Scaling up innovation in health

Case studies supporting the development of the “Global Action Plan for Healthy lives and Wellbeing for All”

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Authors and acknowledgements

Carmen Leon-Himmelstine (ODI) prepared the case studies on Hep C, HIVST and MDiabetes. Rachel Thompson (Independent consultant) prepared the case studies on MenAfricVac and HITAP. Fiona Samuels (ODI) provided supervision and guidance for the 5 case studies and coordinated with R4D and Wellcome Trust. Susan Nicolai (ODI) had overall oversight of this component and the related sister project (Elevating Country Priorities). From Wellcome Trust we would like to thank Alice Jamieson for her support and guidance throughout the process of carrying out the case studies. We would also like to thank our key informants who kindly shared their valuable insights with us and provided us with comments on earlier drafts. Finally we would like to thank Cicely Thomas from R4D for her insightful comments at various stages of the process.

1.0 Introduction

The following set of five case studies were commissioned by Wellcome Trust as part of its support to the delivery of the Global Action Plan for Healthy lives and Wellbeing for All (GAP). Wellcome contributes to the GAP through supporting the development of, and co-leading with the World Health Organization (WHO), one of seven 'Accelerators', i.e. the R&D, Innovation and Access accelerator. One of its focus areas is to generate recommendations on how to scale-up innovations through identifying catalytic actions for governments, national and international organisations and donors to work together to achieve scale and impact. In order to provide such recommendations, learning from existing innovations in health is necessary as the case studies in this document lay out.

Before proceeding to the case studies, this introductory section briefly lays out the approaches and methods used to select and carry out the case studies as well as the challenges and limitations faced. The selection of the case studies was initially informed by a long list of health innovations developed by WHO in collaboration with the other 11 global agencies and international organizations (IGOs) in the GAP which were seen to (a) have the most potential to scale and (b) have significant impact in developing countries. Following this long list, and in discussion with Wellcome Trust and with R4D Centre for Health Market Innovations, a short list of 5 case studies were selected. Criteria for selecting the case studies included: that there was a geographical spread and were not just focused in one region or continent; that they included low and middle income countries as well as countries with different levels of fragility; that some may have a single country focus while others may have a more regional approach; that a range of different solutions, devices and therapeutics were in use across the case studies; that innovations were not restricted just to science or technology innovations but could include process innovations, or those which have innovative ways of managing processes related to, for instance, health planning, setting health priorities, etc; and that they addressed different health related themes. As a second order of priority, contexts where different levels of donor, national, private sector and community engagement in the innovation was apparent was also included.

The final short list included the following case studies:

- Hepatitis C testing, treatment and educational campaign – with a focus on Egypt
- HIV Self-Testing (HIVST) – with a focus on the STAR initiative in Malawi, Zambia, Zimbabwe, South Africa, Eswatini and Lesotho
- MDiabetes – with a focus in India
- MenAfricVac – roll out of Meningitis A vaccine in sub-Saharan Africa's meningitis belt
- HITAP - Health Intervention and Technology Assessment Programme, in Thailand

Following an initial contextualisation of the innovations geographically - within the specific countries and regions – politically and historically where relevant, all the case studies describe the innovation and the impacts (both direct and indirect and/or unintended) it has had. The enablers and barriers to both implementing the innovation and taking it to scale are then explored, also considering how the barriers or challenges were overcome. The role of different actors and their priorities, including donors, government, civil society, private sector and community members in the implementation and scaling up of the innovation, is also a key part of the story as is the extent to which there was collaboration and partnerships. Finally, a set of key lessons are drawn from the findings.

Key approaches used in the case studies included carrying out a literature review of both published and grey materials and carrying out key informant interviews over the phone with government officials, academics, and civil society representatives that were involved in the design, implementation and/or scale-up of the innovations (approximately 5 to 6 per case study). Key informant participants were identified with help from Wellcome Trust and WHO; a snowball approach was also used alongside following-up on authors of secondary literature materials. After the case studies were written they were reviewed by Wellcome Trust and by R4D and revised accordingly; final versions of the case studies were also shared with the key informants to ensure that their perspectives were adequately presented. One main limitation of the case studies is that it was challenging to access in-country government stakeholders to obtain their perspectives of implementation and scale-up. If the case studies had been done in-country obtaining such insights may have been easier. Similarly, these case studies represent a snap-shot of the innovation and not a comprehensive review; in order to obtain a fuller picture, face to face interviews in the country in question would be necessary, including among end users, and accessing a wider array of secondary materials would also be important. Likewise, the literature only included English written sources what may exclude valuable material written in other languages.

The resulting case studies, as highlighted in the summary boxes at the start of each, group the enablers, challenges/barriers and lessons learnt by three main areas: those related to the design/R&D phase, those related to

the implementation phase and those which are crosscutting, i.e. are relevant or important for all stages. Together these studies reveal important detail of factors that support or hinder scaling up innovation in health and its contribution to SDG3 progress.

2.0 Hepatitis C - 'Educate, Test and Treat' Campaign In Egypt

SUMMARY BOX

What is the innovation?

The Hepatitis C 'educate, test and treat' campaign in Egypt is a community mobilisation and education campaign, promoting prevention and facilitating testing linked to treatment. The campaign was piloted in one rural village in northern Egypt and was subsequently scaled up to 73 villages. It consists of four components: (1) community mobilisation by a network of mostly female volunteer village promoters; (2) an educational campaign to sensitise the community; (3) fundraising for public donations among the wealthiest within the communities; and (4) a testing, diagnosis and treatment package. The table below summaries the enablers, challenges and lessons learnt from this innovation.

