levels	JM-105/MBJ-20 correlation, Correlation between TcB measurements and SBR levels, sensitivity, specificity, PPV, NPV	Both devices had high sensitivity and negative predictive values at an SBR level of less than 230 mumol/L and high specificity and positive predictive values at an SBR level of 230 mumol/L and greater. Both devices equally overestimated the actual SBR and had more reliable results if used on the sternum.
Mendoza-Chuctaya et al. (2021)[5]	**Study design**: NRS, prospective, and cross sectional **Population**: Full-term newborns 3,400 m above sea level **N** = 123	**Intervention:** TcB measurement **Comparator:** TSB measurement	TcB and TSB correlation, sensitivity, specificity, area under the curve	TcB measurement is a fast and painless method that can be considered a reliable tool for screening and monitoring jaundice in newborns. It is not a definitive diagnosis tool for deciding use of phototherapy in full-term newborns at 3,400 m above sea level.
Chokemungmeepisarn et al. (2020)[6]	**Study design**: NRS **Population**: Healthy newborns ≥ 35 weeks gestation **N** = 214	**Intervention:** TcB measurement with BiliCare **Comparator:** TSB measurement	TcB and TSB correlation, mean difference of TcB and TSB, sensitivity, specificity, PPV, NPV, area under the ROC	BiliCare TcB and TSB measurements were well correlated. The TcB level + 3 mg/dL could detect all newborns who had hyperbilirubinemia requiring phototherapy during their birth hospitalization.
Lee et al. (2019)[7]	**Study design**: NRS **Population**: Newborns at 2 hospital sites **N** = 790	**Intervention:** Bili-ruler icterometer **Comparator:** Reference standard TcB concentrations, TSB concentrations	Correlation of Bili-ruler measurements and refence standard TcB and TSB levels, sensitivity, specificity,	The Bili-ruler is a noninvasive tool with high diagnostic accuracy for jaundice screening in newborns. It may be used to improve referrals from community or peripheral health centres to higher-level facilities with capacity for bilirubin testing and/or phototherapy.

Study citation	Study design, population	Intervention and comparator(s)	Relevant outcome(s)	Authors' conclusions
Taylor et al. (2017)[8]	**Study design**: NRS **Population**: Diverse sample of newborns, < 7 days old **N** = 530	**Intervention:** BiliCam smartphone app **Comparator:** TSB measurements	Correlation of estimated bilirubin levels and TSB, sensitivity, specificity	BiliCam gave accurate estimates of TSB values, demonstrating that smartphone technology could be used to effectively screen newborns for jaundice.

NRS = non-randomized study; NPV = negative predictive value; PPV = positive predictive value; ROC = receiver operating characteristic curve; SBR = serum bilirubin; TcB = transcutaneous bilirubin; TSB = total serum bilirubin.

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Health Technology Assessments

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Systematic Reviews

No literature identified.

Randomized Controlled Trials

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Non-Randomized Studies

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Economic Evaluations

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Guidelines and Recommendations

10. Hyperbilirubinemia CPG Work Group. Management of hyperbilirubinemia in healthy term and late preterm neonates *(Clinical practice guideline no. 18)*. Toronto (ON): Association of Ontario Midwives; 2019: https://www.ontariomidwives.ca/sites/default/files/2019-11/CPG-Management-of-Hyperbilirubinemia-PUB.pdf. Accessed 2022 Jan 20
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Appendix 1: References of Potential Interest

Previous CADTH Reports

11. Transcutaneous bilirubin measurements in newborns: clinical and cost-effectiveness, and guidelines *(CADTH Rapid response report: summary of abstracts)*. Ottawa (ON): CADTH; 2017: https://www.cadth.ca/sites/default/files/pdf/htis/2017/RB1164%20Transcutaneous%20Bilirubin%20Measurement%20Final.pdf. Accessed 2022 Jan 20.

Non-Randomized Studies

Alternative Outcomes — Relationship Between TcB and TSB Measurements

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Alternative Outcomes — Clinical Utility

13. Konana OS, Bahr TM, Strike HR, Coleman J, Snow GL, Christensen RD. Decision accuracy and safety of transcutaneous bilirubin screening at intermountain healthcare. J Pediatr. 01 2021;228:53-57. PubMed

Mixed Population — Includes Newborns Older Than 10 Days Old

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15. Munkholm SB, Krogholt T, Ebbesen F, Szecsi PB, Kristensen SR. The smartphone camera as a potential method for transcutaneous bilirubin measurement. *PLoS One.* 2018;13(6):e0197938. PubMed

Mixed Population — Newborns With Fewer Than 35 Weeks Gestation and Newborns With 35 Weeks Gestation or More

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Mixed Population — Newborns Discharged From Hospital and In Hospital

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Methodology Not Specified

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See: Table 4. Indications for Bilirubin Testing Modalities and Infant Jaundice Studies; Diagnostic Procedures and Considerations

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