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Infectious Disease Diagnostic Technologies for People Living in Extreme Poverty: An Unmet Need

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Abstract: Diagnostics is believed to drive about 70% of medical interventions, but this may not be true for all demographics. With more than 30% of the African population living in extreme poverty ($1.9 per day - 2022); and healthcare costs competing unfavorably against unbridled access to antibiotics and herbal concoctions, especially in Sub-Saharan Africa, how do you convince such a people to choose diagnostics first? More importantly, how do you design a medical device targeted at meeting the diagnostic needs of this demographic? In developing diagnostic devices for such a market, what is worth sacrificing? How dire is the need for advanced technologies in devices developed for such a demographic? These are questions that remain unaddressed by the technological breakthroughs and current research in medical device development, especially for infectious disease diagnostics. The objective of this paper is to underscore critical concerns which must be considered in the bid to successfully design medical diagnostic devices for Africa and perhaps, other limited-resource settings. It is also written as a suggestive guidance document for researchers whose interest is in the development of infectious disease diagnostic platforms for rural Africa and similar limited-resource environments.

Keywords: Diagnostics; Lower and Middle-Income Countries; Extreme Poverty; Limited-resource settings; infectious diseases; Africa; Sub-Saharan Africa; Nigeria; Antimicrobial; poverty; paper devices; mobile phone; smartphones; microfluidics; multiplexing; inexpensive diagnostics; medical devices; repairability

1. Overview

Considering the economic dispensation of Africa, for business purposes, African countries, much like other low and middle-income countries (LMICs) are classified under emerging markets. However, given that a greater percentage of the annual leading causes of death mostly affect the region, one could argue that there is a high demand for interventions, as such it should be a "developed market". Unfortunately, primarily due to economics, there is little or no hope for the transition from an "emerging" to a "developed" market. For this reason, the region, although in dire need, has fewer advanced technologies targeted at their exact needs.

To paint a clearer picture, 50% of the leading causes of death in LMIC are attributed to infectious diseases (Lower respiratory infections, HIV/AIDS, diarrheal diseases, tuberculosis, and malaria) [1,2], and in 2002 alone, 48% of global deaths due to infectious diseases occurred in Africa [3]. Worse still, the World Health Organbi9zation's (WHO) 2019 mortality estimates showed that about 26% of deaths due to infectious and parasitic diseases occurred in neonates and children 0 – 59 months of age [4]. On account of the disease burden in the LMIC, the WHO summarized that people living in these regions are more likely to die of communicable diseases [1] than any other form of ailment.

2. Poverty-driven Adverse Practices

It is a well-known fact that early and accurate diagnosis could improve the situation in these regions, however, research by Arikpo *et al* [5] and Chipwaza *et al* [6] showed that there is a poverty-

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induced preference for self-medication by the perception of symptoms, the internet, or referrals to diagnostics-informed interventions. Compounding the challenges attendant to self-medication, more than 60% of prescriptions used in Africa are adulterated or counterfeited due to poor antimicrobial stewardship and governance [7]. There is also evidence of dependence on herbal concoctions, notable of which is the national acclaim of herbal treatment for COVID-19 by President Andry Rajoelina of Madagascar in 2020 [8]. These poverty-driven practices that force the adoption of unproven healthcare interventions are often found in regions where drug pricing in clinics and standard pharmaceutical stores force people to depend on the abundance of low-cost "generics" in the open market. Projections of the impact of unchecked antimicrobial resistance on Africa underscore the importance of interventions that transcend current research and development trends from medical device manufacturers and academic researchers. To discourage self-medication and unprofessional healthcare interventions, researchers must therefore drive towards the design and development of diagnostic technologies and platforms whose consumables are inexpensive, rather than at-home kits, especially for non-stigmatized diseases. While there are little or no economic incentives for researchers to develop advanced diagnostic technologies targeted at rural Africa, it would be among mankind's greatest achievements. If it works in Africa, it would work anywhere in the world.

