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Review

A Systematic Mapping Study on Research in Anemia Assessment with Non-Invasive Devices

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Abstract: *Contribution:* This paper examines the literature dealing with the non-invasive estimate of anemia (NEA), and analyzes if the research is developing scientifically with adequate empirical validation. This paper reveals a trend in NEA studies towards an increasing interest in estimating anemia using conjunctiva pallor. *Background:* Supporting clinical developments and processes to reduce personal discomfort and allow extensive screening needs substantial efforts in researching non-invasive techniques to evaluate anemia. *Research Questions:* The main aims of this study are the analysis of the area of interest explored in the NEA literature, the evaluation of the peculiarities of papers, giving special consideration to empirical ones, examining them from the point of view of the daily improvement of doctors and healthcare personnel activities and the daily life of patients; and the identification of any considerable research gap to encourage further investigations on new topics. *Methodology:* The systematic mapping study has been elected as the optimal approach to probe the NEA literature since it defines a rigorous process for data retrieving and interpretation. *Findings:* Research in this sector is very active, especially in the most populated countries in the world and focuses on improving the technologies currently on the market and on proposing new solutions, especially portable and usable by everyone. A new trend in camera and smartphone-based devices is identified.

Keywords: anemia; hemoglobin; human tissues; conjunctiva; non-invasive medical device; systematic mapping study

1. Introduction

In reports published by the World Health Organization, it is claimed that anemia is a global health problem, considering that around 25% of the population is affected, with varying degrees of severity [1–6]. The main factors that cause anemia are iron deficiency, infectious diseases, or genetic factors. Red blood cells and hemoglobin (Hb) concentration levels decrease with anemia and this leads to a reduction in the function of the blood to transport oxygen to the peripheral tissues. The excessive reduction of the availability of oxygen supplied to the cells causes damage to vital organs and then severe anemia has to be monitored steadily. In severe cases, blood transfusion is necessary basing on the Hb measured also daily, normally in the laboratory using a blood sample. This pathology is subtle because it evolves slowly and does not present easily recognizable symptoms. Unequivocal several symptoms appear when the compensatory processes activated by the human body are no more sufficient to guarantee the right quantitative of circulating oxygen. The symptomatology varies according to the severity and type of anemia, but typical symptoms common to all types of anemia include pallor, asthenia, tachycardia, fainting, loss of appetite, nausea, exertional dyspnea [7–11].

Anemia can be detected with invasive and non-invasive techniques. Invasive techniques require blood samples; therefore, they can cause discomfort to patients, can be infection-prone, or require laboratory analysis. Non-invasive techniques are fundamental to patients who frequently take blood tests, or suffer blood loss; these techniques generally exploit the pallor of some body parts to determine whether a patient is anemic or not [12–19]. Patients who need recurrent blood sampling or who cannot easily move from home can benefit greatly from these techniques and then these approaches are of some importance. Furthermore, the recent trend in healthcare is to treat patients at home as far as possible, through new therapeutic care pathways and services like medical records [20,21].

A great effort has been done in recent years to improve non-invasive tool accuracy. Non-invasive devices can be made portable, cheap, and easy-to-use and offer great advantages in rapid pre-diagnosis and self-monitoring. If the devices are low cost, they allow mass screening even in geographic areas with less available economic resources.

As is already the case in other medical disciplines that can benefit from the extensive use, as an example, of the image analysis, sound or signal analysis and artificial intelligence techniques [22–28], it is equally important to stimulate research and development of new technologies to deal with anemia. Among other benefits, the reduction of the costs borne by the national health systems and powering the medical and healthcare services can also be considered important.

Application of non-invasive estimation of anemia in real health care processes could be delayed by divergences between potential interest areas and those dealt with in literature. Marking these divergences can help explore more effective research and experimentation paths to develop and validate the state of the art.

The Systematic Mapping Study (SMS see Appendix B) [29] has been elected as the optimal approach to probe the NEA literature since it defines a rigorous process for data retrieving and interpretation.

The paper has the following structure: related work is discussed in Section 2 along with noting the innovative aspects of this work; the method conducted in this mapping study to classify and select papers is described in Section 3; research questions results are analyzed in Section 4; in Section 5 relevant findings from the research results are discussed, and finally conclusions are drawn in Section 6 where possible research directions are also outlined.

2. The Reason for a Systematic Mapping Study

Medicine was one of the first disciplines that were subject to systematic surveys since it is a branch of knowledge where the research is essentially evidence-driven. Systematic surveys turn up in the past couple of decades as a secondary study method, evolving from researches based on evidence-based primary studies [30,31]. Lately, the systematic survey concept has been transferred to other fields such as information systems [32] and software engineering [33–35]. The lack of studies collecting and summarizing the outcomes of empirical primary studies is addressed by Pickard et al. [36]. The idea of combining the results of primary studies via meta-analysis and the concept of research synthesis have been addressed, respectively, by Miller and Hayes [31]. The work of Basili et al. [37] is the first try to build knowledge by synthesizing primary studies.

Estimating anemia non-invasively is a research area that includes more than one discipline such as medicine, engineering, and computer science; research that provides results based on empirical evidence can benefit those disciplines. The aforementioned communities could take advantage of the results of the present study. Given this research area is recently expanding, the authors considered it appropriate to work on an SMS.

