The Role of Artificial Intelligence in the Diagnosis of Ocular Surface Squamous Neoplasia: a systematic review and meta-analysis

La Inteligencia Artificial en el Diagnóstico de la Neoplasia Escamosa de la Superficie Ocular: una Revisión Sistemática y Metanálisis

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Relevance: Ocular Surface Squamous Neoplasia (OSSN) is the most common malignancy of the ocular surface; timely non-invasive detection can preserve vision. This systematic review and diagnostic meta-analysis revealed that AI-based models performed with high accuracy in diagnosing OSSN. Future research requires comprehensive prospective studies, along with improvements in methodology to strengthen AI-based diagnosis.

Abstract: This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We systematically searched four databases, PubMed, Web of Science, Embase, and Scopus, to explore the use of AI in diagnosing OSSN. The QUADAS-2 tool was used to find the risk of bias across the included studies. A diagnostic meta-analysis was conducted to determine the pooled sensitivity and specificity of AI models used in various studies to diagnose the OSSN. The summary receiver operating curve (SROC) was drawn to calculate the area under the curve (AUC).
A total of 51 studies were found, and 6 studies were included in this systematic review, and four studies were eligible to be included in the diagnostic meta-analysis. All the included studies had at least one significant bias in methodology, leading to an overall high risk of bias. The diagnostic meta-analysis showed a pooled sensitivity of 95.5 % (95% CI: 67.5 to 99.5) and a specificity of 96.4 % (95% CI: 87.7 to 99.0). The summary receiver operating curve (SROC) revealed high accuracy (0.95) of AI models in diagnosing OSSN.

AI-based models demonstrated high sensitivity and specificity in the diagnosis of ocular surface squamous neoplasia. AI can reliably diagnose OSSN with both deep learning and machine learning models.

Keywords: Ocular Surface Squamous Neoplasia, Artificial Intelligence, Machine Learning, Deep Learning.

Relevancia: La neoplasia escamosa de la superficie ocular (NESO) es la malignidad más frecuente de la superficie ocular; su detección temprana y no invasiva puede preservar la visión. Esta revisión sistemática y metanálisis diagnóstico reveló que los modelos basados en inteligencia artificial (IA) presentan una alta precisión en el diagnóstico de la NESO. Las investigaciones futuras deben incluir estudios prospectivos amplios, junto con mejoras metodológicas que fortalezcan el diagnóstico asistido por IA.

Resumen: Esta revisión siguió las directrices de Elementos de Referencia Preferidos para Revisiones Sistemáticas y Metaanálisis (PRISMA). Se realizó una búsqueda sistemática en cuatro bases de datos —PubMed, Web of Science, Embase y Scopus— para analizar el uso de la IA en el diagnóstico de la NESO. Se aplicó la herramienta QUADAS-2 para evaluar el riesgo de sesgo en los estudios incluidos. Se llevó a cabo un metanálisis diagnóstico para determinar la sensibilidad y especificidad agrupadas de los modelos de IA utilizados en diferentes estudios para el diagnóstico de la NESO. Se construyó una curva resumen ROC (SROC) para calcular el área bajo la curva (AUC).

Se identificaron 51 estudios, de los cuales seis fueron incluidos en esta revisión sistemática, y cuatro fueron elegibles para el metanálisis diagnóstico. Todos los estudios presentaron al menos un sesgo metodológico significativo, lo que condujo a un riesgo global de sesgo elevado. El metanálisis diagnóstico mostró una sensibilidad agrupada del 95,5 % (IC 95 %: 67,5–99,5) y una especificidad del 96,4 % (IC 95 %: 87,7–99,0). La curva SROC evidenció una alta precisión (AUC = 0,95) de los modelos de IA en el diagnóstico de la NESO.

Los modelos basados en inteligencia artificial demostraron una alta sensibilidad y especificidad en el diagnóstico de la neoplasia escamosa de la superficie ocular. La IA puede diagnosticar de forma fiable la NESO mediante modelos de aprendizaje profundo y aprendizaje automático.

