



Smartphone Based Point of Care Testing for Infectious Diseases in Rural Settings: A Scoping Review

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Abstract

Diseases spread rapidly around the world and cause lots of deaths each year; most of these deaths occur in rural areas and low resource countries due to limited resources available for diagnosis, the remote location of central laboratories, and prolonged times to correctly diagnose patients to allow them access to proper medical therapy. Recently, we have developed a novel approach to diagnosing and managing infectious diseases using smart phone-based, point-of-care testing (POCT), which incorporates mobile phones as tools for quickly diagnosing patients using images taken by the phone and having the results processed off site via cellular or wireless networks. In this scoping review, we systematically searched PubMed, Scopus, Web of Science, and Google Scholar to identify relevant studies that met pre-established inclusion/exclusion criteria for smartphone POCT applications. The data generated by studies that met the eligibility criteria will be summarized through a process known as descriptive synthesis or thematic synthesis. We identified several POCT applications that can be used to diagnose and/or manage several infectious diseases, including malaria, tuberculosis, HIV, COVID-19, dengue, and hepatitis, utilizing varying technologies, such as the following: smartphone-assisted lateral flow assay readers; electrochemical biosensors; microfluidic lab-on-chip platforms; and artificial intelligence-based image analysis systems. Portable and affordable with quick turnaround time, these technologies require little infrastructure yet allow for real time transmission of collected data to support surveillance efforts. There are challenges with validating these devices for use on a larger scale and meeting regulatory compliance guidelines. Addressing the challenge of training the user and the infrastructure in which to deliver the service will be required for the applications to be applied at the population level. The findings presented here demonstrate the value of smartphone-based POC testing for diagnosing infectious disease in areas with limited resources.

Keywords: smartphone-based diagnostics, point-of-care testing, infectious diseases, rural settings, rapid diagnostic tests.

1. Introduction

According to statistical records, infectious diseases are responsible for a large portion of global morbidity and mortality. Laboratories typically necessitate significant investment in terms of infrastructure (e.g., heavy equipment), qualified personnel and the use of a standardized laboratory, rendering them virtually impossible to implement in various parts of the world. Recent advances in smartphones have

changed this by providing portable, advanced imaging devices and powerful computing capabilities with internet and connectivity capabilities to transfer data for analysis. Thus, it is now possible to develop innovative biomedical platforms that incorporate smartphones with biosensors and microfluidic devices, optical readers and artificial intelligence-based image interpretation for rapid disease

identification at the community level through point-of-care testing of patients using mobile-based test systems [1-3]. Research has demonstrated the efficacy of mobile diagnostic systems for diagnosing Malaria, Tuberculosis, (TB) HIV, Dengue and COVID-19. (Xu et al., 2019; Song J et al., 2018; Turbé et al., 2021; Vashist et al., 2015; Fozouni et al., 2021). There are a variety of new technologies that are being developed for these applications, which include such things as: loop-mediated isothermal amplification (LAMP); CRISPR based means of detecting the target (PATHOGENIC) organisms; rapid test result "readers," mobile microscopy; and deep learning analysis of images using artificial intelligence. (Xu et al., 2019; Fozouni et al., 2021; Mudanyali et al., 2012; Pirnstill & Cote, 2015; Turbé et al., 2021). A wide range of technology is available for developing nations or other under-resourced nations that may not have access to traditional diagnostic labs as well as limited opportunities for performing testing of sample related forces. The purpose of this paper is, therefore, to provide a summary and synthesis of the available literature on smartphone-based diagnostic technologies for infectious disease-related testing and other related technologies.

2. Methods

To complete this study, PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Scoping Reviews) guidelines were utilized for the preparation of this scoping review [4-7]. This scoping review was designed to identify and characterize existing data regarding mobile diagnostic systems based upon smart phones. Scientific databases (i.e., PubMed, ScienceDirect, Google Scholar) were searched and articles relevant to the aforementioned population were identified by utilizing the search terms of "smartphone diagnostics", "mobile health diagnostics", "point of care tests", "infectious diseases", and "mobile biosensors". Only articles that were peer reviewed and published in English were included. The studies included in this review studied the application of mobile diagnostic technology based on smart phone usage to diagnose/infectious diseases, as well as experimental or clinical confirmation of the use of the technology. An initial

search yielded 120 records, but when duplicates (by reviewing titles previews) were removed, only 32 articles were reviewed in full; thus, there were 32 articles that met the initial inclusion criteria. Ultimately, there were 14 articles out of 32 that meet the criteria for this review shown in Figure 1.

