Harnessing innovative HIV point of care testing for health systems strengthening: early lessons from Zimbabwe

Abstract

Questions linking social needs with new technologies have continued to be raised but only very recently have they begun to occupy more of the centre-stage in innovation policy debates. In this narrative review, we draw from innovation and health systems literature and thinking to trace and analyse the deployment and uptake of innovative point of care testing in the early infant diagnosis of HIV in Zimbabwe, one of 15 UNITAID supported early adopter countries. Following a literature review and discussions with policy-makers in Zimbabwe, we distil key lessons from this implementation context and delineate the implications of our findings for the debates on new technological and socio-economic approaches and the health systems strengthening agenda in low-middle income countries (LMICs). We conclude this article by proposing new avenues for future research.

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1. Introduction

Health systems strengthening in sub-Saharan Africa faces many challenges, including an over-reliance on disease-specific interventions and badly functioning health care facilities and, as part of that chronic lack of care provision path-dependency on centralised but often poorly resourced public health referral centres (Kruk et al., 2017). Policy debates in this terrain have focused on issues relating to persistent underfunding, fragmentation, and poor regulation (Mackintosh et al., 2017). The endorsement of Universal Health Coverage (UHC) as a policy mandate by the UN General Assembly in 2012 has raised expectations but its goals remain elusive (Clinton and Sridhar, 2017). It is widely understood that new technological and socio-economic innovation including new governance approaches will be necessary to achieve those goals (Cassiolato and Soares, 2015).

Up to 70 % of all clinical diagnoses rely on the production of a laboratory-based diagnosis. Traditionally, conventional laboratories that are often centrally placed in large hospitals provide this function, however for effective delivery they not only require highly developed infrastructure and complex equipment but also need skilled technical and scientific personnel, both of which are often in short supply in many developing countries. Point of care testing (POCT) is the use of portable and simple-to-operate devices to quickly generate in-vitro diagnostic test results from a range of specimens, including blood, saliva, urine and other sample types, in a range of clinical settings. More fundamentally point of care devices are linked with treatment and care pathways and the routines of everyday clinical work, into a programme of testing that benefits health systems and society (Pai et al., 2012). The increasingly diverse range of new innovative point of care devices is enabling clinicians to diagnose, treat and monitor diseases in ways and with a speed and accuracy not previously thought possible (Pai et al., 2012).

POCT has had a significant impact on health care by bringing clinical testing and monitoring from the central referral hospital to the remote health clinic. However, the task of introducing a new technology on poorly functioning and fragmented health systems is extremely complex. Beisel et al. (2016) for example, on examining the processes of local translation of rapid malaria tests in East Africa have demonstrated the importance of evaluation in the implementation context of a health setting, where deeply-embedded institutional structures, processes and relationships have been shown to be vital in determining clinical and economic outcomes following the introduction of new technologies.

Zimbabwe is one of 15 UNITAID-supported early adopter countries that have successfully trialled HIV POCT as part of an early infant diagnosis (EID) programme jointly implemented by several international partners (Rodriguez, 2017) and the government is considering scaling up this programme. A significant recent development in this area is the release of an implementation tool-kit by UNICEF and its implementing partners, launched at the AIDS 2018 conference in Amsterdam. The implementation context of HIV POCT can therefore serve as a strategic 'window' through which researchers can gain vital insights into the functioning of the broader health system. Bearing this in mind we chose to explore the question: 'how can a developing country innovatively deploy HIV POCT into its health system taking into account key contextual factors and what lessons can be learned from this early adoption context by other countries planning to follow suit?

The main objective of this narrative review is to draw initial lessons from a preliminary investigation into the outcomes of international support for national and sub-national efforts to strengthen health systems and reflects on evidence gathered to date, using current literature and insights gleaned from discussions with policy and decision makers involved with the deployment of HIV point of care testing in Zimbabwe.

Innovation systems and health systems strengthening literatures have been widely used in diverse ways to frame analyses and solutions to the acute challenges of meeting the needs of populations in low and middle-income countries (LMICs). Cassiolato and Soares (2015) and Marjanovic et al. (2017) are just two examples of the multiple ways in which those perspectives have been used and combined. Recent work highlights the related issue of understanding the connections between global health perspectives and their impact on local environments, between the generation and production of treatments and technologies and the ways in which they reach clinics and patients in different contexts (Mackintosh et al., 2018). However, while using that approach to explore tensions and issues related to the deployment and use of HIV point of care testing in Zimbabwe we began to reflect also on new ways of framing and understanding intersects between innovation and healthcare and we adopted several key insights from that literature into analysis. In particular, the weight given to normative aspects of innovation and system development led us to reflect on the importance of governance and participation.

The article is organised as follows: Section 1 - provides an overview of health policy debates, the actors and missions related to diagnostic testing, and we outline the health systems and problem-orientated health innovation approaches to guide later insights. We end this section by presenting a brief methodology. In section 2 we introduce a case study of HIV POCT in Zimbabwe. The key lessons emanating from this implementation context are highlighted in Section 3, and in Section 4 we articulate possible challenges to the more common innovation and health systems strengthening perspectives and conclude by proposing avenues for future research.