	Design/R&D	Implementation/scale-up	Cross-cutting
Enablers	• Trusted and long-established partnership between the villagers and the implementing non-governmental organisation (NGO), ELRIAH (Egyptian Liver Research Institute and Hospital)	• Comprehensive and streamlined approach, which includes prevention through awareness and testing, treatment and care • Community- and demand-led approach, which generated a high degree of ownership along the process • Services such as testing, treatment and delivery of medication were brought to the communities • Prevention, testing and treatment were free • Community funding led by wealthier villagers was key part of the funding base	• Political commitment to scale at the national level was achieved as the model fitted and complemented the government's commitment to eliminate Hepatitis C (HCV) in Egypt • Adaptability to different contexts
Challenges	• Limited knowledge and capacity of village promoters to deliver relatively complex messages	• Tensions among villagers with competing interests • Lower coverage during scale-up due to patients' lack of time and funds to attend clinic • Reaching people from different backgrounds/ages	• Additional funding continues to be necessary • Divergent interests driven by the government's interest to be seen as the champion in efforts to eliminate HCV
Lessons	• Providing services directly in the communities allows low-income patients to be treated and cured • Co-funding between wealthier villagers and implementers promotes a sense of ownership and sustainability • A comprehensive approach – prevention, treatment and care – is important to achieve better results • Providing adequate training for village promoters before they approach	• The awareness campaign achieves better results when there is ongoing contact with people and when it uses various methods and approaches to disseminate information • Having simple diagnostic tools and linkages to care (either in the same day or a single visit) allows patients to complete their clinic evaluation	• The model is more likely to be scaled up when there is government ownership • Countries with similar HCV prevalence could also replicate and adapt the model according to their context • Sustainability (and the elimination of HCV) is more likely to occur when beneficiaries of interventions develop a sense of ownership along the process

	villagers and patients is critical		

1. Introduction

The Global Hepatitis Programme and HIV Department of the World Health Organization (WHO) working with the Association of Liver Patients Care (ALPC) in Egypt implemented the 'educate, test and treat' community mobilisation campaign, which provided education about Hepatitis C virus (HCV) transmission and facilitated testing linked to curative treatment of people in 73 villages. This approach could be an important strategy for adoption in rural settings to complement the national government programme towards the elimination of HCV in Egypt and in other high prevalence countries with a large rural population.

This case study first sets the scene by providing some context on HCV globally and then describes the specific origins and development of the disease in Egypt. This is followed by an analysis of the history and development of the 'educate, test and treat' campaign as well as a more in-depth description of its components. The enablers and challenges faced at different stages are then examined from the perspective of key informants and based on a review of secondary literature, which explored the outcomes of the campaign during its piloting and scale-up. Finally, the case study provides key lessons learnt during the different stages.

2. Context

2.1 The global burden of Hepatitis C virus

Hepatitis is a blood-borne disease usually transmitted through exposure to small quantities of blood and frequently under-diagnosed and untreated, especially in low- and middle-income countries (LMICs) (Unitaid, 2018). According to the WHO (2018a), 71 million people have chronic HCV infection worldwide, most of whom are untreated. This is nearly twice the number of people living with HIV. Furthermore, approximate 400,000 people die each year from HCV-related liver disease (Unitaid, 2018); in 2015, an estimated 290 million people remained undiagnosed (Cooke et al., 2019), and more people were newly infected with HCV (1.75 million) than were cured (843,000) (WHO, 2017).

Until 2015, treatment of HCV had limited efficacy and critical side effects. However, from 2015, new medicines known as direct-acting antivirals (DAAs) have been effective at curing over 95% of HCV infections, usually in 8 to 12 weeks (Unitaid, 2018). Indeed, since the publication of the initial 2014 WHO Guidelines (2016) for screening, care and treatment of persons with chronic HCV, three pangenotypic regimes that are effective across all six major HCV genotypes have been approved by the United States Food and Drug Administration (FDA) and the European Medicines Agency (WHO, 2018b). These regimes reduce the need for costly genotyping and simplify the procurement and delivery of DAAs. As a result, in 2016, the World Health Assembly (the WHO's decision-making body) adopted the goal to eliminate viral hepatitis, including HCV, as a public health problem by 2030, which would entail a 90% reduction in incidence and a 65% reduction in mortality. Reaching this target would entail diagnosing 90% of people living with HCV and treating 80% of diagnosed people with DAAs, along with considerably reducing the number of new infections (WHO, 2018b).

Despite considerable progress in access to medications and diagnostics, viral hepatitis lacks the kind of global funding and support that has gone to tackling HIV, tuberculosis or malaria (Cooke et al., 2019). Other challenges to reach the global targets remain, especially in LMICs, where access to diagnosis and treatment is low. Diagnosis is a two-step process,[1] which makes it costlier for low-income countries, where less than 10% of people infected with HCV had been detected by 2016 (compared with over 40% in high-income countries) (WHO, 2018b). Moreover, HCV diagnostic devices are expensive and often only available in central hospitals and laboratories in main cities (Unitaid, 2018). Other challenges include lack of awareness by doctors and patients, few testing facilities and limited resources for HCV testing services (ibid.).

The WHO has been assisting in drafting and implementing national testing and treatment policies as well as national viral hepatitis plans. By 2017, 84 out of 139 reporting countries had developed such plans – a fivefold increase since 2012 (WHO, 2018b). Some of these countries such as Georgia, Mongolia and Egypt have begun to implement more ambitious national strategies with the goal of reaching the WHO target of eliminating HCV by 2030.

[1] The first test aims to detect the HCV antibodies and the second test, of HCV viral load, aims to differentiate people who have cleared the virus (30% of people infected with HCV clear the infection without needing treatment) from those who have a chronic viraemic infection (WHOa, 2018).

2.2 HCV in Egypt: origins of a unique virus and development of a programme

Egypt has the highest burden of Hepatitis C in the world for its population size (World Bank, 2017a). Estimates for prevalence are based on data reported from the 2015 Egypt Demographic Health Survey, which showed that 5.6 million people were infected – equivalent to 7% of the Egyptian population aged 15–59 years (ibid.). A large number of these infections spread in the 1960s and 1980s (when little was known about Hepatitis and its transmission) as part of a governmental campaign supported by the WHO to eliminate schistosomiasis, an infection acquired through a parasitic worm found in the Nile River that can cause organ failure and cancer if left untreated. Over the 18 years of treatment, 36 million injections were given to more than 6 million people, almost all with unsterilised needles, representing 'the largest ever iatrogenic spread of blood-borne infection' (Gomaa et al., 2017), as confirmed by one of our interviewees:

> *A lot of the Hepatitis infection in some other countries is largely in high-risk populations – injecting drug users, men who have sex with men – but [in Egypt] it's pretty unique to have such a large infection in the general population where you actually have to go proactively and find infections in the villages*. (Global Hepatitis Programme, WHO)

Moreover, initial drug development worldwide focused on infection with HCV genotype 1 (since this was the most prevalent genotype in the USA and Europe), whereas most of the population in Egypt is infected with genotype 4, as in the Middle East more generally (ibid.).

