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A Systematic Review of Noninvasive Blood Glucose Estimation Using Near Infrared

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Abstract: Diabetes is a chronic and lifelong disease, one of the ten highest causes of death in the world. Diabetes management can only be done by carrying out continuous monitoring. Noninvasive blood glucose measuring devices are needed to overcome the weaknesses of invasive methods, but their accuracy still needs to be improved. This review aims to identify factors that influence the accuracy of estimating blood glucose levels using noninvasive methods based on NIR signals and to observe the development of this technology over the last five years. We performed a systematic review based on articles focusing on noninvasive blood glucose level estimation using near-infrared. This systematic review used the PRISMA 2020 guidelines. Primary studies were retrieved from the literature search engine Scopus database, including journals and proceedings: IEEE, Science Direct, Springer Link, MDPI, Word Scientific, and others. This review provides an overview of using NIR and PPG signals, primary and advanced signal processing, conventional and machine learning approaches, and trends. A total of 62 studies were included. Thirty studies used the conventional approach, and thirty-two studies used machine learning. Thirty-eight studies use primary signal processing, and twenty-four studies use advanced signal processing. Forty studies use NIR signals, and twenty-two studies use PPG signals. India, China, and Indonesia are the top 3 countries in publications on this topic. Using advanced signal processing and feature extraction on photoplethysmography signals and machine learning as an estimation method is quite promising for increasing accuracy. The best machine learning method can be analyzed using meta-analysis.

Keywords: *Blood Glucose, Machine Learning, Near Infrared, Noninvasive,*

1. Introduction

The International Diabetes Federation (IDF) states that diabetes is one of the top 10 causes of death in adults. In 2017, it was estimated to cause 4 million deaths, with health expenditure reaching USD 727 billion globally[1]. The prevalence of diabetes will continue to increase globally every year[1][2][3]. In 2019, Indonesia was ranked 7th as the country with the highest number of people living with diabetes, namely 10.7 million people. Indonesia's diabetes population is estimated to increase to 13.7 million in 2030 and 16.6 million in 2045[3]. Indonesia is the only country in Southeast Asia on the list. So, we can estimate Indonesia's contribution to the prevalence of diabetes cases in Southeast Asia.

Diabetes is a chronic disease[4][5][6] which is a metabolic disorder[7][8] characterized by fluctuations in blood glucose levels[8]. Diabetes is a lifelong disease[9]. Uncontrolled hyperglycemia (high blood glucose levels) can cause severe damage to the heart, blood vessels, nerves, eyes, and kidneys [7][8][10][11][12]. On the other hand, hypoglycemia (low blood glucose levels) can cause seizures, coma, arrhythmia, and heart failure [8]. Therefore, managing blood glucose levels is very important to prevent further complications, and diabetes management can only be done by carrying out continuous monitoring[8][9][10][13][14][15][16]. The current blood glucose measurement tools are invasive or minimally invasive, such as performing a prick and taking a blood sample from inside the body. Repeated treatment with this method can cause pain, discomfort, and expensive costs [10][11][12][13]. The most common invasive approach to measuring blood glucose relies on electrochemical methods. These methods utilize disposable test strips, where a small sample drop is placed for analysis. Colorimetric and amperometric techniques are the two most established and widely employed in the electrochemical realm[17]. Unacceptable levels of risk accompany procedures for blood drawing. Blood drawing can result in physical and psychological trauma to the patient. Human blood is a potent vector for various viruses, bacteria, and diseases [18]. For patients with glycemic disorders, the cost of blood glucose measurements may amount to a fourth of their total healthcare expenditures. The most significant expenditure of most patients is on glucose strips, which account for 85% of the biosensor market worldwide [18].

Noninvasive methods are needed to measure blood glucose levels in the human body to overcome the weaknesses of invasive methods [16]. Seeking to replace the painful finger prick method for diabetics, researchers embarked on a two-decade-long study beginning in 1980. Evaluating various body fluids, including tears, saliva, and earlobe, a team at Purdue University ultimately established the superior accuracy of blood-based glucose measurement systems compared to these alternative approaches [7]. Many research groups have found methods for measuring blood glucose noninvasively but have yet to find reliable and accurate methods [11][13][19] [20][21], and this still needs to be improved [11].

Several reviews about noninvasive blood glucose have been conducted, including a review [22] focusing on Near InfraRed (NIR) technology, NIR-Photoplethysmography (PPG) on blood glucose prediction, a review [23] about the development of blood glucose monitoring with minimally invasive and noninvasive techniques, available devices on the market, and the sensors used, reviews [24] and [25] discuss the use of PPG signals and artificial intelligence in estimating blood glucose levels. Meanwhile, this review discusses the noninvasive estimation of blood glucose levels using infrared signals, focusing on research developments and methods to improve the estimation accuracy. Apart from that, this review uses the Systematic Literature Review method, which differs from previous reviews. Review [26] has systematically reviewed but focused on diabetes detection using photoplethysmography and electrocardiographic signals. This review aims to identify factors that influence the accuracy of estimating blood glucose levels using noninvasive methods based on NIR signals and machine learning and to observe the development of this technology over the last five years. Research questions were formulated using the PICOC framework (Population, Intervention, Comparison, Outcome, Context). The population is all related to noninvasive methods used to estimate blood glucose levels using infrared signals and applied to humans regardless of age and diabetes. The intervention was conducted by observing the applied advanced signal processing techniques and machine learning methods. The comparison is against a system with primary signal processing and a conventional method (without machine learning). The outcome of this research is the accuracy of the methods observed in estimating blood glucose levels noninvasively based on infrared signals. The context used in this research is publications in the subject areas of engineering and computer science. Therefore, the research questions were formulated as follows:

RQ1: What is the trend in the use of near-infrared signals in noninvasive estimation of blood glucose levels

RQ2: What factors influence the accuracy of estimating blood glucose levels using infrared signals

RQ3. Can noninvasive methods of estimating blood glucose levels diagnose and monitor diabetes as accurately as invasive methods?

RQ4: What challenges and opportunities exist in developing a noninvasive method for estimating blood glucose levels using infrared signals and machine learning?

