Original article

Developing an approach to differential diagnosis of eye diseases based on knowledge formalization

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Abstract:
Objective: to develop and explore an approach to differential diagnosis of eye diseases based on knowledge formalization, aimed at application in primary health care.
Materials and methods. We proposed a formal model of the subject area, including sets of symptoms, diagnostic hypotheses, linguistic variables, membership functions, inference rules, and a priori assessments of the disease. We developed a hybrid method of diagnostic inference, combining fuzzy logic and Bayesian probability hypothesis refinement. This method served as a basis for the creation of a decision-making system. An experimental evaluation was conducted at the Department of Clinical Diagnosis of the Eye Disease Clinic (Razumovsky State Medical University of Saratov). The results of patient examinations performed by ophthalmologists with at least three years of experience as part of routine practice were compared with the decision-making system conclusion.
Results. The proposed approach ensured the formation of a ranked list of diagnostic hypotheses and an interpretable diagnostic conclusion. In noise-free scenarios, the mean diagnostic accuracy was 82.86%, while in the presence of noise and with contradictory symptoms, it amounted to 85.71% and 76.19%, respectively. This approach demonstrates its superior robustness and lower computational cost vs. a solution based on a large language model.
Conclusion. The developed approach allows for the formalization of diagnostic knowledge, accounts for the ambiguity and incompleteness of clinical information, and ensures the interpretability of diagnostic inference. The obtained results confirm the potential of this approach for use in primary care decision support systems.

Keywords: eye diseases; differential diagnosis; knowledge formalization; fuzzy logic; Bayesian inference.

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Introduction

Timely and high-quality diagnosis of eye diseases remains very important for the contemporary healthcare system, particularly at the primary health care (PHC) level. In remote and sparsely populated areas, PHC often becomes the prime level of medical care, but initial appointments are carried out in conditions of a shortage of specialist doctors and limited availability of specialized diagnostic equipment. Many diseases, such as glaucoma, cataracts, diabetic retinopathy, and age-related macular degeneration (AMD), require early detection. Failure to diagnose eye diseases in a timely manner can lead to irreversible visual impairment and a deterioration in patients' quality of life [3, 7, 9, 11].

In recent years, clinical decision support systems (CDSS) have become increasingly common in this area, as they improve diagnostic accuracy, reduce physician workload, and improve treatment outcomes. As for the factors affecting the development of CDSS, it should be noted that various pathological conditions (for example, AMD or diabetic retinopathy) are often asymptomatic in their early stages. CDSS can detect pathological changes earlier than a physician, which is critical for preserving vision. A shortage of ophthalmologists is also a pressing issue. CDSS offer the opportunity to reduce the workload of eye care professionals. In large clinics and regions with a shortage of ophthalmologists, doctors are faced with a huge influx of patients. Artificial intelligence (AI) systems can be used in initial screening to differentiate patients into those with healthy eyes and those with obvious pathology, and in more detailed examination, to distinguish patients with high risk of disease vs. borderline conditions.

In ophthalmology, CDSS can be used not only as a diagnostic instrument but also as a teaching tool. They facilitate the transfer of knowledge, data interpretation skill improvement, and the development of clinical judgment. Such systems can be effectively used for training and professional development of various categories of specialist doctors and medical students.

The use of CDSS in teaching medical students is possible for mastering the basics of diagnosing eye diseases; learning to read optical coherence tomography (OCT), perimetry, and fundus photographs; and developing the skill of recognizing ocular pathology patterns. Along with normal and pathological values, the system provides prompts and explains the basis for the medical report.

Using the CDSS in resident training is useful for in-depth study of complicated cases and practicing diagnostic algorithms and treatment strategies. CDSS offers cases of varying complexity, provides feedback after image analysis, and can simulate a meeting with experts, demonstrating how different doctors and the artificial intelligence (AI) interpret the same image.

Introducing the CDSS to the practice of young specialists (ophthalmologists with up to three years of experience) is expected to increase their confidence in decision making and help them adapt faster to contemporary technologies. In the test your knowledge mode, the young doctor makes a diagnosis and then compares it with the AI's suggestion. The system helps develop clinical memory by memorizing rare pathology patterns.

CDSS in ophthalmology can also be used by physicians in related specialties (internists, endocrinologists, neurologists, or pediatricians) to apprehend the ophthalmological manifestations of systemic diseases and determine the urgency of referral to an ophthalmologist.

