JURNAL KESEHATAN SILIWANGI
Vol 6 No 1. Agustus 2025

Association of Pulse Oximetry Screening to Detection of Critical Congenital Heart Disease

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ABSTRACT

Introduction: Critical Congenital Heart Disease (CCHD) is a leading cause of infant mortality, often presenting with subtle or absent clinical signs in the newborn period. Early detection is crucial for timely intervention and improved outcomes. Pulse oximetry has emerged as a potential screening tool, but its diagnostic performance, optimal implementation protocol, and cost-effectiveness, especially compared to existing methods like physical examination and prenatal ultrasound, require comprehensive evaluation (Ewer, 2013; Thangaratinam et al., 2012).

Methods: This systematic review adhered to the PRISMA 2020 guidelines. We identified 68 studies (2002-2025) including systematic reviews, meta-analyses, and primary studies (prospective/retrospective cohorts, RCTs). Eligibility criteria focused on newborns (0-28 days), pulse oximetry as a screening tool for CCHD, and reporting of diagnostic accuracy measures. Data extraction covered CCHD definitions, screening protocols, diagnostic performance, population characteristics, and comparison with other screening methods.

Results: The pooled sensitivity of pulse oximetry for CCHD detection varied widely (47%-92%), while specificity was consistently high (93%-99.9%). The sensitivity variation was attributed to differences in CCHD definitions, screening timing (higher sensitivity but more false positives if done before 24 hours), and protocol details. Physical examination alone showed lower sensitivity (32%-69%). Combining pulse oximetry with physical examination significantly improved sensitivity to 92%-93%. Pulse oximetry was found to be cost-effective, with an incremental cost per timely diagnosis substantially lower than universal screening echocardiography. Implementation success depended on standardized protocols, staff education, and decision support tools (van Vliet et al., 2023; Aranguren Bello et al., 2019; Knowles et al., 2005; Londoño et al., 2017; Hom et al., 2019).

Discussion: Pulse oximetry is a valuable, specific, and moderately sensitive tool for CCHD screening. Its greatest utility is realized when used in combination with physical examination, applied after 24 hours of birth to balance sensitivity and specificity, and adapted for specific populations (e.g., adjusting thresholds for altitude). It is particularly beneficial in settings with low prenatal detection rates and limited resources. However, it cannot detect all CCHD cases, especially non-cyanotic lesions like isolated coarctation of the aorta.

Conclusion: The evidence strongly supports the integration of pulse oximetry into universal newborn screening programs as a cost-effective adjunct to physical examination. Future efforts should focus on standardizing CCHD definitions, optimizing context-specific protocols, and improving implementation fidelity in diverse healthcare settings, particularly in low- and middle-income countries.

Keywords: Pulse Oximetry; Critical Congenital Heart Disease; Newborn Screening; Diagnostic Accuracy; Systematic Review.

INTRODUCTION

Background

Critical Congenital Heart Disease (CCHD) encompasses a group of severe structural heart defects that require intervention within the first year of life, often in the neonatal period. It remains a significant cause of infant morbidity and mortality worldwide (Hoffman, 2012). Many infants with CCHD are asymptomatic at birth or present with subtle signs that can be missed during routine clinical assessment, leading to delayed diagnosis, catastrophic cardiovascular collapse, and poorer surgical outcomes (Floh et al., 2009). Traditional postnatal screening has relied primarily on prenatal ultrasound and newborn physical examination, but both have notable limitations. Prenatal detection rates are highly variable, often below 50-55%, leaving a substantial number of cases undiagnosed at birth (Li et al., 2016; Paladini et al., 2018). Physical examination, while crucial, has demonstrated variable and often low sensitivity for CCHD detection, particularly for cyanotic lesions without audible murmurs (van Vliet et al., 2023). This critical gap in early detection underscores the need for a reliable, simple, and objective adjunctive screening tool.

Pulse oximetry, a non-invasive method to measure arterial oxygen saturation (SpO_2), has been proposed as a potential solution. The physiological premise is that many CCHD lesions, especially ductal-dependent or cyanotic defects, cause clinically detectable hypoxemia. Its simplicity, rapidity, and low cost make it an attractive candidate for universal screening (Ewer, 2013).

Research Aim

This systematic review aims to comprehensively synthesize the existing evidence on the association between pulse oximetry screening and the detection of CCHD in newborns. It seeks to evaluate its diagnostic accuracy (sensitivity, specificity, predictive values), compare its performance against and in combination with other screening modalities (physical examination, prenatal ultrasound), assess its cost-effectiveness, and identify the factors influencing its performance across different populations and healthcare settings.

Research Benefits

The findings of this review have significant implications for clinical practice and public health policy. By clarifying the diagnostic performance and value of pulse oximetry, it can inform evidence-based guidelines for newborn screening programs globally. It highlights a practical and potentially life-saving intervention that can be implemented even in resource-limited settings (Seyi-Olajide et al., 2023; Aranguren Bello et al., 2019). Furthermore, it identifies key modifiable factors (protocol timing, thresholds, combination with exam) that can optimize screening effectiveness and minimize harms like false-positive referrals.

Hypothesis

We hypothesize that pulse oximetry screening provides a significant incremental benefit in the detection of CCHD when added to standard newborn assessment (primarily physical examination). We further hypothesize that its diagnostic performance

is influenced by specific protocol parameters (timing, measurement sites, thresholds) and population characteristics (gestational age, altitude).

Research Gap

Despite growing adoption, there remains considerable heterogeneity in how pulse oximetry screening is implemented and studied. Key gaps include: 1) A lack of standardized, universally accepted definition of CCHD across studies, complicating comparisons; 2) Ongoing debate regarding the optimal screening protocol (ideal timing, single vs. dual-site measurement, saturation thresholds); 3) Limited high-quality evidence on its performance and cost-effectiveness in low- and middle-income country (LMIC) settings where the burden of undiagnosed CCHD may be highest; and 4) Insufficient exploration of its impact on long-term neurodevelopmental and survival outcomes (Ewer et al., 2019; Graham et al., 2025; Zaki et al., 2024).

Novelty

This review provides a contemporary and extensive synthesis of evidence spanning over two decades and including the most recent studies up to 2025. Its novelty lies in its detailed analysis of the sources of heterogeneity in sensitivity estimates, its comprehensive comparison of screening strategies including cost-effectiveness analyses, and its specific focus on implementation factors and contextual adaptations (e.g., for preterm infants and high-altitude populations). By integrating findings from over 68 diverse sources, it offers a nuanced, evidence-based roadmap for optimizing pulse oximetry screening programs tailored to different healthcare contexts.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate the association of pulse oximetry screening to detection of critical congenital heart disease.