As far as the authors know, no other SMSs have been carried out on the topic.

The SMS is carefully illustrated and if any threats are found by other researchers in this study, the SMS process can be varied so that the threat can be mitigated, the results reinforced and the time window or the goals of the review changed/extended.

3. Research Method

The proposed research process follows the guidelines proposed by Kitchenham et al. [29] to perform the SMS.

3.1. Research Questions

The SMS uses the paradigm: Population, Intervention, Output (PIO) described in [29], which encourages using a "Comparison" factor. This factor cannot be analyzed in an SMS since papers are partly analyzed and in [29] a description of how such a comparison has been carried out is just hinted.

The PIO paradigm components, for our goals, are below defined:

Population: caregivers, physicians, health assurances, health device manufacturers, researchers, and all people at anemia risk.

Intervention: anemia detection and hemoglobin monitoring using non-invasive techniques and devices.

Output: any benefits leading to an improvement in anemia assessment and hemoglobin screening with non-invasive techniques.

According to the PIO paradigm, we structured SMS' general questions defined by Arksey et al. [38] to match the dimensions investigated in this study. Table 1 reports the resulting research questions.

Table 1. Research questions.

ID	Text	Motivation
RQ1	What is the temporal and geographical distribution of the papers?	To understand how papers develop over time and how they are distributed across countries interested in non-invasive technologies for anemia assessments.
RQ2	What stakeholders do the papers refer to?	To identify NEA stakeholders interested in this research.
RQ3	What are the topics of interest and with what frequency have they been investigated?	To discern the topics that stimulate researchers.
RQ4	What are the most frequent aims of the papers?	To understand why these studies are conducted and to reflect on their utility in improving anemia assessments.
RQ5	What types of empirical studies do the papers refer to?	To analyze what types of empirical evidence were considered so that this study can identify any gaps in the current literature.
RQ6	What solutions are presented in the publications?	To understand the relevance of the research in the literature and the extent to which stakeholders can use it. These data can also be used to suggest interesting approaches to fill research gaps.

3.2. Research Protocol

3.2.1. Research String

A well-built search string ensures to automatically extract a good sample of literature studies relevant to our study. To build the string, knowledge of the popular literature terms relating to the PIO's principles is strictly necessary. These words are picked up via the validation process described in Section 3.2.2; the words are:

Population: anemia, hemoglobin.

Intervention: non-invasive, noninvasive, device, screening, measurement, diagnosis, evaluation, assessment.

Output: improving anemia assessment, non-invasive anemia estimation, non-invasive hemoglobin measurement.

Words and dimensions linked to "OR" and words or dimensions linked to "AND" make up the search string.

3.2.2. Research Strategy

A search string must be assembled before running the research across the entire period considered to ensure that the majority of representative studies in the entire literature on anemia assessment is extracted by the automated research. To build the string, the method suggested by Zhang et al. [39], shown in Figure 1, was followed.

Sensitivity is obtained through the following procedure:

Sensitivity or Recall = NSRR/NSRT;

NSRR: Number of Relevant Studies Retrieved, number of relevant studies identified for the topic being investigated, automatically extracted;

NSRT: Total Number of Relevant Studies, Quasi-Gold Standard

The baseline to reach *Sensitivity* is 80%.

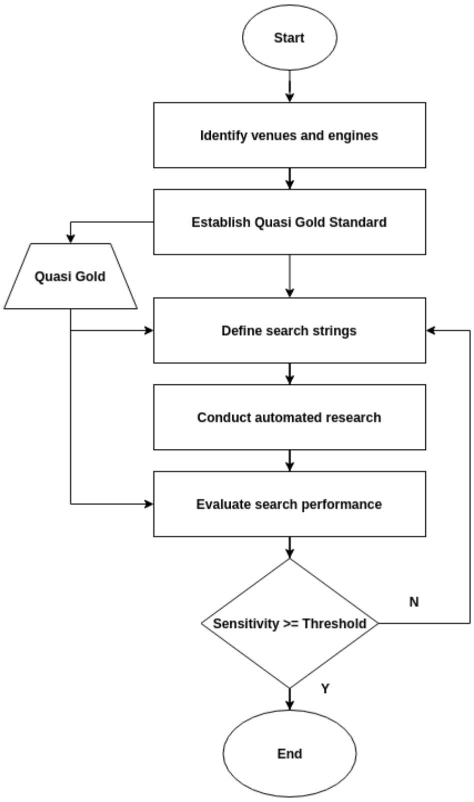

Figure 1. Validation of the research string.

3.2.3. Generation and Validation of the String

The period examined for the search string validation goes from December 2019 to April 2020 (a fifth-month mapping study).

References were identified, collected, and analyzed from each paper of interest. Other relevant papers on the same topic were found thanks to the analysis of the references. Then, citations from each paper of interest were searched, and the most significant were pinpointed. The automatic search was performed through the following search engines:

- Scopus (https://www.scopus.com/);
- Web of Science (http://www.webofknowledge.com/WOS);
- Google Scholar (https://scholar.google.com/).

Using the keywords previously identified by the authors as the most relevant, the first extraction of articles was carried out, the following quantities were reported: extracted papers = 14, sensitivity~87%.

Given the sensitivity greater than the previously defined threshold of 80%, the string is considered definitive. The keywords that make up the string were previously listed in Section 3.2.1.