Palabras clave: Neoplasia Escamosa de la Superficie Ocular, Inteligencia Artificial, Aprendizaje Automático, Aprendizaje Profundo.

INTRODUCTION

Ocular Surface Squamous Neoplasia (OSSN) is the most prevalent ocular surface malignancy. It represents a range of histopathological changes from superficial epithelial dysplasia to potentially progressing invasive squamous cell carcinoma. (1,2) In clinical practice, the interpalpebral limbal conjunctiva is the most common site for OSSN, where it can present as a nodular, superficial, or diffusely invasive lesion. (3) OSSN is mainly associated with prolonged sunlight exposure, male sex, aging (especially over 60), HIV infection, chemical exposure, and vitamin A deficiency. (4–9)

Ocular surface squamous neoplasia usually doesn't cause any symptoms, and it can be wrongly diagnosed as simple benign ocular surface lesions like conjunctival cysts or pterygium. (10) To diagnose OSSN at the early stages is challenging because it resembles common benign eye conditions such as pinguecula and pterygium, especially in regions like East Africa, where such conditions are common. (11) To confirm the diagnosis of OSSN, the most reliable method is biopsy with histopathological examination, which is considered the gold standard. However, this approach needs a trained pathologist for interpretation and may cause complications like infection, scarring, and large excisions. (12) Lack of histopathology facilities is one of the barriers in the early diagnosis of ocular surface squamous neoplasia. (13)

The recent advances in Artificial Intelligence, especially noninvasive image-based diagnosis, have transformed the medical field by increasing the accuracy of disease diagnosis. (14) According to the recent review on the role of AI in ophthalmology, deep learning algorithms used in optical coherence tomography and fundus imaging have gained expert-level performance in detecting diabetic retinopathy, age-related macular degeneration, glaucoma, and other ocular conditions.

Artificial intelligence systems like IDx-DR are FDA-approved for screening diabetic retinopathy. (15)

Current developments in AI models, especially the application of machine learning and deep learning to high-resolution images of anterior segment OCT and slit-lamp images, have shown a remarkably high accuracy in detecting OSSN. (16)

This diagnostic meta-analysis combines the results from various eligible studies to determine the overall sensitivity, specificity, and accuracy of AI models in diagnosing OSSN.

Databases, screening, inclusion, and exclusion

The protocol of this review was registered with PROSPERO under the ID: CRD420251005996 on March 7, 2025. In this review article, we followed and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA). (17) For this systematic review and diagnostic test accuracy meta-analysis, we selected widely used databases in medical literature: PubMed, Web of Science, Scopus, and Embase. A search was carried out using MeSH terms such as Artificial intelligence OR Machine learning OR deep learning OR automation OR Lasso OR support vector machine OR automatic diagnosis OR convolutional neural network OR K-means AND Ocular surface squamous neoplasia OR OSSN. No filters, such as publication year, language, or article type, were applied during the screening of studies on databases. We also conducted a manual search in Google Scholar to identify any studies that might have been overlooked during the database search.

We imported the extracted bibliography into the ZOTERO reference manager, which automatically detected duplicate studies. We removed these studies before screening. We included studies focused on the diagnosis of ocular surface squamous neoplasia using AI; other studies were excluded from this meta-analysis. We selected original, full-text articles with clearly described methodologies and results that focused on the detection of ocular surface squamous neoplasia from ocular surface images using different models of artificial intelligence. We excluded review articles, editorials, and abstracts. Data were extracted independently by two authors according to the criteria.

Extracted Data

From all included studies, we extracted the following data to find the accuracy of AI models in diagnosing the ocular surface squamous neoplasia.