1.1. Background and Context

In 2008 the landmark WHO Maputo declaration identified weak, centralised, poorly functioning, and under-resourced African laboratory systems as a key impediment to global health intervention efforts against infectious disease (WHO, 2008). Efforts were subsequently focused on strengthening laboratory systems in Africa in phases; stepwise laboratory improvement towards accreditation (SLIPTA) based on ISO 15189, in cognisance of the fact that these systems would not achieve world class standards of practice overnight. As argued by Birx et al. (2009), one of the key imperatives in the efforts to strengthen laboratory systems should be in keeping sight of the fact that any attempts to truly address health inequity must transcend the single-disease perspective and move towards systemic integration. That observation reflects broader debate over the focus on global health policy interventions to which we now turn.

1.2. An overview of policy debates about how to support health improvement in LMICs

The last 2 decades have seen an increase in international funding and spending for disease-specific interventions, particularly high-profile diseases, HIV, TB and malaria in sub-Saharan Africa (Nkengasong et al., 2017; UNAIDS, 2017).

While vertical programming has been advertised by its proponents as a clear path by which international donors can support poorer countries to introduce new drugs and treatments and to build capacity to treat disease, it has also been pointed out that the focus on local capacity building by governments should not be lost. Thus, increasing policy focus has turned to horizontal (systems strengthening) as a means for building and ensuring cohesion between key systemic elements; finance, IT service provision, human resources, technology, leadership and governance (WHO, 2007). Whilst these debates about how intervention and support should be provided are complex and, in some cases highly nuanced, it is fair to say that vertical approaches have been more closely aligned with those who see technological innovation as a priority and horizontal approaches with those who view health system support as the top priority (Chataway et al., 2010). Though the distinction between the two approaches is clear, it could be argued that positionality is a significant factor in shaping the views of policy-makers, with those directly involved with global health funding decisions more likely to favour vertical approaches than any other groups.

Those in global health policy with reservations about using the horizontal approach have expressed concern that its adoption would lead to some developing countries neglecting to build their own national health systems, due to assured streams of 'horizontal' funding (Rivers, 2003). Clinton and Sridhar bemoan this persistent debate and liken the shifting discursive boundary between emphasis on vertical and horizontal interventions to a 'pendulum that has swung back and forth over the last half a century'. Spirited debates on this subject however begun to wane off in the last 7 or so years, with the new focus being on UHC, which was endorsed by the United Nations in 2012. UHC is a broad policy goal in which the right to curative, rehabilitative and preventive health services is deemed essential to addressing health inequity. Unfortunately, despite the best of intentions this policy has not been very well-defined which has rendered its achievement difficult.

1.3. The actors and the missions related to diagnostic testing for the strengthening of health systems

There is an increasing policy interest in systems building, among African governments, international policy-makers, and key donors such as WHO, UNAIDS, the Melinda and Bill Gates Foundation, Clinton Health Access Initiative (CHAI), Elizabeth Glaser Paediatric Aids Foundation (EGPAF) and others who have emerged as a powerful constituency driving the scale-up of HIV POCT (Rodriguez, 2017). Leadership by the pan-African aligned African Society for Laboratory Medicine (ASLM), established in 2011 and the African centres for disease control (Africa CDC) founded in 2016, has provided the much needed strategic direction at continental level for strengthening laboratory capacity building, in addition to advocacy roles.

The core focus of policy work in this area builds on the recommendations of the 2008 Maputo declaration with a mandate to build laboratory networks with surveillance capacity and capability, develop specialised facilities that integrate diagnosis across diseases, implement standardised quality management systems allowing for interdisciplinary engagement between professional groups, whilst maintaining an oversight of the interaction between international financiers and technical partners (Nkengasong et al., 2017). HIV POCT has offered a unique opportunity for early adopters such as Zimbabwe to address recurrent challenges emanating from the issues identified by the Maputo declaration, where laboratory systems had traditionally lacked advocacy at the Ministry level and because of the subsequent lack of autonomy, led to laboratory budgets being lumped together and eclipsed by those of medicines (Alemnji et al., 2014).

1.4. Health systems strengthening and problem-orientated health innovation

With so much attention in policy debates on health systems strengthening, unsurprisingly, the spotlight has increasingly been shone on the definition of 'system'. A common approach is to use the WHO definition which refers to the building blocks; leadership, human resources, information technology and IT referred to earlier. It is worthy to note though that the system is more than just the sum of its elements, as its optimum functioning relies on the quality of the relationships and interconnections between the individual components (Lundvall, in Cassiolato and Soares, 2015). 'Strengthening of health systems' may therefore refer to any one of a number of dimensions in systems building across the healthcare continuum. For example, it may be that the building blocks have not matured, have broken down or the interactions, or the 'cement', as described by (Hanlin and Anderson, 2014) that binds these elements requires reinforcement. In all instances it is better not to treat the symptoms but to actively identify and address the root causes. Gilson and colleagues look at this from a different angle and provide a compelling insight: 'health policies and systems are complex social and political phenomena shaped through human action rather than naturally occurring' as such this provides a sound basis for promoting an understanding of health systems and its issues through the lens of social science and interpretivism, complementing the positivist (clinical, biomedical and epidemiological paradigms) that dominate health policy and systems discourses. One perspective could therefore argue for health systems strengthening based on the ability of policy makers to sit between disciplines, actors and perspectives within the health system, thinking and acting in an interdisciplinary manner, to create a shared ground and understanding between perspectives and contending interests (Gilson et al., 2011). We return to the importance of this insight later in the paper.

