

Employing mHealth Applications for the Self-Assessment of Selected Eye Functions and Prediction of Chronic Major Eye Diseases among the Aging Population

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Abstract

In the epoch of advanced mHealth (mobile health) use in ophthalmology, there is a scientific call for regulating the validity and reliability of eye-related apps. For a positive health outcome that works towards enhancing mobile-application guided diagnosis in joint decision-making between eye specialists and individuals, the aging population should be provided with a reliable and valid tool for assessment of their eye status outside the physician office. This interdisciplinary study aims to determine through hypothesis testing validity and reliability of a limited set of five mHealth apps (mHAs) and through binary logistic regression the prediction possibilities of investigated apps to exclude the four major eye diseases in the particular demographic population.

The study showed that 189 aging adults (45- 86 years old) who did complete the mHAs' tests were able to produce reliable results of selected eye function tests through four out of five mHAs measuring visual acuity, contrast sensitivity, red desaturation, visual field and Amsler grid in comparison with a "gold standard" - comprehensive eye examination. Also, part of the participants was surveyed for assessing the Quality of Experience on mobile apps.

Understanding of current reliability of existing eye-related mHAs will lead to the creation of ideal mobile application' self-assessment protocol predicting the timely need for clinical assessment and treatment of age-related macular degeneration, diabetic retinopathy, glaucoma and cataract. Detecting the level of eye function impairments by mHAs is cost-effective and can contribute to research methodology in eye diseases' prediction by expanding the system of clear criteria specially created for mobile applications and provide returning significant value in preventive ophthalmology.

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Abbreviations

<i>AMD</i>	<i>Age-related degeneration</i>
<i>ARED</i>	Age- related eye disease
<i>BLG</i>	Binary logistic regression
<i>CADTH</i>	Canadian Agency for Drugs and Technologies in Health
<i>CNIB</i>	Canadian National Institute for the Blind
<i>CS</i>	Contrast sensitivity
<i>DARI</i>	Kazakh National Center for Expertise in Medicines, Medical Devices, and Medical Equipment
<i>DR</i>	Diabetic retinopathy
<i>ETDRS chart</i>	“Early Treatment Diabetic Retinopathy Study” visual acuity chart
<i>HFA</i>	Humphrey Field Analyzer
<i>LogMAR</i>	The Logarithm of the Minimum Angle of Resolution
<i>mHA(s)</i>	mHealth application(s)
<i>mHealth</i>	Mobile Health
<i>OCT</i>	Optical Coherence Tomography
<i>QoE</i>	The quality of experience
<i>VA</i>	Visual acuity
<i>VF</i>	Visual field
<i>WHO</i>	World Health Organization

Introduction

The rising number of the aging population represents a challenge to any healthcare system due to their healthcare needs (Canadian Medical Association, 2016). Modern approaches to healthcare based on a belief that individuals should play a more active role in the daily self-management of disease, and that self-management plans fit their goals, priorities, and lifestyle (Funnell & Anderson, 2004). These approaches are based on critical aspects of chronic illness care: choices, control, and consequences (R. Rubin et al., 2002).

The prevalent negative trend in the global health of this century is the expansion of chronic diseases requiring complex management, and hence the most critical mission of healthcare today is an elimination of the leading preventable causes of corresponding disability (Bauer et al., 2014). A growing aging population with some form of change in their vision also contributes to this emerging chronic diseases' crisis (Owsley, 2011). Conferring to the WHO, globally there are approximately 1.3 billion people with deteriorated eyesight, and the majority of them are over the age of 50 years ("Blindness and vision impairment," 2018).

Given that the major chronic eye diseases (age-related macular degeneration, cataract, diabetic retinopathy, and glaucoma) are age-related, globally the epidemiological profile of reduced vision and blindness drastically influenced by existing increase in life expectancy; and, on the other hand, these four diseases in total represent the clear majority of cases of avoidable visual impairment all over the world (Flaxman et al., 2017; National Academies of Sciences, Engineering, and Medicine, 2016; Popova T.V, 2007; Schneider et al., 2010). With early intervention as a target, vision screening among adults was identified as one of the top ten priority areas for efficient clinical preventive services, that can be offered in medical settings (Maciosek et al., 2017) and became the hot topic of discussion in Canada, at the government level ("Submission to the House of Commons Standing Committee on Human Resources, Skills and Social Development and the Status of Persons with Disabilities (EN)," 2017).

Ophthalmologists recommend that adults aged over 40 to have an eye exam, at least every two years (Byrne, 2014; Einarson et al., 2006; Hooper et al., 2012; Ministry of Health of Kazakhstan, 2015). In addition, every individual with diabetes must have an annual monitoring for fundus by an eye doctor. However, there is a challenge in the provision of adequate in-time diagnosis, in case of deteriorated eye functions, due to delay or procrastinations barriers of the recommended periodic eye examination (Battakova et al., 2015a; Health Quality Ontario, 2015; Kulzhanov M & Rechel B., 2007; Perruccio et al., 2007a).

It is expected that uncorrectable vision impairment could be doubled worldwide by 2050; unless modern-day solutions for earlier identifications, are made to prevent or slow down the progression and severity of chronic age-related eye diseases and conditions of this population today, and could have a significant impact on eye health of growing aging population of tomorrow (Bourne et al., 2017; Chew & Schachat, 2015; Flaxman et al., 2017; Khanna et al., 2017; National Academies of Sciences, Engineering, and Medicine, 2016).

Today, it is high technologies that determine the effectiveness of the treatment, dramatically improve the quality of people's lives, modernize screening and examination, and ensure prevention of diseases in older adults (Bowles et al., 2015). Lately, 32% of Canadian adults consult health apps; 42 % of apps users find that they are better prepared for meeting with their physician (“Diffusion of Smart Devices for Health in Canada – Final Report | Canada Health Infoway,” 2017). Similarly, 40% of global consumers shared app’s data with their doctor, and 75% believe that mobile health (mHealth) will positively impact their wellness (Accenture LLP (US), 2016).

The ophthalmic viability of the aging individual depends on advanced technologies, including mobile apps; and most importantly, on their active development and instant implementation. Unambiguously, the fast application of such validated technology will result in decreasing of the entire cost of eye diagnostic care. The mobile app allows individuals to conduct a self- assessment of age-related eye diseases at the possible earliest stage, prior to visiting eye specialists(Keane et al., 2015), however, this will not provide exact diagnose. Hence, it is imperative to see an eye specialist for a more comprehensive eye examination, which is an integral part of preventative health care. The gold standard includes, but are not limited to, the following tests, such as contrast sensitivity, gonioscopy, corneal pachymetry, retinal photography, scans of optic nerve or macula, ultrasound, automated visual field testing (Schaneman et al., 2010; Teo et al., 2017).

Though, the implementation of any new technology; especially, disease-related mobile applications require an effective testing approach to application validity and reliability. These types of applications are different from traditional clinical techniques, and increasingly moving towards clinical domains. Nevertheless, disease self-evaluation apps surprisingly not among the frequently validated mHealth apps, although technologically advanced patient-friendly applications; especially, for the screening of various eye parameters, exist(Aleo et al., 2014; Ludwig et al., 2016; Martinez et al., 2012). There are over three hundred fifty mHealth applications for assessment of different eye functions, including visual acuity, contrast sensitivity, assessment of integrity of optic nerve through red desaturation, central and overall visual field and others (Chhablani et al., 2012a; De la Torre-Diez et al., 2015; Moradian & Safi, 2015). And, moreover, 153 of them are for self- testing(Rodin et al., 2017a).

To prevent vision loss and to support surveillance of existing eye disease, it is imperative for the health scientists to address the issue through modern approaches to the screening and comprehensive examination. Despite the high prevalence of ocular disease, only visual acuity app, occupying one - third of all eye applications in the Google Play Store, was studied in great details. Other functional eye health apps practically have not been robustly validated so far (CAOS, 2016). Additionally, these studies often include single or not more than two diseases' evaluation, since the number of eye functions' apps examined by researchers was limited, and did not cover all the parameters used in the comprehensive clinical exam (Bailey et al., 2014; Bursell et al., 2012; Tsui et al., 2014a; Zvornicanin et al., 2014). Furthermore, in the currently existing literature, no adults were surveyed for the quality of experience on any specific set of eye-related apps.

We sought to create a set of apps that are practically identical to the investigations of a real clinical exam to establish its reliability and validity. This combination of five publicly available eye-health mobile applications for self-assessment estimating the five main visual parameters should provide identification of the maximum of significant eye diseases. Furthermore, we wanted to employ this tested set of five apps in the prediction of chronic major eye diseases among the aging population, eventually, to assess it by participants' practice.

Research question and Objectives

The interest in learning more about opportunities of expanding mHealth for out-of-clinic-based individual timely screening and how they are beneficial for ensuring subsequent preventive eye health measures sparked an interest for the following research question to be answered:

The research question

The research question of this study is to identify whether the set of specific mHealth applications (mHAs) used for self-assessment of eye functions is reliable and valid and can be employed to predict a need for an early clinical assessment and further specialists' intervention in the case of age-related eye diseases (ARED).

The objectives

1. To select a limited set of mHAs' tests assessing a wide range of functional abilities relevant to the identification of eye issues associated with four major age-related eye diseases
2. To examine the reliability and validity of the selected mHAs assisting with testing of the various problems related to chronic eye diseases of the target population

3. To assess if this set of mHAs is good at identifying existing cases of functional eye changes in this population.

4. To assess the aging patient's practice related to ophthalmic mHAs through the quality of experience

Research background

A comprehensive literature review was conducted to summarize the existing knowledge regarding employing mHAs for eye assessment, clarifying advantages and disadvantages of these applications, their reliability, and validity. As well as for mHAs' use evaluating chronic eye diseases, including the assessment and the self-testing of age-related eye problems.

Four databases (PubMed, Medline, the Web of Science, and Scopus) were employed for sources search of the literature review. The following four main concepts were used building quires with "AND" operator: 1) "mobile technology," 2) "assessment," 3) "chronic eye disease," 4) "aging population." Search conducted with a use of keywords/MESH terms were used for the concepts with "OR" operator : 1) "mobile technologies", "mobile applications", "smartphone", "iPad", "tablets"; 2) "self-testing", "screening", "assessment", "reliability", "validity", "prediction", "logistic regression"; 3) "eye conditions", "eye disease", "ophthalmology", "age-related disease", "chronic disease", "medical", "healthcare"; 4) "visual acuity", "contrast sensitivity", "Amsler grid", "red desaturation", "visual field". At the later stage, a snowball approach based on the analysis of the references to the found sources as Google Scholar and Bing search engines were used to focus on the latest mHAs.

The search stage yielded 338 articles. After removing duplication and filtering stage, 64 articles were left eligible for the combination of "visual acuity/contrast sensitivity/Amsler grid/red desaturation/visual field mobile application" AND "eye diseases" OR "ophthalmology."

In order to determine the screening stage of best logistic regression approaches, the bibliographic databases PubMed and Science Direct were used as the primary search tools, and the search covered domain of ARED, epidemiology, and web-based health-related mobile applications described between 2001 and 2016. Papers using logistic regression to model age-related eye diseases' presence or susceptibility with explicitly itemized covariates were included in the database. Articles were excluded from the database if they were qualitative, employed expert-driven models, if no statistical method was outlined or if the method used to calculate significant factors was not stated.

Prevalence, the financial burden of age-related eye diseases and their impact on the quality of life

In all countries including Canada life expectancy has sharply increased. Correspondingly, due to overall population growth and the relative increase in the number of seniors, the world population with moderate and severe vision impairment has increased (Stevens et al., 2013).

Despite the high percentage of eye deterioration associated with preventable causes, 5.7% of Canadian aged 40 plus years and 13% after 65 have a visual impairment, and Canada has been an aging society for some time now with more than 1 million Canadians are blind or with partial sight due to ARED (Aljied et al., 2018). Also, one in nine Canadians are still developing irreversible vision loss by age 65 (equal to a number of women affected by breast cancer), and this increases to one out of four by age 75 (Government of Canada, 2016). Analogously, according to Chader and Taylor, (2013), 65% of the visually-deteriorated and 82% of blind world populace are over 50 years of age.

The chronic diseases of a considerable population of people represent an economic burden for any country (Arredondo & Aviles, 2015; Elmslie, 2012). The cost of vision loss will reach worldwide an alarming \$2.8 trillion with indirect costs adding another \$760 billion by 2020 (International Federation on Aging, 2013). Vision loss had the highest health care costs (direct costs) of any disease category in 2009 in Canada. It costs Canadians much more than diabetes, all cancers or cardiovascular diseases (Access Economics Pty Limited, 2009).

Visual impairment doubles the difficulties of daily living, and negatively affects economic well-being for 21% individuals (Welp A., 2016). Untreated, chronic ARED impact employment rates and a patient's independence in performing daily activities, on quality of life with decreasing personal safety, and also are associated with increased mortality and emotional challenges (Crocker Houde, 2001; C. Johnson et al., 2014; Marottoli et al., 1998; Morris et al., 2007; Obstbaum, American Academy of Ophthalmology, American Society of Cataract and Refractive Surgery, & European Society of Cataract and Refractive Surgeons, 2006).

Challenges of patient's screening or monitoring for eye diseases

Age-related macular degeneration, diabetic retinopathy, glaucoma, and cataract are four main chronic eye diseases that represent the leading cause of blindness and disability all over the world (R. Klein & Klein, 2013). Having regular comprehensive eye exams can detect these diseases long before symptoms show up and are part of the regular preventative health routine of an aging individual; and the need for regular eye checkups is demonstrated in both industrialized and developing countries (Klaver et al., 1998; Quillen, 1999). However, regular monitoring of the patients with altered eye parameters is a major eye care challenge all over the world and, also, in Canada ("Submission to the House of Commons Standing

Committee on Human Resources, Skills and Social Development and the Status of Persons with Disabilities (EN),” 2017).

Demographic changes seriously affect any single country concerning access to adequate healthcare (“Aging- foot-sept-2008.pdf,”2008; International Federation on Aging, 2013). Despite the massive health promotion by governments and authorities through mass media based that a central role in preventing chronic disease belongs to the patient (Holman & Lorig, 2004; Lorig et al., 2001), many people still lack basic knowledge of how to sustain their health by managing their chronic condition or engaging in health promotion behaviors (Ryan, 2009). And at the same time, part of the aging population does not have access to medical care because of existing socio-cultural and economic barriers (Doetsch et al., 2017; Yamada et al., 2015).

To start with, there are certain barriers for individuals to obtain timely professional eye assessment (Doetsch et al., 2017; Yamada et al., 2015). According to US national statistics compiled by the Center for Disease Control and Prevention in its Vision Health Initiative, only half of 61 million individuals at high risk of losing their eyesight underwent an eye exam in the past 12 months (“National Data | Data & Statistics | VHI | CDC,” 2015). Thus, populations of particular interest to eye exam include aging individuals, who are at risk of senile cataract, age-related macular degeneration, optic neuropathy, and degenerative myopia, the leading causes of vision loss depending on ethnicity and country/ region location (Chua et al., 2017; Health Quality Ontario, 2006). Glaucoma patients and patients with the wet type of AMD form the second group who suppose regularly monitor their eye function, but 14% of Canadians with glaucoma reported no recent contact with an eye specialist (Perruccio et al., 2007b). The third group to undergo a regular eye exam, and facing certain barriers, is a person at high risk of developing diabetes, especially in case of a high probability of retinal vascular disease and hypertension and associated comorbidities (Eijk et al., 2012). Also, not just those with established diagnoses, since a significant proportion of aging individuals with diabetes or hypertension are unaware of this. According to Jin & Trope (2011), 41% of people aged 65 years or older with established diabetes did not approach eye specialists over a 12-month period in 2011.

Access limitation to primary eye examinations and the presence of significant discrepancy in the expected and actual access to eye care services is similar in many countries and mainly include problems with transportation, communication issues with eye care providers, trusting the doctor, and the cost of eye care (Battakova et al., 2015b; Elam & Lee, 2014; Frazier & Kleinstein, 2009; Kovai et al., 2007; Owsley et al., 2006). For instance, the main barriers to timely eye examination in some countries like Kazakhstan are the problem of mass education in this area of eye care, as well as the shortage of specialists on the countryside (Battakova et al., 2015b; Kulzhanov M, Rechel B., 2007).

The further challenge includes the availability of specialists and proper equipment, the cost of professionals and referrals' issues within a context of limited resources and gaps in provincial health plan coverage for these services (Koenekoop & Gomolin, 1995; Maberley et al., 2003). The cost of professionals increases yearly for government or self-funding, and key examination resources like optical coherence tomography, visual field assessment, and retinal angiography are also costly (Violato et al., 2016). Plus, there are inefficient referrals between primary eye-care and specialized level providers (Ly et al., 2016).

Thirdly, there are elongated national wait times for seen ophthalmologist from 9.3 weeks in 1996 to 20 weeks in 2016 and the high cost of waiting per patient in Canada: \$1,305 if only hours during the average working week are considered "lost" ("Waiting Your Turn," 2017). Besides, there is a growing dissatisfaction with the wait to see a specialist: a significant proportion of Canadians, around 29%, find their delay unacceptable; 14% of patients waited more than three months for their appointment (Ly et al., 2016).

Finally, aging adults very often have a combination of several eye diseases on top of general comorbidities and show considerable variations in their responses to treatment and rates of recurrence within the course of chronic eye diseases. Despite specific self-monitoring tools, like Amsler grid (10-degree central visual field) or acuity test attempt, to alert individuals about magnitudes of change to aid priority assignments, still, there are delays and postponements of the regular comprehensive eye exam in case of complicated patients with already established eye diagnosis. For instance, only 57% of Ontarians with DR (Health Quality Ontario, 2015) and just below 50% Canadians with AMD visit an eye specialist for the periodic eye examination recommended by the Canadian Ophthalmological Society. Even more, 27% of Canadians wait more than five years between comprehensive eye exams with other 39% waiting between two and five years ("Meeting the Eye Health and Vision Care Needs of Canadians," 2018)

Notwithstanding all these issues with regular eye assessments, mass screening eye exams and their cost, early detection of ARED is the vital primary care step, because most individuals do not notice the ocular deterioration due to duality of visual acuity, and, especially, symptoms of separate eye to what extent macular edema and/or neovascularization or eye pressure has already inflicted irreparable damage to the posterior retinal pole (Bressler, 2002; Vashist et al., 2011)

According to World Health Organization, 80% of all visual impairment can be prevented or treated. The visual assessment of the older population may identify individuals at increased risk of visual impairment due to eye diseases, moreover, in two-thirds of adults visual impairment could be eliminated with refractive correction (Dandona & Dandona, 2001). Furthermore, there are researchers that support early diagnosis as a predictor of better outcomes in any stage of eye disease (AREDS2-HOME Study Research

Group et al., 2014; Chew & Schachat, 2015). Timely detection of diabetic retinopathy (DR) can reduce the risk of severe vision loss by 90% and significantly reduce long-term health care costs (Bresnick et al., 2000; Javitt & Aiello, 1996). In the study by Thomas and colleagues (2015), remote tele-assessment of glaucoma in the model was applied to a population aged 50 years and older at a frequency of one screening per year in rural Alberta. This model had a 20% upsurge in ophthalmologist-referral rate. Also, it reduced patient travel times by 61 hours and physician wait times by 30% in comparison to in-person examination (standard of care). Besides, it costs \$872 per patient screened, which was 80% less than in-person examination. Barriers of the health care system including the accessibility of eye specialists and proper equipment, especially in rural areas (Laurent, 2002), as well as, the cost and time of the medical practitioner for the eye exam can be easily overcome by mHealth technology.

mHealth potential

Information technologies are actively being introduced into various fields of healthcare, leading to a fundamental change in the quality of delivery of wide-ranging, flexible interventions for older adults (Vaportzis et al., 2017). There are different definitions for "mobile health" (mHealth) (Park, 2016a). Most of them refer to the use of mobile technologies, as one of the most promising and dynamically developing areas of electronic health (eHealth). According to Zapata and colleagues (2015), mHealth applications started their expansion in the year 2013, and research is therefore still growing (Laurent, 2002). By 2017, there were 325,000 mobile health apps worldwide ("325000 mobile health apps available in 2017," 2017).

There are specific drivers of mHealth market and particularly, of digital health apps, such as governmental policies in the field of supporting the modernization of healthcare, in which separate attention is paid to the issues of mHealth of this sector; reduction of public health financing and growth of paid services in health care all over the world, a significant number of settlements in remote areas, specific clinical requirements, upcoming of patient –centered care models, and importantly, aging population (Banthia, 2016; "The 8 drivers and barriers that will shape the mHealth app market in the next 5 years," 2014). Through the means of mobile devices and apps healthcare providers have more rapid decisions with a lower error rate, high quality of data management and accessibility, and enhanced practice efficiency and knowledge (Ventola, 2014). On the other hand, patients are more actively participating in their care (participatory healthcare), and maintaining contact with their healthcare providers through mobile applications (Boulos et al., 2011) .

Mobile applications offer improved convenience, more active engagement in self-care, and greater health personalization for individuals (Hayes et al., 2014). They create opportunities for better coordination of treatment and enable the remote provision of health services (Fiordelli et al., 2013; Hayes et al., 2014; Kay et al., 2011). As mHealth infrastructure improves, there has been an increase in the use of mHealth

methods in areas such as quantitative informatics about the behavior or condition of the patient and the results of the treatment, disease monitoring, self-tracking, support for decision-making in the provision of health care, the development of comprehensive care, patient education and empowerment for self-help, and increase public awareness as of key aspects of public health (Fjeldsoe et al., 2009; Free et al., 2013; Gómez et al., 2016; Lee et al., 2014; Ludwig et al., 2016; Park, 2016b).

Latest mHAs focus on a wide range of health issues and accumulated objective experience of using mobile health applications (mHAs) shows that mobile healthcare can be very effective in covering the population with chronic diseases which are disproportionately costly in any health-care system (Arean et al., 2016; J. H. Kim et al., 2014; Laing et al., 2014; McManus et al., 2013; Regmi et al., 2017; Swendemant et al., 2015). The mHAs can offers a continuous long-term monitoring and managing conditions such as cardiovascular disease, prostatitis, asthma, epilepsy, or chronic eye conditions (Geryk et al., 2016; Kim et al., 2014; Masterson Creber et al., 2016; McManus et al., 2013; Ranganathan et al., 2015; Yu et al., 2014).

The mHAs' resource can simplify and customize data for individual's eye care provider and acts as a web caregiver for aging patients, so they continue to have support and observation while they are at home. Mobile apps can help make more frequent monitoring of vision, and therefore, have better control of the disease. The use of mobile apps for self-assessment also provides fast results at a convenient time and place that is comfortable for the aging individual with multiple chronic conditions. The only necessary equipment for self-diagnosis and management is a mobile device with the online web application, or offline apps content. Specialized mobile apps for patient self-detection of eye disease could be a potential resource that helps doctors to track the course of the disease remotely and to facilitate treatment decisions. Furthermore, remote assessment such as regular monitoring, population screening, and self- management can be offered by cost-effective applications.

Mobile apps for eye assessment

A majority of ophthalmic diagnostic testing generates digital data, which allows all types of comprehensive eye care to be coordinated through smartphones and tablets (Chhablani et al., 2012a). Compared to the total number of all available medical apps, the number of ophthalmic applications in 2013 was limited to 342 (Tahiri et al., 2013). However, this number increased recently- there were already 355 eye care related mobile apps in June 2017 just in the Canadian iTunes market for IOS devices (Rodin et al., 2017a). Ophthalmic apps are relatively easy to program, and touch-screen functionality of iPad or smartphones grants broad utility, especially, regarding vision testing or contrast sensitivity defects across a broad range level (Allister et al., 2011; Rodríguez-Vallejo et al., 2015).

Visual manifestations are paramount in the diagnosis and monitoring of eye diseases, and their photo, video, the web or mobile app results' registration is a powerful addition to the clinical documentation and continues to be an important element of clinical and scientific ophthalmology. Latest mobile applications are optimal for the facilitation of self - care (Anderson et al., 2016; "Glaucoma Today - The Role of Smartphones in Glaucoma Care (May/June 2015)"; Petersen & Hempler, 2017).

The most significant advantage of touch screen technology is an acceptance by older patients who appear able to interact with the new devices comfortably and efficiently, who can be monitored while remaining at home, and therefore, decreasing the number of hospital visits (Tahir et al., 2014a).