- Publication date and country of origin
- AI model
- Source of images used in the study
- AI model validation technique
- Number of test images
- Specificity – also known as true negative rate, measures the ability of an AI model to identify negative cases correctly. Specificity =True Negatives / (True Negatives + False Positives)
- Sensitivity – also known as true positive rate, measures the ability of an AI model to identify positive cases correctly. Sensitivity = True Positives / (True Positives + False Negatives)
- Accuracy – measures the overall precision of an AI model's output. Accuracy = (True Positives +True Negatives) / (True Positives + True Negatives +False Positives + False negatives

Statistical analysis

The diagnostic test accuracy meta-analysis was conducted by using RStudio (2025.05.0+496 "Mariposa Orchid). A univariate random-effect model was used to find the pooled sensitivity and specificity of different studies separately. Analyses were performed in RStudio, and a summary receiver operating curve was created to visualize the AI model's performance in diagnosing the OSSN.

Results

We performed a search of four major databases on 29th April 2025. A total of 51 studies were identified across all four databases, with 15 studies from PubMed, 15 from Web of Science, 10 from Scopus, and 11 from Embase. We imported all studies into the ZOTERO bibliography manager software. ZOTERO removed 33 detected duplicates before screening. Twelve studies were removed based on their irrelevant titles and abstracts, and six studies underwent full-text screening. Excluded studies included 1 conference abstract and one review article; others were deemed irrelevant based on their titles and abstracts. Among these 6 included studies, four were eligible for diagnostic test accuracy meta-analysis. (12,18–20) The PRISMA flow chart for the literature search is shown in figure 1.

In this systematic review, we included six studies, which were conducted in the USA, Australia, Iran, Hungary, and India. The AI models used in these studies ranged from Machine learning, such as Support Vector Machine (SVM) and K-Nearest Neighbors (KNN), to deep learning, including Masked Autoencoder+ Vision Transformer, EfficientNetB7 (segmentation), GoogLeNet, ResNet50V2, and MobileNetV2. Standard validation methods used in the included studies were patient-level internal splitting, 10-fold cross-validation, and 5-fold cross-validation. The number of testing sizes varied in all studies. The largest sample size was used by Kozma et al, (18) which included 1836 IVCM images, of which 277 were of OSSN. Habibalahi et al. (2019) (21) used non-invasive multispectral autofluorescence imaging and machine learning (K-Nearest Neighbors and Support Vector Machine) for detecting ocular surface squamous neoplasia, and this system achieved high accuracy, >98% in diagnosing OSSN. Later, Habibalahi et al. (2022) (22) used enhanced 59-channel autofluorescence imaging and machine learning (support vector machine) to differentiate normal tissue, pterygium, and OSSN. This machine learning approach achieved high sensitivity (84%), specificity (94%), and accuracy (88%) in diagnosing OSSN.

Table 1 provides the complete overview of the included studies. (12,18–22) This table includes the type of study, the AI model used in the studies, the testing sample size, the validation technique, the reference standard, and the imaging modality.

