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CRITICAL OXYGEN SATURATION-LEVEL ESTIMATION FROM PHOTOPLETHYSMOGRAM (PPG): A PRISMA-COMPLIANT SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Objectives: Photoplethysmogram (PPG) signals have become a crucial tool in the non-invasive monitoring of oxygen saturation levels (SpO2). The main purpose of the present review is to perform a meta-analysis of the involvement and consideration of *critical SpO2 levels* (<90%) in the research papers where SpO2 levels are calculated/predicted from PPG and to elaborate on the impact of the critical levels when presenting the evaluation results. Data sources: PubMed, Science Direct, and Scopus were searched for papers published between January 1, 2016, and September 10, 2022. Results: This study produced several results, concerning the main objective as well as other important issues for improving the SpO2 estimation/calculation. We discovered that only 21 out of 75 papers considered SpO2 values that are in the critical domain. Many papers do not provide access to their databases or disclose the software/models used. Additionally, some studies lack sufficient testing subjects and fail to make their results reproducible. The findings reveal a preference for SpO2 calculation over prediction, limited data availability, undisclosed methodologies, and diverse evaluation metrics hinder replication and direct comparisons between studies. Also, a scoring table is offered that scores higher the papers that are more valuable for SpO2 calculation/prediction.Conclusion: Employing PRISMA guidelines, a comprehensive search across PubMed, Science Direct, and Scopus databases initially extracted 6173 potential papers. Following rigorous screening, 75 papers were selected for detailed analysis, of which only 21 included data from critical SpO2 levels. Furthermore, this research provided information for the filtered 21 paper about the sample size of the study participants, the models utilized to derive the results, the availability of databases, the specific devices employed in the research, the methodologies employed for PPG signal measurement, and the collaborative efforts among authors from different institutions. This information is sublimed in the scoring table which gives higher scoring to those papers that are more valuable for SpO2 calculation/prediction. This study offers references to all these findings that can be used as concrete guidelines for prospective researchers and developers of new sensors for SpO2 estimation/calculation utilizing PPG signals.

Keywords: Photoplethysmogram; Oxygen saturation; Systematic review; Meta-analysis.

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ABBREVIATIONS

PPG = Photoplethysmogram
SpO2 = Blood oxygen saturation
RMSE = Root-mean-square error
MAE = Mean absolute error
RMSPE = Root-mean-square percentage error
TRE = Total relative error
AMAE = Average mean absolute error
AMSE = Average mean squared error
RMSEP = Root mean square error of prediction.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first systematic review and meta-analysis to evaluate the inclusion of critical oxygen saturation levels when estimated from PPG.
- Several other factors are assessed in studies examining critical SpO2 levels, including the number of subjects involved, the types of models used, database availability, device types, methods of PPG signal measurement, and collaboration between different institutions.
- The main limitation of this research is the high level of heterogeneity among the studies in presenting their results, which poses challenges in assessing their quality regarding the interest of this research.

INTRODUCTION

Blood oxygen saturation (SpO2) is the ratio of oxyhemoglobin to the total concentration of hemoglobin present in the blood.[4,86] Alongside heart rate, blood pressure, respiration rate, and temperature, SpO2 is recognized as a crucial vital sign for assessing human health status.[1,87,98] The normal blood oxygen saturation level is 95–100%.[95,96] The abnormalities of oxygenation level, critically below 80%,[3,97] even for a short period may ultimately result in the failure of vital organs, especially the brain and heart, and even death.[1,2,99] Moreover, if the SpO2 level falls below 90%, it may indicate hypoxemia,[100,101] and, if left untreated, can lead to respiratory or cardiac arrest.[3,88]

Photoplethysmography (PPG) is a commonly used technique to measure SpO2 as a noninvasive optical measuring method that considers the changes in blood volume.[3,93,94] Many research papers present SpO2 measurement models based on the PPG signal, including papers on the development of new pulse oximetry devices e.g. Refs. 16, 18, 31, 44, 56, 62, 76, 81, and 84 and also predictions using machine learning models e.g. Refs. 18, 22, 56, and 76. To validate the novice pulse oximetry devices, the researchers perform SpO2 measurements and compare the obtained values with the measurement from commercially available pulse oximeters, or if they propose machine/deep learning models, they use the PPG-SpO2 entries stored in publicly available databases.