Provision of home eye monitoring results in earlier detection of age-related diseases, particularly in AMD, when compared with standard care. There is limited evidence for the utility of current applications and devices for age-related illnesses (Aslam, et al., 2016a). For example, DeBuc in his study described practical advances in the role of mobile technology in diabetic retinopathy and remote assessment of the diabetic eye using a portable retinal camera, smartphone-based devices and telemedicine networks (DeBuc, 2016). Other authors have evaluated the prevalence of smartphone and tablet ownership and patient interest in self-tracking among a retinal clinic population (Ludwig et al., 2016). They found that the execution of mobile health-tracking programs for retinal pathology imposes both access to mobile devices and personal motivation to participate in self-tracking (Ludwig et al., 2016). Self-monitoring of eye parameters would potentially reduce an ever-increasing burden on patients and hospitals. At present, there is limited evidence for the utility of current applications and devices for this (Aslam et al., 2016a). Some other apps started to play a central role as medical diagnostic tools (Bastawrous et al., 2012; Haddock et al., 2013a; Maamari et al., 2014; Russo et al., 2015). However, these current separate eye health' mobile applications provided by different companies evaluate each sign of eye disease separately ("Glaucoma Today - The Role of Smartphones in Glaucoma Care (May/June 2015)"). Moreover, among all available applications, there is no a single application that assesses all of the symptoms of the top four eye problems simultaneously. Having a combination of applications that targets the major eye conditions could help users overcome technological issues described by Mendes and colleagues (2014) such as platform fragmentation, a service of the platform, and the simplicity of the system.

It should also be noted that ophthalmic applications, used for self-assessment or inpatient consultations and emergency room visits, cannot replace of office-based testing under ideal conditions (Lord et al., 2010; Moradian & Safi, 2015; Shah & Pandya, 2015). However, successful self-assessment of eye functions includes specialized eye care applications that are used to its limits, feedback, and supervision during testing and create clear pathways for referral for a complete examination or treatment by a specialized eye care provider.

Three main issues are restricting the large-scale application of self-assessment by mean of mHAs. The first is that web-based vision tests demand the accurate control of luminance, size, and contrast of targets. Scientists are trying to overcome this problem of digital tools (Kagadis et al., 2013; Tahir et al., 2014). The second is the reliability of self-assessment; to what extent can patients be relied upon to carry out self-tests when they are away from a clinical environment, especially in a case of elderly patients who might have a beginning of motor or cognitive decline (Possin, 2010). Also, the last issue is that even the current evidence for eye-related mobile applications suggest increased use in preventing and treating eye disorders, yet inconsistent measures of the reliability of each app contribute to large variability in the interpretation of findings and adherence (Dayer et al., 2017; Perera et al., 2015a). According to Steinhubl and colleagues (2015), most critically needed is real-world clinical trial evidence to provide a roadmap for the implementation of mHealth that confirms its benefits to consumers, clinicians, and payers alike. To date, there is little research examining the online applications' reliability (Perera et al., 2015b). Moreover, obtaining high-validity and reliability test results without using specific mobile applications for specific eye manifestations assumes a high probability of getting biased data.

A summary of research papers on the existing five types of mHAs

At present many separate functional eye parameters tests can be tested by mobile applications (Chang et al., 2015; Chhablani et al., 2012; "Glaucoma Today - The Role of Smartphones in Glaucoma Care", 2015; Meyer et al., 2012; Moradian & Safi, 2015; Rodin et al., 2017b; Zvornicanin et al., 2014). Surveillance data based on latest mobile-based patient assessment tools including visual acuity tests, near vision cards, preferential hyperacuity perimetry, color vision plates, auto refractor applications, pupil gauges and rulers, penlights, imaging cameras and adapters, Amsler grids, Worth 4 Dot tests, fluorescein lights, pediatric fixation targets, visual field assessment, accommodation targets, red desaturation tests, macular mapping test, and optokinetic nystagmus drums (Chhablani et al., 2012a; Keane et al., 2015; Moradian & Safi, 2015; Zvornicanin et al., 2014). Nevertheless, only 44% of them intended for self -assessment (Rodin et al., 2017a). Mostly, eye specialists or neurologists recommend self-assessment through specific application modalities, such as Internet-based shape discrimination test or even specialized expensive hardware as adaptometers or microperimetry, particularly, for the purpose of monitoring of some chronic posterior retinal diseases or multiple sclerosis (Baier et al., 2005; Schwartz & Loewenstein, 2015a; Winther & Frisen, 2015).

The mass retinal screening programs, especially in the case of diabetic retinopathy, also might include a use of smartphone-based imaging and autorefractor cameras, as SV 1, NetraG, Ocular Cellscope, PEEK or Harvard Medical school prototype or interpretation of retinal images by mobile apps (Bourouis et al., 2014a; Ludwig, Murthy, et al., 2016; Panwar et al., 2015; Prasanna et al., 2013). When visual acuity, the

most common test to evaluate the eye functions in mass screening, is measured by Snellen-type tests or by mHAs, even under the most rigidly controlled, standardized conditions, one ignores other parameters that are essential to everyday visual function such as color perception, ability to detect low-contrast objects, capability to recognize side objects, aptitude of motion detection, and ability to function visually in low illumination. These parameters adversely affected by major chronic eye diseases and needed regular surveillance.

Specifically, an early cataract first alters not visual acuity, but contrast sensitivity, diabetic retinopathy and macular degeneration mostly affect posterior retinal pole as macular edema or retinal atrophy with manifestation of visual field defects and alteration of contrast sensitivity as well (Chan et al., 2015; Chandramohan et al., 2016; Ciulla et al., 2003; Lim et al., 2012; Shandiz et al., 2011; Tamura et al., 2015). The diagnosis of glaucoma is mostly based upon a particular pattern of anatomical and functional changes (visual field loss and an increase in eye pressure) but involves visual acuity exam (Hood et al., 2013). Moreover, there is a growing body of evidence that early glaucomatous damage involves the macula (Anctil & Anderson, 1984; Hood et al., 2013).

When any eye parameters' tests are used alone, they do not provide a complete picture of the possible early parametric changes, especially because of intrinsic internal limiting factors. For example, that if one relies only on a visual acuity test, it has properties of pronounced short-term variations of vision/ intersession variability and limited sensitivity to early macular edema (B. J. Kim et al., 2014; Patel et al., 2008; Winther & Frisén, 2015). Also, arterial pressure and effect of light deprivation in cataract might dispossess the visual acuity (Paques et al., 2005). Contrast sensitivity's Pelli–Robson and Mars charts and the Smith-Kettlewell Institute Low Luminance cards may be valuable for functional self- assessment of cataracts and other media problems, and for prediction of future vision loss in an aging population, however, it cannot be used just by itself (Pelli & Bex, 2013; Schneck et al., 2004; Zimmerman et al., 2011). Red desaturation test or visual field assessment alone needs outside assistance to be incorporated into neuro-ophthalmic or glaucoma self- assessment (Behbehani, 2007; Vingrys et al., 2016).

However, given the rapid proliferation of mHealth apps, it is increasingly challenging for users, health professionals, and researchers to distinguish and assess high-quality apps (Cummings et al., 2013). These tests have to be capable of discriminating against groups of altered eye parameters with high reliability and validity. Therefore, for the implementation of mobile health tools that confirm its benefits to consumers, clinicians, and payers alike, most critically needed is real-world evidence (Steinhubl et al., 2015).

While, mHAs offers for individuals convenience, more active engagement in self-care, and greater personalization, especially when considering the significant differences in the populations to be screened,

only specific range of mobile apps might emulate closest array of apps to the primary clinical evaluation set to determine a functional deterioration in case of chronic age-related eye disease. According to the US Committee on Disability Determination for Individuals with Visual Impairments, there are specific seven functional tests that equally important in defining the full functional capabilities of any visual disability (National Research Council, 2002): visual acuity (1) refers to the clarity of vision; contrast sensitivity (2) to the ability to differentiate between light and dark; examination of integrity of optic nerve (3) including red desaturation, criteria of the ocular sensitivity to the red colour; visual field (4) as a measure of side vision; intraocular pressure (5), the Amsler grid (6) as a test for monitoring a person's central 20⁰ visual field; and visualization of the retina (7) by different machines. Eye specialists regularly use these seven ocular parameters to qualify an alteration of retinal thickness or other ocular changes, and these tests are parts of the complete ophthalmic exam common to anyone with different eye problems and issues coming to the outpatient eye clinic for quantification of the quality of vision as perceived by the individual (Piermarocchi et al., 2006).

Notwithstanding, wide-ranging research has assessed mHAs, incorporating the evaluation of phone add-ons that transfigure the camera of the mobile phone into a miniature camera for the visualization of the anterior segment and retina (7), we could not include in review these mHAs because they have specific limitations to the self-assessment (DeBuc, 2016; Haddock et al., 2013; Nazari Khanamiri et al., 2017; Shanmugam et al., 2014). The results of its screening and fundus photography need interpretation only by an eye specialist, and these apps require imaging adapters, integrated to smartphone externally; and up to present-day cannot be used as a self-assessment tool for eye diseases. We also did not find any references to the existing mHA for measuring intraocular pressure (5), although we found one study mentioning its future creation and other using smartphone-based attachment (Lowe & Holeman, 2016; Mariakakis et al., 2016). Thus, our review consists of the remaining five parameters' tests and the corresponding applications such as visual acuity, contrast sensitivity, red desaturation, Amsler grid, and visual field assessments.

The FDA vindicated certain apps for home monitoring and self-assessment (Commissioner, 2018; "First FDA Cleared Ophthalmic App for Monitoring AMD and DR," 2015). In our review of the literature, we focused only on mHAs' tests that allow participants of the study to self-examine mentioned five parameters in out-of-office setting, and, therefore, simulate a set of applications possibly closest to the comprehensive assessment in the eye office, and not just to the screening examination.

The thorough screenings of the extracted literature found a number of studies that tested four mobile apps' tests of the five we are interested in for their alacrity for eye practice (Commissioner, 2018; "First FDA Cleared Ophthalmic App for Monitoring AMD and DR," 2015). Among all ophthalmic mHAs, the

visual acuity's app for different types of electronic devices was the most studied (Akbulut et al., 2017; Allister et al., 2011; Aslam et al., 2016b; Bastawrous et al., 2015a; Pathipati et al., 2016c; Pavindran A Gounder et al., 2014a; Yehezkel et al., 2013). There are very few studies of the reliability of mobile apps for contrast sensitivity, Amsler grid or visual field (Baban et al., 2016; Bullimore et al., 2013; Dorr et al., 2013a; Luk et al., 2015; Rodríguez-Vallejo et al., 2015a; Santos & Morabe, 2016; Spofforth et al., 2017), and no study for validation of red desaturation app was found.

The overall results exhibit that most of the tested eye-related apps do not cover self-management by individual or clinical best practices established by eye professionals. The utmost of the applications studied lacked multiple eye parameters reflecting diverse eye symptoms and did not involve the necessities of the target age group in the testing process. What is more, these studies often involve single or not more than two diseases' evaluation since the number of eye functions' apps examined by researchers did not covered the set of parameters used in the comprehensive clinical exam (Bailey et al., 2014; Bursell et al., 2012; Tsui et al., 2014a; Zvornicanin et al., 2014). There was no one-method-fits-all tool for app testing. The testers, 86% of them were developers of those applications, evaluated various apps by different methods best meeting their testing needs. Also, the majority of these methods evaluated app's usability, accuracy, sensitivity, and specificity.

While studies published till 2013 reported ambiguous results with respect to assessing reliability and validity of mHAs, the recent studies that examined separate health-related applications were confident in the assessment of the quality of visual acuity application and a couple of others. In ophthalmic mobile apps apparently, this is because the researchers took into account such technical factors affecting the outcome of these tests such as the patient effort in assessment, and variable refractive error correction (Pathipati et al., 2016b).

Previous studies have shown that there is room for improvement in both performance and measurement in treatment adherence with the use of a self-monitoring and received electronic medication monitors in case of glaucoma and with the use of self-monitoring and Amsler grid in case of AMD (Bittner et al., 2014). In particular, some studies looking at various mHAs demonstrated the positive attitude of participants using apps with the impression the app was significant to them and benefited them and also feeling more motivated (Almarri & Bhatti, 2015; Peng et al., 2016).

In relation to logistic regression' literature research, up to date, there is only one study analyzing the general public knowledge of risk factors affecting vision in case of three major eye diseases, except diabetic retinopathy, using logistic regression, and it is not related to any mHAs (Noertjojo et al., 2006). Also, there are only two studies predicting eye diseases by mobile application software (Azrak et al., 2015; Chang et al., 2015).

Table (Appendix 9.2) shows the current body of knowledge (64 articles) relating to the evaluation of the top eye functions' apps that we are interested in using for this study. A summary of research papers on existing mHAs shown in Table 1 below.

TABLE 1: A Summary of Research Papers On Existing mHAs

Application under study	N of articles	Max. N of participants /eyes	Intended Eye issues	Cost	Limitations	Test analytics	Methods
<i>Single app</i>							
Amsler grid (central vision)	4	159 with AMD and 51 healthy	AMD, DR	0-1.29 \$		Positive	Wilcoxon signed rank test and sign test, criticality of the score
Central area of visual field (VF) (14°)	1	12% of planned 1400	Screening of VF		Needs specialized skills	Negative	Clinical examination and diagnosis confirming
Contrast sensitivity	9	100	cataract			Positive	Gamma function curve, limits of agreement, mean average precision, a Bland-Altman analysis, Pearson's correlation coefficient data
IOP and other glaucoma- related parameters	2	50	glaucoma		Needs specialized skills		Cross - sectional survey
Red reflex/Bruckner test	1	25			Needs specialized skills		Assessment of red reflex
Superior visual field	1	14	Goldman ptosis			negative	The average of the mean
Visual acuity	32	300	AMD,DR	0-12.9 9\$	Open source, +paid version	Positive, except of 1 art.	Bland-Altman analysis, the coefficient of repeatability, the interclass correlation coefficient, linearly weighted kappa statistics, sensitivity and specificity, Mann-Whitney test, single factor analysis, receiver-operating characteristic curve. Mean-squared difference, one-way ANOVA, a paired sample - t-test and scatterplot, the confident interval of the difference of the scores, agreement measurement, statistically significant difference, meant time scores, semi structured interview, sign and symptoms questionnaire
Visual fields	7	450 eyes	glaucoma	0-3.99 \$	Interpretation only by an eye specialist	Positive only for late stage	Probability level, pattern deviation plot, interclass coefficient, Pearson coefficient, Bland-Altman plot, sensitivity and specificity
<i>Combined apps</i>							

Visual acuity and Amsler grid	1	27	AMD			Positive	Sensitivity
Visual acuity (VA) and contrast sensitivity	5	45				Positive	Tukey and Bland-Altman plots, mean differences and limits of agreement, simple contrast ratio, linear regression
VA, Amsler, color test, stereoscopy, binocularity	1	150	screening		Needs specialized skills	Positive	X-y plot

mHAs FOR TESTING OF SPECIFIC EYE FUNCTIONS

The existing body of knowledge (64 articles) that we are interested in using for this study was divided accordingly to the five specific eye functions’ apps we had been planning to evaluate:

Visual acuity (VA) application

For the past three years, different VA tests’ applications, measuring how clear person can see at various distances, have been clinically validated. The 32 published studies compared the use of Snellen wall charts with apps on tablet devices (Bastawrous et al., 2012; Black et al., 2013; Pavindran A Gounder et al., 2014b), and smartphones, or a comparison between tablet devices and smartphones (O’Neill & McAndrew, 2016). Only one study found error rates between 10%-30% out of eleven tested app (Perera et al., 2015a). All other tested by other authors applications have standard test-retest reliability and demonstrate good concordance with the Early Treatment Diabetic Retinopathy Study (ETDRS) distance visual acuity and standard near vision test (Bodduluri et al., 2016; Brady et al., 2015; Yu et al., 2014). All of the tests are Health Insurance Portability and Accountability Act (HIPAA)-compliant in the case of adult patients. Also, some studies estimated the accuracy of the iOS-based application for the remote self-assessment of near visual acuity (Yehezkel et al., 2013). Handheld shape discrimination hyperacuity test, as representation of visual acuity, has been studied intensely well for diabetic retinopathy and macular degeneration (Azrak et al., 2015; Chen & Adelman, 2016; DeBuc, 2016; Rajalakshmi et al., 2015; Sathiyamoorthy & Kulanthaivel, 2016; Tsui et al., 2014b; Winther & Frisén, 2015), but the validation of applications intended for glaucoma and cataracts, especially in the light of combinations of a number of tests, and most importantly designed for assessment by the patients themselves, is completely missed in related ophthalmic research.

Contrast sensitivity application

The contrast sensitivity function (CSF) is the reciprocal of the degree of blackness to the whiteness of target and the ability to detect decreasing shades in luminance required to be able to see the target. CSF is

a routine clinical tool to monitor the slow progression of blinding eye diseases, such as: advanced diabetic retinopathy and cataract (Chylack et al., 1993) , glaucoma (Hitchings et al., 1981), and neurological disease (Rucker et al., 2006). Contrast sensitivity, but not visual acuity, is a more important factor affecting improvement in the vision-related quality of life (Datta et al., 2008; Fraser et al., 2013).

According to Dorr and colleagues (2013); Kiser and colleagues (2005) CSF evaluation on a mobile device is identical to that obtained with specialized equipment. Also, the application (*ClinicCSF*) to measure Contrast Sensitivity Function (CSF) with tablet devices, did not show any significant differences in all the evaluated spatial frequencies in comparing it against the functional acuity contrast test (Rodríguez-Vallejo et al., 2015a).

Amsler grid application

The Amsler grid is a test for assessing of the total 20-degree central visual field or 10-degree visual field from the point of fixation, and has been used as a self-monitoring for AMD for the past 50-60 years. These days several apps have various Amsler grids available on the go, which is very useful in hospital settings (Baban et al., 2016; Luk et al., 2015). Systematic review and meta-analysis of Faes and colleagues (2014) confirmed the diagnostic screening potential of the Amsler grid in detecting or ruling out wet AMD (Faes et al., 2014). A study by Baban et al. (2016) was the first step in bringing an evidence-based mobile application for self-screening of patients with macular disease. Their research supports the use of Amsler grid via digital interfaces as a validated screening tool and found that the digital Amsler grid is more sensitive than the paper-based grid in detecting visual field losses in eyes affected by the significant macular disease. Qualitatively, participants of this study reported greater clarity of the digital Amsler grid image, ascribed to higher contrast and backlight illumination (Baban et al., 2016).

Red desaturation application

The phenomenon of red desaturation is important in analyzing optic nerve diseases, including the sequelae of optic neuritis. Red desaturation may befall disproportionately to retention of acuity and form perception (Smith, 2004). Sometimes chiasma compression may be detected by red testing at an earlier stage than using traditional methods (Almog et al, 2014). The web-based assessment of red saturation plates can be found in the Eye Handbook and few other mobile applications (Krishna, 2010; Shah & Pandya, 2015). However, we could not find any research assessing these mobile apps.

Visual fields application

A visual field test measures an individual's entire scope of vision including their central and peripheral (side) vision. As we age, there is a normal loss of peripheral view, with the decreasing by approximately

one to three degrees of visual field per decade of life (Quillen, 1999). By the time a person reaches their 70s and 80s, there is typically a peripheral visual field loss (VFL) of 20 to 30 degrees (Johnson et al., 1989; Johnson, M. A., & Choy, D., 1987). Maamari and colleagues (2014) stated that a novel mobile phone application for Goldman ptosis visual field interpretation was highly inaccurate, highly variable, and usually underestimated the field vision loss. Adams and colleagues (2016) employed testing of a web-based comprehensive tele medical visual performance assessment system characterizing visual field defects and based on the 3D Computer- automated Threshold Amsler Grid (3D-CTAG) test, for war fighters, pilots, veterans, and civilians; listing some advantages of their visual field assessment over the Zeiss-Humphrey Visual Field Analyzer, such as detection of the early onset of macular degeneration and glaucoma before they were apparent in standard automated perimetry devices. Additionally, their system was capable of monitoring central visual field loss, e.g., due to macular degeneration, in contrast to conventional visual field tests because of the possibility of peripheral/eccentric fixation markers. In contrast to the mobile apps discussed above, two other mobile applications for visual field testing were clinically validated and performed well when compared to the Humphrey Field Analyzer (“gold standard” of visual field testing). The first is a Melbourne Rapid Fields payable app, a portable perimeter in the form of an iPad app to assess the user’s visual field and detect abnormalities in both central and peripheral locations (Kong et al., 2016; Vingrys et al., 2016). This app is sequel of a free screening app called Visual Fields Easy (VFE), which was validated for developed stage of glaucoma with promising capacity in the field compared with diagnosis based on a Humphrey 24-2 SITA-Standard outcome (C. Johnson et al., 2014; Santos & Morabe, 2016).

Methodology

Research ethics

The Ottawa University and Kazakh-Russian Medical University Human Research Ethics Committees both approved the study. This study was done considering anonymity, confidentiality, and informed consent where the study participants signed a consent form accepting to voluntarily participate in this study before being allowed to respond to the study questions (Tam et al., 2015).

Design

The framework of this research was the pragmatism concerning about what works as solutions to problems (Darke et al., 2002) and the study took the form of new research but on an existing research subject. To control extraneous variables, the one-group test-retest with “gold standard” design was used. Also, different external and internal validity threads were considered in the design: history, maturation, testing, instrumentation, selection, and interaction. The principal purpose in creating our design was to control as many errors as possible, therefore, to minimize and ideally quantify the sources of error study obtained. For all that, appropriate and large sample size using power for the calculation was obtained; conversion of measurements to core parameters of visual impairment was done; standardized procedures were followed. The study consisted of four research methods according to the objectives:

- Method 1: Mapping selection of a limited set of mHAs’ tests
- Method 2: Hypothesis testing of paired samples using different statistic techniques
- Method 3: Binary logistic regression models with a grouping variables’ type
- Method 4: Online survey of the participants.

Method 1: Selection of a limited set of mHAs with conversion of measurements

Researchers should thoroughly assess the apps that already exist in their target domain before testing any mobile health applications (Boudreaux et al., 2014). However, still, there is no comprehensive guidance on identifying health apps that are user-friendly, efficient and providing accurate information (Powell et al., 2014).

The choice of apps in our study and relevance of the set creation

In this study, among multiple eye-care related mHealth applications (mHAs), we wanted to select a set of mHAs’ tests of eye parameters potentially applicable to the ophthalmic assessment. This set supposed to replicate or mimic the comprehensive clinical evaluation as close as possible covering a wide range of functional abilities relevant to ARED and could be used outside of an eye specialist's clinic without the need for professional administration. mHAs were first screened to confirm they had one of the five

required parameters with clearly stated suggestion or recommendation to go for professional help in case of a distorted parameter. Because these mHAs were meant to be used in self-assessment practice of aging population, apps' measures were required to be brief, and to be able to be administered by a non-trained individual.

The choice of apps in our study was relied on the work of Boudreaux with colleagues describing particular strategies that may actively align the app with the available evidence base, such as (1) reviewing the scientific literature, (2) searching app stores, (3) searching app clearinghouse websites, (4) evaluating app descriptions, user ratings, and reviews, (5) piloting the apps, (6) organizing a social media query in professional and, if available, patient networks, and (7) eliciting feedback from participant (Boudreaux et al., 2014).

Conversion of measurements to core parameters of visual impairment

The avoidance of errors in our study also implies that all databases were equalized for identical units of measurement in each considered pair (Appendix, table 18 "Operational coding"). For instance, for two mHAs' tests - visual field assessment and red desaturation we have done transformation and consolidation of the range of their measurements due to that mobile apps' units of measurements were very different from the range of measurement of the professional equipment. Visual field analysis maps the visual fields of each eye independently and can sense blind spots (scotomas) and areas of subdued vision. And that is where the two, "visualEasy field" app and clinical perimetry (visual field investigation at the clinic), methods differ significantly from each other. The mobile version has a smaller number of meridians, which means that the total number of test points is significantly lower, and in addition to this, the app can determine only full scotoma, but not a decrease in the visual sensitivity of the test point. Therefore, their multiple quantitative results (different scotoma types) were reduced in this study to qualitative "yes" and "no." The second example of measurement which was re-coded was a Red Desaturation mobile test's outcome. This test usually detects a suspect of having optic nerve disease in one eye. In this study, red desaturation's result of the app was compared to absolutely different measurement – optical coherence tomography (OCT) of the optic nerve which was revealing a defect in the retinal nerve fiber layer (RNFL). Therefore, in order to be able to do a test that has a measuring for given patient, re-coding was done: "no red desaturation defect" in mHA is equal to "no RNFL defect " on OCT and vice Versa. In both cases, this may have an adverse effect on the interpretation of statistical output from SPSS.

Method 2: Hypothesis testing for paired samples employing parametric, non-parametric techniques and intra-observer agreement

Parametric and non-parametric techniques

The study collected data from a generated set of five mHAs, liable for five eye parameters, attempting closely imitate or reproduce the comprehensive clinical evaluation. The study was measuring the validity and reliability by comparing five mobile application tests' outcomes with the “gold standard”- subsequent clinical testing. Produced data had different parameters including continuous, qualitative and binary. Therefore, we treated tests statistics accordingly (Parab & Bhalerao, 2010).