3. A Few Concerning Approaches adopted In Research Toward Making Inexpensive Diagnostic Devices for Africa

Martinez *et. Al* [9], in 2008 opined that to meet the cost expectation of developing robust diagnostic systems for off-site or rural environments, it may be necessary to compromise sensitivity and specificity standards. Perhaps, a similar perception holds for technologies targeting LMIC such that irrespective of the known sensitivity drawbacks linked to the use of rapid diagnostic test kits (RDTs) [10], most developments targeted at LMICs exploit such concepts. Other concerns include the ideologies behind the application of paper microfluidics as a diagnostic tool in such places as rural Africa [9,11–13]. Citing my field experiences in Nigeria as an example, more standardized benchtop clinical analyzers often break down due to humidity, and short-circuiting and leakage of tubings due to rodent activities, now imagine the fate of paper-based devices against fauna and environmental challenges. Many other attempts at creating inexpensive solutions also cite the benefits of using smartphones as an integral tool for data analysis in remote settings [14–16], while laudable, little concern is expressed about the possibility of theft due to the multi-functionality of the device, power challenges, the perception of exposing the phones to potentially infectious samples, the cost of smartphones, mobile connectivity, etc.

4. Considerations that Must be made in designing Next-Gen Devices for Rural Africa

4.a. Disease Burden and Multiplexing

Given the poor living standards in many rural African communities, people are continuously exposed to myriad infectious agents. Citing Nigeria as an example, more than 90% of the over 200 Million population of Nigeria do not have access to pipe-borne water [17,18]. For these, they must subsist on private or commercial water abstraction systems like wells and boreholes and in some places, streams. There is also a lack of planning, especially in urban slums and rural areas, as such, no regulations are guiding the placement of the sewage disposal system relative to private water abstraction installations. Studies done by Tenebe *et al.* showed that 51 (more than 81%) of the commercial sachet potable waters sampled from the Ado-odo community in Ota, Ogun State, Nigeria were faecally contaminated to alarming levels [19]. Similar tests conducted on river samples from Kaduna State [20] showed the same concerns. To throw more light on exposure to water-borne diseases, a video on Youtube [21] showed the interaction children have with raw sewage and municipal waste-polluted water in Makoko slum, Lagos State, Nigeria. Such contaminations cited above could be a source of diarrheal diseases and infections by highly virulent pathogens such as *Clostridium difficile*, Hepatitis A virus, and other enteric pathogens. The question, therefore is, when who live in such environments present symptoms of diarrheal diseases, and perhaps debilitating

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circumstances which may enable the proliferation of opportunistic pathogens, how do you balance the cost of their care (including diagnostics) and the standard of care? Would you prescribe broadspectrum antibiotics or would you run a barrage of tests to ensure antimicrobial stewardship? The same goes for patients who present with one of the primary symptoms of malaria, fever. Assuming they are willing to part with their meager $1.9/day, what approach would you take to diagnostics?

The examples of water-borne infections showcased above exemplify only a fraction of the day-to-day exposures in most rural African communities which contribute to the death tolls from infectious diseases. While there may not be a simplistic answer to the questions posed earlier, the need to redefine the parameters that must be considered in designing infectious disease diagnostic platforms for rural Africa cannot be overemphasized. For example, multiplexing should be a critical component of devices designed for rural Africa to address the possibility of co-infections and co-morbidities implicated in patients from such regions as Makoko, Lagos State, Nigeria.

4.b. Re-evaluating the REASSURED Criteria

In 2019, Land *et al*. proposed the REASSURED (real-time connectivity, ease of specimen collection, affordable, sensitive, specific, user-friendly, rapid, equipment-free, delivered) criteria, a modification of the WHO Special Program for Research and Training in Tropical Diseases (WHO/TDR) guideline for clinical management of tropical diseases and sexually transmitted infections [10]. While the REASSURED criteria address most of the desired parameters in a diagnostic platform, it does not envelope the requirements for devices designed to meet the needs of a demographic constantly exposed to myriad infectious agents, for example, multiplexing. Studies have also shown poor adoption of the criteria in diagnostic technologies used in Sub-Saharan Africa [22].