3.2.4. Randomly Assigning Papers to Author Reviewers

The reviewing role was assumed by the authors who assessed each selected publication following the exclusion or inclusion rules. So that each of the 950 articles was guaranteed two revisions, the articles were randomly subdivided into 5 groups of 190 articles; each author then picked two groups and reviewed them for a total of 380 papers (see Figure 2).

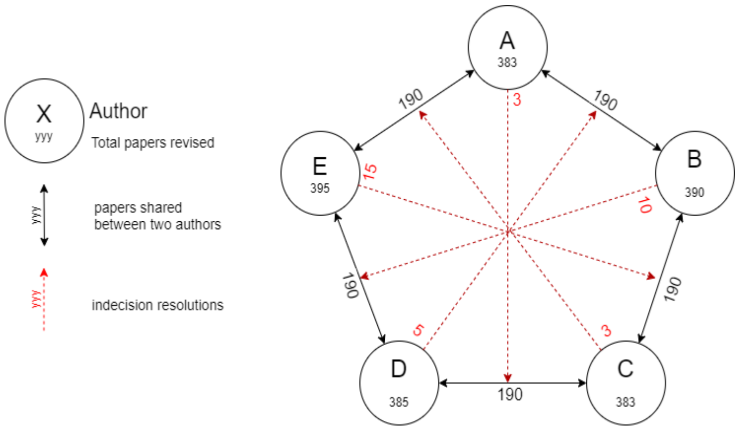

Figure 2. Papers review process diagram.

3.2.5. Screening Relevant Papers for Inclusion and Exclusion

The suitability of each document and therefore its inclusion or exclusion according to the criteria of the protocol was assessed through the following screening process: each article received two revisions from two different randomly selected reviewers, each reviewer independently assessed whether or not to include the document, later the two auditors discussed to reach an agreement if this had not been reached, a third auditor would have taken over, also expressing his opinion to create a majority in favor of the acceptance or exclusion of the document.

Journal papers, technical reports, and conference publications from January 2014 to April 2020 were considered. The period of publications can be chosen as an arbitrary parameter, as suggested in [29]: we consider a 6-years span surely adequate to the aim of this study. Although the search string was built in English, all languages were considered. The quality of the paper has not been considered a critical factor in this study since all in-topic papers can provide valuable information for this type of study (tissue, devices, stakeholders, and so on).

The following table (Table 2) shows the numerical data on the selection and inclusion of publications.

Table 2. Papers selected and included in this study.

Source	Number of Publications			
	Selected	**Excluded**	**Included**	**Included (%)**
Digital Library	950	782	168	17.68

3.2.6. Keywords

The keywords were then extracted from each paper, selecting words that could be convenient to set up classification tables and maps of the RQs.

Reviewers extracted the keywords mainly from the abstracts. If the abstract was inadequate the introductions were analyzed and if necessary, conclusions were also inspected. A paper would be automatically excluded if a reviewer could not mine the keywords and therefore classify the paper and answer the RQs, even though this never happened. A total of 168 papers were classified (see Appendix A).

All the keywords mined by the reviewers underwent comparison and evaluation until they were uncontested. If it was not possible to reach an agreement, the decision was made by the majority. The approved keywords were then linked with the meaning and grouped with semantically related keywords.

If semantic overlapping is detected between a new keyword (K_j) and a previous keyword (K_i), to eliminate the overlap we created an improved definition of K_i and K_j. If the semantics of K_i needed to be adjusted, the reviewers who had analyzed the papers containing K_i aligned the classification to the newly updated semantics.

If papers fitted well with more keywords belonging to a dimension, they were put into multiple classes.

4. Results

In this section the results achieved by answering the six research questions presented in Section 3.1 are presented, the findings concerning each "dimension" are also discussed.

4.1. Temporal and Geographical Distribution of the Publications

Due to the impartial nature of the classification of distributions, the interaction among the reviewers was necessary just to verify the mined data.

Figure 3 shows how the number of non-invasive anemia estimation papers published annually varied from 2014 to 2020.

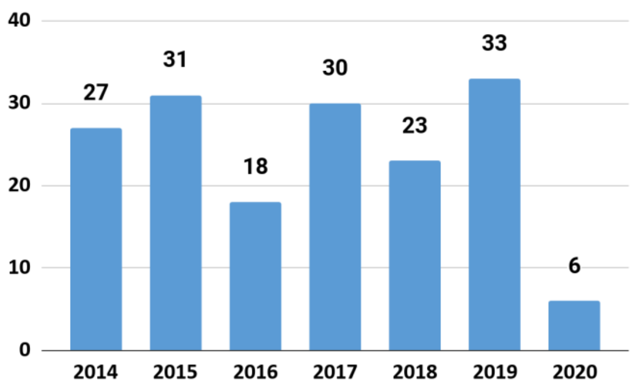

Figure 3. Papers distribution by year.

A significant number of non-invasive anemia estimation studies have been published since 2014 (168 papers). The publication rate seems to remain approximately stable over the years, even if during 2016 there is a slight drop in publications.

The graph in Figure 4 allows to clearly view the geographical distribution of the documents, the countries that have focused mostly on research on the non-invasive estimation of anemia are represented, each with the relative number of articles published: in case an article had had authors from more than one country, this would have been considered a product of the country of origin of the majority of the authors; in the extreme case where there is no clear majority between nationality, then the nation of the first author will win the authorship of that document.