As explained above, the strengthening of a health system is part of a complex jigsaw puzzle. The task of moving a technology from concept to a patient's bedside requires a holistic view which equally focuses on the late stages of the innovation cycle (problem-orientated health innovation) as it does on the production phases. The importance of reflecting on and identifying the 'linkages and disconnects' between the actors and institutions is seen as a key part of issue-focused innovation practice for integrated and sustainable solutions to health system challenges (Chataway et al., 2007; Gilson et al., 2011). The role of socio-cultural and organisational factors in shaping the use of health technologies is articulated by Chataway, Wield and Castle-Clarke (2015) who address this debate from the perspective of disruption and experimentation in health innovation: '…. a physical technology or new scientific formulation does not in itself produce or distribute a new type of innovation'. We reflect on and align with this perspective of innovation throughout the article.

1.5. Methodology

The research design is a narrative case study based on the implementation context of a pilot HIV POCT programme in Zimbabwe. This preliminary study was conducted over four months, during which we reviewed conceptual, peer-referenced, and grey literature; policy proclamations including national strategic plans, guidelines, technical cooperation documents and conference proceedings to gain a clearer understanding of the coordination activities from both government and implementing partner perspectives. Additionally, we interviewed 5 key policy makers who were selected based on their expert knowledge and availability. These included officials from the Ministry of Health, National AIDS Council, a Physician, a Senior Laboratory Scientist and a Programme Specialist for a United States based non-governmental organisation (NGO).

We used various methods to understand the adoption of HIV POCT:

- A review of project reports to understand the implementation context of POCT.
- POCT working group meeting reports covering issues discussed and their proposed solutions, stakeholder resolutions, and feedback from previous meetings.
- A set of focal questions to guide the interviews.
- An exploration of theoretical literature, including innovation and systems perspectives.

The preliminary findings were discussed in detail by the authors. During conceptualising and thinking about the significance of the insights gathered we have reflected on previous POCT adoption meetings attended by one of the authors (VN) and endeavoured to tease out the emergent factors arising from this implementation context and the implications for future research.

2. Zimbabwe's changing diagnostic testing landscape

In this section we briefly explore the location of HIV POCT within Zimbabwe's primary health system, and specifically look at innovative HIV technologies, the HIV EID project and outline the regulatory sphere associated with point of care testing.

2.1. Background

Like its neighbours in Southern Africa, Zimbabwe bears a heavy burden of HIV with its prevalence being the 6th highest in sub-Saharan Africa. Zimbabwe has a population of around 15 million people of whom in 2016, 1.3 million were estimated to be living with HIV and even more staggeringly, HIV accounts for 74% of all orphans (UNAIDS, 2017). The fight against HIV has been a resounding success due to the enormous global support through the Global fund for AIDS and also due to the cumulative impact of multiple vertical programmes, where HIV POCT is just but one of many such interventions. Faced with the twin burdens of non-communicable diseases (NCDs) and infectious diseases, fuelled by unrelenting socio-economic and political challenges, Zimbabwe's decimated health system has also been an experimental ground, from which many important lessons and questions have emerged and continue to emerge.

2.2. HIV POCT technologies

HIV point of care testing methodologies include serological assays that utilise lateral flow strips to detect antibodies to HIV 1 and 2 or the HIV p24 antigen (in saliva or whole blood/ finger prick specimens) and generate results normally within 15 - 20 minutes. In Zimbabwe these third and fourth generation rapid detection tests (RDTs) with 'high sensitivity and specificity' are part of a national WHO-based HIV testing algorithm and have been in use from around 2008 (UNITAID, 2016). The rapid detection kits used for screening were extensively evaluated at market entry from around 2002 and are supplied by a range of leading diagnostic manufacturers through a local network of agents and distributors.

In 2014, global prices for professional HIV rapid tests varied widely; those sourced through the Global Fund ranged from $US 0.50 to $3.30 per blood test and between $4 to $11 per oral fluid test (UNITAID, 2016). This high variation in cost may be reflective of inefficient procurement mechanisms, due to the possible role of 'middle-men', which contributes to driving up the landing prices of diagnostic testing devices and consumables. We reflect on the importance of researching on new financing mechanisms in Section 4.

The other group of HIV tests use molecular detection polymerase chain reaction/PCR techniques and are used primarily for monitoring viral load as part of the local EID programme. In Zimbabwe spare capacity on one such platform, the Gene-Xpert has been innovatively deployed for the detection of multi-drug resistant TB in what is a classic example of integrated diagnosis across diseases (TB and HIV) using a single testing platform. In 2017, Zimbabwe had 135 Gene-Xpert devices in more than 100 public health testing facilities, including provincial and district hospitals. These platforms were sourced from Cepheid® through a complex public-private-partnership (PPP) negotiated by CHAI and have been extensively evaluated in the clinical setting and shown in a recent field study to be feasible for integrated use in Zimbabwe's primary health system (Ndlovu et al., 2018).

