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Taking connected mobile-health diagnostics of infectious diseases to the field

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Preface

Mobile Health or mHealth - The application of mobile devices, their components and related technologies to healthcare is improving patients' access to treatment and advice. Now, in combination with connected diagnostic devices it offers new possibilities to diagnose, track and control infectious diseases and improve health system efficiencies. In this context we look at these technologies and highlight their promise but also the challenges in realising their potential to increase patient access to testing, aid in their treatment and improve the capability of public health authorities to monitor outbreaks, implement responses, and assess the impact of interventions across the world.

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Author Information

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1 Introduction

Rapid advances in portable communications technologies and digital computing have improved the speed of, and efficiency with which data can be processed and exchanged. In particular the arrival of the smartphone and the networks needed to support it, are rapidly reducing the costs of data acquisition and transfer worldwide. As of 2016, global smartphone adoption (the percentage of all mobile phone connections that come from a smartphone) has reached 51 %¹ and by 2020 in sub-Saharan Africa it is forecast to reach 55 %² (Fig. 1). This powerful pocket computer with built-in sensors and wireless connectivity provides researchers and health systems with new opportunities to capture and handle data³. The adoption and capabilities of smartphones and their related technologies in resource-rich settings and resource-limited settings are continually growing with low cost smartphones reducing the affordability barrier⁴ while offering similar sensing and processing capabilities to more costly “high-end” devices (Fig. 1).

The way that we detect and respond to disease is also continually advancing. Step-changes in the development of sensitive and specific immunological and molecular based diagnostics as well as genetic sequencing have allowed the detection and staging of an increasing number of diseases. This has had a large influence on our ability to understand the burden and transmission dynamics of infectious agents as well as to guide clinical decision making and control - no better illustrated than in the field of infectious diseases^{5–7}. Recent advances in nanotechnology, microfluidics and microarray-based systems have brought closer than ever the promise of simple, yet highly sensitive and specific devices, which can be used outside of the laboratory. These areas of use are often described as at or near the “point-of-care” which include places such as the patient’s own home, a primary care setting or by their bedside in a hospital. In pursuit of this, the new generation of nucleic acid tests have been developed that require less than five minutes of hands-on time⁸ and deep sequencing is now possible on a small hand-held device.⁹ These advances, combined with changing consumer attitudes towards self-testing, and increased appetite for wearable biosensors, are enticing healthcare providers to begin to shift towards the new paradigm of P4 Medicine which is *predictive, pre-emptive, personalized and participatory*¹⁰.

These developments have occurred alongside the emergence of the field of mobile health (or mHealth defined by the World Health Organisation as medical and public health practice supported by mobile devices¹¹) and this has spurred the co-development of diagnostics and mobile devices to create connected diagnostics. mHealth interventions have been used to address a range of challenges from disease surveillance to health systems strengthening and health education^{12,13} and the combination of these with these connected diagnostics will impact all areas of healthcare, including those related to infectious diseases.

2 Potential for Infectious Disease Response

Diagnosis and monitoring of disease are key to clinical management. The control of infectious diseases represents a unique challenge because infections can be transmitted to others and thus require a focus on early detection and treatment, surveillance and outbreak control. Diagnostic and monitoring tools must therefore be integrated with effective

surveillance and control measures to limit the spread of infection. mHealth approaches (Table 1) could improve the efficiency, speed and interconnectedness of an integrated clinical and public health response *via* two major mechanisms: (i) increased access to healthcare outside of care settings (e.g. by improved self-testing) and (ii) the real-time or close to real-time reporting of diagnostic results to patients and healthcare professionals to elicit rapid and appropriate clinical and public health responses to both endemic infections and outbreaks of epidemic potential. To date, most mHealth interventions, as exemplified in Box 1 have focused on using established mobile technologies (such as text messages and calls) to connect healthcare workers and patients to each other and to test results¹⁴. Combining this with portable diagnostic devices that connect and report results automatically has the potential to streamline this process.

The global risk of antimicrobial resistant infections is potentially catastrophic, demanding improved diagnostics to better guide antimicrobial therapy¹⁵. Connected diagnostics that can simultaneously detect a pathogen and identify antimicrobial sensitivity and resistance can enable selection of appropriate therapies whilst reporting the required data to surveillance centres. Likewise, for infections leading to chronicity, particularly those requiring long term therapy, mHealth provides major opportunities for home or community-based monitoring. In resource-limited settings, where health services may already be overwhelmed, these approaches are particularly useful. Taking diagnostics outside of formal health facilities and linking the output of testing into pathways of clinical and preventative care that may be delivered in the community could yield more cost effective and user-friendly healthcare. In principle these interventions will increase patient access to precision medicine and in resource-rich settings, connected healthcare systems such as Box 2 are beginning to be used to stratify individual patients into remote treatment and response monitoring programs.

mHealth can also increase system efficiency, by reducing workload and errors associated with paper reporting and preventing stock-outs, through the increased automation of inventory and supply chain management systems¹⁶. Additionally, phone-based decision trees can assist less well trained users in decision making and can play an important role in diagnosis, monitoring or for data gathering more generally¹⁷. Furthermore, in disease surveillance, there is an urgent requirement to more rapidly detect and intervene for newly emerging epidemics (e.g. Ebola or Zika), as well as for increased sentinel surveillance for existing ones¹⁸. The use of connected diagnostics and symptom reporting apps, combined with standardised electronic collection of key epidemiological and clinical data have the potential to greatly enhance the efficiency and speed of management of both epidemic and endemic infections including the management of contacts where appropriate¹⁹. The real time reporting of diagnostic test results can enable this surveillance through the geospatial mapping of infections *via* geotagged test results²⁰ or social network and internet search analysis, providing new tools for assimilation into outbreak control^{21,22}.