India, USA, and China are producing the most (41, 35, and 17 papers, respectively). Regarding them, an explanation could be that they are huge countries, with very dynamic economies, and in two of them anemia is a particularly felt problem, especially in pregnant women and preschool children [2], the USA could also be stimulated by the particular interest in reducing healthcare costs. Only three European countries are listed. Germany is the first (9 papers), Italy and Spain (5 papers published each).

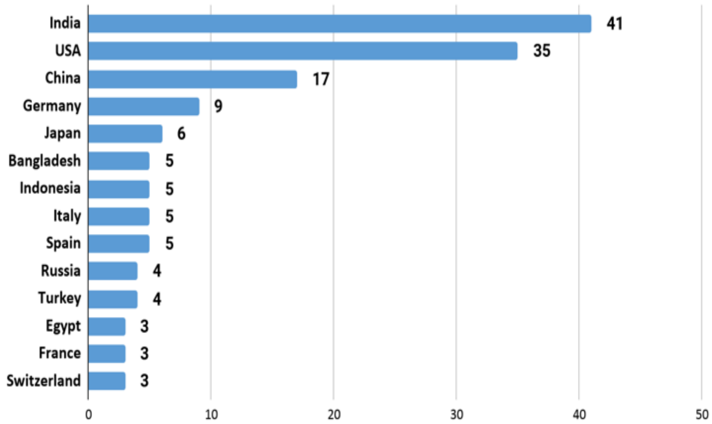

Figure 4. Top productive countries.

4.2. Stakeholders

Table 3 reports identified stakeholders' definitions, while Figure 5 shows the number of papers that a certain kind of stakeholder would be interested in.

Table 3. Identified stakeholders' definitions.

Stakeholder	Description
Health facilities	Include papers that could improve the quality of private and public healthcare services.
Device manufacturers	Includes papers that could improve existing commercial devices or propose innovative solutions that could be implemented. (on sale/commercialized) marketed
National Health System and Health insurance	Papers talk about devices that could save money or time augmenting the system's efficiency.
Doctors and caregivers	Include papers that can make diagnoses faster and easier.
Citizens	Covers tools and techniques usable by non-technical people

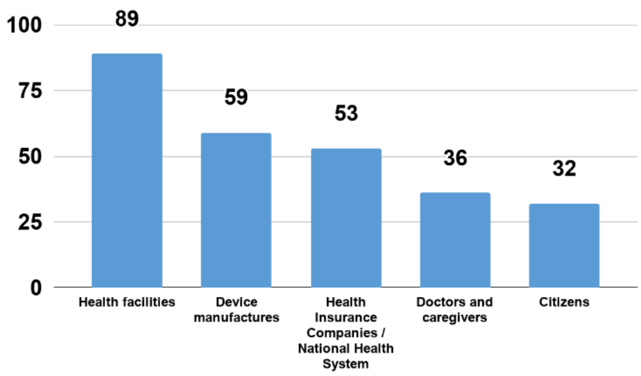

Figure 5. Distribution of stakeholders indicated in the studies.

Most of the papers aim to improve screening efficiency in health facilities (89 papers). A considerable number of the chosen papers propose new technologies that could interest health device manufacturers (59), and a similar number treats cost efficiency aspects (53). In smaller quantities papers focus on aspects that can be significant for caregivers (36) and citizens self-care (32).

Figure 6 gives the distribution of papers by device for the assessment (see Table 4); some papers belong to many classes since often authors compare more than one of them.

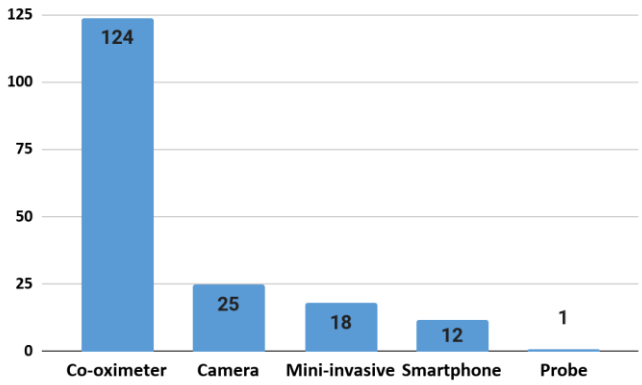

Figure 6. Distribution of papers by device for the assessment.

Table 4. Device types' definitions.

Device	Description
Light reflection/absorbance based	Use devices that indirectly measure hemoglobin levels using light reflection properties to distinguish oxyhemoglobin, and deoxyhemoglobin (pulse co-oximeters).
Camera	Use a digital camera to take pictures or videos, to later extract data from it.
Mini Invasive Device	Use devices that require a small drop of blood to evaluate HB.
Smartphone	Use a smartphone as a measurement tool and/or a user-friendly service to monitor patients' conditions.

Figure 6 shows that the majority refers to co-oximeters (124 papers), perhaps because they are devices easily accessible due to low cost and ease of use. Camera-based solutions are quite popular (25 papers), followed by papers discussing mini-invasive devices (18 papers). Only a few (12 papers) focus on smartphone-centric measurements.

