REVIEW

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

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Mobile health, or 'mHealth', is the application of mobile devices, their components and related technologies to healthcare. It is already improving patients' access to treatment and advice. Now, in combination with internet-connected diagnostic devices, it offers novel ways to diagnose, track and control infectious diseases and to improve the efficiency of the health system. Here we examine the promise of these technologies and discuss the challenges in realizing their potential to increase patients' access to testing, aid in their treatment and improve the capability of public health authorities to monitor outbreaks, implement response strategies and assess the impact of interventions across the world.

Rapid advances in portable communications technologies and digital computing have improved the speed 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 data[3]. 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 barrier[4] while offering sensing and processing capabilities similar to those of more costly 'high-end' devices (Fig. 1).

The ways in which we detect and respond to disease are also continually improving. Step changes in the development of sensitive and specific immunological and molecular-based diagnostics as well as genetic sequencing have enabled 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 realization of simple, yet highly sensitive and specific devices that can be used outside the laboratory. These areas of use are often described as at or near the 'point of care', which may be the patient's own home, a primary care setting or at the patient's bedside in a hospital. In pursuit of this, nucleic acid tests have been developed that require less than five minutes of hands-on time[8] and deep sequencing is now possible on a small hand-held device[9]. These advances, combined with changing consumer attitudes towards self-testing, and an increased appetite for wearable biosensors, are enticing healthcare providers to shift towards the paradigm of 'P4' medicine: 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 devices[11]) 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 in areas such as disease surveillance, health systems and health education[12,13]. The combination of these interventions (see below) with connected diagnostics will impact all areas of healthcare, including those related to infectious diseases.

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 care settings (for example, by improved self-testing) and (ii) the real-time or nearly 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. So far, most mHealth interventions (see Box 1) have focused on the use of established mobile technologies (such as text messages and calls) to connect healthcare workers and

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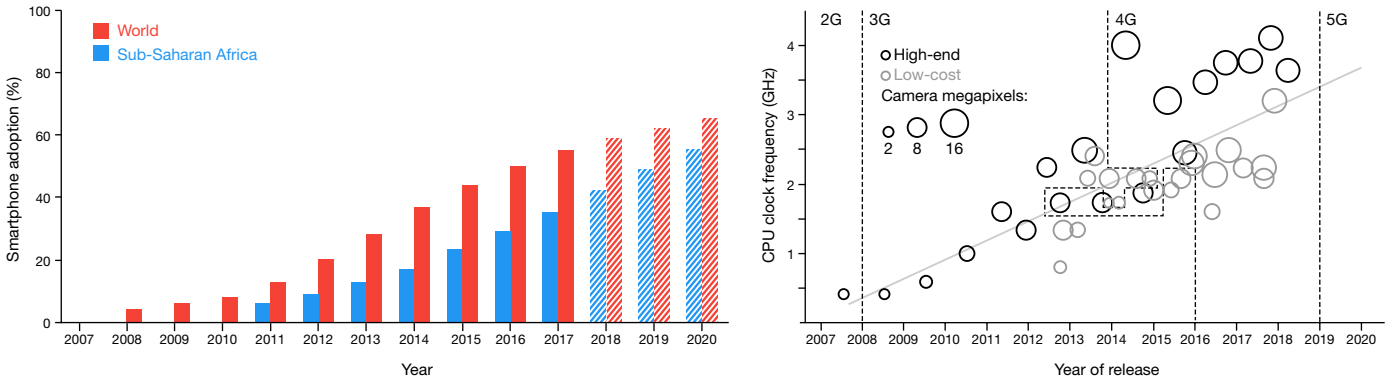

Fig. 1 | The growing power of low-cost smartphones. Smartphone adoption (the percentage of global (red) or sub-Saharan Africa (blue) mobile phone connections that come from a smartphone), processor speed (CPU clock frequency) and camera resolution (primary camera megapixels) of the flagship models of popular smartphone manufacturers. The stated processor speed takes into account multiple processor cores at a parallelization of 50%. 'High-end' models retail for €610–€1,000, whereas 'low-cost' models retail for €60–€160. In order to plot this figure we obtained smartphone adoption data from https://www.gsma.com/mobileeconomy and all smartphone specifications from http://gsmarena.com/. For details on how we generated the graph see Supplementary Information section A. Raw and intermediate data can be found in Supplementary Tables 1 and 2 and at http://doi.org/10.5281/zenodo.1320937.

patients to each other and to test results[14]. 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 guide antimicrobial therapy[15]. Connected diagnostics that can simultaneously detect a pathogen and identify antimicrobial sensitivity and resistance can enable the selection of appropriate therapies while 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 formal health facilities and linking the output of testing into pathways of clinical and preventative care that can 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 (see Box 2) are beginning to be used to stratify individual patients into remote-treatment and response-monitoring programmes.