HIV testing technologies in Zimbabwe are selected using WHO pre-qualification criteria for diagnostic testing products, as a safeguard against the market-entry of poor quality devices by considering such factors as test sensitivity and specificity as shown in table 1. An important argument raised by some is that the stringent clinical performance requirements set by WHO inadvertently acted as a barrier, resulting in delayed access to life-saving diagnostic testing in some low-income countries (Peeling, 2015).

Table 1: HIV rapid detection tests available in Zimbabwe (WHO pre-qualification approved).

Platform/Manufacturer	% Sensitivity	% Specificity
ABON™ HIV 1/2/O Tri-Line Human Immunodeficiency Virus Rapid Test Device (ABON Biopharm (Hangzhou) Co. Ltd, China), for whole blood/finger prick	100	99.7
Alere Determine HIV-1/2 (Alere Medical Co. Ltd, Japan), for whole blood	100	99.4
HIV 1/2 STAT-PAK® Dipstick (Chembio Diagnostic Systems Inc., USA), for whole blood/finger prick	100	99.7
HIV 1/2 STAT-PAK™ (Chembio Diagnostic Systems Inc., USA)	99.3	100
SURE CHECK® HIV 1/2 Assay (Chembio Diagnostic Systems Inc., USA), for whole blood finger prick	99.8	99.9
Uni-Gold™ HIV (Trinity Biotech Manufacturing Ltd, Ireland), for whole blood/finger prick	99.8	99.9
VIKIA HIV 1/2 (Biomérieux SA, France), for whole blood/finger prick	99.4	99.9
OraQuick® HIV 1/2 Rapid Antibody Test (OraSure Technologies Inc., USA), for saliva samples	99.1	99.8

Adapted from: UNITAID 2016. Technology landscape

2.3. The HIV Early Infant Diagnosis project

In 2014, Zimbabwe was one of 9 countries (now 15) including Malawi, Tanzania, Swaziland and others that received a $ US 200 million UNITAID grant to support the adoption and scale-up of innovative HIV POCT in early infant diagnosis. This grant was disbursed through partners such as EGPAF, CHAI and ASLM to address the pressing issue of HIV in children. According to UNAIDS, half of the world's HIV infected children reside in these 15 pilot countries and in 2015 only 43 % of children living with HIV had access to anti-retroviral treatment, unlike 54 % of adults (UNAIDS, 2017). Furthermore, an estimated two thirds of children under the age of 5 years were diagnosed too late and infant mortality is highest between the ages of 2 – 3 months (Ndlovu et al., 2018). The strategy built on an existing programme, prevention of mother to child transmission (PMTCT), to address the dire need for timely diagnosis and commencement of HIV infected infants on treatment programmes. Offering decentralised HIV testing and viral load measurement to infants using highly accurate molecular detection techniques at the earliest opportunity after birth was considered an epidemiologically sound approach supported by policy makers and clinicians alike.

As shown in figure 1 and has been described by Zimuto et al. (2016), Zimbabwe has a tiered laboratory network in which EID testing is strategically located in 3 referral Hospitals; Harare, Mpilo in Bulawayo and Mutare. These are linked to 66 district laboratories which have been the focus of the government's viral load scale-up plan. The more peripheral areas refer specimens for confirmation and further testing to the nearest referral centre, usually a central hospital or reference laboratory, constituting what is effectively a 'hub and spoke model'. Infant HIV screening and viral load testing in at risk groups such as pregnant mothers are prioritised in the district hospitals or in some rural health clinics – in what is called a differentiated model of care.
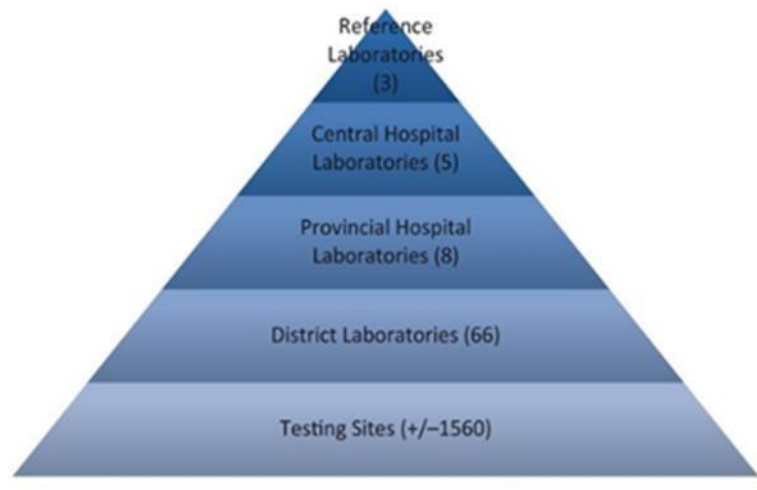
Figure 1: Zimbabwe's laboratory network (Source: Zimuto et al., 2016).