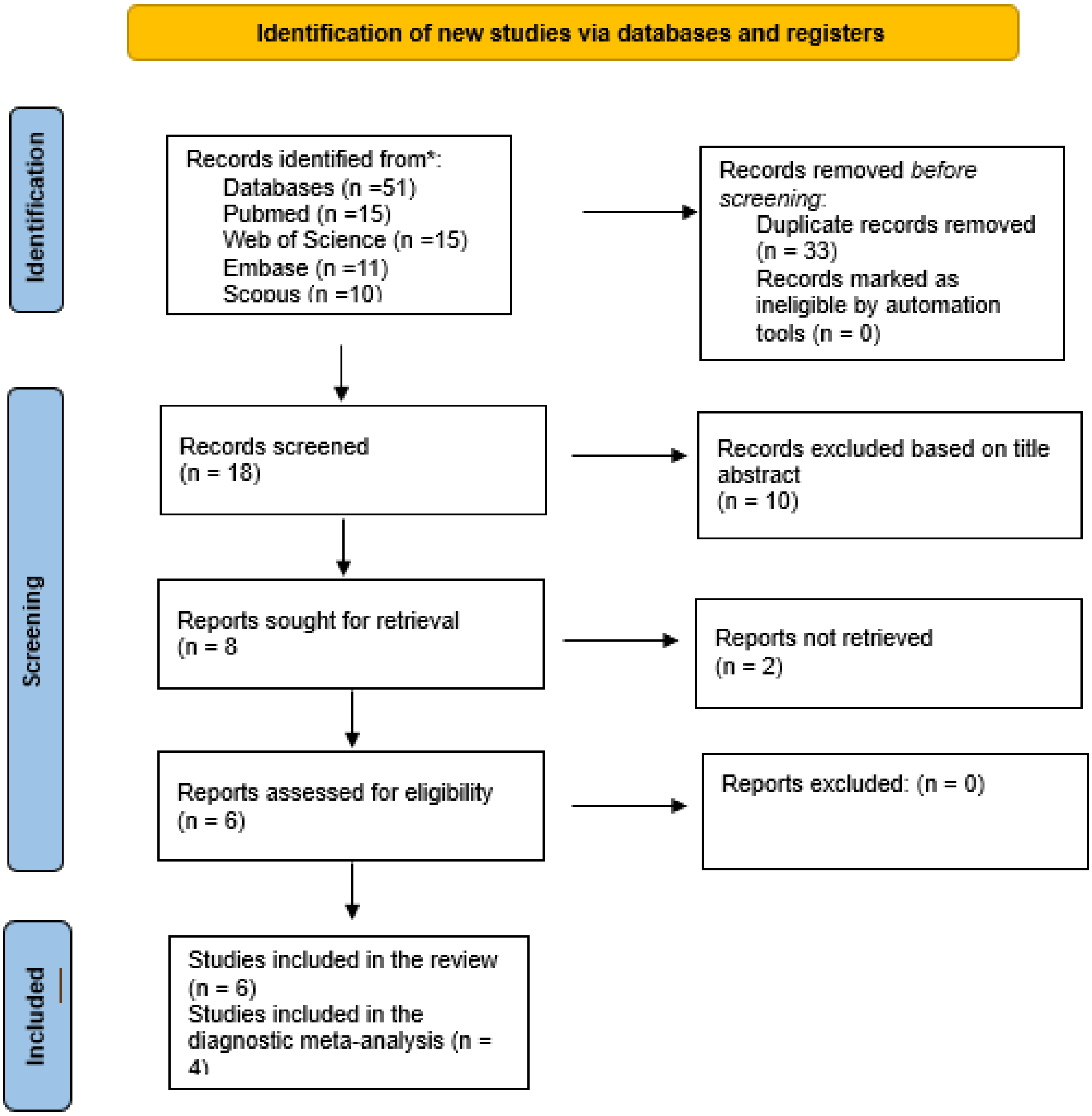

Figure 1: PRISMA flow diagram.

Risk of Bias Assessment

We used the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool to find the risk of bias across different studies. We noted a high risk of bias in 4 studies, and two studies had some concerns of the risk of bias. The studies with high risk of bias were primarily due to the selection of patients or images in the studies. A summary of the bias results of all studies included in this systematic review is shown in figure 2.

Diagnostic Meta-Analysis

In the diagnostic test accuracy meta-analysis, four studies were included. In these 4 studies (12,18–20) only deep learning models were used. The pooled sensitivity of AI models was 95.5 (95% CI: 67.5 to 99.5). High heterogeneity I2 = 66.8%, p = 0.028 was noticed in the pooled sensitivity analysis. The pooled specificity was 96.4 (95% CI: 87.7 to 99.0). Higher heterogeneity was observed in the pooled specificity analysis (I2 = 93.9%, p < 0.0001) compared to the pooled sensitivity analysis. Forest plots of pooled sensitivity and specificity are shown in Figure 3.