As an example, the burden of HIV in sub-Saharan Africa remains unacceptably high. In areas such as KwaZulu-Natal, South Africa, HIV prevalence in the population reaches over 30 % overall, and higher in women²³. This is despite a public health approach to HIV testing and anti-retroviral treatment for all. Reasons for a continuing high rate of new

infections are many fold. The high level of associated stigma leads to poor rates of testing, as well as poor attendance at treatment clinics. High population mobility impedes chronic disease care, as well as being a risk for infection. In this context, there is a need for a precision public health approach to HIV care.²⁴ mHealth provides the ideal framework in which to achieve this through, targeted behavioural change (through interactive apps), care roadmaps (whether community based or clinic) and connected diagnostic monitoring (HIV testing and viral load monitoring). Some examples of this are emerging. The HIVSmart! app²⁵ has been developed from the internet based form used by Pia *et al.* in Box 1 to work with HIV RDTs to support patient linkage to and retention in care worldwide. Now further work is needed to fully develop these and other such interventions and overcome the challenges of integrating connected diagnostics into them.

3 Challenges of delivery

Despite the potential benefits and numerous connectable diagnostic devices being reported, as far as we are aware an mHealth intervention featuring a connected diagnostic linked to a clinical care pathway and/or surveillance system for an infectious disease has yet to be deployed. To fully implement this, systems must be in place for the secure transfer, analysis (either *in situ* or remotely) and storage of the data generated. Once analysed any relevant decisions or conclusions derived from it must be reported to and acted upon by either the patient, healthcare professional or relevant institution along with linkage to a suitable care pathway (Fig. 2). These stages and their challenges will be discussed further below but all have a bearing on how such a device and intervention is developed, regulated and deployed. Moreover, the potential for the misuse of confidential health and personal data requires that, to be acceptable and effective, mHealth approaches must be underpinned by the highest level of community/patient confidence and well-regulated clinical pathways.

4 Target Identification and Sample Acquisition

Identifying relevant diagnostic targets for infectious diseases and developing testing technologies aimed at distinguishing the pathogen or host response to the pathogen from commensal infections or non-specific immune responses is a well-established field²⁶. Targets should be selected both on the predictive capacity for disease identification but also on suitability for use at the point-of-care. This requires careful consideration of what the true requirements and limitations are in each setting. The needs for self-testing at home compared to within a clinical setting are often quite different. The challenges of sample acquisition and processing that are met with ease in a primary care facility are considerably harder to meet in the field or at home. For example sampling using a venous draw requires more specialised equipment and expertise for effective and safe acquisition than a finger-prick blood sample, urine or a swab although these too can be challenging for untrained users²⁷. Some assay systems based on plasma will require a blood centrifugation step prior to testing and swabs or urine samples require pre-processing. Ensuring simplicity of sample processing in the test is key. The development of paper-based centrifugation systems provide promise in this respect²⁸ and controlling the tests *via* a mobile phone has the potential to help further by lowering the training needed to perform and interpret the test. This can be

achieved by displaying step-by-step guides or *via* automating steps previously performed by the user.

5 Developing Connected Point of Care Infectious Disease Diagnostic Technology

The World Health Organization's ASSURED²⁹ criteria defines the paradigm of an ideal point-of-care diagnostic and key design principles are extensively discussed elsewhere^{27,30}. A connected device has an additional requirement whereby the signal generated must be transduced into digital information ready for transmission. Systems for this have been developed³¹ and these technologies are increasingly being used to create connected point-of-care diagnostics with a number of excellent recent reviews on the subject^{32–34}. These systems, either capitalise upon the sensors already built into the phone or use sensors external to the phone and exploit its computational and connective power to create a connected diagnostic (Fig. 3).

In principle, a mobile phone camera can take the place of advanced laboratory-based spectrometers and match their quantitation and multiplexing capability^{35–37} via innovative engineering. These efforts are acting to democratise access to otherwise costly laboratory equipment and reduce the training needed to interpret test results e.g. *via* automated RDT measurements (Box 3). This approach capitalises on mobile phone imaging³⁸ or video capture³⁹ to enable the quantitative⁴⁰ assessment of results with the potential for geotagging⁴¹ and rapid transmission of results to healthcare systems⁴². Similarly, mobile phone-based microscopy⁴³ is now gaining traction in detecting microscopic parasitic infections⁴⁴, and is rapidly approaching that of laboratory based microscopes with a significantly reduced upfront cost. Mobile phone-based microscopy is even yielding portable, handheld routes towards fluorescent imaging of viruses⁴⁵ and DNA molecules⁴⁶.