4.3. Human Body Region of Interest

Figure 7 illustrates the distribution of the parts of the body on which the analysis is carried out. Sometimes studies address various topics, so few papers are classified in more than one class; there are also some papers about technologies exploitable for more than one type of device, so a specific body part could not be identified.

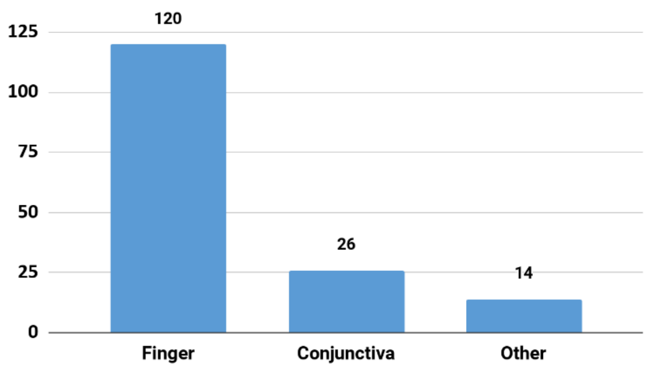

Figure 7. Region of the body investigated in published papers.

The graph in Figure 7 shows how the finger (120 papers) is the most analyzed body part, due to all the papers about devices and technologies that use to extract data from the fingertip capillaries, due to the massive use of co-oximeters which in most cases uses a finger clamp to extract the data; few camera and smartphone devices are also used to take pictures or small videos of the fingertip. Second, with a great gap, the conjunctiva (26 papers in total) comprehends papers that evaluate hemoglobin or anemia using the palpebral or forniceal conjunctiva. Other parts of the body are involved in a small percentage of the papers (14 papers); these papers analyze data from fingernails, eye sclera, retina, hand palms, tongue, or lips.

4.4. Assessment Goals

The assessment goal is the result that is given by the proposed or discussed solution (see Table 5).

Table 5. Assessment goals' definitions.

Assessment Goal	Description
Hemoglobin evaluation	Includes papers that make declarations basing on hemoglobin estimation
Anemia detection	Papers that discuss software or devices whose aim is to state if a patient is anemic or not.

In Figure 8 it is evident that the great majority of the papers focus on devices that estimate hemoglobin (149 papers), while only a few stops on the assertion if a patient is anemic or not.

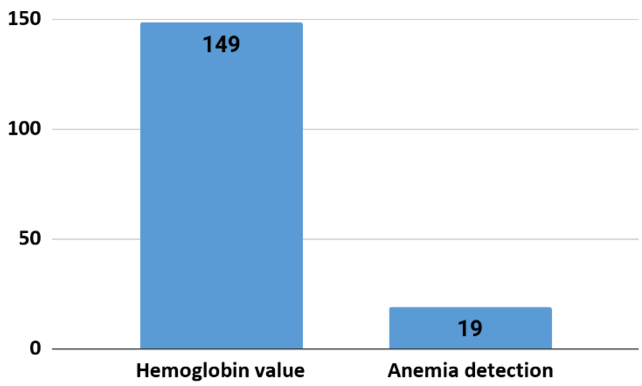

Figure 8. Distribution of assessment goals.

Two factors pallor of the exposed tissue (nails, palpebral conjunctiva, etc.) to obtain influencing this result have been identified. The first is that the majority of the papers relate to co-oximeters, which measure hemoglobin level. The second factor is the experimental nature of some papers, which try to regress the hemoglobin value from the pallor of the analyzed ROI through camera devices. This second group of papers refer to the study of the useful information about the level of hemoglobin concentration in the blood, while co-oximeters estimate it using light reflection properties.

4.5. Type of Studies

Following the identification of the number of articles in the literature that present empirical evidence, the taxonomy introduced in [32] has been adapted to the objectives of this research to better classify the documents. Few papers have a double classification as they present features of more than one type of study.

Figure 9 quantifies the taxonomy of the publications reported in Table 6. Many publications (76) bring new solutions to the literature; several (50) contain empirical evaluation, and some (31) demonstrate their thesis using empirical validation techniques. Other classes, few papers are limited to providing experiences and a few less provide opinions or conceptual scenarios.

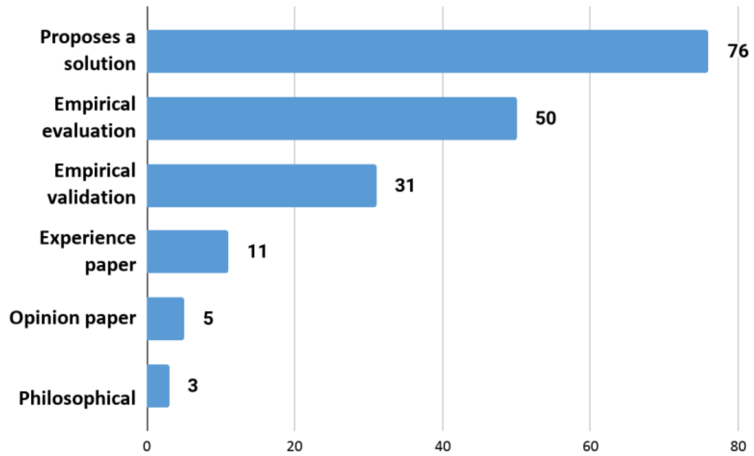

Figure 9. Distribution of papers by classification type.