It is worth noting that the best results are achieved by CDSSs based on explainable AI (XAI): they formalize expert knowledge, since they provide explanations for decisions made, which is important for specialist doctor training.

For experienced ophthalmologists (as part of their advanced training), the CDSS is useful for mastering new technologies (e.g., AI analytics of OCT angiography), training in rare and complicated cases, and preparing for medical accreditation. The system can be integrated into online courses and issue certificates upon passing tests.

The advantages of CDSS-based training include interactivity, instant feedback, accessibility (training at any time, in any remote region), standardization (training on the same high-quality data), and the capability to handle rare cases (AI can detect any rare disease).

Therefore, CDSSs in ophthalmology are already a reality of the present, rather than a matter of the future. They improve diagnostic accuracy, speed up medical examinations, and help doctors make more informed decisions. However, full automation is impossible in the coming years due to the importance of clinical judgment, ethics, and individualized approach to patient care.

We are currently at a stage of human-AI synergy: doctors use technology as a powerful tool while maintaining control over the process. This approach makes ophthalmic care more accessible, accurate, and safe.

CDSSs in ophthalmology are not just a diagnostic tool, but a comprehensive educational resource. They are useful for both novice specialists and experienced doctors, and even for specialist doctors representing related specialties. The sooner a doctor learns to work in conjunction with AI, the higher the quality of care provided and the more patients preserving their vision.

The difficulty of diagnosing eye diseases at the PHC level is determined not only by organizational constraints but also by the specifics of the field per se. A significant share of patient complaints is formulated in subjective and verbally vague terms, such as blurred vision, photophobia, discomfort, eye floaters. Moreover, objective clinical signs in the early stages of the disease may be weakly expressed or unnoticeable without the use of specialized instrumental examination methods. The overlap of symptoms of various eye diseases creates additional challenges, resulting in the diagnostic process in the form of a differential choice between several competing hypotheses [6, 15, 18].

Current intelligent methods of medical diagnosis include machine learning (especially deep learning), probabilistic models, fuzzy logic methods, and XAI approaches. Deep learning methods demonstrate high efficiency in the analysis of medical images and structured data; however, they are characterized by limited interpretability and high dependence on the representativeness of training samples [15–17, 20, 21]. Probabilistic methods allow for the consideration of uncertainty and the formalization of relationships between symptoms and diseases, but are of limited applicability to the processing of qualitative variables [1, 8, 10]. Fuzzy logic methods are well suited to the processing of subjective traits; however, taken alone, they do not provide a mechanism for the probabilistic refinement of diagnostic hypotheses [2, 12, 19]. XAI approaches are largely based on knowledge formalization, thereby allowing to receive explanations of diagnostic conclusions that are important for decision making [4, 13, 14].

Despite the active development of intelligent methods of medical diagnosis, the issue of supporting the differential diagnosis of eye diseases in PHC remains understudied. Many studies have considered hybrid methods combining fuzzy logic and probabilistic models. E.g., a study by Kościelny J. et al. proposed an approach to diagnostic inference based on a combination of fuzzy inference and Bayesian hypothesis refinement, focused on processing uncertain diagnostic data and generating explainable decisions [22]. However, that study was of a general nature and did not address the specifics of ophthalmic diagnostics, including the verbal ambiguity of patient complaints typical of a primary ophthalmological examination.

Furthermore, existing intelligent diagnostic systems are largely focused either on narrow classes of eye diseases or on the use of statistically homogeneous training samples and structured instrumental data [15–17, 20, 21, 23, 24]. Most contemporary studies focused on the analysis of fundus images and OCT data using deep learning methods, while the tasks of supporting primary differential diagnosis based on patient symptoms and complaints remain less explored. Recent reviews noted the limitations of existing AI approaches, including insufficient interpretability of models, limited representativeness of training samples, and the difficulty of extrapolating results to real-world clinical settings [23, 24].

In contrast to existing approaches, we propose a domain-specific model for supporting differential diagnosis of eye diseases based on the formalization of expert knowledge, processing of fuzzy linguistic variables, and probabilistic refinement of diagnostic hypotheses. This approach is oriented toward use in PHC settings and takes into account the incompleteness, inconsistency, and subjective nature of clinical information. Hence, the task of supporting the differential diagnosis of eye diseases in PHC requires the development of an approach that combines interpretability, resilience to incomplete and ambiguous data, the ability to explicitly represent expert knowledge, and a mechanism for probabilistic refinement of diagnostic hypotheses.