Other sensors found in mobile phones have also been explored in a broader context including the accelerometer for monitoring the body's motion which correlates with certain diseases including Parkinson's⁴⁷ and even the microphone for monitoring lung function⁴⁸. Ecology mapping of mosquitos is possible using the microphone⁴⁹ highlighting the broader potential of smartphones to aid disease prevention. Now, new mobile phones and smart watches are actively embracing mHealth with purpose driven intrinsic sensors such as heart rate sensors being built into the back of the device⁵⁰. In addition to this, manufacturers continue to add new sensors and imaging functionalities into the latest handsets. The potential diagnostic applications made possible by these remains to be seen however, 3D sensors such as the infrared depth sensor system found in the iPhone X may assist remote visual diagnosis.

External sensors can be engineered around any suitable biosensor or signal transduction system and connected to share data *via* mobile networks. Importantly, this can avoid the problem of interoperability between different phones and operating systems and reduces device or component heterogeneity which would otherwise hamper approval by regulators. For example, dedicated photodiodes or CMOS chips built into an external device along with

a defined excitation source can yield controlled light environments for microscopy^{51,52} and sensing⁵³.

Once these external sensors are built into a device, they must then transfer the data generated. Many manufacturers have begun to integrate internet connectivity directly into their laboratory based diagnostic equipment, giving users faster access to results and facile integration into laboratory information management systems. As these connected instruments decrease in size these devices are increasingly being deployed at or near to the point-of-care and recently have been deployed in response to the Ebola⁶² and Zika⁶³ epidemics.

For more portable systems, other sensors can also be employed. Biosensors that incorporate electrochemical transduction⁵⁴ are eminently suited to digital interpretation and connection and many connected electrochemical biosensors have been developed⁵⁵. Some of these sensors offer less invasive sample acquisition methods with some incorporated into wearable sensors held near the skin^{56,57} or used to analyse volatile organic compounds in a patient's breath⁵⁸. Other signal transduction methods including micro-cantilevers and surface acoustic wave detection⁵⁹ offer the potential of ultra-rapid testing within 10 seconds⁶⁰.

The advent of nanopore based sequencing⁶¹ has allowed devices that can sequence DNA to be miniaturised to the size of a USB stick offering the possibility of full genomic disease profiling in a handheld device⁹. However, this technology is still limited for use as a point-of-care diagnostic, in part by the need to perform multistep sample preparations unsuited to the untrained user, and because methods for securely handling, analysing, and interpreting the data generated are still in their infancy⁶². This problem is common to all connected diagnostics, but it is especially acute for the large amounts of genomic data generated by sequencing devices⁶³.

6 Data Analysis: On-Phone and on Cloud

Automated result analysis has potential to reduce both trained and untrained user error when interpreting, recording and transmitting results of diagnostic tests. There are a number of methods to automate the visual interpretation of images and their suitability depends on the type of data captured, as well as the resources available in a given setting.

Cloud-based methods are most appropriate for more computationally expensive analysis, such as high-resolution image or video data, in settings where there is sufficient connectivity. However, on-phone feature extraction that reduces the size of the images before their transmission and cloud-based interpretation can mitigate this⁶⁴. Cloud-based systems ensure connectivity to databases and allow algorithms to be updated centrally. It also removes the processing burden from mobile devices, increasing the range of compatible devices. Systems have been developed enabling hands-free automated analysis of HIV RDTs using Google Glass, which sent image data to a remote server⁶⁵. Here a machine learning algorithm qualitatively classified the RDT before the result was sent back and displayed to the user.

On-phone analysis is more appropriate where less complex analysis is required or in remote settings with limited mobile network connectivity and bandwidth. On-phone image and video analysis has been used to detect the fluorescent products of microfluidic nucleic acid amplification⁶⁶ and in cell⁶⁷ and parasite⁶⁸ counting. This allows the asynchronous transmission of data where the results are stored on-phone and uploaded once in range of mobile networks. Although this can reduce the transmission of patient data, on-phone storage poses its own security risks such as the loss or malfunction of the device. On-phone analysis is further enabled by the growing capability of mobile processing hardware (Fig. 1). The introduction of dedicated neural processing units and software frameworks for on-phone machine learning allow increasingly efficient and nuanced image classification⁶⁹ and may improve inference when using defective equipment, or in poor lighting conditions⁷⁰.

7 Data Connectivity to Health Systems

Optimally used mHealth applications have the potential to become the largest source of health data, for use in research and health improvement interventions^{71,72}. However, unlike clinic-based services, where health information from diagnostic testing is currently acquired and stored in laboratory systems that are secure, the data collected from individual mHealth devices may not be securely stored or easily shared across multiple mHealth applications and connected to electronic health records⁷³. Data sharing has been associated with contextual⁷⁴ and ethical⁷⁵ challenges including a lack of standardised data security to assure privacy. What is needed are methods to improve health data sharing and connectivity and develop a consensus on data governance⁷⁶. Broad regulations such as the EU's General Data Protection Regulation (GDPR) are beginning to address this, but more tailored approaches like the voluntary code of conduct on privacy for mHealth apps⁷⁷ are needed. Moreover, recent ethics studies⁷⁸ have highlighted the need for users to understand and consent to all aspects of how their data will be used.

Modular platforms to share information, standardize and coordinate data collection, and improve mHealth device connectivity are currently under development⁷³. However, these platforms such as the Fast Healthcare Interoperability Resources (FHIR)⁷⁹, will still require stakeholder collaboration and substantial standardisation of the interfaces between the hardware and software components in an mHealth system if they are to be put in place.