2.4. Quality assured point of care testing – the last line of defence?

It was recognised early during programme development that in addition to existing internal quality control processes, there was a requirement for external quality assurance (EQA) for POCT in the same manner as for conventional laboratory testing. Quantum leaps in technology have meant that in the last 2 decades sophisticated point-of-care platforms became available to non-expert users in the absence of a supportive regulatory environment (Zimuto et al., 2016; Pai et al., 2012). There is consensus between policy makers that these advancements in diagnostic testing technologies have accentuated the need for the requisite quality safeguards, at the same time it is acknowledged that a quality management system for POCT will significantly increase the cost of testing, hence guidance is increasingly being sought from Health Economists to help model the cost effectiveness of quality assurance.

A mathematical modelling exercise by Terris-Prestholt et al. (2017) and colleagues demonstrated that the annual cost of POCT for EID in Zimbabwe was $365 000 without which misdiagnosis rates were projected at 1.7% per year with a reduction to 0.3% when quality assurance was factored into the model. In the WHO POCT policy adopted for use by all early adopter countries, there is a clear direction for users of these technologies with an emphasis on the need for a quality assurance system to be in place prior to deploying POCT. No study has however sought to independently verify the extent to which this essential policy has been implemented in African countries, which would be an important view in highlighting context-specific implementation challenges.

Given this background highlighting the importance of quality assurance, several organisations have entered the SSA policy arena to lead EQA directly, or to tackle other strata within the regulatory sphere. In a classic example of North-South knowledge flows, this well-resourced and experienced mix of policy players has led discussions on the implementation and harmonisation of quality assurance programmes across SSA countries.

In 2014, through Canadian support a performance monitoring scheme for CD4 analysers was introduced, in the same year the London School of Hygiene and Tropical Medicine (LSHTM) came on board and together with a local quality assurance organisation, the Zimbabwe National Quality Assurance Programme (ZINQAP), exploring ideas around costing of quality assurance to ensure that standards for POCT were in alignment with those defined by ISO 15189.

Some pertinent questions arise. For example, would the country require the provision of a legislative framework to support regulatory capacity (including quality assurance), as is the case in South Africa? Such a move, for example, can be a potential game changer as it would be the most significant expression of political will by the government in clinical laboratory systems regulation to date, with envisaged benefits for the broader health system.

3. The lessons

Reflecting on the findings from our preliminary study we distilled some vital learning points from this early implementation context, some of which unsurprisingly were not new, having been raised in various fora over the last decade. These findings suggest that a lot more global health policy attention will have to be focused on 1) identifying innovative financing mechanisms 2) strengthening coordination and knowledge exchange between policy actors and frontline workers who implement these programmes and 3) enhancing local capacity and involving patients (users) if the goal of strengthening laboratory and health systems is to be achieved.

3.1 Funding and spending priorities – a seasonal matter?

As observed by an official in the National AIDS Council during one of our focused interviews;

> *'We are now in the rather precarious position of knowing that it is time we started to integrate infrastructure and systems to accommodate different diseases, yet targeted funding will not allow this to happen. The message is clear. If you want to integrate, you must use your own funds! And our greatest fear in Health is what will happen to the millions of people on HIV treatment if the plug is pulled on a major bilateral fund like PEPFAR'.* [1]

The dominant view from local policy-makers indicated that international funding supports anywhere between 75-85% of Zimbabwe's health spending, however no current figures were available at the time of this report.

Asked about the challenges associated with vertical programmes, a Ministry of Health official responded:

> *'recently, a motorcycle was dispatched from a reference laboratory to a rural health clinic to collect blood samples for HIV confirmatory testing, but TB sputum specimens at the same health centre had to be left behind by the driver because of the inflexibility of the HIV sample transportation protocol. As a result, a separate motorcycle had to be sent back to collect the sputum samples at an additional cost'.*

Policy makers uniformly reflected on the adverse effects of vertical initiatives, for example, one remarked;

> *'the real danger is that there is verticalisation even within vertical programmes, a case in point is the male circumcision programme in HIV, which is in fact a vertical programme with its own staff, monitoring and evaluation tools and programme motor vehicles!'*

Such accounts by local policy makers on the issue of funding and logistics illustrate in different ways the limitations with vertical approaches thereby raising questions on what can be done locally by stakeholders to address these issues. While international programmes such as PEPFAR and NGOs have begun supporting local pharmaceutical procurement in several Africa countries (Mackintosh et al., 2017) there has been limited discussion on extending this thinking to include diagnostic testing. Given the concerns regarding the long-term sustainability of current interventions such as HIV POCT, more profound questions have been raised concerning whether developing countries will be able to sustain these technologies in the absence of multi-lateral and bilateral funding. Based on our interviews with local policy-makers there is a strong indication that these discussions are timely and would be pivotal in addressing, in the long-term, the issue of health systems strengthening.

