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How the smartphone is driving the eye-health imaging revolution

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Abstract

The digitization of ophthalmic images has opened up a number of exciting possibilities within eye care such as automated pathology detection, as well as electronic storage and transmission. However, technology capable of capturing digital ophthalmic images remains expensive. We review the latest progress in creating ophthalmic imaging devices based around smartphones, which are readily available to most practising ophthalmologists and other medical professionals. If successfully developed to be inexpensive and to offer high quality imaging capabilities, these devices will have huge potential for disease detection and reduction of preventable blindness across the globe. We discuss the specific implications of such devices in high, middle and low-income settings.

Keywords

Smartphone, imaging, mHealth, fundoscopy, ophthalmoscopy, anterior segment imaging, slit-lamp, retina, mobile phone, telemedicine

Introduction

It has long been well established that ophthalmic imaging techniques are of high value to ophthalmologists, general practitioners and other specialists alike[1, 2]. Retinal imaging, for example, is important for the detection of eye diseases, such as diabetic retinopathy[3, 4], age-related macular degeneration[5] and glaucoma[1, 6], as well as the characteristic changes in the fundus that are related to systemic diseases, such as hypertension[7, 8], malaria[9, 10] and neurological conditions[11]. For this reason every medical doctor is expected to be able to use basic ophthalmic imaging devices such as the direct ophthalmoscope[12].

Ophthalmic images have been photographically recorded since the end of the 19th century[13, 14]. The relatively recent introduction of digital imaging technologies has accelerated the advancement of ophthalmic image capture by allowing fast and exact duplication, electronic storage and transmission and instant access to results by dispensing with the need for film development. Digitization of ophthalmic images has also allowed these images to easily interface with computing resources. Consequently, a field of automated image analysis directed at detecting pathology, such as the presence and stage of diabetic retinopathy[15-17], glaucoma[18, 19] and retinopathy of prematurity (ROP)[20], has emerged, presenting the prospect of screening programmes where the number of images requiring manual assessment is dramatically reduced[21-25].

The advancement of mobile telephony in recent years has been rapid and extensive. In particular, the development of smartphones has taken mobile connectivity to a new level. Smartphones are mobile devices which combine the simple communication capabilities of their predecessors, namely voice calls, short text and multimedia message services (SMS and MMS), with capabilities including an operating system allowing application installation and upgrade[26], more powerful computer processing, high resolution digital cameras and global positions systems (GPS), as well as accelerometers and other sensors. As such they are a rich technological resource which, due to their size and intended use, is carried by their user to wherever they go.

Cellular phones with built in digital cameras have been manufactured since the beginning of the 21st century[27]. Improvement in the quality of the images captured by phone-mounted cameras has been quick and profound in the time since their introduction. Recent handsets are capable of capturing images of quality comparable to that of mainstream digital cameras, with Nokia's Lumia 1020, for example, including a 41 megapixel camera sensor[28]. Acquisition of high quality videos by cellular phones has also been developed, with most modern handsets being capable of recording at 1080p resolution (1920 x 1080 pixels per frame), with the latest handsets, such as the Samsung Galaxy Note 3, being able to record 4K video (4096 x 2160 pixels per frame) [29].

It was reported in 2013 that 65% of U.S. adults owned a smartphone, with that proportion being expected to continue rising over the coming months and years[26]. This trend is not only noted in high-income countries but also in middle and low-income countries[30]. China, for example, is reported to have 95% cell phone ownership and 37% smartphone ownership whereas Kenya has 82% cell phone ownership and 19% smartphone ownership[31]. There is therefore no question that smartphones are increasingly becoming part of people's lives globally. In the specific case of medical professionals they offer particular promise, with it being reported as early as 2010 that in the United Kingdom, for example, 80% owned a smartphone[32]. Consequently the new field of mobile health, widely known as "mHealth" has emerged[33-35]. Potential applications of mHealth include patient assessment tools, patient education tools, healthcare professional education and reference tools and patient record and administration tools[36].