The goal of this study was to develop and explore the potential of an approach to supporting the differential diagnosis of eye diseases based on knowledge formalization and targeted for use in PHC settings.

The scientific novelty of this study lies in the development of a domain-specific XAI approach to supporting the differential diagnosis of eye diseases. This approach utilizes a formalized representation of expert knowledge, fuzzy symptom descriptions, and Bayesian probabilistic refinement of diagnostic hypotheses within a unified diagnostic inference model. Unlike existing expert systems and general-purpose intelligent methods, the proposed approach is focused on PHC settings and enables the processing of verbally ambiguous and incomplete clinical data, generating an interpretable diagnostic conclusion. An additional distinguishing feature of the developed model is its expanded range of diagnostic hypotheses, including 39 eye diseases and conditions, as well as the implementation of a mechanism for iterative refinement of the diagnostic conclusion as new features are identified.

Materials and methods

1. Formal model of the subject area. Within the developed knowledge base, we grouped diagnostic hypotheses based on their anatomical and clinical features. The model encompassed diseases of the oculomotor muscles, eyelids, conjunctiva, cornea, anterior and posterior uveal tract, lens, vitreous body, retina, and optic disc.

The proposed approach is based on the formalization of the subject area using set theory descriptions. This approach allows for the formal definition of the main entities of the diagnostic process, their attributes, and the relationships necessary for building a CDSS for the differential diagnosis of eye diseases.

A set of symptoms is defined as follows:

$$S = \{s_1, s_2, \dots, s_n\}, \quad (1)$$

where s_i is an individual symptom or clinical sign characterizing the patient's condition. Symptoms considered include, e.g., eye pain, redness, decreased visual acuity, photophobia, and lacrimation.

Each symptom is described by a set of attributes:

$$S = \{s_1, s_2, \dots, s_n\}, \quad (2)$$

where $name_i$ is the symptom name, $value_i$ is the observed value obtained from the patient or physician, and $severity_i$ is the severity of the symptom, specified linguistically, for example, mild, moderate, or severe.

To formally represent the qualitatively described clinical signs, a set of linguistic values is introduced:

$$S = \{s_1, s_2, \dots, s_n\}, \quad (3)$$

Each linguistic value is associated with a membership function:

$$\mu_{l_j}: X_i \rightarrow [0,1], \quad (4)$$

where Xi is the range of acceptable values for the corresponding symptom.

The use of membership functions allows for fuzzification of the initial clinical information and representation of symptoms as a set of membership degrees in fuzzy sets.

To describe the linguistic variables characterizing the intensity of eye pain, we used mainly trapezoidal membership functions in this study. The choice of this function type was driven by the specifics of expert description of clinical symptoms. In the course of the development of the knowledge base, ophthalmology experts specified ranges of pain intensity, rather than individual point values, corresponding to the linguistic categories of mild, moderate, and severe to determine the severity of signs, such as pain. The use of trapezoidal membership functions allowed formalizing such interval expert assessments and identify regions of complete symptom membership in the corresponding fuzzy set.

The use of trapezoidal membership functions provides:

High interpretability of expert assessments;

Model robustness to minor changes in input data;

The ability to describe smooth transitions between linguistic categories;

Reduced sensitivity of diagnostic conclusion to the subjectivity of the patient's perception of symptoms.

Trapezoidal membership functions have relatively low computational difficulty and are widely used in medical fuzzy inference systems, making them suitable for use in real-time CDSS.

As a result, each symptom can be represented by a set of membership degrees in fuzzy sets characterizing different levels of symptom expression. Thus, for the eye pain symptom, the fuzzy values 'mild', 'moderate', and 'severe' may be used, and the specific observed value will be characterized by a set of numbers from the interval [0,1] reflecting the degree of membership in these categories.

An example of a graphical definition of the membership function for the eye pain symptom is shown in *Figure 1*.

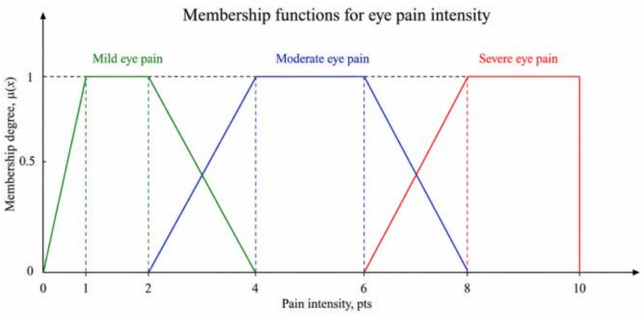

Figure 1. Trapezoidal membership function for the fuzzy set moderate eye pain

The set of diagnostic hypotheses is defined as:

D= {d1, d2,..., dk}, (5)

where each element 〖 d〗 _j corresponds to one of the eye diseases or diagnoses under consideration, the total number of which within the developed model is 39.