8 Challenges in mHealth diagnostic adoption

Regulation

In the past decade, regulatory development has not kept pace with technological innovation. Regulatory authorities, such as the US Food and Drug Administration and the UK Medicines and Healthcare Products Regulatory Agency, have taken a cautious risk-based approach to the regulation of mobile medical applications. Both these institutions are watching closely while exercising their "enforcement discretion" towards medical devices that pose a minimal risk to patients and consumers. This rapidly evolving field however, requires both the development of regulatory frameworks that consider the wide array of medical apps that are emerging and regulatory harmonization amongst different regulatory authorities to avoid the development of regulations that become barriers or disincentives to innovation.

Other challenges arise from the hardware itself. If the test is designed to be used with a range of mobile phones, then their variability in both hardware and software presents challenges for assessing risk in the regulatory review process. This uncertainty is pushing companies to either develop standalone devices with defined components or ship a standardised mobile phone with the diagnostic test and carefully control the software environment all of which influences cost.

Finally, the clinical governance of mHealth based care pathways must be considered. Here a patient may not see a clinician face-to-face and clinical records may be collected remotely *via* standardised questionnaire. Electronic clinical pathways can include a range of linked practitioners including doctors, nurses, pharmacists and other healthcare workers, and the pathway must allow escalation for face-to-face care and referral when needed. All this requires appropriate quality assurance of the clinical decision trees, care pathways and remote prescribing decisions as well as the development of a secure and user friendly interface for remote use⁸⁰.

Cost and Clinical Effectiveness

The decision to employ an mHealth connected diagnostic and how best to integrate into an existing health system requires evidence of its clinical effectiveness and resulting cost effectiveness with particular scrutiny on the context in which it is to be used⁸¹ and how its implementation would function at scale. The cost and clinical effectiveness of point-of-care diagnostics⁸² and some mHealth strategies^{83,84} in infectious disease control have been assessed. However, a connected diagnostic and its associated mHealth intervention have yet to be analysed.

The challenge in this for mHealth connected diagnostics is that they are not a single intervention, but a systems approach involving a complex set of connected and mutually dependent interventions. For a full assessment of such a connected ecosystem all aspects must be considered. Health economic analyses are warranted⁸⁵ to demonstrate value from the increased connectivity made possible through the connected diagnostics (which may not be necessarily cheaper) and how these can be employed as part of broader mHealth interventions. These evaluations need to account for the benefit and potential risk to patients, healthcare professionals and systems in terms of clinical and social outcomes (e.g. time saved or speed of access). Only with this demonstrated, can larger scale studies be employed to assess the impact of the associated increased testing and data generated on national healthcare systems.

Digital Divide

While mHealth technologies have the potential to widen access to testing for many health conditions, it is important to ensure that no one is left behind. Although trends are narrowing, today 35 % of the world's population do not have access to mobile communications. This is predominantly because of lack of access in low and middle income countries¹ although those of lower socio-economic status in resource-rich settings are also affected. Moreover, whilst the developed world awaits the roll out of high-speed 5G networks, many of the least developed countries in the world rely on 2G, and many of the

remote and poor regions have no mobile phone coverage at all. To illustrate this, we have mapped network coverage and distance to healthcare facilities in Uganda, which is one of the three sub-Saharan African nations with publicly available datasets of these factors. We have collated data on healthcare facility location and cell tower location, range and generation, and correlated these to population density (Fig. 4). Here 22 % of the population do not live within 5 km of a healthcare facility (a target set by the Ugandan government⁸⁶). Of this population 45 % live in range of 3G cell towers. An additional 23 % live in range of 2G cell towers, but 32 % are outside the range of cellular networks. Moreover, being in range of a cell tower does not necessarily indicate a good signal and other unforeseen factors, such as power supply interruption, may impact connectivity. Asynchronous data transfer may overcome this problem when reporting results, but further mHealth interventions, such as linkage to care, could be severely restricted. Compounding this are the considerable variations in digital literacy related to socio-economic position and education such that disadvantaged groups who might have the greatest need of a service are the most likely to be excluded.

In this digital era, age and gender gaps are also of concern - it has been estimated that 200 million fewer women than men own a mobile phone in low- and middle-income countries and that even when they do, they are less likely to use it for services, such as mobile internet, that could improve their health⁸⁷. The Pew Research Centre has shown huge age disparities in smartphone ownership: for example 94 % of Chinese people aged between 18-35 own a smartphone compared to 30 % of people aged 50 and over⁸⁸. Trend analysis suggests that these gaps are narrowing, but more needs to be done to ensure that mHealth devices, are made available to all, considering the unmet health need in women and the elderly.

9 Conclusion and Perspective

The convergence of infectious disease diagnostics with mobile phone-based connectivity provides opportunities to deliver potentially disruptive technologies to drive development of novel health systems. These should increase access to testing, diagnosis and treatment of infectious diseases, whilst improving outbreak detection, disease surveillance and guiding a precision public health response. With these technologies the potential for public participation is considerable, either through engagement in outbreak detection through crowd sourced or “citizen science” initiatives or *via* targeted prevention messaging so that individuals and communities can access digital care pathways for an integrated clinical and public health system of detection, care and disease control.