2. Method

A literature review regarding the noninvasive estimation of blood glucose levels using infrared signals was carried out in a systematic and structured manner. A systematic literature review (systematic review) is a systematic, comprehensive, and objective scientific research method for identifying, evaluating, and interpreting all research relevant to a particular topic, research question, or phenomenon of interest[27]. Many research fields have carried out reviews using the SLR method, such as computer networks[28], education[28], the medical field[30], and many others. A thorough search for relevant information was carried out using a digital database. This systematic review used the PRISMA (the Preferred Reporting Items for Systematic Reviews and Meta-Analyses) method. The guidelines used in conducting a systematic review refer to the PRISMA 2020 guidelines [27][[29]. The flowchart for the selection process, including identification, screening, and inclusion, can be seen in Figure 1.

2.1. Eligibility Criteria

The inclusion criteria were (1) a discussion of diabetes detection and noninvasive blood glucose estimation using near-infrared signals, (2) the research subject is humans, regardless of age and diabetes, (3) written in English, (4) articles in the Scopus database from 2018 to 18 September 2023, (5) The subject area of engineering and computer science, (6) Only articles in Journals or Proceedings. Primary studies will be excluded because of (1) irrelevant Topics: focus discussion about sensor design, the absorptivity of glucose, using Middle Infrared, review articles, and the subject of research on animals, (2) abstract only, and (3) insufficient data.

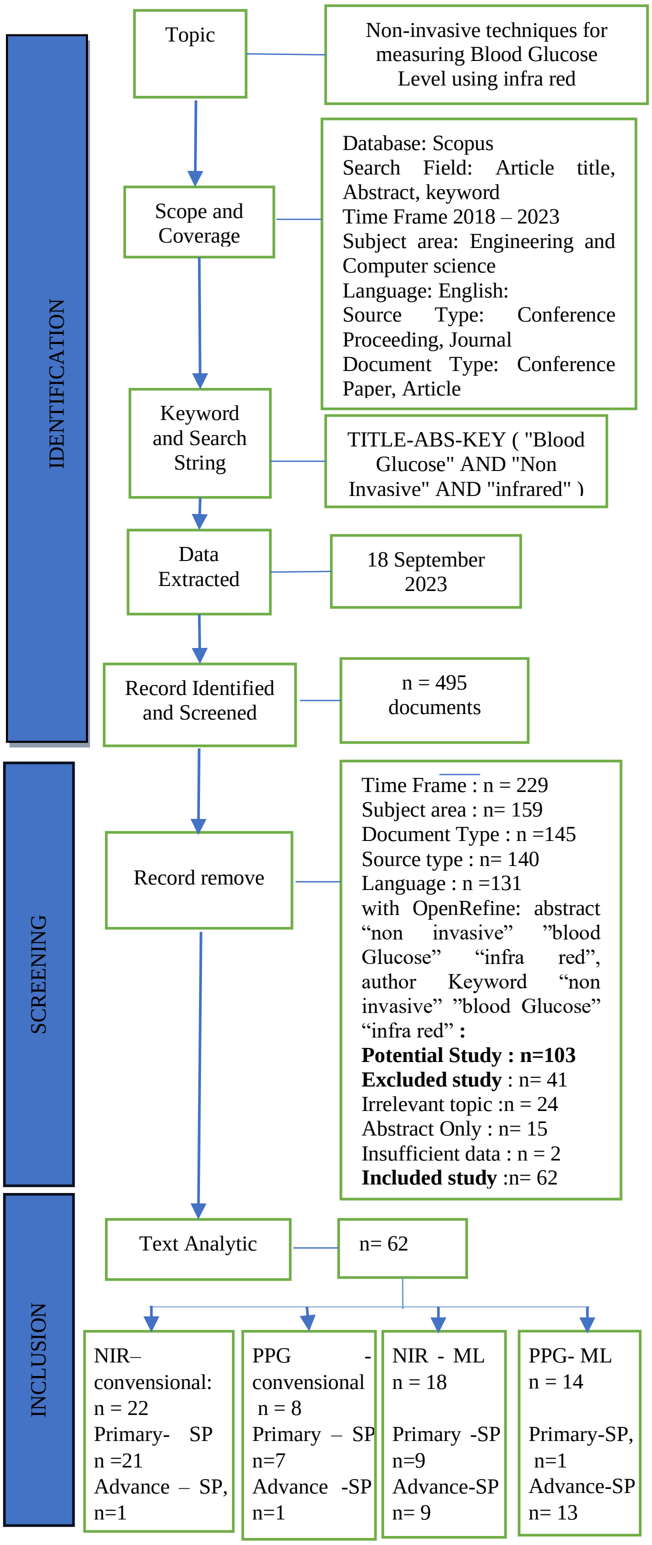


Figure 1. The PRISMA flow diagram

2.2. Data Sources and Search Strategy

Reference articles retrieved from the literature search engine Scopus database, including journals and proceedings, namely IEEE, Science Direct, Springer Link, MDPI, Word Scientific, and others. A search strategy using the keywords "Blood Glucose," "Non Invasive," and "infrared" found 495 documents. Using limitation by year from 2018 to 2023, the search found 229 documents. Subject area restrictions: "Engineering" and "Computer Science" found 159 documents. Document type limitation "Conference Paper and Article" found 145 records. Source type restriction: "Conference Proceedings and Journal" found 140 papers. Limiting the search to English-only articles, it found 131 documents. Therefore, by using the keyword "TITLE-ABS-KEY ("Blood Glucose" AND "Non Invasive" AND "infrared") AND PUBYEAR > 2017 AND PUBYEAR < 2024 AND (LIMIT-TO (SUBJAREA , "ENGI") OR LIMIT-TO (SUBJAREA , "COMP")) AND (LIMIT-TO (DOCTYPE , "cp") OR LIMIT-TO (DOCTYPE , "ar")) AND (LIMIT-TO (SRCTYPE , "p") OR LIMIT-TO (SRCTYPE , "j")) AND (LIMIT-TO (LANGUAGE , "English"))", the search identified 131 articles. Next, the document abstracts were re-selected using the keywords "blood glucose","noninvasive," and "infrared" using OpenRefine software. The search found 103 documents. The 103 identified documents will be read as full text to check whether they meet the inclusion criteria or have exclusion criteria.

2.3. Selection Process

The steps are: 1. Identify the topic and look for related articles; 2. screen the articles to identify essential articles; 3. Select documents to be analyzed. Figure 1 illustrates the stages in a systematic review using the PRISMA method to estimate blood glucose levels noninvasively based on NIR-PPG signals and machine learning.

2.4. Data Extraction

For all included articles, we extract the following information: (1) Type of infrared signal, (2) Data set, (3) Signal processing technique, (4) approach used, (5) output produced. We will discuss the data extraction to determine what factors influence the accuracy.