Parametric tests of statistical inference used to calculate the likelihood that an observed difference between two samples (mHA and doctor) could have arisen by chance – the “null” hypothesis. For instance, when binary categorical variables were applied for outcomes of visual field test we have used a two-proportion z-test. For visual acuity and contrast sensitivity with normal (or Gaussian) distribution, when there were pretest samples from mHAs that need to be compared relatively to the average value of studied clinical tests variable, the paired t-test had been applied. When the model structure was not specified a priori but determined from the data, and the normality was a questionable, nonparametric alternative as the Wilcoxon signed- rank test, paired-sample test, was used (Pettitt, 1979). Table 2 describes the statistical tests used to investigate the eight hypotheses. Unless stated otherwise, all two-tailed tests are based on a 95% confidence interval in the process of hypotheses analyses to sift the variables, which is equal to $\alpha = 0.05$.

TABLE 2: Hypotheses Testing With Statistical Tests Used In This Study

N	Sample pairs	Assumptions	Hypothesis	Test' type	Statistica l test	Formula
1	Visual acuity (VA) on mHA against “gold standard” – clinical exam	The input parameters are continuous numbers. Repeated measurements on the same set of subjects.	Ho: $\mu_1 = \mu_2$, where μ stands for the sample mean. The mean difference between two samples is equal for the repeated subjects. HA: $\mu_1 \neq \mu_2$ There is the difference between two samples	Parametric	A paired t-test	$t = \frac{\bar{x}_1 - \bar{x}_2}{\sqrt{\frac{S_1^2}{N_1} + \frac{S_2^2}{N_2}}}$
2	VA level of ill and healthy participants (pair 1: ill on app vs. doctor, pair 2: healthy on app vs. doctor)	The input parameters are continuous numbers. Two paired samples with equal variance. The normal (or Gaussian) distribution.	Ho: $\mu_1 = \mu_2$, where μ stands for the sample mean. The mean difference between two samples is equal for the repeated subjects. HA: $\mu_1 \neq \mu_2$. There is a difference between two samples	Parametric	A paired t-test	$t = \frac{\bar{x}_1 - \bar{x}_2}{\sqrt{\frac{S_1^2}{N_1} + \frac{S_2^2}{N_2}}}$
3	Contrast	Input variables of this	Ho: The median differe	Nonparam	Wilcoxo	

	sensitivity (CS) on mHA against "gold standard" - Pelli-Robson chart,	comparison are ordinal. The population is not Gaussian in this case, but distribution is approximately symmetric.	nce between pairs of observations is zero. HA: The median difference between pairs of observations is not zero.	etric	n signed-rank test	$W = \sum_{i=1}^{N_r} [\text{sgn}(x_{2,i} - x_{1,i}) \cdot R_i],$ or W= the sum of the signed ranks.
4	Red desaturation (RD) on mHA against OCT measurement for glaucoma's optic nerve asymmetry	Data is paired and comes from the same population. The responses are ordinal. The population is not Gaussian in this case, and measurements from each test are not precisely identical even after converted to similar scale.	Ho: The median difference between pairs of observations is zero. HA: The median difference between pairs of observations is not zero.	Nonparametric	Wilcoxon signed-rank test	$W = \sum_{i=1}^{N_r} [\text{sgn}(x_{2,i} - x_{1,i}) \cdot R_i],$ or W= the sum of the signed ranks.
5	Amsler grid on mHA against clinical paper-based Amsler grid (AG)	Input variables of this comparison are ordinal. The population is not Gaussian in this case, but distribution is approximately symmetric.	Ho: The median difference between pairs of observations is zero. HA: The median difference between pairs of observations is not zero.	Nonparametric	Wilcoxon signed-rank test	$W = \sum_{i=1}^{N_r} [\text{sgn}(x_{2,i} - x_{1,i}) \cdot R_i]$ or W= the sum of the signed ranks.
6	AG, CS, RD, against clinical exam for (1) women and (2) men	Inputs variables of this comparison are ordinal, and assumptions are described above.	Ho: The median difference between pairs of observations is zero. HA: The median difference between pairs of observations is not zero.	Nonparametric	Wilcoxon signed-rank test	$W = \sum_{i=1}^{N_r} [\text{sgn}(x_{2,i} - x_{1,i})]$ or W= the sum of the signed ranks.
7	Visual field assessment from mobile app against automated clinical perimetry	Paired two samples. Binary categorical variables. Since $np > 5$ and $n(1-p) > 5$, normal approximation to binomial is used (n =sample size, p =mean of the binary variable)	H0: VFL is equal on mHA and in doctor's clinic ($p_1 = p_2$). HA: VFL is not equal on mHA and in doctor's clinic ($p_1 \neq p_2$).	Parametric	Two-proportion z-test	
8	AG,CS,RD,VF from mHAs against paper-based AG, Pelli-Robson chart, OCT of optic nerve, VF perimetry	The response data are paired observations of the same phenomenon. The categorical variables are mutually exclusive. The two ratings are independent and unique.			Cohen's kappa agreement	

Testing reliability by a measurement of kappa agreement for qualitative (categorical) items

For this quantitative health study, we needed to estimate the repeatability of the measuring process, and we were also concerned to establish whether two techniques used to measure a particular eye parameter, under identical circumstances, construct the reproducibility or the same result. Both repeatability and reproducibility are measures of reliability which in turn in this study was assessed by Cohen's kappa agreement for Amsler grid, contrast sensitivity, red desaturation, and visual field. Expressly for categorical data, the kappa measurement, subject to proper use and interpretation, delivers valuable evidence on the reliability of diagnostic and other examination procedures (Sim & Wright, 2005). As these two authors stated, when there is a need to measure of agreement between $j \geq 2$ ratings for binary or categorical outcomes, the multifaceted scientific research involving a comparison of various pairs of data extensively uses a coefficient of agreement or kappa (Sim & Wright, 2005). The selection amongst several existing version of the kappa to use depends on the data at hand.

Method 3: Binary logistic regression models with grouping variables' type associated with ARED

According to the Healthline Editorial Team, 56 causes of eye disorders are known, which manifest hundreds of symptoms (The Healthline Editorial Team, 2012). While every patient is different, and the clinical judgment should always prevail, it is imperative to the patient himself to turn to an eye specialist in time according to his symptoms and inherent risk factors for eye disease. Symptoms' surveillance mobile apps to overcome barriers to eye care will be indispensable to inform focused individual health efforts to increase timely access to needed services.

All patient-specific information with data already employed in many of the mHealth applications (K.D. Mandl et al., 2007; Kenneth et al., 2015), and can be used to establish the input for reasonable probability. With help of such data this study identified the most critical risk factors for ARED through the use of logistic regression to find an appropriate discriminant function that helps in the preliminary awareness of the specific disease.

Logistic regression is a multivariate analysis method that expresses the strength of the association between a binary dependent variable and one or more independent variables as adjusted odds ratios (Rosner, 1984), and it was chosen for several reasons for this study: 1. Without logistic regression it is unthinkable to build models in modern medicine and conduct clinical studies, or analysis of data frequently arising in health sciences research, especially in ophthalmology (Lemeshow & Hosmer, 2009); 2. logistic regression analysis generates a statistical significance value for each covariate in the model,

which allows comparison of covariates between diseases (Sperandei, 2014); and 3. logistic regression analysis can generate probabilities of age-related diseases' susceptibility and risk (Li, Fan, & Balluz, 2009; Nano et al., 2013).

The altered visual parameter of the eye coming from the mHAs may indicate the possibility of some underlying eye problem. However, single mobile application test might not signpost the presence of any particular eye problem. Rather, the mobile app is effective if it results in detecting symptoms of eye disease while the patient is asymptomatic and in the commencement of an efficacious therapy that could prevent or retard the advancement of disease to reduce vision loss.

In this regard, our study of weighted binary logistic regression evaluated the main effect of the type of mHAs' test on the possibility of occurrence of four major types of eye disease when monitoring the maturing individual for socio-demographic and clinical characteristics, and the hypothesis of the third objective of the study was:

- H_0 : Aging individual using a limited set of eye - related mHAs, close to the real clinical exam, may predict possibility of major eye disease, and there are relationships between mHAs' predictors and diseases based on the results of the assessment of the tested five applications.
- H_A : No possibility to predict the diseases by tested five apps in aging individual, and no relationships between mHAs' predictors and diseases.

In logistic regression model fitting, there are two common approaches to select the best model of variables: forward selection vs. backward elimination fitting (Bursac et al., 2008). Considering very few logistic-regression based research related to eye-specific diseases (Elsalam, 2015; Ferreras et al., 2010; Lemeshow & Hosmer, 2009; Rosner, 1984), we described the main features of this method. Logistic regression method allows estimating the parameters of the regression equation which helps to forecast the probability (or odds ratio) that a particular risk factor is related to certain age-related condition or disease. Usually, predictors can be nominal, ranking, or categorical variables. The method can be used to predict the probability of certain diseases as for the case of dichotomous dependent variables, and for those cases when the dependent variable has more than two categories. The logistic regression model might predict the probability of the dependent variable Y (age-related eye disease) at various levels of our established independent variables. We used P(x) to represent the probability that Y =1, which is the presence of glaucoma, cataract, AMD, and DR separately. In case of probability that Y =0 or absence of any of four age-related eye diseases, 1-P (x) was expounding. The probabilities are written in the following form:

$$P(x) = P(Y = 1|X1_, 2_, X3_..., Xn)$$

$$1 - P(x) = P(Y = 0|X1_, 2_, X3_..., Xn)$$

All models were controlled for age, sex, race/ethnicity, education, medical comorbidity and health status. Additional models were also constructed that were also adjusted to account for previous eye surgery, reports of a visit to an eye care specialist for the previous 12 months. Since Canadians have the right to be examined free of charge only once a year by the eye specialist, a certain percentage of the participants (28%) did not have an appointment to undergo a clinical study and therefore were not included in this part of the study. To assess the impact of differences in participation rates in the exam, we conducted two sensitivity analyses. First, we compared a sample of Kazakhstanis who underwent an eye exam directly after testing mHAs to cohort of Canadian participants who did not exceed the maximum time (more than a year) between examination by five apps and a clinical examination. As a second sensitivity analysis, the time indicator between the mHAs exam and the subsequent clinical exam was included in all models. Since the results of this analysis did not significantly change the results of the study, the results presented here do not include the adjustment of the time between mobile application and the clinical examinations.

For more elaboration, the statistical tests are used as follows: The relative contribution of individual predictors is expressed by the value of Wald Chi-square statistics providing an index of the significance of each predictor in the equation. If the significance values assessing Wald are less than a value of 0.05, we reject the null hypothesis as the variable does make a significant contribution. If the coefficient is very large, the Wald statistic can become unreliable, in this case, better refer to the change in the log likelihood instead. However, log-odds are not a very straightforward concept. Therefore, we used the multiplicative form of the equation using exp (B), and multiplicative forms were:

Where interest is in coefficients that differ from 1. Values greater than 1 indicate that the variable in question increases the odds of the dependent “event” occurring and values less than 1 (i.e., between 0 and 1) indicate a decrease in the odds. Effectively the odds for the base category are set to 1.

$$\frac{\pi}{(1-\pi)} = e^{\alpha} \times e^{\beta_1 X_1} \dots \times e^{\beta_n X_n}$$

Method 4: Online survey to assess participants’ experience related to mHAs use

The rapid growth of new software industry of smartphones and tablets in the last years propitiated numerous low-quality applications to be reappraised and improved (Martínez-Pérez et al., 2013). Surveys are consistently used to measure opinions and quality of health mobile apps (Stoyanov et al., 2015). The revision of mobile applications for self-assessment of eye diseases by the impact of survey gives a precise picture for developing a new, improved tool for self- evaluation of eye diseases because the many of these mHAs lack a theoretical foundation and the opinion of persons with age-related eye diseases during development or testing.

There are two categories of surveys: 1) according to instrumentation: the questionnaire or the interview; 2) according to the length of time conducting the survey: cross-sectional or longitudinal surveys. The widely known self-administered questionnaires method is the mail survey, and researchers frequently use it. This study decided to use a questionnaire that administered online, as in the form of a cross-sectional web survey, because:

- It is faultless for posing closed-ended questions
- Nowadays, the response rates related to mail surveys had gone low.
- It is valid for consumer research
- The span of conducting the survey should be minimal for the specific age group for quick response and quick data compilation in order to avoid any stoppage to participate

Since the study decided to survey the opinion of the research participants as an additional opportunity to support a mobile developer-led decision-making process, the readymade survey questionnaire based on the article by Martínez-Pérez and colleagues (2013) (Appendix, table 17) was chosen providing a complete tool to measure the Quality of Experience (QoE) of mobile Health (mHealth) applications. Their survey is open for access to anyone in order to assess the quality of the healthcare apps, indicating their positive aspects and the ones, which must be revised and improved, avoiding the releasing of low-quality apps. The questionnaire had already been validated for use by authors of the survey, and as the authors stated, this survey had been developed with the collaboration and advice of psychologists. For this study, this readymade survey was critical due to the possibility to validate the mHealth applications through the quality of experience of the specific-age sample with the array of specific apps. One open-ended question was added by this study to determine the compliance rate.

Setting Modalities, Procedures, and Criteria for Data Collection

After reviewing the selected set of mobile apps, the modalities, conditions, procedures, and criteria for data collection defined to encompass all the steps that will be made by the user, when handling the mHA.

Data collection

The data collection was conducted from July 9, 2016, to March 4, 2017, comparing results from mHAs-based tests to the “gold standard” - actual clinical evaluation by an eye specialist (Ophthalmologists and Doctors of Optometry). This study was nested within the aging cohort in central Canada and south Kazakhstan and included 189 adults aged 45 years and older recruited. Kazakhstan was selected as a place of data collection since of standards for the frequency of screening eye examinations in many developing countries like Kazakhstan are practically identical to adult screening in developed countries, including Canada. Kazakhstanis have a regular eye exam annually for those who are over 60 years old. Every two years applies to individuals aged 40-60 years, whose eyesight is healthy, as well as for those who have diabetes, should have a regular eye screening annually (Battakova et al., 2015b; Botabekova et al., 2016). Moreover, while the provision of special eye investigations such as fundus photography and OCT exam not always available in the optometric office in Canada and has certain cost for patients or even not covered in some provinces (“Eye Physicians and Surgeons of Ontario - OCT Testing,” n.d.; The Canadian Association of Optometrists, 2016), all eye-related complaints in Kazakhstan managed only in ophthalmology office where fundus photography and OCT exam (needed for the “gold standard” of this study) is always presented.

Why benchmark of 45 years was chosen

Whichever observation of demographic trends shaped by the population aging measures. This study’s indicators of aging based on fixed ages contributed to a diminishing evolution of aging sense organ, some of which were associated with the specific eye parameters decline. According to the Ministry of Health and Long-Term Care (2007), 3,7 millions of Ontarians (almost 80%), from the age of 45 had at least one chronic diseases. Furthermore, while individuals 45 years of age and older are more likely to have chronic conditions (WHO, 2005), only about 0.2% of mobile health apps on the market are targeted toward these users despite their increased likelihood of having chronic conditions (Aitken & Gauntlett, 2013). Moreover, aging contributes to the emergence of certain retinal diseases and some types of cataract, and particularly 4.6 % of Canadians between 45 and 64 age group and 27.9% above 65 years had glaucoma or cataract in 2009 (Klein & Klein, 2013; Statistics Canada, 2009; Zhang et al., 2012). Although it is known that after age 40, the number of cases of vision loss doubles every decade(The National Coalition for Vision Health, 2012), the most national population censuses discrete the age group after level of 45 years.

Due to this finding and the possibility of early diagnosis and treatment prior to older age, the current study included middle-aged individuals as well as older adults.

The one group Test on mHAs - Retest with Gold Standard

Assessment of functional eye status was undertaken in two modalities:

- Modality one – *participants self-tested their eye condition with different mHAs from diverse vendors to assess five eye functions prior to their assessment by an eye specialist* (Google play, Healthcare4mobile; Google play, LVPEI - MITRA Innovation; App store, George Kong software). Our method used a combination of computing devices, such as the second-generation Apple iPad (9.7-inch screen), Android tablets (Samsung Galaxy Tab A, 7.0 inches' screen), and smartphones (Samsung Galaxy 6 smartphone 64GB, 5.10-inch and Apple iPhone 6 smartphone 32GB, 4.7-inch screen), since not all the apps can be downloaded to a single device (iOS vs., Android).

- Modality two – *retest by comprehensive eye exam by traditional tests to assess five eye functions: standard, non-illuminated, 3-meter Snellen wall chart or automatic examination of the eye for determining refractive corrections, a paper-based Amsler grid, the Pelli-Robson Contrast Sensitivity Chart, an optical coherence tomography (OCT) and perimeter machines.*

In Kazakhstan, clinical exams were obtained by an ophthalmologist in government clinics and outpatient departments of hospitals directly after testing by mHAs, while Canadian participants went to private offices of doctors of optometry from the same day of testing to less than a year.

Testing conditions: mHAs' testing undertaken in a quiet room separate from the waiting or consultation rooms with ambient lighting levels that are standard for any publicly available room (check limitations). Brightness settings on the tablets and smartphones were set at 50%.

Population sample groups

One hundred and eighty-nine individuals, aged 45 to 98 years were recruited and provided informed consent. Initial screen asked about their vision complaints, hearing, prior computer/cell phone application knowledge/experience, and medical history (screening document is appended, figure 3). A sampling was accomplished by dividing the population into two groups geographically. The groups were differently selected. To ensure that the testing would be easily accessible to participants, the assessment was held at multiple clinics and community sites. The majority of them was recruited from three different community clinics and outpatient departments of two hospitals affiliated with Kazakh-Russian Medical University. The rest of participants were recruited from Bridlewood retirement community in South Kanata of the

Ottawa metropolitan area, Canada. Also, tests were planned at various times for the convenience of patients including late mornings, early afternoons, evenings, and Saturday mornings.

Voluntary response sample:

The study puts out a request for participants of a population to join the sample, and individuals decide whether or not to be in the sample. We asked of total 189 participants, 38 members of the Bridlewood retirement community, Ottawa, Canada, to be tested by mHAs and directly after eye assessment to respond to an online poll. Participants in this cluster were recruited using referrals posters at the retirement community, announcements inpatient newsletters, and referrals from retirement community employers. This sample probably was biased, for participants taking the time to respond tend to have similarly strong opinions compared to the rest of the population, even though there was some randomness in the selection of the sample (Good & Hardin, 2003). The 81.5 % (31) of this portion of the sample had not visited an eye specialist in past year, and 89.5 % (34) were not complaining about any visual or eye disturbance for past year or were asymptomatic (no symptoms) for all the diseases measured. This group self-tested their certain eye parameters with all five apps at the retirement community, and later, from the same day to less than a year, had their scheduled eye assessment with the Canadian optometrist in their private offices. The rationale for this sample was to screen for eye disease in asymptomatic patients. The survey to assess patient's practice related to web-based mobile applications was conducted only in Bridlewood retirement community in Canada because of time limitations and resource constraints in Kazakhstan. The survey was conducted on the same smartphones and tablets.

Cluster random sample:

A cluster of 151 people was the patients from an ophthalmic office. The population in Almaty, Kazakhstan, was first split into five groups. We randomly selected 5 clinics out of 11 affiliated with Kazakh-Russian Medical University. The overall sample consisted of every patient above 45 years on those five ophthalmology clinics on each practice day. This type of sample gets every member from some of the groups, so it was suitable when each group reflects the population as a whole (Moore, 2007). This group was made up of the regular patients who had confirmed eye diagnoses, and individuals were visiting the clinic for the first time with a complaint to eye problems. These patients self-tested their specific eye parameters with all five apps immediately prior to their scheduled assessment with an ophthalmologist. The rationale for the second sample of subjects was to establish a diagnosis in symptomatic patients.

All management and healthcare staff working in both research sites were informed of the recruitment criteria for our study; doctors taken eye exams were blind to the eligibility and purpose of the study.

Eligibility

The initial screen was asking about particular problems from individuals and identifying themselves, place and date to hold the tests (Screening paper can be found in the appendix, figure 3). Also, participants had been asked if they are currently participating in other studies. If they were and that study was interfering with ours, we did not recruit the applicants.

Inclusion criteria:

Participants had to have 12 or more years of education, which could read English, or Russian, could follow simple commands, have no history of a clinically significant audiological disease and have no profound self-reported cognitive decline (Appendix, figure 3 and 4).

Exclusion criteria with rationale:

1. Being under the age of 45 years because study investigates age-related conditions.
2. Bilateral deterioration of vision more than 70%, indicating significant advancement of an eye problem. According to World Health Organization definition the low vision rated in 6/18 (30%) best-corrected acuity level at one eye (Appendix, table 19), and this group of individuals might need special assistive devices to work with technological interfaces used in this study.
3. Inability to participate in routine acuity testing due to apperceptive agnosia, unilateral occipital lobe lesions and age-related profound hearing deterioration. These neurological disorders give rise to impairment in processing visual sensory information, and consequently worsen/prevent a possibility of conventional acuity testing (McCarthy & Warrington, 2013).
4. Not being capable of completing the test due to the profound cognitive decline and severe aphasia which might lead to a failure to adhere to self-test requirements. Also, in the Kungsholmen Study, being cognitively impaired was a predictor of refusal to participate in at least one part of the medical examination (Fratiglioni et al., 1992)
5. Unable to use the mobile medical app owing to visual media problems associated with an acute eye surface disease producing profound tearing or significant corneal/crystalline lens/vitreous body opacities.

Testing procedures

Participants were instructed to sit comfortably at the table in the testing area with the possibility to lean on it in the case of hand tremor. Each eye was evaluated separately, with the contralateral eye covered. Participants were asked to keep their prescription glasses on including for a presbyopia correction and read from the upper line to the smallest line they could understand in case of contrast sensitivity and visual acuity or assess a visual stimulus or shape in other three tests. Each assessment endpoint was the

correct identification of 50% + 1 letters or visual stimulus on every tested eye. The assessment was repeated for each eye and each of five apps, with the patient himself holding the mobile devices at 35 cm (14 inches) distances for viewing (respected distance for a clinical Amsler grid or most of the close-distance eye charts). The order of five mHA assessment was randomized between the participants. No time limits were placed on the participants. For elimination of inter-tester variability issues, the same researcher performed all assessments. Results from mHAs including scores recorded in the individual output file for each participant, a sample output file is included in Appendix, figure 3. Later, all these results were compared with “gold standard” –subsequent clinical evaluation which contain the visual acuity testing on Snellen charts or automated machines, contrast sensitivity on Pelli-Robson chart, Amsler grid test, OCT of optic nerve and macular cube, visual field perimetry, and final diagnosis according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10). For statistical analysis, all results from the mobile application and clinical evaluations were converted accordingly (Appendix, table 18).

Questions of the survey were presented such way: one item per screen and response options in a drop-down list with an answer choice number between one and five to choose; subsequent questions were delivered when the response to the current question had been submitted. Our survey was conducted in a naturalistic setting-patients were surveyed in their usual environment – in the library of the retirement community.

Variables

The assortment of variables used for this research were based on one group test scores evaluated on an individual basis and compared with retest outcomes of clinical examinations. Yet, not much study has been conducted on how these scores from different ocular apps have changed after an intervention has been put in place to help aging population identify some alteration of eye self- exam and consult an eye specialist in time. The statistical variables that are derived from mHA related to this study are (1a) visual acuity; (2a) contrast sensitivity; (3a) red desaturation test; (4a) Amsler grid; and (5a) 30 degree -visual fields. Comparisons of results obtained from mHAs with actual clinical results: We consulted the participant's ophthalmology/optometry clinic chart and outpatient record. The variables that are derived from testing of five eye parameters obtained by the professional equipment ((1b) visual acuity testing on Snellen charts or automated machines, (2b) contrast sensitivity on Pelli-Robson chart, (3b) OCT of optic nerve and macular cube, (4b) Amsler grid test, (5b) visual field perimetry), and (6) final primary and secondary diagnosis according to ICD -10. Covariates (sociodemographic characteristics) in this study include age, education, previous eye-surgeries, other chronic diseases, iris color, familiarity with mobile technology, race/ethnicity.

Results and Data Analysis

In order to adequately address the research question, the study employed a structured method of analysis consisting of two parts.

The first part had an analysis of the collected quantitative data. Statistical analysis was conducted with the SPSS version 22.0 for Windows. The quantitative part of analysis included descriptive and inferential statistics. In this study, parametric and nonparametric tests were measuring a difference in means and proportions, and concordance between clinical rating and mHAs' tests outcomes, and binomial logistic regression forecasted the possibility of age-related eye disease. This approach allowed us to assess the reliability and validity, and also predictive abilities of mHAs' tool.

In the second part, the results of an exploratory survey on the validation through the quality of experience on the set of chosen mHAs described.