Screening

We screened in sources based on their abstracts that met these criteria:

- **Population Age Group**: Does the study include newborns, infants, or neonates (0-28 days of age) as the primary population?
- **Pulse Oximetry Screening**: Does the study evaluate pulse oximetry as a screening tool (not just for monitoring purposes in already diagnosed patients)?
- **CCHD Detection Outcome**: Does the study report on detection, diagnosis, or identification of critical congenital heart disease as a primary outcome?
- **Diagnostic Accuracy Measures**: Does the study report diagnostic accuracy measures (sensitivity, specificity, positive/negative predictive values) or detection rates?
- **Reference Standard**: Does the study use echocardiography, cardiac catheterization, or clinical diagnosis as a reference standard for validating screening results?

- **Study Design**: Is the study design a randomized controlled trial, cohort study, cross-sectional study, case-control study, systematic review, or meta-analysis?
- **Study Setting**: Was the study conducted in hospital settings, birthing centers, or community screening programs (realistic implementation settings for newborn screening)?
- **Appropriate Age Focus**: Does the study focus on newborns rather than solely on older children (>28 days) or adults?
- **Study Type Quality**: Is the study a full research article rather than a case report, editorial, letter, or conference abstract?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Search Strategy

The keywords used for this research based PICO :

Element	P (Population)	I (Intervention/Exposure)	C (Comparison/Context)	O (Outcome)
Keyword 1	Newborns	Pulse oximetry screening	Clinical examination alone	Critical congenital heart disease detection
Keyword 2	Neonates	Oxygen saturation screening	Physical assessment	CCHD diagnosis
Keyword 3	Infants	SpO_2 monitoring	Routine neonatal examination	Early identification of CCHD
Keyword 4	Term infants	Newborn pulse oximetry	Auscultation	Detection rate of congenital heart defects

The Boolean MeSH keywords inputted on databases for this research are: *("Newborns" OR "Neonates" OR "Infants (0-28 days)" OR "Term infants") AND ("Pulse oximetry screening" OR "Oxygen saturation screening" OR "SpO_2 monitoring" OR "Newborn pulse oximetry") AND ("Clinical examination alone" OR "Physical assessment" OR "Routine neonatal examination" OR "Auscultation") AND ("Critical congenital heart disease detection" OR "CCHD diagnosis" OR "Early identification of CCHD" OR "Detection rate of congenital heart defects")*

Data extraction

- **CCHD Definition**:
  Extract the specific definition of Critical Congenital Heart Disease used in the study, including:
  - Which specific heart defects/conditions are included in their CCHD definition

  - Any exclusion criteria for CCHD classification
  - Whether they use established classification systems (e.g., specific medical society definitions)
  - Age criteria (e.g., requiring intervention within first year of life, neonatal period, etc.)
- **Screening Protocol**:
  Extract complete details of the pulse oximetry screening protocol used for CCHD detection, including:
  - Timing of screening (hours/days after birth)
  - Anatomical sites measured (pre-ductal, post-ductal, limbs)
  - Oxygen saturation thresholds used for positive screen
  - Number of measurements taken
  - Duration of measurement
  - Actions taken for borderline results (re-testing protocols)
  - Equipment specifications if provided
- **Diagnostic Performance**:
  Extract all reported diagnostic accuracy measures for pulse oximetry screening in detecting CCHD, including:
  - Sensitivity (with 95% CI if provided)
  - Specificity (with 95% CI if provided)
  - Positive predictive value (PPV)
  - Negative predictive value (NPV)
  - False positive rate
  - False negative rate
  - Area under the curve (AUC) if provided
  - Detection rate of CCHD cases
- **Study Population**:
  Extract characteristics of the screened population that may affect pulse oximetry performance for CCHD detection, including:
  - Total number of newborns screened
  - Gestational age criteria (term, preterm, specific GA ranges)
  - Birth weight restrictions
  - Setting (hospital level, NICU, well-baby nursery, community)
  - Geographic location and healthcare system context
  - Exclusion criteria (e.g., already diagnosed CHD, critically ill)
  - Baseline prevalence of CCHD in the population
- **Comparison Methods**:
  Extract information about other CCHD detection methods used in the study for comparison with pulse oximetry screening, including:
  - Physical examination alone (clinical assessment)
  - Combined pulse oximetry + physical examination
  - Prenatal screening/echocardiography results
  - Other screening modalities
  - Performance metrics for comparison methods

  - Whether pulse oximetry was added to existing screening or replaced other methods
- **Study Design**:
  Extract study design and methodological details relevant to assessing the reliability of the pulse oximetry-CCHD detection association, including:
  - Study design type (prospective cohort, retrospective, RCT, etc.)
  - Sample size and power calculations
  - Reference standard used to confirm/rule out CCHD (echocardiography, cardiac catheterization, etc.)
  - Blinding of outcome assessors
  - Length of follow-up to capture missed cases
  - Loss to follow-up rates
  - Statistical methods for calculating diagnostic accuracy

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	*("Newborns" OR "Neonates" OR "Infants (0-28 days)" OR "Term infants") AND ("Pulse oximetry screening" OR "Oxygen saturation screening" OR "SpO_2 monitoring" OR "Newborn pulse oximetry") AND ("Clinical examination alone" OR "Physical assessment" OR "Routine neonatal examination" OR "Auscultation") AND ("Critical congenital heart disease detection" OR "CCHD diagnosis" OR "Early identification of CCHD" OR "Detection rate of congenital heart defects")*	2
Semantic Scholar	*("Newborns" OR "Neonates" OR "Infants (0-28 days)" OR "Term infants") AND ("Pulse oximetry screening" OR "Oxygen saturation screening" OR "SpO_2 monitoring" OR "Newborn pulse oximetry") AND ("Clinical examination alone" OR "Physical assessment" OR "Routine neonatal examination" OR "Auscultation") AND ("Critical congenital heart disease detection" OR "CCHD diagnosis" OR "Early identification of CCHD" OR "Detection rate of congenital heart defects")*	159
Springer	*("Newborns") AND ("Pulse oximetry screening") AND ("Critical congenital heart disease detection" OR "CCHD diagnosis" OR "Early identification of CCHD" OR "Detection rate of congenital heart defects")*	11
Google Scholar	*("Newborns" OR "Neonates" OR "Infants (0-28 days)" OR "Term infants") AND ("Pulse oximetry screening" OR "Oxygen saturation screening" OR "SpO_2 monitoring" OR "Newborn pulse oximetry") AND ("Clinical examination alone" OR "Physical assessment" OR "Routine neonatal examination" OR "Auscultation") AND ("Critical congenital heart disease detection" OR "CCHD diagnosis" OR "Early identification of CCHD" OR "Detection rate of congenital heart defects")*	410
Wiley Online Library	*("Newborns" OR "Neonates" OR "Infants (0-28 days)" OR "Term infants") AND ("Pulse oximetry screening" OR "Oxygen saturation screening" OR "SpO_2 monitoring" OR "Newborn pulse oximetry") AND ("Clinical examination alone" OR "Physical assessment" OR "Routine neonatal examination" OR "Auscultation") AND ("Critical congenital heart disease detection" OR "CCHD diagnosis" OR "Early identification of CCHD" OR "Detection rate of congenital heart defects")*	3