3. Result and Discussion

3.1. Trends

3.1.1. Publication Trends

The number of potential studies was 103. Forty-one primary studies were excluded. Twenty-four primary studies were excluded because of the irrelevant topic. Fifteen primary studies were excluded because they were not available in full text or abstract only, and two primary studies were excluded due to insufficient data. There were 62 included. Primary studies: 29 primary studies are journal articles, and 33 primary studies are proceeding articles. Figure 2 shows the development of publications about noninvasive blood glucose using infrared signals in the last five years based on these 62 primary studies. Based on 62 primary studies, it was found that IEEE is the publisher that publishes the most articles on this topic, followed by World Scientific, Elsevier, MDPI

(Multidisciplinary Digital Publishing Institute), Springer, and others.

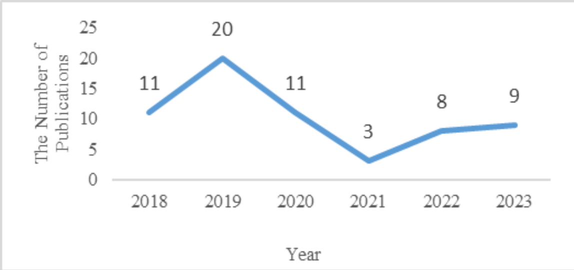


Figure 2 Distribution of publication by years

Based on Figure 2, There was an increase in publications in 2019 and a decrease until 2021. The decline can be influenced by the COVID-19 pandemic throughout the world. Officially, the COVID-19 pandemic began on January 30, 2020, when the World Health Organization (WHO) declared COVID-19 a global pandemic. The effects of the COVID-19 pandemic have negatively influenced the number of publications due to a decrease in research budgets, changes in research priorities, and difficulties in researching because it uses human subjects who must comply with social policies and health protocols. The government and private sector allocate funds quickly for research areas closely related to the COVID-19 emergency. However, research in many areas unrelated to the pandemic has been displaced [29][30]. The COVID-19 publications have suddenly surged, but the non-COVID-19 publications have decreased [29] [30]. After 2021, publications on this topic began to increase. On September 18, 2023, there were nine publications, which will continue to increase. The distribution publication based on the country can be seen in Figure 3.

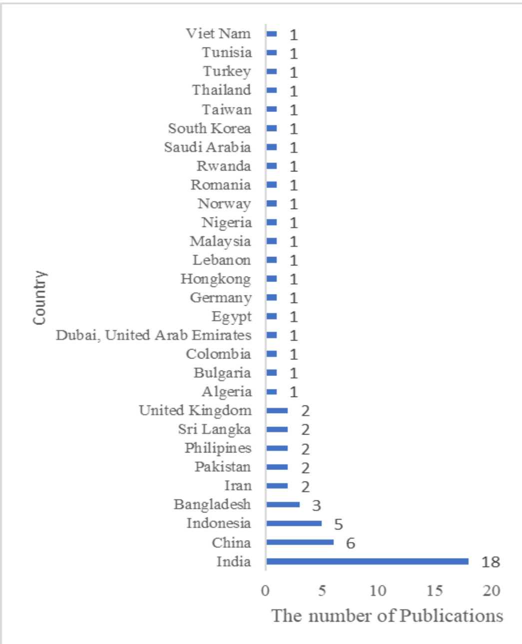


Figure 3. Distribution of the number of publications by country

International Diabetes Federation data shows that China had the most diabetes sufferers in 2019, 116.4 million; in 2030, it is predicted to be 140.5 million, and in 2045, it is predicted to be 147.2 million. Meanwhile, in 2019, India was ranked 2nd with a number of sufferers of 77 million. In 2030, India is predicted to be 101 million and become 134.2 million in 2045. Based on data from the 8th edition of the IDF Atlas, China and India have the highest population of adults with diabetes and total healthcare expenditure for diabetes [1]. Indonesia is ranked sixth, Germany is ranked ninth, and Pakistan is ranked tenth [1]. So, we can estimate the background of many studies on noninvasive blood glucose measurements that are easy, cheap, and accurate, carried out by many countries, especially China, India, and Indonesia.

3.1.2. Research Topic Trends

In this systematic review article, publications about estimating blood glucose levels using noninvasive methods are grouped into four parts: Near Infrared (NIR) with a conventional approach (NIR-Conventional), PPG signals with a conventional approach (PPG-Conventional), NIR signals with Machine Learning (NIR-ML), and PPG signals with machine learning (PPG-ML). We found 22 NIR-Conventional, 8 PPG-Conventional, 19 NIR-ML, and 13 PPG-ML primary studies. The distribution of the number of publications by year in the four categories can be seen in Figure 4. Meanwhile, a graph of the development of Near Infrared (NIR) signals, PPG signals, and the application of machine learning methods in estimating blood glucose levels noninvasively can be seen in Figure 5.

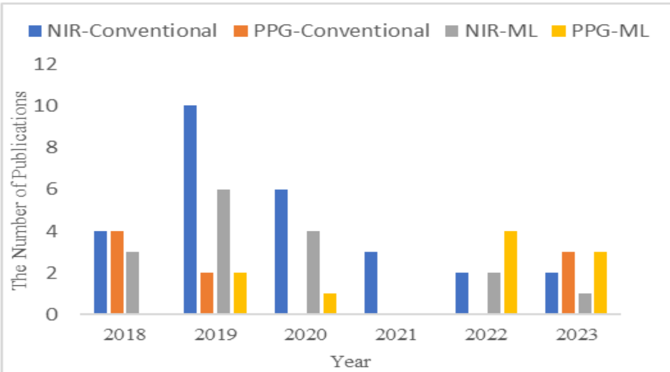
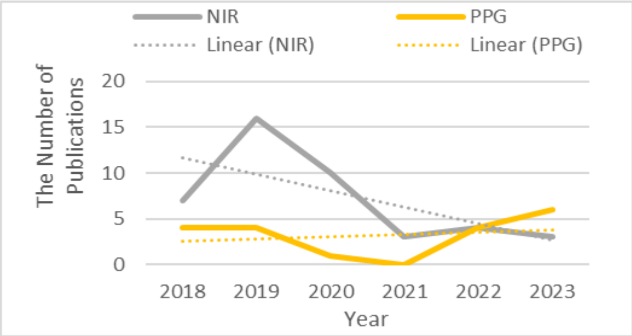
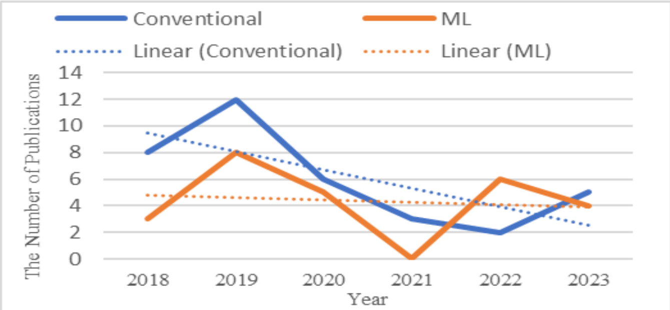