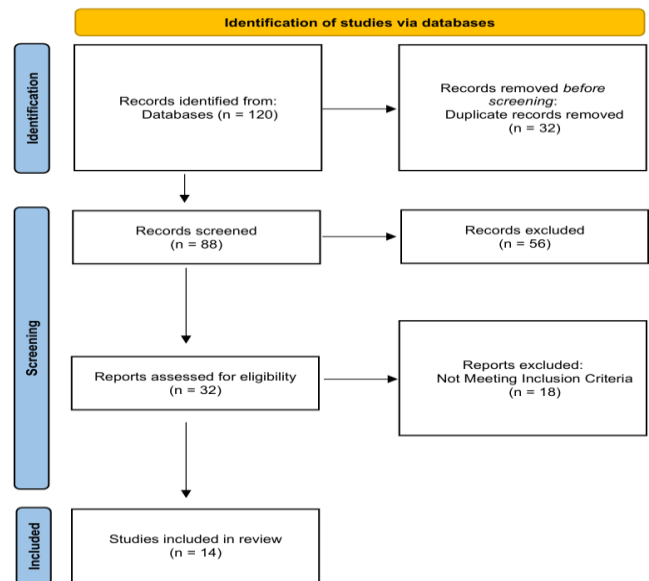


Figure 1 PRISMA flowchart for selection of studies

3. Results

Researchers have demonstrated substantial progress using smartphones to diagnose diseases. (Yetisen et al., 2013; Liu et al., 2017; Jiang et al., 2018; Sun et al., 2021). This includes new diagnostic techniques such as nucleic acid amplification; diagnostic methods performed using optical microscopy, fluorescence, and novel microfluidic devices constructed using paper; and algorithms for detecting images using machine learning. An example of one of these devices is an iPhone-based polarized microscope with digital magnification created by Pirnstill and Coté to detect malaria-infected red blood cells. (Pirnstill & Cote, 2015). In the same way, Xu and colleagues devised a smartphone based RTPCR amplification method to allow for rapid detection/diagnosis of malaria and also for the possibility of using this method in either an outdoor environment or at home by an individual. (Xu et al., 2019) [8-12]. Other researchers have described



potential uses for smartphones in detecting viral infectious

Table 1 Comparative Analysis of Included Studies

Study	Method / Technology	Target Disease	Detection Limit	Sensitivity / Performance
Xu et al., 2019	Smartphone LAMP platform	Malaria	~10 parasites/ μ L	High analytical sensitivity
Pirnstill & Cote, 2015	Smartphone polarized microscopy	Malaria	Microscopic detection	~95% accuracy
Turbé et al., 2021	Deep learning RDT interpretation	HIV	Image-based detection	>98% accuracy
Song J et al., 2018	Smartphone biosensor platform	Tuberculosis	DNA detection	High sensitivity
Yetisen et al., 2013	Paper microfluidic diagnostics	Multiple infections	Varies	Rapid colorimetric detection
Fozouni et al., 2021	CRISPR-Cas13a smartphone detection	COVID-19	~100 copies/ μ L	High specificity
Drain et al., 2022	Smartphone antigen reader	COVID-19	Antigen detection	Clinical screening performance
Vashist et al., 2015	Smartphone quantitative biosensor	Dengue	Low viral concentration	High accuracy
Mujawar M.A. et al., 2020	Fluorescence detection system	Viral infections	Low viral loads	Sensitive detection



Liu et al., 2017	Nucleic acid smartphone platform	Pathogens	Low DNA copies	High precision
Jiang et al., 2018	Multiplex microfluidic smartphone	Multiple infections	Multiplex detection	Simultaneous detection
Mudanyali et al., 2012	Cellphone RDT reader	Multiple diseases	RDT interpretation	Improved accuracy
Poostchi et al., 2019	Mobile microscopy image analysis	Malaria	Parasite detection	High classification accuracy
Sun et al., 2021	Integrated smartphone biosensing	Multiple pathogens	Low detection limits	Portable diagnostics

diseases through the use of apps. Fozouni and others have developed a smartphone based CRISPR-Cas13a based assay for detection of molecules. (Fozouni et al., 2021) [13-15]. The US Food and Drug Administration has approved a method of direct detection for determining the presence of SARS-CoV-2 viral infection. Similarly, Drain et al. evaluated the use of a smartphone as part of community-based rapid antigen testing for detecting the presence of SARS-CoV-2 in local communities. (Drain et al., 2022). With the rapid growth of mobile technologies and the growing implementation of A. I. (Artificial Intelligence) across other new mobile diagnostic devices (including those with added capability for using A. I. to assist in conducting newly developed tests), many new smart devices are using advanced machine learning (A. I.) models to analyze photographic images of rapid HIV testing specimens for accurate test interpretation. (Turbé et al., 2021).