Subgroup analysis was not performed because the included studies in the diagnostic test accuracy meta-analysis used only deep learning models. Figures 2 and 3 display the forest plots of the pooled sensitivity and specificity analyses.A summary ROC curve of the

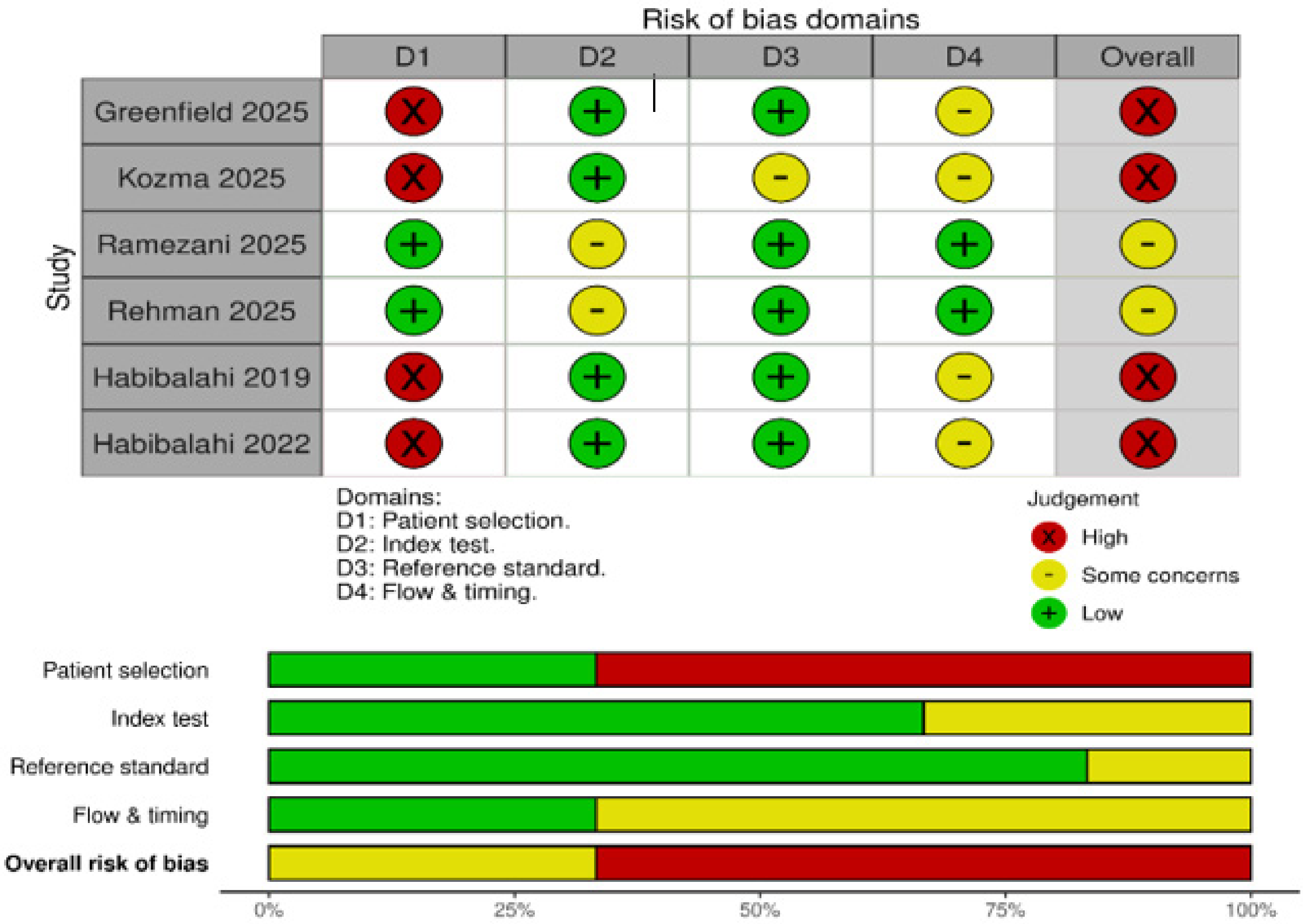

Figure 2: Summary of QUADAS-2 risk of bias of all included studies.

included studies was generated to visualize the overall diagnostic performance across the different studies. The pooled area under the curve (AUC) was 0.95, which showed excellent discriminative ability of the diagnostic AI models. Pooled estimates were plotted from Greenfield (2025)(12), Kozma (2025), (18) Ramezani (2025), (19) and Rahman (2025). (20) The short distance between the pooled points to the upper-left corner suggests a well-supported diagnostic accuracy. Figure 4 illustrates the Summary ROC curve.