During the preparation of our previous research papers,[5,6] which consider the prediction of SpO2 from PPG utilizing machine/deep learning methodologies, we observed a distinct absence of or minimal entries containing SpO2 values of the critical levels (below 90%) in the existing publicly available databases. This may be attributed to the difficulty in obtaining such data, as it is less likely for medical professionals to work with patients who have dangerously low oxygen saturation levels, such as those with terminal cancer.[7,90] Some researchers have resorted to the technique of breath withholding to obtain SpO2 levels below 90% However, most of these results are induced from healthy individuals while in a laboratory setting, and not in a clinical setting.[57,82,91]

In this survey paper, our primary objective is to investigate whether the prevailing trend in the reporting of SpO2 prediction/calculation results is to disregard the critical SpO2 domain in favor of presenting more commending SpO2 prediction outcomes, or if the values below 90% are considered. Notably, the vast majority of SpO2 values within publicly available databases fall within the range of 95–100%. Anticipated results from this investigation aim to provide insights into the extent to which critical SpO2 levels are considered in current SpO2 prediction and calculation methodologies based on PPG signals.

In a practical sense, it is important to use SpO2 estimators that were trained/evaluated on lower levels of SpO2 since we need models that are capable of capturing the sudden drop in oxygen saturation in injured persons/patients — it indicates possible internal bleeding or hypoxemia.

MATERIALS AND METHODS

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.[8,89,92] PRISMA offers a scientific methodology in the form of a guideline checklist and contributes to the quality assurance of research replicability. This section provides a description of the paper's selection criteria, search strategy, and data analysis procedure.

Primary and Secondary Outcomes

The primary research questions addressed in this study are as follows:

Q1: Do authors take into consideration the effect of the critical SpO2 level in their SpO2 prediction/calculation evaluation results?

To address this inquiry, we conducted a comprehensive search across multiple scientific databases using PRISMA guidelines. We postulate that the inclusion of critical SpO2 level values during model validation and calculation/prediction of SpO2 from PPG has the potential to impact the final model validation, i.e. the papers that do not include the critical SpO2 levels tend to have better prediction results compared to the papers that utilize SpO2 less than 90%.

The secondary outcomes are obtained by considering several other issues in the meta-analyses provided in this study, applied only to the selected papers that utilize the critical domain:

Q2: Can we perform a meta-analysis of the existing literature in order to contribute to the existing body of knowledge using the following metrics:

Metric 1: Do the authors provide the software for their developed ML/DNN models (SpO2 predicted), or formulas (SpO2 calculated) to recreate their results?

Metric 2: What is the number of subjects involved in providing the results?

Metric 3: Are there publicly accessible databases that the researchers utilized in their scientific investigations?

Metric 4: What is the type of device utilized to gather the PPG signals in the reviewed papers?

Metric 5: How was the PPG signal measured?

Metric 6: What is the tendency concerning collaboration among the coauthors?

Metric 7: What is the method used for obtaining the SpO2 value?

Data Sources and Search Strategy

A systematic search for papers was conducted in three electronic databases (**Scopus, Pubmed,** and **ScienceDirect**). The period from 2016 to 2022 was selected to capture recent research and advancements in the field of SpO2 estimation using PPG signals. These databases were chosen due to their ability to offer a search option based on user-defined queries, and export data in the preferred format. To increase the inclusiveness of eligible studies using the above-mentioned databases specific, key terms and their combinations using Boolean operators were defined for the topic, paper title, and abstract. We utilized various search phrases and databases, and any discrepancies were resolved through open discussion. These terms and combinations were specified in **Scopus** and **Pubmed** databases' input fields as keywords for the topic, paper title, and abstract, resulting in the following query:

> (*ppg OR* (*photoplethysmogram*) *OR* (*pulse oximeter*) *OR* (*Oxygen sensor*) *OR* (*pulse oximetry*)) ***AND*** ((*oxygen saturation*) *OR* (*blood oxygen*) *OR* (*SpO*2)) ***AND*** ((*prediction*) *OR* (*estimation*) *OR* (*computation*) *OR* (*measurement*) *OR* (*extraction*))).

For the **Science Direct** database, the maximum number of accepted statements in the query used above was eight. Therefore, we defined three different queries, splitting the last ***AND*** expression into (*prediction*) ***OR*** (*estimation*); (*computation*) ***OR*** (*measurement*); *and* (*extraction*), and we obtained the following three queries:

- (*ppg OR* (*photoplethysmogram*) *OR* (*pulse oximeter*) *OR* (*Oxygen sensor*) *OR* (*pulse oximetry*)) ***AND*** ((*oxygen saturation*) *OR* (*blood oxygen*) *OR* (*SpO*2)) ***AND*** ((*prediction*) *OR* (*estimation*))).
- (*ppg OR* (*photoplethysmogram*) *OR* (*pulse oximeter*) *OR* (*Oxygen sensor*) *OR* (*pulse oximetry*)) ***AND*** ((*oxygen saturation*) *OR* (*blood oxygen*) *OR* (*SpO*2)) ***AND*** ((*computation*) *OR* (*measurement*))).
- (*ppg OR* (*photoplethysmogram*) *OR* (*pulse oximeter*) *OR* (*Oxygen sensor*) *OR* (*pulse oximetry*)) ***AND*** ((*oxygen saturation*) *OR* (*blood oxygen*) *OR* (*SpO*2)) ***AND*** (*extraction*))).

