# RESEARCH



# Performance and limitation of machine learning algorithms for diabetic retinopathy screening and its application in health management: a meta-analysis



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# Abstract

**Background:** In recent years, artificial intelligence and machine learning algorithms have been used more extensively to diagnose diabetic retinopathy and other diseases. Still, the effectiveness of these methods has not been thoroughly investigated. This study aimed to evaluate the performance and limitations of machine learning and deep learning algorithms in detecting diabetic retinopathy.

**Methods:** This study was conducted based on the PRISMA checklist. We searched online databases, including PubMed, Scopus, and Google Scholar, for relevant articles up to September 30, 2023. After the title, abstract, and full-text screening, data extraction and quality assessment were done for the included studies. Finally, a meta-analysis was performed.

**Results:** We included 76 studies with a total of 1,371,517 retinal images, of which 51 were used for meta-analysis. Our meta-analysis showed a significant sensitivity and specificity with a percentage of 90.54 (95%CI [90.42, 90.66], P < 0.001) and 78.33% (95%CI [78.21, 78.45], P < 0.001). However, the AUC (area under curvature) did not statistically differ across studies, but had a significant figure of 0.94 (95% CI [– 46.71, 48.60], P = 1).

**Conclusions:** Although machine learning and deep learning algorithms can properly diagnose diabetic retinopathy, their discriminating capacity is limited. However, they could simplify the diagnosing process. Further studies are required to improve algorithms.

**Keywords:** Machine learning algorithms, Artificial intelligence, Diabetic retinopathy, Meta-analysis, Deep learning



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## Introduction

Diabetic retinopathy (DR) has a significant role in vision problems and blindness among individuals in middle age and older populations worldwide [1, 2]. According to estimates, close to 103 million adults worldwide were diagnosed with DR in 2020. Experts project that this number will increase to approximately 160 million by 2045 [3]. It is believed that nearly one-third of people who have diabetes may eventually experience different forms of DR [4], and 10% of those with diabetes are at risk of vision loss [5]. DR consists of several stages: its initial stage includes non-proliferative DR (mild, moderate, and severe), which can progress to diabetic macular oedema or pre-proliferative DR. Pre-proliferative DR itself can lead to proliferative DR. There may be no symptoms in the early stages, or the severity of symptoms is very mild. In asymptomatic patients, the cotton wool and microaneurysms could be found incidentally in fundoscopy. Initial changes can be controlled with proper management. In contrast, the lack of appropriate treatment leads to the progression of DR to the final stages and symptoms, such as blurred vision, blurred vision, flutter, and partial or complete loss of vision [6, 7].

Vision problems resulting from DR have great potential to be considerably improved if detected at the initial stages and cured appropriately [8]. However, less than sixty percent of diabetic patients receive the recommended regular eye examinations due to the high cost and limited access to ophthalmological services [9]. As DR is a sneaky disease, many patients are not consciously aware that they have it, particularly those living in locations with inadequate medical resources. This makes it difficult for ophthalmologists to accurately determine a patient's condition based on fundus pictures [10]. DR's gold standard screening method involves clinical assessments by human clinicians or evaluating color fundus photographs remotely via telehealth services [11]. One of the primary modalities used is optical coherence tomography (OCT). OCT can generate sectional three-dimensional images of the retina's thickness and structure by measuring the amount of light reflection. This technique mainly detects macular oedema in DR [12]. However, these methods require a significant investment of time and effort. In addition, the likelihood of achieving irregular and inconsistent outcomes rises due to natural human subjectivity [13].

Hence, highly sensitive and specific automated systems are essential for widespread implementation of DR screening using color fundus photographs. The advancement of artificial intelligence (AI), particularly machine learning (ML), has made it possible to develop such automated approaches. Machine learning utilizes pre-existing data to instruct a computer on identifying a particular pattern or making predictions about a specific event in a novel data set [11]. The emergence of deep learning (DL), a subset of machine learning (ML), has significantly revolutionized the domain of automated image analysis [14]. In essence, DL approaches refer to representation learning techniques that utilize neural networks with multiple layers. These networks can achieve better performance by iteratively adjusting their internal parameters [11, 12]. Unlike other machine learning algorithms, deep learning does not necessitate image preprocessing or manipulation. After being provided with raw data, the system creates its own representations necessary for pattern identification. It has demonstrated higher accuracy compared to other traditional machine learning methods [11, 13].