Figure 4. Distribution of the number of publications in the grouped categories



(a) Use of NIR and PPG



(b) Use of machine Lealning

Figure 5. Trends in the use of NIR signals, PPG signals, and machine learning methods

Figure 4 shows that in 2022, NIR signals with a conventional approach are used more than NIR signals with machine learning. Figure 5.a shows that NIR signals have a more significant quantity than PPG signals until 2021. Starting in 2021, the use of PPG signals tends to increase, while the use of NIR signals tends to decrease. Beginning in 2022, PPG will be more widely used than NIR. Figure 5.b shows the trend of publications using machine learning and conventional approaches. The use of conventional approaches tends to decline drastically. The use of machine learning in the noninvasive estimation of blood glucose is predicted to be greater than that of conventional approaches in the future. This means that using machine learning to estimate blood glucose noninvasively is an exciting topic that is starting to be widely researched. The use of PPG signals and machine learning in noninvasive blood glucose estimation has increased. Using VosViewer software, the development of research on noninvasive estimation of blood glucose levels using infrared signals based on the keyword (co-occurrence) can be visualized in Figure 6. Overall, It shows that PPG signals and machine learning are exciting and have the potential to be researched further.

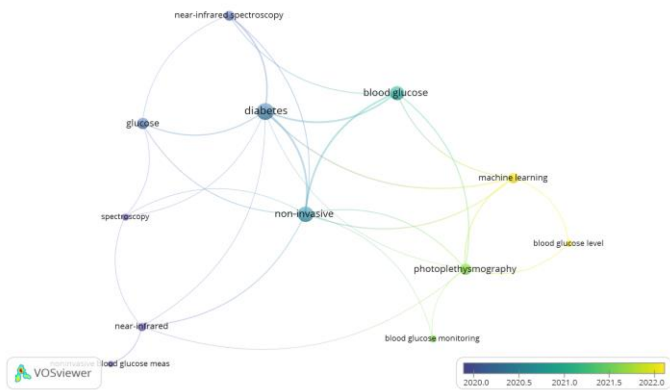


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Figure 6. Overlay visualization based on the keyword (Co-Occurance)

A. Method

In this review, the methods section discusses the use of signal processing techniques on the output of photodiode sensors and the approach used to estimate blood glucose non-invasively. The outcome of concern is the accuracy of blood glucose estimation. Signal processing techniques are divided into two categories, namely primary and advanced signal processing. In the primary signal processing category, we include filtering using low pass, high pass, and amplification, which aims to reduce noise and improve the quality of the photodiode signal. In the advanced signal processing category, we include systems that use signal processing techniques to perform feature extraction on near-infrared or PPG signals. The approaches for estimating blood glucose levels are divided into conventional and machine learning. We include statistical analysis, mathematical modeling, and simple linear regression in the conventional category.

A.1 Blood glucose estimation using near-infrared

Skin tissue consists of three layers, and only the dermis layer has information about blood glucose[9][16]. Infrared wavelengths (780 to 2500nm) can penetrate the dermis layer, avoiding invasive procedures[9]. Electromagnetic waves that enter the body will experience absorption, scattering, and weakening of their power[8][19]. The light entering the glucose concentration will be refracted according to the amount of glucose in the medium[30]. An appropriate wavelength is essential for optical methods[8]. Research [31] focused on optimizing wavelength selection for serum glucose analysis to improve prediction accuracy.

Glucose has light absorption points at wavelengths of 940 nm, 970 nm, 1197 nm, and 1408nm [19][32] and1536 nm, 1688 nm, 1925 nm, 2100 nm, 2261 nm and 2326 nm[32]. Recent research has shown that the most informative region for blood glucose concentration prediction is the 940-1500 nm region[7]. Glucose molecules show peak absorption at 940 nm[4] or 939 nm[8][21]. At a wavelength of 937 nm, attenuation of optical signals by other components, such as water, platelets, and lymphocytes, is minimal [8][31][32]. More than 50% of human blood is water, so the absorption of light by water becomes a complication in signal analysis. This weakness can be overcome by choosing a near-infrared wavelength of 940 nm[33]. Therefore, the desired penetration depth can be achieved at this wavelength [8], and actual blood glucose concentration can be determined [32]. Glucose concentration can be estimated by variations in light intensity transmitted or reflected through glucose-containing tissue[8][33].

The Near Infrared Spectroscopy (NIRS) technique is favorable and globally explored for monitoring and measuring blood glucose levels noninvasively [8][33][34][35]. It is a low-cost technology with greater sensitivity [36]. NIRS is a promising technique for noninvasive glucose measurement due to its low absorption and high penetration of near-infrared light into the skin [21]. The disadvantage of this technique is that it is affected by humidity, environmental factors such as temperature changes, and physical parameters such as pressure and chemicals [36]. When light NIR shines on the skin, some light is absorbed and scattered [11]. Glucose measurements can be influenced by the intervention of physiological parameters such as variations in body temperature, chemical parameters, triglyceride, and albumin levels, and the intervention of environmental variations such as changes in temperature, humidity, carbon dioxide, and atmospheric pressure [8], which is a weakness of NIR Spectroscopy [8][36]. However, due to the weak target signal and low signal-to-noise ratio, the accuracy of noninvasive detection has yet to reach the standard of clinical application. Therefore, basic research needs to be carried out deeply [30].