The result lists of the papers found after the electronic search were downloaded and organized in tables for further analysis.

Eligibility Criteria

The selection of the papers was conducted in three phases.

The first phase was the initial paper screening, where the paper selection was based only on the paper title and abstract. The database queries identified 6173 papers as possible candidates in the databases of interest. After removing the duplicates, 5324 different papers were identified (Fig. 1). The second phase included full-text reading and a deeper analysis of the papers based on the research question. The extensive screening process resulted in 211 studies as eligible

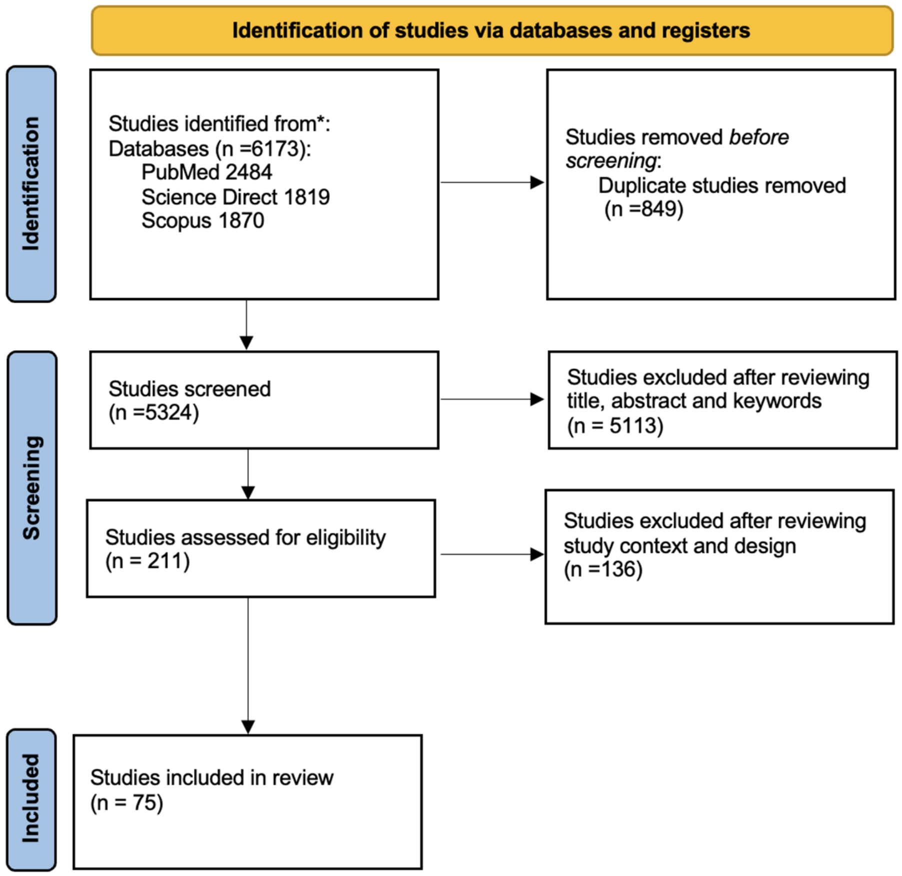

Fig. 1 Schematic representation of the screening and selection process.

candidates. In the third phase, the papers selected in the second phase were subjected to a comprehensive examination. Seventy-five papers that calculate or predict SpO2 levels using PPG signals were finally extracted after reviewing the full context of the papers. More specifics about the considered studies are presented in Sec. 3.1.

Metrics for Studies that Include the Critical SpO2 Levels

To conduct the meta-analysis and rank studies that investigate SpO2 levels below 90%, we utilized a set of standardized metrics and introduced ranking points. The following metrics were considered:

- **Software availability:** Assess whether the model or formulas used for SpO2 prediction or calculation are publicly available (**1** — available, **0** — not available).
- **Number of subjects:** Reflects the number of participants enrolled in the study (**2** — more than 20 subjects; **1** — between 10 and 20 subjects; **0** — less than 10 subjects).
- **Database availability:** Evaluate whether the database used in the study is publicly available (**1** — available, **0** — not available).
- **Device type:** Distinguishes whether the authors used a commercial device or developed a new one for SpO2 prediction/calculation. If the authors compared their device with a commercial one, the commercial device is ranked higher because it is already clinically approved and certified (**3** — new vs. commercial, **2** — commercial, **1** — new, **0** — no information).
- **PPG signal measurement method:** Assess whether the PPG signal measurement is performed by initiating contact with the subject or contactless. The contactless method is ranked lower since it is less reliable (**1** — contact, **0** — contactless).
- **Authors' institutions:** Evaluates the collaborative nature of the research by assessing whether different institutions were involved in the study (**1** — different institutions, **0** — same institution).

