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A systematic review of using clinical decision support systems in corneal diseases

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Abstract

Background: Corneal diseases encompass a wide spectrum of eye diseases, and are among the leading causes of blindness. The use of clinical decision support systems (CDSSs) can assist physicians in timely diagnosis of these diseases and prevent their progression.

Objective: The present study aimed to conduct a systematic review of using CDSSs in corneal diseases to identify gaps in the current knowledge and propose for future research in designing, implementation, and effective use of health information technology in ophthalmology, with a specific focus on corneal diseases.

Methods: This systematic review was conducted in 2024. To retrieve relevant articles, PubMed, Web of Knowledge, Scopus, the Cochrane Library, IEEE Xplore, and ProQuest databases as well as Google Scholar were searched until end of September 2024. After assessing the quality of the articles and risk of bias, the results were reported descriptively.

Results: Out of 279 articles, only eight articles met the research criteria. The results showed that clinical decision support systems were mainly developed for diagnosing corneal diseases, referring patients with low vision for rehabilitation, and identifying extraocular muscle pathology in strabismus. The systems were developed using different programming languages, their input data were patient data and images, and the output was diagnosis and more information about diseases. Most of the systems were active and used a knowledge base. The performance of the systems was evaluated by comparing physicians' diagnosis and the system outputs, investigating users' perspectives, and calculating accuracy, specificity, and sensitivity values.

Conclusion: The use of clinical decision support systems in corneal diseases leads to improve timely diagnosis, error reduction, and user satisfaction. However, further research is recommended to expand the use of new technologies such as artificial intelligence in the diagnosis of corneal diseases.

Keywords

Clinical decision support system, corneal diseases, anterior segment of the eye

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Introduction

The prevalence of corneal diseases varies among different countries and populations. However, it can be leading cause of more than 6 million vision loss worldwide.[1,2] Corneal diseases are the fifth cause of blindness,[3] and includes a wide range of eye inflammations and infections that may lead to corneal ulcers.[4]

Factors such as aging,[5] infections,[6] genetic predispositions,[7] ocular traumas,[8] wearing contact lenses,[9] as well

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as systemic diseases like endocrine disorders, Graves' disease, Addison's disease, hyperparathyroidism, viral and bacterial infections, autoimmune conditions, inflammatory disorders, and genetic abnormalities can lead to damage and dysfunction in cornea.[10] In fact, corneal diseases are among the most significant eye conditions that can lead to cloudiness, deviation, ulcers, and ultimately blindness. The most common corneal diseases are keratitis, dry eye, corneal ulcer, keratoconus, cataract, strabismus, and pterygium.[11,12]

Recently, healthcare organizations started using diverse information technologies and digital tools to provide high quality services.[12] In various medical fields, different information systems, such as clinical decision support systems (CDSS), have been used to facilitate data processing, data management, and disease diagnosis. CDSS are computer systems that influence physicians' decision-making processes in various fields. These systems typically use various computer algorithms to process and analyze medical data, generate alternative decisions, and support diagnostic or therapeutic methods.[12]

The use of CDSS in the field of ophthalmology has also increased. This approach has facilitated decision-making in complex diagnostic and therapeutic cases. Otherwise, the massive volume of generated data, especially in corneal diseases such as keratoconus, dry eye, corneal infection, cataracts, etc., makes the diagnostic process more challenging.[12] Given the importance of providing high quality eye care services and the high cost of potential errors, the necessity of using these systems to assist ophthalmologists is inevitable. Moreover, general practitioners (GPs) and primary eye care practitioners (like optometrists) can use these systems to improve early detection of anterior eye diseases, diagnose diseases quicker, and provide more precise treatment plans. Not only healthcare providers, but also patients can use this technology to monitor their own diseases.[13] Various studies showed that CDSSs have been used in many areas of ophthalmology[14–23]; however, only a few studies have focused on the development and evaluation of these systems for corneal diseases. Therefore, the aim of the present study was to conduct a systematic review of using CDSSs in corneal diseases. The results of this study can be used to identify gaps in the current knowledge and propose opportunities for future research in designing, implementation, and effective use of health information technology in ophthalmology, with a specific focus on corneal diseases.

Materials and methods

This systematic review was conducted in 2024. Before conducting the research, ethics approval was obtained from Iran University of Medical Sciences (IR.IUMS.REC. 1402.192).

Eligibility criteria

In this study, all papers which focused on developing and using CDSS in corneal diseases were searched until end of September 2024. To include articles, they should be published in English with a full-text available and relevant to the aim of the study. Review articles, letters to the editor, protocols, articles in languages other than English, and articles whose full texts were not available were excluded from the study.