Table 6. Taxonomy of types of publication.

Publication Type		Description
Empirical	Propose a solution	Propose a solution to a problem, either an innovation or a significant extension of an existing solution. Potential benefits and applicability are shown with examples and a good rationale.
	Evaluation	Techniques implemented in practice; empirical evaluation; analysis of costs, benefits, and drawbacks carried out. Research methods include case studies, in vivo experiments, field studies.
	Validation	Techniques investigated are innovative, with some sort of experiment, usually in the laboratory or in a realistic (but not real) context. No practical experimentation, even on prototypes.
Non-empirical	Experience paper	Describes the authors' personal experience, explaining what has been done in practice, and how.
	Opinion paper	Expression of personal opinions of good or bad characteristics of a topic and proposes ways to improve them.
	Philosophical paper	Proposes a new method or approach to analyze existing situations by structuring taxonomies or conceptual schemas.

Various devices were used for cumulating empirical evidence, most of them already on the market, analyzing their accuracy in particular conditions or comparing some of them.

Figure 10 exhibits that most of the papers are journals.

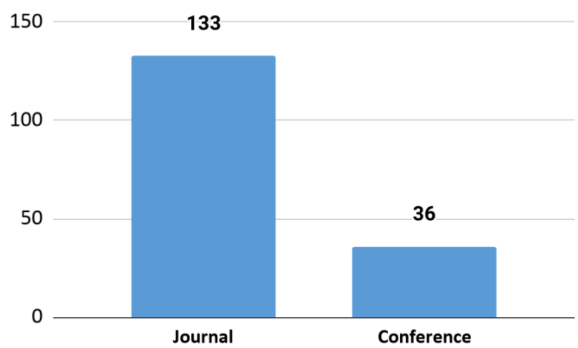

Figure 10. Distribution of where studies are published.

The predominance of journal articles implies that the published results, new technologies, and devices are founded on empirical evidence. This confirms that mature solutions and accurate devices are presented in the literature.

4.6. Solution Status

With regards to the dimension relating to the status of the solution, only articles presenting solutions are included in the considerations, therefore all other types of articles such as philosophical or opinion ones are excluded (see Table 7).

Table 7. Solution status definitions.

Solution Status	Description
Working/on the market	Technologies now beyond the state of experimentation, are already on sale or largely used, even only at an exploratory level.
Prototype	They present tools already implemented and validated with toy examples
Experimental	They offer empirically validated solutions, often accompanied by a working prototype.
Design	Proposals of technologies based only on a theoretical basis, not yet implemented. There are no prototypes available.

Figure 11 represents the status of the solution presented in the paper; if the paper presents or compares more than one solution, it is not classified in any class. Figure 11 shows that most (69 papers) are "working", this is determined by all the papers that discuss the accuracy of already on the market devices. Fewer papers are "prototype" and "experimental" with 37 and 34 papers respectively. A few studies introduce new devices or techniques; therefore the "design" status is less numerous.

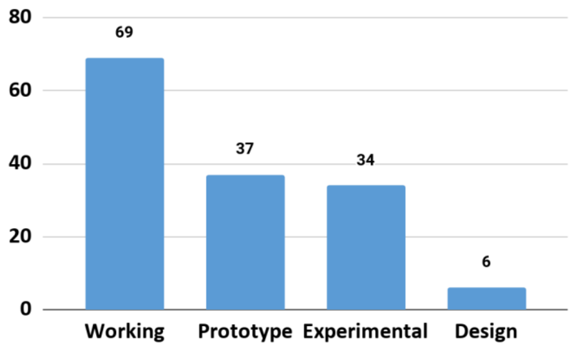

Figure 11. Distribution of solution types presented.

4.7. Mapping

This section examines multiple dimensions to identify patterns, trends, or correlations in the research literature. In particular, four charts express interesting information: device type over years (Figure 12); region of interest over years (Figure 13); region of interest vs. device type (Figure 14); device type vs. solution status (Figure 15).

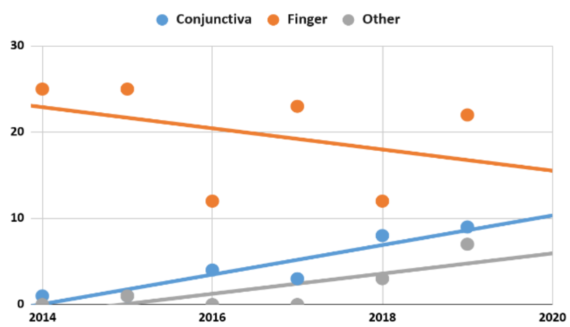

Figure 12. Device Type over Years.

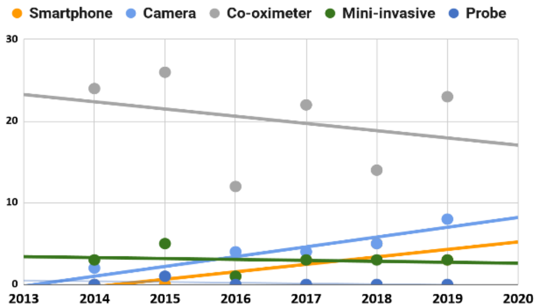

Figure 13. Region of Interest over Years.