The quality of an image captured by a digital camera relies on a number of factors. Firstly the size, separation and number of picture elements (pixels) on the camera detector. However these sensors have advanced such that the most modern smartphone cameras' image quality is limited by factors relating to their optics rather than their detector. The "sharpness" of a digital image, that is the contrast at a particular spatial frequency, (known as the modulation transfer function or the point spread function) is fundamentally limited by diffraction[37]. How close a given camera will come to achieving this fundamental limit depends on the quality of its optics. Further to this, higher order aberrations such as spherical, astigmatic and comatic aberration, field curvature and distortion all reduce the quality of the image formed on the detector[38]. The challenges faced by the engineers who design smartphone camera optics are substantial. Camera modules are generally required to be low-cost and capture a wide range of possible scenes, necessitating that lower quality plastic components be used. The whole camera is also required to be thin, putting a tight constraint on the maximum distances allowed between components. Furthermore, smartphone cameras have a fixed focal length and fixed aperture size with a fairly large “F-number” (the ratio of the focal length to diameter of the entrance pupil, which describes the camera’s ability to collect light)[39] typically ranging from 2.0 to 2.4[40]. It should also be noted that how any digital camera encodes and compresses the image can also lead to loss of image quality[41]. As such the firmware and software of the device also play an important role in the quality of any digital image. Nevertheless, despite the many difficulties associated with the design of smartphone cameras, the increase in image quality captured by these devices in recent years has been so profound that their use in applications such as medical imaging is now a genuine possibility, which ought to be given real consideration.

In this paper we discuss recent efforts to enable smartphones to capture digital ophthalmic images and thus to increase healthcare professionals’ ability to attain the advantages of mHealth within the specialism of ophthalmology. In our analysis, we include commercially available solutions, where they exist, as well as recently reported research in this area.

Displaying Ophthalmic Images with Smartphones

A simple question which should be asked of smartphones is whether they are capable of displaying ophthalmic images, captured using conventional ophthalmic digital cameras, of high enough quality to allow assessment of a patients’ eye health. Kumar et al.[42] conducted a study where 110 fundus images of diabetic patients captured using a non-mydriatic retinal camera (8MP charge-coupled device (CCD) camera, model TRC-NW300, Topcon, Tokyo, Japan), were stored in a secure picture archiving and communication system. They were then assessed by viewing on both the gold standard, a desktop workstation (Optiplex 755, Dell, Round Rock, Texas, USA) via a secure website, and an iPhone 4 (Apple Inc, Cupertino, CA, USA) via second generation (2G) cellular networks. The images were then assessed independently by two ophthalmologists. The detection of retinopathy related were found to be in strong agreement between the phone display and desktop monitor, with the sensitivity (true positives/(true positive + false negative)) and specificity (true negatives/(true negative + false positives)) being greater than 89% except for the detection of microaneurysms. Agreement regarding microaneurysms was a little lower one ophthalmologist recording a sensitivity and a specificity of 72.3% and 89.6% respectively and the other ophthalmologist recording 72.2% and 80.0% respectively. Thus it is clear that microaneurysms are more difficult to detect on an iPhone 4 compared with a standard display. It should also be noted that handsets released since the study was conducted have improved image quality and size. The iPhone 6 Plus (Apple Inc, Cupertino, CA, USA), for example, has a 5.5-inch (diagonal) display with a contrast ratio of 1300:1 and a pixel density of 401 pixels per inch (ppi) compared to the iPhone 4's 3.5-inch display with respective values of 800:1 and 326ppi[42,43]. It would thus be interesting to see whether future studies record an improvement in microaneurysm detection compared to the discussed study or whether the disagreement between devices is due to factors unrelated to display quality.Nevertheless, the authors concluded that the ophthalmic images transmitted through both smartphone and internet techniques matched well with each other. Thus, it should therefore be noted that, even if it were impossible to capture ophthalmic images using a smartphone camera, images captured by means of conventional digital ophthalmic photography may, at least, be assessed by viewing these on a smartphone screen. This in itself is a step forward, given the prevalence of smartphones amongst doctors[32], as it allows such images to be instantly shared between medical professionals, regardless of their location. It also clarifies that any sufficiently high-quality images captured using the following techniques may be viewed on the smartphone in situ as well as on conventional displays upon exporting.

Indirect Ophthalmoscopy Lord et al. reported a method for capture of fundus images on a smartphone apart from a slit-lamp, using standard equipment[44]. Their technique involved holding a 20D lens in one hand, as per traditional indirect ophthalmoscopy, whilst holding and positioning a pen light, for illumination, and an iPhone, for image capture, in the other hand. An example of an image acquired using this technique is shown in Figure 1. This technique was found to be rather cumbersome and thus the acquisition of high quality images difficult[45]. However the widespread introduction of smartphone designs incorporating a light emitting diode (LED) flash on the handset's back face, alongside the phone's camera, allowed for the pen light to be dispensed with and a technique that was much more comfortable for the ophthalmologist, and hence more effective, could be demonstrated, as shown in Figure 2[45]. Using the stock iOS camera application while capturing a video stream with flash enabled, provides a consistent coaxial light source. The use of video also allows individual frames to be extracted after acquisition for use as still images, meaning the practitioner need only get a good view of the fundus at some point during the procedure and does not require an additional action to activate the shutter-release on top of achieving the desired view.