To realise these benefits, the development of connected diagnostics must be undertaken with an understanding of the context in which they are to be used such that they feed seamlessly into their associated mHealth systems. Those introduced in a resource-rich setting may be different and need a different surrounding technical ecosystem compared to those that are to be used in a resource-limited setting. Consumer demand in resource-rich settings may drive the commercial development of these devices in the near term, however they have the potential to transform care in all economic settings if appropriately tailored to local needs. To do this, investment needs to be directed towards the development of appropriate devices

and systems in all socio-economic settings and towards addressing the ongoing digital divide.

In addition to this, if we are to harness the promise of mHealth interventions that use a connected diagnostic the intervention must be designed with a patient-centred focus which improves access and early intervention whilst reducing the burden on patient time and resources. This must be achieved whilst ensuring that overstretched health systems benefit by driving more effective and efficient care and linked public health responses.

The promise of automated or mobile-assisted self-testing with connected, efficient linkage to care is an exciting end-goal and the studies highlighted in boxes 1 to 3 demonstrate the elements of such a system. However, they are yet to be fully integrated and deployed or their effectiveness assessed at scale. For this to occur, we argue for a new approach to the regulation and governance of mHealth devices, interventions and applications, one that addresses the challenges of testing, digital access, data security and clinical governance – for without this user and institutional adoption and public confidence will be limited due to a lack of trust.

The future of diagnostics is likely to be increasingly digital and connected, accelerating changes in the way healthcare is provided. This provides researchers and policy makers with the exciting, if formidable, opportunity to transform healthcare systems in new ways to improve human health and wellbeing in future years to come⁸⁹.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Box 1**An mHealth approach to HIV self-testing**

Studies are increasingly demonstrating the feasibility of self-testing at large scale in resource-limited settings. Choko *et al.* demonstrated that HIV self-testing is safe, accurate and acceptable to over 76.5 % of the 16,600 residents contacted from 14 urban neighbourhoods in Malawi⁹⁴. However as the authors and others⁹⁵ mention, linkage to care remains an issue. mHealth can address this and Pai *et al.* have conducted a small scale study estimating the feasibility of HIV self-testing and remote follow up in South Africa⁹⁶. Here participants performed a HIV rapid diagnostic test (RDT) themselves and were then linked to counselling and treatment. Although the test was not connected, mobile phone calls, internet and text messages enabled post-test linkage to care. Results for the 251 healthcare workers at the Groote Schuur hospital in Cape Town showed a high completion rate of 99.2 % with a 100 % acceptance rate of post-test counselling and referral by mobile phone for those identified as sero-positive (9 patients). This linkage to counselling and advice for patients testing positive was substantially higher than the 56.3 % reported in Malawi however, now larger scale and longer term studies that demonstrate cost-effective integration into a healthcare system are needed⁸⁴.

Box 2**eSexual Health Clinic**

The eSexual Health Clinic⁹⁷ demonstrates the viability and acceptability of online clinical and public health interventions for infectious disease. In this UK study, the first demonstrating a fully developed online diagnosis, care and prevention programme, patients with chlamydia were diagnosed and medically managed *via* an online clinical consultation. 2340 patients were texted a link to access their results online along with, if applicable, links that lead to antibiotic collection from a pharmacy. Discreet partner notification, health promotion and automated surveillance data capture were also integrated into the system to aid prevention for an infection which is asymptomatic, sexually transmitted and potentially stigmatised. While this study relied on a self-swab or urine sample which was posted to a central laboratory for testing or attendance at a genitourinary medicine clinic, there is a clear potential for this to be replaced by a connected diagnostic test which automatically links results. This would act to improve ease of use, time to results and further facilitate the remote testing and the acquisition of treatment, advice and follow up outside of conventional healthcare systems.

Box 3**Mobile phone-based rapid diagnostic test readers**

Dell *et al.* have developed GSID98 an open sourced mobile-phone based system for the capture, transmission and on device analysis of images of RDTs. Comprised of a reader, an app and a central, web-accessible database, it has been applied to the rapid diagnosis of malaria, in five hospitals and clinics in Zimbabwe⁹⁹. User feedback was positive, with the healthcare workers even suggesting extending the range of data that could be inputted into the app to reduce the burden of reporting case notes. A revealing analysis of the frequency and delay in test data transmission, highlighted that on-device analysis and asynchronous data transfer is needed in areas with poor infrastructure.

Going beyond the capture and transmission of results the performance of RDT readers is such that they can be used to support and even improve the training of healthcare workers as shown recently by Laktabai *et al.* for the diagnosis of malaria in Kenya¹⁰⁰.

Furthermore, Brangel *et al.* have recently developed a smartphone app and RDTs to detect patients' antibodies to different ebola subtypes in serum. The app analysed and geotagged captured images of the RDT's test line(s) and could generate a map of test results indicating the survivors' serological state. This prototype has been evaluated in laboratory settings only but has the potential to aid in: survivor identification in clinics, the epidemiological study of neglected tropical disease, and may enable the faster and cheaper evaluation of vaccine effectiveness under outbreak conditions especially in remote areas.