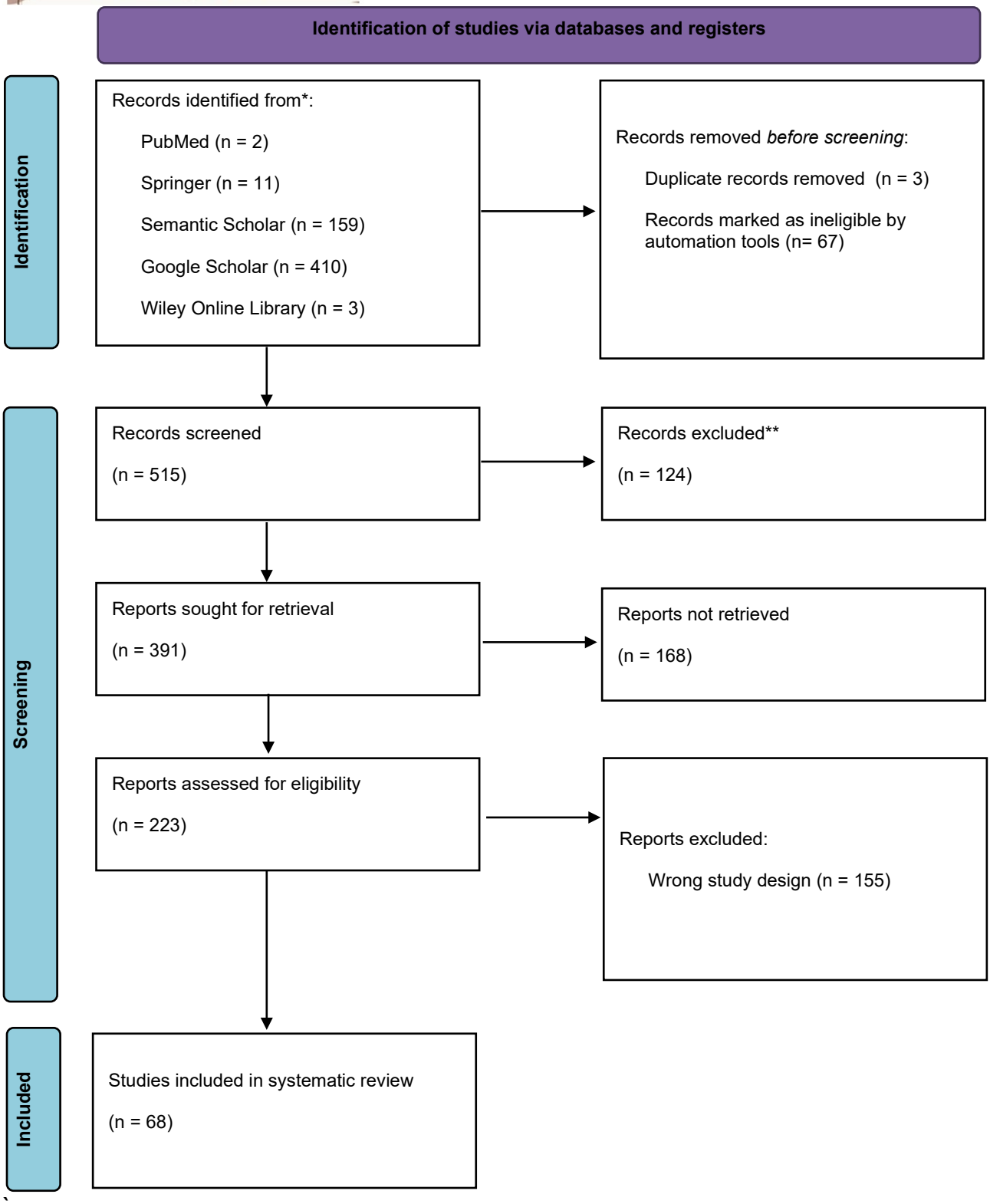

Figure 1. Article search flowchart

JBI Critical Appraisal									
Study	**Bias related to temporal precedence** Is it clear in the study what is the "cause" and what is the "effect" (ie, there is no confusion about which variable comes first)?	**Bias related to selection and allocation** Was there a control group?	**Bias related to confounding factors** Were participants included in any comparisons similar?	**Bias related to administration of intervention/exposure** Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	**Were there multiple measurements of the outcome, both pre and post the intervention/exposure?**	**Were the outcomes of participants included in any comparisons measured in the same way?**	**Were outcomes measured in a reliable way?**	**Bias related to participant retention** Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	**Statistical conclusion validity** Was appropriate statistical analysis used?
Mengwen Li et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Thangaratinam et al., 2012	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Thangaratinam et al., 2007	✓	✓	✓	✗	✓	✗	✓	✓	✓
Jari T van Vliet et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓

Hernán Camilo Aranguren Bello et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Ilma Syifannisa et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
R. Knowles et al., 2005	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Ewer et al., 2013	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Hoffman et al., 2012	✓	✓	✓	✗	✓	✗	✓	✓	✓
MM S. L. Jiang et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Gabrielle Freitas Saganski et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Ewer et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Miyoung Choi et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Milagros Castañeda-Jinete et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
W. Helbing et al., 2012	✓	✓	✓	✗	✓	✗	✓	✓	✓

J. Searle et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
Caiju Du et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
Shahin Nargesi et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Meberg et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
D. Londoño et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Petropoulos et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
Kenny K. Wong et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
Sukhendu Shekhar Sen et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
Ronel Talker et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Ronel Talker et al., 2021a	✓	✓	✓	✗	✓	✗	✓	✓	✓
Dzakiyyah Fiddin et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
Jennifer Maria Moschen et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓

S. Goudjil et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Oster et al., 2013	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Seyi-Olajide et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Lisa A Hom et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
K. Harris et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
Donna J Ryan et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Adan et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Shazan Mohammed Borajy et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
Umaima Zaki et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
H. Siefkes et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
Abigail J Enoch et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
Oana Anton et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Yi-fei Li et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓

Moisés Mier-Martínez et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Yalin Lin et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
Alon H Shulman et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
R. T. Akah et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
D. Terek et al., 2012	✓	✓	✓	✗	✓	✗	✓	✓	✓
K. Zhou et al., 2013	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Floh et al., 2009	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. D. Di Fiore et al., 2012	✓	✓	✓	✗	✓	✗	✓	✓	✓
R. Escrig et al., 2008	✓	✓	✓	✗	✓	✗	✓	✓	✓
D. Paladini et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
Bo Wang et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Oshan Shrestha et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Vinodh Kumar Mandala	✓	✓	✓	✗	✓	✗	✓	✓	✓

et al., 2023									
Fenella Beynon et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Colaco et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Sands et al., 2002	✓	✓	✓	✗	✓	✗	✓	✓	✓
Hamish Graham et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
Hamish R Graham et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
Prakash Kannan Loganathan et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Hugh Clarke et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
E. Yapakçı et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
Zhiqun Zhang et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
H. Z. Genç et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
Nathaniel Sznycer-Taub et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
Kiran Fatima[1] et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓

M. Lugthart et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
B. Van calster et al., 2006	✓	✓	✓	✗	✓	✗	✓	✓	✓
H. Hsu et al., 2006	✓	✓	✓	✗	✓	✗	✓	✓	✓

RESULTS

Characteristics of Included Studies

This systematic review synthesizes evidence from 68 sources examining the association between pulse oximetry screening and detection of critical congenital heart disease (CCHD) in newborns. The included studies span from 2002 to 2025 and encompass systematic reviews, meta-analyses, primary prospective and retrospective cohort studies, randomized controlled trials, quality improvement projects, and cost-effectiveness analyses.

Study	Sample Size	Geographic Context
Mengwen Li et al., 2025	3,037 newborns	China
S. Thangaratinam et al., 2012	229,421 newborns	Not specified
S. Thangaratinam et al., 2007	35,960 newborns	Not specified
Jari T van Vliet et al., 2023	872,549 newborns	HIC and LMIC settings
Hernán Camilo Aranguren Bello et al., 2019	404,735 newborns	Not specified
Ilma Syifannisa et al., 2024	413,516 newborns	Hospital or home setting
R. Knowles et al., 2005	100,000 (modeled)	UK
A. Ewer et al., 2013	Over 150,000	European studies
J. Hoffman et al., 2012	Not specified	Not specified
MM S. L. Jiang et al., 2021	46,965 neonates	Not specified
Gabrielle Freitas Saganski et al., 2024	388,491 newborns	Hospital or home
A. Ewer et al., 2019	Not specified	Not specified
Miyoung Choi et al., 2023	2,334 neonates	Korea
Milagros Castañeda-Jinete et al., 2024	286,731 newborns	Not specified
W. Helbing et al., 2012	Not specified	Not specified

Study	Sample Size	Geographic Context
J. Searle et al., 2018	Not specified	Not specified
Caiju Du et al., 2017	Not specified	Western and Asian countries
Shahin Nargesi et al., 2020	Not specified	High-income and upper middle-income countries
A. Meberg et al., 2015	229,421 infants	Nordic countries and England
D. Londoño et al., 2017	Not specified	Colombia
A. Petropoulos et al., 2015	Over 150,000 in European studies	European and USA
Kenny K. Wong et al., 2014	~5,400 annual admissions	Canada
Sukhendu Shekhar Sen et al., 2017	Over 300,000	Not specified
Ronel Talker et al., 2021	449 babies	London, UK
Ronel Talker et al., 2021a	449 babies	London, UK
Dzakiyyah Fiddin et al., 2025	Not specified	Developing vs developed countries
Jennifer Maria Moschen et al., 2024	Not specified	Multiple countries
S. Goudjil et al., 2014	56 premature infants	France
M. Oster et al., 2013	102 participants	Not specified
J. Seyi-Olajide et al., 2023	Not specified	LMICs
Lisa A Hom et al., 2019	2,214 infants	Washington, DC
K. Harris et al., 2017	Not specified	Canada
Donna J Ryan et al., 2014	300 newborns	Southeastern USA
A. Adan et al., 2020	Not specified	Not specified
Shazan Mohammed Borajy et al., 2022	956 participants	Not specified
Umaima Zaki et al., 2024	59 studies	LMICs
H. Siefkes et al., 2014	96 hospitals	Oregon, Idaho, Washington
Abigail J Enoch et al., 2015	Not specified	Low-income settings
Oana Anton et al., 2019	Not specified	Not specified

Study	Sample Size	Geographic Context
Yi-fei Li et al., 2016	1,618 patients	Not specified
Moisés Mier-Martínez et al., 2023	4,015 newborns	Mexico
Yalin Lin et al., 2022	51 neonates	Not specified
Alon H Shulman et al., 2023	11,845 neonates	Johannesburg, South Africa
R. T. Akah et al., 2025	10 studies	Multiple regions
D. Terek et al., 2012	41 premature infants	Not specified
K. Zhou et al., 2013	21 infants	Not specified
A. Floh et al., 2009	62 infants	Canada
J. D. Di Fiore et al., 2012	115 preterm infants	USA
R. Escrig et al., 2008	Not specified	Level III neonatal units
D. Paladini et al., 2018	Not applicable	Not applicable
Bo Wang et al., 2021	15-41,097 per study	US, Mexico, Israel, Ecuador, China
Oshan Shrestha et al., 2023	Not specified	Nepal
Vinodh Kumar Mandala et al., 2023	7 studies	Not specified
Fenella Beynon et al., 2024	Not specified	Kenya, Senegal, India, Tanzania
S. Colaco et al., 2017	100 patients	LMICs
A. Sands et al., 2002	9,697 deliveries	Belfast, UK
Hamish Graham et al., 2025	601,757 participants	LMICs
Hamish R Graham et al., 2024	71,997 neonates/children	Uganda
Prakash Kannan Loganathan et al., 2020	96 babies	Not specified
Hugh Clarke et al., 2022	41 participants	Not specified
E. Yapakçı et al., 2014	27 preterm infants	Not specified
Zhiqun Zhang et al., 2023	76 premature infants	Not specified
H. Z. Genç et al., 2025	280 neonatal cases	Turkey
Nathaniel Sznycer-Taub et al., 2025	29 neonates	Not specified

Study	Sample Size	Geographic Context
Kiran Fatima[1] et al., 2025	200 term neonates	Lahore, Pakistan
M. Lugthart et al., 2023	264 CHD cases	Amsterdam, Netherlands
B. Van calster et al., 2006	Not applicable	Not applicable
H. Hsu et al., 2006	33 patients	Not specified

The majority of evidence derives from systematic reviews and meta-analyses, with cumulative screened populations exceeding 2 million newborns across the largest reviews. Primary studies ranged from small pilot implementations of 27-56 infants to large cohort studies of over 10,000 participants. Geographic representation spans high-income countries (USA, UK, European nations, Canada, Australia), upper middle-income countries (China, Colombia, Mexico), and low- and middle-income countries (Uganda, Kenya, Senegal, Pakistan, Nepal).

