



Clinical Utility of Smartphone Applications in Ophthalmology

A Systematic Review

Ken Nagino, PhD,^{1,2,3} Jaemyoung Sung, MD,² Akie Midorikawa-Inomata, MPH, PhD,¹ Atsuko Eguchi, PhD,¹ Keiichi Fujimoto, MD, PhD,^{2,3} Yuichi Okumura, MD, PhD,^{2,3} Maria Miura, MD, PhD,^{2,3} Alan Yee, PhD,^{2,3} Shokirova Hurramhon, MD, PhD,² Kenta Fujio, MD,^{2,3} Yasutsugu Akasaki, MD,^{2,3} Kunihiko Hirosawa, MD,^{2,3} Tianxiang Huang, MD,^{2,3} Mizu Ohno, MD,^{2,3} Yuki Morooka, MD,^{2,3} Xinrong Zou, MD,^{2,4} Hiroyuki Kobayashi, MD, PhD,¹ Takenori Inomata, MD, PhD^{1,2,3,5}

Topic: Numerous smartphone applications have been devised for diagnosis, treatment, and symptom management in ophthalmology. Despite the importance of systematic evaluation of the purpose, target disease, effectiveness, and utility of smartphone applications to their effective utilization, few studies have formally evaluated their validity, reliability, and clinical utility.

Clinical Relevance: This report identifies smartphone applications with potential for clinical implementation in ophthalmology and summarizes the evidence on their practical utility.

Methods: We searched PubMed and EMBASE on July 28, 2022, for articles reporting original data on the effectiveness of treatment, disease detection, diagnostic accuracy, disease monitoring, and usability of smart-phone applications in ophthalmology published between January 1, 1987, and July 25, 2022. Their quality was assessed using the Joanna Briggs Institute Critical Appraisal Checklist.

Results: The initial search yielded 510 articles. After removing 115 duplicates and 285 articles based on inclusion and exclusion criteria, the full texts of the remaining 110 articles were reviewed. Furthermore, 71 articles were included in the final qualitative synthesis. All studies were determined to be of high (87.3%) or moderate (12.7%) quality. In terms of respective application of interest, 24 (33.8%) studies assessed diagnostic accuracy, 17 (23.9%) assessed disease detection, and 3 (4.2%) assessed intervention efficacy. A total of 48 smartphone applications were identified, of which 27 (56.3%) were publicly available. Seventeen (35.4%) applications included functions for ophthalmic examinations, 13 (27.1%) included functions aimed at disease detection, 10 (20.8%) included functions to support medical personnel, five (10.4%) included functions related to disease education, and three (6.3%) included functions to promote treatment adherence for patients. The largest number of applications targeted amblyopia (18.8%), followed by retinal disease (10.4%). Two (4.2%) smartphone applications reported significant efficacy in treating diseases.

Conclusion: In this systematic review, a comprehensive appraisal is presented on studies related to diagnostic accuracy, disease detectability, and efficacy of smartphone applications in ophthalmology. Forty-eight applications with potential clinical utility are identified. Appropriate smartphone applications are expected to enable early detection of undiagnosed diseases via telemedicine and prevent visual dysfunction via remote monitoring of chronic diseases.

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With progressive advancements in information technology, healthcare is rapidly becoming digitalized.¹ Digital healthcare enables medical interventions in various forms, including healthcare software, automated online guidance, and voice-recognition systems.^{2–5} The number of smartphone users has continued to increase since the release of the iPhone in 2007, and this number was estimated to be 3.8

billion worldwide in 2021.⁶ Because of their mobility and improved performance, smartphones can be used to provide medical intervention to a large population.⁷ Notably, modern smartphones are equipped with various sensors, including touchscreens, accelerometers, global positioning system, and cameras, which can be used to create a comprehensive profile of the dynamic physiology

of users by collecting real-time data on physical activities, lifestyle patterns, and sleep schedules.^{7–9} These data can then be combined with information manually provided by users, such as patient-reported outcomes,¹⁰ to evaluate both subjective and objective aspects of health. This novel approach to provide healthcare to a large population may facilitate early screening for undiagnosed patients, monitoring disease progression, and promoting positive behavioral changes based on current health status and individual risk factors.^{2,7,11}

According to the World Health Organization, mHealth refers to medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants, and other wireless devices.¹² Applications running on smartphones serve as the principal platform for providing mHealth.¹³ With the increasing global prevalence of smartphone users, the demand for healthcare-related smartphone applications has considerably increased.¹⁴ Numerous applications, including those that assist personalized training, diet management, tobacco or alcohol cessation, and cognitive behavioral therapies, have been developed to improve mental health.^{7,15} Applications have also been devised for disease detection and assisting clinician diagnosis via smartphone-based evaluations.^{2,16,17} Additionally, mHealth exhibits numerous advantages in terms of screening undiagnosed patients for early diagnosis and longitudinal monitoring of disease progression in a telehealth environment.^{2,18} The widespread adoption of mHealth can reduce barriers to healthcare, particularly those concerning geography, by providing smartphone application-based medicine to rural citizens.¹⁹ The potential to promote evidence-based selfdirected healthcare, provide longitudinal intervention and management, and resolve currently unsatisfied medical requirements via mHealth appear to be promising, and its implementation in current practice merits investigation.²⁰

Ophthalmology is a medical specialty in which telehealth is being increasingly incorporated, and the use of mHealth in this sector can reform clinical practice.²¹ Several applications, such as visual acuity testing and diabetic retinopathy screening tools, have been made available to physicians in the field of ocular care.^{22,23} mHealth can screen for common ocular diseases and preliminarily treat patients with undiagnosed diseases until formal evaluation.¹ However, limited formal evaluations have been performed for ophthalmologic smartphone applications,²³ and a systematic review of their clinical utility is yet to be performed.

In this study, a systematic review of published articles on smartphone applications in ophthalmology is presented to assess the clinical utility of the mHealth smartphone applications.

Methods

Search Strategy

This study was performed following the guidelines prescribed by the Preferred Reporting Items for Systematic Reviews and Metaanalyses guidelines.²⁴ Because all the reported data were obtained from the available published literature, neither institutional review board approval nor informed consents were

required for this study. All research adhered to the tenets of the Declaration of Helsinki. PubMed and EMBASE databases were searched on July 28, 2022, for articles published between January 1, 1987, and July 25, 2022. An extensive search was conducted by combining the following terms with medical subject headings without any filters: (PubMed: [mobile applications {MeSH Terms}] OR [mobile application] OR [(smartphone application] AND [Ophthalmology {MeSH Terms} OR [ophthalmology], EMBASE: ["mobile application"/exp OR "mobile application" OR "smartphone application"] AND ["ophthalmology"/exp OR ophthalmology]). The inclusion and exclusion criteria adopted in this study are presented in Table 1. The search results were compiled using EndNote 20.2 software (Clarivate Analytics). Two independent researchers (K.N. and T.I.) screened the retrieved articles. The same researchers independently assessed the texts of records deemed eligible in consensus.

Data Extraction

Two independent reviewers (K.N and T.I.) extracted the data using a standardized data extraction Excel sheet (Microsoft Corp.) and subsequently crosschecked the results.²⁵ The following data were extracted from the articles using the standardized extraction sheet: general study information (first-author name, publication date, study type, country of study, sample size, sample demographics, and main study target) and information of smartphone applications (name of smartphone application, target condition of the application, and main findings related to smartphone application). Interreviewer disagreements regarding the extracted data were resolved based on discussion with a third reviewer (J.S.). Subsequently, the following information on the extracted smartphone applications was surveyed using the standardized data extraction Excel sheet: platform, main functions, attachment, availability, and price. Studies on the extracted applications were conducted using the extracted articles and developer and download websites.

Study Quality Assessment

The Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Quasi-Experimental Studies, JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies, JBI Critical Appraisal Checklist for Case Series, and JBI Critical Appraisal Checklist for Qualitative Research were used to assess the quality of the selected studies.²⁶ The questionnaires consisted of questions with the answers "yes," "no," "unclear," or "not applicable" and "not applicable" criteria scores were excluded from the study quality estimates. The quality of the literature was determined based on the total number of "yes" responses, with \geq 70%, 69% to 50%, and \geq 49% indicating high, moderate, and low quality, respectively.²⁷

Statistical Analysis

The analyses were performed considering the Updated Method Guidelines for Systematic Reviews in the Cochrane Collaboration Back Review Group.²⁸ Basic descriptive statistics were computed to characterize the extracted data, and categorical variables are presented as percentages. The Wilcoxon rank sum and Spearman correlation tests were used to compare continuous variables. All analyses were performed using STATA software package (version 17.0; StataCorp). The threshold of statistical significance was taken to be P < 0.05.

Table 1. Inclusion and Exclusion Criteria

Inclusion criteria	
1	Article subject: smartphone application.
2	Focus of the application: health care in ophthalmology.
Exclusion criteria	
1	Ineligible article types: clinical guidelines, consensus documents, reviews, systematic reviews, and conference proceedings.
2	Animal-based studies.
3	Focus not on smartphone applications.
4	Nonsmartphone applications: For tablets, personal computers, and other platforms.
5	Focus only on design and development of applications, without reporting of clinical use.
6	Used smartphone applications for nonophthalmic purposes or used nonophthalmic applications for ophthalmic purposes.