Egypt now is predicted as being on track for eliminating its HCV epidemic by 2030 and has been perceived as a model for other LMICs experiencing similar HCV epidemics (WHO, 2018b; World Bank, 2017a). Efforts in Egypt began in 2006 when the National Committee for Control of Viral Hepatitis (NCCVH) was established by the Ministry of Health and Population, whose primary policy was to provide medications to all patients at either reduced cost or free (Gomaa et al., 2017). This was followed by the development of a Plan of Action for the prevention, care and treatment of HCV for 2008–2012 by the Ministry, which was updated for 2014–2018 (Shiha et al., 2018). The current Plan covers six main components: surveillance; infection control; improving blood safety; Hepatitis B vaccination; health education to providers and communities; and care and treatment (Ministry of Health and Population, 2014). Egypt's goal is to reduce prevalence to < 2% in 10 years and to <1% by 2030, potentially preventing more than 250,000 deaths between 2015 and 2030 (Cooke et al., 2019). The highest prevalence is found in low-income rural communities, which were more affected by schistosomiasis (11.7% compared to 7.1% in urban areas) (World Bank, 2017b; Shiha et al., forthcoming). Similarly, prevalence for men is somewhat higher than for women (12.4% and 8.1% respectively) and lower for young people compared to the age groups who were exposed to schistosomiasis treatment (World Bank, 2017b).

Under the Plan, the government implemented different strategies to achieve its goals. When DAA regimens became available to cure infections with HCV genotype 4, the government accelerated registration of DAAs and negotiated in 2014 with drug manufacturers (especially with Gilead Sciences, a US-based drug manufacturer) to reduce prices for the expansion of access to treatment in large numbers (World Bank, 2017a). As a result, 18 generic versions of medication (including sofosbuvir, sofosbuvir/ledipasvir and daclatasvir) are available in Egypt and about 1.5 million people had received HCV treatment by 2017 (World Bank, 2017b). To continue reducing medication prices, the government also supported the domestic pharmaceutical industry, and there are now more than a dozen Egyptian companies licensed to manufacture DAAs (World Bank, 2017a). The country had also opened 56 new treatment centres by 2016 (with plans to reach 100) and created electronic portals to enrol new patients for testing and receiving treatment, if necessary, free of charge (World Bank, 2017b).

However, the Ministry of Health and Population initially focused its efforts on treatment and not on infection control and education, which began to challenge the success of the campaign (Elgharably et al., 2017). This and other challenges led to the 'educate, test and treat' mobilisation campaign and programme for the elimination of HCV. It was implemented by a non-governmental organisation NGO, the Association of Liver Patients Care (ALPC), which had a very strong influence on the current governmental campaign to test and cure HCV.

2.3 Evolution and history of the 'educate, test and treat' campaign

ALPC and its 'village free of hepatitis' campaign (also referred to as a 'model' by key stakeholders) started in 2013, before the government initiated its campaign in rural areas, according to key informants. The aim of this initial project was to have villages free of liver disease, targeting people in their homes and providing education to raise awareness (African Liver Patients Association (ALPA), 2018).

The ALPC campaign aimed to complement the existing government treatment programme and to support the goal to eliminate HCV in the country by 2030 (Shiha et al., 2018). For example, although a large number of individuals had been able to access treatment under the large-scale government campaign, much of the expansion of treatment in 2015 and

2016 only reached people who registered on the web-based system set up by the government. This was mainly used by those who already knew they were infected and eligible for treatment (World Bank, 2017b), while others were unable to be diagnosed and seek treatment on their own (World Bank, 2017a). Thus, the focus turned to the challenge of identifying undiagnosed individuals. Latest data showed that although prevalence of HCV infection decreased from 10% in 2008 to 7% in 2015, between 3.5 million and 4.2 million people were still living with HCV and in need of treatment (Shiha et al., forthcoming). The main challenge to screening and treatment is in low-income rural communities (57% of Egypt's 92 million population), where people face more financial constraints to access care (ibid.). This was confirmed by one stakeholder involved in the design of the 'village free of hepatitis' model:

> *One of the key issues was that about 60% of the Egyptian population live in villages so there was a question of how to best reach the villages ... There were all these treatments around the country [through the national campaign] but that requires travel, it requires cost and time. The national programme was successful, but it was not necessarily reaching everybody and particularly those in the villages and those who were poorer*. (Global Hepatitis Programme, WHO)

As Hepatitis C in Egypt is characterised by a high prevalence and burden of HCV infection in rural areas, also among lower socioeconomic groups (World Bank, 2017b), the strategy to eliminate HCV in the country had to be directed towards finding those infected through mass screening in rural communities, which would allow for identification and treatment of those not yet aware of their diagnosis (Kandeel et al., 2017). High rates of new infections also guided the design of the model, according to one key informant:

> *The second issue we identified was that there was still a high rate of new infections. Even if most people were being treated, a lot of people were still getting newly infected because there was a lot of unsafe practices going on be it at healthcare settings, barber shops, informal healthcare settings, with re-use of needles, syringes and unsafe practices. So the WHO Global Hepatitis Programme established a collaboration with ALPC and ELRIAH [Egyptian Liver Research Institute and Hospital] group in the northern part of Egypt where there is a high density of villages and a high prevalence of HCV infection to establish a model of education and prevention to stop new infections alongside testing and treatment in the villages*. (Global Hepatitis Programme, WHO)

For example, in 2016, nearly 150,000 Egyptians were estimated to have been newly infected (World Bank, 2017a), with each person transmitting the infection to around 3.54 individuals (Waked et al., 2016). The Ministry of Health and Population (2014) suggests that contact with infected blood through medical procedures (primarily through re-use of disposal syringes) is the primary mode of HCV transmission in the country. The main reason is the popular belief among Egyptians that injections are more effective to cure health issues than oral medications, contributing to an average use per person per year of 4.2 injections compared to 1.5 in other countries. Injections in many cases are also given by informal providers (e.g. pharmacists, housekeepers and barbers) with no medical education or training (ibid.). All these issues highlighted the need for a large-scale awareness-raising and education campaign to prevent new infections, particularly in poorer rural settings (Shiha et al., forthcoming).