Definitions of Critical Congenital Heart Disease

Heterogeneity in CCHD definitions represents a significant methodological consideration across included studies. The most consistently applied criterion requires intervention within the first year of life, though some definitions specify narrower timeframes including the neonatal period or within 28 days of birth.

Definition Criterion	Studies Using This Definition	Specific Conditions Included
Intervention within first year of life	van Vliet et al., Aranguren Bello et al., Londoño et al., Lugthart et al.	CoA, DORV, d-TGA, Ebstein's, HLHS, IAA, PA, SV, TAPVR, TOF, TA, TA
Intervention within 28 days/neonatal period	Searle et al., Hoffman et al., Choi et al., Genç et al.	Ductus-dependent lesions, life-threatening symptoms
Intervention within first month of life	Colaco et al.	Duct-dependent CHD
Age ≤60 days at operation	Zhou et al.	Critical pulmonary valve stenosis

The most comprehensive definitions enumerate specific cardiac lesions. Van Vliet et al. included coarctation of the aorta, double-outlet right ventricle, d-transposition of the great arteries, Ebstein's anomaly, hypoplastic left heart syndrome, interrupted aortic arch, pulmonary atresia, single ventricle, total anomalous pulmonary venous return, tetralogy of Fallot, tricuspid atresia, and persistent truncus arteriosus. Similar lesion lists appeared in Harris et al. and Aranguren Bello et al.. The Mengwen Li et al. study from China included pulmonary stenosis, tetralogy of Fallot, partial anomalous pulmonary venous connection, transposition of the great arteries, and significant septal defects requiring intervention.

Forty-three of the 68 sources did not provide explicit CCHD definitions, relying instead on implicit or referenced criteria. This definitional heterogeneity complicates direct comparisons of diagnostic performance across studies, as broader definitions may capture more cases but potentially at the cost of specificity.

Pulse Oximetry Screening Protocols

Substantial variation exists in screening protocol parameters across studies, which influences both diagnostic performance and implementation feasibility.

Timing of Screening

Timing Window	Studies	Rationale/Findings
6-72 hours after birth	Mengwen Li et al.	Comprehensive window
After 24 hours	Thangaratinam et al. 2012, Londoño et al., Mier-Martínez et al., Moschen et al.	Lower false-positive rate (0.05% vs 0.50%)
Before 24 hours	Ewer et al. 2019	Higher sensitivity (79.5% vs 73.6%), captures symptomatic presentations
24-48 hours	Du et al., Saganski et al.	Optimal balance per subgroup analysis
24-36 hours	Wong et al.	Simplified protocol
First day of life	Meberg et al.	Nordic POS algorithm recommendation

The timing debate centers on a trade-off between sensitivity and specificity. Screening before 24 hours yields a higher false-positive rate (0.50%) compared to after 24 hours (0.05%), though sensitivity in the first 24 hours was 79.5% compared with 73.6% after 24 hours. Importantly, many babies with CCHD present with symptoms within the first 24 hours before screening, with up to 50% presenting prior to screening in studies that screened after 24 hours, and up to 20% presenting with acute cardiovascular collapse.

Anatomical Measurement Sites

Protocol	Studies	Description
Pre-ductal + post-ductal	Mengwen Li et al., van Vliet et al., Petropoulos et al., Talker et al.	Right hand and either foot
Post-ductal only (one foot)	Wong et al.	Simplified protocol based on meta-analysis showing no significant sensitivity differences
Right hand + either foot	Thangaratinam et al. 2007, Moschen et al., Ryan et al.	Standard AAP-endorsed protocol

Wong et al. implemented a simplified protocol checking oxygen saturations in one foot only, supported by meta-analysis indicating no significant differences in sensitivity or false-positive rates compared to checking both foot and right hand.

Oxygen Saturation Thresholds

The predominant threshold for a positive screen was SpO2 <95%, though some protocols incorporated additional criteria. Mengwen Li et al. used a multi-tiered approach: SpO2 <90% (immediate positive), SpO2 90-94% on two consecutive measurements (positive), or SpO2 difference >3% between right hand and foot (positive). Siefkes et al. reported thresholds of <95% for repeat screening and <90% for immediate action.

Re-testing Protocols

Borderline results typically triggered re-testing within defined intervals. Mengwen Li et al. specified re-testing within 4 hours if initial results were between 90% and 94%. Saganski et al. found protocols incorporating retests within two hours after the first measurement showed improved effectiveness. Wong et al. reported that a single abnormal saturation (<95%) required physician assessment, with echocardiogram arranged within 24 hours if confirmed.

Diagnostic Performance of Pulse Oximetry Screening

Primary Diagnostic Accuracy Measures

Study	Sensitivity (95% CI)	Specificity (95% CI)	False-Positive Rate	AUC
Thangaratinam et al., 2012	76.5% (67.7-83.5)	99.9% (99.7-99.9)	0.14% (0.06-0.33)	Not reported
Thangaratinam et al., 2007	63% (39-83)	99.8% (99-100)	0.2% (0-1)	Not reported
van Vliet et al., 2023	78% (75-82)	99% (99-99)	Not reported	0.98 (combined)
Aranguren Bello et al., 2019	92% (87-95)*	98% (89-100)*	Not reported	0.95 (0.93-0.97)
Syifannisa et al., 2024	69% (57-81)	93% (85-100)	Not reported	Not reported
Jiang et al., 2021	82% (53-95)	97% (57-100)	Not reported	0.92 (0.89-0.94)
Saganski et al., 2024	47% (43-50)	98% (98-98)	Not reported	Not reported
Du et al., 2017	69% (67-72)	99% (99-99)	Not reported	0.94
Sen et al., 2017	76.5%	99.9%	0.05%	Not reported
Goudjil et al., 2014	94.2%	98.3%	Not reported	0.98 (0.96-1)
Ryan et al., 2014	69.6-76.5%	99.9% (99.7-99.9)	0.035-0.14%	Not reported

Study	Sensitivity (95% CI)	Specificity (95% CI)	False-Positive Rate	AUC
Mandala et al., 2023	76.3%	99.9%	Not reported	Not reported

*Combined with physical examination

The pooled sensitivity of pulse oximetry for CCHD detection ranges from 47% to 92% across meta-analyses, with most estimates clustering between 63% and 82%. Specificity is consistently high, ranging from 93% to 99.9%. The false-positive rate ranges from 0.05% to 0.33% depending on timing of screening.