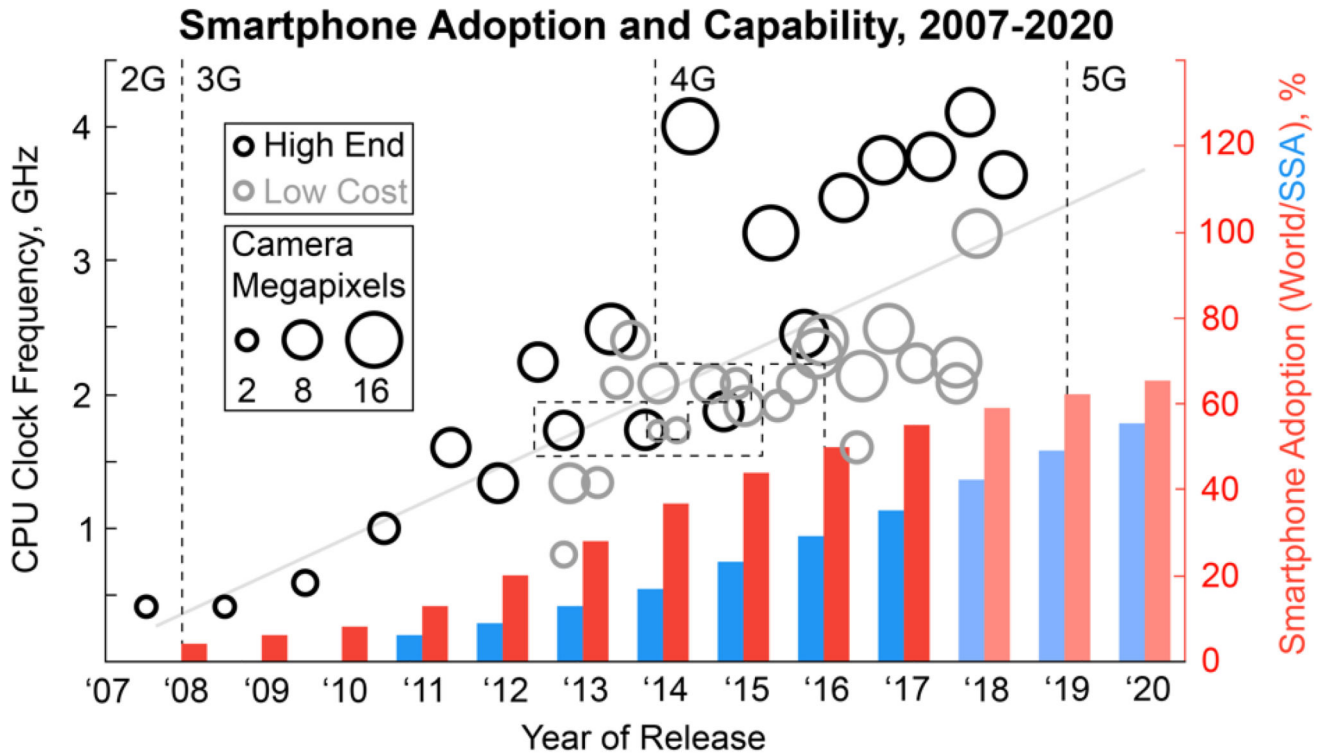


Figure 1.

The growing power of low cost smartphones. Smartphone adoption (the percentage of global (red) or sub-Saharan Africa (blue) mobile phone connections that come from a smartphone), processor speed (CPU clock frequency) and camera resolution (primary camera megapixels) of the flagship models of popular smartphone manufacturers. The stated processor speed takes into account multiple processor cores at a parallelisation of 50 %. “High End” models retail for between approximately €610-1000 whereas “Low Cost” models retail for between €60-16090.