Table 1 summarizes the metrics that were included, as well as the value ranges and meaning of each metric.

Table 1. Evaluation Framework Metrics and Value Ranges.

Metric	Value Range	Criteria
SpO2 values range	0–1	1 — if measured SpO2 values lower than 85%
		0 — SpO2 values higher than 85%
Software availability	0–1	1 — if a model or formula is available
		0 — otherwise
Number of subjects	0–2	2 — more than 20
		1 — between 10 and 20
		0 — <10
Database availability	0–1	1 — if there are available links with the used data
		0 — otherwise
Type of device	0–3	3 — new vs commercial
		2 — commercial
		1 — new
		0 — no information
PPG signal measurement	0–1	1 — contact
		0 — contactless
Authors institution	0–1	1 — authors from at least two institutions
		0 — all authors are from one institution

RESULTS

Included Studies

Using the abovementioned criteria for database search, in the first, **Identification** step, the three databases were searched to identify the relevant papers (the Search strategy, Sec. 2.2). Namely, **6173** potential papers were identified: **2484** from Pubmed, **1819** from Science Direct, and **1870** from Scopus. As an outcome of this step, **849** papers were eliminated as duplicates. In the second, **Screening** step, the initially obtained papers were processed by title, abstract, and keywords. Out of the remaining **5324** papers, **5113** were excluded as they did not cover the topic of interest. Following, **136** papers were eliminated after reviewing the study context, design, findings, and contribution. In the third, **Included** step, the final list of papers was confirmed, to be used for the review study, i.e. **75** papers met the inclusion criteria and were selected for the final analysis in the third phase.

Figure 1 shows the selection process in detail.

Only peer-reviewed papers written in English were considered in this selection process. Any discrepancies in the selection of the final papers were solved by consensus among the co-authors.

Characteristics of the Included Studies

In this section, we will describe the characteristics of the 75 included studies, put in a broader context.

Figure 2 depicts the frequency of published papers per year. Our findings indicate an unremarkable rise in the number of published research papers in 2021 based on a comparison of publication counts across the years 2016–2022.

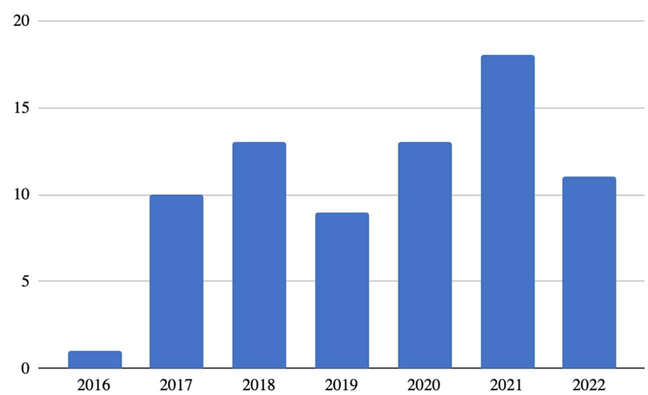

Fig. 2 Frequency of published papers per year.

Research published across 57 distinct journals on the subject under analysis, indicates the increasing significance of the topic across diverse fields of knowledge. Figure 3 depicts journals with more than one paper dedicated to the estimation of SpO2 from PPG.

Main Findings

This section provides the answer to the Primary outcome Q1 of this paper, points out the different approaches for evaluation metrics and presents a scoring table according to Sec. 2.4.

Table 2 summarizes the included 75 papers, the method used to acquire SpO2 values (prediction(P) or calculation(C)), and the range of SpO2 levels examined in the paper.