Although the use of AI in the medical domain is being steadily developed [15], the impact and performance of AI diagnostic tools are not consistent across all research [16, 17], so questions remain regarding whether ML techniques have enough reliability to be used for actual medical needs, specifically in DR screening. Due to this heterogeneity among the studies, the present meta-analysis is conducted to update the performance and limitations of ML algorithms for DR screening and its application in health management.

### Methods

In this systematic review, we intend to scrutinize the performance and limitations of a machine learning algorithm for diabetic retinopathy screening and its application in health management. The design protocol of this review was registered in the Open Science Framework (OSF: osf.io/3prs8).

#### Search strategy

Our methodology follows the PRISMA (preferred reporting items for systematic reviews and meta-analysis). It is critical to state that this manuscript's search strategy, screening, and data selection were all checklist-based. Databases, including PubMed (Medline), Scopus, and Google Scholar, were searched up to September 30, 2023, without any time restriction. The search strategy for each database is defined in Table 1. By searching the references of the found studies, we manually added studies with relevant titles that were not discovered during the database search. The studies were manually filtered to exclude non-diabetic studies. Duplicated studies were found automatically and manually by two independent researchers. After complete screening, studies compatible with our inclusion criteria were included.

#### Inclusion and exclusion criteria

In this study, all articles that explore a machine-learning or deep learning algorithm for diabetic retinopathy screening using color fundus photographs were included. In addition, we only used English papers. It is worth noting that the inclusion was not limited to specific types of diabetes (type 1 or 2) or age groups. However, all letters to editors, case reports, case series, posters, and abstracts were excluded.

Database	Search strategy	Date
PubMed	(retinopathy[Title]) AND ((artificial intelligence [Title]) OR (Al[Title]) OR (machine learning [Title]) OR (ML[Title]) OR (deep learning [Title]) OR (DL[Title]))	September 30, 2023
Scopus	TITLE ((retinopathy AND ("artificial intelligence" OR "machine learn- ing" OR "deep Learning")))	September 30, 2023
Web of science	TITLE ((retinopathy AND ("artificial intelligence" OR "machine learn- ing" OR "deep Learning")))	September 30, 2023

Table 1	Search	strateqv	for	online	databases
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#### Quality assessment and data extraction

The Joanna Briggs Institute's (JBI) checklist was used in our manuscript study quality assessment. Two reviewers evaluated the full text of the papers to exclude improper studies. If there was any dispute, it was resolved by consultation. Two other researchers extracted data, including author, year, country, study design, total image number, sensitivity, specificity, and area under the curve (AUC).

#### Statistical analysis

Data analysis was conducted using STATA 13.1 software, developed by StataCorp LP in College Station, TX, USA. Results were presented as pooled sensitivity and specificity with a 95% confidence interval (CI), visualized in a forest plot. Heterogeneity among included studies was assessed using the  $I^2$  statistic, and the random effects model was applied in the presence of significant heterogeneity ( $I^2 > 50\%$ ). In addition, we calculated the AUC. Eventually, the publication assessed using a funnel plot and Egger's regression test.

## Result

#### Study selection and study characteristics

A total of 1861 studies were obtained by searching online databases, including PubMed, Scopus, Google Scholar, and manual search. Duplicated reports were removed, of whom 576 cases were done automatically. After screening the remaining articles, 969 irrelevant studies were excluded. Finally, 76 studies with a total of 1,371,517 images were included in the systematic review (Fig. 1). Of which, 51 studies were used for meta-analysis. The remaining 25 studies were excluded from the meta-analysis due to insufficient data. These studies were published between 2013 and 2023 (Table 2). Both private and public data sets were used in these studies. Our findings showed that studies suggested a range of approaches used in diabetic retinopathy screening, from traditional manual grading to advanced machine learning methods like convolutional neural networks (CNNs) and deep learning models. Some studies used smartphone-based imaging for more accessible screening, especially in resource-limited settings. Hybrid models combining different algorithms were also utilized, showing potential for improving screening processes (Table 2).

#### Meta-analysis

We performed a meta-analysis to assess the accuracy (including sensitivity and specificity) of machine learning detection in diabetic retinopathy in 51 studies. Our result revealed a significant sensitivity and specificity with a percentage of 90.54% (95%CI [90.42, 90.66], P<0.001) and 78.33% (95%CI [78.21, 78.45], P<0.001) (Figs. 2 and 3). We observed a severe heterogeneity between studies in both cases ( $I^2$ >99%). In addition, we observed a substantial AUC with an amount of 0.94 (95% CI [- 46.71, 48.60]); however, it was not statistically significant (P=1) (Fig. 4).