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 systems[16]. Additionally, phone-based decision trees can assist less-well-trained users in decision making and can be helpful in diagnosis, monitoring or for data-gathering more generally[17]. Furthermore, in disease surveillance, there is an urgent requirement to detect and intervene more rapidly in emerging epidemics (for example, Ebola or Zika), as well as for increased sentinel surveillance for existing ones[18]. The use of connected diagnostics and symptom-reporting apps, combined with standardized electronic collection of epidemiological and clinical data, has great potential to enhance the efficiency and speed of management of both epidemic and endemic infections, including the management of contacts where appropriate[19]. The real-time reporting of diagnostic test results can enable this surveillance through the geospatial mapping of infections via geotagged test results[20] 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 in South Africa,

Table 1 | mHealth opportunities in 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 characterization	Portable genetic sequencing of samples (for example, to identify emerging drug resistance)
	Syndromic surveillance	Multi-source data capture and passive reporting (for example, 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, fewer 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	Rapid geospatial and phylogenetic mapping
	Outbreak response	Real-time reporting to public health agencies to implement control strategies via connected clinical and public health systems
	Epidemic control	Social media queries capture and mapping during outbreaks
		Electronic implementation of control measures
		Data visualization for epidemiological and clinical mapping, contact management and monitoring the effectiveness of interventions
		Targeted information dissemination

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.[94] 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 Malawi. However, as they[94] and others[95] mention, linkage to care remains an issue. mHealth can address this. Pai et al.[96] have conducted a small-scale study estimating the feasibility of HIV self-testing and remote follow-up in South Africa, in which participants performed an HIV 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, larger-scale and longer-term studies that demonstrate cost-effective integration into a healthcare system are needed[84].

Box 2

eSexual Health Clinic

The eSexual Health Clinic[97] 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. 2,340 patients were texted a link to access their results online along with, if applicable, links that led 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 this infection, which is asymptomatic, sexually transmitted and potentially stigmatized. Although 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 clearly potential for this to be replaced by a connected diagnostic test that automatically links to results. This would act to improve ease of use, time to results and to facilitate remote testing and acquisition of treatment, advice and follow-up outside of conventional healthcare systems.

HIV prevalence in the population reaches over 30% overall, and is higher in women[23]. This is despite a public health approach to HIV testing and anti-retroviral treatment for all. Reasons for the continuing high rate of new infections are manifold. 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 (via interactive apps), care roadmaps (whether community-based or in the clinic) and connected diagnostic monitoring (HIV testing and viral load monitoring). Some examples of this are emerging. The HIVSmart! app[25] has been developed from the internet-based form described in Box 1 to work with HIV rapid diagnostic tests (RDTs) to support patient linkage to care and retention in care worldwide. Now further work is needed to fully develop these and other such interventions and to overcome the challenges of integrating connected diagnostics with them.

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 such an intervention, 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 the data 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 and patient confidence and by well-regulated clinical pathways.

Target identification and sample acquisition

The identification of relevant diagnostic targets for infectious diseases and development of 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 field[26]. Targets should be selected both by their capacity for disease identification and their suitability for use at the point of care. This requires careful consideration of what the true requirements and limitations are in each setting. What is needed for self-testing at home often differs from what is needed within a clinical setting. 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 specialized 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 users)[27]. Some assay systems based on plasma will require a blood centrifugation step before testing and swabs or urine samples require pre-processing. Ensuring the simplicity of sample processing in the test is key. The development of paper-based centrifugation systems is promising in this respect[28] and controlling the tests via a mobile phone has the potential to help further by reducing the training needed to perform and interpret the test. This can be achieved by displaying step-by-step guides or via automated steps previously performed by the user.

Connected point-of-care diagnostic technologies

The World Health Organization's ASSURED[29] 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 developed[31] 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 capitalize on 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 democratize access to otherwise costly laboratory equipment and to reduce the training needed to interpret test results, for example, via automated RDT measurements (Box 3). This approach capitalizes on mobile phone imaging[38] or video capture[39] to enable the quantitative[40] assessment of results with the potential for geotagging[41] and rapid transmission of results to healthcare systems[42]. Similarly,