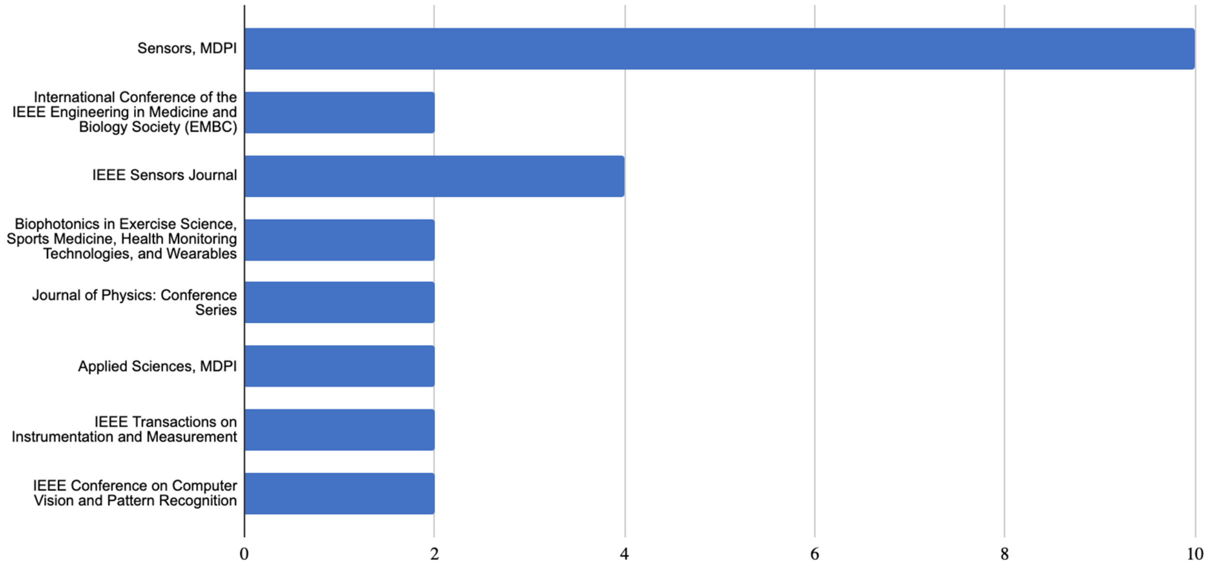

Fig. 3 Frequency of papers relevant to our study per journal.

The papers that address the levels of SpO2 lower than 90% are highlighted in grey in Table 2. We discovered that only 21 out of 75 papers considered SpO2 values that are in the critical domain (Fig. 4). In other words, over 56% of these papers (42 out of 75) did not take the critical SpO2 level into account e.g. Refs. 12, 14, 21, 26, and 45, and 16% did not provide information of the SpO2 level values.

Considering the methods used to acquire SpO2 values, 10 of the papers in our research use prediction, and 65 calculate the SpO2 values by analyzing how much of each wavelength is absorbed by the blood. SpO2 critical level values below 90% were included in six out of those ten papers that predicted SpO2 values from PPG, and four of them even included values below 85%. In comparison, only fifteen of the 65 papers that calculate SpO2 values from PPG consider the SpO2 critical level below 90%, and 9 of them consider the SpO2 critical level below 85%.

The next point of this section is about the used evaluation metrics. Just a small number of the papers that explore only SpO2 values above 90% have presented the metrics they used for the evaluation of their results.

Table 3 is created only from the papers that elaborated on the evaluation metrics used in their research. As one can observe, the authors used very different approaches for evaluation in those papers.

Table 3 also contains the evaluation metrics results for the prediction or calculation of SpO2 from PPG achieved in the papers that address SpO2 levels below 90%. They are given on the right side of Table 3 and marked in grey.

Comparing these studies is challenging since they use different evaluation metrics, which practically makes them noncomparable. For instance, RMSE of 2.3 for SpO2 is reported by Pirzada *et al.*,[13] Ijaz *et al.*[65] achieved RMSE of 0.5589. At the same time, Mohan *et al.*[27] attained RMSE in the range of 2.05–2, while Vogels *et al.*[52] reported MAE of 4.11. The absolute mean error is used in.[22,75] The average R^2 is used only in.[22] Other authors use metrics such as standard error,[40] deviation,[30] accuracy,[49] average MSE,[22] and percentage error rate.[62]

Concerning the evaluation of the papers that considered SpO2 values below 90%, only 16 papers, e.g. Refs. 18, 44, 31, and 40, out of these 21, presented information on the evaluation metrics they used in obtaining their results. We noted a tendency for these studies to report lower overall accuracy and other evaluation metrics assessing model performance compared to those focusing on SpO2 levels between 95% and 100%. However, direct comparison between these results is challenging since different authors use different evaluation metrics.

Our methodology produced the scoring table, Table 4, which shows the results of the assessment of the selected 21 papers that use SpO2 critical levels, according to the metrics described in Sec. 2.4 and presented in Table 1.

In the Total column, the sum of all the other columns is provided, with a higher score indicating that the particular paper presents more valuable information.

Thirteen research papers take SpO2 values lower than 85% into account e.g. Refs. 22, 56, 18, 61, 62, and

Table 2. Summary of the Data Extracted from the Studies Included in the Systematic Review.