DISCUSSION

This systematic review and diagnostic meta-analysis evaluated the diagnostic accuracy of various AI models in detecting ocular surface squamous neoplasia. The data synthesis from qualifying studies indicated that AI models demonstrate high sensitivity and specificity for detecting this condition. Given the limited number of eligible studies, we performed a meta-analysis of diagnostic accuracy using four studies that employed deep learning models, including EfficientNetB7, GoogLeNet, ResNet50V2, and MobileNetV2.

The pooled sensitivity and specificity of AI models were 95.5% (95% CI: 67.5-99.5) and 96.4% (95% CI: 87.0-99.0), respectively. The summary ROC curve (AUC) was 0.95, indicating excellent diagnostic performance. These high diagnostic values suggest that AI-based models can provide accurate clinical diagnoses, facilitating early detection, particularly in lower-income countries where standard diagnostic labs, such as histopathology labs for OSSN diagnosis, are not available.

To the best of our knowledge, this is the first diagnostic meta-analysis evaluating the efficacy of artificial intelligence in diagnosing ocular surface squamous neoplasia. As noted by Sinha et al. (2024), (16) AI has the potential to facilitate the early and accurate detection of OSSN, benefiting both highly developed and low-resource clinical settings. They also discussed how AI tools, such as conventional neural networks (CNN), can be used in screening programs for early disease detection. Such methods can enhance early detection and referral pathways for OSSN. However, we quantitatively demonstrated the role of AI in OSSN detection in our meta-analysis, which further strengthens the diagnostic accuracy of AI models in OSSN detection.

There is a growing investigation into the use of AI for diagnosing and differentiating ocular surface diseases. Recent studies have focused on the role of artificial intelligence in screening and monitoring different ophthalmological conditions. Various authors have applied AI in ocular oncology, achieving positive outcomes. (23,24) In another study by Xu W. et al. (2021), (25) they developed an AI-based diagnostic system utilizing deep learning to identify pterygium from anterior segment images captured with a digital single-lens reflex camera connected to a slit-lamp microscope. Very close to our findings, Xu W et al. AI model achieved 94.68% accuracy on 470 test photos and AUC values of 100% for group 1 and 95% for groups 2 and 3. It could detect PTG and classify its severity.

The outstanding diagnostic capabilities of AI models facilitate their incorporation into teleophthalmology workflows or screening initiatives in regions with limited or non-existent access to histopathology labs. This integration can reduce diagnostic delays and decrease dependence on invasive biopsy procedures, which often cause risks of ocular scarring and sampling errors. This meta-analysis demonstrates that AI models are effective in diagnosing ocular surface squamous neoplasia (OSSN), but some limitations exist, such as a small number of eligible studies, most studies used a retrospective study design, and variations in reference standards, raising concerns about real-world applicability. The high risk of bias was mainly because of the selection of patients or images used in the analysis. Future studies should use a more refined architecture of AI models with prospective validation systems, standardized image processing technologies, and researchers should employ a high volume of high-quality images to train and test AI models to diagnose the OSSN.

CONCLUSIONS

AI models demonstrated high accuracy in diagnosing OSSN. The AI-based models could help in the early detection of OSSN in both low-resourced clinical settings and fully developed clinical setups. Future large prospective studies with improvement in conduct are needed to strengthen AI-based diagnosis.

