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## Review article

# Artificial intelligence applications and cataract management: A systematic review



Daniele Tognetto, MD<sup>a</sup>, Rosa Giglio, MD<sup>a,\*</sup>, Alex Lucia Vinciguerra, MD<sup>a</sup>,  
Serena Milan, MD<sup>a</sup>, Robert Rejdak, MD<sup>b</sup>, Magdalena Rejdak, MD<sup>c</sup>,  
Katarzyna Zaluska-Ogryzek, MD<sup>d</sup>, Sandrine Zweifel, MD<sup>e</sup>,  
Mario Damiano Toro, MD<sup>e,f</sup>

<sup>a</sup> Eye Clinic, Department of Medicine, Surgery and Health Sciences, University of Trieste, Trieste, Italy

<sup>b</sup> Chair and Department of General and Pediatric Ophthalmology, Medical University of Lublin, Lublin, Poland

<sup>c</sup> Medical University of Warsaw, Warsaw, Poland

<sup>d</sup> Department of Pathophysiology, Medical University of Lublin, Lublin, Poland

<sup>e</sup> Department of Ophthalmology, University of Zurich, Zurich

<sup>f</sup> Department of Medical Sciences, Collegium Medicum, Cardinal Stefan Wyszyński University, Warsaw, Poland

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## ABSTRACT

Artificial intelligence (AI)-based applications exhibit the potential to improve the quality and efficiency of patient care in different fields, including cataract management. A systematic review of the different applications of AI-based software on all aspects of a cataract patient's management, from diagnosis to follow-up, was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. All selected articles were analyzed to assess the level of evidence according to the Oxford Centre for Evidence-Based Medicine 2011 guidelines, and the quality of evidence according to the Grading of Recommendations Assessment, Development and Evaluation system. Of the articles analyzed, 49 met the inclusion criteria. No data synthesis was possible for the heterogeneity of available data and the design of the available studies. The AI-driven diagnosis seemed to be comparable and, in selected cases, to even exceed the accuracy of experienced clinicians in classifying disease, supporting the operating room scheduling, and intraoperative and postoperative management of complications. Considering the heterogeneity of data analyzed, however, further randomized controlled trials to assess the efficacy and safety of AI application in the management of cataract should be highly warranted.

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\* Corresponding author: Rosa Giglio, MD, Eye Clinic, Department of Medicine, Surgery and Health Sciences, University of Trieste, Trieste, 34134, Italy

E-mail address: [giglio.rosam@gmail.com](mailto:giglio.rosam@gmail.com) (R. Giglio).

## 1. Introduction

Globally, cataract is one of the primary causes of visual impairment. In medium- and low-income countries, more than 50% of cases of blindness can be attributed to cataract.<sup>55</sup> In 2010 alone about 33.3% and 18.4% cases of worldwide blindness and visual impairment, respectively, were traced back to the emergence of cataract.<sup>37,69</sup> A previous review reported a cataract prevalence rate of 64% in European people aged 70 years or older.<sup>55</sup> Cataract surgery is one of the most cost-effective healthcare interventions<sup>13,74</sup> that effects improvement physically as well as psychologically.<sup>68,69</sup>

Cataract surgery has previously been shown to enhance the cognitive function among Alzheimer and other dementia patients.<sup>4,13,74</sup> A previous study found that elderly patients who underwent cataract surgery exhibited enhanced cognitive function, alleviated depressive mental status, and improved quality of life.<sup>35</sup> Another study reported that cataract surgery, in conjunction with adequate cardiac care, led to an increase in the life expectancy of the elderly by 1.8 years.<sup>13</sup> Furthermore, Tseng and coworkers determined that elderly patients who underwent cataract surgery had a lower risk of hip fracture compared to those who did not.<sup>70</sup>

Recently, several factors, such as early intervention, higher eye surgery frequency, and population aging, have led to an increase in the frequency of cataract surgeries.<sup>75</sup> Limited resources and longer wait times, however, pose major roadblocks to cataract management in countries that depend primarily on public healthcare systems.<sup>74</sup>

It is well known that an early diagnosis and therapeutic intervention for this pathology helps to avoid complications and reduce healthcare costs.<sup>77</sup> The recent Coronavirus disease–COVID-19-pandemic has forced healthcare organizations, including ophthalmology services, to reorganize, making it hard to pursue these aims.<sup>68</sup>

Artificial intelligence (AI)-based applications have shown great potential in several areas related to patient care.<sup>64</sup> Thanks to the digital revolution, AI technology has entered almost all parts of society, and the COVID-19 pandemic has significantly accelerated this process. Hence, with advancement in developing countries and general population aging, AI systems could become an important part of the screening, staging, and treatment of eye conditions. This, in turn, could lead to higher population coverage within a short time, timely and adequate diagnosis and treatment, and reduction in the number of tedious tasks to be conducted by experts.<sup>5</sup> In this scenario, AI could contribute to filling these gaps and has thus gained an interest regarding its role in cataract management. Additionally, neural networks (NNs), as a set of algorithms, are impacting diverse areas of science, including ophthalmology.<sup>67</sup>

Here, we provide a systematic review of the different applications of AI-based software on all aspects of cataract management, including diagnosis and follow-up. A glossary of the main concepts related to AI is provided to facilitate the comprehension of this complex theme for neophytes (Supplementary Material, Table 1S).

## 2. Methods

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>49</sup> The review protocol was not recorded, and no registration number is available for consultation. We performed a systematic search for all available articles exploring the AI applications in the field of human adult cataract management.

Only original studies on adults were included in the current review, with no restriction on study design. Exclusion criteria included: review studies, editorials, and conference reports. Articles dealing with animal models and/or not written in English were also excluded. The level and quality of evidence of the selected studies were evaluated based on the Oxford Centre for Evidence-Based Medicine (OCEM) 2011 guidelines<sup>33</sup> and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system,<sup>23</sup> respectively.