Photoplethysmography (PPG) is a technology that has become popular in the last decade for monitoring the physiological condition of patients [37][38]. PPG is a noninvasive method that can provide information about the cardiovascular and respiratory systems. In addition, PPG is widely applied in portable devices and pulse oximeters because of its convenience and ability to take continuous readings, and it does not require complicated devices.[38][25]. PPG is a noninvasive optical technique that measures changes in blood volume based on variations in light intensity passing through or reflected by human organs [2][5]. PPG signals can be used to estimate blood glucose levels. This method is still very popular because it is easy to use, inexpensive, and noninvasive. During routine PPG measurements, errors can occur due to physical differences in the subjects, resulting in insufficient PPG to extract components from the blood [14]. The absorption value of skin, muscle, bone, and fat should be liminated. They have permanent absorption values and must be excluded from the blood absorption values during measurement and eliminated or minimized from the PPG signal [14]. In addition, the PPG signal obtained is usually contaminated with baseline drifts or additional noise due to motion artifacts and environmental noise [15][34]. It reduces the quality of the PPG signal, thereby affecting the extracted features and ultimately resulting in poor accuracy in estimated blood glucose values[34]. Therefore, PPG signal processing is essential[15][34] to reduce noise and other unwanted signals and increase signal quality and features to make estimates more accurate. By maintaining the quality of the PPG signal from the beginning, optimal accuracy values in machine learning can be achieved[2]. This review found eight primary studies using PPG with a conventional approach and fourteen primary studies using PPG with machine learning to estimate blood glucose levels. This review groups signal processing techniques into primary and advanced. We found that thirty-eight primary studies used primary signal processing, and twenty-four primary studies used advanced signal processing. Twenty-eight primary studies used primary signal processing with the conventional approach to estimate blood glucose levels, as seen in Table 1. Based on Table 1, The NIR and PPG signals used also have a variety of wavelengths, but the one widely used uses a wavelength of 940 nm (19 out of 28 primary studies). Data sets used in the research include glucose solution [4][8][47][48], human subjects on fingers [33][39][40], and human subjects on ears.

A.2. Estimation Of Blood Glucose Level Using Primary Signal Processing and Conventional Approach

Research that estimates blood glucose using primary signal processing generally uses electronic circuits to conduct filtering, amplification, and analog-to-digital conversion (ADC). In general, primary signal processing is almost the same as pre-processing a signal to reduce noise, remove unwanted signals, and increase the SNR of the signal. Primary studies that use primary signal processing with conventional approaches can be seen in Table 1. The filters used include HPF to remove low-frequency noise, as in research [8][9][39], LPF to remove high-frequency noise, as in research [4][9][16][32][39][41][42] and a combination of both. Research [32] combines a normal LP-RC Filter and a twin t-notch filter to reduce all unwanted signals from the sensing module and the environment. Nevertheless, research [11][29] uses raw signals from analog to digital conversion without filters and amplifiers and then models them mathematically. Research [4] also used HPF with Fc 0.5 Hz, followed by a second-order Butterworth low pass filter with fc 180 hz and a notch filter with a frequency of 50 Hz to reduce all unwanted signals. Notch filters are typically used to eliminate noise added to the original signal due to motion artifacts and slight finger movements [32][36]. Almost all studies amplify the signal to obtain the actual visible output [36] and make the signal compatible with noise filters and microcontrollers [41].

Table 1. Primary studies using primary signal processing and the conventional method

Author	*Input Signal*	*Data Set*	*Signal Processing*	*Approach*	*Outcome*
Aswathy S.A 2018 [11]	NIR at 650 nm	5 Subjects	ADC	Mathematical Model	Error varies from 4 - 11 mg/dl
Venkataramanan S.2018[35]	NIR-PPG at 940 nm	22 Patients	HPF, LPF, Amplifier, ADC	Linear Regression	Mean Error = 0.8585
Lakshmi. 2018[30]	RL at 650 nm	5 Samples	ADC	Mathematical Model	Accuracy varies around 85 % -90 %
Javid B. 2018[8]	NIR at 940, 1550, and 1650 nm	in vitro: 22 glucose solution in vivo: 24	Filtering, Amplification, and Signal Isolation, ADC	Linear Regression	Average Percentage Error: 8.27, RMSE: 18.52 mg/dL,

Table 1 (cont). Primary studies using primary signal processing and the conventional method

Author	*Input Signal*	*Data Set*	*Signal Processing*	*Approach*	*Outcome*
Gayathri B. 2018[9]	PPG	24 Subjects	HPF, LPF, Amplifier, ADC	Linear Regression And Polynomial	An error of ±12 mg/dL An error of ±7 mg/dL.
Sen P.K. 2019 [12]	NIR at 940 nm, 660 nm	50 patients.		Statistical Regression Analysis	P-Value: 1,4E-27
Bagais K. 2019[36]	NIR at 730-2500 nm	The glucose solution.	Preamplifier, Filter Noise, ADC	Mathematical Modeling	not mentioned
Deepthi S. 2019[37]	NIR at 940nm	15 Subjects	ADC	Linear Regression	Accuracy 88.18 %
Sarkar K. 2019[16]	PPG signal at 940 nm	27 Subjects	Active LPF, amplifier ADC	Regression Analysis	R^2 is 0.9873, and the average percentage error is 3.4765%.
Sithara S.K.T 2019[33]	NIR at 940 nm	Two sets of data	ADC, Amplifier, LPF, and a twin t-notch filter.	A Simple Linear Regression Analysis	R = 0,61
Marius I. 2019[17]	NIR at 600 nm – 900 nm	8-10 scan at ear	Glucose solution: 200,400,600,800 mgdl	A Polynomial Mathematical Function	Not mentioned
Asekar M.S. 2019[4]	NIR-PPG	Glucose Solution	Butterworth LPF, Notch Filter, Amplifier	Linear Regression	Percentage Error from (1%-7%)
Olakanmi O. 2019[38]	NIR at 1,450 nm and 1,550 nm	15 Patients	Noise Filter, ADC	Linear Regression	CEG : 62 % region A, 23 % region B, 15% region C