Information sources

To retrieve relevant articles, PubMed, Web of Knowledge, Scopus, the Cochrane Library, IEEE Xplore, ProQuest databases, as well as Google Scholar search engine were searched. In addition, the OpenGrey database was searched to find any relevant grey literature. The search process was carried out with reference checking and citation tracking, and all relevant articles were examined.

Search strategy

In order to develop a search strategy, MeSH Terms (Medical Subject Headings) such as clinical decision support system, computer assisted diagnosis, clinical decision-making, computer assisted decision making, anterior eye segments, and cornea were used. Search strategies in different databases are presented in Appendix I.

Selection process

The screening process was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram. After retrieving relevant articles, reference management was conducted using EndNote software (version X7), and duplicate items were removed. Titles, abstracts, and full texts of the retrieved studies were screened. The initial search and screening processes were conducted by one of the authors (FE). Then, the remaining articles were independently screened and evaluated by other authors (HA). Any discrepancies were resolved via discussion with the third author (KZ).

Data collection process

Data were extracted using a data extraction form that included the name(s) of author(s), year of publication, country, research objective, research methodology, system characteristics, evaluation criteria, and a summary of the findings. The first author (FE) initially collected the data, and the reports were independently reviewed by other researchers. In case of any disagreement, researchers discussed the issue and resolved it through consensus.

Data elements

In this study, the characteristics of the designed systems, as well as the methodologies used to evaluate these systems were examined and compared in various studies.

Quality and risk of bias assessment

Since the selected articles aimed at diagnosing diseases or addressing corneal problems in patients, and included various qualitative, quantitative, and mixed-methods studies, the Mixed Methods Appraisal Tool (MMAT) was used to assess quality of these articles. This checklist consists of two general questions and five sections, each containing five questions for qualitative studies, quantitative randomized controlled trials, quantitative nonrandomized studies, quantitative descriptive studies, and mixed-methods studies. The responses to the questions include Yes, No, Can't tell, and Comments.[24] The MMAT results were deemed acceptable, allowing inclusion of identified studies, as no articles presented low quality or high risk of bias. Moreover, a checklist from the Joanna Briggs Institute (JBI) was used to assess the risk of bias in the selected studies. This checklist consisted of eight questions, and each question had four options: Yes, Unclear, No, and Not Applicable.[25] The assessment was independently conducted by two researchers (FE and HA).

Synthesis methods

After extracting the necessary data using the data collection form, the results were categorized and reported descriptively. To summarize data, tables were developed based on the data extraction form, and the results were synthesized narratively. As different systems were developed and evaluated, it was not possible to conduct a meta-analysis. Therefore, the system characteristics and evaluation methodologies were described.

Results

Study selection

Initially, 279 articles were identified, and 39 duplicate records were removed. The remaining papers were 240 which were examined in terms of their title and abstract relevancy with the aim of the current study. In this process, 209 irrelevant papers were removed and 31 papers remained to get access to their full texts. There was no access to the full texts of three articles and they were excluded. Then, the full texts of 28 remaining articles were fully reviewed, and some papers were excluded. The main reasons for excluding papers were as follows: the CDSS was not developed ($n = 15$), and the system was developed for other eye diseases ($n = 5$). Finally, eight studies were selected for further review. Figure 1 illustrates the process of article selection in a PRISMA diagram.

Study characteristics

The findings indicated that the selected studies were conducted between 1994 and 2022 in Iran,[18] the United States,[14,23] Ukraine,[12] India,[19] Lebanon,[15] Spain,[21] and Singapore.[22]

The main objective of these studies was diagnosing and determining the severity of dry eye,[18] identifying patients for low vision rehabilitation,[14] identifying extraocular muscle pathology in patients with strabismus,[12] diagnosing anterior segment eye abnormalities,[19] grading and mapping corneal haze,[15] diagnosing red eye,[21] automatic grading of nuclear cataract,[22] and differentiating keratoconus patterns from other conditions.[23] A summary of the selected papers is presented in Table 1.

Quality and risk of bias assessment in the studies

The results of quality and risk of bias assessment are presented in Tables 2 and 3. According to the results, most of the studies were acceptable in terms of quality and had a low risk of bias.