## 3. Results

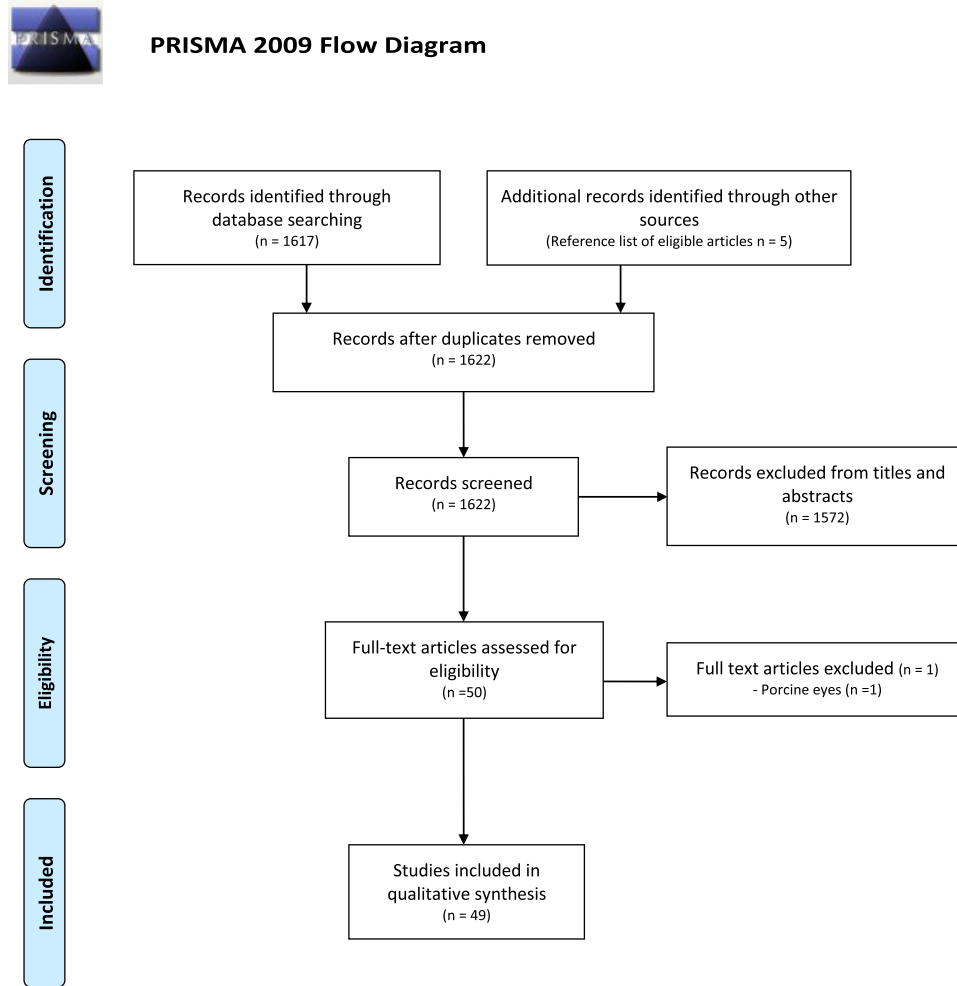
The results are summarized in a flow diagram according to PRISMA guidelines (Fig. 1). Of the initially extracted 1617 articles, 44 abstracts met the inclusion/exclusion criteria. One article was excluded after full-text reading because it involved porcine eyes. Five additional articles included in the analysis were derived from the selective review of the list of references during the full-text review of the original articles (Fig. 1).

No data synthesis was possible because of the heterogeneity of available data and the design of the available studies. Thus, the current systematic review reports a qualitative analysis in a narrative fashion below. To facilitate a more comprehensive overview, all the included studies were subgrouped into four main topics (“diagnosis”, “intraocular lens power calculation”, “surgery”, and “complications”). The level and quality of the available evidence are summarized in Supplementary Material, Table 2S.

### 3.1. Diagnosis

There have been significant signs of progress in the processing of medical images in different settings, allowing more reliable diagnosis and more accurate measurements of pathological features.<sup>3</sup> Teleophthalmology screening programs exploiting AI-based software could reduce the pressure on tertiary referral centers providing screening evaluations before referring the patients to specialized hospital services. The effectiveness of NNs in detecting and classifying lens opacities has been assessed by different authors, who mainly focused on the evaluation of anterior segment images.<sup>3,17,20,38,44,45,47,77,80</sup>

In 2003, Fan and coworkers proposed an automatic nuclear cataract classification system based on slit lamp photographs.<sup>17</sup> The project included approximately 1000 images. After the detection of the visual axis and the identification of ocular landmark features from slit lamp photographs, they devised a linear grading function to detect nuclear sclerosis



**Fig. 1 – PRISMA flow chart. Flow diagram of the study according to PRISMA guidelines.**

severity based on landmark intensity. The machine grades were compared with the human grades. The linear grading function showed a 95.8% grading accuracy within 1 grade using the Age-Related Eye Disease Study (AREDS) grading system (in human grading, one grade fluctuation is considered acceptable). Moreover, the machine grading reduced the time necessary for classification to less than 2 seconds versus the previous 2 minutes.<sup>17</sup>

In 2009, Acharya and coworkers employed the Artificial Neural Network (ANN) classifier to distinguish cataract from normal and post-cataract eye images.<sup>3</sup> They analyzed 140 optical images belonging to the three different classes (normal, cataract, and postoperative). First, the specific features of the three classes were extracted using image processing and application of Fuzzy K-means clustering algorithm to the raw optical images. For image classification, a back-propagation algorithm (BPA) was used. They showed that the ANN classifier could correctly classify 100% of normal eye images and 90% of abnormal eyes, with an average accuracy rate of 93.3%. Their system exhibited 98% sensitivity and 100% specificity.<sup>3</sup>

Wu and coworkers validated a universal AI platform for cataract diagnosis and management based on datasets derived from the Chinese Medical Alliance for AI (CMAAI).<sup>77</sup> The

dataset employed for the AI agent training included 37,638 slit lamp photographs of normal lenses, cataracts (of different etiologies and degrees), and pseudophakic eyes (postoperative eyes). Each image was analyzed and labeled by at least 2 ophthalmologists, and all the images were employed to train the AI agent that was then employed to create a multicenter validated system. A deep learning convolutional neural network (CNN) was employed for training and classification. The first step was the identification of the type of capture mode (mydriatic, mydriatic-diffuse, non-mydriatic, and non-mydriatic-diffuse). The second step was the diagnosis (normal, cataract, or postoperative), and the last step was the degree of severity evaluation (follow-up or referral). Conditions for referral included: nuclear grades III-IV and significant anterior and/or posterior capsular opacification. The authors highlighted the importance of testing under the non-mydriatic-diffuse mode. As a matter of fact, in previous studies and cataract classifications, slit lamp and cycloplegics were traditionally applied, implying costs, risk of complications, and difficulty in community-based screening settings. In this study, it was found that the performance of non-mydriatic mode in cataract diagnosis, even in diffuse conditions, was comparable to that of 'gold-standard' mydriatic mode, with