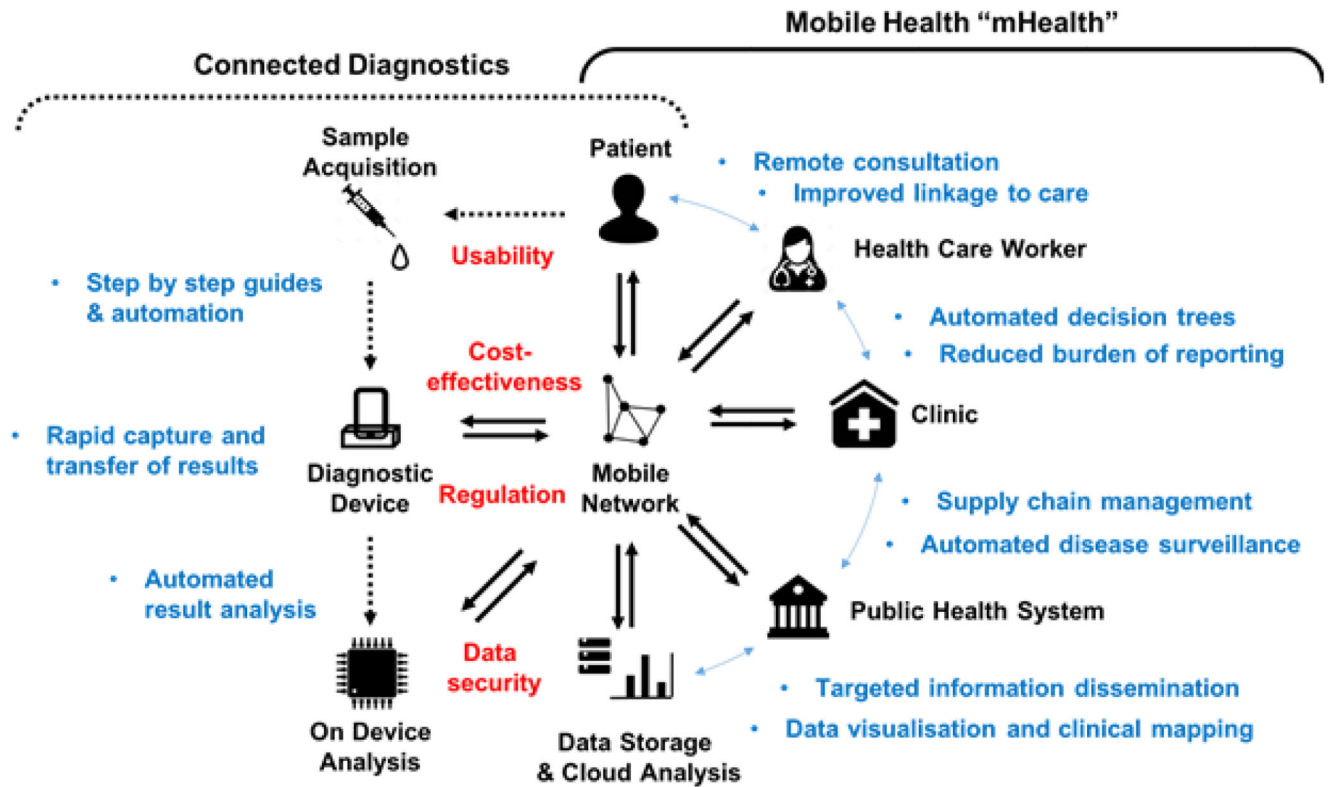


Figure 2. Deploying an mHealth connected diagnostic. The stages, stakeholders, example outcomes (blue) and challenges (red) to deploying an effective mHealth intervention that employs a connected diagnostic device.

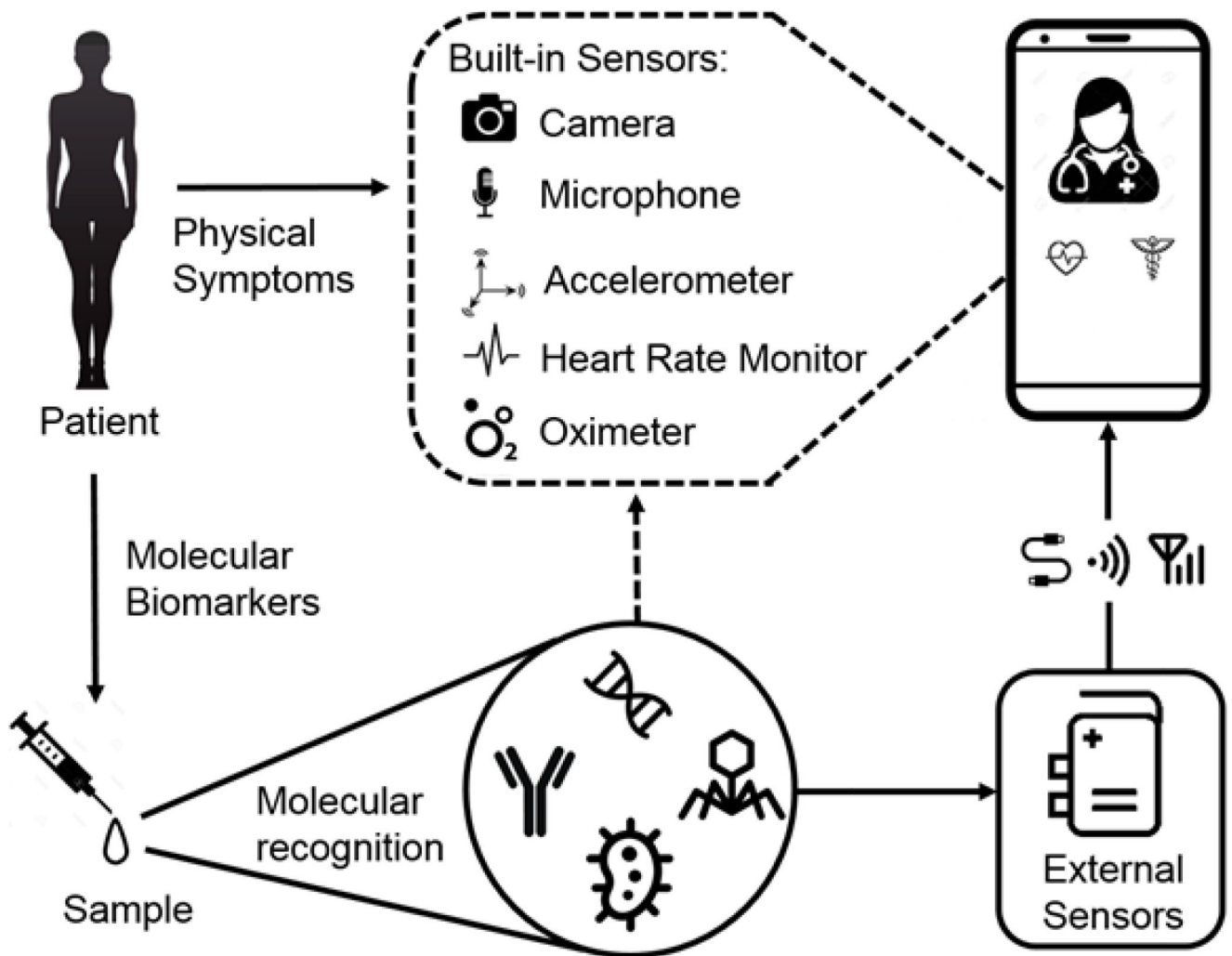


Figure 3. Diagnosis by device. How a connected diagnostic test can be used to detect disease markers - from the physical to the molecular - *via* sensors either built into or external to the phone.