A.rocha Jr N. 2020[39]	NIR at 940nm, 1450nm, 688nm	15 Subjects	Filter, Amplifier, ADC	Statistical Analysis: Mhc And Multivariate Analysis	for 15 samples 100% region A,
Javier R.I.R. 2020[15]	NIR	70 Testing	Not Mentioned	Statistical Analysis	97% of the tests passed the standard, and 3% failed.
Mamilov 2020[40]	NIR at 660 nm, 850nm, 940nm	Four subjects: 84 test points	Filter, Amplifier, Multiplexer, ADC	Statistical Analysis	CEG: 74% in zone A, 26 % in zone B
Kassem A. 2020[41]	NIR at 850 nm	Not Mentioned	Filter, Amplifier, ADC	Linear Regression	errors ranging from 10% to 20 %;
Al-Dhaheri M.A 2020[42]	NIR-PPG 940 nm	10 Subjects	Butterworth Filter, Amplifier	Linear Regression	RMSE 10.44 mg/dl (R^2) 0,839
Piyapan S. 2020[43]	NIR-PPG 940 nm	40 Subjects	Filter, Amplifier	Linear Regression	accuracy 95.13 %
Taghizadeh-Behbahani R. 2021[44]	NIR at 950 nm.	Glucose concentration and participant	Amplifier and LPF	Linear Model	Measurement error does not exceed 25%
Hepriyadi S.U.,2021[45]	NIR at 900 - 1300 nm	Glucose solution	Amplifier, Filter, ADC	Linear Model	R^2= 0.98
Sathishkumar S.2022 [46]	NIR at 660 nm and 880 nm	20 Subjects	RC LPF, Amplifier	Mathematical Modeling	Accuracy:88.0494%
Khan T.R. 2023[47]	NIR at 940 nm	10 participants: 40 data	Filter, Amplifier, ADC Notch Filter 50 hz	Linear Regression	Accuracy: Diffused Transmittance: 93.04 % Diffused Reflectance: 89.83%
Nanayakkara N.D.2018 [19]	NIR 940 nm	20 Measurements	LPF and Hamming digital low pass FIR filter	Least Squares Linear Regression Model.	CEG : Region A : 73.3% Region B: 26.7%

Table 1 (cont). Primary studies using primary signal processing and the conventional method

Author	***Input Signal***	***Data Set***	***Signal Processing***	***Approach***	***Outcome***
Acharya K.N 2019[48]	NIR	33 subjects	Filter, Amplifier, ADC	Parametric Bayesian Regression (BR) non-parametric Gaussian Process Regression (GPR)	BR-RMSE: 3.7mg/dL GPR-RMSE: 3.28mg/dL
Naresh M. 2023 [49]	NIR at 950 nm	184 samples	ADC, amplification,	Polynomial Expression	MARD: 1.61 %, MAD: 3.02 mg/dl, RMSE: 4.81 mg/dl
Diana Selsiya.	NIR at 940	25 data	filter, amplifier,	a 2nd order	percentage errors: +7% to -

2023[50]	nm	points	ADC	polynomial regression	7%
Godfrey K 2023 [51]	NIR-PPG at 940 nm	100 volunteers: 15 for testing	filter, amplifier, ADC	the Pearson correlation coefficient	error varies from -14 mg/dl to +48 mg/dl

Table 1 shows 28 primary studies that used primary signal processing and conventional approaches. Twenty primary studies use a linear regression approach, four primary studies use statistical analysis, and four primary studies use mathematical models. The mathematical model approach in research [11][29][41] creates a mathematical relationship between the ADC value and the blood glucose value (mg/dl) of the invasive tool to estimate noninvasive blood glucose values. Research [49] makes a mathematical relationship between the NIR intensity variation values obtained using The Beer-Lambert Law to obtain noninvasive blood glucose estimation values. The accuracy for the mathematical model approach varies around 85 – 90%, but the number of testing samples was very small.

Research [12],[15][39][40] uses statistical analysis to estimate blood glucose levels. Research [12] studies the variance between observed data sets using the ANOVA test. The ANOVA model helps test the variability of a data set using statistical tests between sample distributions [12]. Research [40] conducted a study for BGL measurements using near-infrared spectroscopy and metabolic heat conformation studies using multivariate analysis. Research [40]compared changes in transmittance data on NIR signals with wavelengths of 850 nm and 940 nm with commercial glucometer readings so that they could calculate calibration coefficients to translate transmittance values into absorption intensity due to blood glucose to calculate blood glucose level values used the corresponding ratio. Research [9][17] [49][50] uses simple polynomial regression. The independent variable in research [9] is the PPG signal voltage, and in research [17], it is channel length. 13 Other research using a linear regression approach uses a single variable independent, namely NIR or PPG signal voltage, to predict the blood glucose values.

A.3 Estimation Of Blood Glucose Level Using Primary Signal Processing And Machine Learning Approach

Table 2 shows ten primary studies that estimated blood glucose levels noninvasively using NIR or PPG using primary signal processing and machine learning approaches. 9 out of 10 primary studies use NIR signals. The Primary studies [7] [21] and [52] use ANN. Primary study [21] used the Levenberg–Marquardt (LM) based Artificial Neural Network (ANN) to predict the blood glucose level from the voltage signal of photodiodes. LM combines the steepest descent and the Gauss-Newton method. The proposed method in research [7] is a Feed-Forward Backpropagation Neural Network, and weights and bias values are updated according to the Levenberg-Marquardt optimization. This Study compares the proposed method with Linear PLS and poly PLS. Based on the correlation coefficient between actual and predicted blood glucose values, the proposed method is better than linear PLS and poly-PLS. Primary Study [60] used PLS, and primary Study [57] used MPR. PLS is a development of the MPR model. PLS is a robust machine learning algorithm widely used in spectral and chemical engineering, where measuring data requires regression and modeling [7]. Primary studies [5] and [55] use deep learning. Primary study 57 proposed two methods, DNN and MPR3, with two types of samples: serum and capillary. This research found that the DNN method performed better than MPR3 for both serum and capillary samples. Meanwhile, testing on serum samples is more accurate than capillary.

Table 2. Primary studies using primary signal processing and machine learning methods

Author	***Input signal***	***Data set***	***Signal processing***	***Method***	***Outcome***
Yadav J. 2018[21]	NIR at 940 nm	Two data sets: 84 and 52 data patterns	BPF fc 0.5 - 10 Hz amplification	LM-based ANN	CEG : 83.33% Region A : 16,67%
Pathirage K.D.2019	NIR multi wavelengths 660, 940,	A total of 395 data samples were collected from a	The trans-impedance amplifier, a	Multivariate Linear Regression,	MARD: 13,6, accuracy: 86,4 %