The REASSURED criteria assume that such a demographic is ready for at-home tests, on account of the inclusion of "ease of sample collection" and does not consider the negation of "affordability" by the addition of "real-time connectivity" technologies. Perhaps, there is need for a new and more refined guidance criteria for technologies designed specifically for rural Africa and similar resource-poor settings.

In consideration of the cost (direct and indirect) of current diagnostic platforms, equipment-free, rapid, sample-in-answer-out platforms have been of utmost interest. Agreeably, rapid diagnostics are needed to ensure patients are provided appropriate treatment regime within their first visit. Some approaches, however, have been directed toward creating cost-effective equipment-free devices (EFD) that empower at-home personalized diagnostics. A major concern with EFDs for this demographic as discussed earlier, there is a preponderance of self-medication and polypharmacy. In these environments, the choice of medication is easily incited by verbal recommendations from individuals who have had similar symptoms. Although the development of equipment-free devices stands as a very crucial advancement in diagnostics, especially for stigmatized diseases such as HIV/AIDS; it stirs up questions about sustainability concerning control and limits in developing countries. Clinic-based monitoring has been emphasized as a critical consideration for point-of-care diagnostic technologies for Africa [23].

4.c. Quantification

In addition to the aforementioned considerations, a very important parameter has eloped researchers – the need for pathogen quantification. Population density per settlement, chronic groundwater pollution from decentralized sewage disposal systems, food handling culture, inadequate water treatment facilities, exposure to disease vectors, etc. are a few conditions that predispose LMIC to endemic diseases. Mere detection and identification of a pathogen in these environments do not necessarily justify treatment steps. For example, in Nigeria, malaria and typhoid parasites are known to be endemic, therefore, the availability of the pathogen-specific analytes above threshold titers constitute signal for treatment. This justifies the need for diagnostics in LMIC to include the means of quantifying biomarkers especially while diagnosing endemic diseases.

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4.d. Ease of Repair

More than 95% of medical equipment in Africa are sourced from developed countries primarily via donations. A downside of sourcing devices for Africa from developed countries is the logistical nightmare facing the procurement of spare parts, repair of broken parts, or availability/ accessibility of suitably trained biomedical engineers to repair them [24]. These challenges have greatly impacted the life span of devices designed for developed countries but donated or purchased for use in Africa. Studies have shown that only about 10 – 30% of devices donated to Sub-Saharan Africa become operational [25]. It is therefore crucial that devices built for rural Africa and other similar demographics be robust, and have locally-sourced parts such that biomedical engineers local to the area can repair or service them effectively.

4.e. Sustainability of Technologies via Creative Common Licensing

Most advancements made in the world of computation and information technology were possible through open-source developmental platforms. To advance the development of cost-effective multiplex diagnostic assays, there is a need to empower researchers in LMIC via creative common licenses. This way assay developers and engineers from around the globe can develop adaptable assay cartridges and data interpretation algorithms certified by relevant regulatory bodies such as the FDA and its equivalents in the LMICs. With an open-source platform, source files and design schematics used in the development of modular parts will be made available via online repositories thereby enabling a contributive approach to the creation of the robustsystems.

5. Conclusion

Poverty, literacy gaps, environmental conditions, access, and other sociopolitical factors may justify barebone diagnostic technologies available commercially in rural Africa today. However, the potential impact of AMR and the re-emerging economic effects of the disease burden in Africa and other low and middle-income polities, justify the need for more. The question remains, how do you design infectious disease diagnostic platforms for such a demographic? In an attempt to suggest parameters to be considered while developing diagnostic technologies for LMIC, we suggested multiplexing, quantification, repairability and creative common licensing. However, these suggestions are not exhaustive, thus, more contributions are needed from researchers in the LMIC regions because regardless of the form of the diagnostic technology adopted, a lot is misunderstood or unknown about the challenges of people living on less than $1.9/ day.

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