The ease-of-use of the above technique was further enhanced by Haddock et al.'s introduction of the 'Filmic Pro' (Cinegenix LLC, Seattle, WA, USA) specialist smartphone photography application[46]. The software allows independent control of the focus, exposure and flash light intensity during video filming. Still images could then be extracted from the video after recording. They reported that this allowed high quality images of fundus images of animals, as well as comatose and awake adults, to be more consistently produced compared to the methods described above.

Similarly, Lin et al. were able to capture fundus images of neonatal patients using the camera and LED flash of an iPhone 4S and HTC One (HTC Corp, New Taipei City, Taiwan) in conjunction with a 30D lens[47]. Specifically, the authors investigated the feasibility of using smartphones in screening for retinopathy of prematurity (ROP). Although the technique still required scleral indentation, a method which often causes the patient distress, the use of smartphones allowed photographic records to be made, as opposed to drawings or written notes alone, without the use of an expensive retinal camera. An example image from the study, from which the authors were able to detect plus disease is shown in Figure 3. The study therefore shows the considerable advantage of techniques involving smartphones in ROP screening, particularly given the importance of good record keeping when monitoring neonatal patients' retinal development.

Myung et al. recently developed a prototype which aims to aid digital image capture from indirect-ophthalmoscopy using a smartphone[48]. The system, shown in Figure 4, consists of a light-weight 3d printed arm that attaches to an iPhone 5 (Apple Inc, Cupertino, CA, USA) and holds a condensing lens at an adjustable fixed distance from the camera optic. As per Haddock et al. the authors also used the 'Filmic Pro' app for video frame extraction and illumination brightness adjustment. The smartphone's native LED flash was used as light source and the handset's autofocus adjusted for any differences in participant refractive error. The authors used the system to capture images of firstly, a model eye, and then latterly a sample of good quality, normal and abnormal fundal images on dilated study participants. Although the working distance of the system was adjustable, the authors' found that extending this beyond a certain distance caused overall size and stability issues. They also found that allowing this distance to be adjusted during imaging greatly reduced the system's ease of use. Nevertheless, such a solution does appear to offer a feasible means for acquiring digital images during indirect ophthalmoscopy and promises to be a useful tool for the field ophthalmologist and even non-specialists.

Anterior Segment Imaging and Slit-lamps

Barsam et al. demonstrated a technique for capturing digital anterior segment images using a smartphone by simply aligning, by hand, the camera optic of an iPhone 3G (Apple Inc, Cupertino, CA, USA) with one of the eyepieces of a BM 900 slit lamp[49]. Although this method allowed capture of digital anterior segment images without the need for an expensive slit-lamp camera (typical cost

15000 USD), it is more difficult than the standard technique and still requires a slit-lamp, meaning the full system is still rather expensive and relatively immobile. Since this study was published, a host of smartphone slit-lamp adapters have been made commercially available with prices varying from 75 to 520 USD. It has even been shown that a “Do-it-yourself” adapter can be assembled for approximately 15 USD using simple, readily available components[50]. Whilst such adapters improve on Barsam et al.’s study, by removing the need for the user to hold the handset in position for the duration of the examination, they are still dependent on the availability of a slit-lamp and on the expertise to use such an instrument. This can often be an issue for acquiring such images outside of well-equipped ophthalmology department. For example, Myung et al. have recently demonstrated a means of eliminating the need for a slit-lamp in the acquisition of digital anterior segment images[51]. The authors first attempted to acquire images by attaching a commercially available smartphone camera macro lens and using the native flash of an iPhone 5 at a working distance of approximately 2.5cm from the subject’s eye. However it was found that, even when using Filmic Pro to control the illumination intensity, the brightness of the flash was too uncomfortable for study participants at the close working distance necessitated by the macro-lens’ focal length. This prompted the authors to develop a simple adapter, Figure 5, which combined the macro lens with an external LED light source with a brightness selected for patient comfort. The adapter is pocket-sized and can be easily attached and detached from any handset. There are a number of limitations to the adapter, notably that it does not have the ability to create a slit of light that can be used to estimate the depth of a corneal pathology or for capturing cells or flare. Also, the relatively short working distance results in the necessity for disinfection between uses. However the authors were able to use this system to capture high quality anterior segment images of subjects displaying a number of different pathologies, allowing them to claim that they had sufficient quality images with regards to the clarity of the cornea, quality of the epithelium, fluorescein uptake, state of the conjunctiva, shape of the pupil, health of the iris, presence or absence of a hyphaema or hypopyon in the anterior chamber and the appearance of the eye-lids and lashes. Thus, given the low production cost, ease of use and reported quality of images this design offers the potential for a very useful anterior segment imaging tool, applicable to a variety of settings, included those in which resources are limited.