Results of individual studies

System development

Two main approaches were used to develop CDSS. In the studies conducted by Ebrahimi et al., Guo et al., and López et al. the relationships between variables were first identified using If-Then rules (conditional statements used in logic and programming, and consist of two parts: the "if" part (antecedent) states a condition, and the "then" part (conclusion) specifies an action or result that follows if the condition is met). Subsequently, the coding was completed and the final system was developed.[14,18,21] However, in other studies, an image processing methodology was used to develop the system.[12,15,19,22,23] The designed systems were either passive (the system operated independently and there was no need for the user to wait) or active (the user directly interacted with the system and had to wait to get feedback to continue working with the system). The results showed that a passive system was used only in one study,[14] and other systems worked actively.[12,15,18,19,21–23]

In addition, three studies designed knowledge-based systems, as the relationships between variables (independent and dependent) were established according to the opinions of corneal specialists,[18] experts[14] and guidelines.[14,18,21] The other five systems were not knowledge-based, but simply identified patterns based on the trained data.[12,15,19,22,23]

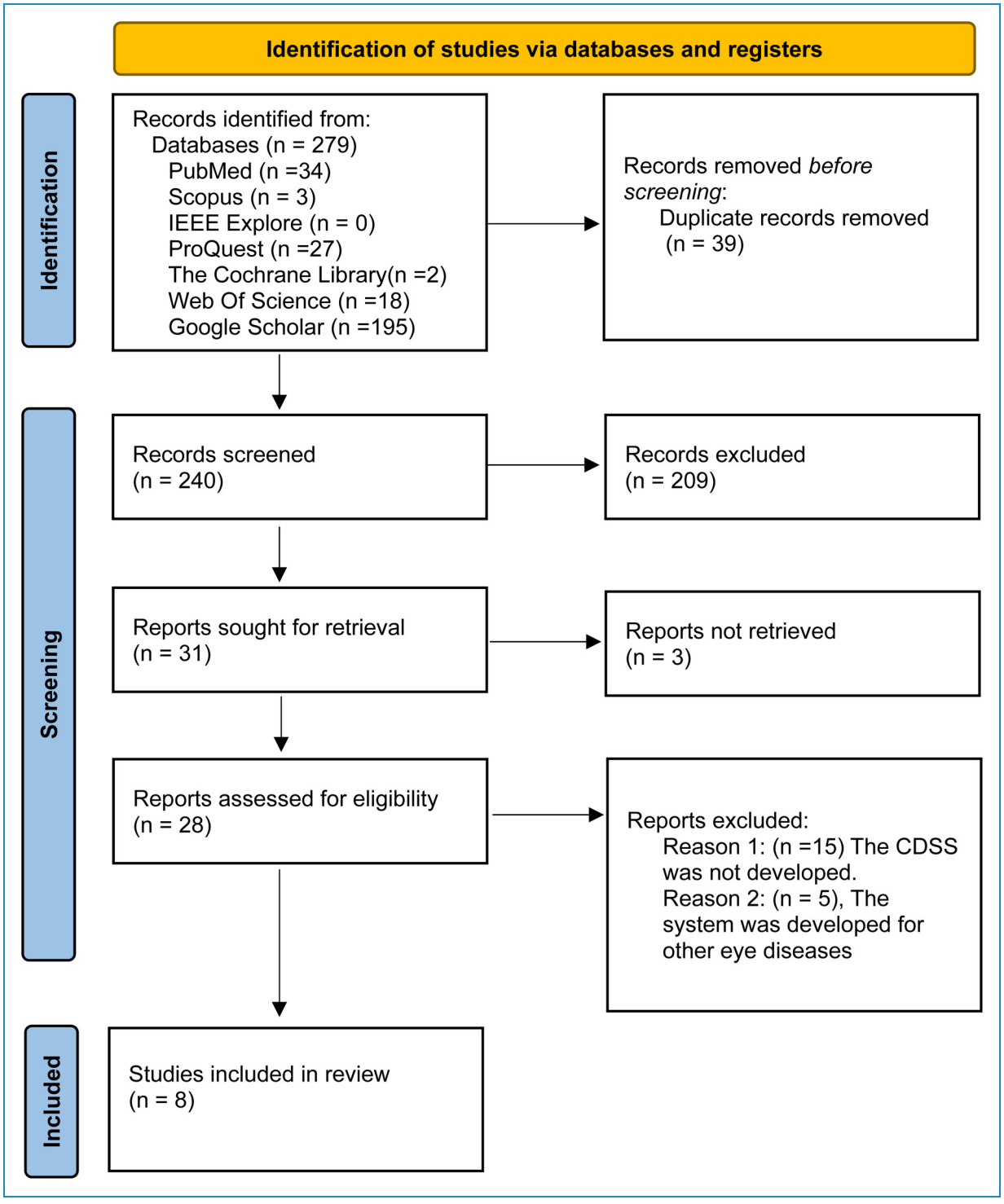

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram.