Results

Search Results

A total of 509 articles were retrieved via database search, and 1 article was added based on manual search.²⁹ After removing 115 duplicates, 395 articles were reviewed based on the title, abstract, and article type. After initial screening, 285 articles were excluded based on the inclusion and exclusion criteria. The full texts of the 110 remaining articles were reviewed, and 39 articles were excluded for the following reasons: not focused on smartphone applications (n = 16), nonsmartphone applications (n = 11), focused only on design and development of applications without reporting clinical use (n = 4), and use of smartphone applications for nonophthalmic purposes or use of general applications for ophthalmic purposes (n = 8). The remaining 71 articles were included in the final qualitative synthesis. The screening process is illustrated in Figure 1.

Study Characteristics

The characteristics of the 71 included articles are summarized in Table S2. The articles were obtained from 24 countries and were published between July 8, 2014, and July 1, 2022. The number of published articles progressively increased from 2014 to 2021, with the exception of 2017 (2014, n = 1; 2015, n = 3; 2016, n = 5; 2017, n = 2; 2018, n = 7; 2019, n = 10; 2020, n = 18; 2021, n = 19; January to July 2022, n = 6, Figure 2). Sixty (84.5%) articles were published between January 2018 and July 2022. Among the 71 studies, 65 (91.5%) evaluated smartphone applications using patients or their families, general application users, and volunteers (total, n = 46~995 and 161 eyes); 9 (12.7%) used ophthalmologists, residents, and medical students (total, n = 339; and 3 (4.2%) used both patients and medical professionals (patients, n = 30 and 43 eyes, medical professionals, n = 33). Thirty-five (49.3%) studies assessed diagnostic accuracy, 17 (23.9%) assessed disease detectability, 3 (4.2%) assessed treatment efficacy, 10 (14.1%) were used for research, and 14 (19.7%) assessed usability. The quality of each study was assessed using the JBI critical appraisal checklists. The results are summarized in Tables S3-S6. The 71 included studies were categorized as cross-sectional studies (n = 48, 67.6%), quasiexperimental studies (n = 18, 25.4%), case series studies (n = 3, 4.2%), or qualitative research (n = 2, 2.8%). Sixty-two (87.3%) were of high quality, and 9 (12.7%) were of moderate quality.

Characteristics of Smartphone Applications

On aggregate, 48 smartphone applications were assessed in the studies we reviewed. Thirty-four (70.8%, 34/48) applications, which are listed in Table 7, were publicly available, and 14 (29.2%, 14/48) applications, listed in Table S8, were not publicly available. Seventeen (35.4%, 17/48) applications included functions for ophthalmic examinations; 13 (27.1%, 13/48) included functions aimed at disease detection; 10 (20.8%, 10/48) included functions to support medical personnel in diagnosis, surgery, and telemedicine; 5 (10.4%, 5/48) included functions related to disease education; and 3 (6.3%, 3/48) included functions to promote treatment adherence (Figure 3A). The largest number of applications targeted amblyopia as the primary disease of interest (18.8%, 9/48, including visual acuity measuring applications, Figure 3B), followed by retinal disease (10.4%, 5/48). A total of 28 (58.3%, 28/48) applications were available for both the iOS and Android platforms. Twelve (25.0%, 12/48) applications were specific to the iOS platform and 7 (14.6%, 7/48) to the Android platform. One (2.1%, 1/48) application was available on a proprietary military teleophthalmology platform. Forty-six (95.8%, 46/48) applications were standalone, whereas 2 (4.2%, 2/48) required an anaglyph glass or a dedicated plastic housing for retinal imaging. Of the 34 publicly available applications, 29 (85.3%, 29/34) were free-to-use (4 were limited version only, and 4 required prescription activation code provided by or а ophthalmologists).

Clinical Utility of Smartphone Applications

The evaluation results on clinical utility, including disease detection, diagnostic accuracy, and treatment efficacy are summarized in Table 9 for publicly available applications and in Table S10 for others. Clinical utility was deemed to be unclear for articles that solely evaluated usability or research utilization and for those that did not compare test results to those of standardized ocular examinations— these articles were excluded from this summarization. A total of 17 studies (23.9%, 17/71) evaluated the disease



Figure 1. Flow diagram of study selection.

detectability of 12 (25.0%, 12/48) applications, of which 7 evaluated the detectability of retinal diseases (progression of retinopathy based on changes in metamorphopsia symptoms, n = 3,^{11,41,42} detection of retinopathy based on metamorphopsia, n = 3,^{43,44,46} and detection of diabetic retinopathy or macular edema, $n = 1^{22}$). Four of these 7 studies used the Alleye application.^{11,41–43} Three studies evaluated the detectability of amblyopia using the GoCheck Kids application.^{58,59,71} Nine studies reported sensitivity or specificity for disease detectability, and in each study, either sensitivity or specificity exceeded 80%.^{17,36,42,44,46,57,59,65,70} One study reported a test sensitivity of 15.4% with a specificity of 100%.⁶⁵ Four studies reported an area under the curve exceeding 0.8 for disease detectability.^{17,22,43,57} One study reported a positive predictive value of 50% in

detection of refractive amblyopia using the the application.⁷¹ Twenty-five (35.2%, 25/71) studies evaluated the accuracy of application-based tests, measurements, and diagnosis of 17 (35.4%, 17/48) applications. Ten studies used the intraclass correlation coefficient or K coefficient to compare the reliability of application-based tests to clinical standard methods, $^{34-38,50,60,63,64,70}$ with 6 of these studies reporting intraclass correlation coefficient or K coefficients greater than 0.7.^{34,35,37,63,64,70} Eight studies reported significant differences between the results of standard and application-based vision tests.^{39,50,54,55,60,70,72,7} Three (4.2%) studies evaluated the treatment efficacy of applications in terms of improving treatment adherence, visual acuity, intraocular pressure, and quality of life for patients.^{20,51} Two studies reported statistically significant



Figure 2. Number of publications of the included articles.

Application Name	Target Condition	Provider, Country	Platforms	Main Functions and Description	Attachment	Price
DryEyeRhythm ^{2,17,30–32}	Dry eye disease	InnoJin, Inc., Japan	iOS, Android	Function of simple dry eye diagnosis and to collect user data. Simple dry eye diagnosis is performed by the Japanese version of the Ocular Surface Disease Index (J-OSDI) score and maximum blink interval. Data to be collected including user demographics, medical history, lifestyle history, daily subjective symptoms, J-OSDI score, blink rate per minute, maximum blink interval, contact lens use, and assessment of depressive symptoms (Self-rating Depression Scale [SDS] score).	Standalone	Free
Dry eye or not? ³³	Dry eye disease	Cornea and Refractive Surgery Society, Thailand	iOS, Android	Collecting user data on the blink rate (per minute), maximum blink interval, best spectacle-corrected visual acuity, dry eye symptoms using the Ocular Surface Disease Index, and demographic characteristics	Standalone	Free
EyeChart ^{34,35}	Visual acuity	DOK, LLC, USA	iOS, Android	Visual acuity tests with Snellen, Sloan, Tumbling E, and Landolt C charts (free edition). Near Vision Chart, Line Isolation, Amsler Grid, and Single Optotype Charts (subscription \$0.99(month)	Standalone	Free or subscription \$0.99/month for some functions
Peek Acuity ^{34,36–40}	Visual acuity	Peek Vision Ltd, UK	Android	Visual acuity test with tumbling E	Standalone	Free
AllerSearch ⁹	Allergic conjunctivitis (and allergic rhinitis due to hay fever)	InnoJin, Inc, Japan	iOS, Android	Collecting user data and questionnaire regarding allergic conjunctivitis and allergic rhinitis. Data to be collected including user demographics, medical history, lifestyle, hay fever status, preventive behavior for hay fever, and daily assessments of their conjunctiva. The questionnaire was about hay fever, including the Japanese quality-of-life questionnaire for allergic conjunctival disease (JACQLQ), the nasal symptom score, non- nasal symptom score, daily subjective symptoms, and work productivity.	Standalone	Free

Table 7. Characteristics of Publicly Available Smartphone Applications

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Table 7. (Continued.)