Access to Health Facilities and Mobile Networks in Uganda

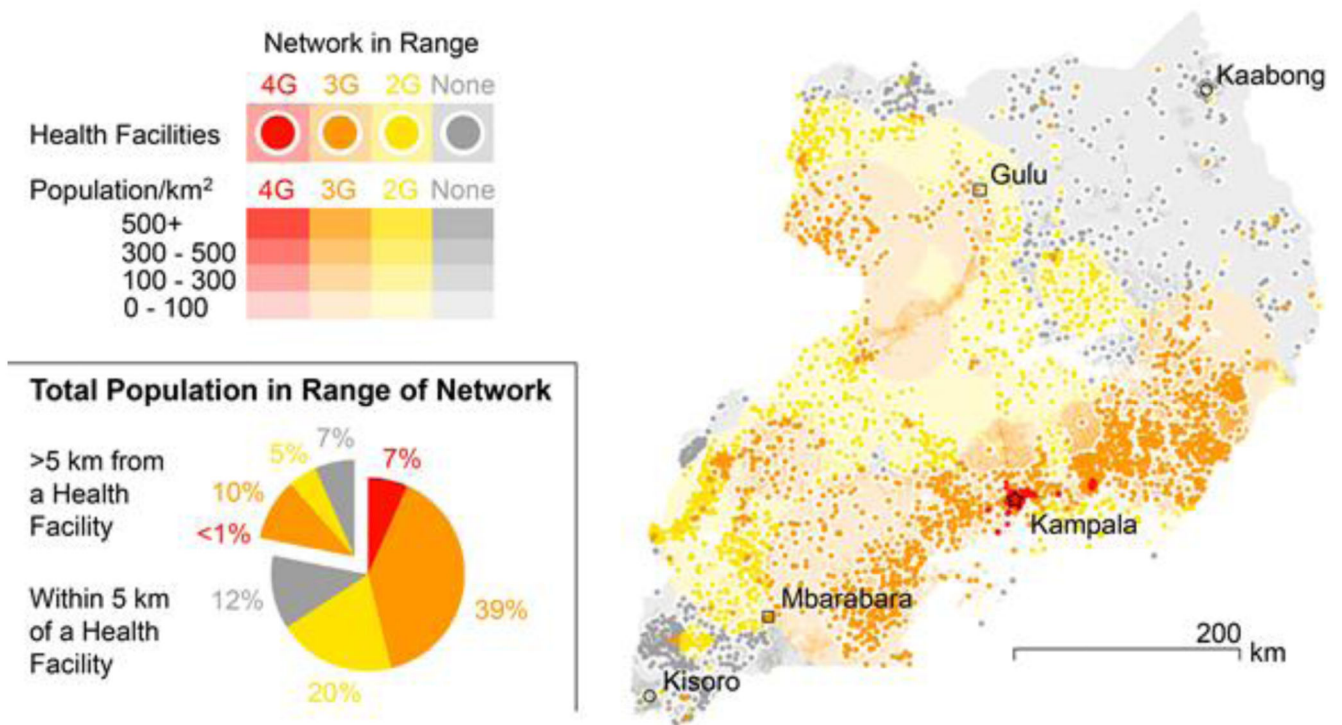


Figure 4. The digital and healthcare divide in Uganda. Map of healthcare facilities (2012)⁹¹ and the population density (2015)⁹² >5 km from healthcare facilities. Areas and healthcare facilities are coloured according to the generation of cellular network in range, where the range is calculated from cell tower location and the distance of the furthest measured signal⁹³. The white circles around the health facilities indicate the 5 km radius threshold⁹⁰.

Table 1
Examples of mHealth enhancement of infectious disease diagnosis, treatment and control.

Area	Function	mHealth Opportunities
Outbreak Identification	Novel outbreak monitoring	Electronic collection of epidemiological and clinical data
Diagnosis	Community or self-testing	Early detection, automated result capture and analysis
	Disease characterisation	Portable genetic sequencing of samples (e.g. to identify emerging drug resistance)
	Syndromic surveillance	Multi source data capture and passive reporting (e.g. activity levels and location history)
Treatment and Patient Management	Linkage to clinical care	Mobile connection to clinical care (decision trees, electronic prescribing)
	More efficient and effective use of stakeholder time	Automated report generation and supply chain management, reduce transcription errors in reporting
	Chronic infection monitoring and response to therapy	Long term biomarker reporting and analysis to guide community-based medication and care
Disease Control and Elimination	Cluster 'hot spot' identification Outbreak response Epidemic control	Rapid geospatial and phylogenetic mapping Real time reporting to public health agencies to implement control strategies via connected clinical and public health systems Social media queries capture and mapping during outbreaks Electronic implementation of control measures Data visualisation for epidemiological and clinical mapping, contact management and monitoring the effectiveness of interventions Targeted information dissemination