Aware of these challenges, the ALPC, working with WHO, developed the community-based 'educate, test and treat' campaign, for the prevention, diagnosis and treatment of HCV, as a strategy to eliminate Hepatitis C across villages in rural Egypt (Shiha et al., forthcoming). The origins of this innovation were described by the Chief Executive Officer (CEO) of ELRIAH, the subsidiary hospital of ALPC:

> *When the oral drugs, the direct-acting antiviral [DAA] regimens became available in Egypt, especially with the generics, we were able to treat a very large number of patients because the drugs were available, and the price was not very high, so through donations we started to treat larger numbers of patients. But there was a challenge ... We found that many people could not even afford the costs of travelling [to the hospital to ask for treatment], so with our project we decided to go to the patients. That was our slogan – we go to them in their villages ... But then the main obstacle was the budget, who will sponsor? So, we negotiated with the villagers and told them "we are a charity and we can offer some help but we need the cooperation of the rich people in the villages, the majority in the villages are poor but there are some who can afford the cost of treatment and can donate to others". So we made this as a research project we call it the 'educate, test and treat' model, we started to work more than five years ago in 2013.*

The overall objective of the project was 'to establish a comprehensive community-led model programme for the prevention, diagnosis, and treatment of hepatitis C in one Egyptian village, and identify knowledge that could inform scale up to other villages and rural settings' (Shiha et al., 2018: 3). The programme was first tested in Al-Othmanya

village, one of the 317 villages in the governorate of Gharbiah Al-Othmanya, with a population of 6,997 living in about 1,242 households. The village was chosen as the first to implement this model because the community leaders approached ELRIAH to develop an intervention to eliminate HCV from their village, aware that it was a major challenge. Between June 2015 and June 2018, the model was scaled to 73 villages across 7 governorates in Egypt, covering more than 300,000 villagers and keeping the same components of the first village. However, implementation by ELRIAH stopped recently because, according to key informants, the national screening programme had begun:

> *The sequence was like this: we started in one village as a model and after we succeeded, we had requests from many, many villages. We went to five more villages, nearby villages and when we started in these five villages, we had requests from 10 more villages. Then we had a waiting list and we were working in more than 100 villages, we stopped last, say, five or six months ago because there was a national screening programme in the whole country, so we stopped our project. But this model is ready for re-implementation in Egypt or anywhere*. (CEO, Egyptian Liver Research Institute and Hospital)

3. Key elements

This section begins by describing the four key components of the 'educate, test and treat' model followed by an analysis of the stakeholders that were involved at different stages. We also offer insights about how the campaign evolved from piloting in the first village to being scale up to the 73 other villages.

3.1 Characteristics of the innovation

The model comprises four main components: (1) community mobilisation by a network of mostly female volunteer village promoters and establishment of partnerships between ELRIAH and community-based organisations; (2) an educational campaign to sensitise the community about HCV and its transmission and promote behavioural changes; (3) fundraising for public donations among the wealthiest within the communities; and (4) a testing, diagnosis and treatment package. Details of the components are briefly described in Table 1, using information from Shiha et al. (2018), Shiha et al. (forthcoming), and the views of key informants interviewed for this study.

Table 1 Components of the 'educate, test and treat' campaign

Component	Description
Community mobilisation	• Establishment of a partnership between ELRIAH (based 30km from Al-Othmanya village) and a village community committee and two community-based organisations with the purpose to promote community participation, ownership and accountability • Main activities of the committee were to fundraise donations to ensure economic resources for the treatment of low-income villagers, motivate households to undertake and maintain safe practices, supervise the activities of the village promoters, and provide ongoing contact with ELRIAH • 60 villagers were recruited as volunteer promoters, most of whom were women. Their main roles were to deliver the educational and motivational messages to spread information and promote behavioural change among the population, organise the door-to-door testing activities and support individuals to adopt safe practices
Awareness-raising and educational campaign	• Sensitisation of the community about HCV and transmission of information about HCV preventive strategies, making use of public awareness events, door-to-door household visits and promotional materials (cartoon films, posters, booklets, or songs) targeting the general population and groups working in higher-risk settings in the communities (e.g. informal healthcare providers and barbers) • Use of promotional materials aimed to share optimistic messages, address stigma and move from awareness to action • Use of a village hotline and a local 'satellite' channel to regularly broadcast educational information in the community-based organisations, healthcare facilities, youth clubs and schools

Fundraising	• Fundraising campaign to collect donations from the wealthier villagers to pay for treatment of low-income villagers
Testing, diagnosis and treatment	• Identification of the population aged 12–80 years infected with HCV followed by linkage to care and treatment • Testing was done using rapid diagnostic tests, inviting households to attend a screening at a convenient location such as the local healthcare unit or school. At this point, patients who tested positive were asked to provide an additional blood test sample (to be tested for HCV- ribonucleic acid (RNA) polymerase chain reaction (PCR) to confirm infection) • People with confirmed results attended the ELRIAH clinical centre in groups with transport provided to receive care and were offered a 24-week DAA treatment with an assessment cure at 12 weeks after completion of treatment • Stages of liver disease and fibrosis (levels of damage to the liver) were assessed using transient elastography (fibroscan). Likewise, patients were assessed at ELRIAH at weeks 4, 8, 12, 16 and 20 to collect medication, and monitor adverse events and treatment adherence

Following positive effects of the programme, the model was scaled up by ELRIAH to the other 73 villages across 7 of the 27 governorates: Gharbiah, Dakahlia, Damietta, Port-Said, Beni-Swef, Sohag and Red Sea (Shiha et al., forthcoming).

3.2 Stakeholder's involvement: main actors during design, implementation, scale-up; type of involvement; coordination and partnerships

International level: A key stakeholder was the WHO Global Hepatitis Programme, which was involved in the design and assessment of the project, and dissemination of its results, as noted by WHO's Senior Scientist in the Global Hepatitis Programme:

> *Part of what we do at WHO in viral hepatitis is related to work on innovations in service delivery and simplification of the care pathway. So you often want to work with a university or with a non-governmental organisation or with a set of partners to do these types of demonstration projects to drive innovation ... and what you are hoping is that by getting good results, by disseminating it, by showing its impact, that you influence national government policy and approach. And I think we certainly have.*