Two notable, commercially available smartphone-compatible slit lamps are the PSL One and Classic (Keeler, Windsor, U.K.). Both these models have many of the features of a regular slit lamp with the added benefit of being lightweight and durable[52]. The combination of these slit lamp models and Keeler's iPhone 4 adapter provides the user with the genuine ability to conduct mobile digital slit lamp photography. However, with the portable slit lamps costing between 2750 GBP[53] and 4000 GBP[54] and the adapter costing an additional 90 GBP[55] this remains an option that has a price beyond that which most non-specialists are able to afford. It has been reported that the slit lamp adapter is also compatible with the Hagg-Streit 900 BM and SL-3F (Topcon Corp., Tokyo, Japan) slit lamps if a varying degree of adaptation is applied[56].

Direct and Monocular Indirect Ophthalmoscopy

Currently, the most widely used smartphone compatible monocular indirect ophthalmoscope is the 'Panoptic' with 'iExaminer' attachment (Welch-Allyn Inc., Skaneateles Falls, NY, USA). The Panoptic itself, according to its manufacturer, is of a design that improves upon that of a classical monocular indirect ophthalmoscope by introducing 'Axial PointSource Optics' allowing a field-of-view of 25° (compared to approximately the 5° of conventional direct ophthalmoscopes) along with an increased magnification[57], with the distance between the operator's and patient's eye being a fixed distance between two eye-pieces, reducing the complexity of the procedure compared to standard ophthalmoscopes. Indeed, it has been reported that whilst accuracy of diagnosis for various pathologies remains at least as good compared to conventional direct ophthalmoscopy, ease of use and patient comfort are significantly increased[58, 59].

Blanckenberg et al. used a Panoptic which was customised, as shown in Figure 6, so to allow fundus images to be captured using a wireless enabled digital camera[60]. These images were then communicated to a mobile phone via Wi-Fi and uploaded to a web application via 2G/3G cellular networks. An image analysis algorithm was then applied which determined whether the images were of acceptable quality and the results reported back to the field via SMS. The system was thus capable of capturing images with a 25° viewing angle for a cost significantly less than the commercial options available at the time, the authors estimating that twelve healthcare centres could be equipped with such a system for the same cost as a single standard fundus camera, however they noted that even this is a cost which the district health service in Cape Town, where the trial was conducted, could not afford.

Following the work of Blanckenberg et al., Welch Allyn released the ‘iExaminer’ attachment in February 2013. The attachment is an adapter that allows an iPhone 4 or 4s to be inserted in place of the operator’s eyepiece allowing fundus images to be viewed through the phone’s camera, thus allowing digital images to be captured and distributed via wireless or cellular networks. To date the iExaminer is the only ophthalmoscope capable of smartphone integration which has achieved FDA approval[61]. However as the instrument is only compatible with the iPhone 4 and 4s models, the system is already two generations behind the smartphone market with Welch Allyn expressing that a version compatible with the iPhone 5 series will not be available in 2014. The Panoptic, iExaminer and 'pro' application (enabling emailing, printing, and storing additional patient files within the storage capacity of the phone) together typically cost the end user more than 700 USD in total (www.medisave.com), putting it in the premium ophthalmoscope price range.–

The ‘Ocular Cellscope’ (Maamari et al, Figure 7) entails independent LEDs, with multiple lenses and polarizers, in a configuration similar to that of the Panoptic with iExaminer, producing mydriatic images comparable with commercial dedicated desktop fundus photography systems (Topcon TRC-50EX)[62]. Working with the iPhone 4S (Apple Inc, Cupertino, CA), the Ocular Cellscope captures high resolution (2652x2448 pixel) images with a wide 55 degree field of view in a single capture, with potential to expand this field using digital mosaic techniques of multiple captures.