However, such matters are rarely straightforward as noted by an official from the National AIDS Council during an interview:

> *'The diagnostic analysers that our organisation purchased for CD4 counts were rendered useless as soon as we adopted the latest WHO HIV treatment and care guidelines in 2015, which recommend treatment monitoring based on viral load. The lesson for us is that rather than buying equipment outright we ought to be establishing managed service contracts with the manufacturers, which will allow us to get updated diagnostic equipment whenever the technology changes'.*

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[1] President's Emergency Plan for AIDS Relief

This is an important view from the National AIDS Council and offers a practical argument which governments across the continent would do well to explore further in diagnostic testing, possibly through innovative financing mechanisms involving private-public-partnerships.

3.2. The opinions and voices of front-line workers and patients do matter

Until around 2008 the Zimbabwean government had funded, developed, and implemented policies for the delivery of most of its health services based predominantly on the perceptions of top-level decision-makers in a top-down approach. What had been lacking in all these efforts had been the patient's line-of-sight and that of front-line workers.

This shift in the approach to policy development is highlighted by an observation from a technical expert who works for an NGO supporting POCT adoption and health systems strengthening in Zimbabwe: *'…. In 2015 during the development of treatment guidelines, we involved community advisory groups of people living with AIDS and they played an active role in consultations…'.* Writing about the need for good quality of care in LMICs, Kruk et al. (2017) observe that rarely is there a full picture of care, especially one captured from the patient's view. There is no specific mention in the documents on POCT that we reviewed, of patient and citizen involvement (bottom-up) approaches in Zimbabwe, but this may possibly be explained by the fact that these programmes are still relatively new. This picture may however be different elsewhere, as at a recent POCT meeting in Amsterdam we were pleasantly surprised to observe an HIV positive activist from Kenya included as part of the discussion panel.

While the public health arguments supporting POCT are in many ways compelling, it is important to acknowledge that assumptions are made regarding the simplicity of using point of care devices, but there is no extensive evidence base examining how these assumptions unfold in real clinical settings, especially in SSA. This concern is rather disconcertingly echoed by Beisel et al. (2016);

> '*Despite relative simplicity of the technology some users of rapid diagnostic tests in malarial testing where observed to take short-cuts due to time pressures and a lack of a full appreciation of the technological constraints'.*

The above sentiment highlights an important concern in the HIV testing context, where the diagnostic testing devices can be seen as inextricably linked with the clinical care and treatment pathway, which leads us to believe that 'linkage with clinical care' should take centre-stage in the discussion. Beyond this, programmes such as POCT run the risk of creating a sense of 'techno-optimism', where technology can be misconstrued as being capable of making fundamental change on its own.

As in many other such cases, global policy makers, researchers and clinicians concerned with introducing POCT to facilitate health systems strengthening would do well to take heed of the rallying call by Beisel and colleagues for a more analytic appraisal to 'processes of local translation and appropriation of technology'. In section 3.3 we explore issues related to absorption, resistance and how knowledge flows in the POCT implementation context.

3.3. From systems to facilitating transitions: knowledge flows matter

The last section argued that a key consideration in thinking about how POCT should be implemented and might make the biggest impact is the importance of multiple perspectives that constitute a holistic understanding of change. This includes drawing on patient, nurse and clinician perspectives.

A clear implication of this, is that a vertical approach which isolates one set of disease-based intervention priorities will have limited impact.

Interdisciplinary thinking (which can also be viewed as a diagonal approach) offers the single most important route to best capture the different 'ways of seeing' for this diverse range of actors and constituencies; the public health clinicians, laboratory professionals, programme implementers, patient groups and NGOs who will have to meet regularly to review progress and iron out differences for the successful leveraging and scale up of POCT. Lundvall, (p 12 in Cassiolato and Soares, 2015) draws our attention to an important point: 'the notion of innovation as a process that takes place between users and producers of knowledge has been lost' and he observes that those involved in these debates are from 'different fields of thought'. Reflecting on the above point, the degree to which implementing partners and donors have shown a common understanding on the necessity of organising themselves to stimulate learning and capacity building across sectors is debateable, but efforts are being made as demonstrated by the accomplishments made by African governments and their international partners after the Maputo declaration. Alemnji et al. (2014) provide evidence of the engagement between experts in North-South and South-South collaboration.

In the literature on POCT, some researchers have highlighted the issue of laboratory professionals being opposed to testing that occurs outside of the standard laboratory facilities and concerns have been raised over ceding control of testing to other health care workers (Alemnji et al., 2014; Pai et al., 2012). In Zimbabwe this concern around 'protectionism' was raised by a Ministry official and National AIDS council expert whom we interviewed, however ways to address this issue have not been proffered at the policy level. A qualitative study investigating perceptions around protectionism and the effects on systems building would shed key insights into the problem. There is real potential in gaining a deeper understanding of the implementation context and exploring issues such protectionism as a possible route to rethinking the roles of the laboratory professionals. Innovative ways to address this challenge could entail, for example, that rather than the laboratory staff conducting POCT, they could focus on quality management and regulatory oversight and cascade training of other health professionals.