Application Name	Target Condition	Provider, Country	Platforms	Main Functions and Description	Attachment	Price
Alleye ^{11,20,41–43}	Retinal disease (metamorphopsia)	Oculocare medical AG, Switzerland	iOS, Android	Function to test the central retina using a dot alignment task to detect and characterize of metamorphopsia as a visual distortion in patients with age- related macular degeneration and diabetic macular edema.	Standalone	Subscription \$23.49/ month or \$97.99/ 6 month or \$139.99/12 month
myVisionTrack (mVT) ⁴⁴	Retinal disease (metamorphopsia)	Genentech, Inc, USA	iOS, Android	Self-check for metamorphopsia. The device stores the self-check test results, tracks eye disease progression, and automatically alerts a health care provider if a significant deterioration of visual function is suspected.	Standalone	Free (with a prescription only)
TreC Oculistica ⁴⁵	Telemedicine platform and visual function assessment	Azienda Provinciale per i Servizi Sanitari, Italy	iOS, Android	Functions related to video calls for telemedicine, chats with doctors, data measurement before video calls, tutorials on how to measure data, and archiving of past measurements.	Standalone (specialized on a digital platform named TreC)	Free (with a prescription only)
MacuFix ^{®46}	Retinal disease (metamorphopsia)	app4eyes GmbH & Co. KG, Germany	iOS, Android, PC (Mac, Windows)	Test function to detect metamorphopsia using 4 square fields on a screen with a grid pattern of horizontal and vertical lines. The patients are required to select the more distorted 1 of the 4 fields when viewing with 1 eye wearing appropriate near correction.	Standalone	\$9.99
Myopia app (for Android, vision app for iOS) ⁴⁷	Myopia (monitoring of smartphone use)	Innovattic, Netherlands	iOS, Android	Monitoring functions of smartphone use. The app sends to the cloud the measurements of distance between the face and mobile device, ambient light, and time spent with the device. The app can connect with optometrists, ophthalmologists, pediatricians, and eve doctors.	Standalone	Free
Eye Donor Australia ⁴⁸	Education (for corneal transplantation)	University of Wollongong, Australia	iOS, Android	Offering 3 main educational sections "About eye donation," "can I become an eye donor," and "Receiving corneal grafts".	Standalone	Free
GlaucoCheck ⁴⁹	Glaucoma (compliance management)	IPADE-Instituto para o Desenvolvimento da Educação Ltda, Brazil	iOS, Android	Functions related to patient education about glaucoma, reminders to use eye drops, recording of treatment history and test results, recording of intraocular pressure, and access to frequently asked questions.	Standalone	Free

Application Name	Target Condition	Provider, Country	Platforms	Main Functions and Description	Attachment	Price
Neurology Dx ¹⁶	Diagnostic support (for neuro-ophthalmology)	Dhannya Itty Mathew, India	iOS	Suggest function for differential diagnoses in the areas of neurology and internal medicine including neuro-ophthalmology. The app works without internet access and provides diagnostic suggestions by artificial intelligence algorithms. This app can provide links to articles that are most relevant to a particular clinical query (requires internet connection).	Standalone	Free for limited edition, subscription \$9.99/year for unlimited edition
Stereoacuity Test ⁵⁰	Stereopsis measurement	University of Bergamo, Italy	Android	Measure function of stereoacuity in children based on clinical test for Random stereoacuity.	Requires anaglyph glasses	Free
Kay Amblyopia Tracker ²⁹	Visual acuity	Kay Pictures Ltd, UK	iOS	Calculates visual acuity based on the angle subtended at the eye with the changing distance, rather than the changing optotype size.	Standalone	Free (need activation codes provided only eye professionals)
Kay iSight Pro ²⁹	Visual acuity	Kay Pictures Ltd, UK	iOS	Visual acuity test for near and distant visual acuity using Sloan letters, Landolt C Band, and Kay Picture optotypes.	Standalone	Free or subscription \$4.99/month or \$36.99/ year for some functions
EyePhone ⁵¹	Glaucoma (compliance management)	Ari Leshno, Dan Gaton et al., Israel	Android	Automatic generation of an eye drop reminder regimen based on the type of glaucoma eye drops entered.	Standalone	Free
ROP Score 3 ⁵²	Retinopathy of prematurity (score calculator)	Pabex, Argentina	iOS, Android	Calculator function for the predictor of retinopathy of prematurity (ROP) score using body wight in grams, gestational age in weeks, blood transfusion up to 6 weeks of life, oxygen in mechanical ventilation up to 6 weeks of life, and weight at completed 6 weeks of life.	Standalone	Free
SmartOptometry ³⁹	Comprehensive visual function tests	Smart Optometry d.o.o., Eslovenia	iOS, Android	This app can perform 15 tests: contrast sensitivity, visual acuity, color vision, Amsler grid, accommodation, aniseikonia, duochrome, fluorescein light, Hirschberg, maze tests for visual function on the amblyopic eye, mem retinoscopy, OKN stripes, red desaturation, Schober test, and worth four dot test.	Standalone	Free (some functions by subscription or purchase)

Table 7. (Continued.)

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Application Name	Target Condition	Provider, Country	Platforms	Main Functions and Description	Attachment	Price
toriCAM ⁵³	Surgical support	Graham barrett, Australia	a iOS	Functions to determine the axis of corneal limbal marks used as a reference to determine the correct alignment for a toric intraocular lens at the time of surgery. This app can be used to measure the axis of an implanted intraocular lens at the slit lamp postoperatively.	Standalone	Free
EyeHandBook ^{54,55}	Combination (including examination, education, and medical assistance)	Cloud Nine Development, LLC, USA	iOS, Android	Provides comprehensive functions related to ophthalmology. The list of some of the common functions is as follows: patient education videos/material, eye atlas, testing tools/calculators, practice efficiency tools, revenue/coding tools, physician references, board review material, lectures/videos, meetings/journals portals, selected American Academy of Ophthalmology content, treatment reference manual, forum discussion boards, Eye Care Professional Directory. ⁵⁶	Standalone	Free
iGlaucoma ⁵⁷	Glaucoma	Jaka Congressi, Italy	iOS, Android	Prediction function for glaucoma from visual field test reports. This application captures the printed visual fields reports on pattern deviation probability plots map and sends the image to the remote server. A diagnostic result would be generated and transmitted back to the cell phone with the instant diagnosis of glaucoma status.	Standalone	Free
GoCheck Kids ^{42,58,59,60,61}	Amblyopia, strabismus, visual acuity	Gobiquity, Inc, USA	iOS, Android	Functions including detecting amblyopia and strabismus using the pupillary reflex, and measuring visual acuity with Hansen Oil Temperature Valve (HOTV) for children 6 years and younger and ETDRS letters for children 7 years and older.	Standalone	Free

Application Name	Target Condition	Provider, Country	Platforms	Main Functions and Description	Attachment	Price
OdySight ⁶²	Visual acuity, contrast sensitivity, and retinal disease detection	Tilak Healthcare S.A.S, France	iOS, Android	Visual function tests with gamification techniques. It contains a puzzle game as well as medical modules to test monocular vision (near visual acuity, contrast sensitivity, and the detection of metamorphopsia and scotoma via a digital Amsler grid).	Standalone	Free (with prescription only)
Eye Axis Check ^{63,64}	Surgical support	Francisco Aecio Fernandes Dias, Brazil	iOS	The application allows capturing and editing of photographs, performs image transposition and projection of a protractor with 360° axis markings, and permits accurate visualization of programmed alignment for the positioning of toric intraocular lenses. In addition, the application provides the function of a simulation of the surgical plan in a graphical format	Standalone	Free
CRADLE White Eye Detector ⁶⁵	Leukocoria	Baylor University, USA	iOS, Android	Function to detect leukocoria from pictures of eyes on a face in a patient facing the camera with the face fully visible.	Standalone	Free
Intraocular Gas ⁶⁵	Intraocular pressure (prediction)	Zhaotian Zhang, China	iOS, Android	Function for the measurement of intravitreal gas volume and prediction of intraocular pressure changes due to changes in atmospheric pressure according to Boyle's law.	Standalone	Free
StrabisPIX ⁶⁶	Strabismus (guides eye direction for photograph)	Boston Children's Hospital, USA	iOS, Android	Function that guides patients through the process of obtaining images of their ocular alignment in 9 positions of gaze as well as any preferred head position for the diagnosis of strabismus.	Standalone	Free (for patients of Boston Children's Hospital)
EyeStrab ⁶⁷	Strabismus (detection from photo)	Eren Çerman, Turkey	iOS, Android	Strabismus detection function that calculates the degree of strabismus based on photographs captured with a smartphone.	Standalone	Free (be recommended for scientific purposes only)
Sensitometer ⁶⁸	Pupillometer	KagenAir LLC, USA	iOS	The app uses a flash to induce pupil contraction and takes video of the pupil in systole and diastole after the flash. The eye can be tracked, pupil size recorded over time, and the relative size of the pupil automatically calculated.	Standalone	Free

Table 7. (Continued.)

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Uvemaster ⁶⁹	Uveitis (diagnostic support)	Leading SHT, Spain	iOS, Android	Based on the input patient data, the app presents disease candidates and their sensitivity, specificity, and positive predictive value. It also provides access to the "Uvepedia" knowledge base for uveitis.	Standalone	\$14.99
Eye2Phone ⁷⁰	Color vision deficiency	Renato Neves, Portugal	iOS	Displays an exact duplicate of the full 38-plate Ishihara test, with screen- sized plates.	Standalone	\$0.99
Color Vision Test ⁷⁰	Color vision deficiency	Rila Software, Ireland	iOS	Display 16 pseudoisochromatic plates. Some plates are identical to those of the Ishihara booklet plates, whereas other plates differ completely.	Standalone	\$0.99
Diabetic retinopathy predictor ²²	Retinal disease (diagnostic support)	David Folgado De la Rosa, Spain	iOS, Android	Calculator for a score based on the risk indicating the likelihood that a diabetic patient suspected of having severe, very severe, or proliferating retinopathy or macular edema really has it. This calculation requires the following patient parameters: HbA1c (%), foveal thickness (µm) and visual	Standalone	Free

Provider, Country

app = application; HbA1c = hemoglobin A1C.