Giardini et Al. have demonstrated a novel approach in creating a smartphone adapter, shown in Figure 8, which deflects the phone's LED flash in a way so that a light source co-axial to the phone's camera is created, allowing fundus images to be displayed and captured using the phone's stock camera app or using bespoke software[63]. An example image is shown in Figure 9 alongside that of a standard retinal camera for comparison. As the operator is not required to put their eye in contact with an eye-piece the device can be kept at arms' length from the operator whilst images are captured, increasing comfort for the patient and making the experience less intimidating, particularly for children. The retina is brought into focus by the camera's autofocus feature by simply by tapping on the screen. The device can therefore be used by any operator familiar with the use of a smartphone after a brief induction session, without the need for any clinical training. The authors demonstrated a design using a Galaxy SIII GT-I9300 (Samsung C&T Corp., Seoul, Republic of Korea) smartphone. The authors report that interim results for 300 of 2100 dilated eyes imaged in Nakuru, Kenya show no clinically significant difference between remotely graded vertical cup to disk ratios measured using the smartphone unit's images compared to those measured using a standard retinal camera images (DRS+ Haag Streit CenterVue, Italy) ,with a p-value, the probability that differences occurred by chance, of 0.98. Such low-cost solutions, when compared to existing smartphone-based solutions, present a potential means for overcoming the cost barriers highlighted by Blanckenberg et al.[60].

Safety considerations

All of the techniques and devices discussed in this paper require some form of illumination. The safe limits for the intensity a subject's eye may be exposed to, across the electromagnetic spectrum, are clearly outlined in ISO15004-2:2007[64]. It is important that, if trying to replicate any of the techniques detailed in this paper, that the illumination source being used meets these standards. It has been verified that the indirect ophthalmoscopy technique detailed by Bastawrous falls within these limits when an iPhone 4 is used[65], however it should be noted that some smartphones now include exceptionally bright xenon flashes[28] and, as such, it is important to check the applied illumination source's adherence to the referenced standard. If the move to brighter smartphone flashes becomes a general trend then there may be a need in the future to decouple entirely from the native flash and use LED sources independent from the flash. Smartphone flashes are, after all, designed for general purpose photography and not with ophthalmic applications in mind.

Expert Commentary

There are currently appropriate commercially available means for ophthalmic specialists to capture good quality digital images of the anterior segment and fundus using smartphone cameras. However the specialist skills required and/or the cost of the instruments currently available has thus far either prevented or severely limited general practitioners and other non-ophthalmic specialists from also gaining this ability. Whilst inexpensive and non-specialist-friendly means have been demonstrated, the publication of more robust analyses of these prototypes' capacity to detect common eye pathology, compared to standard techniques, is required in order to consolidate the scientific literature validating their clinical use. Hence, these instruments are not currently commercially available. As such, accessibility to the ability to easily electronically store, share and display ophthalmic images presently remains reserved to ophthalmic specialists.

Five Year View

80% of all blindness is avoidable[66]. There is therefore tremendous scope for reducing blindness and visual impairment by introducing effective screening in situations where it currently doesn't exist, dramatically improving millions of lives. The World Health Organization (WHO) recently announced its 'Global Action Plan 2014-2019' for universal eye-health[67]. This document calls for "eye care services to become an integral part of primary health care and health systems development". As commercially available smartphone ophthalmic imaging devices are developed over the next five years, their ease-of-use will approach that of a smartphone. The availability of such affordable, high quality and easy to use smartphone imaging devices will have profound effects on eye care worldwide. The resulting changes to eye care will differ depending on the current state of the healthcare system in question. What is certain, however, is that the global impact to eye-health will be extensive, providing that adequate resources are supplied to developing and integrating these emerging devices across all income settings.

The initial impact will be in helping to achieve the first objective of the Global Action Plan by generating evidence with respect to the magnitude and cause of visual impairment, in order to advocate for greater political and financial commitment by respective governments. The devices will then become an integral part of on-going screening programmes allowing the continued early detection of what are presently the main causes of blindness, dramatically reducing the number of persons suffering from preventable blindness.

In the final part of this review we discuss the possible nature of the changes to eye care in low, middle and high income settings.

Diabetic retinopathy is currently the leading cause of blindness in those between the ages of 20 – 74 years in high-income countries, such as the United States[68]. However, a number of high-income countries lack effective screening programmes for the disease[69, 70]. Given the prevalence of type-2 diabetes globally[71] the development of a means of screening for and treating patients in the early stages of the disease is of paramount importance if the development of blindness in diabetes patients is to be slowed or prevented[72].