System evaluation

Except one study,[12] other studies evaluated the clinical decision support system. Evaluation was performed through investigating users' opinion about usefulness and user interface[14,21] or comparing final diagnoses,[18] images[17,19] and videos[23] with the system performance. The accuracy, sensitivity, and specificity of the system developed for dry eye were 96.9%, 97.5%, and 93.7%, respectively. Moreover, the system's performance and the opinions of corneal specialists were compared using

Table 1. A summary of the selected papers.

No	Author, year	Country	Objective	Methods	System characteristics	Evaluation criteria	Results
1	Ebrahimi et al. 2022[18]	Iran	To develop a clinical decision support system for diagnosing and determining severity of dry eye disease	This research was carried out in two phases: 1) a questionnaire was designed to identify the most important diagnostic parameters from the cornea specialists' perspectives (n = 37), 2) a CDSS was designed and evaluated using patient data (n = 50).	The system interface consisted of three parts: demographic information of a patient, diagnostic parameters, and results for diagnosing and determining severity of dry eye disease. It was designed using MATLAB environment.	The specificity, sensitivity, and accuracy of the system performance were calculated and compared to the specialists' diagnoses using Kappa statistical test.	The diagnostic parameters for dry eye disease were filamentary keratitis, meibomian gland dysfunction, score of ocular surface disease index, Schirmer's test result, tear meniscus height, tear breakup time, and fluorescein staining score. The system output variables were the diagnosis and severity of dry eye disease at four levels for the right and left eyes, separately. The results of the evaluation study showed that the accuracy, sensitivity and specificity of the system were 96.9%, 97.5%, and 93.7%, respectively. The results of the Kappa test revealed a very good agreement between the system performance and the specialists' diagnoses.
2	Guo et al. 2021[14]	USA	To develop and evaluate an electronic health record (EHR) -based clinical decision support system (CDSS) to identify patients meeting criteria for low vision rehabilitation (LVR) referral.	The project included three phases: 1) developing a prototype based on the guidelines. 2) updating the system after 7 months. 3) incorporating further refinement of the alert appearance during the patient encounter. In total, 15 ophthalmologists from 8 subspecialties participated in the design and implementation process.	CDSS was based on EHR and appeared as an alert. Alert firing relied on visual acuity and International Classification of Diseases (ICD)-10 diagnosis (hemianopia/ quadrantanopia) criteria.	False positive rates (firing for encounters with suppression reasons, firing without criteria met), and false negative rates (not firing when visual acuity or diagnosis criteria met) were calculated.	The alert suppression considerations included age < 5 years, recent surgeries, prior LVR visit, and related alert actions. False positive rate was 0.2%, and the overall false negative rate was 5.6%. Among 13 physicians who completed the survey, 8 agreed that the alert was easy to use, and 12

(continued)

Table 1. Continued.

No	Author, year	Country	Objective	Methods	System characteristics	Evaluation criteria	Results
							would consider ongoing usage.
3	Kochina et al. 2020[12]	Ukraine	To substantiate and develop an automated CDSS for extraocular muscle (EOM) pathology in strabismus	To develop an extraocular muscle pathology classification based on corneal interference patterns, the researchers used (1) parameters of interference patterns for 147 strabismic patients in whom the presence of pathology of specific EOM was confirmed, and (2) parameters of calculated isochromes produced by modeling of the stress-strain state of the cornea in various structural and functional states of the EOM.	The system included a user interface and a database for storing and retrieving information. The database included patient information, eye images, the diagnostic patterns, and the angles of the target patterns.	Not reported	By using patient data, fuzzy models and interference pattern processing software were developed. The main features of the interference patterns for various types of strabismus were identified, and an automated system using the above informative interference pattern parameters was proposed for extraocular rectus muscle pathology in strabismus.
4	Mahesh Kumar and Gunasundari, 2018[19]	India	To propose a multiclass computer-aided diagnosis (CAD) system using visible wavelength (VW) eye images to diagnose anterior segment eye abnormalities	The support vector machine (SVM) by Sequential Minimal Optimization (SMO) algorithm was used for classifying 228 VW eye images.	The normal and abnormal VW eye images were used as input for the diagnostic system, which was developed in the MATLAB software environment.	Three different classes of anterior segment eye abnormalities were identified and sensitivity, specificity and accuracy of the system were calculated.	The proposed system achieved a predictive accuracy of 96.96% with 97% sensitivity and 99% specificity.
5	Dhaini et al. 2018[15]	Lebanon	To evaluate a proposed technology for offering objective grading and mapping of corneal haze as detected by corneal spectral domain optical coherence tomography after corneal cross-linking	A retrospective study to evaluate corneal optical coherence tomography images performed on 44 eyes of 44 patients who underwent corneal cross-linking.	The system was designed using the OpenCV image processing library to take Optical Coherence Tomography (OCT) images of the OCT video file cube sections as input. It provided diagnosis, classification, and statistical information on corneal opacity.	Descriptive statistics were used to report mean and SDs for continuous variables. The paired t-test was used to compare haze intensity and area between different time points. Two-way repeated measures analysis of variance with the Bonferroni correction for post hoc analysis was used to compare	Overall average brightness of the cornea was markedly increased from 43.4% (±6.0) at baseline to 50.2% (±4.4) at 1 month, 47.9% ± 4.4) at 3 months, and 46.4% (±5.7) at 6 months with $P < 0.001$, < 0.001, and <0.005, respectively. In the anterior stroma, the average brightness significantly increased at 1, 3, and 6 months with