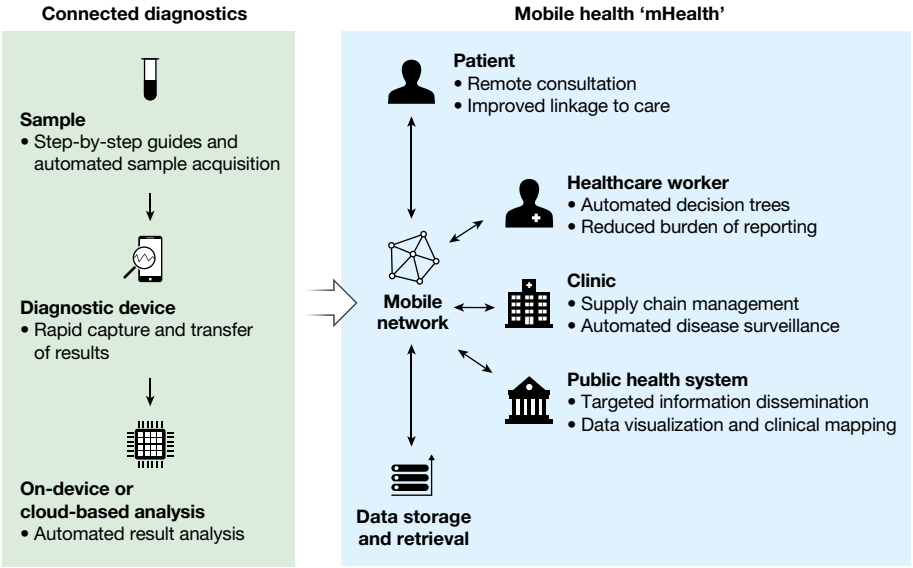

Fig. 2 | Deploying an mHealth connected diagnostic. The stages, stakeholders and possible outcomes of deploying an effective mHealth intervention that uses a connected diagnostic device.

mobile-phone-based microscopy[43] is now gaining traction in the detection of microscopic parasitic infections[44], and is rapidly approaching the standard of laboratory-based microscopes with a substantially reduced upfront cost. Mobile-phone-based microscopy is even yielding portable, handheld routes towards fluorescent imaging of viruses[45] and DNA molecules[46].

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 such as Parkinson's[47], and the microphone, which can be used to monitor lung function[48]. Ecological mapping of mosquitoes is possible using the microphone[49], highlighting the broader potential of smartphones to aid disease prevention. Mobile phones and smart watches are now actively embracing mHealth, with purpose-driven sensors such as heart-rate sensors being built into the back of the device[50]. 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, three-dimensional 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 could 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 sensing[53].

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, such devices are increasingly being deployed at or near to the point of care and have recently been deployed in response to the recent Ebola[54] epidemics.

For more portable systems, other sensors can also be used. Biosensors that incorporate electrochemical transduction[55] are eminently suited to digital interpretation and connection and many connected electrochemical biosensors have been developed[56]. Such sensors can offer less invasive sample acquisition methods, with some incorporated into wearable sensors held near the skin[57,58] or used to analyse volatile organic compounds in a patient's breath[59]. Other signal transduction methods including micro-cantilevers and surface acoustic wave detection[60] offer the potential of ultra-rapid testing within ten seconds[61].

The advent of nanopore-based sequencing[62] has allowed devices that can sequence DNA to be miniaturized to the size of a USB stick, offering the possibility of full genomic disease profiling in a handheld device[9]. 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 infancy[63]. This problem is common to all connected diagnostics, but it is especially acute for the large amounts of genomic data generated by sequencing devices.

Data analysis on-phone and on-cloud

Automated result analysis has the 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.

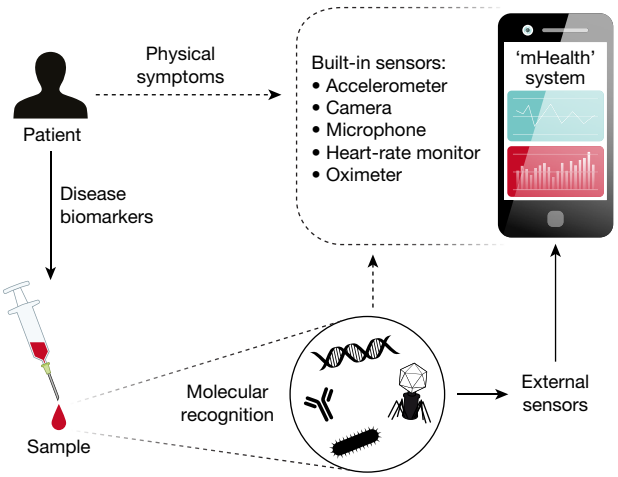

Fig. 3 | Diagnosis by device. A connected diagnostic test can be used to detect disease markers—from the physical to the molecular—via sensors either built into or external to the phone.