National level: As mentioned, ALPC was another key stakeholder. Established in 1997, the NGO provides free treatment, free investigation and free medications for poor patients. ELRIAH, a liver and gastrointestinal disease hospital, research institute, clinical laboratory and clinical trials centre, was established in 2011 by ALPC. ELRIAH's funding sources are mostly from pharmaceutical companies, with a small proportion coming from donations and membership fees. The main hospital is in Sherbin near Mansoura, Dakahlia. ELRIAH has also established another 20 secondary facilities throughout Egypt (including in Cairo, Sharkia, Upper Egypt, Menoufia, Gharbiah, BeniSwef, Dakahlia, Damietta, Port-Said, Sohag and Red Sea) that were used to expand the programme. The roles of ALPC and ELRIAH in the model were described by ELRIAH's CEO:

> *The Association of Liver Patients Care (ALPC) is a charity … The aim was to combat Hepatitis in general, especially Hepatitis C, and to help poor people who cannot afford the costs of treatment and investigations, to create awareness about Hepatitis as an infection and how people can protect themselves and to offer care for Hepatitis or liver diseases in general, and that was achieved in 2011 with the Egyptian Liver Research Institute and Hospital (ELRIAH), which is working as a centre of excellence giving treatment for patients, and doing other investigations like radiology, interventional radiology, and even surgery, in addition to the clinical trial unit for clinical research...*

Local level: In addition, other relevant stakeholders are those involved in the design and implementation of the process within the villages and ELRIAH's hospital:

> *The champions are the people who donate, the village promoters and, of course, the whole team of our Association, including doctors, nurses, lab specialists … The whole team were champions because they go*

very frequently to the villages. Some villages are remote and the weather sometimes is not good but doctors, nurses, they go regularly and complete the work, so they are the real champions. (CEO, ELRIAH)

4. Impacts/effects of the innovation

This section first presents the overall impact of the 'educate, test and treat' campaign with a description of the indicators used to measure impact. It then explores the direct and indirect effects of the campaign in Al-Othmanya village, before moving on to examine the results in the 73 villages and its subsequent adoption and scale-up by the Egyptian government at national level.

4.1 Overall impact of the innovation

The model achieved high uptake of HCV testing, high levels of linkage to care and DAA treatment, and high attainment of cure. The key outcomes that have been monitored to measure the success of the model are described in Table 2.

Table 2 Indicators used to measure outcomes and effects of the 'educate, test and treat' campaign

Outcomes of interest	Indicators
Screening, treatment and cure	• Number and proportion of those who took up serological testing • Number and proportion of those who linked to testing to confirm viraemic infection and assessment of stage of liver disease • Number and proportion of those who initiated treatment in those who were HCV positive • Number and proportion of those who completed treatment and were cured (assessed by a viral load test 12 weeks after completion of treatment)
Educational and awareness campaign (only measure in Al-Othmanya village)	• Number and proportion of villagers who participated in the campaign • Improvement in the awareness and knowledge scores, reduction in unsafe behaviours and practices[2] • Uptake of Hepatitis B virus vaccination among patients who were HCV viraemic but HBsAg seronegative[3]
Costs of the campaign	• Costs of the diagnosis process (rapid diagnostic tests and HCV-RNA PCR, the second stage of HCV diagnosis), costs of drugs • Excluding costs of staff, maintenance and infrastructure

The overall effect of the project is described by one stakeholder as follows:

We have now extended this whole model to 73 villages with testing of more than 200,000 villagers identifying about 33,839 (who tested positive), of which 15,892 had viraemic infection and needed treatment. There was almost complete linkage to care, and a very high uptake of treatment. Almost everybody who needed treatment got treatment and was cured, so it's been very successful. We have also done some follow-up work

[2] Changes in knowledge and awareness of HCV and adoption of good practices were assessed on the basis of survey scores before and after the educational campaign intervention in key subject areas (e.g. sharing of toothbrush with other family members; use of non-sterilised equipment during dental procedures; use of own shaving instruments at the barber shop; checking for use of sterilised tools at dental clinic; not sharing loofah and sponge for personal cleaning among family members; informing the dentist if they have or previously had HCV, among other areas).

[3] The Ministry of Health and Population's plan of action includes Hepatitis B vaccination as one of its six components, aiming to eliminate Hepatitis B and C as a public health threat by 2030. As such, prevention, testing and treatment are also at the core of an effective Hepatitis response by ALPC.

to check how many people who were originally negative for HCV infection when tested before got infected in the couple of years after the project. Our finding is that there's still some people getting infected in these villages but it's less than it was before. The markedly reduced number of people with HCV in the villages following mass treatment means there are fewer people to transmit the infection. But prevention is still far from perfect, and some people are still being infected through unsafe healthcare practices. (Global Hepatitis Programme, WHO)

4.1.1 Direct and indirect (unintended) impacts / effects – in Al-Othmanya village

Direct effects

Testing, treatment coverage and cure

The programme screened 89% of all adult individuals, of whom 13% were HCV positive. These individuals had a second level of screening using HCV-RNA PCR and 59% were positive. A total of 96% of these patients were given DAA. Of those who completed treatment, 98% were cured. In 2017, the programme conducted a second screening at village level, with no new positive cases identified. Overall, it was estimated that the intervention of testing, treatment and cure covered an estimated 92% of all those people infected with HCV in the village aged between 12 and 80 years (Shiha et al., forthcoming).

Ongoing transmission

In a follow-up study (Shiha et al., 2019a) that took place between May and July 2018, individuals of the same village who were HCV negative during the original screening intervention three years earlier were re-tested. Only two villagers were positive for HCV, confirming the near elimination of HCV infection in Al-Othmanya village, alongside the treatment and cure of more than 90% of the infected population.

Awareness and behavioural change

After the educational campaign, the proportion of survey participants who showed awareness of high-risk practices increased to 70%. In addition to awareness, there was a 70% increase in the adoption of good practices to reduce transmission, as participants reported using their own shaving devices at the barber shops, checking for use of sterilised tools at the dentist, or not sharing personal hygiene items such as toothbrushes or nail clippers.

Costs

The total cost of testing and treatment for 312 individuals who were infected with HCV was $117,980, with 80.5% of the costs covered by ELRIAH and 19.5% covered by villagers. The awareness-raising and educational campaign cost $1,698 (Shiha et al., 2018). However, as mentioned by stakeholders, the village promoters were volunteers and the costs of the campaign were also reduced through using existing promotional materials published by ELRIAH.