Use of an ophthalmoscope for fundoscopy in a primary healthcare setting is useful for the diagnosis of a host of eye and non-eye related pathologies. However, those primary healthcare physicians who are entirely comfortable performing a patient examination using an ophthalmoscope are in the minority. For example, it has been reported that in Canada only 52.3% of resident family care doctors feel competent in performing fundoscopy, even though over 95% felt it was an important skill to have[73]. The proportions comfortable performing other eye assessments, such as slit-lamp examination and anterior depth assessment, were equally poor (45% and 10% respectively). The field data reported by Giardini et al.[63] suggests that there is potential for smartphone imaging to improve general practitioners' and non-eye specialists' comfort in performing fundoscopy and provides a strong basis for our prediction that smartphone imaging devices similar to their adapter will greatly increase the proportion of practicing doctors who feel comfortable performing basic ophthalmic examinations. This can consequently reduce the number of referrals to ophthalmologists, delivering faster diagnoses and reducing the time and resource burdens on healthcare systems. This improvement can be further compounded through the introduction of complementary technologies such as mid-price (1000-3000 USD), portable, smartphone incompatible fundus cameras, such as the Epipole[(Epipole Ltd., Rosyth, UK) and CAVCAM (Retivue LLC, Charlottesville, VA, USA) fundus cameras, the latter of which is based on a commercial digital single lens reflex (DSLR) camera and produces images comparable to those of current desktop systems[74].

Furthermore, as Giardini et al. report that even operators with a minimal background in ophthalmology were able to capture sufficiently good quality optic nerve images compared to the reference standard[62]. Indeed, Farley et al. showed in their study of community health centres that primary care physicians, advanced practice nurses and physicians' assistants equipped with a nonmydriatic retinal camera can detect a high instance of microvascular abnormalities in patients, once given training in identifying such abnormalities from fundus photographs and if provided with good quality images[75]. We predict that the development of the smartphone based ophthalmoscopes discussed in this paper will allow cost effective, primary care based screening programmes to be established, potentially reducing the complications of diabetic retinopathy, along with a variety of other eye related pathologies such as glaucoma and macular degeneration, in high-income settings. Such programmes may be particularly important in the case of diabetic retinopathy in the coming years given that it has been predicted that, in the United States alone, the number of those suffering from the condition is to almost treble by 2050[76].

Similarly, papiloedema, which describes swelling of the optic nerve head, a sign of clinically significant brain involvement in many disease processes, including intra-cranial lesions such as tumour, haemorrhage or aneurysm, as well as such systemic diseases as malignant hypertension, is typically detected with direct ophthalmoscopy outside specialist eye centres. Any technology that improves the ease of examination and transmission of disc images has potential to improve detection of the many life-threatening conditions in which optic nerve head swelling is a hallmark.

90% of those suffering from visual impairment live in low-income countries[77], where the lowest concentration of ophthalmologist is found[78, 79]. There is therefore tremendous scope for smartphone imaging to facilitate the prevention and curing of avoidable blindness in low-income countries.

Patient navigation by the deployment of “community healthcare workers”, that is non-clinical staff native to a local population or sub-population, has been noted to be an effective means of tackling many of the issues preventing effective healthcare in low-income settings[80]. Within eye-care such barriers include lack of community or family support[81], lack of awareness of available treatments[82] and scepticism of evidence based medicine[83]. Smartphone ophthalmology will allow such non-clinically trained workers to be armed with the tools that are needed to conduct a screening programme where they can reach the most isolated patients without the need for expensive equipment, infrastructure or medical training.

The ability to conduct screening programmes for pathologies related to preventable blindness will allow governments and non-government organisations to mount campaigns to address the imbalance in the quantity of blind people distributed in low-income regions. We predict that the ability to do so in combination with the training and retaining of significantly more ophthalmologists and eye-health workers in low-income countries will allow many of these countries to achieve the Global Action Plan goals laid out by the WHO.

Moreover, smartphone ophthalmology will not only allow for a one-off drive to achieve the Global Action Plan but will also allow the infrastructure to be put in place for long-term, ongoing, population-wide screening for the causes of preventable blindness in low and middle-income countries, meaning that the reduction in instances of preventable blindness achieved in order to reach the WHO's targets can be maintained over the short, medium and long term.

Further to this, as in high-income settings, granting non-specialists the ability to comfortably diagnose eye pathologies will improve the care administered to those who are suffering from diseases which are not primarily eye problems. Smartphone fundus imaging will, for example, provide a simple means of diagnosing infectious diseases[9, 10, 84-87] such as dengue fever[87] and malarial retinopathy[9, 85, 86], a unique set of retinal abnormalities related to cerebral malaria which is commonly over-diagnosed when other non-imaging tests are used. Therefore smartphone ophthalmoscopes such as those detailed in this paper promise to provide a feasible means of triage, even when an ophthalmologist is not present.