4. Discussion

In today's world, advances in mobile technology and increased use of artificial intelligence (AI) across other new mobile diagnostic devices, including those that utilize artificial intelligence (AI) to assist with

conducting newly developed tests, have resulted in many smart mobile devices using sophisticated AI machine learning models to analyze photographs of rapid HIV test specimens for accurate test interpretation. (Xu et al., 2019; Pirmstill & Cote, 2015; Turbé et al., 2021; Song J et al., 2018). A broad spectrum of technologies has emerged, including nucleic acid amplification-based techniques, CRISPR-based detection systems, microfluidic devices, mobile microscopy, and AI-assisted interpretation, as well as demonstrating the diversity of smartphone-based diagnostic systems. (Yetisen et al., 2013; Fozouni et al., 2021; Jiang et al., 2018; Sun et al., 2021). The introduction of molecular diagnostic methods such as LAMP (loop-mediated isothermal amplification) and CRISPR technologies have provided highly sensitive detection of pathogens with little need for sophisticated laboratory infrastructures. (Xu et al., 2019; Fozouni et al., 2021). Unlike traditional polymerase chain reaction (PCR) methods, isothermal amplification techniques are better suited for point-of-care environments since they are operated at a single temperature and require very little additional equipment. (Xu et al., 2019).



Also, by utilizing smartphone imaging and real-time data processing capability, the time taken to produce results is greatly reduced while maintaining a high level of analytical sensitivity. (Liu et al., 2017; Sun et al., 2021). Microscopy using smartphones has quickly become an alternative to traditional methods for examining diseases like malaria and has shown similar accuracy with wider access in developing countries. (Pirnstill & Cote, 2015; Poostchi et al., 2019). Artificial Intelligence (AI) and machine learning has improved diagnostics by reducing the chance of subjective interpretation errors, especially for rapid diagnostic tests (RDTs). (Turbé et al., 2021). Image analysis powered by AI increases reproducibility of diagnosis while allowing the identification of small diagnostic features that the human eye may have missed. (Turbé et al., 2021; Mudanyali et al., 2012). Also, biosensors and microfluidics that are integrated with smartphones allow for simultaneous multiplex detection and quantitative analysis of multiple pathogens, resulting in cost- or resource-effective and quick diagnostics. (Yetisen et al., 2013; Jiang et al., 2018). In particular, microfluidic systems made from paper provide benefits such as low cost, simple operation, and applicability for large-scale testing in out in the field. (Yetisen et al., 2013). In addition, connectivity in real-time (RT) for smartphone-based diagnostics allows for automatic collection, processing and transmittance of data for epidemiological purposes including disease surveillance and remote patient monitoring. (Drain et al., 2022). Epidemiological tracking could be improved through geolocation and networking capabilities, which could help quickly respond to public health crises during an outbreak. (Drain et al., 2022; Sun et al., 2021). While there are many benefits from using smartphone-based diagnostics, there are also a number of challenges that exist. Variability in smartphones (e.g., hardware, software, camera quality; processing power; operating systems; etc.) create obstacles to standardization and/or consistent diagnostic results. (Mujawar M.A. et al., 2020). In addition, very few of these tools have been through clinical trials on a large scale or validated in a clinical environment. (Mujawar M.A. et al., 2020; Liu et al., 2017). There

are a number of regulatory challenges that would impede widespread clinical use, including issues related to safety, quality, software validation, and data security. (Drain et al., 2022). There are also several important logistical issues that will have to be addressed before smartphone-based diagnostic tools can be successfully implemented. These include: ensuring that healthcare providers receive the necessary training to use the tools effectively; providing infrastructure, such as reliable internet access and electricity, especially in rural and resource-poor areas; (Sun et al., 2021) and dealing with issues related to variability in study design, sample sizes, and evaluation methodology, which limit our ability to compare the diagnostic performance of different technologies. (Liu et al., 2017; Jiang et al., 2018). As a result of these issues, the establishment of standard evaluation protocols for mobile-based diagnostic systems is essential if we are to make appropriate comparisons among these systems and make evidence-based decisions about continued research into this area of technology. (Sun et al., 2021). As a result of these issues, the establishment of standard evaluation protocols for mobile-based diagnostic systems is essential if we are to make appropriate comparisons among these systems and make evidence-based decisions about continued research into this area of technology. (Yetisen et al., 2013; Drain et al., 2022).

Conclusion

By decentralizing testing, reducing reliance on central laboratories, and providing diagnostic services to people in underserved communities, these types of technologies will significantly enhance health equity in low- and middle-income countries. Mobile diagnostic technology represents a significant milestone for the movement to decentralize healthcare delivery. As the studies show, mobile diagnostic technologies can provide accurate, portable answers to patients' health problems as compared to laboratory-based tests. As technological advancements continue, increased clinical trials and evidence of regulatory acceptance will enable wider use of this technology in global health care.

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