To describe the relationships between symptoms and diseases, we introduced a set of rules of inference:

$R=\{r_1,r_2,...,r_t\}$, (6)

Each rule complies with the following expression:

$$IF\ (s_i\ is\ l_i) AND (s_2 is l_2) AND \dots AND\ (s_p\ is\ l_p)\ THEN\ (d_j\ is\ h), \quad (7)$$

where l1, l2,...,lp ∈ L are the linguistic meanings of the symptoms, and h is a linguistic or numerical estimate of the degree of support for the diagnostic hypothesis dj.

For each hypothesis, an a priori certainty is specified:

$$P(d_j), \text{where } P(d_j) \in [0,1]. \quad (8)$$

This expression reflects the initial assessment of the certainty of the corresponding disease before taking into account the individual data of a particular patient. This certainty is determined based on expert assessments by specialist doctors.

A specific clinical case is described by a set of observed traits:

$$X = (x_1, x_2, \dots, x_n), \quad (9)$$

where x_i is the value of the symptom s_i recorded for the considered patient. The values of x_i can be quantitative, categorical, or verbal.

After the fuzzification procedure, each symptom value is assigned a set of membership degrees:

$$F(x_i) = \{\mu_{l_1}(x_i), \mu_{l_2}(x_i), \dots, \mu_{l_m}(x_i)\}, \quad (10)$$

The fuzzy description of the patient's condition is represented as:

$$F(x_i) = \{\mu_{l_1}(x_i), \mu_{l_2}(x_i), \dots, \mu_{l_m}(x_i)\}, \quad (11)$$

2. Method of differential diagnosis. The proposed method of differential diagnosis is based on the consecutive application of fuzzy inference and Bayesian probabilistic refinement of diagnostic hypotheses.

The first stage involves fuzzification of the input data. Observed symptom values are converted into membership degrees in fuzzy sets characterizing different levels of symptom severity.

For example, for the eye pain symptom, we used the linguistic values 'mild', 'moderate', and 'severe'; their membership functions are shown in *Figure 1*. To describe the fuzzy sets for the linguistic values of mild and moderate as applied to the eye pain symptom, the following trapezoidal membership functions are employed:

$$\mu(x) = \begin{cases} 0, & x \le a, \\ \frac{x-a}{b-a}, & a < x \le b, \\ \frac{c-x}{c-b}, & b < x < c, \\ 0, & x \ge c, \end{cases} \quad (12)$$

where a, b, c, d are the function parameters defining the boundaries and shape of the fuzzy set; a and d define the region outside which the membership degree is 0; b and c define the interval of complete membership. We chose trapezoidal membership functions because they naturally convey uncertainty, which is convenient for clinical experts, reflecting both full confidence in the expert assessment and areas of doubt. Furthermore, linear sections simplify the fuzzification and defuzzification algorithms, thereby reducing the computational load, compared with smoothed curves.

For the linguistic value 'severe', we used a membership function with a rectangular right-hand side.

After fuzzification, the degree of support for each diagnostic hypothesis is calculated using rules from the set R. We denote the fuzzy inference obtained for the hypothesis d_j as:

$$\alpha(d_j), \quad (13)$$

where $\alpha(d_j)$ reflects the degree to which the observed symptoms comply with the hypothesis d_j in terms of the rule base and membership functions.

The next step involves probabilistic refinement of the hypotheses. Considering a priori certainties and the results of fuzzy inference, an updated estimate of a specific disease probability is achieved. In general, Bayesian refinement can be expressed as follows:

$$P(d_j \mid X) = \frac{P(X|d_j) \cdot P(d_j)}{\sum_{q=1}^{k} P(X|d_q) \cdot P(d_q)}, \quad (14)$$

Fuzzy inference results in the proposed approach are used as a mechanism affecting the plausibility of hypotheses. Consequently, the fuzzy degree of support $\alpha(d_j)$ acts as a factor determining how well current symptoms match the suspected disease and influence the recalculation of prior probabilities.