Study	Design	AI Model	Testing Sample Size (OSSN cases/ images)	Validation method	Reference standard	Imaging Modality
Greenfield et al., 2025 USA (12)	Retrospective DTA study	DL (Masked Autoencoder + Vision Transformer)	48 cases (OSSN 27 cases)	Patient-level internal splitting	Biopsy-proven diagnosis	AS_OCT
Kozma et al., 2025 Hungary (18)	Diagnostic accuracy study	ResNet50V2,	1836 IVCM images (277 OSSN)	Patient-wise split + Leave-One-Out CV	Histopathology confirmed cases	In Vivo Confocal Microscopy (IVCM)
Ramezani et al., 2025 Iran (19)	Retrospective DTA study	EfficientNetB7 (segmentation) + GoogLeNet (classification)	162 (77 OSSN)	10-fold cross-validation	Impression cytology	Slit lamp Photography (BX900 HAAG-STREIT)
Rehman et al., 2025 India (20)	Retrospective observational study	MobileNetV2	Images 120 (40 OSSN)	5-fold cross-validation	-	Slit Lamp Photographs
Habibalahi et al., 2019 Australia (21)	Exploratory diagnostic study	SVM (inter-patient), KNN (intra-patient)	18 OSSN Patients	10-fold cross	Histopathology	Multispectral Autofluorescence Microscopy
Habibalahi et al., 2022 Australia (22)	Prospective laboratory-based diagnostic study	Support Vector Machine (SVM) with PCA (fused classification)	50 patients with PTG and/or OSSN (specific number of OSSN cases not separated, but spectral sectors analyzed)	K-fold cross-validation and Leave-One-Patient-Out	(H&E-stained tissue by pathologist)	Auto-fluorescence Multispectral Imaging

Table 1: Baseline characteristics of included studies.