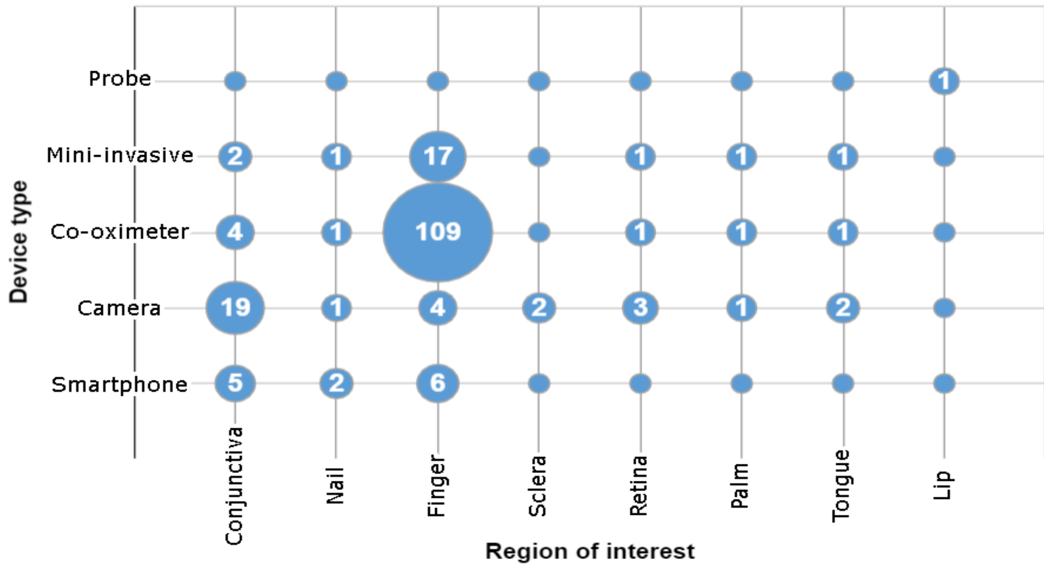

Figure 14. Region of interest (ROI) vs. device type.

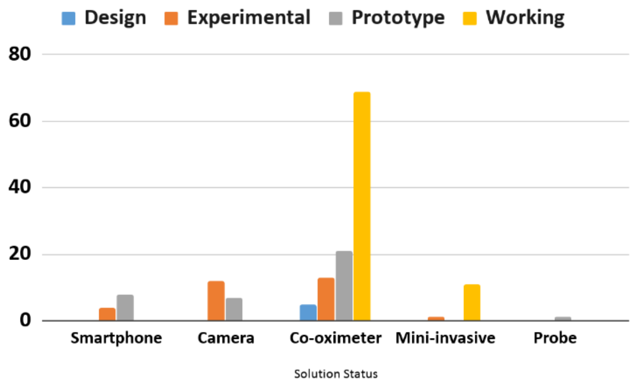

Figure 15. Device Type vs. Solution status.

The trend charts in Figures 12 and 13 do not include the year 2020 because data from this year, only refers to the months from January to April, so including it in a trend chart would distort the trends making them steeply go down.

Figure 12 clearly shows how the interest of the scientific community has changed over time, in particular, while co-oximeter research papers decrease, camera-based and smartphone-based research papers increase, it may be associated with the increasing availability and low prices of this kind of devices, thus the increasing interest in the conjunctiva (Figure 13) that is suitable for simple and fast hemoglobin evaluation through more common devices such as cameras and smartphones that also show an increase in popularity. The finger as a region of interest shows a decreasing trend even if numbers are still high, correlated with the decrease in research interest, and the still massive use of co-oximeters that rely on finger clamps as a source of inputs. An increment is also revealed in other ROIs that are relatively new such as sclera, retina, hand palm, tongue and lip, due to their novelty the number of paper referring to them is yet small, but their popularity is increasing due to the discovery of new non-invasive techniques and devices that allow self-diagnosis.

The chart in Figure 14 shows that proposed solutions that analyze the conjunctiva are all based on photos of it; most of them use smartphone cameras to take the picture, though only a few go further by embedding the measurement in an app addressed to self-care.

Fingertips are certainly the most used ROI for non-invasive and mini-invasive measurements, which are mostly made with co-oximeters and similar proposed devices; some studies acquire data from this ROI using cameras (3) or smartphones (4). Papers using sclera, retina, palm, tongue, and nail are all using cameras. This data merged with the trend of these ROIs shown in Figure 13, marks the increasing importance that image analysis techniques are gaining in non-invasive diagnosis. This approach lets researchers easily experiment with new ROIs without requiring specialized hardware, and aims to build a new generation of wide-spread, inexpensive tools.

The following chart (Figure 15) underlines that no camera and smartphone solutions are on the market.

Co-oximeters are the only kind of non-invasive device already on the market, although a lot of papers propose improvements to this technology: 13 papers published in 2019 have been identified as setting a proposal to improve measurements by the use of optical sensors. The main trends to enhance co-oximetry are the use of artificial intelligence approaches [40–46], find the optimum wavelengths [40–43,47–52], noise reduction [45,46], and minimize illumination influence [45].