After probabilistic update, the results of the fuzzy and Bayesian stages are combined. The final integrated hypothesis score (dj) is defined as a function of $\alpha(d_j)$ and $P(d_j \mid X)$:

$$I(d_j) = f\left(\alpha(d_j), P(d_j \mid X)\right), \quad (15)$$

The aggregation function in the proposed approach aims to combine qualitative expert support and probabilistic hypothesis assessment into a single measure of preference. Based on the values of $I(d_j)$, a ranked list of diagnostic hypotheses is formed.

Therefore, the proposed method combines three key components: a formalized representation of the subject area knowledge, a fuzzy description of symptoms, and probabilistic disease refinement. This allows, on the one hand, to take into account the qualitative and subjective nature of clinical information, and on the other hand, to formalize the diagnostic conclusion and ensure its interpretability.

3. Algorithm of the diagnostic system functioning. The developed diagnostic system algorithm implements an iterative refining of diagnostic hypotheses and is designed for use in conditions of incomplete and ambiguous clinical information.

The algorithm's input data include the following:

A list of patient symptoms;

Values of the features characterizing their severity grade;

Prior probabilities of diagnostic hypotheses;

Parameters of the membership functions of fuzzy sets;

Diagnostic process termination threshold ε;

Maximum permissible number of iterations, Tmax.

The algorithm's output data are as follows:

A ranked list of diagnostic hypotheses;

A final diagnostic conclusion;

An explanation of the diagnostic conclusion;

Recommendations for further examination of the patient.

First, the diagnostic session is commenced and the patient's initial data is entered, including complaints, anamnestic information, and the results of the initial physical examination.

Next, fuzzification of symptoms is performed, in which each observed feature is assigned membership degrees to the corresponding fuzzy sets.

After fuzzification, fuzzy inference rules are activated and the degrees of support for the diagnostic hypotheses are calculated. The obtained values are used during the probabilistic refinement stage to calculate the posterior probabilities of specific diseases.

After calculating the integral scores of hypotheses, a ranked list of the most likely diagnostic conditions is generated.

The diagnostic process is terminated when one of the following conditions is met:

The maximum integral score of the hypothesis exceeds the threshold value (ε);

The maximum allowable number of iterations (Tmax) is reached;

The user forcibly terminates the diagnostic session.

If the conditions for the termination are not met, the system generates a request for additional diagnostically significant features and proceeds to the next iteration of the diagnostic process.

4. Design of experimental study. We conducted an experimental evaluation of the developed approach on a set of simulated clinical cases modeling typical scenarios of initial patient appointments with ophthalmological complaints in PHC settings.

The input data comprised expertly generated clinical case descriptions, including:

Subjective patient complaints;

Anamnesis details;

Objective symptoms as a result of the initial examination.

The study modeled clinical scenarios of varying complexity, including the following:

Cases without diagnostic noise;

Cases with irrelevant symptoms;

Cases with inconsistent symptoms.

Diagnostic noise was specified as the presence of signs unrelated to the primary diagnostic hypothesis but potentially encountered in clinical practice. Inconsistent symptoms were defined as signs that strengthen alternative diagnostic interpretations.

Values of the following parameters varied during the study:

Number of symptoms in the clinical case;

Level of diagnostic noise;

Proportion of inconsistent symptoms;

Number of competing diagnostic hypotheses.

Expert assessment of the accuracy of diagnostic conclusions was performed with the participation of ophthalmologists. The inference rules, membership function parameters, and prior probabilities of diagnostic hypotheses were generated by experts as well.

The experimental set included 210 clinical cases modeled by experts with the participation of ophthalmologists. The set included scenarios without diagnostic noise, cases with irrelevant symptoms, and cases with inconsistent features that strengthened alternative diagnostic hypotheses.

The development of diagnostic rules, the assignment of prior probabilities of diseases, and the parameters of membership functions for fuzzy sets were based on expert knowledge and did not involve the use of machine learning methods. Consequently, the set was not divided into training and test parts. The experimental sample was used solely to assess the quality of the developed approach in terms of the diagnostic inference.

Additionally, we compared the developed approach with an intelligent system based on the DeepSeek large language model. This comparison was implemented on an identical set of input data with the same noise parameters and symptom inconsistencies.

5. Methods of quality assessment and statistical processing. The following factors varied in the experimental study: number of test cases; noise level; proportion of inconsistent symptoms; and number of symptoms per diagnosis. Noise was defined as the addition of irrelevant features to the clinical case description that are potentially encountered in practice but are not specific to the expected hypothesis. Inconsistent symptoms were defined as features that reinforce alternative interpretations of the patient's condition.