Paper	SpO2 P/C	SpO2 values Range	Paper	SpO2 P/C	SpO2 values Range
Longmore *et al.*[9]	C	No info	Umar *et al.*[47]	C	95–99%
Li *et al.*[10]	C	No info	Naguszewski and Weremczuk[48]	C	88–100%
Fan *et al.*[11]	C	No info	Banik *et al.*[49]	C	94–100%
Ballaji *et al.*[12]	C	>97%	Luo *et al.*[50]	C	90–99%
Pirzada *et al.*[13]	C	No info	Jarchi *et al.*[51]	C	92–96%
Zhang *et al.*[14]	C	95–100%	Vogels *et al.*[52]	C	No info
Krizea *et al.*[15]	C	95–100%	Ferlini *et al.*[53]	C	No info
Chan *et al.*[16]	C	70–100%	Davies *et al.*[54]	C	94–100%
Fan *et al.*[17]	C	90–100%	Ashisha *et al.*[55]	C	95–99%
Venkat *et al.*[18]	P	81–100%	Aguirregomezcorta *et al.*[56]	P	70–100%
Dai *et al.*[19]	C	95–100%	Purwiyanti *et al.*[58]	C	89–99%
Kim *et al.*[20]	C	90–98%	Al-Naji *et al.*[59]	C	90–100%
Alharbi *et al.*[21]	C	95–98%	Rosa and Betini[60]	C	95–98%
Vijayarangan *et al.*[22]	P	60–100%	Takahashi *et al.*[61]	C	80–100%
Toral *et al.*[23]	C	92–100%	Bui *et al.*[62]	C	82–97%
Anagha *et al.*[24]	C	94–97%	Bui *et al.*[63]	C	>90%
Wu *et al.*[25]	C	88–100%	Merkepci *et al.*[64]	C	90–96%
Bhattacharjee *et al.*[26]	C	96–99%	Ijaz *et al.*[65]	P	No info
Mohan *et al.*[27]	C	No info	Moço and Verkruysse[66]	C	85–100%
Casalino *et al.*[28]	C	>95%	Han *et al.*[67]	C	No info
Fan *et al.*[29]	P	>95%	Jakachira *et al.*[68]	C	95–100%
Azhari *et al.*[30]	C	89–100%	Raghuram *et al.*[69]	C	92–96%
Tanveejul *et al.*[31]	C	70–100%	Xuedan *et al.*[70]	C	94–99%
Chen *et al.*[32]	C	95–99%	Shen *et al.*[71]	P	90–99%
Krizea *et al.*[33]	C	No info	Bejgam *et al.*[72]	C	95–100%
Van Beers *et al.*[34]	P	>87%	van Gastel *et al.*[73]	C	94–100%
Gupta *et al.*[35]	C	No info	Jakachira *et al.*[74]	C	96–99%
Alharbi *et al.*[36]	C	>90%	Bui *et al.*[75]	P	82–97%
Tian *et al.*[37]	C	94–98%	Berwal *et al.*[76]	C	95–100%
Haque *et al.*[38]	C	95–100%	Von Chong *et al.*[77]	C	No info
Khalid *et al.*[39]	C	97–99%	Song *et al.*[78]	C	90–99% (Simulator)
Tang *et al.*[40]	C	71–100%	Ma *et al.*[79]	C	90–100%
van Gastel *et al.*[41]	P	86–100%	Wang *et al.*[80]	C	80–100% (Simulator)
Naeem *et al.*[42]	C	>85%	Rodriguez-Labra *et al.*[81]	P	90–99%
Budidha *et al.*[43]	C	95.5–100%	Celka *et al.*[83]	C	70–100%
Naresh *et al.*[44]	C	70–100%	Wei *et al.*[84]	C	90–100%
Cao *et al.*[45]	C	96–100%	Brieva *et al.*[85]	C	95–100%
Ali *et al.*[46]	C	95–98%			

Notes: "P" — Prediction, "C" — Calculation.

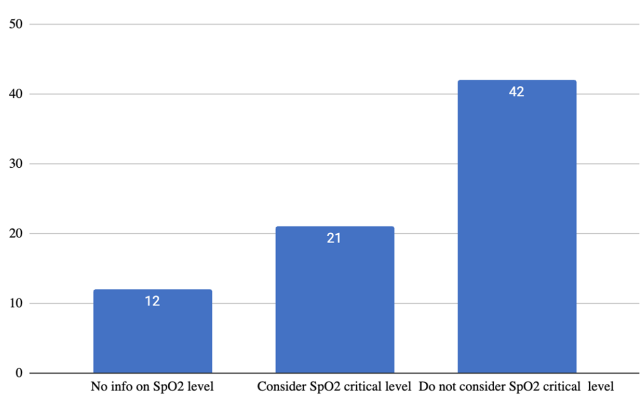

Fig. 4 Comparison between the number of studies that did not report SpO2 levels and those that reported critical and non-critical levels of SpO2.

84, whereas eight do not. Among these 21 papers, 11 include information regarding the specific methodology (software or formulas) employed to calculate or predict the SpO2 values e.g. Refs. 57, 40, 62, and 76. The included studies also raise some important questions about the reproducibility of the results. Additionally, in 20 out of 21 papers the data used in the research are not accessible for further study, making it difficult for other researchers to verify the findings. Only the authors of Ref. 40 provided info on the database used for their SpO2 estimation.