Table 1. Continued.

No	Author, year	Country	Objective	Methods	System characteristics	Evaluation criteria	Results
						the change in haze after corneal cross-linking.	values of 54.8% (±3.9), 52.5% (±5.2), and 49.7% (±6.9) with $P <$ 0.001, < 0.001, and <0.003, respectively. In the mid stroma, the change was clinically significant at 1 and 3 months, whereas in the posterior stroma, it was only significant at 1 month compared with baseline (P = 0.003).
6	López et al. 2016[21]	Spain	To develop OphthalDSS, a mobile decision support system for red eye diseases diagnosis	The decision support system was supported by an algorithm that provided diagnosis for more than 30 diseases. Diseases were classified in four big groups attending the form of hyperaemia.	The CDSS was developed by using the Java language for Android smartphones. The algorithms were developed by using if/then rules	Quality of users' experiences were evaluated by a short questionnaire.	The OphthalDSS was capable of diagnosing more than 30 eye's anterior segment diseases. A total of 67 medical students evaluated the system. Most of the students agreed that OphthalDSS did the function that they expected, the information was reliable, it was intuitive, effective, and had an appropriate interface
7	Li et al. 2010[22]	Singapore	To develop a system for automatic grading of nuclear cataract (AGNC).	Anatomical structure in the lens image was detected using a modified active shape model. On the basis of the anatomical landmark, local features were extracted according to the clinical grading protocol. Support vector machine regression was used for grade prediction using 5850 slit lamp images.	The system was developed in MATLAB, and had three components: structure detection, feature extraction, and grade prediction of nuclear cataracts	For the accuracy of feature extraction, lens structure detection results were evaluated, and the automatic grades from AGNC system were compared to the grader's grading results.	The AGNC system achieved 96.9% success rate for lens localization and 95% success rate for lens structure detection. The comparison results showed that average grading difference was 0.36 on a scale of 5.0.
							A paired t-test between automatic grades and grader's grades was

(continued)

Table 1. Continued.

No	Author, year	Country	Objective	Methods	System characteristics	Evaluation criteria	Results
							performed, and the results showed that there was a good agreement between AGNC automatic grades and clinical grades.
8	Maeda et al. 1994[23]	USA	To develop an automated system to differentiate keratoconus patterns from other conditions using computer-assisted videokeratoscopy.	The developed system combined a classification tree with a linear discriminant function derived from discriminant analysis of eight indices (simulated K1, simulated K2, surface asymmetry index, differential sector index, opposite sector Index, center/surround index, irregular astigmatism index, and analyzed area) obtained from topography maps and videokeratoscope data. 200 cornea images were used for training and system validation.	The system was developed using the Pascal programming language. It had eight quantitative parameters as input variables from a videokeratoscope and provided the user with information regarding the presence or absence of keratoconus.	One hundred corneas with a variety of diagnoses were used for training, and a validation set of 100 additional corneas were used to evaluate the system. The efficacy of the discriminant analysis classifier and expert system was compared by using the validation set. The results, were described in terms of sensitivity, specificity and accuracy.	In discriminant analysis 19 out of 22 cases of clinically diagnosed keratoconus were detected, with no false-positive cases in the training set. In the validation set, 19 out of 28 keratoconus cases were detected with one false-positive case. Sensitivity, specificity, and accuracy were 86%, 100%, and 97% in the training set, and they were 68%, 99%, and 90% in the validation set, respectively. The optimum cutoff value in the expert system was 0.28 for the most sensitive and accurate results in the training set. Therefore, sensitivity, specificity, and accuracy were 100%, 96%, and 97% in the training set, and 89%, 99%, and 96% in the validation set, respectively. The sensitivity with the expert system classifier (89%) was significantly better than the sensitivity with discriminant analysis alone (68%).