We employed the following metrics to assess the quality of the diagnostic inference: diagnosis accuracy (Y1), accuracy of identifying the affected anatomical structure of the eye (Y2), mean time necessary to make a diagnostic conclusion (Y3) (ms), and a normalized estimate of computational costs (Y4).

Diagnosis accuracy (Y1) was calculated as the proportion of clinical cases in which the primary diagnostic hypothesis generated by the system matched the expected diagnosis:

$$Y_1 = \frac{N_{correct}}{N} \cdot 100\%, \quad (16)$$

where $N_{correct}$ is the number of cases with a correctly identified diagnosis, while N is the total number of clinical cases.

The accuracy of determining the affected anatomical structure of the eye (Y2) was determined as the proportion of cases in which the system correctly identified the anatomical region of the eye corresponding to the suspected disease:

$$Y_2 = \frac{N_{structure}}{N} \cdot 100\%, \quad (17)$$

where $N_{structure}$ is the number of cases with a correctly identified affected anatomical structure of the eye.

The mean time necessary to make a diagnostic conclusion Y3 was calculated as the mean time to complete the full diagnostic conclusion cycle:

$$Y_3 = \frac{1}{N}\sum_{i=1}^{N} t_i, \quad (18)$$

where t_i is the processing time of the i-th clinical case n milliseconds

To evaluate the computational efficiency of the developed approach, we used a normalized estimate of the computational costs (Y4):

$$Y_4 = \frac{t_i}{t_0}, \quad (19)$$

where t_i is the mean time to generate a diagnostic conclusion by the studied method, ms; t_0 is the threshold response time of the system.

In this study, the t_0 value was set to 1,000 ms (i.e., 1 s), which corresponds to the acceptable interactive response time of CDSSs during initial patient consultations.

Using a normalized assessment allows for a comparison of computational efficiencies of different intelligent methods relative to the requirements for diagnostic conclusion time. Values of Y4<1 correspond to CDSSs that meet the requirements for interactive use in real time.

In this article, we present the experimental results as mean values of the studied parameters. To process the results, we used standard Python 3.12 programming language tools, along with the pandas and NumPy libraries.

Results

The results of our study indicate that the addition of irrelevant symptoms does not lead to a critical deterioration in the quality of the diagnostic conclusion. For scenarios without diagnostic noise and irrelevant symptoms, the mean values of diagnosis accuracy (Y1) and accuracy of identifying the affected anatomical structure of the eye (Y2) were 82.86% and 92.63%, respectively. The mean time required for generating a diagnostic conclusion (Y3) was 3.2 ms, and the normalized computational cost estimate (Y4) was 0.0032.

In scenarios with diagnostic noise and irrelevant symptoms, the values of the Y1, Y2, Y3 and Y4 metrics were 85.71%, 92.11%, 4.0 ms, and 0.0040, respectively. These results demonstrate that the proposed approach is robust to the presence of irrelevant symptoms and does not exhibit a substantial increase in computational costs.

Inconsistent symptoms have the most significant impact on the quality of diagnostic conclusions. Under these conditions, Y1 metric decreased to 76.19%, and Y2 to 87.72%. The mean time necessary for generating the diagnostic conclusion generation was 2.67 ms, and the Y4 value was 0.00267. Hence, inconsistency in clinical information is a more significant factor in diagnostic quality reduction than sheer data redundancy.

Analysis of the time characteristics showed that the developed approach generates a diagnostic conclusion in significantly shorter time than the system's interactive response threshold, thereby confirming its applicability to real-time CDSSs in PHC.

Additionally, we compared the developed approach with an intelligent system based on the DeepSeek large language model, which utilizes a transformer architecture and mixture of experts (MoE) technology. The comparison was conducted with identical input data and identical parameters of diagnostic noise, irrelevant symptoms, and symptom inconsistency.

For DeepSeek, in scenarios without noise and irrelevant symptoms, the Y1, Y2, Y3 and Y4 were 71.43%, 88.42%, 30,703.60 ms, and 30.70, respectively. With diagnostic noise and irrelevant symptoms added, these metrics increased to 57.14%, 86.84%, 34,043.67 ms, and 34.04 ms, respectively. In the case of inconsistent symptoms, their values increased to 47.62%, 85.96%, 34,104.00 ms, and 34.10 ms, respectively.