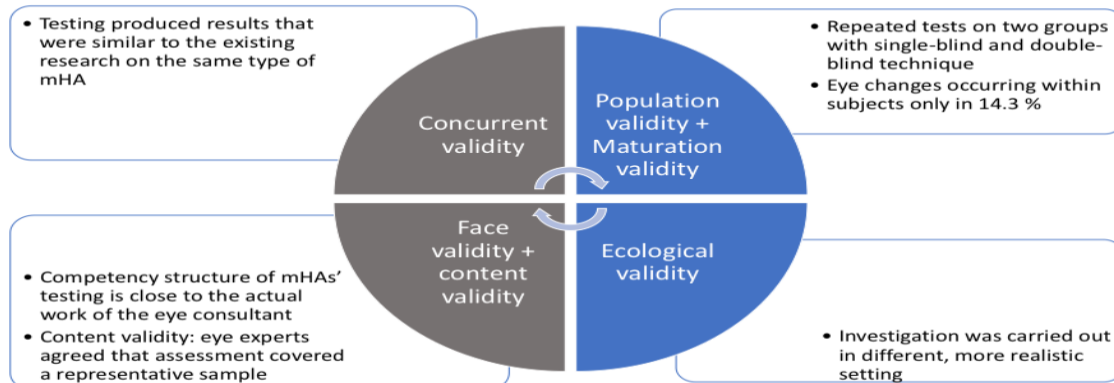
Validity and reliability in this study

Generally, reliability is the extent to which a tested instrument consistently has the uniform results if it is used in the identical situation or on repeated occasions (Fratiglioni, Viitanen, Bäckman, Sandman, & Winblad, 1992). Reliability in this study was defined as the assessment of outcomes provided by independent but comparable measures of the same object through the test and retest design and referred to the same result of paired measures between the mHAs scores obtained by the individual self-assessment and the subsequent clinical evaluation of his eye condition. In terms of enumeration of the reproducibility of the same variable, the second goal of this research was to assess the relations between the variables of interest. Eternally, reliability is a segment of the assessment of validity.

Many forms of validity exist, making it a unitary idea (Howell, 2005; Malterud, 2001; Onwuegbuzie, 2000). In this study, Hammersley's viewpoint to validity was followed. In 1987 he defined an instrument as valid or true if it represents credible features of the phenomena that proposed to be describe, explain or theorize (Hammersley, 1987). Therefore, validity in this study can be characterised by outcomes that are replicable or convincing, and also by the scope to which a test measures what it claims to measure. Content validity evidence of this research was required to determine whether the set of five mHAs matches the "gold standard." In this research, the content validity relates to how well the set measures the main result of interest, in particular, the final diagnosis in case of logistic regression. This evidence was gathered throughout final full diagnosis by eye experts performing "gold standard" –comprehensive eye exam.

Results of internal and external validity

Goal: To assess if all five mHAs are reliable and valid



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FIGURE 1: Results of Internal And External Validity

Descriptive statistics of the sample

The sample consisted from 189 participants/378 eyes. Mean age was 66.5 years (45 to 98 years; SD=14.07). Also, the individual involvement was not equably distributed between women and men (71% women, 29% men). Nonetheless, this might not be a limitation since it could represent the actual distribution of the gender of aging populace. Sixty-seventy eyes were with a normal vision (visual acuity (VA) 1,0 diopter), 185 eyes with mild visual impairment (VA normal to 0.5), 111 eyes with moderate visual impairment (VA 0.5-0.1), and 15 eyes with a low vision in one eye (VA less than 0.1). 189 (100%) participants underwent 945 mHAs' tests; 178 participants (94%) went for subsequent full clinical exam (734 monocular VA, 50 bilateral contrast sensitivity, 191 bilateral OCT of optic nerve, 82 bilateral paper-based Amsler grid and 124 bilateral visual field assessments). 62,6% of total eyes diagnosed with common age-related eye diseases and conditions on a clinical exam. More than 20 ophthalmic nosology's revealed in 237 eyes (appendix, table).

The objectives of this study did not include an epidemiological profile of the prevalence of age-related eye disease in this particular population, but we would still like to clarify that a specialized glaucoma clinic fell into a random selection of sites for examining participants of this research, and therefore this sample is not representative for the incidence of age-related eye diseases.

Results of selection of a limited set of mHAs' tests

To select a limited set of mHAs' tests assessing a wide range of functional abilities relevant to the identification of eye issues associated with four major age-related eye diseases, our study was looking for specific ocular apps for the particular eye functions from any of the available for the public -use-internet

stores. Because these mHAs were meant to be used in self-assessment practice of aging population, apps' measures were required to be brief, and to be able to be administered by a non-trained individual in out-of-clinic setting. The procedure of selection of apps in our study was based on the work of Boudreaux with colleagues.

Reviewing the scientific literature

An analysis of the literature on mobile applications of interest for this study was presented earlier.

Searching app stores

A recent study by Rodin and colleagues (2017b) identifies, describes, and categorizes mobile apps related to eye care that are available to users only in the Canadian iTunes market (Rodin et al., 2017). They reviewed 355 eye apps, and out of them, 153 were for self-testing. All mobile apps available on the Internet in December 2015 and targeting iOS and Android, the two most widely-used mobile operating systems, were entitled to inclusion. Our study searched each of the keywords related to specific eye-function tests in the Google Play and the App Store. It was found 326 IOS-specific apps available with the keyword 'eye test', in the Canadian App Store, including 43 with 'visual acuity', 27 with 'Snellen', 14 with 'visual field', 4 with 'Amsler grid', 1 with 'low contrast sensitivity', 1 with 'variable contrast sensitivity', and 1 with 'red desaturation'. Very similar numbers returned the search of Android-based applications. Of these mobile applications, we only considered free versions not previously studied (check limitations' part).

The five apps freely available from different Internet sources (Google Play and Apple store) were presented to the patient as one self-assessment (including all five apps), which simplifies the presentation. Total time is taken for four tests (visual acuity test, contrast sensitivity, Amsler grid and red saturation test) in a total of 3-7 min depending on the age and level of experience with mobile devices of the patient. The most prolonged test was a visual field assessment application with 3-10 min duration alone. Technical resources for the study shown in Table 3 below.

In this study, we have used:

a. Visual acuity test, contrast sensitivity, central visual field-analog of Amsler grid, and red desaturation test from a single vendor "Healthcare4mobile" for the convenience. According to the website description visual acuity mobile applications' outcome was estimated in percentage as arithmetic means of five standard clinical visual acuities: Snellen eye test, LogMAR chart, Golovin-Sivtsev table, Landolt C/Japanese Vision Test, Tumbling E chart.

b. VisualFields Easy, an app designed at the University of Iowa (Iowa City, IA). It provides a rapid assessment of gross visual field abnormalities and it has a 0.79 mean deviation in comparison with Humphrey visual field analysis (Santos & Morabe, 2016).

c. Since the central visual field (Amsler test) from “Healthcare4mobile” was different from the actual clinical exam and included qualitative description questions in quantifying Amsler grid defects, a second Amsler grid, identical to the "gold standard," from LVPEI - MITRA Innovation was chosen.

TABLE 3: Resources

Information Technology, Screening Equipment:	Examinations:
Five systems and software: Researchers: Two types of smartphones (android and IOS based), Samsung Android tablet, iPad, and Smartphones of 12 participants, who were not willing to conduct the evaluation on the equipment of researchers Application for the visual field was tested on the iPad by 100% participants. None of these services and equipment was purchased for the purpose of this study.	Visual Acuity Test, Contrast Sensitivity Test, Central Vision (Amsler Grid) Test, Red Desaturation Test, (Offered by Google play, healthcare4mobile), Amsler grid (Central Vision) test (Offered by Google play, LVPEI - MITRA Innovation), visualFields easy (Offered by George Kong software, App store).

Searching app clearinghouse websites

Also, assessment identified the extent of data protection principles concerning disclosure of data use and apps’ user rights. Unfortunately, the app clearinghouse websites did not reveal any specific information on apps which we choose for our study may be because they are not from USA or UK vendors.

Evaluating app descriptions, user ratings, and reviews

The following inclusion criteria were applied: (1) app available in the English and Russian language (from the app description in the app stores) due to the oral language of the study samples, (2) relevance to the eye and (3) to self- assessment. Exclusion criteria were: (1) medical apps targeting only health professionals; and (2) focus on eye parameters not included in clinical eye exam for outpatients, (3) focus only on fitness, physical exercise or calorie counts/diets. Applications which we used for our study were available through the iTunes store and Google Play store, had complete descriptions, good user ratings/ reviews and scored an average user rating of 4.1 out of 5. The chosen five mobile apps from different vendors (description of commercial names and trademark signs of mobile apps in the Table 1 below) were easy self-assessment exams. The “healthcare4mobile” vendor had four out of five required apps with two supported languages: English and Russian.

Piloting the apps

We acquainted a small proportion of participants (three in Canada and five in Kazakhstan) with the assessing apps. We piloted mHAs on them to test the characteristics and functions of the applications, to studying the behavior of the application during data collection and transmission and received positive reviews from them. To maintain the unbiasedness of the experiments, we did not introduce such apps to the eye specialists who were performing clinical exam (“gold standard”). To obtain feedback from participants after self-assessment, we surveyed some of them after running all tests.

Organizing a social media query in professional and, if available, patient networks

We have distributed written information as an e-mail letter about nature and purpose of use of the mHealth apps testing to the administration and heads of the clinics and the retirement community where mHAs had been tested. However, neither the doctors performing “gold standard” or participants were informed about specific to avoid any biases.

Eliciting feedback from participant

Feedback from participants on the tested mHAs was gained by surveying, as the 4th method of this study.

Results of parametric, non-parametric techniques and intra-observer agreement

This study analyzed differences amid outcomes of mHAs and clinical assessment by paired *t*-test, Wilcoxon signed- rank test, two-proportion z-test, and Cohen's kappa-test according to the data. Goal of collected quantitative data in this part of the thesis was to assess if five mHAs assisting with testing of the various problems related to chronic eye diseases of the target population are reliable and valid.

Test-retest reliability

All statistics were two-tailed and *P* values <.05 were considered statistically significant. The five types of mHAs testing allowed constructing outcomes for seven hypotheses. Two findings reported on the visual acuity, one result reported on the visual field testing and rest on the contrast sensitivity, Amsler grid, and red desaturation. In a trial for four mHAs, the P-value was more than 5%. Then, we leave our null hypothesis (H_0) because the difference between means of the mHAs tests and clinical testing was not found for visual acuity outcomes. The sample for contrast sensitivity, red desaturation, and Amsler grid is not normally distributed. Therefore, using non-parametric test was a better choice. Since, measurements are ordinal, paired and came from the same population; Wilcoxon signed rank test was the best fit. Wilcoxon signed rank test results (Table 5) showed that difference in median rank is not significant; supporting that contrast sensitivity, red desaturation, and Amsler grid testing by an app is somehow equivalent to clinical examination conducted using professional equipment. Finally, hypothesis

testing rejected our null hypothesis that visual field is equal in the app and doctor assessment with statistical significance -5.13. Detailed results of test-retest reliability are provided in Table 4.

Because the z-test revealed the statistical difference between visual field assessment on app and doctor, and 94 % of those differences between application and the clinical evaluation were due to glaucoma, therefore, we run cross tabulation specifically for glaucoma cases (figure 2).

TABLE 4: Parametric And Nonparametric Tests Performance Results

N	Sample pairs (test-retest)	N of pairs	Statistical test	Hypotheses	Results
1	Visual acuity (VA) on mHA against “gold standard” –clinical exam	356 eyes	A paired t-test	H ₀ : $\mu_1 = \mu_2$, where μ stands for the sample mean. The mean difference between two samples is equal for the repeated subjects. H _A : $\mu_1 \neq \mu_2$. There is the difference between two samples	Failed to reject H ₀ as p-value= 0.079. No difference between VA on mHA and clinical chart outcomes
2	VA level of ill and healthy participants (pair 1: ill on app vs. doctor, pair 2: healthy on app vs. doctor)	80 healthy eyes and unhealthy 276 eyes	A paired t-test	H ₀ : $\mu_1 = \mu_2$, where μ stands for the sample mean. The mean difference between two samples is equal for the repeated subjects. H _A : $\mu_1 \neq \mu_2$. There is the difference between two samples	Failed to reject H ₀ as p-value=0.117 for healthy participants; and p-value=0.154 for unhealthy ones No difference between VA on mHA and clinical chart for healthy and unhealthy participants
3	Contrast sensitivity (CS) on mHA against "gold standard."	50 eyes	Wilcoxon signed-rank test	H ₀ : The median difference between tested pairs of observations is zero. H _A : The median difference between pairs of observations is not zero.	Failed to reject H ₀ as p-value=0.157. No difference between CS on mHA and Pelli-Robson clinical chart
4	Red desaturation (RD) on mHA against OCT measurement for glaucoma’s optic nerve asymmetry	210 eyes	Wilcoxon signed-rank test	H ₀ : The median difference between pairs of observations is zero. H _A : The median difference between pairs of observations is not zero.	Failed to reject H ₀ as p-value= 0.076. No difference between RD on mHA and OCT outcomes
5	Amsler grid on mHA against clinical paper-based Amsler grid (AG)	88 eyes	Wilcoxon signed-rank test	H ₀ : The median difference between pairs of observations is zero. H _A : The median difference between pairs of observations is not zero.	Fail to reject H ₀ as p-value=0.527. No difference between Amsler grid on mHA and clinical paper-based Amsler grid.
6	CS, RD, AG against clinical exam for (1) women and (2) men	348 eyes in total	Wilcoxon signed-rank test	H ₀ : The median difference between pairs of observations is zero. H _A : The median difference between pairs of observations is not zero.	Fail to reject H ₀ as p-value for males: OCT=0.177, Amsler=0.157, CS=0.593, and p-value for females: OCT=0.957, Amsler=0.739, CS=0.319. No difference between CS, RD, AG on mHA and clinical exam.
7	Visual field (VF) assessment from mobile app against automated clinical perimeter	124 eyes	Two-proportion z-test	H ₀ : VF is equal on mHA and in doctor’s clinic ($p_1=p_2$). H _A : VF is not equal on mHA and in doctor’s clinic ($p_1 \neq p_2$).	The null hypothesis was rejected as p-value= - 5.128648 VF assessment by app and doctor are not equal.

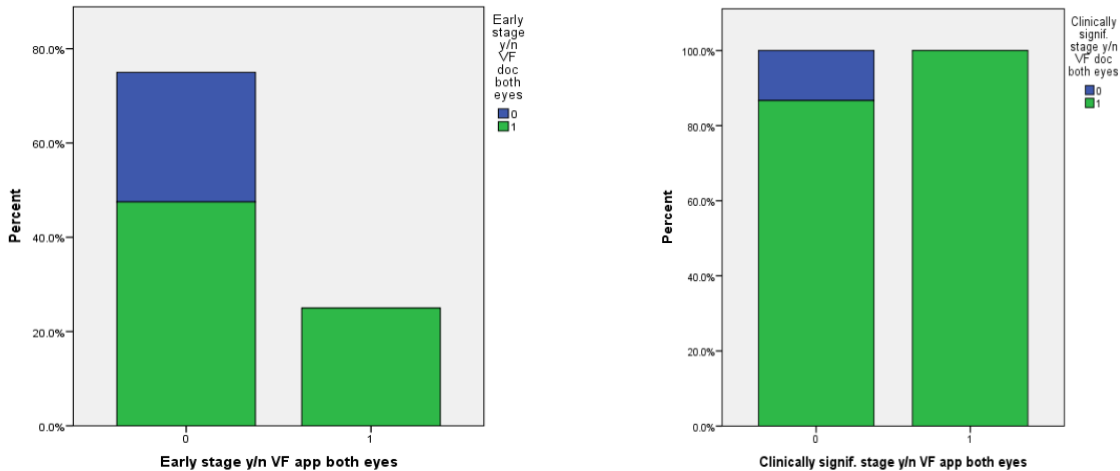


FIGURE 2: Comparison Of Visual Field Assessment By mHA Against Clinical Perimetry For Early And Clinically Significant Stages Of Glaucoma

In the graph above 0 is the indicator for mHA’s visual field assessment and one is for clinical perimetry. On early stage of glaucoma, the app is overestimating the presence of visual field loss (VFL), and in clinically significant stages of glaucoma, the app is underestimating the occurrence of VFL.

Inter-rater reliability

Also, for categorical scales of four tests, we used inter-rater reliability exploiting Cohen's kappa-test. We have not performed this reliability for visual acuity test only because it was very thoroughly researched in existing literature. Summarizing only for “CS on mHA vs. Pelli-Robson chart “and for “Amsler mHA vs. paper-based Amsler “pairs, the Cohen coefficient was in the “almost perfect: 0.81-1.0” interval in agreement to the gradation proposed by Landis & Koch (1977). However, for “red desaturation vs. OCT of optic nerve” and “visual field assessment by mHAs vs.by clinical perimetry” the pairwise agreement was less because the coefficient kappa belongs to the “fair - 0.21-0.40” interval.

We also should mention that a test of parallel reliability was conducted for the Amsler grid app only because “Central Vision (Amsler Grid)” app from healthcare4mobile vendor was operating by categorical measurement while “Amsler grid (Central Vision)” app offered by LVPEI - MITRA Innovation was identical to the real chart of clinical paper - based Amsler grid. And the parallel accuracy of the Amsler Grid application was as high as the kappa test.

Binomial logistic regression (BLR) analysis

A data of this method included 189 participants and is composed of a binary dependent variable which represents the presence or absence of four ARED and different independent categorical variables which indicate various risk factors related to each age-related eye disease. For logistic regression analysis, we decided to determine α at 10%. In this study goal of BLR was to test if mHAs plus sociodemographic variables accurately predict a possibly chronic eye disease. Therefore,

- For categorical predictors, the odds ratio compares the odds of the event occurring at different levels of the predictor
- The age-related eye disease (any of four or combination) was the binary dependent variable (coded 0= no disease, 1= disease)
- Putative risk factors were the age at the time of testing by mHAs, measurements obtained from five mobile tests, socioeconomic characteristics and whether or not there were any comorbidity and previous eye surgery related to these diseases

Binary Logistic Regression assumptions and imitations.

A study was conducted on participants undergoing five functional eye tests on mHAs identifying whether or not a set of these tests can predict an age-related eye disease as AMD, DR, cataract or glaucoma. Estimation of the influences of several indices on the development of these diseases and forecast of the probability of its development are executed by the method of binary logistic regression (Lemeshow & Hosmer, 2009; Mitchell et al., 1995). The selection of the variables for each of four diseases included in our model for logistic regression was achieved with the aid of the estimation of the significance of the differences between the individuals with the presence of DR, AMD, cataract, and glaucoma, and its absence for each test on mHAs and based on the literature review. Different sets of independent variables were used to run the logistic regression with different dependent variables (four common ARED). BLR analysis uses maximum likelihood estimation to predict AREDs in this specific age – group population. The analysis of the study dataset conducted to observe if the assumptions of BLR were met and presented below.

The correlation coefficients, absence multicollinearity, crisscross interaction

Firstly, we run Pearson correlation between five mHAs, and the correlation coefficients range between .552 and -.474. As can be seen from table 5, the correlations between independent variables are not so high, and, therefore, multicollinearity was not a serious problem here.

The table shows that most of the mHA's presenting results in agreement with scientific evidence from

related research. For instance, table revealed positive correlation coefficient between visual acuity and contrast sensitivity (0.55) identical to the moderate correlation between the two measures described by other authors (correlation coefficient ≥ 0.5) (G. S. Rubin et al., 1994; G. S. Rubin et al., 1997). Also, increased visual field loss correlated with a decrease in the visual acuity and contrast sensitivity at the mHAs similarly to results of Humphrey visual field testing in glaucoma in the study by Wilensky & Hawkins (2001). We did not crisscross interaction between two independent variables to make our model simple, but we consider that future research can be done using different interactions.

TABLE 5: Cohen Kappa Symmetric Measures For Amsler, CS, Red Desaturation And VF Pairs

		Value	Asymptotic Standard Error ^a	Approximate T ^b	Approximate Significance	N of Valid cases
Measure of Agreement Amsler app - Amsler doc	Kappa	.842	.046	14.544	.000	82
Measure of Agreement CS app - CS doc	Kappa	.940	.042	9.388	.000	50
Measure of Agreement Red desaturation - OCT	Kappa	.314	.054	6.020	.000	191
Measure of Agreement VF app-VF doc	Kappa	.380	.070	5.393	.000	124
a. Not assuming the null hypothesis.						
b. Using the asymptotic standard error assuming the null hypothesis.						

Independence, ratio of cases to variables and dummy variables

BLR necessitates meticulous groupings for the each dependent variable, and for each category of the categorical variables, that are unrelated to each other (Good & Hardin, 2003). This requirement was met since each of the mHAs' responses come from an isolated testing of discrete eye test on each participant so there was no adjunct responses. Moreover, all variables used in this study were based on current literature review related to specific set of variables for isolated ARED. Predictive factors of risk of four major ARED are systematized with the prognostic significance related to the rise of DR, AMD, cataract, and glaucoma dependent on age. In this study knowing the age of diseased individual was important because we wanted extra power to detect other effects. Also, this study tried to include a sufficient number of individuals and diseases to avoid the possibility of augmentation of parameter estimates when having so few observation in relation to the number of discrete variables will unlikely detect meaningful effects, and created dummy variable indicating whether a tested person has any of four AREDs (table 6).

There were 138 people who have at least one eye disease out of four and 51 people don't have any conditions. Using a cut-off probability of 0.50, our logistic model predicted 155 people have any of the

four diseases, out of which only 128 people have eye problems. 27 people don't have any eye conditions, but the logistic model is predicting at least one condition (false positive). On the other hand, ten people have eye disease, but the logistic model is predicting no eye problems (false negative).

TABLE 6: Cross-Correlations Among mHAs

Five mHAs		VA	CS	RD	AG	VF
Visual Acuity (VA)	Pearson Corr.	1	.552**	-.204**	-.474**	-.324**
	Sig. (2-tailed)		.000	.000	.000	.000
	N	378	378	356	356	124
Contrast sensitivity (CS)	Pearson Corr.	.552**	1	-.408**	-.378**	-.337**
	Sig. (2-tailed)	.000		.000	.000	.000
	N	378	378	356	356	124
Red desaturation (RD)	Pearson Corr.	-.204**	-.408**	1	.205**	.218*
	Sig. (2-tailed)	.000	.000		.000	.015
	N	356	356	356	356	124
Amsler Grid (AG)	Pearson Corr.	-.474**	-.378**	.205**	1	.146
	Sig. (2-tailed)	.000	.000	.000		.107
	N	356	356	356	356	124
Visual field (VF)	Pearson Corr.	-.324**	-.337**	.218*	.146	1
	Sig. (2-tailed)	.000	.000	.015	.107	
	N	124	124	124	124	124

** . Correlation is significant at the 0.01 level (2-tailed).

* . Correlation is significant at the 0.05 level (2-tailed).

The output of logistic regression in Table 7 shows that only age and reduction of contrast sensitivity can be considered as statistically significant risk factors associated with four major ARED. Individuals with reduced contrast sensitivity are five times more likely to develop any of the four age-specific eye conditions. For further research data with enough variation in a dependent variable could be used and it might help for more precise and reliable prediction.

TABLE 7: Dummy Variable Table For The Presence Of Any Of Four Diseases

Observed			Predicted		
			Four Common Eye Diseases		Percentage Correct
			.0	1.0	
Step 1	Eye Diseases	.0	24	27	47.1
		1.0	10	128	92.8
Overall Percentage					80.4

The cut value is .500

Results of the BLR for each disease separately

For senile cataract, statistically significant risk factors (SSRF) was the age. For glaucoma, SSRF was an alteration of red desaturation and some visual field loss for late stages only. For age-related macular degeneration (AMD), SSRF were age and distorted Amsler grid. For diabetic retinopathy, none of the SSRF found to be statistically significant (8 /189).

There is only one research has been done that is similar to our approach, but that paper used logistic regression only for glaucoma and used different sets of predictors; and does not base on the outcome of any mobile app (Elsalam, 2015). Below you will find our model for prediction of glaucoma with our set of risk factors (Table 8).