Table 2. Quality assessment of articles using MMAT

Category of study designs	Methodological quality criteria	Ebrahimi et al.	Guo et al.	Kochina et al.	Mahesh Kumar and Gunasundari	Dhaini et al.	López et al.	Li et al.	Maeda et al.
Screening questions (for all types)	S1. Are there clear research questions?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	S2. Do the collected data allow to address the research questions?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Further appraisal may not be feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.								
1. Qualitative	1.1. Is the qualitative approach appropriate to answer the research question?	Yes	Yes	Can't tell			Yes		
	1.2. Are the qualitative data collection methods adequate to address the research question?	Yes	Yes	Can't tell			Yes		
	1.3. Are the findings adequately derived from the data?	Yes	Yes	Can't tell			Yes		
	1.4. Is the interpretation of results sufficiently substantiated by data?	Yes	Yes	Can't tell			Yes		
	1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?	Yes	Yes	Can't tell			Yes		
2. Quantitative randomized controlled trials	2.1. Is randomization appropriately performed?								
	2.2. Are the groups comparable at baseline?								
	2.3. Are there complete outcome data?								
	2.4. Are outcome assessors blinded to the intervention provided?								
	2.5 Did the participants adhere to the assigned intervention?								
3.Quantitative nonrandomized	3.1. Are the participants representative of the target population?	Yes			Yes	Yes		Yes	Yes
	3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?	Yes			Yes	Yes		Yes	Yes

(continued)

Table 2. Continued.

Category of study designs	Methodological quality criteria	Ebrahimi et al.	Guo et al.	Kochina et al.	Mahesh Kumar and Gunasundari	Dhaini et al.	López et al.	Li et al.	Maeda et al.
	3.3. Are there complete outcome data?	Yes			Yes	Yes		Yes	Yes
	3.4. Are the confounders accounted for in the design and analysis?	Yes			Yes	Yes		Yes	Yes
	3.5. During the study period, is the intervention administered (or exposure occurred) as intended?	Yes			Can't tell	Can't tell		Can't tell	Can't tell
4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the research question?		Yes						
	4.2. Is the sample representative of the target population?		Yes						
	4.3. Are the measurements appropriate?		Yes						
	4.4. Is the risk of nonresponse bias low?		Yes						
	4.5. Is the statistical analysis appropriate to answer the research question?		Yes						
5. Mixed methods	5.1. Is there an adequate rationale for using a mixed methods design to address the research question?	Yes	Yes						
	5.2. Are the different components of the study effectively integrated to answer the research question?	Yes	Yes						
	5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted?	Yes	Yes						
	5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?	Yes	Yes						
	5.5. Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?	Yes	Yes						

Table 3. Risk of bias assessment

	Studies Questions	Ebrahimi et al.	Guo et al.	Kochina et al.	Mahesh Kumar and Gunasundari	Dhaini et al.	López et al.	Li et al.	Maeda et al.
1	Were the criteria for inclusion in the sample clearly defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2	Were the study subjects and the setting described in detail?	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
3	Was the exposure measured in a valid and reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4	Were objective, standard criteria used for measurement of the condition?	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
5	Were confounding factors identified?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6	Were strategies to deal with confounding factors stated?	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
7	Were the outcomes measured in a valid and reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8	Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Overall appraisal		Included	Included	Included	Included	Included	Included	Included	Included

Kappa statistics, demonstrating very good agreement.[18] In Guo et al.'s study, the system performance, ease of use, and usefulness were evaluated. For performance evaluation, the focus was on the accuracy of alerts firing, and false positive (0.2%) and negative rates (5.6%) were calculated. Eight physicians found alerting and working with the system easy, and twelve were interested in using the system.[14] Mahesh Kumar and Gunasundari evaluated their system using 228 eye images, and reported system accuracy (96%), sensitivity (97%), and specificity (99%).[19]

For corneal haze detection system, a paired t-test was used to compare the haze intensity and area at different times. The overall corneal clarity significantly increased from 43.4% initially to 50.2% at 1 month, 47.9% at 3 months, and 46.4% at 6 months.[15] In the study conducted by López et al. OphthalDSS was able to diagnose more than 30 anterior segment eye diseases, and most students agreed that the developed system worked well, provided reliable information, was understandable, and had a suitable user interface.[21]