In nine papers, the results are obtained from studies that consider less than 10 subjects e.g. Refs. 40, 48, 61, and 76, six studies include between 10 and 20 subjects, e.g. Refs. 49, 81, 84, and 34 and six studies

Table 3. Evaluation Results in Papers that Included Info on the Means of Evaluation.

Papers with Levels of SpO2 > 90%	Evaluation Metrics Results	Papers with Levels of SpO2 < 90%	Evaluation Metrics Results
Zhang *et al.*[14]	RMSE = 1.8	Chan *et al.*[16]	RMSE = 2.64
Dai *et al.*[19]	RMSE = 0.0572	Venkat *et al.*[18]	Absolute mean error of 0.5% with an accuracy of 96 ± 2%
Kim *et al.*[20]	MAE = 0.537	Vijayarangan *et al.*[22]	AMAE = 1.81, AMSE = (5.17–8.21), AVG R^2 = (−0.55–2.9)
Alharbi *et al.*[21]	Pearsonr = 0.98	Azhari *et al.*[30]	Deviations less than 2%
Anagha *et al.*[24]	Maximum difference 3%	Van Beers *et al.*[34]	RMSEP of 1.86%
Bhattacharjee *et al.*[26]	Average error = 1,4%	Tang *et al.*[40]	Standard error ±1–±3%
Alharbi *et al.*[36]	Personr = 0.982, p-value = 0.894	van Gastel *et al.*[41]	RMSPE of <2%
Haque *et al.*[38]	MAE = 1.08	Naresh *et al.*[44]	RMSPE = 3.3654%
Khalid *et al.*[39]	MAE = 2.063, RMSE = 2.401	Aguirregomezcorta *et al.*[56]	RMSPE = 3%
Cao *et al.*[45]	Error range is within 0.71%	Purwiyanti *et al.*[58]	Average error 1.02%
Ali *et al.*[46]	Maximum deviation of 2%	Bui *et al.*[62]	3.5% error rate
Umar *et al.*[47]	Percentage error results less than 1%	Moço *et al.*[66]	RMSE = 2.9
Davies *et al.*[54]	RMSPE = 1.47%	Bui *et al.*[75]	Mean abs error of 2%
Ashisha *et al.*[55]	Error range 0–2%	Wang *et al.*[80]	Mean error <1%
Al-Naji *et al.*[59]	MAE = 3.02, RMSE = 3.62	Wei *et al.*[84]	RMSPE = 3.03% ± 0.14%
Rosa *et al.*[60]	Maximum difference 2%	Banik *et al.*[49]	Accuracy 98.96%
Shen *et al.*[71]	R^2 = 0.97, TRE = 0.46%, Accuracy = 99.4%		
Bejgam *et al.*[72]	Error range (%) = [2.3—4]		
van Gastel *et al.*[73]	MAE = [0.43—0.85]		
Song *et al.*[78]	RMSPE = [0.31—0.74%]		
Ma *et al.*[79]	Deviation of 1%		
Rodriguez-Labra *et al.*[81]	RMSE = 0.07, Accuracy=99.5%		
Brieva *et al.*[85]	RMSE = [1.5—2]		
Chan *et al.*[57]	RMSE = 0.6		

Notes: RMSE — Root mean square error, MAE — Mean absolute error, TRE — Total relative error, RMSPE — Root mean square percentage error.

Table 4. Assessment of the Selected 21 Papers that Include SpO2 Below 90%.

Authors	Values Lower Than 85%	Software Availability	Number of Subjects	Database Availability	Type of Device	PPG signal Measurement	Authors Institution	Total
Chan *et al.*[16]	1	1	1	0	3	1	1	8
Venkat *et al.*[18]	1	0	2	0	3	1	1	8
Vijayarangan *et al.*[22]	1	0	2	0	3	1	0	7
Tanveejul *et al.*[31]	1	0	2	0	3	1	1	8
Tang *et al.*[40]	1	1	0	1	0	1	0	4
Naresh *et al.*[44]	1	1	2	0	3	1	0	8
Naguszewski *et al.*[48]	1	0	0	0	2	1	0	4
Aguirregomezcorta *et al.*[56]	1	0	1	0	3	1	0	6
Takahashi *et al.*[61]	1	1	0	0	3	0	1	6
Bui *et al.*[62]	1	1	0	0	3	0	1	6
Bui *et al.*[75]	1	1	0	0	3	1	1	7
Wang *et al.*[80]	1	1	1	0	3	1	0	7
Celka *et al.*[83]	1	0	1	0	3	1	1	7
Wu *et al.*[25]	0	1	0	0	3	1	1	6
Azhari *et al.*[30]	0	0	0	0	3	1	1	5
Van Beers *et al.*[34]	0	1	1	0	3	1	1	7
van Gastel *et al.*[41]	0	0	0	0	2	0	1	3
Naeem *et al.*[42]	0	1	0	0	3	1	1	6
Banik *et al.*[49]	0	0	1	0	3	1	1	6
Purwiyanti *et al.*[58]	0	0	2	0	3	1	0	6
Raghuram *et al.*[69]	0	1	2	0	3	0	1	7

include more than 20 subjects e.g. Refs. 31, 22, 66, 58, 18, and 44. Eighteen of the papers considered in our study elaborate on the results obtained by their measuring device and compare them to the results obtained from a commercial device e.g. Refs. 16, 18, 61, 30, 62, and 34. This aspect further enhances the significance and applicability of their respective studies. Two of the papers use commercial devices only and one does not specify this information.