area under the curve (AUC) values > 99% in all tests. Moreover, even if this mode implied difficulties in the detection of complicated referable conditions, it still achieved an AUC > 91%. These findings suggested that this AI agent could be used via a mobile application by the patients on their own. A web platform was thus established. After uploading their files, users could obtain remote real-time disease monitoring (to avoid misdiagnoses, data were weekly analyzed by doctors, who could even update the semantic logic according to the most recent guidelines). These findings led to the establishment of a new tertiary healthcare referral pattern that included three monitoring levels: self-management, primary healthcare, and secondary specialized services. Through this system, users could upload self-information (such as basic personal data and history, visual acuity, etc.). When a suspicious case occurred, a notification was sent to community-based facilities, where a slit lamp image was obtained and uploaded to the AI platform. If the platform classified the cataract as a “referral”, the doctors were immediately alerted. When a comprehensive examination was needed, the patients were informed. It was found that this tertiary referral system could improve assistance, increasing the ophthalmologist-to-population service ratio by 10.2-fold compared to traditional cataract management (for which, Zhongshan Ophthalmic center was taken as an example). The universal AI platform showed a robust diagnostic performance for the three-step tasks suggesting, in a real-world setting, 30.3% of people to be ‘referred’.<sup>77</sup>

Li and coworkers devised a computer-aided system for the diagnosis of nuclear cataract based on slit lamp image analysis.<sup>44</sup> Their automatic grading of nuclear cataract (AGNC) system was structured in three components: feature extraction, grade prediction, and structure detection. They included more than 5000 images in their work. The nuclear opacity grading was automatically valued using the Support Vector Machine (SVM) regression. The automatic classification was then compared to human grader classification. They reported success rates of 95% and 96.9% in lens structure detection and localization, respectively. The grading difference for more than 97.5% of the value images was less than one grade (Wisconsin cataract grading system).<sup>44</sup>

In 2013, Xu and coworkers introduced a new feature and a new approach for automatic grading of nuclear cataracts based on slit lamp images.<sup>80</sup> They performed parameter selection, regression model training, and feature selection simultaneously through the employment of a group sparsity-based constraint for linear regression (GSR). Compared to the conventional model, their method generated superior results with respect to clinical grading in terms of agreement ratio, mean absolute error (MAE), and decimal grading error.<sup>80</sup>

In 2015, Gao and coworkers proposed another method for automatic detection and grading of nuclear cataracts based on slit lamp images.<sup>20</sup> They chose to adopt the convolutional-recurrent neural networks (CRNN)-based deep learning framework, the only system that could extract information from realistic-sized images. Their approach achieved a 70.7% exact agreement ratio against clinical grading, integral grading error  $\leq 1$  in 99.0% of tests, decimal grading error  $\leq 0.5$  in 88.4% of tests, and MAE of 0.304.<sup>20</sup>

Kim and coworkers developed a new form of CNN they named Tournament-based Ranking CNN that was able to

aggregate outputs of multiple binary NNs.<sup>38</sup> Since cataract grading using multi-label classification models and regression models degrade the performance because these models simplify the opaque patterns of cataract into linear forms, this work proposed a tournament-based CNN and very deep pre-trained binary models to grade cataract efficiently. By dividing classes into two sets in a way that recorded the highest AUC, the accuracy of the model increased (68.36% of exact match accuracy).<sup>38</sup>

Even visible wavelength eye images taken by a compact digital camera could be applied for automatic cataract diagnosis. The Computer-Aided Diagnosis (CAD) program proposed by Mahesh Kumar and coworkers, based on an SVM, was characterized by high values of sensitivity (97%), specificity (99%), and predictive accuracy (96.96%).<sup>47</sup>

AI algorithms typically rely on high-quality data to achieve optimal training.<sup>45</sup> Li and coworkers devised a novel workflow named “Visionome” (DSV) to annotate pathological features and to segment anatomical structures in slit lamp images. Their workflow was employed to improve the performance of a deep-learning algorithm for multiregional detection and classification of abnormal eyes (including age-related cataracts) and normal eyes. They established a densely annotated dataset based on anatomical structures and pathological features of selected lesions. Their algorithm was tested in different clinical scenarios (mass screening, comprehensive clinical triage, hyperfine diagnostic assessment, and multipath treatment planning). Compared to the image-level-annotated classification technique, the Visionome (DSV)-based diagnostic system showed better diagnostic performances.<sup>45</sup>

In 2008, Abdul-Rahman and coworkers evaluated the efficacy of Fourier analysis of digital retinal images in grading cataract severity.<sup>1</sup> In their method, discrete Fourier transforms (DFT) were employed to assess the optical degradation of a fundus image of a cataract-affected eye to detect and assess the severity of cataracts. They compared the DFT’s predictive value in classifying cataract severity with LogMAR visual acuity and the Lens Opacity Classification System (LOCS III) grading. Using the Fourier analysis technique, they achieved 72.4% sensitivity and 52.7% specificity. The results for cataract severity grading were moderately correlated with LOCS III (regression coefficient value -  $R_2 = 0.59$ ). DFT analysis demonstrated a comparable correlation with LogMAR visual acuity ( $R_2 = 0.39$  - as LOCS III,  $R_2 = 0.44$ ), while a poor correlation was found in clear ( $R_2 = 0.05$ ) and pseudophakic lenses ( $R_2 = 0.07$ ), as with LOCS III score. Using this technique, however, they were not able to distinguish corneal defects or vitreous haze from lenticular opacities, nor could they determine the cataract type.<sup>1</sup>

Until 2015 existing methods for automatic fundus image classification used a single learning model.<sup>81</sup> Since it was widely accepted that a combination of multiple learning models could provide more accurate classification compared to any of the constituent models, Yang and coworkers proposed an ensemble method.<sup>81</sup> In their system, three independent feature extraction techniques and two base learning models (Support Vector Machine and Back Propagation Neural Network) were employed for base classifier construction. Then, two ensemble approaches (majority voting and stacking) were used to combine the multiple base classifiers. It was

found that the ensemble classifier achieved 93.2% accuracy for cataract classification (two-class task) and 84.5% accuracy for cataract grading (four-class task). This approach outperformed the single learning models significantly considering that for single learning models, the maximum accuracy was 91.9% for cataract detection, achieved by Wavelet-BPNN - and 83.2 for cataract grading - achieved by All-SVM).<sup>81</sup>