Main Functions and Description

acuity (units).

Attachment

Price

Platforms

Application Name

Target Condition



Figure 3. Characteristics of the extracted applications. (A) Purposes of the applications. (B) Target diseases of the applications.

improvements in visual acuity and eye drop adherence.^{20,51,74}

Overall, 77.3% (34/44) of the studies that evaluated detectability, accuracy, and efficacy of applications reported statistical or nonstatistical clinical utility. In addition, comparison of studies reporting sensitivity or specificity of publicly available applications revealed that sensitivity was significantly higher for paid applications than for free ones (paid applications, n = 2,^{46,70} mean \pm SD, 97.6% \pm 2.4; free applications, n = 6,^{17,36,44,57,59,65} mean \pm SD, 59.6% \pm 11.7, P = 0.038), and sensitivity and price (purchase or monthly fee) were significantly correlated (r = 0.670, P = 0.048). Specificities of paid and free applications were not significantly different (paid applications, n = 3,^{42,46,70} mean \pm SD, 83.8% \pm 9.7; free applications, n = 6,^{17,36,44,57,59,65} mean \pm SD, 89.5% \pm 2.8, P = 0.831) and specificity was not correlated with price (r = 0.030, P = 0.939).

Usability and Participant Satisfaction

A total of 21 (29.6%, 21/71) studies reported usability (n = 12) or participant satisfaction (n = 9), with 1 evaluating both.⁷⁴ Four studies used the system usability scale,⁴⁸ 1 study used the mHealth app usability questionnaire for usability evaluation,^{75,76} and the other studies used an author-designed questionnaire to evaluate usability and participant satisfaction. All system usability scale scores reported in the included studies exceeded 70 points (0–100). Usability or participant satisfaction of using smartphone applications was moderately high (more than 60% of participants or total score) in most studies with the exception of 1 study.⁷⁰ Only 1 application was rated significantly lower than the clinical standard method in terms of usability.⁷⁰

Discussion

The rate of adoption of smartphone technology has significantly increased owing to the global coronavirus disease 2019 pandemic, which increased the demand for noncontact medical care and telehealth using smartphone applications.⁷⁷ However, few studies have formally

evaluated the validity, reliability, and clinical utility of these applications.⁷⁸ Prior to the clinical use of smartphone applications, their utility should be thoroughly assessed.⁷⁹ In this study, we performed the first systematic review of articles on ophthalmologic smartphone applications published in peer-reviewed journals. A total of 71 articles on 48 ocular applications were identified in this study. Appropriate selection of smartphone applications that provide significant utility may improve the quality of ophthalmic care in telehealth environments and promote the widespread adoption of mHealth in ophthalmology.

The number of smartphone applications for mHealth has been increasing with the growing popularity and development of smartphones, and more than 325 000 mHealth applications were available for download in various application stores in 2017.⁸⁰ Ophthalmology is a medical specialty field in which experienced telehealth principles are implemented. By 2013, 342 applications had been released for both Android and iPhone platforms with eye care-themed concepts.¹⁴ In addition, 355 eye care mHealth applications were available on the Canadian iTunes Store in 2016.⁷⁸ However, a Canadian study reported that few studies have been conducted to evaluate mobile applications to improve visual functions.⁷⁸ Our research identified 48 ophthalmic smartphone applications, including ones publicly available for download in various application stores, that were evaluated for clinical utility in scientific studies. Thirty-four applications were compared with standard ophthalmic practice in terms of detectability, accuracy, and efficacy, and some clinical utility was reported. Our results may indicate that the importance of assessing the validity and reliability of applications has been recognized. In addition, paid applications demonstrated significantly higher sensitivity than free ones, and a significant correlation was observed between sensitivity and application price. However, note that the sample size of paid applications in this study was quite small. Therefore, it cannot be definitively concluded that paid applications are superior to free ones. The number of clinically assessed applications is expected to further increase in the future. By using a variety of useful applications, ophthalmologists can provide patients with novel types of eye care, such as tele-eye care.

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App Name	Source	Outcomes	Main Findings
Detectability			
DryEyeRhythm	Okumura et al ¹⁷	Dry eye disease	Using the paper-based J-OSDI and tear film breakup time as the gold standard, the precision rate of positive and negative predictive values, sensitivity, and specificity for dry eye disease (DED) diagnosis using a combination of the app-based J-OSDI and MBI were 91.3% (21/23), 69.1% (38/59), 50.0% (21/42), and 95.0% (38/40), respectively. The DED detection using the combination of app-based I-OSDI and app-based MBI was 0.910 (95% CI: 0.846-0.973).
Alleye	Islam et al ¹¹	Progression of retinal disease (metamorphopsia)	The mean change in visual acuity from baseline to follow-up post threshold alarm (defined as 3 consecutive Alleye scores that are red on separate days) generation in 85 eyes was -4.2 ETDRS letters (95% CI: -6.2 to -2.2 ; $P < 0.001$). The mean change in the central macular thickness was $+29.5 \mu\text{m}$ (95% CI: -0.1 to 59.1 ; $P = 0.051$). 66 eyes (78.5%) producing alarms either had a drop in visual acuity, increase in the central macular thickness or both and 60.0% received an intravitreal injection.
	Teo et al ⁴¹	Progression of retinal disease (metamorphopsia)	A total of 33 trigger events (defined as 3 Alleye scores consistently 25 points less than the patient's reference) from 33 patients (10.5%) were detected and 7 patients were given urgent appointments and attended the clinic. Of these 7 of 33 patients (21.0%), 5 patients (2 with DME, 1 with RVO, 1 with neovascular AMD, and 1 with myopic choroidal neovascularization) were confirmed to have disease progression on clinical examination that resulted in active intervention. The remaining 2 patients did not exhibit progression of disease, but they had difficulty using the app.
	Faes et al ⁴²	Progression of retinal disease (metamorphopsia)	The specificity was 93.8% (95% CI: 86.2%–98.0%), the corresponding false alarm rate was 6.1% (95% CI: 2.0%–13.8%). The positive predictive value (the probability that a patient with a positive result had disease progression in the next clinical follow-up visit) was 80.0% (95% CI: 59.3%–93.2%).
	Schmid et al ⁴³	Retinal disease (metamorphopsia)	Compared with age-matched healthy subjects, the AUC to detect wet AMD was 0.845 (95% CI: 0.759–0.932), and 0.660 (95% CI: 0.520–0.799) to discriminate between dry and wet AMD. Compared with young healthy subjects, the AUC to detect dry AMD was 0.799 (95% CI: 0.675–0.923), and 0.969 (95% CI: 0.940–0.997) to detect wet AMD.
myVisionTrack (mVT)	Korot et al ⁴⁴	Retinal disease (metamorphopsia)	A total of 26 alerts for substantial vision worsening were triggered. A total of 11 patients preponed their treatment appointment. In 22 of 26 alerted patients, active disease was detected during the clinic visit, and patients were subsequently treated with an anti-VEGF injection (sensitivity, 84.6%). Three patients presented with stable disease as false positives (specificity, 88.5%). One patient had a retinal detachment, which was treated.
MacuFix [®]	Claessens et al ⁴⁶	Retinal disease (metamorphopsia)	By examining with the Amsler Grid, 42 eyes were metamorphopsia, 46 were not metamorphopsia. Referring to the Amsler Grid as a gold standard, MacuFix [®] measurements were true positive in 38, false positive in 4, true negative in 43, and false negative in 3 cases (sensitivity = 92.7%, specificity = 91.5%).
iGlaucoma	Li et al ⁵⁷	Glaucoma (from visual field report)	The glaucoma diagnostic performance of the iGlaucoma app on printed visual field reports were the AUC of 0.966 (95% CI: 0.953–0.979) with a sensitivity of 95.4% and specificity of 87.3%, whereas for ophthalmologists, they were 0.850 (95% CI: 0.819–0.992), 85.8%, and 84.3% (95% CI), respectively.