#### **Publication bias**

The funnel plot and Egger's test were performed to investigate the possible publication bias. The funnel plot showed a symmetrical pattern, indicating no publication bias (not shown). In addition, Egger's test supported this result.



Fig. 1 PRISMA diagram for present study

#### Discussion

Incorporating ML algorithms into healthcare, particularly in DR screening, represents a significant advancement in medical diagnostics. Diabetic retinopathy stands as a major cause of blindness among adults globally, necessitating early detection and prompt management to prevent irreversible vision loss. With the emergence of machine learning and AI, the approach to DR screening and diagnosis has undergone a transformative shift, capitalizing on these technologies' immense potential to bolster accuracy, efficiency, and accessibility in healthcare [10, 18].

This meta-analysis consolidates existing evidence and assesses the diagnostic accuracy of ML algorithms in detecting DR using color fundus photographs.

Having completed a comprehensive meta-analysis, we have investigated the diagnostic accuracy of ML algorithms in detecting DR using color fundus photographs. Our analysis, which involved data from 76 studies encompassing 1,357,517 images, has concluded. The results, showing a sensitivity of 90.54% (95% CI [90.42, 90.66]), specificity of 78.33% (95% CI [78.21, 78.45]), and an area under the receiver operating characteristic curve (AUC) of 0.94, underscore the high diagnostic accuracy of ML models in identifying DR from retinal images. These findings suggest the capability of ML algorithms to detect the presence of DR accurately, a critical step toward preventing vision loss in diabetic patients.

The high sensitivity rate indicates that ML algorithms are proficient at identifying those individuals with DR, minimizing the risk of missed diagnoses. Meanwhile, the specificity rate reflects the algorithms' ability to correctly identify those without the

 Table 2 Baseline characteristics of included studies and performance of color fundus image screening

Code	Author (year) [Ref.]	Total images	Sensitivity	Specificity	AUC	Approach for screening
2	Jain (2021) [26]	1294	100	89.55		Kowa VX-10a mydriatic camera & Remidio FOP NM-10
3	Keel (2018) [27]	96	92.3	93.7	0.95	DLA
4	Jiang (2020) [ <mark>28</mark> ]	3228	93.9	94.4	0.94	Grad-CAM
5	lpp (2020) [ <mark>29</mark> ]	893	95.5	85		ETDRS scale
6	lbáñez-Bruron (2021) [30]	89	100	55.4		DART
7	Yo-Ping Huang (2020) [31]	52	96.6	95.2	0.99	VGG16, VGG19, MobileNet, InceptionV3, DenseNet
8	Hsu (2021) [ <mark>32</mark> ]	13,410	96.84	89.44	0.97	DLA
9	Yi-Ting Hsieh (2019) [33]	7524	92.2	97.5	0.95	CNN (VeriSee)
10	Heydon (2020) [34]	30,405	95.7	68		EyeArt v2.1
11	He (2019) [35]	889	90.79	98.5	0.94	Airdoc
12	Hao (2022) [ <mark>36</mark> ]	6146	79.2	87.1		VoxelCloud
13	Guo (2021) [ <mark>37</mark> ]	978	54	95	0.88	ResNet & U-Net
14	Gulshan (2019) [ <mark>38</mark> ]	3049	83.5	98.7	0.96	ICDR scale
15	Gulshan (2016) [ <mark>39</mark> ]	4997	90.3	98.1	0.99	DLA
16	Grzybowski (2021) [40]	60	93.33	94.45	0.94	Retinalyze
17	González-Briceño (2020) [41]	3368	89	92		Cross-industry standard process for data mining
18	Gargeya (2017) [ <mark>42</mark> ]	75,137	94	98	0.97	DLA
19	Glinton (2022) [43]	597	91	95	0.93	Python (version 3.6.9)
20	Gadekallu (2020) [44]	1151	90.4	94.3		DLA
21	Fleming (2023) [45]	179,944	89.19	77.41	0.99	DLA
22	M. Al-hazaimeh (2022) [46]	88,702	99.2	96.4	0.98	SVMGA
23	TamoorAziz (2023) [47]	219	94.21	97.46	0.98	DLA
24	Ghadah Alwakid (2023) [48]	12,522	89	99		CLAHE, ESRGAN
25	Eman AbdelMaksoud (2022) [49]	3662	96	69	0.99	CNN
26	Marc Baget-Bernaldiz (2021) [50]	1200	97.92	99.91	0.99	DLA
27	Anas Bilal (2022) [51]	98	96.9	96.9	0.97	U-NET, CNN-SVD
28	Usharani Bhimavarapu (2023) [ <mark>52</mark> ]	88,702	96.34	96.74	0.89	CNN
29	Wejdan L. Alyoubi (2021) [53]	13,673	89	97.3	0.95	CNN512, YOLOv3
30	Miao (2022) [54]	35,126	79.01	89.07	0.79	DLA
31	Penha (2023) [ <mark>2</mark> 1]	686	93.6	71.7	0.86	EyerMaps
32	Lee (2021) [55]	311,604	80.47	81.28		VA HCS
33	Lam (2018) [ <mark>56</mark> ]	1346	95	96		DIGITS
34	Nugroho (2021) [ <mark>57</mark> ]	200	95	81		DLA
35	Nneji (2022) <mark>[58]</mark>	35,126	98.9	98	0.99	WFDLN
36	Zhang (2022) [ <mark>22</mark> ]	1089	98.23	74.45	0.95	EyeWisdom V1
37	Yang (2021) [59]	1418	79.6	79.9	0.81	XGBoost, RF, naïve Bayes, KNN, AdaBoost, Light GBM, ANN, LR
38	Zhao (2022) [60]	7943	88.9	74	0.8	RF, XGBoost, LR, SVM, KNN
39	Pinedo-Diaz (2022) [61]	420	97.66	98.33	0.98	DLA
40	Surya (2023) [62]	1085	83.33	98.86	0.83	Dr Noon
41	Zhang (2020) [63]	47,269	83.3	92.5		DLA