In addition to the North-South knowledge flows seen during technical support and capacity building programmes involving a range of international partners, the Early Infant Diagnosis consortium made up of early adopter countries such as Tanzania and Zimbabwe has been a vital platform for South-South collaboration. This group convened in Johannesburg in 2016, to exchange experiences and share knowledge. Zimbabwe for example shared with other members data from its evaluation of the PIMA CD4 instrument (Carmona et al., 2016).

Learning and cooperation are recognised as being fundamentally important by many scholars across innovations thinking. Pessoa de Matos et al. (2015) for example, use the local innovative and productive systems (LIPS) conceptual framework to trace and analyse how 'processes of learning, cooperation and innovation' are uniquely shaped by geographical and organisational contexts. This suggests to us the plausibility of focusing on the angle of learning and knowledge flows in the POCT implementation setting as a way of understanding systems strengthening and one warranting further exploration. This approach underscores the importance of looking at the way in which technological 'recipes' are understood and implemented by those who are using them.

3.4. Integration and local capacity building

Integration/diagonal approaches have been proffered as an alternative to vertical and horizontal modes of delivering health services. Though there is agreement on the merits of integrating healthcare programmes, there is no consensus on the mechanisms for its delivery. The laboratory system lends itself well for integration as newer POCT technologies allow multi-plexing, thereby increasing access to tests such as Hepatitis C, Human Papilloma virus, TB or even Ebola on the same point of care platform without increasing fixed costs - we expand on this under point 1 below. To achieve equitable access and systems strengthening there is a need for integration efforts to be multi-dimensional and focus on integration from a range of perspectives for example; between vertical programmes, funding, supply chains, training, health information systems and monitoring and evaluation tools.

Integration can also be viewed from the standpoint of the combined use of facilities, both within the context of district and centralised health centres as well as between hospitals and industrial production plants. Diagnostic device manufacturers recommend that guanidine thiocyanate, a chemical used to denature nucleic acids and a toxic end-product of molecular testing should be disposed of by incineration at very high temperatures (1000°C). A recent study in Zimbabwe by Ndlovu et al. showed that many district level health centres lack the requisite disposal facilities, so used Gene Xpert catridges are transported to central hospitals once a month for incineration.

Cement production factories have been proposed as an alternative for outsourcing molecular testing waste (Ndlovu et al., 2018) which is an example of an innovative integrated approach that may be worthy of pursuit in some LMICs. Another integrative path is the National AIDS Council programme in which cervical cancer screening, treatment and monitoring have been added to the repertoire of what were traditionally HIV treatment and care services. Despite the relatively embryonic state of this project, it offers a clear growth route for integration (Author discussion with NAC official, 27 October 2017). Integration could be further explored though combining HIV POCT with counselling, mental health services and nutrition programmes.

This research identified a number of local capacity building initiatives in the POCT context:

1. In 2015 of the 132 Gene Xpert devices available for viral load monitoring across Zimbabwe, only 11 % of the total capacity was utilised. Following an integration pilot project supported by UNITAID and CHAI to combine HIV with TB testing using the Gene Xpert analysers, capacity utilisation was increased to 67 % and turnaround times for TB testing were reduced from 3 weeks to 1 day with excellent clinical outcomes for the combined TB-HIV treatment pathway.[2]

2. A laboratory mentorship programme introduced by the government in 2012 (in 19 laboratories across the country) has greatly aided this integration thinking. This mentorship project has been central in building local capacity and in establishing the national quality management system linked to an international standard ISO 15189, guided by a local quality assurance body, ZINQAP [3] and supported by WHO and ASLM (Zimuto et al., 2016). More innovative approaches will continue to be needed to build on current initiatives and address the health systems strengthening agenda.

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[2] Zimbabwe country POCT feedback report at AIDS 2018 presented by Raiva Simbi.
[3] Zimbabwe National Quality Assurance Programme – first referred to in sub-section 2.4

3. Zimbabwe has run an IT information skills development programme in conjunction with the Harare Polytechnic over the last 2 decades promoting the development of information management capabilities in the health sector, however these programmes have not specifically focused on laboratory systems. Further research should therefore explore the development of stronger and problem-orientated innovation linkages at country level – integration across service functions.

With respect to health systems in LMICs, arguments for the local production of medicines in Africa (Mackintosh et al., 2017) have been raised and have been of significant interest to international policy makers which in turn raises compelling questions about the implications of these debates for diagnostic testing. Whilst this perspective will need to be discussed in a separate article, we found that discussions about technology transfer in diagnostic testing were already underway in Zimbabwe. The local production of external quality assurance testing panels has been proposed, for example, and is not only seen as a viable route with clear economic benefits, but one with a clear potential to improve diagnostic performance since the molecular characterisation of the test panels will closely resemble those of the local population (Zimuto et al., 2016).

4. Conclusions

This article endeavoured to explore and investigate the issues, lessons and experiences arising from the wider implementation context of POCT, through discussions with policy makers and implementers in Zimbabwe, unpublished interviews, a review of the literature and meetings on POCT. The insights gleaned point to an increasingly complex policy picture shaped by a diverse ensemble of policy players (at least 48 organisations), which highlights the need for an exploration of the governance aspects of the relationships among these policy actors and the extent to which these relationships aid or hinder learning and knowledge sharing, and drive processes of local translation of POCT.