Li et al. evaluated the AGNC system using 5850 slit-lamp images and compared the automatic AGNC system grades with the grader's grading results. The success rate was 96.9% for determining lens location and 95% for detecting lens structure. Furthermore, the result of a paired t-test between the automatic grading system and the human grader demonstrated a strong agreement between these two.[23]

Maeda et al. used a videokeratoscope to evaluate their automated system against discriminant analysis on 100 corneas with various diagnoses. In discriminant analysis, the sensitivity, specificity, and accuracy of keratoconus detection system were 68%, 99%, and 90%, respectively. For the automated system, the sensitivity, specificity, and accuracy were 89%, 99%, and 96%, respectively. Sensitivity with the automated system classifier (89%) was significantly better than the sensitivity with discriminant analysis (68%).[23]

Results of syntheses

Due to the importance of corneal diseases and the possibility of vision loss in case of the late intervention or misdiagnosis, the use of CDSS has been suggested to help ophthalmologists, optometrist, and other eye care professionals to diagnose diseases as soon as possible and prevent patients serious conditions at the later stages of disease progression. The evaluation results of several studies also showed that these systems were successful in accurate diagnosis. According to the results, in addition to several clinical parameters, the analysis of eye images can be helpful for accurate diagnosis. Therefore, it seems that future CDSSs can use the potentials of artificial intelligence (AI) and imaging informatics to analyze eye images and facilitate making decisions by eye care providers.

Discussion

In this research, articles related to the use of CDSS in corneal diseases were reviewed. Although the number of studies which met the inclusion criteria was limited, the results indicated that the system characteristics as well as the method of system development and evaluation were different. The designed systems were mainly developed to support clinical diagnosis, were either active or passive, and divided into the knowledge-based or non-knowledge-based systems. The input and output variables were also different based on the main purpose of system development. Apart from differences, using these systems could improve accuracy, sensitivity and specificity of diagnosis, and users were satisfied with using these systems in clinical decision making.

The results showed that most of the systems were designed to assist making the right diagnosis and screening patient condition. Moreover, in most studies, the system was developed to facilitate diagnosing one[12,15,18,22,23] or multiple corneal diseases.[19,21] However, in one study, the focus was on diagnosing and referring visually impaired individuals to the rehabilitation services.[14] It should be noted that different types of CDSS are responsible for various tasks, such as presenting clinical guideline, generating documentation templates, computerized alerts and reminders, diagnostic support, management support, and contextually relevant reference information. Many systems can be developed and used for each task in different areas of eye care to improve healthcare quality.[26] CDSSs are also effective in managing diseases that frequently lead to medical visits and directly impact quality of life, such as ocular morphological pathology.[21]

In terms of active or passive performance, most studies designed an active system, and only one study developed a passive system.[14] In fact, active systems help users to be informed about doing the right things automatically, and this approach is much more effective than using passive systems, in which users need to inquire about the correct things to do. The active CDSS works in real-time and requires more accurate design with special focus on the details, which might be very essential. However, these systems may also generate too many false-positive alerts, which can be annoying. In addition, passive CDSS require more users' effort, and users must make a specific query to request advice.[27]

Moreover, some systems were knowledge-based,[14,18,21] and some others were non-knowledge-based systems.[12,15,19] In knowledge-based systems, IF-THEN rules are generated, and the system uses data to evaluate the rules, and producing an output or a recommendation. Rules can be made using literature, best practices, or evidence. Those CDSSs that are non-knowledge-based require a data source, but it is based on AI, machine learning (ML), or statistical pattern recognition. While the use of non-knowledge-based system is increasing, there are still concerns over the accuracy of decisions made by these systems.[26] However, due to the advancement of AI, it is expected that the future CDSSs do not use a knowledge base and rely on the computational analysis.

In three studies, the clinical decision support systems were developed using the MATLAB software environment,[8,19,22] while in other studies, the systems were development using other languages and environments.[12,14,15,21–23] In fact, a specific programming language is chosen based on the suitability of it for certain tasks or specific operating systems.[27]

The system inputs included both numerical/textual data[14,18,21] and images.[12,15,19,22,23] A variety of data input indicated that there are many opportunities for system development in the future and AI can be used to facilitate this process. Clinical data in the form of unstructured text, images, or signals are remained unexplored and could be potentially used to develop effective CDSS. The use of multi-type clinical data in a CDSS is another area of research which is worth investigation.[28] Regarding the CDSS for corneal diseases, it seems that in addition to signs and symptoms, eye images are helpful for diagnosis and future systems can be developed by using different types of data.