Author	*Input signal*	*Data set*	*Signal processing*	*Method*	*Outcome*
[53]	1050, and 1550 nm	group of 125 subjects	passive LPF	Random Forest regression Gradient Boosting regression	MARD: 9,3. Accuracy 90,7 % MARD: 13,1; accuracy: 86,9 ~~%~~
Ghozzi D. 2019[7]	NIR at 950 nm	300 Human serums	Differential amplifier, LPF, ADC	The ANN regression model	RMSE: 0.0784; R=0.99 CEG: 97.33% in Region A
Hossain S. 2019[5]	NIR at 900 – 1700 nm	30 Subjects	Filtering, Eliminating corrupted signals	CNN	R:0,95
Cheng J 2019 [54]	NIR at 1550 nm	14 Subjects with 205 sample	Filter, Amplifier, ADC	7Vs BPN 4VsBPN SA - NARX model	RMSE:1.05 mmol/l; Corr :0.66; 80% region A, 20% region B RMSE: 0.97 mmol/l; Corr: 0.7; 83.41 % region A, 16.59 % region B RMSE:0.72 mmol/l; Corr : 0.85; 90.27 region A, 9.73 region B

Table 2 (cont). Primary studies using primary signal processing and machine learning methods

Author	*Input signal*	*Data set*	*Signal processing*	*Method*	*Outcome*
Joshi A.M 2019 [55]	NIR at 940 nm and 1300 nm	Capillary glucose:113 samples serum glucose: 74 samples	Acquisition circuit, ADC	Deep Neural Network (DNN), Multiple Polynomial Regression (MPR)	RMSE: 13.57 mg/dl 100 % Region A
Dinh D.T.-M. 2019 [52]	NIR at 980 nm	D-glucose samples	Filter, amplifier	ANN	Not mentioned
Alfandi O 2022.[56]	NIR	Multivariate Time-Series data set	Filter, Amplifier	Linear Regression and Decision Tree algorithm	Absolut diference varies 0 - 32 mg/dl
Ibrahim H 2022 [57]	NIR at 950 nm	Not mentioned	Filter, Amplifier, ADC	Regresi Kuadrat Terkecil Parsial (Pls)	Not mentioned
Hina A. 2022[22]	PPG	200 subjects,	TIA- a switched integrator-based LPF	Ensembled Boosted Trees	Not mentioned

A.4 Estimation Of Blood Glucose Level Using Advanced Signal Processing And Feature Extraction

Table 3 shows 24 primary studies that used advanced signal processing and feature extraction to estimate blood glucose noninvasively using NIR or PPG. The advanced signal processing category is signal processing that carries out preprocessing stages using filters, amplifiers, ADC, or digital signal processing methods to reduce noise and improve signal quality, then continues with feature extraction. Two primary studies that use advanced signal processing use statistical analysis (conventional approach). The primary study [10] used ANOVA and the Pearson Correlation Coefficient to estimate blood glucose, the Standard Normal Variable (SNV) preprocessing method to remove baseline drift, and then dimension reduction using Singular Value Decomposition (SVD). Primary study [75] uses The Pearson Correlation Coefficient to estimate blood glucose, electronic circuit (HPF Fc: 0.7; LPF fc:10 hz, first Op-Amp with gain:100 and second Op-Amp with gain:10) to preprocessing signal and then followed by feature extraction using the peak detection method to find Perfusion Index/PI (peaks and troughs) of PPG signals.

Primary studies [15] and [58] use digital wavelet transform (DWT) to preprocess PPG signals. The primary study [15] used DWT and wavelet decomposition (WD) to remove baseline drift from the collected PPG signal, a simple moving average algorithm for data smoothing to remove some residual noise that may originate from other sources (e.g., body movement), and Local maxima algorithm was used for PPG signal peak detection.

In Table 3, twenty-two primary studies use machine learning approaches. Five primary studies use PLS [30],[15],[64],[67],68]. Nine primary studies use ensemble learning: the random forest method [62][63][70][71][72][77], Ensembled Boosted Trees-SVR [69], The ensemble regression trees model [74], and the Ensemble Bagging Tree [2]. Three primary studies use ANN-based methods [18][65][73]. Five primary studies use supervised machine learning to predict continuous values: SVM [76], FGSVR [66], Exponential Gaussian Process machine learning regression[34], A kernel-based regression algorithm[61], and multiple linear regression analysis[14]. The use of non-linear machine learning provides better estimation results compared to linear machine learning (regression models) [7][68].

Table 3 . Primary studies using advanced signal processing and feature extraction

Author	***Input signal***	***Data set***	***Signal processing***	***Approach conventional/ML***	***Outcome***
Suryakala S.V. 2018[10]	NIR at 780 nm-2500 nm	33 Subject diabetes	SNV and SVD technique	Conventional: Statistical Analysis	P-value<0.05 Pearson Correlation Coefficient = 0.967
Akkaya I. 2018[14]	PPG signals	24 Non-diabetic subject	HPF Notch filter, amplification, LPF filter Saviztky Golay, The Welch Power Spectral Density Estimation Method.	Multiple Linear Re-Regression Analysis	The R2: 0.97. CEG 79.17%: zone A, 20.83%: zone B
Pai P.P. 2018 [59]	NIR at 905 nm and 1550 nm	In vitro on glucose solutions and in vivo on tissues	The Coherent Averaging Module	A Kernel-Based Regression Algorithm	MARD: 8.84% CEG Zone A: 92,86% , Zone B: 7,14%
Zhou X. 2019 [60]	NIR	Training 8 subjects, testing 168 samples	Joint Empirical Mode Decomposition and Singular Spectrum Analysis-Based Pre-Processing Method	Random Forest Regression Model	Average RMSE: 1,.44 mg/dl CEG: 80,35 %di Region A

Table 3 (Cont). Primary studies using advanced signal processing and feature extraction