Zhang and coworkers proposed an automatic method for cataract diagnosis and grading based on fundus image evaluation.<sup>84</sup> The more the lens opacifies, the more the images get blurred. In order to describe cataract evolution, they identified a new 6-stadium grading classification of lens opacity depending on what structures could be detected during fundus examination: non-cataractous (in which structures were clear and distinguishable), slightly mild (small retinal vessels still visible), mild (fuzzy, small retinal vessels), medium (only optical disc and thick vessels could be seen), slightly severe (only optical disc was detectable), and severe (fundus was not visible at all). In their study, they proposed a new AI method (called “multi-feature & stacking”) based on deep learning that could detect the above-mentioned characteristics by analyzing fundus images captured by a specialized fundus camera to automatically diagnose and grade cataracts. They reported an average accuracy of 92.66%, with differences depending on the degree of disease severity. The highest sensitivity and specificity values were reached in normal lenses (95.68% and 99.37%, respectively) and severe cataracts (98.52% and 96.43%, respectively). The other levels were characterized by lower levels of accuracy, with the lowest values in mild cataracts (sensitivity of 81.33% and specificity of 82.40%). They concluded that although their method could not detect other diseases that could modify image quality, it might be useful in narrowing down the number of patients who needed to be examined by ophthalmologists.<sup>84</sup> Zhou and coworkers analyzed 1355 retinal images from more than 1000 consecutive cases from the Beijing Tongren Hospital to develop automatic cataract classification algorithms.<sup>85</sup> In addition, they compared their algorithms with other cataract detection and grading methods. They proposed some classification methods, such as exponential DST (EDST-MLP) or multilayer perceptron with discrete state transition (DST-MLP), for cataract grading (four-category classification). They proposed NNs with discrete parameters (EDST-ResNet, DST-ResNet, EDST-MLP, and DST-MLP) for cataract classification (two-category classification). The authors concluded that other classification methods that possess prior knowledge are better suited for complex tasks, such as classification of complicated medical images, whereas deep NNs, without prior knowledge, showed the better performance to perform simple tasks, such as cataract detection.<sup>85</sup>

Xu and coworkers employed CNN to directly investigate the input data and deconvolution network method to investigate how CNN characterized cataract layer-by-layer.<sup>79</sup> They found that vascular information played a key role in cataract grading.<sup>79</sup>

In 2021, Tham and coworkers proposed a new method for disease-related visual impairment diagnosis, employing retinal photograph-based deep learning.<sup>65</sup> Patients affected by different major age-related eye diseases such as cataract, diabetic retinopathy, and maculopathy were included, and a deep CNN was used (Residual Neural Network ResNet-50 architec-

ture). First, they determined the AUC for the detection of any disease-related visual impairment. Then, they assessed the performance of the algorithm for the detection of cataract-related visual impairment. The AUC was 94.8% (95% CI 93.4–96.3) for any disease-related visual impairment and 95.0% (95% CI, 92.6–97.4) for moderate or worse disease-related visual impairment. The tested algorithm needed a single macular-centered retinal photograph as input, without requiring an expert intervention. Consequently, it could potentially help identify cases that should be referred to a specialist.<sup>65</sup>

Computer-aided cataract diagnosis (CACD) existing algorithms have not been optimized for the presence of noise in digital fundus retinal pictures, which is a severe concern because even minor noise levels might compromise cataract diagnosis efficiency. Pratap and coworkers studied a CACD method against a noisy environment that was found superior to existing CNN based CACD methods at different noise levels.<sup>54</sup>

Peissig and coworkers developed and validated an Electronic Health Records (EHR)-based algorithm for the identification of age-related cataract-affected subjects.<sup>53</sup> They found a positive predictive value (PPV) of 95.6% and a negative predictive value (NPV) of 95.1%. For the first time, a multimodal phenotyping strategy was tested to increase and optimize the accuracy of identification of cataract patients. This method combined three different detection methods, applying them in the following order: conventional data mining (CDM), which used data from data warehouse, natural language processing (NLP), which analyzed electronic text documents, and optical character recognition (OCR), which valued scanned images. Data from 2159 cataract subjects were analyzed: 752 (34.8%) were identified by CDM, 767 (35.5%) were recognized by NLP, and 640 (29.6%) were assessed by OCR. Consequently, multimodal strategy helped increase the detection of cataract subjects compared to single-mode approach, while keeping high PPV. Focusing on nuclear sclerotic cataract subtype, the most common subtype, only 493 (26.7%) subjects were identified by CDM, which represented the approach that is first used to identify subtypes in actual practice, since it required the least effort. Furthermore, 1213 (65.6%) subjects were detected by NLP, while OCR methods recognized 813 (44%) subjects. Multimodal phenotyping increased the number of subjects with NS subtypes from 493 (11.6%) to 1849 (43.6%). For cataract severity and location, no coded values were found in the EHR, so CDM could not be used. NLP detected cataract location (right or left eye) with high reliability in 53% subjects. The OCR yield was low because only a limited number of data were processed (only the cases not diagnosed using NLP). Finally, the authors validated the transportability of their algorithm by testing it on Group Health Research Institute/University of Washington’s data. A PPV of 96% was obtained; however, because of did not use the digital forms, only CDM and NLP were implemented at the electronic MEDical Records and GENomics (eMERGE) institutions participating in the study.<sup>53</sup>

The Ophthatome™, a knowledge base of ophthalmic diseases, was introduced by Raj and coworkers.<sup>58</sup> They constructed a licensed database containing patient-contributed data to create highly specialized disease cohorts for ophthalmology and vision science research utilizing combination

search terms and built-in logical processes. Ophthatome™ contained comprehensive clinical data captured from the electronic medical record at Narayana Nethralaya, a multi-specialty tertiary eye hospital in Bangalore, India, between September, 2012 and January, 2018. The Ophthatome™ database contained clinical and phenotype data from 581,466 subjects with 524 distinct ophthalmic disease types and 1800 disease sub-types. Age, disease diagnosis, quantitative traits, systemic diseases, prescription drugs, family history, diagnostic procedural images, visual impairment, and longitudinal data were all captured in Ophthatome™. ICD10 codes were used to diagnose diseases in the EMR. The ICD diagnosis was divided into disease types and subtypes to allow for more comprehensive and informative data querying. For example, all types of cataracts, such as cortical, nuclear, and anterior subcapsular cataracts, were first classified as cataracts and then subclassified into their respective subtypes. Comprehensive ophthalmic clinical variables such as refraction, intraocular pressure, central corneal thickness, slit lamp examination details, diagnosis, medications, surgical interventions, and thirteen clinical diagnostic images were included in the knowledgebase. Each subject's clinical variables were mapped longitudinally, beginning with the most recent value.<sup>58</sup>