TABLE 8: Variables In The Equation For Presence Of Any Of 4 Major Age-Related Eye Diseases

Variable(s)	B	S.E.	Wald	df	Sig.	Exp(B)
Age (45-98)	0.03	0.016	3.621	1	0.057	1.03
Race (Caucasian or Asian)	-0.424	0.462	0.844	1	0.358	0.654
Sex (Male or Female)	0.44	0.451	0.948	1	0.33	1.552
Vascular Disease (Either presence or absence)	-0.136	0.42	0.106	1	0.745	0.872
Eye Surgery (Either presence or absence)	1.63	1.098	2.204	1	0.138	5.105
Visual acuity (below 50% no or yes)	0.069	0.554	0.016	1	0.901	1.071
Contrast sensitivity (below 50% no or yes)	1.634	0.441	13.721	1	0	5.126
Red desaturation (normal, suspicion, abnormal)	0.21	0.629	0.111	1	0.739	1.234
Amsler grid changes (Either presence or absence)	0.175	0.598	0.086	1	0.769	1.192
Visual field changes (Either presence or absence)	20.188	5799.358	0	1	0.997	585460587
Constant	-2.494	1.242	4.034	1	0.045	0.083

TABLE 9: Binary Logistic Regression (BLR) For Glaucoma

Variables	B	S.E.	Wald	df	Sig.	Exp(B)
Age	-0.032	0.035	0.841	1	0.359	0.969
Race (1)	0.493	0.63	0.613	1	0.434	1.637
Gender (1)	0.057	0.715	0.006	1	0.936	1.059
Education			0.138	2	0.933	
Education (1)	0.178	0.842	0.045	1	0.833	1.194
Education (2)	0.343	0.934	0.134	1	0.714	1.409
Red desaturation			3.366	2	0.186	
Red desaturation (1)	0.875	1.039	0.71	1	0.4	2.399

Red desaturation (2)	1.291	0.709	3.321	1	0.068	3.637
Visual Field Loss (1)	0.486	0.701	0.48	1	0.488	1.626
Myopia (1)	1.081	0.918	1.387	1	0.239	2.948
Circulatory disorders in the vessels of the brain (1)	0.037	1.506	0.001	1	0.98	1.038
Visual acuity reduction (1)	-1.118	0.716	2.437	1	0.119	0.327
Contrast Sensitivity reduction (1)	0.282	0.794	0.126	1	0.723	1.325
Constant	2.521	2.637	0.913	1	0.339	12.435

a. Variable(s) entered on step 1: Race (Caucasian, Asian), Gender (Male, Female), Education (School, College, University), Red desaturation (normal, suspicion, abnormal), Visual Field Loss (Either presence or absence), Myopia (Either presence or absence), Circulatory disorders in the vessels of the brain (Either presence or absence), Visual acuity changes (below 50% no or yes), Age (45-98 years old), Contrast Sensitivity (below 50% no or yes).

For glaucoma, only significant risk factor (at $\alpha = 0.068$) was a red desaturation test changes on mHA: If someone has been identifying Red Desaturation plates as orange or with shades, he is 3.6 times more likely to have glaucoma. Since we did not find any work on red desaturation alteration as a significant risk factor for glaucoma, we run BLG removing mHA indicators and controlling for the socio-economic factors only, which revealed that the age, education level and race are significant (Appendix, table 25).

Next tables 10 and 11 showed that age was a significant risk factor associated with senile cataract. For example, compare with reference age group (45-49), people between 70 to 74 years old are eight times more likely to have senile cataract. People in the range of 95-98 years old have even more chances to develop senile cataract (11-fold compare to reference age group with 0.078 p-value). Our study finds similar results like some research related to senile cataract that support history of previous eye surgery as significant risk factor linked to development of cataract (J. R. Chang et al., 2011).

The output of logistic regression in Table 7 shows that only age and reduction of contrast sensitivity can be considered as statistically significant risk factors associated with four major ARED. Individuals with reduced contrast sensitivity are five times more likely to develop any of the four age-specific eye conditions. For further research data with enough variation in a dependent variable could be used and it might help for more precise and reliable prediction.

TABLE 10: BLR For Senile Cataract

Variables	B	S.E.	Wald	df	Sig.	Exp(B)
Age	0.058	0.017	11.336	1	0.001	1.059
Race	-0.188	0.385	0.238	1	0.625	0.829
Female	-0.422	0.399	1.122	1	0.29	0.656
Diabetes type 2	-0.402	0.615	0.427	1	0.514	0.669
Previous Eye Surgery	1.699	0.576	8.686	1	0.003	5.468
Visual acuity (less than 50 %)	-0.228	0.429	0.283	1	0.595	0.796
Contrast sensitivity (less than 50 %)	1.33	0.421	9.962	1	0.002	3.782
Constant	-4.414	1.221	13.079	1	0	0.012
Observations	163					

TABLE 11: BLR For Age Variations In Case Of Senile Cataract

Variables	B	S.E.	Wald	df	Sig.	Exp(B)
Age group (reference 45-49 y. o)			17.606	9	0.04	
Age group (50-54)	0.144	0.738	0.038	1	0.846	1.154
Age group (55-59)	-0.223	0.683	0.106	1	0.744	0.8
Age group (60-64)	0.216	0.695	0.097	1	0.756	1.241
Age group (65-69)	-0.096	0.719	0.018	1	0.894	0.908
Age group (70-74)	2.088	0.982	4.523	1	0.033	8.065
Age group (75-79)	1.696	1.007	2.837	1	0.092	5.451
Age group (80-84)	2.078	1.036	4.023	1	0.045	7.986
Age group (85-90)	1.927	1.14	2.859	1	0.091	6.87
Age group (95-98)	2.375	1.35	3.096	1	0.078	10.755
Race	-0.243	0.414	0.344	1	0.557	0.784
Gender	-0.464	0.408	1.29	1	0.256	0.629
Diabetes, type 2	-0.389	0.641	0.369	1	0.544	0.678
Previous eye Surgery	1.7	0.595	8.164	1	0.004	5.475
Visual acuity less than 50 %	0.049	0.497	0.01	1	0.922	1.05
Contrast sensitivity less than 50 %	1.567	0.48	10.674	1	0.001	4.794
Constant	-1.427	0.716	3.979	1	0.046	0.24
Obs			163			

None of the risk factors in table 11 found to be statistically significant predictors of diabetic retinopathy, maybe because of very few people in our sample have diabetic retinopathy (only 8 out of 189). Thus, we

can't conclude whether mHA's are a good predictor of diabetic retinopathy. Sample with more significant numbers of DR patients can estimate more reliable predictors for mHA's.

TABLE 12: BLR For Diabetic Retinopathy

Variables	B	S.E.	Wald	df	Sig.	Exp(B)
Age	0.085	0.142	0.363	1	0.547	1.089
Race	-0.177	2.033	0.008	1	0.931	0.838
Sex	2.341	2.339	1.001	1	0.317	10.386
Diabetes type 2	82.816	4678.725	0	1	0.986	9.25979E+35
Dyslipidemia	49.602	3395.073	0	1	0.988	3.48211E+21
Hypertension	34.313	2565.248	0	1	0.989	0
Amsler changes	16.816	1508.191	0	1	0.991	20100505.9
Constant-DR	89.609	4678.756	0	1	0.985	0
Obs	8					

Logistic regression to identify risk factors associated with age-related macular degeneration shows that age and presence of distorted Amsler grid are statistically significant which implies that older adults and people with changes in the central 20-degree visual field have higher chances of being detected with AMD using mHAs.

BLR for a combination of AREDs in single individual

We also looked if the presence of any eye disease affects the possibility to develop other age-related eye disease and changes on mHAs' tests (Table 13).

TABLE 13: BLR For Age-Related Macular Degeneration (AMD)

Variables	B	S.E.	Wald	df	Sig.	Exp(B)
Age	0.05	0.024	4.338	1	0.037	1.052
Race	0.703	0.511	1.894	1	0.169	0.495
Female	0.45	0.55	0.67	1	0.413	1.569
Dyslipidemia	0.051	0.761	0.004	1	0.947	1.052
Contrast sensitivity	0.094	0.63	0.022	1	0.882	1.098
Visual acuity	0.332	0.56	0.353	1	0.553	1.394
Amsler grid changes	1.922	0.553	12.094	1	0.001	6.832
Constant	5.956	1.705	12.198	1	0	0.003
Obs.	161					

Logistic regression revealed the correlation of cataract with a presence of diabetic eye changes and age; and correlation of glaucoma with the existence of all other three AREDS in this sample. AMD was correlated with glaucoma and cataract factors and age. Diabetic retinopathy does not show any effect of other conditions on it.

The online survey data was compiled from individuals who were completing the self-administered survey as part of an elaborate self-assessment intervention. The analysis of this particular survey was based on a five-point Likert system: 1. Strongly disagree 2. Disagree 3. Neither agree nor disagree 4. Agree 5. Strongly agree.

TABLE 14: BLR For Relation Of Any Of Four Age-Related Eye Diseases (AREDS) With Other AREDS

Cataract	Sig.	Exp(B)
DR	.006	.026
Glaucoma	0	.025
AMD	0	.036
VA below 50%	.708	1.24
CS less than 50 %	.015	4.458
RD (normal, abnormal)	.068	0.345
Amsler grid changes	.951	.962
Visual field loss	.016	4.321
Eye Surgery	.001	13.744
Age	.003	1.064
Race	.998	1.001
Gender	.349	0.598
Constant	0	.001

Glaucoma	Sig.	Exp(B)
DR	.009	.012
Cataract	.017	.238
AMD	.003	.087
VA below 50%	.550	.679
CS less than 50 %	.006	4.742
RD (normal, abnormal)	.007	4.767
Amsler grid changes	.234	.448
Visual field loss	.000	42.805
Eye Surgery	.003	11.022
Age	.237	1.026
Race	.959	1.027
Gender	.252	1.873
Constant	.015	.025

DR	Sig.	Exp(B)
AMD	.993	.000
Cataract	.717	1.549
Glaucoma	.993	.000
VA below 50%	.206	.164
CS less than 50 %	.799	1.347
RD (normal, abnormal)	.994	.000
Amsler grid changes	.240	4.704
Visual field loss	.992	276.....
Eye Surgery	.542	2.504
Age	.790	1.009
Race	.098	.067
Gender	.037	.098
Constant	.464	.123

AMD	Sig.	Exp(B)
DR	.998	.000
Cataract	.030	.268
Glaucoma	.006	.087
VA below 50%	.924	.942
CS less than 50 %	.212	2.339
RD (normal, abnormal)	.894	.910
Amsler grid changes	.000	9.509
Visual field loss	.059	5.685
Eye Surgery	.029	5.221
Age	.003	1.071
Race	.302	.550
Gender	.521	1.511
Constant	.000	.001

Using a random sample, we surveyed 38 individuals between July and December of 2016; age ranged from 81 to 98 with mean age 87. These results reflect only Canadian sample of older participants of the study (ranged from 45 to 98). The questionnaire was administered online. Considering the demographics of our survey sample (N=38), 86,84% were female, 13,16% were male. In terms of education, 31,58 %

had secondary-level education, 44,7% completed a college, and 23,68.4% had higher education. In terms of familiarity with any health –related mobile application, 76,32% of the participants were familiar with mHealth, and 23,68% never used any mobile app for health purpose (Appendix, figure 4).

Results of online survey

When constructing the survey, we used several methods to minimize bias in the data. The survey was distributed to the residents of the Bridlewood Retirement Community at the West end of Ottawa, N=38 patients were recruited (no refusals); and, it was distributed among the participants through providing online link via smartphone, tablet or iPad. The survey was administered remotely (online submission) to reduce researcher pressure on participants recording their answers. Every participant of the study was provided with an entirely anonymous, online Google- based self-administered questionnaire right after finishing the mobile assessment of their vision. The survey was distributed in this manner in order to ensure maximum awareness and response. Out of 38 participants of the retirement community, only four had a personal e-mail, rest of them used the retirement community e-mail. All the participants were able to fill out the survey on the spot. Immediately after collection of eye status by mHAs, each participant replied to the survey questionnaires. There were 38 responses to the survey, providing us with a response rate of 100% at the Ottawa site.

The survey included online Google based, completely anonymous, codified close-ended, structured, standardized questionnaire to assess their quality of experience (QoE), with an additional open-ended part, including the way of eye evaluation was set up, easiness of use of a mobile application, possible features of the single future application. Close-ended part of survey retrieved from an article of Martínez-Pérez and colleagues (2013) open for access to anyone in order to assess the quality of the healthcare apps. We added an open-ended question to this survey which allowed the participants to clarify their preferences: a validated set of mobile applications vs. clinical evaluation.

After finishing the evaluations, we analyzed the quantitative data of survey based on Linkert scale introduced in a program for statistical calculation, IBM SPSS Statistics, with eight variables of the survey. Data collected from this survey were grouped into a hierarchy of four levels of measurement: nominal, ordinal, interval, and ratio data. Data analyses using nominal, interval and ratio data are straightforward and transparent. However, initial analysis of Likert scalar data was not involving parametric statistics but relied on the ordinal nature of the data. Besides, a frequency histogram of the responses for each question created to demonstrate the variation in the replies and a bar chart used to display the percent of respondents selecting particular responses. Finally, to analyze answers to open-

ended questions, we have not implemented the full qualitative methodology, because this part of the study was mostly exploratory. We just looked to some of the interesting paths of the responses from the point of validity and reliability. With this analysis plan, the quality and comprehensiveness of the information on understanding how patients interpret and use the advice from mHA set and the impact of self- assessment on care seeking, was assessed. Reliability of the survey was ensured by the consistency among the questions.

Types of outcome measured:

Primary outcomes

Response rates: the number of completed questionnaires divided by the total number of eligible sample units was satisfactory (38/38=100%). Data completeness: no missing items between participants. Data accuracy: comparison of the proportion of errors or questionable items between age-groups for delivering the same survey question: out of the eight aspects just 50 % were replied positively, the quality content, easiness to use, performance and appearance was questionable for the participants.

Secondary outcomes

Difference between participants and between types of technical devices they used in the time taken to complete a survey questionnaire: Even it was not our objective; we have not recorded any differences between three delivery modes (IPad, Android tablets, and smartphone) in acceptability to respondents. Also, the presented population sample was reasonably homogenous due to specific retirement status (retirement community) and therefore, due to similar financial and sociodemographic condition.

Differences in respondents' adherence to the original sampling protocol: respondents' adherence to a pre-specified schedule (both in terms of duration and frequency) of survey completion. Because the participants have been surveyed immediately after the mHAs' testing they had a 100 % adherence to the protocol, but different time consuming was due to the speed of typing, the presence of presbyopia (age-related changes of near vision) and some motor function disturbances in some of the responders.

The study obtained the evaluation of the different characteristics representative of medical apps, which can be very valuable for future developers:

1. Content quality: users' perception of the quality of the content offered by the mobile application.
2. Security: Data security level that the mobile application provides.
3. Ease of Use: Determines the difficulty of managing the application by the user.
4. Performance: Errors, unexpected stops of running, a response time of the application.
5. Appearance: Describes the general look of the product.
6. Learning:

Specifies the ease to learn how to use the application. 7. Precision: Quantifies the accuracy of the calculations of the application. 8. Future contribution to development of the mobile apps.

TABLE 15: Surveyed Features Of mHealth Applications

Age groups	Count of Age	Average(Av.) of Content quality	Av. of Security	Av. of Ease to use	Av. of Performance	Av. of Appearance	Av. of Learning	Av. of Precision	Av. of Future Directions
80-84	29%	3	4	3	3	3	5	4	5
85-89	45%	3	4	3	3	3	4	3	5
90-94	21%	3	3	3	3	3	4	3	5
95-99	5%	3	3	3	3	2	4	4	5
Total	100%	3	4	3	3	3	4	4	5

When asked if the participants felt that this mHealth application was as practical as their doctor's eye examination most were unsure about the validity/reliability of the tested mHAs. Assessing it proportionally within the gender group and within the ownership of any technological device related to mHA, only 31% of the female sample and 34% of the male sample have a smartphone or iPad/Android tablet. The Pearson chi-square shows that there is no significant gender difference in ownership of a mobile phone with $p = 0.338$. On easiness to use, performance and appearance questions 89% of responders found it difficult to distinguish between negative and positive aspects. Meanwhile, the easiness to learn, security and precision were evaluated positively by 84.2% for ease to learn, 81.5% for security and 36,8% for the precision. It is worth stating that 42% think they can be sure for the accuracy of the app only after clinical evaluation by an eye specialist with whom only 27 out of 38 participants secured an appointment in coming months after the testing of five mHAs. The other functions seemed ensured to the participants.

According to the Pew research centre, every third old-age client uses a smartphone, but only 9% uses mobile applications (Fox, 2011). Moreover, several studies have been showing that age is one of the leading factors of the digital divide. Mobile apps and Internet usage are negatively correlated with age (Norris et al., 2001; Rice & Katz, 2003). However, data from this study does not reveal digital divide even among sample population over 80 years old. The two responders of the survey of this study emphasized that with any mHA, it will take some time to fully master the capabilities to use them, especially in case of the unknown new mHA. Therefore, it is desirable that at the first acquaintance with the specialized medical application there was some healthcare assistant who guides the self-assessment. As for questions about future aspects of the development of the mHAs such as an individual benefit for

the patient himself, for the quality of his life, and for society as a whole, 93% of the responders answered maximum positively from the possible five-point Likert system choices. Because all the questions were related to the mobile application, all the answers were fairly consistent.

However, some questions were difficult to understand from the point of three pilot participants; therefore, we offered session explaining the purpose of questionnaire and presentation on the use of an Android tablet and iPad to all participants, including those who wanted to complete the survey questionnaire using a smartphone.

Of the 38 respondents, 26 responded very briefly, and 12 gave detailed replies to the open-ended question "Which method, if it is valid and reliable (mobile app or usual clinical evaluation by an eye doctor), would you prefer and why?". Fifteen participants preferred full clinical examination with a doctor, while the other 23 considered a validated mobile application to be a more convenient method of evaluation of the eye status in their cases. Because our survey does not specify the type of convenience, further studies of this aspect are required.

Discussion

To evaluate a useful tool predicting the need for full clinical evaluation and possible intervention, this study explored the specific limited set of five mHealth eye-care applications and revealed their validity and reliability in the process of using it by elderly individuals, which is an evidence-based, guided online intervention for a person without and with eye concerns. We applied a hypothesis testing approach to investigate the validity and reliability of all five mobile applications because research on validity and reliability of sets of different eye-related mobile applications from plural vendors is rare (Norris, Engelgau, & Narayan, 2001; Rice & Katz, 2003) and critical to better overall eye care for the most common eye issues. The validity and reliability aspects are essential for setting prospective usage patterns and possible creation of single, ideal, eye health evaluating mobile application that comprises more than one measure of vision. This study also demonstrated the opinions on the perceived validity of the tested apps by surveyed individuals through the quality of experience survey within the study.

In contrast to all the further-mentioned studies that have demonstrated statistical significance by criteria of sensitivity, specificity and accuracy for the evaluation for mobile apps' efficacy on small sample sizes and evaluated only a single or couple ophthalmic mobile test, we conducted a usability study by hypothesis testing as a method of statistical significance on a set of mHAs and on a large population sampling. Parametric, non-parametric and Cohen approaches of hypothesis testing allowed synchronized validation of all five mobile apps' tests most closely simulating the real comprehensive eye exam. Logistic regression analysis, as part of hypothesis testing, endorsed the possibility of exploring the predictive abilities of the set of chosen mHAs. The survey elements of this study focused specifically on validation of the use of the selected set of mobile applications by specific-age-group population.

Discussion of statistical methods

This study showed that those aging adults who did complete the mHealth apps' tests were able to produce reliable results of eye function tests through four out of five mHAs measuring visual acuity, contrast sensitivity, red desaturation and Amsler grid in comparison with "gold standard" measurements of a comprehensive eye examination. While Pathipati and colleagues (2016a) suggested that smartphone-based apps measuring visual acuity are more accurate than Snellen chart testing by emergency department providers, our hypothesis testing objectively confirmed that test of visual acuity by the mHAs is reliable and valid, as the standard Snellen test, for ill and healthy participants.

In our study z-score testing reveals a difference between visual fields assessment in mHA vs. clinical tests. It means that a free "visualFields easy" app was not statistically reliable for glaucoma, contrary to that, this application for the iPad proved to be reliable in a different study for the early manifest of glaucoma in combination with frequency-doubling technology, blue arc entoptic phenomenon testing, and

quick contrast sensitivity function clinical testing (Groves, 2016). Also we noticed the shortcomings of the mobile app for the assessment of visual field (Kong et al., 2016; Vingrys et al., 2016), as that application only available on iPad, has difficulty in which quadrant to look at, restrained or limited range of visual field meridians. These limitations are well described by inventors themselves and other authors in other studies overly. Opposing to the articles describing the quantitative parameters and accuracy of this application our study also found reduced reliability in case of suspicion or early stage of glaucoma, and we assumed that this was the reason of overall statistical unreliability of the application. We know that the authors of this free application are working on an improved paid version of this app, where they undoubtedly consider taking into account all the above disadvantages (Kong et al., 2016).

Valid and reliable results were shown for the test-retest measures because differences in the mHAs total score of apps with a clinical examination by an eye specialist and the corresponding effect sizes were established using a *t*-test, two-proportion z-test, Wilcoxon signed-rank test, and Cohen's kappa coefficient respectively. The *P* values for four outcomes from mobile applications were all greater than 0.05, indicating that there is no difference in measuring of visual acuity, contrast sensitivity, red desaturation and Amsler grid between mobile application score and its corresponding clinical evaluation result. Also, the *t*-test illustrated that the grade of each of two scales for ophthalmic ill and healthy patients were not statistically different between the mobile applications' group and its corresponding clinically-evaluated group. By the same token, the reliability established because standard error values ranged from 0.0207 to 0.199, much smaller compared to their mean values (Appendix, table 21).

Since the kappa scores displayed an almost perfect strength of agreement between the mHAs and doctors' measurements for contrast sensitivity and Amsler grid and , the study shown fairly confidence that both test -retest procedures are identifying outcomes in a similar manner. However, for “red desaturation vs. OCT of optic nerve” and “visual field assessment by mHAs vs.by clinical perimetry” the pairwise agreement was less and belongs to the “fair ” interval. Most likely there was this type of agreement because first pair vaguely differently asses the optic nerve concerning disease stage , and second pair for visual field had low reliability according to the *t*-paired test. To be precise, red desaturation refers to a qualitative inter-eye test difference in color perception that mostly tested in chronicity of optic nerve changes while number of studies have found that a greater advances of glaucomatous optic neuropathy seen on OCT's quantitative evaluation of inner retinal layers and the optic nerve head, contrary to what OCT sometimes falsely miss or oversight early glaucoma in substantial proportions of subjects. Second tested pair of “visual field assessment by mHA vs. by clinical perimetry” had “fair” agreement in contrary to the general low reliability of “EasyField” app uncovering changes in case of early glaucoma. To continue, in our study, visual field assessment on mHAS revealed visual field losses mainly in patients

whom a complete clinical examination revealed glaucoma, and specifically moderate or advanced stage. And that is why, and despite the fact that the two - proportion z test failed the hypothesis of equality of the assessment of visual fields by mobile application and standard stationary perimeter, the kappa test still revealed a connection, although not expectedly high, between these two research methods.

Nevertheless, we are confident on the reliability of all four annotations as the annotators agree on labelling the same pairs of words. This allows us to prove the validity of the annotation. Since the scores displayed a sufficient strength of agreement between the four mHAs and four doctors' measurements, the study shown fairly confidence that both test -retest procedures are identifying outcomes equally. Though, it is worth noting that even if two ratings strongly agree, this does not necessarily mean that their decision is correct (e.g., both mHAs or doctors could be misinterpreting the level of deterioration of eye parameter).

All tested applications reflecting the functional abilities of the eye were separate applications from different developers. So, results received from disparate mobile applications indicated that mHAs use could be further enhanced by combining these distinct forms into a single one that is tailored towards specific visual impairments, simplifying the database, and increasing the number of functional eye tests that can be stored as favorites.

Amending in these areas could lead to a set of capacities using mHAs that matches the reliability and usability of regular eye self-assessment and monitoring, but with several key advantages. Firstly, the ophthalmic data is accessible via a smartphone or tablets, which are more reliable than a standard paper-based Amsler grid for home testing or Snellen test (Adams et al., 2016; Dutta & Palta, 2014; Pathipati, Wood et al., 2016c), and allows patients to record their functional changes easily throughout the specific time-period. Secondly, smartphones and tablets often combine features such as image enlargement and high-contrast screens that can assist an aging individual as operational reduced vision aids (Crossland et al., 2014). It may be the case, that mHA would minimize the anxiety of adults who are concerned about their vision changes because it may reassure them, especially when the medical practitioner prescribes a long testing interval. Additionally, this may reduce the number of visits to the health care practitioner if the eye status has not changed, providing convenience. Tested apps could evade problems with recall when it comes to adherence to chronic therapy in asymptomatic disease, both for AMD and glaucoma. Such mHealth supporting adherence to therapy may liberate eye practitioner time and minimize unnecessary appointments for older adults with multiple medical appointments.