Furthermore non-communicable disease and their associated complications are not restricted to high-income settings. Indeed it is in middle-income countries where the highest numbers of those between the ages of 20 and 79 suffering from type-2 diabetes are to be found, a number which is due to increase by 50% by 2030[70]. Thus it is in these settings, where practicing ophthalmologists are few and difficult to access, where population-wide screening for associated complications such as diabetic retinopathy is most sorely needed. However, given the prevalence of smartphones in low and middle-income countries and its expected rise[88], so will the proportion of health workers comfortable with operating smartphone-based ophthalmic devices. Thus such smartphone based devices will offer a vital tool in preventing an epidemic of non-communicable disease related eye complications.

However, a note of caution must be sounded with regards to our above predictions. Despite its immense potential, thus far a very low proportion of the relatively numerous mHealth technology pilot studies conducted have gone on to full integration into healthcare systems[89-91]. Smartphone ophthalmic imaging's full potential will only be realised if mHealth in general is accepted into healthcare systems at large. It has therefore been noted that it is vital that technologists, clinicians and policy makers work together to develop the common standards and frameworks that are necessary for integration of mHealth in general[89, 91].

Finally, the future development of smartphone imaging for ophthalmology is tied to the future development of smartphones themselves. Herein lies both one of the greatest opportunities for these emerging techniques and one of the greatest challenges. The rapid development of smartphones has seen their image capture quality increase drastically over recent years, as has processing power, data storage and many other features. However the physical design of smartphones has also altered greatly, which is a key parameter whose continued evolution could pose problems for any ophthalmic imaging industry attempting to piggy-back on the mainstream mobile phone industry. By means of example, established ophthalmic imaging manufactures already appear to have fallen behind with the failure to implement device updates following the launch of the iPhone 5 series (the iExaminer, for example, being the only smartphone ophthalmoscope on the market with FDA approval, has yet to be adapted to integrate with handset updates). As such new smartphone-centric manufacturers may need to emerge in order to develop an industry capable of innovating and providing robust clinical verification of these innovations at a pace matching that of the wider mobile phone market.

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Key Issues: 8 – 10 bullet points summarizing the review

- Smartphones, mobile devices capable of telephony, installing and running software applications are evolving towards being ubiquitous devices owned by large portions of the global population.
- Studies have shown that display quality on smartphones is sufficient to assess ophthalmic images with equal or better quality than desktop monitors.
- Smartphones are increasingly being fitted with high quality digital cameras.
- A number of hardware solutions have been developed which allow anterior segment, indirect and direct ophthalmoscopy images to be captured using a smartphone camera.
- Several studies have so far reported smartphone ophthalmic imaging as having comparable quality to reference standards.
- Commercially available solutions remain above the affordability threshold for many settings.
- There has been recent progress which suggests that in the coming one to three years genuinely inexpensive solutions may emerge.
- The benefits of these devices will be felt across high, middle and low income settings.

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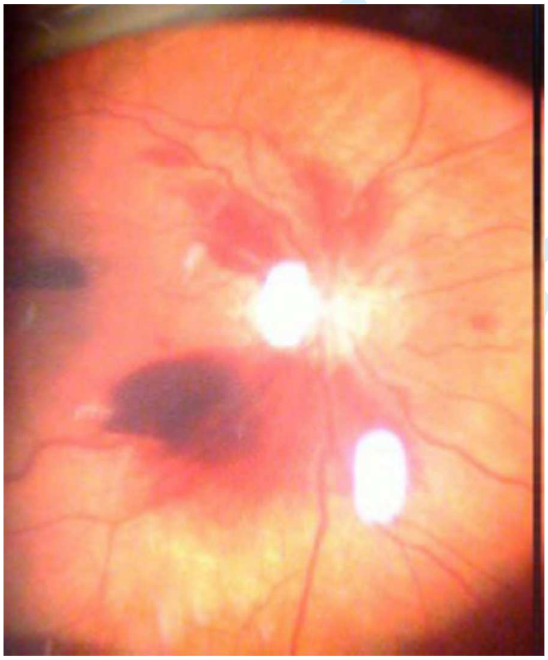

Figure 1. Fundus image captured using a 20D lens, iPhone (Apple Inc, Cupertino, CA, USA) and a pen torch.

Reproduced with permission from [44].