Indirect effects

Increased social cohesion and reduction of stigma

Testing and treating at the village level enabled an increase in social cohesion among people in the community as those who were infected found support from others in their community who were not infected, which also helped to reduce stigma. The intervention also generated cooperation, sharing of information among members of the community, and a sense of collective achievement:

The wider social benefits are a sense of empowerment, as the community felt that they had made this happen. So, there was ownership of the fact that they had largely eliminated Hepatitis C in their village. We estimated about 90% of everyone who was infected in that village between the ages of 12 to 80 years got tested, treated and cured. (Global Hepatitis Programme, WHO)

4.1.2 Effects/impacts at different levels (community/user, sub-national, national, regional, global)

Results of scale-up to the 73 villages also showed a high level of success at all steps along the diagnosis, care and treatment process in the villages. The acceptance and uptake of testing reached 92.3% of persons using rapid diagnostic tests, a 100% linkage of all HCV-positive individuals through same-day confirmatory viral testing, initiation of DAA treatment in 91.2% (with the rest referred to the government treatment programme as they were formal sector workers), completion of treatment by 99.9%, and cure in 98.3% of those treated (Shiha et al., forthcoming). Overall, the campaign achieved treatment, coverage and cure of 84.6% of the estimated infected individuals aged 12–80 years old (ibid.). The effectiveness of the educational campaign was not assessed at this stage as it was shown to achieve positive results in Al-Othmanya village. However, the success during scale-up was achieved through addressing challenges that were identified during implementation in Al-Othmanya village, as section 5will examine.

Although ELRIAH no longer implements the model, it has influenced the current government programme to eliminate HCV and there are plans to implement a similar model in Pakistan with assistance from WHO, most likely with modifications to adapt the model to that context, as one key informant noted:

> *What you are hoping is that by getting good results, by disseminating it, that you influence the policy and approach at a national level. And I think we certainly have, that they [the government] are now going into the communities, which they were not before, they are now also doing exactly what we were doing, which is screening for diabetes and hypertension at the same time, and making testing more accessible and being much more proactive ... But they have not been able to do it in the same way with the village workers ... But we think we have strongly influenced the government approach to their national programme and we are wanting to adopt and implement this same approach in Pakistan, which has a very similar epidemic – it's in the general population, a lot of people in the villages are not getting access and there's a lot of new infections. So, this is an example where I think we have influenced national policy and now we think we can apply the same model as a demonstration model in Pakistan, in Punjab, and that's what we are planning to do at the moment.* (Global Hepatitis Programme, WHO)

Thus in 2017 and with support from the World Bank, the Ministry introduced a Hepatitis C pilot screening programme in the Upper Nile region using teams of community health workers travelling across villages to screen for the virus (World Bank, 2017a). By October 2018, the Ministry had initiated a 'huge screening effort' to identify most individuals with HCV who were to be treated, using rapid diagnostic tests. This was to be the first time that 'a screening and treatment programme of this magnitude is attempted ... and will be a large step towards disease elimination in Egypt' (Esmat et al., 2018: 665).

5. Innovation enablers and barriers

This section begins by explaining the main enablers of the 'educate, test and treat' model in three different stages: (1) during design/R&D; (2) during implementation/scale-up; and (3) cross-cutting. Afterwards, the section will present the challenges and how ELRIAH's team solved these, when possible.

5.1 Enablers of success

During design/R&D

Trusted and long-established partnership: Before implementation, a long-term established relationship was built-on between the villagers and ELRIAH, which had been working in those villages and providing treatment to patients since 2011:

> *We are in close contact to the people since our existence, we started to treat people with the oral drug at its early stages and we were effective and people were coming to us to treat more people ... Many from the villages come to me or talk to my colleagues and ask, "we want to treat our villages, but they won't come easily and many don't know what they have so please come and do screening and treat us", so the need comes from the people themselves*. (CEO, ELRIAH)

The presence of ELRIAH in these villages was supported by its 20 satellite facilities throughout Egypt, which also provided villagers with a team of experts and the necessary infrastructure and equipment. Thus, an established relationship of trust was already developed, which contributed to the acceptance of the project.

During implementation/scale-up

Comprehensive and streamlined approach: The model uses a comprehensive approach that includes prevention through awareness-raising, and also testing, treatment and care. Initially, when people were confirmed with HCV, they needed to attend the ELRIAH clinic a few times over a two-week period to obtain additional tests, receive care and start treatment. To simplify the process and reduce visits to the clinic, ALPC has recently implemented an 'all in one day' project to achieve complete linkage to care by offering testing and treatment to villagers on the same day as screening, as described by one key informant:

> *We had the idea and you can consider it an innovation ... I asked my colleagues can we do all in one day? ... Can we do the screening, the PCR, the abdominal ultrasound, liver function tests, in addition to fibroscan for staging of liver disease, clinical evaluation and treatment on the same day? Can we go to a village in the morning and test 500 people and at the end of the day we give treatment? ... The obstacle was the viral load test because ... we needed a portable device that gives us the result on the same day and that is done ideally*

by a GeneXpert[4] [device], we have had a GeneXpert at our hospital since June 2017 ... So we decided to do a pilot and we have done a pilot in one village for Hep C and B, which gives the results in 1–2 hours ... and it was very successful. We repeated this not in a village but in one governmental building where there are 3,500 employees, we did this in three days, almost 1,000 every day and ... we were successful, treatment and screening on the same say. So, this work can be easily replicated either in low-income countries or even in some settings in rich countries. (CEO, ELRIAH)

The pilot for this new innovation took place in Beeden village, Tanah district, Dakahlia, in northern Egypt, where all laboratory instruments and the team were transferred. By implementing screening, testing, clinical evaluation and treatment on the same day, ELRIAH achieved almost complete linkage to care (Shiha et al., 2019b).

Community- and demand-led approach: Involvement of the community was crucial not only during fundraising but also during implementation through the village promoters, who were influential and trusted by villagers. All stakeholders considered that the community-based associations and the volunteer village promoters were a key component for the success of the model at all stages:

In each village they had a village committee, which invited and identified village promoters who were largely women at the front line going to the houses with the healthcare workers, getting people to come out and get tested, organising community sessions, community education … They were the key lynchpin, they were the ones that when the results were available made sure that the patients were aware, had transport to the clinic. And they were central in the enthusiasm and motivation at the village to get the poorer people to get tested and treated. (Global Hepatitis Programme, WHO)

As mentioned by our stakeholders, the village promoters were also members of the community who were influential, trusted, and listened to by the villagers. They were the ones who persuaded the villagers to go through the entire process of screening, treatment and care. Moreover, everyone had someone or knew of someone who was affected by HCV, which contributed to the communities themselves approaching ELRIAH to also have access to treatment. This generated a high degree of ownership of both the process and results.