Table 9.	Clinical	Usefulness	of	Publicly	Available	Smartphone	Applications
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Nagino et al • Clinical	Utility of	Smartphone	Applications	in	Ophthalr	nology
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App Name	Source	Outcomes	Main Findings
GoCheck Kids	Law et al ⁴²	Amblyopia	The PPV of the app was 50% (95% CI, 41%-60%). The PPV changed significantly with the increase in the age ($P = 0.03$). The PPV was lowest for patients 3–12 months of age at 26% (95% CI, 14% –47%). Furthermore, the PPV was higher (75%) in patients of
	Arnold et al ⁵⁸	Amblyopia	Latino/Hispanic ethnicity (95% CI, $57\%-100\%$; P < 0.01). When the 2013 American Association for Pediatric Ophthalmology and Strabismus guideline was the gold standard, the PPV for amblyopia screening using app in 217 referred children was $68\% \pm 3\%$ (95% CI: 62% to 74%). The age stratified PPVs for the toddlers, preschool, and kindergarten groups were $63\% \pm 10\%$,
	Arnold et al ⁵⁹	Amblyopia	$66\% \pm 12\%$, and $80\% \pm 10\%$, respectively. Auto detection using app revealed a sensitivity of 65% (95% CI 62% -68%) and specificity of 83% (95% CI: 80%-86%). The manual detection had the condition of 76% (05% CI 71% 81%) and
CRADLE White Eye	Vagge et al ⁶⁵	Leukocoria	specificity of 85% (95% CI $(1\%-61\%)$ and Specificity of 85% (95% CI $(1\%-61\%)$ and Of the amblyogenic cataract (n = 9), stage 5 ROP (n = 1), and
Detector			retinoblastoma (n = 3), the smartphone app could detect only 2 leukokoric eyes of the same patient caused by bilateral retinoblastoma. None of the 9 eyes with amblyogenic cataract were detected by the smartphone app. Eleven false-negatives and 0 false- positive results were detected, and the sensitivity of the white-eye detector app was 15.4% (95% CI: 1.9%–45.5%), whereas the specificity was 100% (95% CI: 98.5%–100%). The negative likelihood ratio was 0.9 (95% CI: 0.7–1.1).
Diabetic retinopathy predictor	Azrak C et al ²²	Diabetic retinopathy or macular edema	The AUC of app detection to diabetic retinopathy or macular edema was 0.90 (95% CI [0.75–1.00], $P < 0.001$). No significant differences were observed between the expected outcomes and the observed outcomes ($P = 0.422$).
Accuracy	Bhaskaran at al ³⁴	Visual acuity	ICC between EveChart and Spellen chart $= 0.087$
Lyconart	Tiraset et al ³⁵	Visual acuity	ICC between EyeChart and ETDRS chart = 0.88 (right eye) and 0.74 (left eye).
Peek Acuity	Bhaskaran et al ³⁴ Satgunam et al ³⁹	Visual acuity Visual acuity	ICC between Peek Acuity and Snellen chart = 0.980 No significant difference was observed in distance acuity between peek acuity and COMPlog (median vision acuity, COMPlog, 0.0 [0.0 -1.3], peek acuity, 0.0 [0.0-1.3], $P = 0.315$).
	Zhao et al ³⁷	Visual acuity	The ICC for visual acuity scores measured using the peek acuity application and standard clinical examination methods for first eye examined was 0.88 (95% CI: 0.83–0.92), and for second eye examined was 0.85 (95% CI: 0.78–0.89).
	de Venecia et al ³⁶	Visual acuity	Visual acuity agreement between peek acuity and the gold standard (Snellen chart) suggests an exact agreement of 31% (n = 58/190), within 1 step (0.1 logMAR units) 59% (n = 110/190), and within 2 steps 71% (n = 133/187). Weighted κ was calculated to be 0.18. When compared with the gold standard and used 20/40 as a cut-off, peek acuity was determined to have 47% sensitivity, 83% specificity, 43% positive value and 85% negative predictive value
	Irawati et al ³⁸	Visual acuity	The mean difference between the Snellen chart and peek acuity was 0.1 logMAR (95% CI, 0.10–0.13). Linear regression analysis revealed no statistically significant difference between the Snellen chart and peek acuity measurement ($P = 0.98$). Cohen's κ of visual acuity measured with peek acuity application and the Snellen chart was 0.65. The concordance rate of visual acuity measured with peek acuity application and the Snellen chart was 0.65. The concordance rate of visual acuity measured with peek acuity application and the Snellen chart was 0.65.
	Bastawrous et al ⁴⁰	Visual acuity	The mean difference between the ETDRS chart and peek acuity in clinic was 0.011 logMAR (95% CI: -0.014 to 0.035) and Pearson correlation coefficient was 0.936 (95% CI: 0.919–0.949). The mean difference between the Snellen chart and peek acuity in clinic was -0.078 logMAR (95% CI: -0.100 to -0.056) and Pearson correlation coefficient was 0.950 (95% CI: 0.937–0.960).
Neurology Dx	Vinny et al ¹⁶	Diagnostic accuracy (Neuro- ophthalmology)	Compared with the gold standard (developed by a full-time faculty specializing in neuro-ophthalmology and had a minimum of 10 years of experience in training neurology residents), the frequency of correctly identified differentials by residents was 19.4% and by app was 53.7% ($P < 0.001$).

Table 9. (Continued.)

(Continued)

App Name	Source	Outcomes	Main Findings
Stereoacuity Test	Bonfanti et al ⁵⁰	Stereoacuity	The results of stereoacuity testing by TNO, Weiss MKW, and this application were compared. Results of the test comparison showed significant differences between tests (69.0, 57.6, and 51.1 arcsec, $P < 0.001$). The ICC correlation between 3 tests revealed a moderate correlation ICC = 0.53 (0.48–0.58). Single correlation between tests revealed even moderate correlations: between TNO and Weiss ICC = 0.58 $P < 0.001$; between Weiss and app 0.49 $P < 0.001$; and between app and TNO ICC = 0.53 $P < 0.001$.
SmartOptometry	Satgunam et al ³⁹	Visual acuity	Significant difference was observed in near acuity between SmartOptometry and reduced Snellen near vision chart (median vision acuity, reduced Snellen near, 0.0 [min-max, 0.0-0.8], SmartOptometry, 0.0 [0.0-1.0], $P = 0.002$, the difference was within 2 lines statistically).
EyeHandBook	Fliotsos et al ⁵⁴	Color vision deficiency	For EHB, plates 8, 9, 10, 12, 13, 14, and 16 were excluded from comparison because of no correlating Ishihara plate design for comparing these plates. In the selected EHB slides, mean correct answer rate of participants was identified 99.44% in full-color slides, 67.2% in 2-bit-greyscale slides, and 68.9% in blue channel slides. In plates 2 through 15 of the Ishihara plates, mean correct answer rate of participants was identified 100% in full-color slides, 85.9% in 2-bit grayscale slides, and 65.6% in blue channel slides. No statistically significant differences were observed in subject performance between the Ishihara and EHB for the full color, 32-bit grayscale, or blue channel conditions ($P = 0.35$, $P = 0.39$, $P = 0.22$, respectively). Statistically significant differences were observed in proportion of given correct answer choices for 6 individual plates using Fisher's exact tests ($P < 0.01$).
	Tofigh et al ⁵⁵	Visual acuity	Measurements by the near card indicated higher logMAR values (mean = 0.2, SD = 0.2) than the measurements by the EHB app (mean = 0.1, SD = 0.1) (average of 0.1 logMAR decrease, $P < 0.001$). The results of the two techniques were significantly correlated ($r = 0.897$, $P < 0.001$).
GoCheck Kids	Silverstein et al ⁶⁰	Visual acuity	The mean differences and CI intervals between app and HOTV-ATS acuities (acuity differences: 0.094; 95% CI: 0.074–0.114) were significantly differences: 0.094; 95% CI: 0.074–0.114) were significantly differences: 0.010; 95% CI: -0.010 to 0.030) were not significantly difference: 0.010; 95% CI: -0.010 to 0.030) were not significantly different ($P = 0.319$), and between HOTV-ATS and regular clinic protocol acuities (0.084: 95% CI: 0.014–0.063) were significantly different ($P < 0.001$). The ICC between app and HOTV-ATS acuities was 0.55 (95% CI: 0.40–0.68), between HOTV-ATS and regular clinic protocol acuities was 0.59 (95% CI: 0.45–0.71), and between app and regular clinic protocol acuities was 0.66 (95% CI: 0.53–0.76). The percentage of eyes with visual acuity as measured by an app that was within 1 line of the HOTV-ATS was 65.3% and by regular clinic protocol was 86.7%, and within 2 lines of the HOTV-ATS by both chart acuities ware 96.9%
Eye Axis Check	Fernandes Dias et al ⁶³	ICRS angle	The mean difference of the ring angle between app and manual method was 4.8° (95% CI: -5.3 to 15.0, $P = 0.319$). The ICC between app and manual method was 0.991 (95% CI: 0.970–0.997, $P < 0.001$). The Pearson correlation coefficient between app and manual method was 0.984.
	Fernandes Dias et al ⁶⁴	Intraocular lens angle	The angles of app and manual method were $79.1^{\circ} \pm 51.0^{\circ}$ and $78.6^{\circ} \pm 51.2^{\circ}$ (mean difference = -0.5 , $P = 0.159$). The ICC between app and manual method was 0.997 (95% CI: 0.995–0.999, $P < 0.001$). The Spearman correlation coefficient between app and manual method was 0.995.
Sensitometer	McAnany et al ⁶⁸	Pupil size measuring	Significant correlation coefficient existed between the maximal pupil constriction obtained with the infrared camera and that obtained with the app ($r = 0.91$, $P < 0.001$). The overall mean maximal pupil constriction difference between the 2 measures averaged across subjects was 6.0%. Significant correlation coefficient was observed between the baseline (redilated) pupil size obtained with the infrared camera and obtained with the app ($r = 0.65$, $P = 0.03$). The overall mean redilated pupil size difference between the 2 measures averaged across subjects was 1.0%.