We are aware of separate studies examining single apps to predict AMD and DR (Azrak et al., 2015; M.-L. Chang et al., 2015; Faes et al., 2014; Hartmann, 2014; Prasanna et al., 2013), however, our study is significantly different from the aforementioned studies in a number of ways. Only two out of sixty-three

studies related to the evaluation of apps for eye disease used a higher number of participant compare with our research, to best of our knowledge (appendix, table 1). Moreover, our study assessed more apps than any other research listed in appendix, table 1. Other studies either described one disease examined by a single mobile application (Rajalakshmi et al., 2015; Wang et al., 2013) or only one type of app-based test for a particular eye function. However, the validation of a single app based on a single disease, as an example AMD, does not necessarily mean validation of other illnesses, as an example macular hole or DR. In comparison with only a paper that used binary logistic regression for DR to validate the mobile apps (Azrak et al., 2015), our work is distinguished by a set of multiple statistical methods that allows working with large data consist of different eye diseases. Besides, there is no previously published work containing confirmation of the quantitative data for mobile applications by exploratory survey assessing the effectiveness of multiple apps.

The researched set of five mHAs' tests for eye diseases assessed in the aging patients' sample showed promising mHAs test performance characteristics for predicting models for four AREDs. The results of this study exhibited that, in order to estimate the accuracy of age-related eye disease prediction, along with such influential clinical manifestations as: a reduction of visual acuity, contrast sensitivity, red desaturation disabilities or defect in 20 or 30-degree visual field, other predictors also have a significant contribution. There is one study by Canadian authors analyzing the general public knowledge of risk factors of three major eye diseases, except diabetic retinopathy, using logistic regression (Noertjojo et al., 2006). Even so, this study does not include certain factors considered in our work, factors known to affect vision in case of any of the ARED or their combination. There are two other studies predicting eye diseases by mobile application software (Azrak et al., 2015; M.-L. Chang et al., 2015). The range of risk factors related to the progression of age-related macular degeneration considered in these papers also notably differs from ours. Our set of risk factors included a more extensive range of risk factors and made it possible to identify the most significant of the numerous predictors characterizing the visual functional state of aging individuals, in addition to their predictive value. These results can be used in preventive interventions taking into account the individual spectrum of risk factors for four common eye diseases per World Health Organization (WHO) recommendations on stratification of the risk of those conditions. More promising and targeted schemes of complex ophthalmic treatment or vision correction can be implemented depending on the outcome target value of five mobile apps tests.

In our study, no gender bias was found in predicting visual acuity and contrast sensitivity. The examined mHAs tended to provide operational result in detecting symptoms of four major eye disease while the patient is asymptomatic and perhaps facilitate commencing of an efficacious therapy that could prevent or retard the advancement of disease to reduce vision loss in the active aging period.

As can be seen from the results of logistic regression, the aging element (0.057) and reduction of contrast sensitivity (0) can be considered as statistically significant risk factors associated with the presence of any of four major ARED without clear identification of which one. Individuals with reduced contrast sensitivity are five times more likely to develop any of the four age-specific eye conditions.

Furthermore, isolated logistic regression for each disease revealed that in case of senile cataract, only age was a significant probability in contrary to age-related macular degeneration (AMD) where identified risk factors were age and distorted Amsler grid. Considering, the diabetic retinopathy, none of the risk factors found to be statistically significant predictors may be because the prevalence of DR in our sample was low and in line with prevalence of it in this age constraint described literature (8 /189).

Two types of risk factors for glaucoma- increased pressure and loss of visual field- are main factors for the development of glaucoma. However, the detection of visual field loss on mHAs do not show advantages over the clinical evaluation in ruling out glaucoma in our model and could thus be not useful in the mHAs self-evaluation context at the moment, especially in case of early glaucoma. Besides, to date, there is no app for measuring eye pressure, although there are some attempts ([Araci et al., 2014](#); [Molaei et al., 2018](#)). While we could not use the intraocular pressure as the primary predictor factor for glaucoma (no such mobile app is available to measure it now), this does not detract from the fact that we used patient's socioeconomic characteristics serving as a broad –range base for a number of accompanying risk factors. The logistic regressions suggested that altered red desaturation with another variable as the age became substantial risk factor around 60 years for glaucoma and coincided with the literature on glaucoma but for other diseases the significance occurring at somewhat later ages. Reckon that, we did not find any study related to detection of red desaturation using the mobile application, much less a single work on the quality of the experience of testing these apps by the participants themselves, and in particular, by aging population.

Customarily, the red desaturation test able to give the practitioner a quantitative measure of red loss in the optic nerve. Since the optic nerve is sensitive to red, the eye with damaged optic nerve sees red colors as washed out a pink-orange color. Anecdotally, when we view the red desaturation plates separately, not in a row, to compare (Appendix, figure 6), it was occasionally awkward to discern the differences in the colors of plates. Therefore, we assumed that the patient might exhibit the same differences in visual perception and be prone to errors. These findings need to be taken into consideration for creating an ideal mobile app for eye diseases.

Finally, when we used regression to diagnose possible combinations of these four diseases in one eye of the same participant, since with age individuals are at higher risk of developing concurrent AREDs and conditions in the same eye, the results showed the following: Senile cataract correlated with a presence of

diabetic eye changes and age. Glaucoma allied with the existence of DR and AMD in this sample. AMD was interrelated with glaucoma, presence of cataract, and age. Exploiting a predictive mHA model can support primary care physicians diagnosing ARED, intensely in adults with concomitant chronic disorders, and referring this patient to the relevant eye specialist in a timely manner. The predictive mHA model's outcome can contribute directly to the aging individual's quality of life (Klein & Klein, 2013). A low risk (predicted by the app) for ARED can relieve concerns of the adult over 45+ or his/her caregivers, especially in case of age-related retinopathy (Cimarolli et al., 2012). On the other hand, a high risk may help the aging individual understand symptoms of diseases, increase their treatment adherence, and modify lifestyle and living conditions by evading unnoticed loss of peripheral visual field or ignored loss of visual acuity.

The results of the analysis have not only prognostic capabilities identifying the stage of the disease through these mHAs tests but also have differential-diagnostic significance for clarifying the stage of eye-disease in the cohort of aging patients under study and identifying the timeline for intervention (i.e., surgery for cataract). The prospect of this approach is realized in follow-up clinical observations, which makes it possible to retrospectively check previous results and makes it useful in upcoming studies.

In closing, on the basis of tests performed, the visual acuity, contrast sensitivity, and the Amsler grid showed some advantages in ruling-in cataract and AMD and could thus help in monitoring these diseases. Also, these findings utterly correlated with the data of modern literature. Though, to what extent our results can be transferred to a real situation still needs to be established. Arguing that this set of mHAs may be appropriate in the evaluation of cataract and AMD; it must be noted that five types of the app test that we assessed were not enough to predict diabetic retinopathy and need some redesigning in the future development of such mHA set. We agree with other authors that the ideal mobile app for health screening still needs to be found (Teo et al., 2017).

Discussion of survey

As part of an elaborate self-assessment intervention, the Canadian participants (a sub-sample) rated, on a five-point Likert system, the validity of five healthcare apps which they tested, indicating the positive and negative aspects of the quality of experience. Answering twenty-three close and one open-ended question the participants also discussed the future aspects and contributions of mHAs, how the apps could improve quality of life and contribute to the future development of high-quality apps. This study allowed us to understand the perception of the validity of the mHAs by the elderly population through the quality of experience (QoE). The QoE covers user interaction with their app, motivation to sustain usage.

Despite the low usage of any personal smartphone or computer, the future perspectives of the mHAs by the respondents were mostly positive. The majority agree that mHAs are essential for the development of

the personal use and improved quality of life (87% and 79%, respectively). Also, 72 % of seniors were willing to learn how to use a mHA.

According to the responses to the open-ended question, twenty-three participants preferred validated mHAs to a routine clinical eye examination for some reasons: "I prefer this thing if it can define the state of my eyes, and on its basis, the pharmacist will prescribe the medication. I don't like doctors anymore; they always find the different diseases in me..." - Survey discussion, Participant, 91 years' old.

"If in fact, your study confirms that the applications can be relied upon with one hundred percent scientific certainty, I will choose a mobile app. I don't need to go anymore anywhere, and I can send all the results directly to my doctor. He will invite me to the clinic when he considers its necessity. However, I don't complain much about my vision, but my wife goes to doctors endlessly. She always wants to describe everything to the physician in person" - Survey discussion, Participant, 81years old.

"Of course, the ideal would be that through this app I had the opportunity to be constantly in touch with my eye doctor or, at least, with his assistant. It is so hard to reach them in time..." - Survey discussion, Participant, 92 years old.

Nevertheless, a significant portion of participants still prefer the full exam by their doctors, especially those who have already established their ophthalmic diagnosis: "I felt that these apps are straightforward to use and offering convenience and enhance efficiency for both I and my health provider, but I'm not sure if they can replace real medical judgment" - Survey discussion, Participant, 84 years old.

"If a nurse or personal support worker taught me how to use these mobile applications correctly, I would regularly check the Amsler grid on the iPad. The last four years, my eyesight in my left eye is rapidly deteriorating thanks to macular degeneration... And therefore, my doctor advised me to repeat Amsler at home regularly. However, he is not satisfied with the quality of the grid due to my hand tremor. I believe that your app is much more convenient for me; at least I can tap the screen quickly. Otherwise, I would prefer to check all the other tests with my Doctor of Optometry..."- Survey discussion, Participant, 84 years old.

In addition to a questionnaire, the users were asked regarding their opinion of the survey, and the majority of them (27 out of 38 users) were positive about it. This suggests that this survey can be used for assessing the Quality of Experience of this mHA set. Despite this, we are not sure that the tool created by Martínez-Pérez and colleagues can be very useful for developers of specialized apps in order to assess the quality of particular healthcare apps. However, the importance is that self-administered survey questionnaire has in generating the evidence base for public health and epidemiology (for use, and uptake

of health applications, particularly in older populations), and the number of researchers already using apps for delivering self-administered survey questionnaires.

Results of the survey about experiences and attitudes of older participants towards mHAs show that study does not reveal any digital divide among different age groups. There was good familiarity with mHealth mobile applications in general. However, according to their final responses to survey, at present such technologies are not exclusively intended to meet aging adults' needs, and capabilities, however, older adults are enthusiastic and motivated to learn (or continue to learn) to use mHAs.

We believe that the role of the proposed mobile app, consideration of age-associated changes in lifestyles and cognitive decline, are the main factors influencing the further development of the ideal mobile application for visual function assessment in older samples. And thus, we assume that the surveyed part of the sample was not representative of the general older adult population for some reasons. At first, the mobile apps we offered for evaluation was very particular. Secondly, the population sample consisted only of very aged individuals of the Caucasoid race with an income level above the middle whose acquaintance with mobile health technologies was far higher than usual. Finally, we have not run on them specialized full cognitive function test; we just asked some specific questions related to their general memory, let them count the proposed numbers backward. From the very beginning, the dwellers of specialized "memory floor" of this particular retirement community with cognitive impairment or dementia were excluded from the study.

Strength and limitations

Our study applied the conventional methodology and used state of the art statistical methods for quantitative summaries. Our battery of five mHAs is suitable for use outside a clinical setting for non-trained aging adults, combining short familiarization tasks and engaging the participant with the freely available web-based application tests, with the potential for a reliable result even in senior adults as old as 98 years.

There were some limitations to the study. Firstly, the eye self-assessment was not ascertained from professional medical equipment, there might be an underestimation of eye nosology prevalence and incidence. The model assumed that the mHA is a perfect screening system in theory; this true cannot be tested without the real development of the full application and its use in clinical trials. Our study used a combination of computing devices such as iPads, Android tablets, and smartphones because not all apps can be downloaded to a single device (iOS vs., Android). Different technological means which are usually used in real scenery, had various screen size and different luminescence, and, also, testing itself in clinics or community settings cannot control the light in the room. Therefore, future studies could measure differences in ambient light and the best means to deliver this battery of apps and monitoring for this. We

did not include already validated mobile applications in this study: we assume that almost all of them were verified subjectively because they were tested by their inventors. We also excluded paid version of mobile apps because the Kazakhstan sample was not able to afford it.

The level of adherence to intervention varied considerably within the intervention group due to the elderly age of patients and burden of other chronic diseases. The most critical risk factor for glaucoma as a level of eye pressure has been missed in the prognostic plan because still, no such mobile application exists on iTunes or Google Play. Part of the final results of full clinical evaluations did not reach us for some administrative reasons. We were not able to guarantee the participation of two other retirement communities due to the resistance of some Canadian Doctors of Optometry to cooperate specifically regarding mobile application for eye evaluation. A certain number of participants (11 out of 189 studied) could not get an appointment for financial reasons since a free eye consultation is held annually once in Canada. We were not controlling for other chronic diseases that could have an impact on the quantitative results of our study. In our study, even if some older participants with some degree of cognitive impairment had found the mobile application difficult to use they did not fail the testing. Close-ended questionnaire's evaluation of responses on the Likert scale was limiting the researcher's comprehensive understanding of the respondent's answers and required budget for reproduction of survey questionnaires. Finally, the number of individuals with incident eye problems was relatively small in studied sample, restricting the power, and precision of risk estimates.

The impracticality of conducting this study on the entire study population implies the researcher will utilize tested participants (R. B. Johnson & Onwuegbuzie, 2004). Self-assessment by a patient may become an essential tool for doctors in an attempt to identify a higher number of individuals in need of urgent intervention, but the success and compliance of the use of these devices will vary with the eagerness present in different patients (Huckvale & Car, 2014).

Overview

The tested mHAs offer valid and reliable self- assessment set and demonstrate initial promise, to be considered a useful tool for self-assessment of changes in eye function and timely evaluation for the dynamics of a newly diagnosed age-related eye disease or a pre-existing condition. The outcome of these specialized mobile applications tests are simple to understand and encourage an aging patient to consult an appropriate specialist. Especially in comparison with the complex and costly solutions based on a multistage reference from an optometrist and a primary general practitioner to an ophthalmologist. It is important to note that mHAs cannot substitute key in-person comprehensive eye examinations with counseling and management. Instead, apps supplement eye services as an instrument for conveying high-risk adults into professional care.

The results should assist ophthalmic apps developers to evaluate other mHAs, especially paid ones, for real user. Improvement of the set needs to be done before the final release with possible additions, such as the introduction of online optical coherence tomography (OCT), built –in smartphones fundus camera and the connection of a tonometer, which will significantly optimize instant diagnostics based on complete criteria for the potential risk of four major eye diseases. We can assume that in a concise time the patient can be diagnosed by OCT through the appropriate mobile application outside the doctor's office, since Mehta et al., (2017) already developed wireless interactive control of an OCT system using mobile devices.

Ideally, our study hopes to develop a tool that consistently reveals vision changes that were not well appreciated subjectively but was confirmed by proper clinical examination. With this practical endorsement, the mHA tool would be ready for field use with particular attention to “at risk” populations who are currently unserved or underserved for any eye problem (including self-assessment and care avoidance).

Practical contribution

"Research and innovation within the field of mobile assistive technology for the visually impaired patients highlight the need for successful collaboration between domain users, computer science, and clinical expertise to realize the potential benefits of such technologies fully" ([Hakobyan et al.,2013, p.513](#)). We envision that the ideal screening test based on evaluated in this study mHAs will also have valid and reliable test performance in the relevant clinical setting and will be easy to handle, apply, and interpret.

Despite that tested individual applications are not yet combined into a practical single tool, but now, after verifying their reliability and ability to predict the presence of age-related eye disease, they can be used as

an offered set of mHAs and maybe wished-for in places where eye specialists may just not be available, especially in case of low-income countries where preventable blindness is still a significant health problem (Holden, 2007; Naidoo, 2007), and where the cloud-based system functioning without Internet connection by storing data and then syncing it when a signal is available (“A New Smartphone App Is Revolutionizing Eye Care in Developing Countries,” 2015).

There is a challenge in the accuracy of the reflection of the entire population based on our model since 20 percent of the sample was recruited based on voluntary participation, which implies certain biases. However for the first time, a validated practical instrument was proposed for self-assessment of eye condition by mHAs already accessible to the general public use. The self-assessment and monitoring of eye-health by the individual could help identify risk for age-related eye disease early and could become a valuable tool to recognize the need for follow-up with an eye doctor to prevent illness or implement treatment earlier. Detecting age-related eye problems early with timely alteration of therapy has long-term benefits including slowing of vision loss (Bressler, 2002), reduced maintenance dose of intravitreal medication for wet type of AMD (Muether et al., 2013), reduced frequency of intravitreal shots (Moutray & Chakravarthy, 2011), lowered healthcare costs (International Federation on Aging, 2013), diminished the need for rehabilitation (Roets-Merken et al., 2017), decreased risk of hemorrhages from DR (Sayin et al., 2015), improved quality of life (Schwartz & Loewenstein, 2015b) and reduced risk of permanent vision loss (Brody et al., 1999; Crocker Houde, 2001; Hakobyan et al., 2013). Moreover, timely treatment can benefit both aging individuals with severe age-related eye changes and with mild stages (Chew et al., 2012). Recently, a number of works have also demonstrated that these applications themselves contribute to strengthening the health behavior modification. These apps are more than ever significant for the employed part of our sample, and most of all for those who are unaware of the presence of glaucoma or undiagnosed diabetic retinopathy, because further aggravation of these diseases leads to loss of working days and a corresponding economic disadvantage. Most importantly, these mobile applications are relevant for self-assessment of age-related diseases, since they meet the needs and priorities of age-related consumers.

Incorporating self-assessment, in particular by means of any technological device, into the daily routine of clinical practice can be challenging. Not all individuals are able or willing to self-manage their chronic conditions, and this should be respected. Some older adults may need encouragement before they embrace the idea of self-managing (Grady, 2011). Some health providers may not be prepared to see individuals as full partners either, and this can pose a substantial hurdle. These attitudinal encounters to self-management may diminish over time as the health system changes proposed by the Chronic Diseases

Prevention Management Framework are put in place (Ministry of Health and Long-Term Care, Canada, 2007).

A doctor can prescribe this set of apps for home use for monitoring of individuals at increased risk of an eye condition, such as a dry form of macular degeneration or to a healthy person with a family history of diabetic retinopathy or glaucoma. By analogy with a portable glucometer allotted for a long-standing diabetic patient, this array of mHAs' tests must be implemented for the patients with an established diagnosis of macular edema due to various types of maculopathies. Especially, validate set is appreciated to monitor the progress of clinically significant stages of glaucoma when the prescribed eye drops regime is not respected by the patient. Even more, a new thoroughly developed mHA- assisted "crash –diagnostic set" can be put in a Family Physician clinic or be an integral part of a corner office in Drugstore, where trained health care providers will carry out investigations as an external site, and the clinician will review the results in a hospital. Arguably, test performance will decline in clinical practice if the mHA test is performed without explicit instructions and monitoring of patients. In our study, every second patient was diagnosed with one of four common eye diseases in case of a distorted vision when using mHAs on their own. However, again, it requires an adequate number before assessing its usefulness in screening.

Understanding how patients interpret and use the advice from mHA system and the impact of self-evaluation on care seeking should be a key focus for future research. Notably, “it becomes apparent that the design of any assistive technology or device for older adults requires a basic understanding of how this population perceives and processes sensory information. Vision, hearing, and touch hold a central role in the successful integration of technologies into the lives of older adults, whether they are impaired or not” (Sunkyo Kwon, 2016, p.28). The providers of self-tracking technology will be able to offer new tools that meet the standards of expectations from older individual and his eye-care specialist, and accuracy in recognizing eye problems.

Academic contribution and further research

Both the mHealth and the eye-related mobile applications are ongoing developments and moving the health science as we know. This study aimed to explore health informatics field by (1) conducting an empirical study revealing: “verified reliability + validity = reproducibility of the mHAs, assessing eye functions”, (2) developing predictive models for age-related eye diseases based on mHAs results and other clinical predictors. The study contributes to research methodology in eye diseases' prediction by bolstering the system of clear criteria particularly created for mobile applications. This thesis is therefore complementary to the current literature in interdisciplinary ophthalmic and mHealth research. The results of the analysis provided a deeper insight into mHealth self- assessment by specific age group and the effect of mHAs on clinical satisfaction for employing new algorithms of self-examining different

disorders. Finally, diseases' prediction by mHAs is a fairly novel topic in the literature. Quantitative exploration of validity and reliability of the set of specialized mobile applications in eye care will guide future research projects that work towards enhancing mobile-application guided diagnosis in joint decision-making between clinicians and individuals. Another line of further research might cover detailed rules for mobile apps' predictive employment distinguishes the types and causes of cataracts and retinal abnormalities. This study identified that the age became substantial risk factor around 60 years for glaucoma but for other diseases the significance occurring at somewhat later ages. Hence, subjects with these age factors should be given closer monitoring or intervention of challenges in the provision of the periodic eye exam recommended by the Canadian Ophthalmic Society. Publication of this study might accelerate the acceptance of mHAs by eye health providers.

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Appendixes

APPENDIX, TABLE 16: Evaluation Of Ophthalmic mHAs In The Present Scientific Literature

#	Articles	Evaluated eye tests	Evaluated eye function	Methods used	Number and age of participants/or number of eyes
	A Comparison of the Paxos Mobile App to Standard Vision Assessment Tools. Clinical trial NCT02871817, SPD02000-01. July 2016-October 2016	The CLEAR study is testing the level of agreement between in office visual acuity and Amsler grid testing using a mobile vision testing application, Paxos Checkup Study and standard in office methods. In addition, the percent of patients able to successfully complete home testing on the digital device will be assessed.	Visual acuity and Amsler grid	An observational study for sensitivity	27 participants 18 years of age and older
	Adams, C., Cerwin, J., & Fink, W. (2016, May). Ceeable Visual Field Analyzer (CVFA TM) for the Portable, Comprehensive, and Tele-Medical Assessment of Visual Performance over Time in Warfighters, Pilots, Veterans, and Civilians. Society of Photo-Optical Instrumentation Engineers (SPIE).	To develop a Web-based, portable (i.e., iPad or tablet), tele-medical, and comprehensive visual field test and characterization system based on the 3D Computer-automated Threshold Amsler Grid (3D-CTAG) test.	Visual field defects	assessing the system by psychophysical method	Not find
	Aslam, T. M., Murray, I. J., Lai, M. Y., Linton, E., Tahir, H. J., & Parry, N. R. (2013). An assessment of a modern touch-screen tablet computer with reference to core physical characteristics necessary for clinical vision testing. <i>Journal of the Royal Society Interface</i> , 10(84), 20130239.	This report investigates the pertinent physical characteristics behind one of the most common highest specification tablet computers (iPad 3, Apple Inc.) with regard to its capacity for vision testing.	Contrast sensitivity	Plotting of a gamma curve allows a reasonable range of contrast sensitivity to be tested.	Not find
	Aslam, T. M., Tahir, H. J., Parry, N. R., Murray, I. J., Kwak, K., Heyes, R., ... & Ashworth, J. (2016). Automated Measurement of Visual Acuity in Pediatric Ophthalmic Patients Using Principles of Game Design and Tablet Computers. <i>American journal of ophthalmology</i> , 170, 223-227. DOI: 10.1016/j.ajo.2016.08.013	To report on the utility of a computer tablet-based method for automated testing of visual acuity in children based on the principles of game design.	Visual acuity	Reliability of MAVERIC-C near visual acuity score and agreement of MAVERIC-C score with near ETDRS chart for visual acuity.	112 patients
	Baban, K., Mishra, K., Esperanza, K., & Brodie, S. E. (2016). AutoAmsler: Envisioning Secondary Prevention Through Digital Health. <i>Investigative Ophthalmology & Visual Science</i> , 57(12), 4972-4972.	Amsler grid is often digitally reproduced on mobile devices and web sites, interfaces that allow a greater range of supportive functionalities (reminders, history tracking, resources), but for which diagnostic validity has not been demonstrated.	Amsler grid	Wilcoxon signed rank test and sign test	145 eyes in 100 patients