Our results show that using a large language model is associated with significantly higher computational costs and a deterioration in the robustness of diagnostic conclusion with increasing input uncertainty. Unlike DeepSeek, the developed approach maintains low diagnostic inference time and ensures the interpretability of the resulting diagnostic conclusion.

A key advantage of the proposed method is the ability to obtain explanations for conclusions, which is crucial for improving the skills of doctors performing diagnostics. It should be noted that the use of large language models does not provide an explicit formalized mechanism for explaining diagnostic conclusion comparable to the system of rules and the hypothesis activation sequence implemented in the proposed approach.

A comparative analysis confirms that using formalized knowledge and hybrid inference mechanism provides greater robustness, better reproducibility of results, and more acceptable computational efficiency vs. a universal approach based on a large language model.

The developed model of knowledge presentation forms the basis for the implementation of the CDSS in the form of a software application for a step-by-step scenario of supporting the differential diagnosis of eye diseases.

During system operation, diagnostic hypotheses are iteratively refined through consecutive query of additional diagnostically significant features and re-execution of the diagnostic inference (*Figure 2*).

The final stage of the CDSS operation involves the formation of a diagnostic conclusion, including the main diagnosis, alternative diagnostic hypotheses and recommendations generated on the basis of the knowledge base (*Figure 3*).

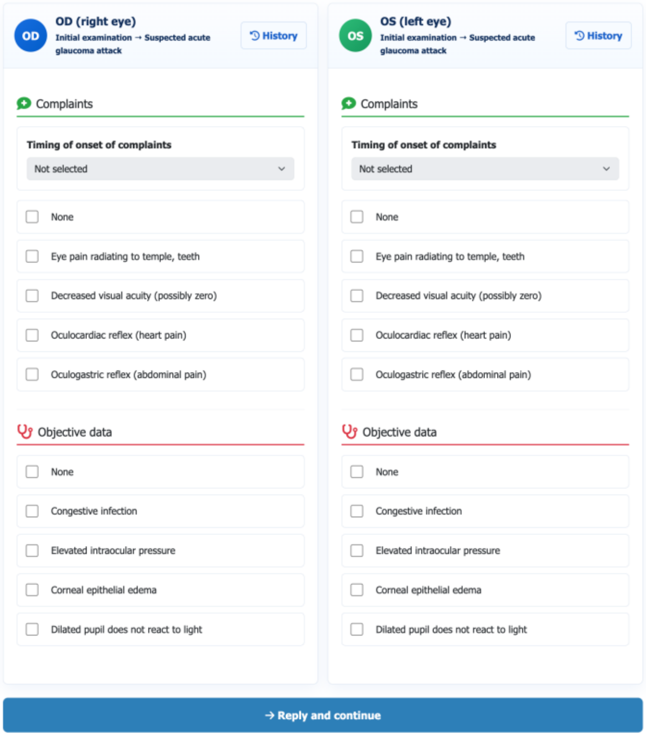

Figure 2. Diagnostic process screen

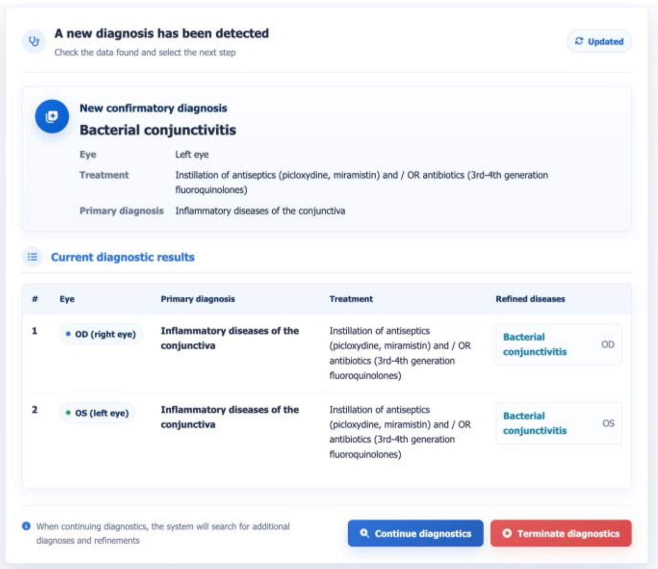

Figure 3. Diagnostic conclusion screen

Discussion

Contemporary studies of CDSS in ophthalmology mainly use the methods of deep learning and medical image analysis [15–17, 20, 21, 23, 24]. Such systems demonstrate high accuracy in resolving specific tasks of fundus image and OCT data classification, but their use typically requires structured instrumental information and representative training samples.