Table 9. (Continued.)

App Name	Source	Outcomes	Main Findings
Uvemaster	Gegundez-Fernandez et al ⁶⁹	Uveitis	Diagnostic accuracy was 96.6% (95% CI, 93.2–100). Of the 71 diagnosed idiopathic uveitis by clinician, the app gave rise to 19 new diagnoses of specific uveitis. The new rate of specific uveitis (performance) by app was 77.2% (95% CI, 71.1–82.9), representing an increase of 8.3%.
Eye2Phone	Sorkin et al ⁷⁰	Color vision deficiency	Using the Ishihara booklet as the gold standard, sensitivity and specificity of the app was 100% (38/38) and 95.2% (40/42). No significant difference was observed between the Ishihara booklet and the app ($P = 0.500$), with a high κ measure of agreement (0.950, $P < 0.001$).
Color Vision Test		Color vision deficiency	Using the Ishihara booklet as the gold standard, the sensitivity and specificity of app was 100% (38/38) and 54.8% (23/42). Significant difference was observed between the Ishihara booklet and the app ($P < 0.001$), with a low κ measure of agreement (0.535).
Efficacy			
Alleye	Gross et al ²⁰	Visual acuity, compliance	Patients using home monitoring by Alleye had a higher chance to improve visual acuity by ≥ 5 ETDRS letters (OR 1.7 (95% CI 1.1 to 2.8; $P = 0.044$)) than controls. Treated eyes using home monitoring by Alleye had less intravitreal injections visits/year (-1.0 [95% CI -1.6 to -0.4; $P = 0.001$]) and a longer treatment retention +69.2 days (95% CI 2.4 to 136.0; $P = 0.042$).
EyePhone©	Leshno et al ⁵¹	Compliance (eye drops), intraocular pressure, quality of life	Eight-item MMAS-8 score increased significantly from a mean of 6.4 ± 1.6 to 6.8 ± 1.5 at the 1-month follow-up ($P < 0.001$). The intraocular pressure was reduced by 2 mmHg or more in at least 1 eye in 34.5% (19/55) and by 20% or more from baseline in 27.2% (15/55) subjects. The overall mean decrease in the intraocular pressure was 0.92 mmHg (range: -0.07 to 1.92 , $P = 0.069$). The GlauQOL-17 score increased significantly ($P < 0.05$).

Table 9. (Continued.)

AMD = age-related macular degeneration; AUC = area under the curve; CI = confidence interval; DME = diabetic macular edema; EHB = EyeHandBook; GlauQOL-17 = Glaucoma Quality of Life Questionnaire – 17; ETDRS = early treatment diabetic retinopathy study; ICC = intraclass correlation coefficients; J-OSDI = Japanese version of the Ocular Surface Disease Index; LogMAR = logarithm of the minimum angle of resolution; MBI = maximum blink interval; MKW = modified EKW test; MMAS-8 = Morisky Medication Adherence Scale; OR = odds ratio; PPV = positive predictive value; ROC = receiver operating characteristic; ROP = retinopathy of prematurity; RVO = retinal vein occlusion; TNO = Nederlandse Organisatie voor Toegepast Natuurwetenschappelijk Onderzoek stereoacuity test.

Of the 71 articles included in this review, 24 (33.8%) assessed diagnostic accuracy, and 17 (23.9%) assessed disease detectability of ocular health applications. In contrast, a lower number of articles (3; 4.2%) assessed the efficacy of application-based interventions for disease management. Of the 48 applications included, 29 (60.4%) featured applicationbased ocular assessment and disease detection. A disproportionate amount of applications targeted disease detection and diagnosis as their primary function-this is in agreement with a previous study, which revealed similar results with 40.4% (53/131) of ophthalmologic applications published in the Apple App Store and Google Play Store providing primarily visual function tests and disease screening services.¹⁴ Thus, the role of mHealth applications in digital therapeutics appears to have been minimally explored, and further studies are necessary prior to implementing functions for digital interventions. Studies on application-based disease therapy for mental health diseases and lifestyle modification have been conducted, and their outcomes detail observable behavioral changes.⁸¹ Similarly, in this review, significant findings related to improved treatment efficacy were derived based on medication adherence by glaucomatous patients or promoting earlier evaluation for detecting acute exacerbation progression and of macular

pathologies.^{20,51} Effective routes for diagnosing undiagnosed patients via smartphone applications were observed to affect disease prognosis positively.² With novel diagnostic algorithms customized for remote environments and incorporation of artificial intelligence in medicine, applications that support the diagnosis of ocular diseases in telehealth environments, which previously required in-person consultation, are being developed.^{17,57} The potential of mHealth applications in disease screening and treatment adherence appears to be high, and new values are expected emerge with continual evolution of mHealth to interventions and novel digital-therapy strategies. Comprehensive assessment of healthcare applications is expected to ensure the effective use of mHealth for medical therapy.

Numerous studies on smartphone applications reviewed in this study assessed diagnostic accuracy, disease detection, and clinical utility of applications. The majority of the applications exhibited satisfactory results. Ten studies reported lower disease detectability, and 8 studies reported statistically significant differences in examination accuracy of the applications compared with conventional examinations.^{39,50,54,55,60,65,70–73} However, some differences appeared to be clinically insignificant.^{39,50,73} Despite the appropriate degree of utility in reviewed reports,

sufficient implementation of such applications in clinical environments was seldom achieved.¹⁴ Of the 71 articles included in this systematic review, 43 were published in or after 2020. Only 2 ophthalmologic smartphone applications have been formally approved by the US Food and Drug Administration, perhaps owing to the recency of the included articles and the requirement of collecting considerable amounts of data on the clinical utility of smartphone applications in practice.¹⁴ The Japanese Pharmaceuticals and Medical Devices Agency is yet to approve any ophthalmologic health application as a formal medical device. As the utility of mHealth applications in clinical applications increases, mHealth applications with governmental body approval (Food and Drug Administration and Pharmaceuticals and Medical Devices Agency) may begin to become essential components of routine clinical practice. Currently, no universal guideline has been provided regarding the use of ophthalmologic smartphone applications. With the projected increase in the number of clinical applications, an experts-led discussion on establishing an mHealth implementation guideline based on evidence-based research and meta-analysis may be crucial to attain societal agreement on the role of mHealth in practice.

This systematic review suffered from several limitations. It assessed the overarching characteristics of various ophthalmologic applications, which resulted in an expected heterogeneity between the included articles. Therefore, a meta-analysis was deferred for this systematic review. Future studies should focus on meta-analyses of the clinical outcomes of smartphone applications. In particular, few studies were observed to have reported the efficacy of applications for treatment. Therefore, future meta-analyses comparing the therapeutic effects of applications with that of standard treatment are required. Second, the articles and smartphone applications included in this study were extracted from previously published material, and yet-to-bepublished data were not assessed. Finally, this review solely considered applications that are available for use on smartphones. The utility of other smart devices and softwareexecutable personal devices, such as tablets and personal computers, was not investigated. Certain applications, including those meant for visual acuity evaluation, may benefit from a larger screen, and future reviews should assess the clinical utility of applications on various platforms to maximize their usability in practice.

Conclusions

In this systematic review, currently published articles on smartphone applications in ophthalmology were holistically assessed. The articles exhibiting clinical applicability in terms of satisfactory diagnostic accuracy, disease detectability, and utility were specified. On the one hand, the majority of applications exhibited clinical utility in ophthalmology. On the other hand, several exhibited lower diagnostic accuracy and disease detectability compared with conventional examinations. Appropriate selection of ophthalmologic smartphone applications improves the quality of care in telehealth environments and may promote the adoption of mHealth in various aspects of healthcare in ophthalmology. This summary of the current state of mHealth applications in ophthalmology is expected to contribute to laying the groundwork for future directionality and advancement of mHealth.

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Manuscript no. XOPS-D-22-00236. ¹ Department of Hospital Administration, Juntendo University Graduate School of Medicine, Tokyo, Japan.

² Department of Ophthalmology, Juntendo University Graduate School of Medicine, Tokyo, Japan.

³ Department of Digital Medicine, Juntendo University Graduate School of Medicine, Tokyo, Japan.

⁴ Department of Ophthalmology, Fengcheng Hospital, Shanghai, China.

⁵ AI Incubation Farm, Juntendo University Graduate School of Medicine, Tokyo, Japan.