Table 2	2 (continue	ed)
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Code	Author (year) [Ref.]	Total images	Sensitivity	Specificity	AUC	Approach for screening
42	Sosale (2020) [64]	922	93	92.5	0.9	Medios Al
43	Mehboob (2022) [65]	25,600	78	44		DLA
44	Mujeeb Rahman (2022) [66]	560	93.65	95.13	0.97	DNN, SVM
45	Abramoff (2016) [67]	1748	96.7	87	0.98	IDx-DR X2.1
46	Palaniswamy (2023) [68]	813	94.28	99.34	0.96	DLA
47	Ting (2017) [69]	71,896	90.5	91.6	0.93	DLA
48	Jebaseeli (2019) [70]	201	80.61	99.54		DLBSVM
49	Jena (2022) [71]	100	99.2	99.4	0.99	2-branch CNN
50	Jiang (2019) [72]	30,244	85.57	90.85	0.946	DLA
51	Khan (2023) [73]	45	79.63	98.63	0.98	Inception v3 & DenseNet-121
52	Shankar (2020) [74]	541	98.54	99.38		SDL
53	Kuna (2023) [75]	1200	98.9	99.7		DL-DRDC
54	Ludwig (2020) [76]	92,364	89	89	0.89	CNN
55	Sosale (2020) [77]	297	98.84	86.73	0.92	ICDRS scale
56	Li (2022) [ <mark>23</mark> ]	1674	95	85.1	0.94	Deep learning algorithm
57	Roy (2020) [78]	1330	94	95		DLA
58	Romero-Aroca (2020) [79]	1748	96.7	97.6		DLA
59	Pei (2022) [80]	324	91	81.3	0.86	EyeWisdom
60	Rayave (2022) [81]	650	65.54	100		CNN, RNN, SVM, FKM, DA
61	Paradisa (2020) [82]	89	99.3	98		CNN, SVM, KNN, RF, XGBoost
62	Li (2022) [83]	950	97.96	93.88	0.99	NNs, SVM, XGBoost, DT, LR, GNB, KNN
63	Roychowdhury (2013) [84]	1200	100	53.16	0.87	GMM, SVM, KNN, AdaBoost
64	Sarao (2020) [ <mark>85</mark> ]	165	90.8	75.3	0.07	EyeArt
65	Li (2021) [ <mark>86</mark> ]	32,452	70	90	0.9	LR, XGBoost, RF, SVM
66	Wu (2022) [ <mark>87</mark> ]	7033	100	37.8	0.9	OC-Net, SE-Net
67	Ruamviboonsuk (2022) [88]	138	91.4	95.4		DLA
68	Ruamviboonsuk (2019) [89]	25,326	97	96		DLA
69	Saxena (2020) [90]	56,839	81.02	86.09	0.92	CNN
70	Sayres (2019) [91]	1612	79.4	96.6		DLA
71	A. Shah (2021) [ <mark>92</mark> ]	2680	100	81.82	0.98	IDx-DR
72	P. Shah (2020) [93]	1533	99.7	98.5	0.99	CNN
73	Rajalakshmi (2018) [94]	296	95.8	80.2		ICDR
74	Reddy (2022) [95]	89	90.2	95.2	0.88	DLA
75	Rom (2022) [ <mark>96</mark> ]	363	45	94	0.81	CNN
76	Rogers (2021) [97]	22,180	81.6	81.7	0.98	Pegasus
77	Ryu (2022) [98]	918	67.5	94.4		CNN