Figure 2. Capturing fundus images using an iPhone 4's (Apple Inc, Cupertino, CA, USA) native light emitting diode (LED) flash rather than a pen torch.

Reproduced with permission from [45].

Figure 3. Plus disease in a pre-term infant could be diagnosed from an image captured using a smartphone's camera and light emitting diode (LED) flash by applying an eyelid speculum and performing scleral indentation.

Reproduced with permission from [47].

Figure 4. The '3D Printed Smartphone Indirect Lens Adapter' developed by Myung et al. consists of a condensing lens held at a fixed length from the Smartphone's camera by a 3d printed adapter. Reproduced with permission from [48].

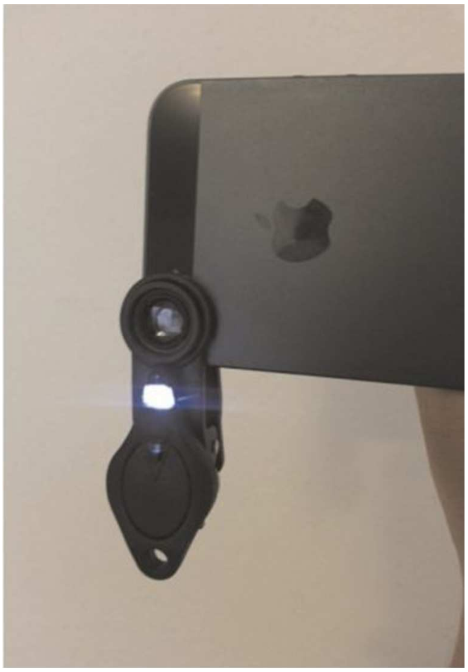

Figure 5. Smartphone adapter for anterior segment imaging developed by Myung et al. Reproduced with permission from [51].

Figure 6. Panoptic monocular indirect ophthalmoscope (Welch-Allyn Inc., Skaneateles Falls, NY, USA) customised so to capture images with a wireless enabled digital camera. A cellphone then received these images for long-distance transmission.

Reproduced with permission from [60].

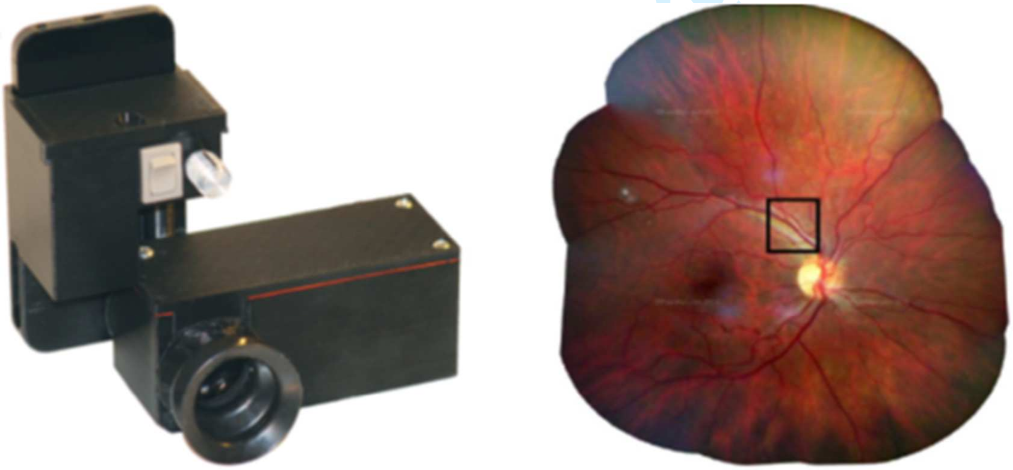

Figure 7. The Ocular Cellscope (left) captures fundus images with a 55 degree field of view. Multiple images can then be “stitched” together by specialist software to produce an image with an even

wider field of view (right).

Reproduced with permission from [62].

Figure 8. A simplified smartphone adapter developed by Giardini et al. promises to overcome the cost barriers presented to screening in many settings.

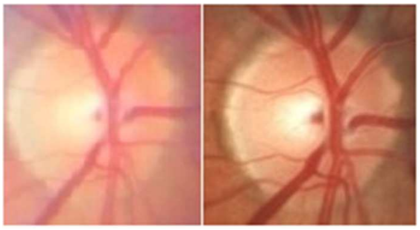

Figure 9. Optic nerve as captured by the adapter reported in Giardini et al. (left) and a standard desktop fundus camera (Topcon Corp., Tokyo, Japan) (right).