	<p>Bastawrous, A., Rono, H., Livingstone, I. A., Weiss, H. A., Jordan, S., Kuper, H., & Burton, M. (2015). The Development and Validation of a Smartphone Visual Acuity Test (Peek Acuity) for Clinical Practice and Community-Based Fieldwork. <i>JAMA Ophthalmology</i>, 133(8), 930–937. http://doi.org/10.1001/jamaophthalmol.2015.1468</p>	<p>To design and validate a smartphone-based visual acuity test that is not dependent on familiarity with symbols or letters commonly used in the English language. Validation study comparing results from smartphone Peek Acuity to Snellen Acuity (clinical normal) and the Early Treatment Diabetic Retinopathy Study (ETDRS) LogMAR chart (reference standard).</p>	<p>Visual acuity</p>	<p>The correlation (scatter) plots and Bland-Altman difference plots. Mean time scores between Snellen and Peek Acuity tests were compared using paired <i>t</i> tests.</p>	<p>Three hundred adults aged 55 years and above (6-years follow up)</p>
	<p>Black, J. M., Jacobs, R. J., Phillips, G., Chen, L., Tan, E., Tran, A., & Thompson, B. (2013). An assessment of the iPad as a testing platform for distance visual acuity in adults. <i>BMJ open</i>, 3(6), e002730.</p>	<p>To assess whether measurements of distance visual acuity using LogMAR letter charts displayed on an iPad tablet computer were in agreement with standard clinical tests of visual acuity in adults with normal vision.</p>	<p>Visual acuity</p>	<p>Diagnostic test study</p>	<p>85 participants</p>
	<p>Brady, C. J., Eghrari, A. O., & Labrique, A. B. (2015). Smartphone-Based Visual Acuity Measurement for Screening and Clinical Assessment. <i>JAMA</i>, 314(24), 2682–2683. http://doi.org/10.1001/jama.2015.15855</p>	<p>Outcome measures were monocular logMAR visual acuity scores for each test: ETDRS chart logMAR, Snellen acuity, and Peek Acuity.</p>	<p>Visual acuity</p>	<p>Same as in article of Bastawrous and colleagues</p>	<p>Same as in article of Bastawrous and colleagues</p>
	<p>Bullimore, M., Jansen, M., Kollbaum, E., & Kollbaum, P. (2013). An iPad Test of Letter Contrast Sensitivity. <i>Investigative Ophthalmology & Visual Science</i>, 54(15), 5331-5331.</p>	<p>An iPad-based letter contrast sensitivity test was developed by Ridgevue Vision (ridgevue.com) consisting of two letters on each page of an iBook. Agreement and repeatability of this iPad test was compared to the Pelli-Robson Chart and the computer-based Freiburg Visual Acuity and Contrast Test (FrACT, version 3.7).</p>	<p>Contrast sensitivity</p>	<p>Repeatability and agreement were assessed by determining the 95% limits of agreement (LoA): ± 1.96 SD of the differences between administrations or tests.</p>	<p>Twenty normally sighted subjects were recruited (age 21-38 years).</p>
	<p>Charters, L. (2012). New test helps patients self-monitor for AMD lesions; Macular computerized psychophysical exam able to detect lesions better than Amsler grid. (A pilot trial). <i>Ophthalmology Times</i>, July 1, 2002, Vol.27(13), p.26 [Peer Reviewed Journal]</p>	<p>A new exam, the macular computerized psychophysical test (MCPT), seems to be more effective than the Amsler grid for identifying patients with lesions related to age-related macular degeneration.</p>	<p>Amsler grid</p>	<p>The responses were automatically analyzed and an algorithm showed the areas of abnormality perceived by the patients on a grid</p>	<p>159 patients with AMD and 51 healthy age-matched controls</p>

	<p>Chew, E. Y., Clemons, T. E., Bressler, S. B., Elman, M. J., Danis, R. P., Domalpally, A., ... & Garfinkel, R. A. (2014). Randomized trial of the ForeseeHome monitoring device for early detection of neovascular age-related macular degeneration. The HOME Monitoring of the Eye (HOME) study design—HOME Study report number 1. <i>Contemporary clinical trials</i>, 37(2), 294-300.</p>	<p>To evaluate the effects of a home-monitoring device with tele-monitoring compared with standard care in detection of progression to choroidal neovascularization (CNV) associated with age-related macular degeneration (AMD), the leading cause of blindness in the US. The basis for this test is preferential hyperacuity (or vernier acuity) perimetry which potentially detects the earliest functional abnormalities associated with CNV, prior to patient's awareness of symptoms or visual acuity changes.</p>	<p>Visual field (the central area of the visual field of 14°)</p>	<p>Progression to CNV was determined by the investigator, based on clinical examination and ancillary office testing. Ocular images obtained for the documentation of CNV were graded by a central reading center to confirm the diagnosis of CNV onset.</p>	<p>No exact number of participants (men and women, 55 to 90 years old) were mentioned. A sample size of 1400 participants (700 per arm) was considered. About 12% of the participants (~50 per arm) with AMD were anticipated to have progression to neovascular AMD by 3 years.</p>
	<p>Chhetri, A. P., Wen, F., Wang, Y., & Zhang, K. (2010, November). Shape discrimination test on handheld devices for patient self-test. In <i>Proceedings of the 1st ACM International Health Informatics Symposium</i> (pp. 502-506). ACM.</p>	<p>The paper presents an iPod/iPhone implementation of the test method and reports initial experimental results.</p>	<p>Visual acuity</p>	<p>The software solutions include proper UI considerations like simplicity and visual clarity for patients with eye problems, and also the provision for local and remote extraction of test data.</p>	
	<p>Dorr, M., Elze, T., Hui, W., Lu, Z. L., Bex, P. J., & Lesmes, L. A. (2017). New precision metrics for contrast sensitivity testing. <i>IEEE journal of biomedical and health informatics</i>.</p>	<p>To evaluate the test-retest variability of a tablet-based quick Contrast Sensitivity Function (CSF) implementation</p>	<p>Contrast sensitivity</p>	<p>Rank-precision analysis such as Mean Average Precision</p>	<p>100 subjects</p>
	<p>Dorr, M., Lesmes, L. A., Lu, Z. L., & Bex, P. J. (2013). Rapid and Reliable Assessment of the Contrast Sensitivity Function on an iPad. <i>Investigative ophthalmology & visual science</i>, 54(12), 7266-7273.</p>	<p>To improve the current state of home testing for vision, we have developed and validated a computerized adaptive test on a commercial tablet device (iPad) that provides an efficient and easy-to-use assessment of the CSF.</p>	<p>Contrast sensitivity</p>	<p>A Bland-Altman analysis</p>	<p>Four observers (aged 28–36 years; three males, one female) plus six subjects (aged 21–46 years; five males, one female)</p>

	Dutta, A., &Palta, A. (2014, November). Computerization of the Amsler Grid test for detecting macular degeneration. In <i>Medical Imaging, m-Health and Emerging Communication Systems (MedCom), 2014 International Conference on</i> (pp. 60-63). IEEE.	To provide an electronic version of the Amsler Grid with options to mark for blurred vision, black spots and no vision.	Amsler grid	This marked grid is then automatically scored and based on the criticality of the score, consequential diagnosis is provided.	Not found
	Giardini, M. E. (2015). The Portable Eye Examination Kit: Mobile phones can screen for eye disease in low-resource settings. <i>IEEE pulse</i> , 6(6), 15-17.	The Portable Eye Examination Kit (Peek) is being tested in field trials in Kenya, Mali, Malawi, Tanzania, Botswana, Madagascar, India, and the United Kingdom, and testing in more countries is planned in the future.	Visual acuity and contrast sensitivity	No statistics	Just description of trials without N of participants
	Gounder, P. A., Cole, E., Colley, S., &Hille, D. M. (2014). Validation of a portable electronic visual acuity system. <i>Journal of Mobile Technology in Medicine</i> , 3(2), 35-39.	To compare the visual acuity measurements obtained from EyeSnellen iPad app with a standard illuminated Snellen Chart.	Visual acuity	Bland-Altman analysis	67 participants (122 eyes) (average age 57, range 19–89)
	Hartmann, M. (2013). Evaluation of vision auto-testing in patients with AMD using an iPad App. <i>Investigative Ophthalmology & Visual Science</i> , 54(15), 5018-5018.	This project was designed to evaluate whether iPad-based vision auto-testing is a feasible method for patients with AMD compared to established instruments. Visual acuity was measured by a) distance vision testing by projection of Landolt rings (EN ISO 8596) b) near vision test charts (Oculus) with Landolt rings and c) auto-measurement with Landolt rings using the iPad App “Eyetest - Control your visual acuity”. Patients were initially advised how to use the iPad App.	Visual acuity		112 patients of 57 to 92 years of age (mean 77.2 yrs)
	Hartmann, M. G. (2014). Home vision auto-testing in patients with AMD using an iPad App. <i>Investigative Ophthalmology & Visual Science</i> , 55(13), 5604-5604.	This study was designed to evaluate whether iPad-based vision auto-testing at home is a feasible method for patients with AMD to safely check for changes in visual acuities controlling their visual status.	Visual acuity		152 patients of 58 to 91 years of age (mean 79.4 yrs)
	iPad Screenings Effective for Detecting Early Signs of Glaucoma in Underserved, High-Risk Populations. Newspaper article.PR Newswire, Oct 20, 2014 or States News Service, Oct 20, 2014		Visual field		

	Johnson, C. A., Thapa, S., & Robin, A. L. (2016). Visual field screening to detect glaucoma and diabetic retinopathy in Nepal using an iPad application program. <i>Am AcadOptom</i> . 2014.	To perform visual field screening in Nepal using a free program on the iPad, "Visual Fields Easy" to distinguish among visual field characteristics of healthy normal control eyes, glaucomatous eyes with visual field loss, and eyes with diabetic retinopathy that produce visual field loss.	Visual field	Probability level and Pattern deviation plot	450 eyes (about 200 healthy normal eyes, 200 glaucoma eyes, and 50 diabetic retinopathy eyes)
	Kaiser, P. K., Wang, Y. Z., He, Y. G., Weisberger, A., Wolf, S., & Smith, C. H. (2013). Feasibility of a novel remote daily monitoring system for age-related macular degeneration using mobile handheld devices: results of a pilot study. <i>Retina</i> , 33(9), 1863-1870.	This pilot study evaluated the feasibility of the Health Management Tool (HMT), a novel computing system using mobile handheld devices, to remotely monitor retinal visual function daily in patients with neovascular age-related macular degeneration treated with ranibizumab.	Visual acuity	Signs and Symptoms Questionnaire	160 patients (64% >=75 years of age)
	Kingsnorth, Alec ; Drew, Tom ; Grewal, Bikramjit ; Wolffsohn, James S. Mobile app Aston contrast sensitivity test. <i>Clinical and Experimental Optometry</i> , July 2016, Vol.99(4), pp.350-355 [Peer Reviewed Journal]	This study validates the accuracy and inter-test repeatability of a swept-frequency near and distance mobile app Aston contrast sensitivity test, which overcomes this limitation compared to traditional charts.	Contrast sensitivity	Bland-Altman coefficient of repeatability (COR) and Pearson's correlation coefficients data	20 patients
	Knox, P. C., Milling, A. F., & O'Connor, A. (2014). Effects of age and blur on, and test-retest variability of, a handheld radial shape deformation test. <i>Invest Ophthalmol Vis Sci</i> , 55(5).	The performance of a radial shape discrimination test on an Apple Ipad touch developed by Wang and colleagues examined against ETDRS chart and Pelli Robson Contrast Sensitivity chart	Visual acuity and contrast sensitivity	Linear regression, Tukey and Bland-Altman plots	84 participants aged 16-80 years.
	Kollbaum, P. S., Jansen, M. E., Kollbaum, E. J., & Bullimore, M. A. (2014). Validation of an iPad test of letter contrast sensitivity. <i>Optometry & Vision Science</i> , 91(3), 291-296.	An iPad-based letter contrast sensitivity test was developed (ridgevue.com) consisting of two letters on each page of an iBook. The test was compared to the Pelli-Robson Test and the Freiburg Acuity and Contrast Test.	Contrast sensitivity	Repeatability and agreement were assessed by determining the 95% limits of agreement (LoA) ± 1.96 SD of the differences between administrations or tests.	Twenty normally sighted subjects and 20 low-vision subjects
	Kong, Y. X. G., He, M., Crowston, J. G., & Vingrys, A. J. (2016). A comparison of perimetric results from a tablet perimeter and Humphrey field analyzer in glaucoma patients. <i>Translational vision science & technology</i> , 5(6), 2-2.	To determine the correlation between the perimetric outcomes from perimetry software Melbourne Rapid Fields (MRF) run on an Apple iPad tablet and those from the Humphrey Field Analyzer (HFA).	Visual field	Intraclass coefficients; Linear regression to derive Pearson coefficients and a least squares method; Bland-Altman plots	90 eyes from 90 participants
	Ku, J. Y., Milling, A. F., Pitrelli Vazquez, N., & Knox, P. C. (2016). Performance, usability and comparison of two versions of a new macular vision test: the handheld Radial Shape Discrimination test. <i>PeerJ</i> , 4,	Handheld radial shape discrimination (hRSD) tests were performed using an Apple iPod Touch and the myVisionTrack® (mVT®) application. The Radial Shape Discrimination (RSD) test	Visual acuity	Bland-Altman plots for test-retest analysis	186 participants

e2650. http://doi.org/10.7717/peerj.2650	measures the threshold at which distortions in a radial frequency pattern can be detected and there is evidence that it is more sensitive to macular pathology than visual acuity (VA). It also provides a more quantitative measure of macular function than the commonly available Amsler grid. Study investigated the characteristics of the hRSD test in healthy participants.			
Livingstone IAT, Tarbert CM, Giardini ME, Bastawrous A, Middleton D, Hamilton R (2016) Photometric Compliance of Tablet Screens and Retro-Illuminated Acuity Charts As Visual Acuity Measurement Devices. PLoS ONE 11(3): e0150676. https://doi.org/10.1371/journal.pone.0150676	This study photometrically characterized seven tablet computers (iPad, Apple inc.) and three ETDRS (Early Treatment Diabetic Retinopathy Study) visual acuity charts with room lights on and off, and compared findings with visual acuity measurement standards.	Visual acuity and contrast sensitivity	The simple contrast ratio was calculated and overall luminance was calculated as the mean of the nine measurements across the screen or chart	
Livingstone, I. A. T., Lok, A. S. L., & Tarbert, C. (2014, August). New mobile technologies and visual acuity. In <i>Engineering in Medicine and Biology Society (EMBC), 2014 36th Annual International Conference of the IEEE</i> (pp. 2189-2192). IEEE.	The present research activity relates to design and validation of a novel tablet-based infant acuity test.	Visual acuity		
Lodhia, V., Karanja, S., Lees, S., & Bastawrous, A. (2016). Acceptability, usability, and views on deployment of peek, a mobile phone mHealth Intervention for eye care in Kenya: qualitative study. <i>JMIR mHealth and uHealth</i> , 4(2).	This qualitative study evaluated the acceptability and usability of Peek in addition to perceptions regarding its adoption and nationwide deployment.	Visual acuity	Semi structured interviews	20 patients, 8 health care providers (HCPs), and 4 key decision makers in ophthalmic health care provision in Kenya
Luk, S., Chen, K., & Davies, N. (2013). Variation of online Amsler grid from mobile apps, YouTube and Google. <i>Acta Ophthalmologica</i> , 91(s252), 0-0. doi:10.1111/j.1755-3768.2013.F060.x	To analyze and evaluate the dimensions and instructions of Amsler grid from three sources: Mobile Phone Apps, YouTube and Google.	Amsler grid	Online search	10 apps and 7 videos
Maamari, R. N., D' Ambrosio, M. V., Joseph, J. M., & Tao, J. P. (2014). The efficacy of a novel mobile phone application for goldmann ptosis visual field interpretation. <i>Ophthalmic Plastic & Reconstructive Surgery</i> , 30(2), 141-145.	To evaluate the efficacy of a novel mobile phone application that calculates superior visual field defects on Goldmann visual field charts.	Superior visual field (SVF)	The average of the mean percent error of the oculoplastic surgeons' visual estimates of SVF defects	14 practicing ophthalmology board certified and fellowship-trained oculoplastic surgeons who routinely use Goldmann VF testing

	Malone, C. P., McCourt, C., Al Daqqaq, N. T., & Murphy, C. (2014). Evaluation of Tablet Computers in the Assessment of Visual Acuity: Can iPads™ Replace the Snellen Chart? <i>Investigative Ophthalmology & Visual Science</i> , 55(13), 5599-5599.	This study seeks to assess the accuracy of a popular tablet application (Kybervision Visual Acuity XL software) used for measuring VA and to examine the effects of decreased luminance on test validity.	Visual acuity	Statistically significant difference	79 ambulatory care patients
	Mariakakis, A., & Patel, S. (2016, September). Ocular symptom detection using smartphones. In <i>Proceedings of the 2016 ACM International Joint Conference on Pervasive and Ubiquitous Computing: Adjunct</i> (pp. 435-440). ACM.	The system emulates fixed-force tonometry using a low-cost mechanical attachment to the smartphone. Video is captured through the attachment and then processed in real-time to provide an absolute estimate of the patient's intraocular pressure.	Intraocular pressure	The clinical measurements validated by Adolph Posner tables	Ex vivo porcine eyes
	Maturi, R. A. (2015). New Self-Testing System for Patients with AMD or DME. <i>Retinatoday.com</i>	This article examines how mVT; Vital Art and Science company tool could be useful for patients with DME or wet AMD, and for follow-up in patients with high-risk dry AMD.	Visual acuity	Describes myVisionTrack system	Not applicable
	Nesaratnam, N., Thomas, P. B., Kirolos, R., Vingrys, A. J., Kong, G. Y., & Martin, K. R. (2017). Tablets at the bedside- iPad-based visual field test used in the diagnosis of Intraocular Haemangiopericytoma: a case report. <i>BMC ophthalmology</i> , 17(1), 53.	Report how timely investigations, including an iPad-based visual field test (Melbourne Rapid Field, (MRF)) conducted at the bedside aided swift and appropriate management of the patient.	Visual field	Case presentation	a single 73-year-old lady
	O'Neill, S., & McAndrew, D. J. (2016). The validity of visual acuity assessment using mobile technology devices in the primary care setting. <i>Australian family physician</i> , 45(4), 212.	The objective of this study was to evaluate the assessment of distance visual acuity using two mobile technology devices (iPhone, iPad) against the commonly used 3-metre Snellen chart in a primary care setting.	Visual acuity	Interclass correlation coefficient (ICC) assessment	60 participants
	Pathipati, A. S., Wood, E. H., Lam, C. K., Sáles, C. S., & Moshfeghi, D. M. (2016). Visual acuity measured with a smartphone app is more accurate than Snellen testing by emergency department providers. <i>Graefe's Archive for Clinical and Experimental Ophthalmology</i> , 254(6), 1175.	To assess the accuracy of best-corrected visual acuity (BCVA) measured by non-ophthalmic emergency department (ED) staff with a standard Snellen chart versus an automated application (app) on a handheld smartphone (Paxos Checkup, San Francisco, CA, USA)	Visual acuity	A paired, two-tailed <i>t</i> -test.	64 patients (128 eyes)
	Perera, C., Chakrabarti, R., Islam, F. M. A., & Crowston, J. (2015). The Eye Phone Study: reliability and accuracy of assessing Snellen visual acuity using smartphone technology. <i>Eye</i> , 29(7), 888–894. http://doi.org/10.1038/eye.2015.60	This study aimed to evaluate the equivalence of a smartphone-based visual acuity chart with a standard 6-m Snellen visual acuity (6SVA) chart. 11 Snellen chart applications in the Apple 'App Store' were compared for ratings, cost, test distances, and inaccuracy	Visual acuity	A paired <i>t</i> -test for a sample size of 28 and Pearson correlation for total sample	88 subjects above 16 years old

	Phung, L., Gregori, N. Z., Ortiz, A., Shi, W., & Schiffman, J. C. (2016). Reproducibility and comparison of visual acuity obtained with sightbook mobile application to near card and snellen chart. <i>Retina</i> , 36(5), 1009-1020.	To investigate test-retest reproducibility of visual acuities obtained with a popular mobile application (app) and to explore the agreement with the standard clinic charts. Snellen chart, Rosenbaum near vision card, and SightBook mobile app were reviewed.	Visual acuity	The agreement and test-retest reproducibility	One hundred and twenty-six patients
	Razmaria, A. (2015). Development and Validation of a Smartphone-Based Visual Acuity Test (Peek Acuity) for Clinical Practice and Community-Based Fieldwork. <i>JAMA</i> , 314(16), 1763.	An abstract of a study by Bastawrous et al designing and validating a smartphone-based visual acuity test that is not dependent on familiarity with symbols or letters commonly used in the English language is presented.	Visual acuity	Same as in art.1	Same sample of patients as in art.1
	Reading, V. M., & Weale, R. A. (1993). Self-administered automatic sight-testing. <i>Documentaophthalmologica</i> , 83(1), 43-54.	A feasibility study to estimate the extent to which self-administered computerized sight-testing instruments would be acceptable to patients and staff in a hospital outpatient eye department has been carried out.	Visual acuity		86 patients in the age range 20–79 years
	Rhiu, S., Lee, H. J., Goo, Y. S., Cho, K., & Kim, J. H. (2016). Visual Acuity Testing Using a Random Method Visual Acuity Application. <i>Telemedicine and e-Health</i> , 22(3), 232-237.	The log minutes of arc (logMAR) VA results were compared with those from the iPad-based application, which contains a Snellen chart, a Tumbling E chart, a Landolt C chart, and a VA chart consisting of Arabic figures.	Visual acuity	Repeatability and agreement between the VA chart were assessed using the Bland–Altman method. The repeatability of each VA charts was compared by using paired t test.	43 subjects
	Rodríguez-Vallejo, M., Llorens-Quintana, C., Furlan, W. D., & Monsoriu, J. A. (2016). Visual acuity and contrast sensitivity screening with a new iPad application. <i>Displays</i> , 44, 15-20.	To present a new iPad application (app) for a fast assessment of Visual Acuity (VA) and Contrast Sensitivity (CS) whose reliability and agreement was evaluated versus a commercial screening device (Optec 6500).	Visual acuity and contrast sensitivity	Bland-Altman analyses for the agreement and Deming regressions to calculate Mean Differences (MDs) and Limits of Agreement (LoAs).	Forty-five healthy subjects
	Rodríguez-Vallejo, M., Llorens-Quintana, C., Montagud, D., Furlan, W. D., & Monsoriu, J. A. (2016). Fast and reliable stereopsis measurement at multiple distances with iPad. <i>arXiv preprint arXiv:1609.06669</i> .	To present a new fast and reliable application for iPad (ST) for screening stereopsis at multiple distances. Results were compared with other commercial tests: TNO (at near) and Howard Dolman (at distance)	Visual acuity	Agreement measurement	65 subjects
	Rodríguez-Vallejo, M., Monsoriu, J. A., & Furlan, W. D. (2016). Inter-Display Reproducibility of Contrast Sensitivity Measurement with iPad. <i>Optometry & Vision Science</i> , 93(12), 1532-1536.	To evaluate the reliability of measuring CS with uncalibrated iPads.	Contrast sensitivity		6 iPads

	Rodríguez-Vallejo, M., Remón, L., Monsoriu, J. A., &Furlan, W. D. (2015). Designing a new test for contrast sensitivity function measurement with iPad. <i>Journal of optometry</i> , 8(2), 101-108.	To introduce a new application (<i>ClinicCSF</i>) to measure Contrast Sensitivity Function (CSF) with tablet devices, and to compare it against the <i>Functional Acuity Contrast Test (FACT)</i>	Contrast sensitivity	Bland–Altman plots	42 subjects
	Ruamviboonsuk, P., Sudsakorn, N., Somkijrunroj, T., Engkagul, C., &Tiensuwan, M. (2012). Reliability of visual acuity measurements taken with a notebook and a tablet computer in participants who were illiterate to Roman characters. <i>J Med Assoc Thai</i> , 95(Suppl 3), S109-S116.	To assess test-retest reliability of VA scores determined with this method	Visual acuity	The confidence interval (CI) of the difference of the scores from the test and retest. The t test was used to analyze differences in mean VA scores between the test and retest in each group	49 and 50 participants in the tablet and keyboard group
	Santos, A. S., &Morabe, E. S. (2016). “VisualFields Easy”: an iPad Application as a Simple Tool for Detecting Visual Field Defects. <i>Philipp J Ophthalmol</i> , 41, 22-26.	This study aims to determine the reliability of the “VisualFields Easy” application in detecting visual eld loss among ophthalmology patients; and to determine the sensitivity, specificity, positive predictive and negative predictive values of this examination using the Humphrey Visual Field Analyzer as the gold standard.	Visual field	Sensitivity and specificity with the True Positive (TP) and True Negative (TN) values	137 eyes of 77 patients
	Schrage, N., Simonsen, F., Dudziak, C., &Dutescu, M. (2014). Self-assisted Online visual testing. <i>Investigative Ophthalmology & Visual Science</i> , 55(13), 5603-5603.	Control of visual acuity in near and far vision, amsler grid, colour testing, stereoscopy and evaluation of binocular functions is under evaluation in an online system since 5 years.	Visual acuity, Amsler grid, colour testing, stereoscopy and evaluation of binocular functions	x-y plots of known clinical patterns. The correlation coefficients (r2) between online self testing and visual acuity	150 known subjects of defined ophthalmologic al diagnosis and known clinical data out of 3000 users
	Silva, A. R. O. (2014). <i>Design of a Mobile Application for Eye Signs Screening</i> (Doctoral dissertation, Instituto Politécnico do Porto. Instituto Superior de Engenharia do Porto.).	This application, to apply the defined protocol, was designed keeping in mind the target user, the parents, who can use it at home as a tool to trace the visual health of their children, given that an ophthalmologist follow-up is scarce or nonexistent in many places. Finally, some results of a Hospital field study are portrayed with complementary medical opinions about the application and also about the protocol designed, which is assessed as a necessary complement to an early diagnosis for important diseases like amblyopia or strabismus that have large incidence in children.	Red reflex/Brockner test	the assessment of red reflexes	25 children, with ages between 3 and 4 years' old