DLA: Deep-learning algorithm; VA: Veterans Affairs; HCS: Puget Sound Health Care System; DIGITS: Deep Learning GPU Training System; WFDLN: weighted fusion deep learning network; XGBoost: extreme gradient boosting; KNN: k-nearest neighbour; ANN: artificial neural network; RF: Random Forest; LR: Logistic Regression; SVM: Support Vector Machine; DNN: deep neural network; DLBSVM: Deep Learning Based Support Vector Machine; SDL: Synergic deep learning; CNN: convolutional neural network; ICDRS: International Clinical Diabetic Retinopathy Severity Scale System; RNN: Recurrent Neural Network; FKM: Fuzzy K-means cluster; DA: Discriminant Analysis; GNB: Gaussian Naive Bayes; LR: Logistics Regression; DT: Decision Tree; NNs: Neural Networks; GMM: Gaussian Mixture model; OC-Net: occurrence network; SE-Net: a severity network; DL-DRDC: w deep learning empowered diabetic retinopathy detection and classification



Fig. 2 Forest plot for sensitivity showed a significant amount of 90.54%

condition, although there is room for improvement to reduce false positives. The AUC, a measure of the algorithm's overall diagnostic ability, further confirms the efficacy of ML in DR screening, suggesting that these technologies can reliably distinguish between affected and unaffected individuals.

However, the implementation of ML in DR screening is not without challenges. The variation in specificity rates points towards the need for further refinement of algorithms to enhance their discriminative capacity, minimizing the occurrence of false positives that could lead to unnecessary anxiety or interventions for patients. In addition, the effectiveness of ML algorithms can vary based on factors such as image quality, the diversity of the data sets on which the algorithms are trained, and the prevalence of DR in the screened population. Ensuring that ML models are trained on diverse, high-quality data sets is crucial to enhancing their generalizability and accuracy across different populations and settings.

Moreover, integrating ML algorithms into clinical practice necessitates a multidisciplinary approach involving technologists, data scientists, clinicians, patients, and policymakers. The meta-analysis of ML algorithms for DR screening represents a significant step forward in applying AI in health management. The high diagnostic accuracy of



Fig. 3 Forest plot for specificity showed a significant amount of 78.33%

these models holds the promise of revolutionizing DR screening, making it more accessible, efficient, and effective. However, realizing this potential requires addressing the limitations and challenges associated with the deployment of ML in healthcare. ML can play a significant role in transforming healthcare delivery, and improving patient outcomes through continuous refinement of algorithms, adherence to ethical standards, and collaboration across disciplines.

The results show diverse techniques utilized across the studies, reflecting the evolving landscape of approaches to screening diabetic retinopathy, where different algorithms cater to specific needs in clinical settings. Traditional methods, such as manual grading by trained professionals, are contrasted with advanced machine learning techniques, including CNNs and deep learning models, which have demonstrated remarkable improvements in sensitivity and specificity, underscoring the potential of artificial intelligence to enhance diagnostic accuracy. Several studies adopted smartphone-based imaging systems, highlighting a shift towards more accessible screening methods, particularly significant in resource-limited settings where conventional imaging equipment may not be available. The integration of AI with portable devices facilitates rapid screening and timely referrals, potentially improving patient outcomes. Furthermore, the table



Fig. 4 Forest plot for area under the curve (AUC) showed the amount of 0.94; however, it was not significant

indicates that some studies utilized hybrid models, combining various algorithms to leverage their strengths, which may enhance the robustness of screening processes and address limitations often encountered with single-algorithm applications; the effectiveness of these hybrid models, as evidenced by their reported performance metrics, suggests a promising avenue for future research and implementation.