Services were brought to the communities: As the name of the 'educate, test and treat' programme suggests, the model focused on both prevention to reduce transmissions (through the awareness-raising and education campaign) as well as testing and treatment. Likewise, the fact that the entire project was taking place within the communities and individuals were receiving information and testing services at their household (rather than villagers having to commute to get tested or receive treatment) contributed to the high uptake and equity in access regardless of sex, income level or stage of disease, as reported by the results of the studies (Shiha et al. 2019a; 2018; forthcoming) and stakeholders:

At the villages they wanted to be treated ... The people were not believing that someone was caring for them to the extent that they will come and see them at their place, it looks easy but this is not that simple. People, especially the poor, feel marginalised, so if doctors and hepatologists bring their devices and mobilise to their villages rather than them [patients] going to the main city, the specialists come to them at their place. This was emotionally very important for people at the villages, they were very grateful and at the beginning they did not believe it, so this atmosphere that we were welcomed by the people, and when they discovered that many were treated, they told the others about the success in those villages. (CEO, ELRIAH)

Similarly, when the model was scaled up, patients did not have to collect medication from the clinic as a health worker travelled to the villages to deliver medication every month at designated times.

***Services were free*:** Delivery of free services is also linked to community ownership of the project, which motivated wealthier villagers to donate so that individuals received testing services and treatment for free, allowing those who were previously unable to afford it to be cured:

Every family in the village had one relative with Hepatitis or died from Hepatitis so people already knew there was a problem, but they didn't know how to solve it and they didn't have the money. So the most successful factor was that we offered the treatment for free, so people were eager and willing to be treated because they were poor and couldn't afford the treatment. So that's a key factor that motivated the people to come, we offered treatment and testing for free. (Hepatologist, ELRIAH)

[4] The GeneXpert does not require PCR room settings and uses a sputum sample, being able to give a result in less than two hours.

***Community funding*:** Donations by wealthier villages (linked also to *zakat*[5]) were an important part of the funding base. Funding of treatment contributed by the villagers ranged from 10% to 80% across different villages, and the rest was covered by ELRIAH's donations.

Cross-cutting

Political commitment: The model fitted and complemented the government's interest and commitment to eliminate HCV in Egypt. As has been documented (World Bank, 2017a), the Egyptian President has spoken several times in high-profile speeches and statements about his commitment to eliminate the disease. Similarly, one key informant noted that the President shared his personal interest to implement the model in the country. Although the government has not adopted all components of the model (particularly the use of village promoters), many of the other components (such as mass screening in rural communities in a proactive and systematic way) have been taken up and this campaign is currently underway.

Adaptability: Key informants highlighted the ease of the model to adapt to different contexts. As mentioned, it is planned to adapt and implement the model in Pakistan and one key informant mentioned the interest shared by African countries also affected by HCV. Another key informant noted the feasibility to adapt the model not only to rural areas but also to urban contexts across different settings (e.g. government offices, universities, mosques, etc.).

5.2 Challenges faced and solutions identified

Although, the 'educate, test and treat' model has been successful, certain components have been modified to improve the scale-up process and to overcome the challenges faced during implementation. This section outlines those challenges and describes the solutions that were developed to address them.

During design/R&D

***Limited knowledge and capacity of village promoters*:** Village promoters struggled to deliver relatively complex messages related to infection and transmission, since some had only basic education. To overcome this, ELRIAH offered a more structured and tailored community training package of 1–2 days using printed materials, booklets and videos to prepare the promoters (Shiha et al., forthcoming). This training was more intense than what had been offered in the pilot village, and covered topics related not only to HCV transmission and prevention but also skills in talking to people, answering typical questions, fundraising, data collection and mapping, and preparing work plans and reports.

During implementation/scale-up

***Tensions among villagers*:** In some villages, success during implementation was affected by existing social tensions among influential families competing with each other. Some of these families were encouraging some community members not to test or get treatment:

> *In Egypt we were 100% successful in some villages and 80% successful in others. Success is not linear because we are dealing with people ... In some villages we were confronted with big families that were competing with each other. Sometimes we were in a village through someone and that person had enemies, either political or whatever, but this happened, although this did not prevent us from screening the whole village or giving treatment to most of the patients, the implementation was quite difficult ... This is not always the case, it happened in some villages*. (CEO, ELRIAH)

This challenge was overcome by village promoters facilitating communication between community members and by showing the positive results of the campaign.

***Lower coverage during scale-up due to time and funds to attend clinic*:** Estimated coverage of treatment and cure of infected villagers in the 73 villages was about 84% (compared to 92% in the pilot) (Shiha et al., 2018; forthcoming). According to key informants, this was largely because it was not possible for ELRIAH to provide transport to all patients during scale-up to complete their clinical evaluations and start treatment:

> *When we first started after people had that first test in the village, they all had to go to the [ELRIAH] clinical centre and that involved getting people onto buses and taking them there, having them there all day, bringing them back, and then they used to come back to pick up their treatment ... That was a barrier, that costed money and we thought we had to make it even simpler to people, you've got to make it simple*. (Global Hepatitis Programme, WHO)

[5] Wealthy people in the village were motivated to donate for the project due to several reasons, one being *zakat*, whereby they considered their donation a religious obligation.

Similarly, limited availability and/or cost of transport as well as lack of time due to work commitments (opportunity costs) may have been a disincentive for patients to return to the clinic to complete their clinical evaluation. These challenges motivated ALPC to implement the 'all in one day' project.

Reaching all: Although the awareness-raising, and educational campaign about household transmission was highly successful, it did not cover promotion of the exclusive use of syringes in healthcare facilities or the reduction of unnecessary injections (Shiha et al., 2018). Likewise, sharing the messages to different kinds of people from different background and ages was challenging. To solve this, the campaign diversified materials, the messages were repeated and delivered using different channels (lectures in the villages, at the mosque, at houses), and additional sessions were delivered to local barbers and health workers who were target groups of the campaign:

> *The awareness campaign was not easy to implement ... It was one of the advantages of the project but also one of the most difficult things to achieve ... We had a lot of brochures, videos, songs, all the material that can help, so we used these when we went to the villages. So it was not only giving lectures or talking to the people but giving something to listen, something to see, something to read*. (CEO, ELRIAH)

Cross-cutting issues

Funding: There is an ongoing need for funding for the project. While part of the solution was to fundraise among the wealthier villagers, additional funding continues to be necessary. As mentioned, no government funding was received, according to key informants.