Unlike these approaches, our original system is designed to support primary differential diagnosis in conditions of limited diagnostic data and implements a formalized expert knowledge, fuzzy inference, and probabilistic hypothesis refinement. The proposed approach is not intended to compete with highly specialized medical image analysis systems, but rather to support diagnostic searches at the initial patient consultation stage.

A reliable comparison with existing CDSS is problematic due to differences in the datasets used, diagnosed disease lists, quality assessment criteria, and experimental conditions. Most published studies focused either on specific ophthalmic pathologies, or else on binary or multiclass image classification tasks, whereas our study examined iterative differential diagnosis based on symptoms, patient complaints, and expert inference rules.

Our findings showed the potential for the effective application of a hybrid approach based on a combination of fuzzy inference and Bayesian probabilistic refinement to process incomplete, inconsistent, and linguistically ambiguous clinical information in PHC settings.

The results of our experimental study demonstrated the robustness of the developed approach to the presence of irrelevant symptoms. Moreover, the greatest impact on the quality of diagnostic inference was demonstrated by inconsistent features, which reinforce alternative diagnostic interpretations. This result is consistent with the specificities of clinical practice, in which the overlap of symptoms in various eye diseases is a major cause of diagnostic errors.

A comparison with a system based on the DeepSeek large language model revealed the advantages of the proposed approach in terms of accuracy of diagnostic conclusions and computational cost. The differences may be due to the fact that large language models are primarily focused on processing generalized text patterns and do not utilize an explicitly formalized structure of subject area knowledge. In contrast, the proposed approach relies on diagnostic dependences defined by experts and provides a controlled mechanism of issuing a diagnostic conclusion.

An additional advantage of the proposed method is its capability of explaining diagnostic results. The final conclusion is formed based on the consecutive activation of diagnostic rules and update of probabilistic hypothesis assessments, which allows identifying the features with the greatest impact on the choice of diagnostic solution. This has practical significance both for clinical decision support and for educational purposes.

We compared the proposed CDSS for diagnosing eye diseases with routine clinical practice. This research was conducted at the Department of Clinical Diagnostics of the Clinical Hospital #2 (Clinic for Eye Diseases) at Razumovsky State Medical University of Saratov (RSMUS), Russia. The results of routine patient examinations by ophthalmologists (with three years of experience or more) were compared with the findings of the proposed CDSS. The experts were T.G. Kamenskikh (Doctor of Medicine, Professor, Chair of the

Department of Eye Diseases, RSMUS); I.O. Kolbenev, PhD, Associate Professor, Department of Eye Diseases, RSMUS; and E.V. Veselova, PhD, Associate Professor, Department of Eye Diseases, RSMUS. A total of 100 clinical cases were analyzed, including both patients with ophthalmic pathology and healthy subjects undergoing a medical examination. The developed CDSS can evaluate and issue a diagnostic conclusion on both anterior segment eye diseases (of the ocular adnexa, cornea, choroid, and lens) and posterior segment eye diseases (of the retina and optic nerve).

The resulting diagnostic accuracy of the CDSS was comparable to that of ophthalmologists, and in some cases even superior to them, particularly in detecting minimal clinically important differences (89–93% for the CDSS and 85–91% for physicians). In terms of analysis time, the CDSS outperformed physicians (10–15 s vs. 3–7 min).

Promising areas for further research include expanding the diagnostic rule base, conducting clinical testing of the system on actual medical data, and integrating medical image analysis methods and electronic medical records into unified diagnostic framework.

Conclusion

This paper develops an approach to supporting the differential diagnosis of eye diseases, based on the formalization of subject area knowledge and oriented toward application in PHC settings.

We proposed a formal model for representing diagnostic knowledge, including descriptions of symptoms, diagnostic hypotheses, fuzzy linguistic variables, inference rules, and prior disease probabilities. Based on the developed model, we implemented a hybrid diagnostic inference method combining fuzzy logic and Bayesian probabilistic hypothesis refinement.

An experimental evaluation demonstrated the robustness of the developed approach to incomplete and ambiguous clinical information, as well as its superior computational performance and interpretability, compared with an alternative approach based on a large language model.

Our results confirm the potential of the developed approach for use in intelligent CDSSs for PHC.

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