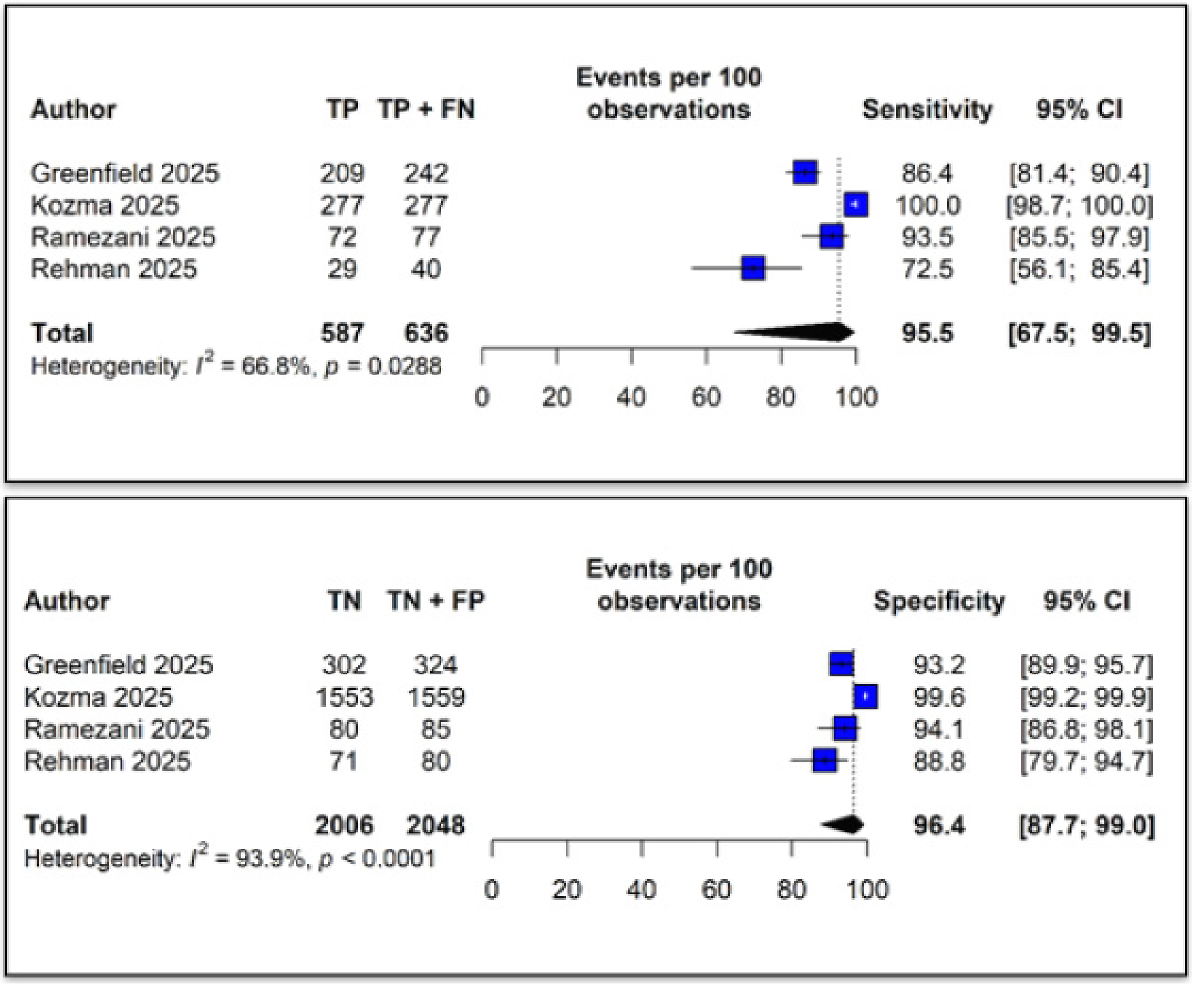

Figure 3: Forest plots of sensitivity and specificity.

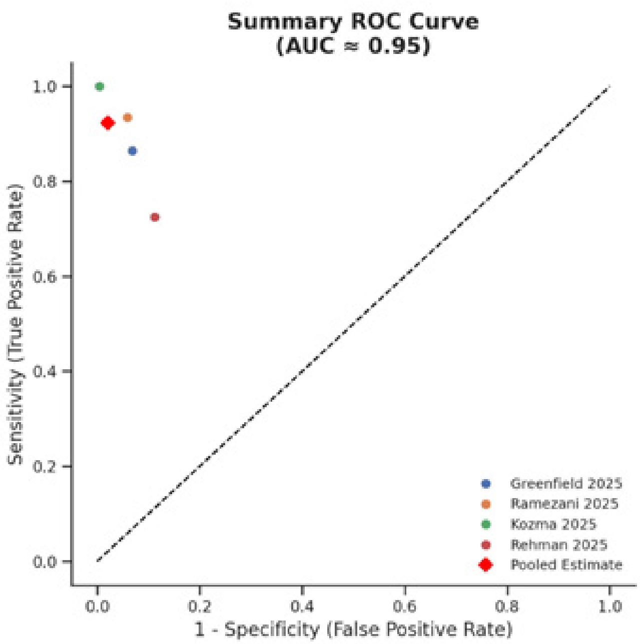

Figure 4: Summary ROC curve.

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ABBREVIATIONS

- AI: Artificial Intelligence
- AUC: Area Under the Curve
- AS-OCT: Anterior Segment Optical Coherence Tomography
- CNN: Convolutional Neural Network
- CV: Cross-Validation
- DTA: Diagnostic Test Accuracy
- FDA: Food and Drug Administration
- H&E: Hematoxylin and Eosin
- HSROC: Hierarchical Summary Receiver Operating Characteristic
- IDx-DR: AI System for Diabetic Retinopathy Detection
- IVCM: In Vivo Confocal Microscopy
- KNN: K-Nearest Neighbors
- MeSH: Medical Subject Headings
- ML: Machine Learning
- OCT: Optical Coherence Tomography
- OSSN: Ocular Surface Squamous Neoplasia
- PCA: Principal Component Analysis
- PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
- PROSPERO: International Prospective Register of Systematic Reviews
- QUADAS-2: Quality Assessment of Diagnostic Accuracy Studies, version 2
- ROC: Receiver Operating Characteristic
- SROC: Summary Receiver Operating Characteristic
- SVM: Support Vector Machine