When PPG results are obtained through direct contact with the subject, they are considered to be more reliable, especially given the current technological capabilities. The majority of the papers in our study use devices that directly measure data from the subjects' skin e.g. Refs. 58, 49, 25, 84, and 34. Furthermore, if the data are derived from a collaborative research effort involving multiple institutions, it indicates a broader consensus regarding the relevance of the obtained data. Fourteen of the papers in our research stem from collaborations between two or more institutions, e.g. Refs. 31, 61, 62, 84, and 34.

DISCUSSION

SpO2 has significant implications for clinics and clinical research across various domains, such as clinical monitoring, diagnosis and disease management, clinical care and triage, research and development, and epidemiology (e.g. COVID-19 pandemic). By analyzing and comparing the various approaches considered in different studies utilizing this PRISMA approach, the researchers can make informed decisions regarding which methodologies, technologies, and evaluation metrics for SpO2 extraction from PPG are important for their own studies. This review can also aid in quantifying the studies by assessing different characteristics, such as software and database availability, number of subjects included in the study, type of devices used, and authors' collaboration (scoring table 4). However, we are aware that comparison of these studies is challenging. Many of them include missing information on the used methodology, insufficient subjects' health status, and highly diverse error metrics. Overall, the paper exhibited a high level of heterogeneity, posing challenges in assessing their quality.

We believe that it is of great importance to make the SpO2 extraction models accurate for a wider range of SpO2 values, i.e. to use SpO2 estimators that were trained on lower levels of SpO2. This is especially important when there is a sudden drop in SpO2 values from normal values to the critical domain since the sudden drop in oxygen saturation indicates possible internal bleeding and the need for priority treatment of these critical patients or victims in triage situations with a high volume of casualties.

CONCLUSION

The primary objective of this review is to examine the incorporation and significance of critical SpO2 levels (<90%) in research papers related to the calculation or prediction of SpO2 using PPG signals. The goal is to raise awareness regarding this issue and emphasize its significance within the field. Additionally, it aims to elucidate the impact of these critical levels when presenting evaluation results. To address this inquiry, we conducted a comprehensive search across multiple scientific databases using the PRISMA guidelines in three databases: PubMed, Science Direct, and Scopus where **6173** potential papers were identified. Through an extensive screening process, only **75** papers were chosen for further analysis, out of which only **21** included data from critical SpO2 levels.

Considering the secondary outcome, this research included the sample size of the study participants, the models utilized to derive the results, the availability of databases, the specific devices employed in the research, the methodologies employed for PPG signal measurement, and the collaborative efforts among authors from different institutions.

Furthermore, some of the papers do not give an insight into the software models or the formulas used for obtaining the results. Many of the studies produce the results in laboratory settings and do not include a significant number of testing subjects. The findings of this review indicate a preference among researchers for utilizing SpO2 calculation rather than prediction, with approximately 86.7% of the analyzed papers employing SpO2 calculation as the primary method for deriving values.

A notable concern arising from the included studies relates to the reproducibility of the results. Most of the data are not made available to other researchers, limiting the ability to replicate and verify the findings. Additionally, the adoption of diverse evaluation metrics across the studies makes them practically incomparable.

In our future work, we aim to actively monitor the developments around the primary question, the incorporation of critical SpO2 levels in the development of new algorithms for SpO2 prediction/calculation.

Designing a model for SpO2 estimation from PPG signals is challenging, as it is difficult to collect SpO2 data with levels lower than 95% since these subjects are usually with low health status in hospitals. Even more, the subjects with SpO2 lower than 90% can be possibly found only in intensive care units.

Future SpO2 estimation studies should consider critical SpO2 levels below 90% for their results to be more relevant and usable within the medical systems. The databases and the models should be made available to the wider research community, to make the experiments reproducible. The studies should also include researchers from diverse institutions especially medical doctors.

To the best of our knowledge, there is no similar research that specifically analyses the coverage of SpO2 critical levels in relevant published papers, including several important points (reproducibility of the results, availability of databases, number of testing subjects). By elaborating the first and the secondary outcomes, we hope to have given directions to the prospective researchers and developers of new sensors in the domain of SpO2 estimation/calculation utilizing PPG signals.

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