### 3.2. Intraocular lens power calculation

After phacoemulsification and implantation of intraocular lens (IOL), changes in trabecular-iris angle width (TIA) and anterior chamber depth (ACD) are expected, and these variations play a crucial role in IOL calculation. Although the qualitative relationship between baseline eye anatomy and surgery-induced variation is clear, its quantitative character is still difficult to determine. Rekas and coworkers proposed a new method for the evaluation of the phacoemulsification-related anterior segment anatomical changes, to establish their correlation with baseline anatomical parameters.<sup>59</sup> Included patients were previously divided into 4 groups, depending on their phenotype characteristics (ACD, TIA, central lens thickness, and axial length (AL)). They detected a linear connection; however, the degree of the over-mentioned phenomenon could not still be explained. It was shown that the application of NNs could help generalize the results. They showed that the network's data and actual data achieved a positive correlation coefficient that, based on the network used, ranged as follows:

- Training set: 0.75 to 0.83
- Testing set: 0.72 to 0.77
- Validation set: 0.79 to 0.83

The highest error was obtained when phenotype clusterization was removed from the network structure.<sup>59</sup>

Accurate IOL calculation performed during the preoperative assessment of cataract surgery is a critical step to achieve the desired refractive outcome. Several formulas, used to determine the best IOL power, require the ACD, AL, and keratometry values for. Other formulas also require lens thickness (LT).<sup>78</sup> To date, optical biometer devices have been the gold standard to provide ocular biometric parameters.<sup>71</sup> On the basis of ocular biometric variations, the surgeon can choose the

most adequate formula. A crucial weakness of all these formulas is the need for an accurate estimation of the postoperative IOL position (ELP), a parameter that can be predicted considering biometric measurements and the lens as constant.<sup>78</sup>

Since the ideal refractive outcome, emmetropia, is obtained only in about 80% of cases, this has led the researchers to continue searching for new formulas through ray-tracing software (Okulix10) and AI (Hill-RBF-based calculators, Kane method, Pearl-DGS, FullMonte IOL software system, Ladas Super Formula (LSF) AI). As the number of available data increases the AI approaches to IOL power calculation might provide higher accuracy.<sup>51</sup> Fernandez-Alvarez and coworkers trained one of these networks, Multilayer Perceptron (MLP) to predict the IOL power, given average corneal K power, AL, the desired refraction, and the predicted refraction using a theoretical formula.<sup>18</sup>

The advantages of NNs against traditional linear regression formulas have been discussed since this topic first emerged in 1997 by Clarke and Burmeister.<sup>14</sup> Mean postoperative error and absolute error from predicted refraction were +0.271 diopters (D) and -0.217 diopters and +0.630 and +0.930 for NN and Holladay personal groups, respectively. Both these errors differed significantly ( $P < 0.022$ ; nonparametric Mann-Whitney test). An error of less than  $\pm 0.75$  D was observed for 72.5% and 50.0% of the NN and Holladay groups, respectively.<sup>14</sup> Findl and coworkers conducted a study aimed at optimizing postoperative refractive outcome through a more accurate prediction of the pseudophakic ACD, necessary for the prediction of the effective lens position (ELP).<sup>19</sup> They used a neural-network-type multilayer perceptron (MLP) and a linear regression technique, but in the end they found that predictions from the artificial network were less accurate than those done by the linear regression model.<sup>19</sup>

Sramka and coworkers investigated the potential improvements to IOL power calculation that could be made by employing the Support Vector Machine Regression model (SVM-RM) and the Multilayer Neural Network Ensemble model (MLNN-EM).<sup>62</sup> Using a dataset of pseudophakic eyes whose IOL was calculated using the SRK/T formula (with an optimized A constant of 119.1), they investigated how the refraction outcome might have differed if an SVM-RM-based or an MLNN-EM-based IOL calculation had been used. When compared to clinical outcomes, both models were found to have much lower absolute error; nevertheless, the difference between the two AI approaches was not significant. When it came to prediction errors (Pes), both models had a significantly greater overall percentage of eyes with PEs of 0.25, 0.50, 0.75, and 1.00 D than clinical outcomes. The percent of eyes within a prediction error (PE) of  $\pm 0.25$  was 33.4% for clinical results, 48.2% for SVM-RM and 48.9% for MLNN-EM. The percent of eyes within a PE of  $\pm 0.50$  resulted 57.7 % for clinical results, 82.8 % for SVM-RM and 82.3% for MLNN-EM. The percent of eyes within a PE of  $\pm 0.75$  was 79.4 % for clinical results, 93.4% for SVM-RM and 93.7% for MLNN-EM. The percent of eyes within a PE of  $\pm 1.00$  resulted 91.8 % for clinical results and 97.7% for both SVM-RM and MLNN-EM; however, the differences between SVM-RM and MLNN-EM were not statistically significant.<sup>62</sup>

Nemeth and coworkers analyzed the biometric results of Hill-radial basis function (RBF) method 2.0 (online version), comparing its outcomes with those provided by the Barrett

Universal II formula and the SRK/T formula.<sup>52</sup> This AI-driven method was linked to the best percentage of subjective and objective PEs fewer than 0.5D, as well as the best percentage of subjective refraction errors, whereas the SRK/T formula was linked to the worst. Furthermore, the Hill-RBF system had the narrowest range of PE, whereas the SRK/T formula had the broadest.<sup>52</sup>

Carmona González and coworkers developed a new IOL power calculator based on machine learning approaches.<sup>9</sup> This approach, like the Hill-RBF system, is data driven, but it contains more calculation factors than the former: WTW distance, central LT, and the ratio between the curvature of the anterior and posterior corneal surfaces. A novel nonlinear regression model (called “Karmona”) was tested. The accuracy of this novel approach was compared to Holladay 2, Haigis, Barrett Universal II, and Hill-RBF v2.0: it was observed that the Karmona method had the lowest SD of the refractive prediction error (RPE), followed by Haigis, Holladay 2, Barrett Universal II, and Hill-RBF v2.0. Furthermore, significant variations in the MAE and the median of the absolute error (MedAE) were found between Karmona and Hill-RBF.<sup>9</sup>