Box 3

Mobile-phone-based rapid diagnostic test readers

Dell et al.[98] have developed GSID[99], an open-source mobile-phone-based system for the capture, transmission and on-device analysis of images of RDTs. Comprising a reader, an app and a central, web-accessible database, GSID has been applied to the rapid diagnosis of malaria in five hospitals and clinics in Zimbabwe. User feedback was positive, with the healthcare workers even suggesting extending the range of data that could be input into the app to reduce the burden of reporting case notes. An analysis of the frequency and delay in test data transmission revealed 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.[100] for the diagnosis of malaria in Kenya. Furthermore, Brangel et al.[41] 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 help with survivor identification in clinics and the epidemiological study of neglected tropical disease, and it may enable faster and cheaper evaluation of vaccine effectiveness under outbreak conditions, especially in remote areas.

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. Where connectivity is low, on-phone feature extraction that reduces the size of the images before their transmission and cloud-based interpretation can mitigate this problem[64]. Cloud-based systems enable connectivity to databases and allow algorithms to be updated centrally. They also remove the processing burden from mobile devices, increasing the range of compatible devices. Systems have been developed that enable hands-free automated analysis of HIV RDTs using Google Glass, which can send image data to a remote server[65]. In that case, 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 amplification[66] and in cell[67] and parasite[68] counting. This can reduce the amount of data that needs to be transmitted and can aid its asynchronous transmission where the results are stored on-phone and uploaded once in range of mobile networks. On-phone storage, however, 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 classification[69] and may improve automated inference when using defective equipment, or in poor lighting conditions[70].

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 records[73]. Data sharing has been associated with contextual[74] and ethical[75] challenges including a lack of standardized data security to ensure privacy. Ways to improve health data sharing and connectivity and to develop a consensus on data governance are needed[76]. Broad regulations such as the EU's General Data Protection Regulation (GDPR) are beginning to address this, but more tailored approaches such as the voluntary code of conduct on privacy for mHealth apps[77] are needed. Moreover, recent ethics studies[78] 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, to standardize and coordinate data collection, and to improve mHealth device connectivity are currently under development[73]. However, these platforms, such as the Fast Healthcare Interoperability Resources (FHIR)[79], will still require stakeholder collaboration and substantial standardization of the interfaces between the hardware and software components in an mHealth system if they are to be put in place.

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 the approval of medical devices (such as smart watches that include heart-rate monitors) 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 among 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 standardized mobile phone with the diagnostic test while carefully controlling the software environment—a limitation as both approaches increase 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 standardized 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 to face-to-face care and referral when needed. To ensure this happens when necessary, appropriate quality assurance of the clinical decision trees, care pathways and remote prescribing decisions is required, as well as the development of a secure and user-friendly interface for remote use[80].

Cost and clinical effectiveness

The decision to use an mHealth-connected diagnostic and how best to integrate it 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 used[81] and how its implementation would function at scale. The cost and clinical effectiveness of point-of-care diagnostics[82] 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 difficulty of such an analysis lies in the complexity of the system: an intervention and its connected diagnostic may involve a