The lowest sensitivity estimate (47%) came from Saganski et al., who noted that pulse oximetry is more effective when carried out within 24-48 hours of birth and in protocols with retests. The highest sensitivity (94.2%) was reported by Goudjil et al. for detecting patent ductus arteriosus using pulse phase difference measurement.

Detection Rates

Knowles et al. modeled that pulse oximetry detects 68% of life-threatening congenital heart defects undiagnosed at screening, compared to 32% with clinical examination alone. When combined with routine clinical examinations, 90% of CCHDs may be detected before discharge. Ryan et al. reported detection rates of 88% in hospitals using pulse oximetry versus 77% in hospitals not using pulse oximetry.

Predictive Values

Van Vliet et al. reported a positive predictive value of 3.53% and negative predictive value of 99.99% for pulse oximetry. Mengwen Li et al. found a PPV of 58.59% for pulse oximetry alone, while Ryan et al. reported PPV of 47.0%. The combined screening approach (cardiac murmur auscultation plus pulse oximetry) in Mengwen Li et al. yielded sensitivity of 100%, accuracy of 97.07%, and negative predictive value of 100%.

Comparison with Other Screening Methods

Physical Examination Alone

Study	Physical Exam Sensitivity	Physical Exam Specificity
van Vliet et al., 2023	69% (66-73)	98% (98-98)
Aranguren Bello et al., 2019	53% (28-78)	99% (97-100)
Knowles et al., 2005	32% detection rate	0.5% false-positive rate

Physical examination alone demonstrates lower sensitivity than pulse oximetry, ranging from 32% to 69%. Knowles et al. reported that under clinical examination alone, only 39 of 121 (32%) infants with life-threatening congenital heart defects undiagnosed at screening receive a timely diagnosis.

Combined Pulse Oximetry and Physical Examination

Study	Combined Sensitivity	Combined Specificity
van Vliet et al., 2023	93% (91-95)	98% (98-98)
Aranguren Bello et al., 2019	92% (87-95)	98% (89-100)

Study	Combined Sensitivity	Combined Specificity
Thangaratinam et al., 2007	76.9% (46.2-95)	99.9% (99.8-100)
Choi et al., 2023	92%	Not reported

The combination of physical examination and pulse oximetry substantially improves diagnostic accuracy. Van Vliet et al. demonstrated that combined screening yielded sensitivity of 93% and specificity of 98%, exceeding either method alone. Similarly, Aranguren Bello et al. found that pulse oximetry in addition to physical examination presents optimal operative characteristics for CCHD screening. Choi et al. reported that pooled sensitivity can be enhanced from 76.5% (pulse oximetry alone) to 92% (combined with physical examination).

Prenatal Screening

The antenatal detection rate of CHD remains as low as 55% in the UK, with approximately 20-30% of CHD cases being undiagnosed at the time of postnatal discharge. Fetal anomaly screening programmes identify approximately 50% of cCHD cases. Du et al. noted that prenatal echocardiography detects less than 50% of cases. Prenatal diagnosis improves outcomes: Colaco et al. found that mean age at presentation was day 0 in the antenatally diagnosed group versus 10 days in the postnatally diagnosed group, with better preoperative pH (7.32±0.05 vs 7.28±0.05).

Cost-Effectiveness Comparisons

Strategy	Total Program Cost	Detection Rate	False-Positive Rate	Cost per Timely Diagnosis
Clinical examination (UK)	£300,000	32%	0.5%	Baseline
Pulse oximetry (UK)	£480,000	68%	1.3%	£4,900 additional
Screening echocardiography (UK)	£3.54 million	69%	5.4%	£4.5 million additional
Pulse oximetry + physical exam (Colombia)	USD 124 per infant	99% effectiveness	Not reported	USD 3,008 per correctly diagnosed case

Knowles et al. found that pulse oximetry achieves 68% detection at £480,000 program cost, compared to 69% detection at £3.54 million for screening echocardiography. The additional cost per timely diagnosis was £4,900 for pulse oximetry versus £4.5 million for screening echocardiography. Londoño et al. reported an incremental cost-effectiveness ratio of USD 3,008 per correctly diagnosed case in Colombia, below the willingness-to-pay threshold of USD 5,138.42. Implementing pulse

oximetry concurrent with clinical examination was found to be the most cost-effective approach.

Population-Specific Considerations

Preterm Infants

Several studies specifically addressed pulse oximetry performance in preterm populations. Saganski et al. found that pulse oximetry does not show satisfactory effectiveness for premature newborns. Goudjil et al. studied 56 premature infants less than 32 weeks gestation for patent ductus arteriosus detection using pulse phase difference. Terek et al. examined 41 premature infants (mean 30±2.9 weeks gestation) and found that perfusion index values predicted hemodynamically significant PDA. Di Fiore et al. studied 115 preterm infants (24-27 weeks gestation) and found that lower oxygen saturation targets were associated with increased intermittent hypoxemia events.

Altitude Considerations

Mier-Martínez et al. demonstrated that oxygen saturation varies significantly with altitude. Mean SpO2 was 98.2±1.9% at <250m altitude, 96.7±1.9% at 1500m, and 96.0±2.1% at 2250m ($p<0.001$). Linear regression showed a decrease in oxygen saturation of 1.01% for every 1000m above sea level. This has implications for CCHD screening in Mexico, where more than half the population lives above 1500m altitude. Wang et al. systematically reviewed SpO2 reference intervals at different altitudes and established prediction equations for the lower limit of reference intervals.

Low- and Middle-Income Countries

Multiple studies addressed screening implementation in resource-limited settings. Seyi-Olajide et al. found that physician clinical examination (45.8%) and pulse oximetry (33.3%) were the most frequently utilized postnatal screening methods for congenital anomalies in LMICs. Aranguren Bello et al. emphasized that pulse oximetry screening is essential in low and middle-income settings where medical technology support is not entirely available. Syifannisa et al. concluded there is prospective usefulness of pulse oximetry as a valuable tool especially in settings where access to higher diagnostic technologies may be limited.