Another study led by Cheng and coworkers looked at how AI-based constant optimization for SS-OCT biometry improved the accuracy of current formulas (Barrett, Emmetropia Verifying Optical 2.0, Haigis, Hoffer Q, Holladay 1, Holladay 2, Olsen, STK/T and T).<sup>11</sup> They specifically looked at how refraction outcomes (i.e., mean PE, MAE and MedAE, and percentages of eyes within different PE ranges) were affected when compared to those associated with standard User Group for Laser Interference Biometry (ULIB) constants. Both optimized constants (obtained by using Kane, PEARL-DGS, and RBF 2.0) and ULIB constants were used. The MedAE of the Haigis, Barrett, and Hoffer formulas were much lower than those obtained using the single ULIB a0 constant, but the SRK/T and Holladay 1 formulas showed no significant difference. With the Kane formula, the lowest MAE was attained. Kane (45.4%) came in third in terms of eye proportions within 0.25 D, behind Olsen (47.1%) and Barrett (45.9%), while the PEARL-DGS (42.7%) and RBF 2.0 (41.2%) formulas performed poorly. Furthermore, the Kane formula had the highest value for the 0.50 D endpoint (77.1%) and the lowest probability of refractive surprise (> 1.00 D from intended refraction, 3.7%). Finally, it was observed that applying the same formula to different axial length subgroups was associated with different outcomes. The Hoffer formula provided the lowest MedAE, while the PEARL-DGS formula produced the lowest MAE; the RBF 2.0 formula produced the worst results in short eyes. The Olsen formula produced the lowest MedAE in medium eyes. The Barrett formula had the lowest MedAE while the Kane formula had the lowest MAE in both medium and long eyes.<sup>11</sup>

Szalai and coworkers investigated the performance of three types of IOL power calculators: five third- and fourth-generation vergence IOL power calculation formulas (Barrett Universal II, Haigis, Hoffer Q, Holladay 1, and SRK/T), an artificial intelligence-based method (Radial Basis Function 2.0), and two combined IOL power calculation methods (Kane and LSF).<sup>63</sup> The Kane approach produced good results, with one of the lowest MAEs (second only to Haigis), followed by LSF and RBF 2.0, and the other systems achieving much higher values. Moreover, the Kane method was associated with the second

highest percentage of eyes (41%) within  $\pm 0.25$  D PE, following Haigis formula (56%) and with the highest percentage (79%) of eyes within  $\pm 0.50$  D PE, followed by Haigis formula (78%), Hoffer Q (63%), LSF (62%) and RBF 2.0 (61%).<sup>63</sup>

Ladas and coworkers recently tested three formulas (SRK, Holladay I, and LSF) and three supervised learning algorithms (Support Vector Regression, Extreme Gradient Boosting, and Artificial Neural Network).<sup>39</sup> The use of each type of AI method on each formula was found to result in a lower mean and median AE than the baseline formula; all differences were statistically significant. For instance, SRK was associated to a mean AE of  $0.499 \pm 0.012$ ; this value was reduced to  $0.439 \pm 0.026$  for SRK + ANN, to  $0.325 \pm 0.023$  for SRK + SVR and to  $0.314 \pm 0.022$  for SRK + XGB. As regards Holladay 1, its baseline MAE was  $0.392 \pm 0.013$ ; when adding SVR, it ameliorated to  $0.307 \pm 0.021$ ; for Holladay 1 + XGB, it was  $0.309 \pm 0.022$ ; adding ANN, it was  $0.326 \pm 0.022$ . As regards LSF, its MAE at baseline was  $0.355 \pm 0.017$ ; when adding SVR, it was  $0.311 \pm 0.021$ ; for LSF+XGB, it was  $0.310 \pm 0.024$ ; with ANN, MAE was  $0.319 \pm 0.024$ . Furthermore, the use of this “fusion method” was associated with higher percentages of eyes falling within 0.5 diopters of the predicted refraction than the baseline formula: for example, when the XGB algorithm was applied to LSF, the percentage increased from 76 to 82 percent. Both the SVR and XGB algorithms increased the Holladay 1-associated percentage from 72 to 82 percent. When the XGB algorithm was applied to SRK, which had a percent of 61 percent at the start, it achieved a maximum of 81 percent.<sup>39</sup>

Nemeth and coworkers compared the accuracy of results from Barrett Universal II to three AI-based methods for calculation of the IOL power (Hill-RBF 2.0, Kane method, Pearl-DGS method).<sup>51</sup> They retrospectively collected and calculated the differences between the manifest and objective postoperative refractions of 114 eyes (PE). They found significant differences for PEs among the AI-based methods both for subjective and objective refractions (all  $P < 0.05$ ). When compared to BU II, the Hill-RBF 2.0 method provided better PE accuracy. When compared to BU II, the Kane and Pearl-DGS techniques performed similarly.<sup>51</sup>

Cheng and coworkers compared new AI formulas (Kane and RBF 2.0) to other formulas in eyes with high to extreme myopia (AL  $\geq 26.0$  mm), including Wang-Koch adjustment methods for Holladay and SRK/T, BU II, EVO 2.0, and Haigis.<sup>12</sup> The Wang-Koch AL adjustment was created to improve the accuracy of standard formulas and prevent postoperative hyperopia surprises. Kane was comparable to RBF 2.0, BU II, H1-MWK and H1-WK in highly myopic eyes with an AL  $\geq 26.0$  mm, and was better than BU II and RBF 2.0 in extremely myopic eyes with an AL  $\geq 30.0$  mm.<sup>12</sup>

Langenbacher and coworkers attempted to model the measured postoperative position of an intraocular lens implant after cataract surgery using machine learning techniques.<sup>42</sup> Based on preoperative effect sizes of AL, corneal thickness, internal ACD, LT, mean corneal radius, and corneal diameter, 17 machine learning algorithms were tested for prediction performance for calculation of internal anterior chamber depth (AQD<sub>post</sub>) and axial position of the equatorial plane of the lens in the pseudophakic eye (LEQ<sub>post</sub>). In terms of root mean squared error for AQD<sub>post</sub> and LEQ<sub>post</sub> prediction, the Gaussian Process Regression Model with an exponential

kernel outperformed the machine learning algorithms. Thus, the advantage of machine learning algorithms appeared to be limited when compared to a standard multivariate regression model.<sup>42</sup>

A detailed discussion of the best available methods for IOL power calculation, including special cases (i.e., premium IOLs, post-refractive surgery, keratoconus, etc.) goes beyond the scope of this review. We strongly encourage interested readers to consult more resources to obtain more in-depth information.<sup>2,6,61,72,73,76,78,10,15,21,22,31,32,36,60</sup>

### 3.3. Surgery

There has been increased interest in modeling surgical procedures during the last decade. Besides operating room (OR) organization, the implementation of modeling into clinical practice could improve the evaluations done using surgeons and surgical tools.