5. Discussion

This paper has analyzed how non-invasive anemia assessment develops, has assessed the results obtained from different points of view, recognized some shortcomings in the literature, and gave ideas for future research. The following results are the result of the careful analysis of the generated data maps that led to answering the research questions listed in Table 1.

(RQ1) As seen in Section 4.1 the total number of researches relative to non-invasively estimating anemia seems to remain approximately stable over the years. Section 4.1 also highlights a trend that varies from area to area, and seems to be increasing in the most populated countries and fast-growing economies, where anemia is a particularly felt problem or cost-saving objectives are particularly pursued.

(RQ2) Figure 5 shows that most studies refer to health facilities while a good part refers to device manufacturers and Health Insurance Companies/National Health System, with very few studies addressing doctors, caregivers, and citizens.

(RQ3) The great majority of the papers investigate different regions of interest and different types of non-invasive devices. As seen in Figure 14, the most discussed device is the co-oximeter and the finger as ROI; camera devices follow and are used to examine different ROIs, but the conjunctiva seems to be the most promising one among the others.

(RQ4) As already told in Section 4.5 there is a predominance of papers that propose a solution, followed by a good number of empirical evaluations and validations, suggesting that the majority of the researchers try to find and evaluate new solutions and technologies to further improve the anemia assessment by making it faster and simpler.

(RQ5) The literature demonstrates its effectiveness through empirical evidence, therefore most of the papers were categorized as "empirical" (see Figure 8). The overall empiricism exhibits a deep analysis of explored arguments. Few publications express an opinion or review existing technologies.

(RQ6) Different kinds of devices are proposed as a solution; they are driven by different technologies, thus making them suitable or not to certain situations.

The most common solution is to use light absorption and reflection properties through co-oximeters. These devices can distinguish oxyhemoglobin and deoxyhemoglobin measuring the absorption of light passing through blood, light that is often emitted by a finger clamp that shines it through the fingertip. However, it must be specified that using oxygen saturation of hemoglobin is an indirect way to evaluate hemoglobin itself thus its values can be influenced by external factors that can alter the oxygen availability in the blood or blood circulation such as respiratory failure; also available outside health facilities the device has good accuracy but it can be influenced by some external factors such as skin tone [6].

Another solution discussed by a considerable number of papers is to use a digital camera to take photos or small videos to a body part (conjunctiva, retina, sclera, fingernail) to later analyze it and provide information to the user. The solution is advantageous because it only needs common devices to be used but it has the disadvantage of being a two-step process (take a photo and analyze it); furthermore, taken photos can be largely biased by light conditions, so particular attention has to be played in the acquisition phase [12,13].

An alternative to the camera solutions is smartphone-based, which have the great advantage of local analysis of the taken photo that quickens the diagnosis process. Smartphone-based solutions are designed to be used by anyone and can embed tools that go further to the lone measurement.

Both camera and smartphone solutions have to face the problem of variable light conditions that greatly influence the shots and therefore the diagnosis outcomes. Hence camera adapters that artificially illuminate the ROI have been proposed [14–16].

6. Conclusions

In recent years, a great number of methods have been employed to assess anemia non-invasively. A systematic mapping study that summarizes the existing information on devices and technologies used or still in development to evaluate anemia in a non-invasive way has been presented here. From an initial group of 950 papers, a total of 168 were selected for this mapping study. The chosen papers allowed the authors to discuss the state of the art in the field of Estimating anemia non-invasively and to identify research gaps. The well-defined review protocol applied in this study could allow us and other researchers to efficiently update and extend the systematic mapping study.

The results highlight the need for novel non-invasive devices to estimate anemia that can be accurate in most of the situations without being influenced by external factors and also being portable, cheap and usable by the majority of the people; growing interest is noted in application and software that can satisfy all most of these needs by using and running on simple and cheap devices such as smartphones or commercial cameras.

We hope that the findings of this study will be useful in the development and improvement of the current non-invasive anemia estimation research, and will provide an outline to which tools and devices are used and/or in development and how they are employed.

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Appendix A. Papers Considered for This Study (168)

A1. Reich, C.A.; Glaum, A.; Weimann, J. 24 Hour-Accuracy of Continuous Non-Invasive Hemoglobin Measurement By Pulse Co-Oximetry (SPHB) In ICU Patients With Different Inflammatory States. In Proceedings of The Intensive Care Medicine; Springer 233 Spring St, New York, NY, USS, 2014; Volume 40, pp. S281–S282.

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Appendix B. The Systematic Mapping Study

Systematic Mapping Studies are designed to provide a wide overview of a research area, to establish if research evidence exists on a topic and provide an indication of the quantity of the evidence. The results of a mapping study can identify areas suitable for conducting Systematic Literature Reviews and also areas where a primary study is more appropriate. They have broad and multiple research questions driving them.

Unlike the reviews, in the SMS the search terms are less highly focused and are likely to return a very large number of studies. This is a value than with large numbers of results during the search phase of the systematic review as the aim here is for broad coverage rather than narrow focus.

As a matter of fact, one of the main aims of this study is to classify papers with sufficient detail to answer the broad research questions and identify papers for later reviews without being a time consuming task.

The analysis stage of a mapping study is about summarizing the data to answer the research questions posed. It is unlikely to include in depth analysis techniques such as meta-analysis and narrative synthesis, but totals and summaries. Graphical representations of study distributions by classification type is an effective reporting method.

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