	Spofforth, J., Codina, C., & Bjerre, A. (2017). Is the 'visual fields easy' application a useful tool to identify visual field defects in patients who have suffered a stroke?. <i>Ophthalmology Research: An International Journal</i> , 7(1), 1-10.	To determine the level of agreement between the visual Fields easy application (VFE) for iPad and a standard clinical test for assessing peripheral vision in stroke survivors.	Visual field	clinically assessing the results for normality	50 participants with a diagnosis of stroke and a suspected visual problem
	Tahir, H. J., Murray, I. J., Parry, N. R., & Aslam, T. M. (2014). Optimisation and assessment of three modern touch screen tablet computers for clinical vision testing. <i>PLoS One</i> , 9(4), e95074.	In order to produce clinically valid tests, it is important to identify the limits imposed by the screen characteristics, such as resolution, brightness uniformity, contrast linearity and the effect of viewing angle. Previously they have conducted such tests on the iPad 3. Here extension of investigations to 2 other devices and outline a protocol for calibrating such screens, using standardized methods to measure the gamma function, warm up time, screen uniformity and the effects of viewing angle and screen reflections. Three devices were tested for this study, an iPad 3 (Apple Inc.) a Google Nexus 10 (Google Inc.) and Galaxy Tab 2 10.1 (Samsung Electronics).	Contrast sensitivity	Gamma function assessment and calculation of range of programmable contrasts and uniformity of luminance and contrast of targets with different angles of view	Not applicable
	Tariq M. Aslam, Neil R. A. Parry, Ian J. Murray, Mahani Salleh, Caterina Dal Col, Naznin Mirza, Gabriela Czanner, Humza J. Tahir. Development and testing of an automated computer tablet-based method for self-testing of high and low contrast near visual acuity in ophthalmic patients. <i>Graefes Archive for Clinical and Experimental Ophthalmology</i> , 2016, Volume 254, Number 5, Page 891	To present a new automated, computer tablet-based method for self-testing near visual acuity (VA) for both high and low contrast targets. To report on its reliability and agreement with gold standard measures.	Visual acuity	the Bland-Altman comparison method	173 patients
	Tofigh, S., Shortridge, E., Elkeeb, A., & Godley, B. F. (2015). Effectiveness of a smartphone application for testing near visual acuity. <i>Eye</i> , 29(11), 1464-1468. http://doi.org/10.1038/eye.2015.138	The purpose of this study was to evaluate the discrepancy between the near visual acuity (VA) measurements using the EyeHandBook smartphone application and the conventional method of using the near vision card.	Visual acuity	A paired sample <i>t</i> -test and scatterplot	100 eyes
	Toner, K. N., Lynn, M. J., Candy, T. R., & Hutchinson, A. K. (2014). The Handy Eye Check: a mobile medical application to test visual acuity in children. <i>Journal of American Association for Pediatric Ophthalmology and Strabismus</i> , 18(3), 258-260.	To compare visual acuity results obtained with the Handy Eye Chart to results obtained using the Handy Eye Check, a mobile medical application that electronically presents isolated Handy Eye Chart optotypes according the Amblyopia Treatment Study (ATS)	Visual acuity	Linear correlation and an intraclass correlation coefficient	60 children 6-18 years of age

		protocol.			
	Waisbourd, M., Dhami, H., Zhou, C., Hsieh, M., Abichandani, P., Pro, M. J., ... & Myers, J. S. (2016). The Wills Eye Glaucoma App: Interest of Patients and Their Caregivers in a Smartphone-based and Tablet-based Glaucoma Application. <i>Journal of glaucoma</i> , 25(9), e787-e791.	To evaluate the interest of glaucoma patients and their caregivers in a smartphone-based and tablet-based glaucoma application (App), developed by the Wills Eye Glaucoma Research Center in collaboration with Drexel University.	Intraocular pressure and other glaucoma related parameters	Cross-sectional survey of patients with glaucoma and their caregivers	50 subjects
	Wang, Y. Z., He, Y. G., Mitzel, G., Zhang, S., & Bartlett, M. (2013). Handheld Shape Discrimination Hyperacuity Test on a Mobile Device for Remote Monitoring of Visual Function in Maculopathy. <i>Investigative ophthalmology & visual science</i> , 54(8), 5497-5505. doi:10.1167/iovs.13-12037	This study evaluated a handheld shape discrimination hyperacuity (hSDH) test iPhone app designed for visual function self-monitoring in patients with AMD and DR.	Visual acuity	Bland-Altman analysis and One-way ANOVA	One hundred subjects (27 visually normal, 37 with AMD, and 36 with DR)
	Wang, Y. Z., He, Y. G., Mitzel, G., Zhang, S., & Bartlett, M. B. (2014). Compliance and Test Variability of Patients with Maculopathy in Using an iPhone-Based Shape Discrimination Hyperacuity Test at Home. <i>Investigative Ophthalmology & Visual Science</i> , 55(13), 5602-5602.	Assessing the compliance and test variability of patients with diabetic retinopathy (DR) and age-related macular degeneration (AMD) in using the mobile SDH test at home.	Visual acuity	Mean-squared differences between the supervised test and retest and the average standard deviation	35 DR and 9 AMD patients
	Winther, C., & Frisén, L. (2015). New rarebit vision test captures macular deficits hidden to acuity tests. <i>Acta ophthalmologica</i> , 93(5), 481-485.	Evaluation of a new personal-computer-based vision test aimed for rapid and accurate assessment of macular conditions such as age-related macular degeneration (AMD).	Visual acuity	Mann-Whitney tests, single-factor analysis of variance, product-moment correlation coefficients, and receiver operating characteristic (ROC) curves	Thirty-seven patients
	Winther, C., & Frisén, L. (2015). Self-testing of vision in age-related macular degeneration: a longitudinal pilot study using a smartphone-based rarebit test. <i>Journal of ophthalmology</i> , 2015.	There is a need for efficient self-tests of vision in patients with neovascular age-related macular degeneration. A new tablet/smartphone application aiming to meet this need is described and its performance is assessed in a longitudinal pilot study.	Visual acuity	Linearly weighted kappa statistics. Sensitivity and specificity were analyzed using receiver-operating characteristic (ROC) curves.	Twenty-eight patients with neovascular AMD
	Yu, S. Y., Yang, J. H., Kim, Y., Kwak, H. W., & Blumenkranz, M. (2014). Reliability of Smartphone-Based Electronic Visual Acuity Testing: (Applications in Remote Monitoring and Clinical Research of Macular Pathology). <i>Investigative Ophthalmology & Visual</i>	To assess the feasibility and accuracy of a smartphone-based electronic method of visual acuity (VA) testing for remote monitoring and clinical research, and to evaluate its test-retest reliability and concordance with standard Early Treatment for Diabetic Retinopathy Study (ETDRS) testing.	Visual acuity	Reliability and concordance were calculated using the Bland-Altman limits of agreement, the coefficient of repeatability (COR), and the intraclass	69 normal, 35 cataract, 55 diabetic, and 41 age-related macular degeneration patients (n=200).

	<i>Science</i> , 55(13), 5598-5598.			correlation coefficient (ICC).	
	Zhang, Z. T., Wei, Y. T., Jiang, X. T., Yang, Y. Z., Qiu, S., & Zhang, S. C. (2015). Novel use of smart tablet computer for ophthalmology. <i>Int Eye Sci</i> , 15(1), 8-10.	To identify and categorize ophthalmology-relevant apps for the iPad tablet computer as a source for ophthalmic practices on the Apple's App Store	Visual field	Review of ophthalmology - relevant apps on Apple store	
	Zhang, Z. T., Zhang, S. C., Huang, X. G., & Liang, L. Y. (2013). A pilot trial of the iPad tablet computer as a portable device for visual acuity testing. <i>Journal of telemedicine and telecare</i> , 19(1), 55-59.	Evaluating the accuracy of an app for the iPad tablet computer (Eye Chart Pro) as a portable method of visual acuity (VA) testing.	Visual acuity	Bland-Altman analysis	120 consecutive patients (240 eyes)

APPENDIX, TABLE 17: Survey To Measure The Quality Of Experience In mHealth Applications*

Content quality	The Likert scale
Does it make the function that you expected?	1 2 3 4 5
Can you do the same without the application?	1 2 3 4 5
Does the application receive updates regularly?	1 2 3 4 5
Do you think the data are reliable?	1 2 3 4 5
Can you identify with this application health problems?	1 2 3 4 5
Do you have possibility to send information about your status to your doctor?	1 2 3 4 5
Do you have better quality of life by using this application?	1 2 3 4 5
Security	
Do you think that this application has appropriate security methods to protect data that are introduced?	1 2 3 4 5
Do you think that the data obtained with this application are sufficiently protected?	1 2 3 4 5
Ease of use	
Do you find what you need?	1 2 3 4 5
Do you think that the traditional method used so far is more difficult or does not exist?	1 2 3 4 5
Is this application useful for monitoring the disease?	1 2 3 4 5
Performance	
Do you think you might have a more optimized performance?	1 2 3 4 5
Do you find some kind of error or problem while using the application?	1 2 3 4 5
Appearance	
Do you find adequate the appearance of this application?	1 2 3 4 5
Would you change or add something from this application?	1 2 3 4 5
Learning	
Do you think that the time for learning the use of the application is appropriate?	1 2 3 4 5
Precision	
Do you think the calculations done by this application are correct?	1 2 3 4 5
Future research applications' content quality	
Would you use the app if developed?	1 2 3 4 5
Do you think that in the future it can be useful to society?	1 2 3 4 5
Do you think it will improve the quality of life of the users?	1 2 3 4 5
Will this future application help in treating diseases?	1 2 3 4 5
*survey retrieved from the article of Martínez-Pérez, B., Torre-Díez, I., Candelas-Plasencia, S., & López-Coronado, M. (2013). Development and evaluation of tools for measuring the quality of experience (QoE) in mHealth applications. <i>Journal of Medical Systems</i> , 37(5), 1-8. doi:10.1007/s10916-013-9976-x	

APPENDIX, TABLE 18: Operational coding (equalization of units of measurements between mHAs’ tests and professional medical equipment)

Pairs of mHA – eye clinic	Units of measurements of mHAs	Units of measurements of doctor’s equipment	Equalization and/or Transformation
Visual acuity	Percentage (%) from 0 to 100	Decimals and fractions on Snellen and ETDRS charts (from 20/20; 6/6 or 1.0 to 0)	Step 1. Percentage and fraction were changed to decimals. Step 2. Decimals are recoded to LogMAR according to Holladay formula, 1997: $\text{Decimal Acuity} = \text{antilog}(-\text{LogMAR}) = 10^{-\text{LogMAR}}$
Contrast sensitivity	% from 0 to 100 Contrast sensitivity is usually stated as a percent, where the ratio is multiplied by 100. The maximum contrast is thus 100% contrast.	The Pelli-Robson Contrast Sensitivity Chart, the 16-bit file, and the log contrast of the letters range from 0 to 2.25.	Contrast sensitivity = 100 percent or log 2 transposed to qualitative scores similar to Pelli-Robson score. A Pelli-Robson score of 2.0 represents normal contrast sensitivity of 100 percent. Less than 2.0 scores signify poorer contrast sensitivity, and result of less than 1.5 is consistent with visual diminishing and a score of less than 1.0 signifies visual disability (Parede, Torricelli, Mukai, Vieira Netto, & Bechara, 2013)
Red desaturation	Qualitative categorical measurement (0- the same red; 1-looks pinker; 2- looks more orange; 3- shades of red in the center and rear; 4- cannot see).	OCT of the optic nerve: qualitative measurements (0- Retinal Nerve Fiber Layer within normal limits, 1- borderline, 2-outside of normal limits)	Step 1. Awarded a numerical value for each categorical description Step 2. Measurements of mHA were re-coded from five categorical measurements to three categorical measures equal to the OCT readings; 0 to 0, 1 to 1, all above 2 to 2.
Amsler grid	Two apps were used. All patients tested by central vision app (analog of Amsler) from “healthcare4mobile” where categorical measurement: 1-bent or wavy lines, 2- boxes differ in size or shape, 3- lines are missing, blurry or discolored; 0- none of the above. Then the part of the sample with/without any of VF defects was selectively compared by other Amsler test’s mHA	Paper-based Amsler grid test: 1-wavy, 2-broken or 3- distorted lines OR 4-a blurred or missing area of vision.	Awarded a numerical value for each categorical description and equalized the defects of Amsler grid

	identical to clinical paper-based Amsler grid test		
Visual field (VF)	Counting of missing points on VF of mHA to obtain the presence of scotoma	VF loss and types of scotoma was defined by the attending eye specialist	Transformed to binominal variables “yes” for any visual field loss and “no” for absence of VF loss

APPENDIX, TABLE 19: Vision Acuity Level Divided Into Four Groups For Statistical Analyses

N	Visual acuity level	Description
1	20/20; 6/6 (1.0)	Normal vision
2	20/40; 6/12 (0.5)	Reduced vision, Canadian/Kazakhstan legal driving limit
3	20/60; 6/18 (0.3)	Low vision (World Health Organization definition)
4	Less than 20/200; 6/60 (0.1)	Legal blindness (eligible for various entitlements)

**Evaluation to Sign an Informed Consent Document for Research
[DeRenzo EG, et al. J Health Care Law Polic 1998;1:66-87]**

Subject Identifier: _____ Date of Evaluation: _____

Directions

Make a subjective judgment regarding item 1. Ask the subject questions 2-5 and record responses. The evaluator may use different wording in asking the questions in order to assist the subject's understanding.

1. Is the subject alert and able to communicate with the examiner? Yes ____ No ____

2. Ask the subject to name at least two potential risks of participating in the study.

3. Ask the subject to name at least two things that he/she will be expected to do during the study.

4. Ask the subject to explain what he/she would do if he/she no longer wanted to participate in the study.

5. Ask the subject to explain what he/she would do if he/she experienced distress or discomfort during the study.

Evaluator's Signature

It is my opinion that the subject is alert, able to communicate, and gave acceptable answers to the questions above.

Evaluator's Signature

Date

HSO 06/03

**FIGURE 3, APPENDIX: Evaluation To Sign An Informed Consent Document For Research
[Derenzo Eg, Et Al. J Health Care Law Policy 1998;1:66-87]**

Information/ Информация

Name/Ф.И.О

Name of data collection site/ Название учреждения сбора данных

Date of birth (age) / Дата рождения(возраст)

Race/ethnicity/ Раса / этническая принадлежность

Gender/ Пол

Level of Education / Уровень образования

Computer familiarity and knowledge of health app/ Умение пользоваться компьютером и Знание приложения для здоровья

Language/ Язык

Telephone/ Телефон

E-mail address/ Адрес электронной почты

Code of the participant/ Код исследуемого

Medical history/ Медицинская История

Last date visiting eye specialist/ Дата последнего посещения окулиста

Tests results / результаты исследования	Mobile applications/ Моб. приложения	Mobile applications/ Моб. приложения	Clinical evaluation with ISD -10 diagnosis/primary, secondary/ Клиническая оценка с ISD -10 диагноз / первичный, вторичный	
Visual acuity /Острота зрения	OD	OS	OD	OS
Red desaturation test/ Цветовая камиметрия	OD	OS	OD	OS
Amsler grid /Амслер сетка	OD	OS	OD	OS
Contrast sensitivity Контрастная чувствительность	OD	OS	OD	OS
Visual field assessment/ Поле зрения	OD	OS	OD	OS

Comments/ Комментарии:

FIGURE 4, APPENDIX: Sample Output File**APPENDIX, TABLE 20: Diagnoses Discovered By Full Clinical Examination**

Diagnosis	Right eye, N	Left eye, N
Glaucoma open-angle, different stages	36	31
Glaucoma narrow -angle, different stages	11	10
Glaucoma close-angle, different stages	3	3
Suspicion of glaucoma	16	22
Senile cataract, different stages	47	51
Other types of cataract	12	11
Pseudophakia	24	25
Diabetic retinopathy	8	8
Age related macular degeneration	28	31
Drusen	4	7
Macular changes including macular hole, non- specified etiology	18	26
Serous chorioretinopathy	1	1
Retinal changes due to high degree myopia	8	9
Vitreoretinal traction		1
Optic nerve neuropathy or atrophy not related to glaucoma	4	4
Error of refraction	92	93
Retinal vein occlusion, residual changes	2	
Hypertensive retinopathy	11	10
Posterior vitreous detachment	1	2
Uveitis		1
Lattice degeneration	1	1

APPENDIX, TABLE 21: Apps And Clinical Exams Paired Variables

Variables	Mean	N	Std. Deviation	Std. Error Mean
VA (Visual acuity) on mobile app	.280	356	.3897	.0207
VA Doctor (Doc)	.270	356	.3954	.0210
CS (Contrast sensitivity) on app	.980	50	.8449	.1195
CS, Doc	.940	50	.8430	.1192
Red desaturation on app	0.99	191	0.957	.069
OCT of optic nerve, Doc	1.15	191	.872	.063
Amsler Grid on app	1.88	82	1.717	.190
Amsler, Doc	1.90	82	1.789	.198
VF (visual field) on app	.56	124	.498	.045
VF Doc	.85	124	.362	.032

APPENDIX, TABLE 22: Paired T-Test For Visual Acuity For Total, Healthy And Unhealthy Participants

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	VA app - VA doc	.0107	.1143	.0061	-.0012	.0226	1.762	355	.079
Pair 2	Healthy participants VA app - VA doc	.01	.0565	.0063	-.0026	.0226	1.584	79	.117
Pair 2	Unhealthy participants VA app - VA Doc	.0108	.1263	.0076	-.0040	.0258	1.430	275	.154

APPENDIX, TABLE 23: Wilcoxon Signed Ranks Test For CS, Amsler, And RD Pairings

		N	Mean Rank	Sum of Ranks
CS doc – CS app	Negative Ranks	2 ^a	1.50	3.00
	Positive Ranks	0 ^b	.00	.00
	Ties	48 ^c		
	Total	50		
Amsler doc – Amsler app	Negative Ranks	4 ^e	5.50	22.00
	Positive Ranks	6 ^e	5.50	33.00
	Ties	72 ^f		
	Total	82		
OCT – Red desaturation	Negative Ranks	29 ^g	45.86	1330.00
	Positive Ranks	53 ^h	39.11	2073.00
	Ties	109 ⁱ		
	Total	191		
a. CS doc < CS app				
b. CS doc > CS app				
c. CS doc = CS app				
d. Amsler doc < Amsler app				
e. Amsler doc > Amsler app				
f. Amsler doc = Amsler app				
g. OCT < Red desaturation				
h. OCT > Red desaturation				
i. OCT = Red desaturation				

APPENDIX, TABLE 24: Wilcoxon Signed Ranks Test Statistics For CS, Amsler And RD Pairs

	CS doc – CS app	Amsler doc - Amsler app	OCT – Red desaturation
Z	-1.414 ^a	-.632 ^a	-1.774 ^a
Asymp. Sig. (2-tailed)	.157	.527	.076

a. Based on positive ranks.

APPENDIX, TABLE 25: Wilcoxon Signed Ranks Test For Males And Females For AG, CS, RD Tests

	OCT in doctor office - RD for pairing on mHA	Amsler/doc - MA Amsler	Pelli-Robson CS - CS on mHA
Z	-1.350 ^b	-1.414 ^b	-.535 ^b
Asymp. Sig. (2-tailed) for males	.177	.157	.593
Z	-.054 ^b	-.333 ^c	-.998 ^b
Asymp. Sig. (2-tailed) for females	0.957	0.739	0.319

a. Wilcoxon Signed Ranks Test
 b. Based on negative ranks
 c. Based on positive ranks

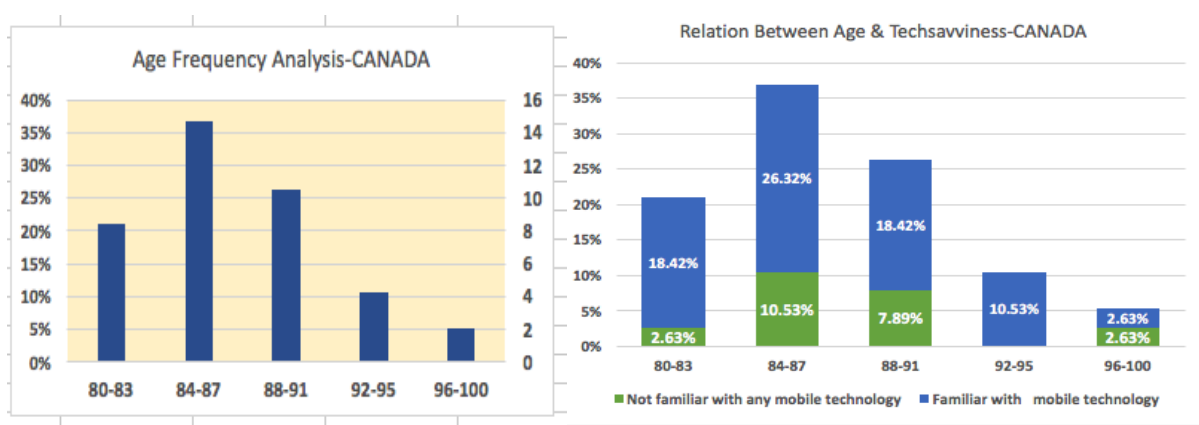


FIGURE 5, APPENDIX: Age-Frequency And Tech Savviness Among Surveyed Participants

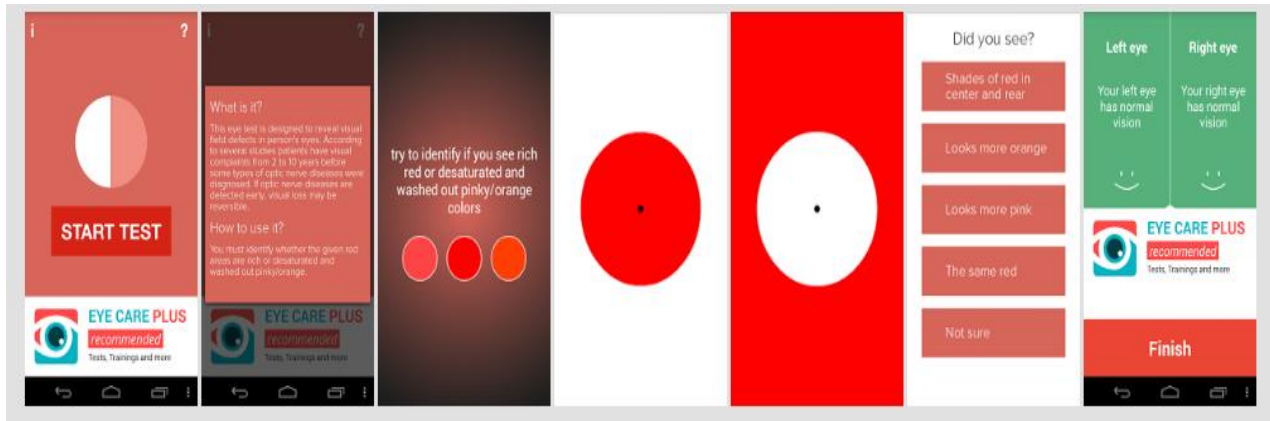


FIGURE 6, APPENDIX: Screenshot Of “Red Desaturation” Mobile App Used For This Study

APPENDIX, TABLE 26: BLR For Glaucoma And The Socioeconomic Factors Only

Variables ^a	B	S.E.	Wald	df	Sig.	Exp(B)
Race (1)	0.777	0.266	8.538	1	0.003	2.174
Gender (1)	0.343	0.261	1.727	1	0.189	1.409
Education			17.021	2	0	
Education (1)	0.508	0.342	2.207	1	0.137	1.661
Education (2)	-0.62	0.344	3.238	1	0.072	0.538
Age group			16.634	10	0.083	
Age group (1)	0.077	0.488	0.025	1	0.875	1.08
Age group (2)	0.735	0.444	2.741	1	0.098	2.086
Age group (3)	0.913	0.444	4.229	1	0.04	2.491
Age group (4)	0.448	0.452	0.981	1	0.322	1.565
Age group (5)	0.648	0.562	1.332	1	0.248	1.912
Age group (6)	0.746	0.588	1.609	1	0.205	2.109
Age group (7)	0.33	0.538	0.377	1	0.539	1.391
Age group (8)	-1.239	0.849	2.133	1	0.144	0.29
Age group (9)	-0.97	0.856	1.282	1	0.258	0.379
Age group (10)	1.654	1.111	2.219	1	0.136	5.23
Constant (Glaucoma)	-1.516	0.516	8.626	1	0.003	0.22

Variable(s) entered: Race (Caucasian or Asian), Gender (Either male or female), Education (high school, college or university), Age groups (45-49(reference), 50-54,55-59,60-64, 65-69,70-74,75-79,80-84,85-89,90-94,95-98).