#### 3.3.1. Scheduling and perioperative management

Proper scheduling of the OR is the first important step to guarantee access to treatment while providing an adequate level of care.<sup>16</sup> Devi and coworkers developed three novel prediction models to optimize and estimate the duration of three different types of ophthalmic surgeries, including cataract surgery.<sup>16</sup> In their work, they considered different variables, including surgeon and staff nurse experience and the type of anesthesia. Mathematical models and algorithms were utilized to obtain an ANN system, an adaptive neuro fuzzy inference system (ANFIS) and a multiple linear regression analysis (MLRA) system and the results of estimation were subsequently compared. They demonstrated on computer simulations of the OR how a good system of planning and scheduling could enable more work to be carried out within a reasonable time.<sup>16</sup>

Despite the introduction of checklists, the risk of medical errors, including wrong-site surgeries, remains, especially in high volume settings and in the presence of concomitant comorbidities. Yoo and coworkers designated a deep-learning-based smart speaker in ocular surgery, including age-related cataract surgery, to confirm surgical information, especially during the time-out phase.<sup>82</sup>

#### 3.3.2. Video-monitored surgery and intraoperative assistance

Video-recording systems in the OR are increasingly common because they can generate reports and can be employed for critical review of surgical skills. Real-time analyses of video-monitored surgeries might be useful to communicate information to the surgeon in due time, especially for less experienced surgeons. Thanks to the development of novel techniques relying on AI, such as machine learning and deep learning techniques, videos of cataract surgery could be segmented into constituent phases for subsequent automated skill assessment and feedback. With these tools, recommendations on how to deal with the next surgical tasks and warnings about possible task complications might be communicated to the surgeon.

Quellec and coworkers developed an automatic video analysis system based on a new algorithm capable of recognizing surgical tasks in real-time.<sup>56</sup> A content-based video retrieval

(CBVR) model was used to detect key video subsequences and to categorize surgical tasks. These subsequences were then decomposed into an optimal set of overlapping basic image intervals. They successfully applied a system that could retrieve such subsequences to recognize surgical tasks in eye surgeries.<sup>56</sup> In 2015, an algorithm for phase segmentation and recognition was proposed.<sup>57</sup> Key spatiotemporal polynomials were identified in videos to detect key gestures, and therefore, to recognize the target surgical tasks.<sup>57</sup> Morita and coworkers performed groundwork for a broader and safer cataract surgery training doing real-time phase segmentation from cataract surgical video recordings using an NN.<sup>50</sup> Real-time extraction of two important phases (i.e., the curvilinear capsulorhexis and nuclear extraction phase) was obtained with the aim of preventing complications by evaluating the surgical techniques of inexperienced surgeons too.<sup>50</sup> Yu and coworkers designed five deep learning algorithms to classify a given video segment (belonging to a phase of cataract surgery), previously pre-segmented manually.<sup>83</sup> Al Hajj and coworkers carried out a series of interesting works on AI-based tools for surgical video analysis.<sup>24–27</sup> In 2017, they developed a detector of surgical tools in surgical videos based on CNNs analyzing the sequences of consecutive images. Features extracted from each image by the CNN were fused inside the network using the optical flow to combine different views of the same object.<sup>24</sup> In the same year, they addressed the surgical detection tool problem and generated datasets of artificial surgery videos to train the CNNs and evaluating two classification methods to detect tool presence.<sup>25</sup> In another report, Al Hajj and coworkers monitored usage of surgical tools in cataract videos analyzing each frame of the video by CNNs and temporal relationships between events by RNNs.<sup>27</sup>

In 2017, the Automatic Tool Annotation for catarACT Surgery (CATARACTS) challenge was organized to evaluate tool annotation algorithms in the context of cataract surgery.<sup>26</sup> This challenge relied on more than nine hours of videos of 50 cataract surgeries, of which the presence of 21 surgical tools was manually annotated by two experts. Manual annotations were compared with deep learning solutions proposed by 14 different teams. The authors concluded that automatic annotations were comparable to manual annotations.<sup>26</sup> Annotation of surgical videos is a difficult and time-consuming task, but it is necessary for the training of deep learning algorithms. Lecuyer et al developed a semi-automated method to assist annotation of phases and steps of surgical procedures based on CNN, to reduce the duration of annotation procedure while increasing its accuracy.<sup>43</sup>

Surgical process models (SPMs) have been defined as models of a set of one or more related activities or procedures performed to achieve a surgical objective. Lalys and coworkers developed a new method for the automatic detection of the phases of the surgery from videos (high-level tasks).<sup>41</sup> They eventually extended their method for the detection of low-level surgical tasks (activities). An activity was defined by a triplet <surgical tool, action, anatomical structure>. An example of a phase in cataract surgery was represented by corneal incisions. During this phase, one of the actions identified was <1.1 mm knife, incise, cornea>. In their work, they moved from high-level to low-level tasks using a complex system with validated methods that included formalization of surgi-



cal activities, surgical tool detection, and anatomical structure detection. They reported a mean accuracy of the recognition of surgical activities of 64%, a specificity of 76.3%, and a sensitivity of 54.9%.<sup>40</sup>

Phacoemulsification is a critical phase of cataract surgery. The amount of energy released can be controlled by the surgeon and is considerably influenced by the level of experience of the first operator. For this reason, Tian and coworkers introduced a Video-Based Intelligent Recognition and Decision (VeBIRD) system to automatically track the operation process and to classify the cataract grade.<sup>66</sup>

This system included an iris detector, a phacoemulsification probe tracker, and an intelligent discriminator to detect the cataract grade. The hardness of the lens nucleus, and correspondingly, the release of the ultrasonic energy were automatically decided by a computer-aided system with intelligent programs in real-time.<sup>66</sup>

Although small incision cataract surgery has become a safe and quite reproducible procedure, the integration of robotics systems into it could improve accuracy, dexterity, and prevent some complications. Hubschman and coworkers developed electromagnetic tracking to quantify and accurately evaluate the range of motion of each instrument during the five main surgical steps of cataract surgery.<sup>34</sup> The aim was to help design new robotic systems that could give assistance during ophthalmological procedures.<sup>34</sup> The integration of AI and robotics might represent the future for telesurgery, but further steps, including the analysis of big data to deploy deep-learning models, would be necessary for building intelligent robots that are independent of human intelligence.<sup>7</sup>

### 3.4. Complications

Artificial models and NNs have also been applied in the field of cataract surgery complications to improve patient care in terms of diagnosis, prognosis, and planning. Antibiotic injection into the anterior chamber is considered an effective approach to reduce the risk of postoperative endophthalmitis. Despite the intraoperative administration of antibiotics, the development of a posterior capsular rupture is a well-known risk factor for postoperative endophthalmitis following cataract surgery.<sup>8,28</sup> Liu and coworkers performed a natural language processing (NLP) to identify two crucial intraoperative variables from surgical reports: the rupture of the posterior capsule and the injection of intracameral antibiotics.<sup>46</sup> This could support the monitoring of complications and the identification of their incidence by simplifying the data analyses. Moreover, this work could help other specialists to develop and implement NLP protocols in their own settings.<sup>46</sup>