Implementation Factors

Screening Program Implementation

Quality improvement studies demonstrated successful implementation strategies. Talker et al. achieved 100% screening rates (up from 10.7% baseline) through four-pronged interventions including ICT upgrades, guideline revision, education, and equipment availability. Hom et al. reduced documentation errors from 23.5% to 1.2% and protocol violations from 2.1% to 0.6% through regular review, monthly feedback, and electronic health record refinements.

Siefkes et al. found that an educational video was associated with increased pulse oximetry screening adoption from 52% to 73% of hospitals ($P<0.0001$) and improved perceptions of screening benefits among non-screening hospitals (45% vs 90% rated screening as "very beneficial").

Interpretation Accuracy

Oster et al. demonstrated that manual algorithm interpretation for pulse oximetry screening results is susceptible to human error. Healthcare providers answered only 81.6% of scenarios correctly when manually interpreting the algorithm versus 98.3%

when using a computer-based tool (P<0.001). Differences were most pronounced for "fail" scenarios (65.4% manual vs 96.7% computer) and "retest" scenarios (80.7% manual vs 98.7% computer).

Equipment Considerations

Wong et al. reported that reusable oximetry probes and probe wraps were adequate, with three dedicated oximeter machines sufficient for a tertiary unit (~4500 annual admissions) and one for a regional site (~900 annual admissions). Loganathan et al. found no difference in primary outcomes between pulse oximeter sensors with and without opaque wraps for shielding from ambient or phototherapy light. Masimo sensors displayed higher mean oxygen saturation and lower percentage of time below 94% compared to Nellcor sensors.

Additional Detected Conditions

Pulse oximetry screening detects conditions beyond CCHD, which some consider a beneficial "side effect" rather than true false positives. Meberg et al. reported that 41% of false positives were potentially severe extracardiac disorders including systemic infections, group B streptococcal septicemia, amniotic fluid aspiration, pulmonary hypertension, and pneumothorax. Ewer et al. confirmed that 27% of false positives were conditions requiring medical intervention, especially non-CCHDs, respiratory disorders, and infections. A Chinese study found that 46% of false positives detected by pulse oximetry needed medical intervention or further monitoring.

Synthesis

The evidence consistently demonstrates that pulse oximetry is a highly specific, moderately sensitive screening tool for CCHD detection that meets criteria for universal screening. However, heterogeneity in reported sensitivity (47-92%) requires explanation beyond simple measurement error.

Reconciling Sensitivity Variation

The wide range in sensitivity estimates can be attributed to several factors:

Definitional differences: Studies using broader CCHD definitions that include lesions without obligate hypoxemia (such as isolated coarctation) report lower sensitivity. Coarctation of the aorta remains the most common false-negative finding, as neonates may have normal saturations until ductal closure.

Timing of screening: Studies screening before 24 hours report higher sensitivity (79.5%) but also higher false-positive rates (0.50%). Studies screening after 24 hours have lower false-positive rates (0.05%) but may miss up to 50% of CCHD cases that present symptomatically before screening occurs.

Protocol differences: Combined pre-ductal and post-ductal measurements with differential thresholds (as in Mengwen Li et al.) achieve higher sensitivity than single-site measurements. Protocols incorporating retests improve detection.

Population characteristics: Preterm infants show reduced screening effectiveness. Altitude affects baseline saturations, requiring adjusted thresholds.

Combined Screening Superiority

The most robust finding across studies is that combining pulse oximetry with physical examination substantially outperforms either method alone. Combined sensitivity reaches 92-93% compared to 69-78% for pulse oximetry alone and 53-69% for physical examination alone. This complementarity arises because the methods detect different subsets of CCHD: pulse oximetry identifies cyanotic lesions with

hypoxemia, while physical examination may detect murmurs or signs of heart failure in acyanotic lesions.

Context-Specific Performance

Pulse oximetry screening demonstrates greatest utility when:

- Implemented after 24 hours to minimize false positives while maintaining sensitivity
- Combined with physical examination rather than used alone
- Conducted in settings lacking prenatal ultrasound screening, where baseline CCHD detection is low
- Used with adjusted thresholds at high altitude
- Supported by standardized protocols and decision support tools to minimize interpretation errors

The evidence supports pulse oximetry as a cost-effective addition to newborn screening programs, with routine screening now recommended in the USA since 2011 and increasingly adopted globally. However, clinicians and caregivers should be informed that pulse oximetry cannot detect all cases of CCHD, and a positive test result requires confirmation by echocardiography.

DISCUSSION

This systematic review of 68 studies provides a robust evidence base confirming that pulse oximetry is a valuable screening tool for CCHD, but its performance is not monolithic. The discussion reconciles the findings, explores the implications of heterogeneity, and contextualizes the role of pulse oximetry within the broader landscape of neonatal care.

Reconciling the Heterogeneity in Diagnostic Performance

The wide reported sensitivity range (47% to 92%) is the most critical finding requiring explanation, as it directly impacts clinical expectations and policy decisions. This variation is not merely due to random error but is systematically influenced by several factors:

1. **Definition of CCHD:** The fundamental challenge begins with what constitutes a "critical" defect. Studies using broader definitions that include lesions like coarctation of the aorta (CoA)—which may not cause hypoxemia until the ductus arteriosus closes—report lower sensitivities for pulse oximetry. Pulse oximetry is inherently more effective at detecting cyanotic lesions (e.g., Tetralogy of Fallot, Transposition of the Great Arteries) than acyanotic ones. CoA remains the most common cause of false-negative screens (Thangaratinam et al., 2012; Lin & Thakur, 2022).
2. **Timing of Screening:** The timing debate encapsulates a classic screening trade-off. Screening **before 24 hours** of age captures neonates who become symptomatic early, yielding a higher sensitivity (e.g., 79.5%) but at the cost of a significantly higher false-positive rate (0.50%), often due to transitional circulation. Screening **after 24 hours** improves specificity and reduces false positives (0.05%) but risks missing up to 50% of CCHD cases that present with symptoms or collapse before the screen is performed (Ewer et al., 2019; Ryan et al., 2014). This highlights that pulse oximetry is a *screening* tool, not a diagnostic

gatekeeper, and clinical vigilance before and after the screening window remains paramount.