Whilst disease specific interventions have very likely been a contributory factor for the remarkable strides in the global fight against HIV, in part this success is also attributable to the sheer volume of funding. For example, between 2000 and 2016, US$ 109.8 billion developmental assistance was channelled to HIV/AIDS programmes (Schneider et al., 2016). This success is most noticeable in sub-Saharan Africa which has half of the world's HIV positive population. UNAIDS statistics reveal an HIV incidence of 300 000 in 2010, this figure decreased by about 50% to 160 000 in 2016 (UNAIDS, 2017). Hard targets such as the Sustainable Development Goal (SDG) target 3.3 which calls for the end of the AIDS epidemic by 2030, have been easy to sell as key policy tools that have greatly aided the focusing of intervention efforts.

Person power development, enhanced laboratory capacity and capabilities, including the development of strong laboratory networks within and between countries and the citizen voice will play a central role in accelerating the pace at which this can be achieved. This will require concerted efforts between global health policy-actors and decision-makers at the national and sub-national levels. Thus, while disease-specific interventions have allowed for experimentation in the way that new technologies and new management approaches combine to allow for better health care, cordoned off to some extent from broader and complex health systems and governance challenges these initiatives created space for new coalitions of actors to coalesce around more specific challenges.

The problem has, as clearly noted in many studies now, been that these vertical interventions have had limited positive impact on overall health systems strengthening and that early successes derived from vertical initiatives will be limited by a lack of integration. It is evident from the observations made by policy makers in HIV POCT in Zimbabwe, and from the debates in the literature that one of the key insights for organisational learning is the realisation in policy spheres that continuation on this trajectory of vertical programming will not result in the same success that we have witnessed in the past decades and that at some point issues of organisational and institutional learning across different components of health care and of governance become critical and essential to sustainable approaches for a more profound impact.

To recap on earlier points, the deployment and uptake of POCT in Zimbabwe shows:

1) The necessity of regulatory considerations 2) funding and sustainability are crucial 3) the voices and opinions of front-line workers and patients must be heard 4) POCT could offer a realistic route for delivering integrated health care and 5) the need to explore newer ways of harnessing learning and interdisciplinary approaches to build synergies from this implementation context.

Recent research, backed up by evidence in this paper suggests that thinking across production, delivery and use, and involving perspectives from all spheres will be critical. Based on this preliminary evidence gathering and literature review, we propose a research agenda:

- To seek deeper insights of the wider POCT implementation context by employing social science perspectives to explore the emergent factors including, governance, new innovative finance mechanisms, possible roles of public and private partnerships, universities and industry linkages for long-term sustainability of POCT.
- The future evaluation of POCT, its implementation and routinisation will need to be grounded in theory, which can for example inform theory of change exercises. Hitherto this has not been the case. Most evaluation to date has been informed from clinical, biomedical and epidemiological standpoints which has led to a somewhat asymmetric development of policy and understanding.

In relation to developing solid theoretical perspectives and in ending this article, it is useful to reflect on the implications of what we have said for innovation and health systems concepts and literatures. We made the point earlier in the paper that innovation systems perspectives (Mahoney, 2011) have tended to focus on technological innovation and therefore tended towards more vertical approaches for achieving change. Health systems strengthening perspectives have stressed the importance of the range of human capability, financing and governance issues which affect profoundly the ways in which healthcare can meet people's needs.

Whilst there is more work needed to develop concepts which integrate both perspectives, it is clear that these insights have already opened up a range of new questions:

1. What will be the fate of the POCT technologies and national health systems beyond the US$ 200 million UNITAID funding?
2. Can the emergent P-P-P arrangements such as the one between CHAI and Cepheid be viewed as a key 'head-wind' supporting the future delivery of diagnostics in LMICs? If so, how can early adopters harness learning from these arrangements to address the question of long-term sustainability and delivery of diagnostic testing?

3. How can collaboration between local institutions contribute to local capacity building, for example can ministries of health co-design POCT curricular in tandem with universities and other tertiary education institutions?

This paper has highlighted the importance of learning, integration, and governance in the case of successful and sustainable adoption of HIV POCT. We have drawn on both innovation and health systems framings to understand the challenges and are aware of the importance of both perspectives in informing how learning and integration happen and in thinking about governance. One of the frustrations in using both literatures to frame arguments and discussions is that they tend to result in a type of stand-off between approaches which start from radically different principles. In future work we plan to explore the possibilities opened up by the sustainability transitions literature which is now being increasingly being thought about in the context of health (Broerse and Grin, 2017). This literature offers perspectives on how experimental socio-technical approaches designed to challenge existing technological, social and organisational routines and processes, can achieve broader transformation. The advantage of beginning to adopt this thinking is that it side steps problems which emerge in trying to reconcile two alternative visions of thinking and focuses from the outset on the importance of the range of factors involved in new socio-technical innovations, both for introducing new approaches to delivering better healthcare but also in sustaining that delivery. Potentially, the approach allows for a way of reframing partially at least, the rich insights offered by both innovation and health systems literatures.

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