Furthermore, Wang et al. conducted a meta-analysis utilizing multiple algorithms to assess the diagnostic efficacy of DR. Their study included 21 original studies involving 129,759 eves. The pooled sensitivity, specificity, and area under the curve (AUC) of the AI model for diagnosing DR were reported as 0.880 (0.875-0.884), 0.912 (0.99-0.913), and 0.9798, respectively [10]. Similarly, Wu et al. conducted a meta-analysis utilizing machine learning algorithms for DR screening, encompassing 60 color fundus photograph studies involving 445,175 interpretations. Their study reported high ML accuracy in diagnosing various categories of DR, with a pooled AUROC ranging from 0.97 (95% CI 0.96-0.99) to 0.99 (95% CI 0.98-1.00) and a pooled sensitivity and specificity ranging from 0.93 to 0.97 and 0.90 to 0.98, respectively. They concluded that ML algorithms' performance detecting DR based on color fundus photographs is likely comparable to human clinicians [19]. Ryu et al. developed an end-to-end deep learning-based classification system for DR and referable DR diagnoses using optical coherence tomography angiography (OCTA) images. They achieved high accuracy, sensitivity, and specificity for detecting the onset of DR and referable DR, further supporting the efficacy of ML algorithms in DR detection [20]. In their study, Penha et al. utilized an AI system, which included 686 individuals. Their findings demonstrated high sensitivity for DR screening using only one image per eye, suggesting a simpler protocol than the traditional approach [21].

In addition, Zhang et al. conducted a prospective, multi-center clinical trial study utilizing AI software to diagnose DR. Their study reported high sensitivity for DR detection compared to manual grading, highlighting the potential of AI in improving DR diagnosis [22]. Li et al. surveyed using deep learning algorithms (DLA). The DLA graded retinal fundus images; for all 1674 gradable images the AUC, sensitivity, and specificity of the DLA for referable DR were 0.942, 85.1%, and 95.6%, respectively [23]. Besides that, Li et al. conducted a study using DLA. They achieved an AUC, sensitivity, and specificity of 0.955, 92.5%, and 98.5%, respectively, for detecting referable DR in their independent multiethnic data sets [24]. Finally, Joseph et al. conducted a survey encompassing 34 studies utilizing AI algorithms for diagnosing DR based on real-world fundus images. Their study reported overall pooled accuracy, sensitivity, and specificity, further emphasizing the potential of AI in DR diagnosis [25].

One drawback of our analysis is that we had limited access to the data sets and the complete text of articles [18]. Furthermore, we exclusively incorporated materials written in English. The collected data on DR did not include the proliferative diabetic subtype or other categories of DR, which could affect the assessment of its diagnostic usefulness [10].

In addition, bias may have been incorporated by poor description of patient characteristics in the included studies. By the reason of spectrum bias, there is a possibility of ML's performance being overestimated in real-world scenarios, and this factor should be considered [19] It is reasonable for another complementary study to initiate using this algorithm in primary care settings; other applications and research are necessary to improve the this algorithm's clinical validity [24].

In conclusion, machine learning algorithms can potentially diagnose diabetic retinopathy using retinal images. Although this capability was insignificant in discriminating true positives from false positives, it could be used for faster and better evaluation. However, further studies are required to develop improved algorithms.

### **Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s12938-025-01336-1.

Supplementary Material 1.

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#### Author contributions

Study design and conception: M.AA; Search and study selection: M.M, FJ; Data extraction: T.D, AM.K; Quality assessment: R.B, M.R; Statistical analysis and interpretation: MRJ, F.S; Drafting the manuscript: M.M, FJ,A.M, SKSR, YK, T.D, AM.K, R.B, M.R, MRJ, F.S, M.AA; Critical revision: M.AA All authors were approved the submitted version.

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#### Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

#### Declarations

**Ethics approval and consent to participate** Not applicable.

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**Consent for publication** Not applicable.

#### **Competing interests**

The authors declare no competing interests.

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