Posterior capsule opacification and cystoid macular edema (ME) are the most frequently occurring postoperative complications after uncomplicated cataract surgery.<sup>48</sup> Mohammadi and coworkers generated three back-propagation ANNs, trained them using 282 randomly selected eyes, and tested them using 70 eyes, to predict posterior capsule status that would require capsulotomy.<sup>48</sup>

In case of diabetic patients affected by ME shortly after cataract surgery, identifying the real underlying pathology can be challenging and of crucial importance to determine the proper treatment.<sup>30</sup> Hecht and coworkers developed an auto-

mated classifying algorithm based on machine learning methods using different spectral-domain optical coherence tomography (SD-OCT) parameters to develop a simple clinical classifier capable of distinguishing the underlying pathology of ME between pseudophakic ME, diabetic ME, or “mixed” ME.<sup>30</sup> Hecht and coworkers also developed a simple web tool for use on a personal computer or mobile phone specifically designed to accurately diagnose the underlying pathology of ME post-cataract surgery and to implement the research into this field.<sup>29</sup>

## 4. Conclusions

The application of AI-driven diagnostics has been reported to be comparable and, in selected cases, even to exceed the accuracy of experienced clinicians in correctly classifying eye diseases, including cataract. More recently, other applications of AI in cataract surgery have included OR scheduling, intraoperative support, and postoperative management of complications. With advances in technology, there has been an emergence of several AI-based imaging tools and smartphone applications to provide support for clinical decisions. Such application can help deliver ophthalmology care across triage, diagnosis, and monitoring.

The unique features of these AI tools, however, make them vulnerable to distinct biases with respect to training data that, in turn, might decrease their efficiency in improving patient outcomes in clinical settings. AI algorithms perform advanced computational analysis of a huge amount of “training data” to devise a mathematical function that can be used for further extrapolation. The training set might comprise text or labeled images (as in ophthalmology). Such data reflect a reference frame for real-world scenarios; hence, it is important that the data also reflect the setting in which the AI algorithm would be used. For instance, the studies demonstrating the use of AI-based diagnostic tools must at least provide the specificity, sensitivity, NPV, and PPV values for these tools. The datasets that are used for AI algorithm generation may contain incomplete clinical metadata. This limitation makes it difficult to extrapolate population characteristics to assess the disease spectrum. In addition, AI algorithms often dichotomize diagnostic tools with unclear thresholds, which may result in inaccurate prediction of the disease spectrum as well as inefficient diagnostic potential.

Several AI algorithms have been created and tested using experimental designs and datasets; however, these cannot replicate the real-world scenarios, leading to generalizability issues.<sup>42</sup> Machine learning datasets cannot effectively represent the actual human population. Hence, for patients beyond these groups, the results obtained from the application of AI algorithms become less predictable, which may lead to undesirable inferences. The real-world applicability and generalizability of these algorithms might be limited owing to the challenges in their development and validation. Prior to their real-world application, these AI algorithms must be evaluated through randomized trials to assess their safety, cost-effectiveness, and efficacy in clinical settings. Recent studies have shown that AI algorithms have the potential to exhibit comparable or higher accuracy compared to that of ex-

perienced clinicians.<sup>42</sup> Using rigorous validation approaches, these AI applications might be optimized to support clinicians and patients while delivering ophthalmology care across triage, diagnosis, and monitoring.

Optimization of cataract patient management is crucial now more than ever. COVID-19 has significantly increased the waiting lists to access cataract surgery. International guidelines have suggested a reduction of the number of unnecessary visits for the patients and minimizing the number of OR staff without negative effects of training of young surgeons. AI tools could meet the increased needs of both surgeons and patients by optimizing preoperative management and surgery and, eventually, by reducing the incidence of complications. The implementation of AI into the clinical practice could expand the access to care and safety for the patients. Moreover, AI-guided systems could support surgeons in training as well.

To date, only a few clinical trials have compared the efficacy of AI systems in real-world settings. Indeed, only a few algorithms have also been shown to be reliable in a clinical setting. Given the possibility of potential biases, however, it is essential that more randomized controlled trials be conducted to evaluate the efficacy of AI algorithms.

## 5. Method of literature search

The following terms were combined as shown: (“Eye Diseases” [MESH] OR “Cataract Extraction”[Mesh] OR “Cataract/analysis”[Mesh] OR “Cataract/classification”[Mesh] OR “Cataract/complications”[Mesh] OR “Cataract/diagnosis” [Mesh] OR “Cataract/diagnostic imaging”[Mesh] OR “Cataract/drug therapy”[Mesh] OR “Cataract/economics”[Mesh] OR “Cataract/epidemiology”[Mesh] OR “Cataract/etiology”[Mesh] OR “Cataract/prevention and control”[Mesh] OR “Cataract/rehabilitation”[Mesh] OR “Cataract/surgery”[Mesh] OR “Cataract/therapy”[Mesh]) OR (“Lens, Crystalline/abnormalities”[Mesh] OR “Lens, Crystalline/analysis”[Mesh] OR “Lens, Crystalline/anatomy and histology”[Mesh] OR “Lens, Crystalline/diagnosis”[Mesh] OR “Lens, Crystalline/diagnostic imaging”[Mesh] OR “Lens, Crystalline/pathology”[Mesh] OR “Lens, Crystalline/physiopathology”[Mesh] OR “Lens, Crystalline/surgery”[Mesh] OR “Lens, Crystalline/therapy”[Mesh] OR “Lenses, Intraocular”[Mesh] OR “Lens Implantation, Intraocular”[Mesh] OR CATARACT OR LENS\* AND “Artificial Intelligence”[Mesh].

For this comprehensive review, a literature search of all original articles published up to 1st March 2021, was performed in parallel by three authors (A.L.V., S.M. and K.Z.-O.) from PubMed.

Three reviewers (A.L.V., S.M. and K.Z.-O.) independently screened the titles and the abstracts of articles identified by the initial search using Rayyan QCRI Software. The full texts of the relevant articles were then analyzed, and the bibliography of eligible articles were assessed to identify any study not obtained through electronic search. A fourth reviewer (R.G) was consulted in case of disagreement. The same reviewers independently extracted the following data: study title, year of publication, author, number of participants, study design, type of AI-related application, and main outcomes measured.

## Declarations of interest

None

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.sipas.2020.100009](https://doi.org/10.1016/j.sipas.2020.100009).

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