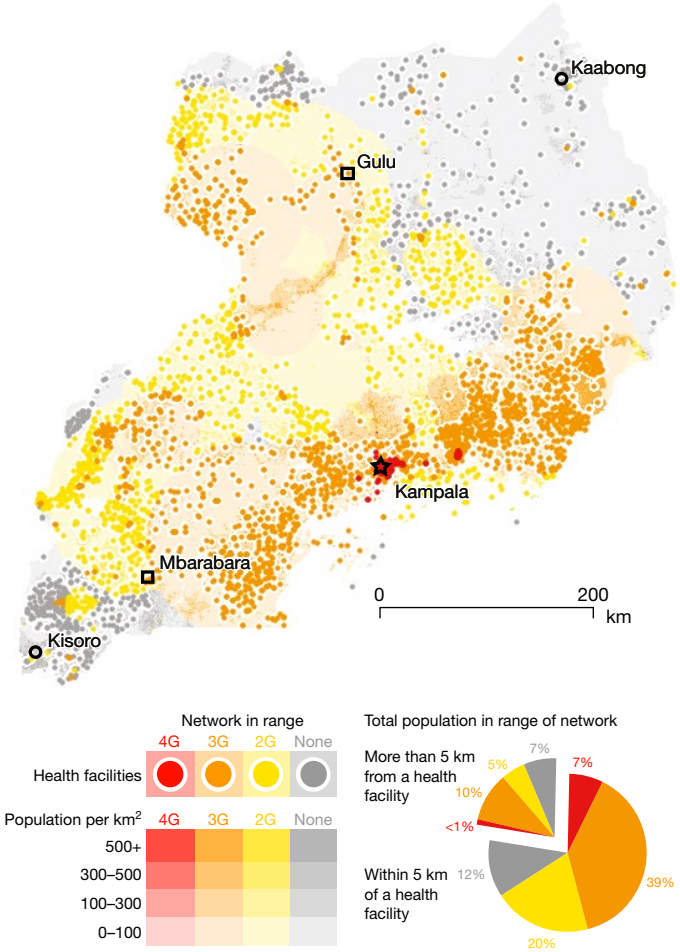

Fig. 4 | The digital and healthcare divide in Uganda. Map of healthcare facilities (in 2012)[90] and the population density (in 2015)[91] living more than 5 km from healthcare facilities. Areas and healthcare facilities are coloured according to the generation (2G to 4G) of the cellular network in range, where the range is calculated from cell tower location and the distance of the furthest measured signal[92] within the Uganda national boundary[93]. The white circles around the health facilities indicate the 5-km-radius threshold. This figure is a remapping of publicly available data using the open source geographical information system application QGIS (https://www.qgis.org). We chose Uganda as an example country owing to the availability of the required data. We downloaded healthcare facility locations and ranges from http://maps.data.ug/layers/geonode%3Ahealth_centres_ubos_and_others_merged, cell tower location from https://opencellid.org/ (OpenCelliD Project is licensed under a Creative Commons Attribution-ShareAlike 4.0 International License), and population data from http://www.worldpop.org.uk/data/summary/?doi=10.5258/SOTON/WP00283 (WorldPop datasets are available under the Creative Commons Attribution 4.0 International License). For details on how we generated this graph see Supplementary Information section B. Raw and intermediate data can be found in Supplementary Table 3 and at http://doi.org/10.5281/zenodo.1320937.

set of mutually dependent interactions. For a full assessment of such a connected ecosystem many aspects must be considered. Health economic analyses are warranted[85] to demonstrate value from the increased connectivity made possible through the connected diagnostics (which may not necessarily be cheaper) and how these can be used 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 (for example, time saved or speed of access). Only once all of this has been demonstrated can larger-scale studies assess the impact of the associated increased testing and data generated on national healthcare systems.

Digital divide

mHealth technologies have the potential to widen access to testing for many health conditions, and 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 countries[1], although those of lower socio-economic status in resource-rich settings are also affected. Moreover, while 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 for 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 government[86]). Of this remote 22%, 45% live in range of 3G cell towers, 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 factors, such as power supply interruption, may affect 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, which mean that disadvantaged groups in the greatest need of a service are the most likely to be excluded from obtaining it.

In this digital era, age and gender gaps are 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 health[87]. The Pew Research Centre has shown huge age disparities in smartphone ownership: for example 94% of Chinese people aged between 18 and 35 own a smartphone, compared to 30% of people aged 50 and over[88]. Trend analysis suggests that these gaps are narrowing, but more needs to be done to ensure that mHealth devices are made available to all, especially considering the unmet health needs in women and the elderly.

Conclusion and perspectives

The convergence of infectious disease diagnostics with mobile-phone-based connectivity provides opportunities to deliver potentially disruptive technologies to drive the development of health systems. These should increase access to testing, diagnosis and treatment of infectious diseases, while 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 realize these benefits, the development of connected diagnostics must be undertaken with an understanding of the context in which they are to be used so 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 from those 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, but 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 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 that improves access and early intervention while reducing the burden on patient time and resources. This must be achieved while ensuring that overstretched health systems benefit, by driving more effective and efficient care and linked public health responses.

Automated or mobile-assisted self-testing with connected, efficient linkage to care is an exciting goal and the studies highlighted in Boxes 1 to 3 describe the elements of such systems. However, they have not yet been fully integrated and deployed, nor has their effectiveness been assessed at scale. For this to occur, the regulation and governance of mHealth devices, interventions and applications must address the challenges of testing, digital access, data security and clinical governance. Without this, user and institutional adoption and public confidence will be limited by a lack of trust.

The future of diagnostics is likely to be increasingly digital and connected, accelerating changes in the way healthcare is provided. Researchers and policy makers now have an exciting and challenging opportunity to use them to transform and improve healthcare systems[89].

Data availability

All data and methods relevant to the development of Figs. 1 and 4 can be found in the Supplementary Information and at https://doi.org/10.5281/zenodo.1320937.

Online content

Any methods, additional references, Nature Research reporting summaries, source data, statements of data availability and associated accession codes are available at https://doi.org/10.1038/s41586-019-0956-2.

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Additional information

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