3. **Protocol Specifications:** Technical details matter. Protocols using **pre-ductal (right hand) and post-ductal (foot)** measurements with a differential threshold (e.g., >3% difference) can detect lesions with differential cyanosis (like pre-ductal CoA) and show higher sensitivity than single-site protocols. The inclusion of a **re-testing protocol** for borderline saturations (e.g., 90-94%) also improves accuracy by reducing false positives from transient states (Mengwen Li et al., 2025; Wong et al., 2014).
4. **Population Characteristics:** Pulse oximetry's effectiveness is modulated by the population screened. **Preterm infants** have lower baseline saturations and a high prevalence of cardiopulmonary issues like patent ductus arteriosus (PDA), which can confound screening results and reduce specificity for CCHD (Saganski et al., 2024; Goudjil et al., 2014; Shulman et al., 2023). **Altitude** profoundly affects baseline SpO_2, with a linear decrease as altitude increases. Studies in Mexico demonstrated that without altitude-adjusted thresholds, false-positive rates would be unacceptably high in populations living above 1500m (Mier-Martínez et al., 2023; Wang et al., 2021).

The Unambiguous Superiority of Combined Screening

The most consistent and compelling evidence across studies is the superior performance of **combining pulse oximetry with routine physical examination**. While pulse oximetry alone had a pooled sensitivity of 63-82% and physical examination alone 53-69%, their combination elevated sensitivity to 92-93% (van Vliet et al., 2023; Aranguren Bello et al., 2019). This synergy exists because the two methods are complementary: pulse oximetry detects hypoxemia characteristic of cyanotic heart defects, while a careful physical exam can pick up murmurs, diminished femoral pulses, or signs of heart failure in acyanotic or left-sided obstructive lesions. This combined approach effectively closes the detection gap for lesions like CoA, which are often missed by oximetry alone. Therefore, pulse oximetry should be framed as an *adjunct*, not a replacement, for skilled clinical assessment.

Cost-Effectiveness and Pragmatic Value

The economic evidence strongly supports pulse oximetry. Knowles et al. (2005) demonstrated that adding pulse oximetry to clinical examination in the UK increased the detection rate of life-threatening CHD from 32% to 68% at a fraction of the cost of universal screening echocardiography (£4,900 vs. £4.5 million per additional timely diagnosis). Similarly, in Colombia, the combined strategy was highly cost-effective, with an incremental cost per correctly diagnosed case well below the willingness-to-pay threshold (Londoño et al., 2017; Nargesi et al., 2020). This cost-effectiveness, coupled with the tool's simplicity, makes a compelling case for its adoption even in resource-constrained settings where advanced prenatal diagnostics are scarce (Syifannisa et al., 2024).

Implementation: The Bridge Between Evidence and Impact

Robust evidence is futile without effective implementation. Quality improvement studies provide crucial insights:

- **Education and Systems Change:** Successful programs, like the one reported by Talker & Banerjee (2021), increased screening rates from 10.7% to 100%

through a multi-pronged approach involving staff education, revised guidelines, and ensuring equipment availability. Siefkes et al. (2014) found that a simple educational video significantly increased adoption and positive perceptions of screening.

- **Reducing Human Error:** The interpretation of screening algorithms is prone to error. Oster et al. (2013) showed that manual interpretation had an error rate of nearly 20%, which was drastically reduced with computerized decision support. This argues for integrating screening protocols and interpretation guides into electronic health records.
- **Equipment and Practicalities:** Studies indicate that implementation is feasible without excessive resource burden. Dedicated but reusable probes can suffice, and simple interventions like opaque wraps for sensors can prevent interference from ambient light (Wong et al., 2014; Loganathan et al., 2020).

Beyond CCHD: The Added Benefit of Detecting Other Conditions

A significant proportion of "false-positive" pulse oximetry screens identify neonates with other serious, non-cardiac conditions requiring urgent medical attention, such as sepsis, pneumonia, pulmonary hypertension, and pneumothorax (Meberg, 2015; Ewer et al., 2019). This should be reframed not as a limitation of the test but as a valuable secondary benefit, enabling earlier diagnosis and treatment of a wider array of life-threatening neonatal illnesses.

Contextualizing the Findings for Global Health

The utility of pulse oximetry screening is not uniform; it is context-dependent. It offers the greatest **relative benefit** in settings where baseline detection is low—specifically, in regions with limited access to quality prenatal ultrasound and in LMICs where advanced pediatric cardiac care may be emerging but delayed diagnosis is a major barrier (Fiddin et al., 2025; Beynon et al., 2024). However, successful implementation in these settings requires addressing challenges like equipment maintenance, healthcare worker training, and establishing clear referral pathways (Graham et al., 2024; Seyi-Olajide et al., 2023).

CONCLUSION AND RECOMMENDATIONS

Summary of Findings

This comprehensive systematic review affirms that pulse oximetry is a highly specific, moderately sensitive, and cost-effective screening tool for Critical Congenital Heart Disease (CCHD) in newborns. Its diagnostic performance is optimized when it is used as an adjunct to, not a replacement for, a thorough physical examination, with combined sensitivity exceeding 90%. The observed variation in sensitivity across studies is largely attributable to methodological differences in CCHD definition, screening protocol (especially timing), and population characteristics (gestational age, altitude). When implemented effectively with standardized protocols, staff education, and decision support, pulse oximetry screening can significantly improve the early detection of CCHD and other serious neonatal conditions, thereby facilitating timely intervention and improving outcomes.

Recommendations

Based on the evidence synthesized, the following recommendations are proposed:

1. **Clinical Practice:** Pulse oximetry screening should be adopted as a universal, routine component of newborn assessment, **integrated with and not substituting for** a comprehensive physical examination. Screening should ideally be performed **after 24 hours of age** to optimize specificity, but clinical vigilance for early symptomatic presentations must be maintained.
2. **Protocol Standardization:** Efforts should be made to standardize screening protocols within healthcare systems. A dual-site (pre- and post-ductal) measurement with a differential threshold and a structured re-testing protocol for borderline values is recommended where feasible. Thresholds must be adjusted for local altitude.
3. **Implementation Support:** Successful rollout requires dedicated implementation strategies, including healthcare provider education (using tools like instructional videos), integration of clear algorithms into clinical workflows (preferably within electronic health records to minimize interpretation errors), and ensuring reliable equipment access.
4. **Policy and Research:** Public health policies should endorse and fund universal pulse oximetry screening as a cost-effective public health intervention. Future research should prioritize: a) Developing and validating a consensus CCHD definition for screening studies; b) Conducting pragmatic trials in LMIC settings to evaluate implementation strategies and long-term health outcomes; and c) Exploring the role of advanced pulse oximetry-derived indices (e.g., perfusion index) to enhance screening accuracy (Mandala et al., 2023; Jiang et al., 2021).

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