In order to evaluate CDSSs, either the real data were used,[15,18,19,22,23] the system results were compared to the physicians' opinions in the patient records, or users' perspectives were investigated. The evaluation results might be presented quantitatively and qualitatively. Overall, the system evaluation results were satisfactory, and users evaluated the system as useful, reliable, and effective tools.[14,21] The evaluation of a CDSS should validate its efficacy, safety, usability, reliability and reproducibility. However, validation methods vary depending on the type of CDSS and its purpose. The value of a CDSS should also be considered in terms of its long-term implications and the need to improve it based on new research findings and discoveries.[24]

Overall, it seems that the use of CDSS in corneal diseases may have received less attention compared to other eye diseases. Therefore, with respect to the advancement of technology, it seems that future research can be directed to use new technologies such as AI to examine the effectiveness of the new systems in terms of reducing the rates of misdiagnosis and improving patient outcomes.

Research limitations

Although a comprehensive search was conducted in six databases as well as Google Scholar, there might be papers that were not included in the current study. These papers might not be in English, their full texts were not available, were indexed in other databases, or were published after submitting the current study. Moreover, mobile-based applications were not considered in this research, as they may not be specifically developed for corneal diseases. Future research can focus on investigating the applications of other computer-aided tools for diagnosing different eye diseases.

Conclusion

In this study, the use of clinical decision support systems in corneal diseases was investigated. These systems were mainly developed to aid diagnosis and included active/passive, knowledge-based and non-knowledge based systems. In addition, different methodologies were used to evaluate their performance. The results showed that the use of CDSS in ophthalmology aided in disease diagnosis and improved quality of patient care services. As the number of the retrieved studies related to corneal diseases was quite limited, it seems that further research can contribute to improve the use of CDSS in teleophthalmology, referral refinement, and resource management especially in deprived geographical areas with a focus on corneal diseases. This can help patients and healthcare providers to make more efficient decisions, and can improve quality of care.

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Appendix I: Search strategies

Search strategy	Databases
((“Clinical decision support system"[Title/Abstract] OR “Clinical decision support system"[MeSH Terms] OR “Computer Assisted Diagnosis"[Title/Abstract] OR “Clinical Decision-Making"[Title/Abstract] OR “Computer Assisted Decision Making"[Title/Abstract] OR “Computer Assisted Diagnosis”[MeSH Terms]) AND (“Anterior Eye Segments"[Title/Abstract] OR (“Anterior Eye Segments"[MeSH Terms] OR “cornea"[Title/Abstract] OR “cornea"[MeSH Terms]))	PubMed
TS:(((“Clinical decision support system” OR “Computer Assisted Diagnosis” OR “Clinical Decision-Making” OR “Computer Assisted Decision Making”) AND (“Anterior Eye Segments” OR “cornea”))) OR AB = (((“Clinical decision support system” OR “Computer Assisted Diagnosis” OR “Clinical Decision-Making” OR “Computer Assisted Decision Making”) AND (“Anterior Eye Segments” OR “cornea”)))	Web of Knowledge
TITLE-ABS-KEYWORDS ((“Clinical decision support system” OR “Computer Assisted Diagnosis” OR “Clinical Decision-Making” OR “Computer Assisted Decision Making”) AND (“Anterior Eye Segments” OR “cornea”))	Scopus
(“Clinical decision support system” OR “Computer Assisted Diagnosis” OR “Clinical Decision-Making” OR “Computer Assisted Decision Making”) AND (“Anterior Eye Segments” OR “cornea”) in Record Title OR (“Clinical decision support system” OR “Computer Assisted Diagnosis” OR “Clinical Decision-Making” OR “Computer Assisted Decision Making”) AND (“Anterior Eye Segments” OR “cornea”) in Abstract–(Word variations have been searched)	The Cochrane Library
(“All Metadata":(”Clinical decision support system” OR “All Metadata":"Computer Assisted Diagnosis” OR “All Metadata":"Computer Assisted Decision Making”)) AND (“All Metadata":(”Anterior Eye Segments” OR “All Metadata":"cornea"))	IEEE Xplore
Title (((“Clinical decision support system” OR “Computer Assisted Diagnosis” OR “Clinical Decision-Making” OR “Computer Assisted Decision Making”) AND (“Anterior Eye Segments” OR “cornea”))) OR abstract(((“Clinical decision support system” OR “Computer Assisted Diagnosis” OR “Clinical Decision-Making” OR “Computer Assisted Decision Making”) AND (“Anterior Eye Segments” OR “cornea”)))	ProQuest
((“Clinical decision support system” OR “Computer Assisted Diagnosis”) AND (“Anterior Eye Segments” OR “cornea”))	Google Scholar