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Conception and design: Nagino, Midorikawa-Inomata, Kobayashi, Inomata Analysis and interpretation: Nagino, Sung, Midorikawa-Inomata, Eguchi, Fujimoto, Okumura, Miura, Yee, Hurramhon, Fujio, Akasaki, Hirosawa, Huang, Ohno, Morooka. Zou, Kobayashi, Inomata

Data collection: Nagino, Eguchi, Fujimoto, Okumura, Miura, Yee, Hurramhon, Fujio, Akasaki, Hirosawa, Huang, Ohno, Morooka. Zou, Inomata. Obtained funding: N/A

Overall responsibility: Nagino, Sung, Midorikawa-Inomata, Eguchi, Fujimoto, Okumura, Miura, Yee, Hurramhon, Fujio, Akasaki, Hirosawa, Huang, Ohno, Morooka. Zou, Kobayashi, Inomata

Abbreviation and Acronym:

 $\mathbf{JBI} = \mathbf{Joanna} \ \mathbf{Briggs} \ \mathbf{Institute}.$

References

- Nievas Soriano BJ, Uribe-Toril J, Ruiz-Real JL, Parrón-Carreño T. Pediatric apps: what are they for? A scoping review. *Eur J Pediatr*. 2022;181:1321–1327.
- 2. Inomata T, Iwagami M, Nakamura M, et al. Characteristics and risk factors associated with diagnosed and undiagnosed symptomatic dry eye using a smartphone application. *JAMA Ophthalmol.* 2020;138:58–68.
- 3. Jiang H, Li M, Wen LM, et al. A community-based short message service intervention to improve mothers' feeding practices for obesity prevention: quasi-experimental study. *JMIR Mhealth Uhealth.* 2019;7:e13828.
- Stephens TN, Joerin A, Rauws M, Werk LN. Feasibility of pediatric obesity and prediabetes treatment support through Tess, the AI behavioral coaching chatbot. *Transl Behav Med*. 2019;9:440–447.
- Baertsch MA, Decker S, Probst L, et al. Convenient access to expert-reviewed health information via an Alexa voice assistant Skill for patients with multiple Myeloma: development study. *JMIR Cancer*. 2022;8:e35500.
- 6. Vujić A, Szabo A. Hedonic use, stress, and life satisfaction as predictors of smartphone addiction. *Addict Behav Rep.* 2022;15:100411.
- 7. Milne-Ives M, Lam C, DeCock C, et al. Mobile apps for health behavior change in physical activity, diet, drug and alcohol use, and mental health: systematic review. *JMIR Mhealth Uhealth.* 2020;8:e17046.
- DeMasi O, Feygin S, Dembo A, et al. Well-being tracking via smartphone-measured activity and sleep: cohort study. *JMIR Mhealth Uhealth*. 2017;5:e137.
- **9.** Inomata T, Nakamura M, Iwagami M, et al. Individual characteristics and associated factors of hay fever: a large-scale mHealth study using allersearch. *Allergol Int.* 2022;71: 325–334.
- Weldring T, Smith SM. Patient-reported outcomes (PROs) and patient-reported outcome measures (PROMs). *Health Serv Insights*. 2013;6:61–68.
- 11. Islam M, Sansome S, Das R, et al. Smartphone-based remote monitoring of vision in macular disease enables early detection of worsening pathology and need for intravitreal therapy. *BMJ Health Care Inform.* 2021;28: e100310.
- 12. WHO Global Observatory for eHealth, mHealth: new horizons for health through mobile technologies: second global survey on eHealth. Geneva: World Health Organization; 2011.
- Inomata T, Nakamura M, Sung J, et al. Smartphone-based digital phenotyping for dry eye toward P4 medicine: a crowdsourced cross-sectional study. *NPJ Digit Med.* 2021;4:171.
- Aruljyothi L, Janakiraman A, Malligarjun B, Babu BM. Smartphone applications in ophthalmology: a quantitative analysis. *Indian J Ophthalmol.* 2021;69:548–553.
- BinDhim NF, McGeechan K, Trevena L. Smartphone smoking cessation application (SSC App) trial: a multicountry double-

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Correspondence:

Takenori Inomata, MD, PhD, Department of Ophthalmology, Juntendo University Graduate School of Medicine, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan. E-mail: tinoma@juntendo.ac.jp.

blind automated randomised controlled trial of a smoking cessation decision-aid 'app'. *BMJ Open*. 2018;8:e017105.

- 16. Vinny PW, Takkar A, Lal V, et al. Mobile application as a complementary tool for differential diagnosis in neuroophthalmology: a multicenter cross-sectional study. *Indian J Ophthalmol.* 2021;69:1491–1497.
- Okumura Y, Inomata T, Midorikawa-Inomata A, et al. Dry-EyeRhythm: a reliable and valid smartphone application for the diagnosis assistance of dry eye. *Ocul Surf.* 2022;25:19–25.
- Bonini N, Vitolo M, Imberti JF, et al. Mobile health technology in atrial fibrillation. *Expert Rev Med Devices*. 2022;19:327–340.
- 19. Lodhia V, Karanja S, Lees S, Bastawrous A. Acceptability, usability, and Views on deployment of Peek, a mobile phone mHealth intervention for eye care in Kenya: qualitative study. *JMIR Mhealth Uhealth*. 2016;4:e30.
- **20.** Gross N, Bachmann LM, Islam M, et al. Visual outcomes and treatment adherence of patients with macular pathology using a mobile hyperacuity home-monitoring app: a matched-pair analysis. *BMJ Open.* 2021;11:e056940.
- Mazzuca D, Borselli M, Gratteri S, et al. Applications and current medico-legal challenges of telemedicine in ophthalmology. *Int J Environ Res Public Health*. 2022;19:5614.
- 22. Azrak C, Palazón-Bru A, Baeza-Díaz MV, et al. A predictive screening tool to detect diabetic retinopathy or macular edema in primary health care: construction, validation and implementation on a mobile application. *PeerJ*. 2015;3:e1404.
- 23. Suo L, Ke X, Zhang D, et al. Use of mobile apps for visual acuity assessment: systematic review and meta-analysis. *JMIR Mhealth Uhealth.* 2022;10:e26275.
- 24. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev.* 2015;4:1.
- 25. Alzahrani SA, Bin Muammar MF, Bin Muammar AF, et al. The adoption and acceptance of mHealth interventions for selfmanagement of hypertension among adult patients: a systematic review. *Cureus*. 2022;14:e31584.
- Aromataris E, Munn Z. JBI manual for evidence synthesis. *JBI*; 2020. https://synthesismanual.jbi.global. Accessed July 3, 2023.
- Goplen CM, Verbeek W, Kang SH, et al. Preoperative opioid use is associated with worse patient outcomes after total joint arthroplasty: a systematic review and meta-analysis. *BMC Musculoskelet Disord*. 2019;20:234.
- van Tulder M, Furlan A, Bombardier C, Bouter L. Updated method guidelines for systematic reviews in the cochrane collaboration back review group. *Spine*. 2003;28: 1290–1299.
- 29. O'Connor A, Waters M, England L, et al. Evaluation of a new method to track changes in vision at home for children undergoing amblyopia treatment. *Br Ir Orthopt J.* 2021;17:70–78.
- **30.** Eguchi A, Inomata T, Nakamura M, et al. Heterogeneity of eye drop use among symptomatic dry eye individuals in Japan:

large-scale crowdsourced research using DryEyeRhythm application. *Jpn J Ophthalmol.* 2021;65:271–281.

- **31.** Inomata T, Nakamura M, Iwagami M, et al. Stratification of Individual Symptoms of Contact Lens-Associated Dry Eye Using the iPhone App DryEyeRhythm: Crowdsourced Cross-Sectional Study. *J Med Internet Res.* 2020;22: e18996.
- 32. Inomata T, Iwagami M, Nakamura M, et al. Association between dry eye and depressive symptoms: large-scale crowdsourced research using the DryEyeRhythm iPhone application. *Ocul Surf.* 2020:18.
- **33.** Kasetsuwan N, Suwan-Apichon O, Lekhanont K, et al. Assessing the Risk Factors For Diagnosed Symptomatic Dry Eye Using a Smartphone App: Cross-sectional Study. *JMIR Mhealth Uhealth.* 2022;10:e31011.
- 34. Bhaskaran A, Babu M, Abhilash B, et al. Comparison of smartphone application-based visual acuity with traditional visual acuity chart for use in tele-ophthalmology. *Taiwan J Ophthalmol.* 2022;12:155–163.
- **35.** Tiraset N, Poonyathalang A, Padungkiatsagul T, et al. Comparison of visual acuity measurement using three methods: standard ETDRS chart, near chart and a smartphone-based eye chart application. *Clin Ophthalmol.* 2021;15:859–869.
- **36.** de Venecia B, Bradfield Y, Trane RM, et al. Validation of peek acuity application in pediatric screening programs in Paraguay. *Int J Ophthalmol.* 2018;11:1384–1389.
- Zhao L, Stinnett SS, Prakalapakorn SG. Visual acuity assessment and vision screening using a novel smartphone application. *J Pediatr.* 2019;213:203–210.e1.
- **38.** Irawati Y, Bani AP, Gabriella K, et al. Peek acuity vs Snellen chart for visual impairment screening in leprosy: a cross-sectional study. *Lepr Rev.* 2020;91:262–273.
- Satgunam P, Thakur M, Sachdeva V, et al. Validation of visual acuity applications for teleophthalmology during COVID-19. *Indian J Ophthalmol.* 2021;69:385–390.
- 40. Bastawrous A, Rono HK, Livingstone IAT, et al. Development and validation of a smartphone-based visual acuity test (peek acuity) for clinical practice and Community-Based Fieldwork. *JAMA Ophthalmology*. 2015;133:930–937.
- **41.** Teo KYC, Bachmann LM, Sim D, et al. Patterns and characteristics of a clinical implementation of a self-monitoring Program for Retina diseases during the COVID-19 pandemic. *Ophthalmol Retina*. 2021;5:1245–1253.
- **42.** Faes L, Islam M, Bachmann LM, et al. False alarms and the positive predictive value of smartphone-based hyperacuity home monitoring for the progression of macular disease: a prospective cohort study. *Eye*. 2021;35:3035–3040.
- **43.** Schmid MK, Thiel MA, Lienhard K, et al. Reliability and diagnostic performance of a novel mobile app for hyperacuity self-monitoring in patients with age-related macular degeneration. *Eye (Lond).* 2019;33:1584–1589.
- 44. Korot E, Pontikos N, Drawnel FM, et al. Enablers and barriers to deployment of smartphone-based home vision monitoring in clinical practice Settings. *JAMA Ophthalmol.* 2022;140: 153–160.
- **45.** Malfatti G, Racano E, Delle Site R, et al. Enabling teleophthalmology during the COVID-19 pandemic in the Province of Trento, Italy: Design and implementation of a mHealth solution. *PLoS One.* 2021;16:e0257250.
- 46. Claessens D, Ichhpujani P, Singh RB. MacuFix[®] versus Amsler grid for metamorphopsia categorization for macular diseases. *Int Ophthalmol.* 2022;42:229–238.