Author	***Input signal***	***Data set***	***Signal processing***	***Approach conventional/ML***	***Outcome***
Lin Y. 2019 [31]	NIR	A total of 191 serum samples	FT, NDF, EC-PLS	The PLS Regression	the average correlation coefficient (Rp):0.846 SPE: 0.348 mmol/l
Rachim V.P. 2019 [15]	PPG	In vivo with 12 subjects	DWT, WD	The PLS Regression	the average correlation coefficient (Rp):0.86 SPE: 6.16 mg/dl
Jenie R.P. 2019[18]	NIR at 1550–1700 nm	An in vitro trial using 110 participants	FFTW	Fast Artificial Neural Network	RMSE:10.8 mg/dl 93.75% A and 6.25% B
Li Z. 2019[61]	NIR	Two subjects, each subject 23 sample	Emd-Based Hierarchical Multiresolution Analysis	Random Forest Regression Algorithm	CEG: 78,26 % region A, 21.74% region B
Solihin M.I 2019[62]	NIR at 900-1700nm.	45 subjects, with a total of 90 sample	Smoothing, MSC, SNV	Interval PLS (IPLS)	Determination Coefficient(R2) =0,91
Hina A. 2019[58]	PPG	200 Patients (training: 80%, testing: 20%)	DWT: Daubechies wavelet (db4)	Exponential Gaussian Process Machine Learning Regression	mARD of 8.97%. CEG: 97.5% region A, 2,5 % region B
Nampoothiri S.N. 2020 [63]	PPG	172 Patients	Subsampling, Detrending, And Denoising.	ANN	Most data points are in regions A and B, but there are data points in regions C and D.
Hina.A. 2020[64]	PPG	200 Subjects	DPF and MAV filter+ Feature Extraction	FGSVR	R^2 = 0.937, mARD = 7.62%
Heise H.M. 2021[65]	PPG		Spectral Wiener Filter method	PLS	not mentioned
Yu,2021[66]	NIR 900~1700 nm	26 Subject	Pre-processing + feature extraction: SI and GA	PLS ELM Si-GA-ELM-Tradaboost	R: 0.966, RMSEP:0.137
Hina A. 2022[34]	NIR-PPG	200 subjects	Pre-processing + Feature extraction	Ensembled Boosted Trees -SVR	a mean absolute relative difference (MARD) of 5.83%
Ding X.	NIR-PPG		Preprocessed, Feature	Random Forest for	MARD= 0.207;

2022[67]			Extracted, feature smoothed.	Regression Analysis	RMSE =1.3732
Wei Y. 2022[68]	PPG	8 Subjects: 465 data	Denoised using SSA + Feature Extraction	Random Forest	MARD: 12,19 %, CEG: 87,0588 % region A
Huang C. 2022 [69]	NIR-PPG: at 1450 and 1650 nm	232 data:	Statistical Feature Filter and Feature Extraction	Random Forest	MARD:1.769 RMSE:1.3568
Chih-Ta Yen, 2023[70]	PPG at 660 nm and 900 nm+ bioimpedance	40 participants	Principal Component Analyses	Back-Propagation Neural Network (BPNN).	MSE :40.736; RMSE: 6.3824; MAE, :5.0896; MARD: 4.4321, R2: 0.997
Hammour G. 2023[71]	PPG at 880 nm	4 Subjects	Pre-processing + feature extraction	The Ensemble Regression Trees Model	CEG: 82.05% in region A, 17.95 % region B
Argüello-Prada E.J. 2023[72]	PPG at 940 nm	53 volunteers: 19 diabetics	Signal Acquisition: HPF, LPF, Amplifier + Feature Extraction	Conventional: Statistical Analysis	CEG: 91,57 % region A, 9.43 % region B
Susana E. 2023[2]	PPG	80 subjects:400 original PPG	Pre-Processing: Electronic Circuit +Feature Extraction	The Ensemble Bagging Trees	accuracy: 98 %
Pham, 2023[73]	NIR at 445, 590, 730, 760, 810, and 910 nm	65 sample	The ANOVA F-test and Standard Scaler methods	SVM	CEG:92% in Region A, 8% in Region B
Sun Y. 2023[74]	NIR at 1370 nm and 1640 nm + RF	5 healthy volunteers	(Filter, Amplifier, ADC) Feature Extraction	Random Forest	MARD: 7.31% RMSE: 21.06 mg/dl

Tables 1, 2, and 3 show the various variations in the research, such as signal selection (NIR, PPG, and wavelengths used), number of data sets and how the sample testing procedures are carried out, signal processing techniques (electronic circuits, pre-processing, and feature extraction method), estimation methods (conventional, machine learning). The digital signal Proceessing commonly used are Discrete Wavelet Transform (DWT), Wavelet Decomposition (WD), Moving Average Filter (MAV), Elliptical Filter, Digital Smoothing Polynomial Filter, Fast Fourier Transfor In The West (FFTW), Spectral Wiener Filter Method, Discrete Fourier Transform (DFT), Welch Power Spectral Density Estimation Method, Normal Variate (SNV), Singular Value Decomposition (SVD), The Coherent Averaging Module, Joint Empirical Mode Decomposition, Singular Spectrum Analysis-based Pre-processing Method, Norris Derivative Filter (NDF), Multiplicative Scatter Correction (MSC). The feature extraction commonly used are Logarithmic Energy Entropy Feature, Kaiser-Teager Energy Feature (KTE), Spectral Entropy Feature (SE), Autoregressive Model of PPG Signal, the difference of optical density between the pulsatile PPG_{AC} components (ΔOD_{λ}), Peak-to-Peak interval (PPI), Detrended Fluctuation Analysis (DFA), Power spectral density (PSD), Wavelet Entropy (WE). All these things aim to increase the accuracy of estimating blood glucose levels and obtain a robust system. The research results are expressed in various measures: RMSE, correlation coefficient (R), coefficient of determination (R^2), MARD, CEGA, and SPE. The 62 primary studies included in the review used varying amounts of data, signal processing methods, estimation approaches, and accuracy performance parameters. Therefore, this systematic review can be continued with a meta-analysis of the meta-correlation type to find the best method. Meta-correlation is carried out to determine which method can provide the highest correlation between predicted (noninvasive) values and actual (invasive) values.

4. Conclusion

Research on noninvasive blood glucose estimation using NIR signals tends to increase. The wavelength selection can affect the estimation accuracy because the NIR wavelength value affects the attenuation of glucose and other particles. The most widely used wavelength is 940 nm. The use of PPG signals is quite promising in the future. The signal processing of the NIR and the PPG signal is essential because it can affect the quality of the signals and the extracted features. By maintaining the quality of the PPG signal from the beginning, optimal accuracy values in machine learning can be achieved. Therefore, developing digital signal processing methods to reduce noise, improve signal quality, and perform feature extraction is important to increase the accuracy of noninvasive blood glucose estimation. The conventional approach is used because it is simple, but the machine learning approach promises better accuracy and robustness. Using non-linear machine learning provides better.

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Author contributions

Fitrilina: Conceptualization, Methodology, Writing-Original draft preparation; Rusydi: Validation, data extraction; Kurnia: Validation, retrieving primary studies; Sunaryo: retrieving primary studies, data extraction, collecting data. Ramadhani: retrieving primary studies, data extraction, collecting data

Conflicts of interest

The authors declare no conflicts of interest.

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