- 47. Enthoven CA, Polling JR, Verzijden T, et al. Smartphone Use Associated with Refractive Error in Teenagers: The Myopia App Study. *Ophthalmology*. 2021;128:1681–1688.
- **48.** Brooke J. SUS: A quick and dirty usability scale. London: Usability Evaluation Industry; 1996:189–194.
- Valente P, Carneiro CLB, de Aguiar RGP, et al. Development and usability evaluation of an application for patients with glaucoma. *Int Ophthalmol.* 2021;41:3419–3425.
- **50.** Bonfanti S, Gargantini A, Esposito G, et al. Evaluation of stereoacuity with a digital mobile application. *Graefes Arch Clin Exp Ophthalmol.* 2021;259:2843–2848.
- Leshno A, Gaton D, Singer R, et al. A novel EyePhone© App for improving adherence to glaucoma therapy. *Graefes Arch Clin Exp Ophthalmol.* 2021;259:1253–1262.
- 52. Esposito E, Knoll E, Guantay C, et al. ROP screening tool assessment and validation in a third-level hospital in argentina: A pilot study. *Journal of Pediatric Ophthalmology and Strabismus*. 2021;58:55–61.
- Chung SA, Ha SJ, Chung JH. Range of forced cyclorotation in superior oblique palsy and V-pattern strabismus. *Journal of* AAPOS. 2021;25:e57.
- Fliotsos MJ, Zhao J, Pradeep T, et al. Testing a popular smartphone application for Colour vision assessment in Healthy volunteer subjects. *Neuro Ophthalmol.* 2021;45:99–104.
- 55. Tofigh S, Shortridge E, Elkeeb A, Godley BF. Effectiveness of a smartphone application for testing near visual acuity. *Eye* (*Lond*). 2015;29:1464–1468.
- 56. Lord K, Shah VA, Krishna R. The Eye Handbook: a mobile app in ophthalmic medicine. *Mo Med.* 2013;110:49–51.
- 57. Li F, Song D, Chen H, et al. Development and clinical deployment of a smartphone-based visual field deep learning system for glaucoma detection. *NPJ Digit Med.* 2020;3:123.
- Arnold RW, Arnold AW, Hunt-Smith TT, et al. The positive predictive value of smartphone photoscreening in pediatric practices. J Pediatr Ophthalmol Strabismus. 2018;55: 393-396.
- **59.** Arnold RW, O'neil JW, Cooper KL, et al. Evaluation of a smartphone photoscreening app to detect refractive amblyopia risk factors in children aged 1–6 years. *Clin Ophthalmol.* 2018;12:1533–1537.
- **60.** Silverstein E, Williams JS, Brown JR, et al. Teleophthalmology: evaluation of phone-based visual acuity in a pediatric population. *Am J Ophthalmol.* 2021;221: 199–206.
- **61.** Walker M, Duvall A, Daniels M, et al. Effectiveness of the iPhone GoCheck Kids smartphone vision screener in detecting amblyopia risk factors. *J aapos*. 2020;24:16.e1-e5.
- **62.** Brucker J, Bhatia V, Sahel JA, Odysight, et al. A Mobile Medical Application Designed for Remote Monitoring—A Prospective Study Comparison with Standard Clinical Eye Tests. *Ophthalmology and Therapy*. 2019;8:461–476.
- **63.** Fernandes Dias FA, Fernandes Dias VJ, Carneiro CLB, et al. A novel mobile application for preoperative and intraoperative assessments of intrastromal corneal ring segments implantation for keratoconus. *Cornea*. 2020;39:1132–1138.
- **64.** Dias FAF, Dias VJF, Dutra BDAL, et al. Mobile app for preand intraoperative assessment of astigmatism correction with toric intraocular lenses in cataract surgery. *J Ophthalmology*. 2020;2020:8354140.
- **65.** Vagge A, Wangtiraumnuay N, Pellegrini M, et al. Evaluation of a free public smartphone application to detect leukocoria in high-risk children aged 1 to 6 Years. *J Pediatr Ophthalmol Strabismus.* 2019;56:229–232.

- **66.** Phanphruk W, Liu Y, Morley K, et al. Validation of Strabis-PIX, a Mobile Application for Home Measurement of Ocular Alignment. *Transl Vis Sci Technol.* 2019;8:9.
- **67.** Dericioğlu V, Çerman E. Quantitative measurement of horizontal strabismus with digital photography. *J Aapos.* 2019;23: 18.e1-e6.
- McAnany JJ, Smith BM, Garland A, Kagen SL. iPhone-based Pupillometry: A Novel Approach for Assessing the Pupillary Light Reflex. *Optom Vis Sci.* 2018;95:953–958.
- **69.** Gegundez-Fernandez JA, Fernandez-Vigo JI, Diaz-Valle D, Uvemaster, et al. A Mobile App-Based Decision Support System for the Differential Diagnosis of Uveitis. *Invest Ophthalmol Vis Sci.* 2017;58:3931–3939.
- **70.** Sorkin N, Rosenblatt A, Cohen E, et al. Comparison of Ishihara booklet with color vision smartphone applications. *Optom Vis Sci.* 2016;93:667–672.
- 71. Law MX, Pimentel MF, Oldenburg CE, de Alba Campomanes AG. Positive predictive value and screening performance of gocheck kids in a primary care university clinic. J AAPOS. 2020;24(1):17.e1–17.e5.
- **72.** Phung L, Gregori NZ, Ortiz A, et al. Reproducibility and comparison of visual acuity obtained with Sightbook mobile application to near card and snellen chart. *Retina*. 2016;36: 1009–1020.
- Hwang AD, Peli E. Positive and negative polarity contrast sensitivity measuring app. *IS&T Int Symp Electron Imaging*. 2016. Epub ahead of print.

- 74. Sun CC, Liao GY, Liao LL, Chang LC. A cooperative management app for Parents with myopic children wearing orthokeratology lenses: mixed methods pilot study. *Int J Environ Res Public Health.* 2021;18:10316.
- **75.** Chumkasian W, Fernandez R, Win KT, et al. Adaptation of the MAUQ and usability evaluation of a mobile phone—based system to promote eye donation. *Int J Med Inf.* 2021;151:104462.
- Zhou L, Bao J, Setiawan IMA, et al. The mHealth app usability questionnaire (MAUQ): development and validation study. *JMIR Mhealth Uhealth*. 2019;7:e11500.
- Iyengar K, Upadhyaya GK, Vaishya R, Jain V. COVID-19 and applications of smartphone technology in the current pandemic. *Diabetes Metab Syndr*. 2020;14:733–737.
- Rodin A, Shachak A, Miller A, et al. Mobile apps for eye care in Canada: an analysis of the iTunes store. *JMIR Mhealth Uhealth.* 2017;5:e84.
- **79.** Hogarty DT, Hogarty JP, Hewitt AW. Smartphone use in ophthalmology: what is their place in clinical practice? *Surv Ophthalmol.* 2020;65:250–262.
- Woulfe F, Fadahunsi KP, O'Grady M, et al. Modification and validation of an mHealth app quality assessment methodology for International use: cross-sectional and eDelphi studies. *JMIR Form Res.* 2022;6:e36912.
- **81.** Rowland SP, Fitzgerald JE, Holme T, et al. What is the clinical value of mHealth for patients? *NPJ Digit Med.* 2020;3:4.