***Divergent interests*:** Although ALPC's model clearly influenced the current government campaign and official documentation invites civil society to collaborate through screening for reaching and prioritising the diagnosis and treatment (Ministry of Health and Population, 2014), it was reported that the project stopped when the government scaled up its own campaign to avoid duplication of efforts. However, one key informant also shared that it was important to have a unified approach and for the government to have a protagonist role and be seen as the champion in efforts to eliminate HCV in Egypt.

6. Lessons learnt

This section presents the lessons learnt by the 'educate, test and treat' campaign during the same three stages: design/R&D; implementation and scale-up. These lessons are based on the literature provided by the campaign as well as interviews with key informants.

During design/R&D

- HCV diagnosis, linkage to care and treatment provided directly in the communities allows low-income patients (who cannot afford transport costs and time to travel for multiple visits) to be diagnosed, receive treatment and be cured.
- Co-funding between wealthier villagers and ALPC has been important to create a sense of ownership among villagers and to promote the sustainability of the project.
- It is important that studies are conducted to understand the differences in prevalence, transmission patterns, and the state of HCV across the population to help develop the most appropriate programme design.
- It is critical that a comprehensive approach is taken so that awareness-raising (through an educational campaign) aimed at prevention takes place alongside testing and treatment.
- Partnerships between government, the private sector, civil society and the media are critical to ensure that messages reach different audiences and to encourage the adoption of safe practices by the general population and in a range of high-risk settings (e.g. hospitals, informal health settings, barber shops, dentists, tattoo parlours).
- The village promoters are key, so it is vital that they receive adequate training before approaching villagers and patients. As they are volunteers, implementers need to make sure that they are motivated and supervised from the beginning and throughout the process.

During implementation/scale-up

- An awareness-raising campaign where there is ongoing contact with the people, responding to the most frequently asked questions, and distributing information through various methods/approaches (videos, posters, etc.) facilitates implementation and scale-up.
- It is important to have simple diagnostic tools and linkage to care (either in the same day or in a single visit) to overcome the barriers that patients face to complete their clinical evaluation.

- Targeting the general population is as important as targeting specific groups of people such as barbers, dentists, and healthcare providers who give injections.

Cross-cutting issues

- Countries with similar HCV prevalence that affects the majority of the population and where many live in rural communities (e.g. Pakistan, Indonesia and Mongolia) could also replicate and adapt the model according to their healthcare infrastructure and epidemiological context. Assessments will be needed to understand the kinds of partnerships and expertise that would be necessary in those particular contexts to make it happen, the role of different members of the community as well as the necessary infrastructure and equipment that would be available and needed (e.g. a hepatologist, his/her lab team and clinical team, nurses, pharmacists, etc.).
- The model is more likely to be scaled up when there is government ownership and political will to eliminate HCV. However, this could also challenge the involvement of NGOs to continue implementation. Partnerships between government and civil society are crucial to maximise positive results.
- To achieve scale-up and reach populations in different settings, substantial investments by governments will need to take place to cover the costs of diagnosis, linkage to care and treatment of those who cannot afford it, including those who are not covered by health insurance or who are unemployed. Currently, there is limited funding at the international level to support national hepatitis elimination plans (WHO, 2017). Governments will need to undertake economic analyses to make an investment case.
- Investing in effective monitoring and evaluation (M&E) and establishing standardised criteria to confirm elimination of HVC, as has been developed for other infectious diseases, is also a key lesson from this case study.
- Real sustainability (and the elimination of HCV) is more likely to occur when the beneficiaries of interventions to eliminate HCV develop a sense of ownership along the process.
- Linked to the above, ownership can be developed by involving the local population (as investors, village promoters) by consulting with them at different stages of the process, and by sharing with them the achievements of their own actions.
- Support to civil society organisations and collaboration between them and the government is important to achieve acceptability and greater coverage.

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3.0 HIV Self-testing case study

SUMMARY BOX

What is the innovation?

HIV self-testing (HIVST) is a process in which a person collects his or her own specimen (oral fluid or blood from a finger print), then performs a rapid HIV test and interprets the result, often in a private setting. HIVST kits take between 5 and 7 steps and between 1 and 45 minutes to provide results. The table below summaries the enablers, challenges and lessons learnt from this innovation.

	Design/research and development (R&D)	Implementation/scale-up	Cross-cutting
Enablers	• Clear, easy and understandable instructions in local language • Privacy and user-led focus	• Diversification of delivery models made testing accessible and appealing to users	• Funding from donors and agreement with the Bill & Melinda Gates Foundation enabled tests at low cost in high HIV burden settings • Political support from government representatives as well as the release of the World Health Organization (WHO) guidelines • Close and constant consultation between communities, researchers and manufacturers
Challenges	• Most kits are second generation assays, which cannot detect the acute phase of HIV	• Concerns and doubts about potential social harms such as suicide, gender-based violence and coerced testing • Stigma and other behavioural challenges (re-testing) continue	• Funding and price point. For example, market competition is limited due to only two WHO prequalified tests • Non-existent, time-consuming or unclear national registration and regulatory processes for HIVST
Lessons	• Involving policy-makers in discussions is a first step • There must be consultations with beneficiaries and efforts to tailor HIVST kits according to users' needs	• Consultation with the target communities gives an opportunity to provide information about what HIVST is, and to discuss doubts, concerns and entry points • Delivering HIVST using several different models is more effective to reach target groups • Providing continued information to users about how to use the test and how to interpret the result is key	• Donors should be involved in consultations with countries across regions and from different income levels to support them on the supply of kits • Effective collaboration through working groups is critical to achieve adequate regulations and national HIVST policies • Support from the media is critical during design and implementation and in disseminating information

1. Introduction

More than 30 years ago, in 1986, the World Health Organization (WHO) first evaluated rapid diagnostic tests for HIV. During the intervening decades, HIV testing services became widely available – routinely through clinical settings and to higher-risk populations through community-based approaches. By 2017, 75% of the people estimated to be living with HIV (28 million out of 37 million) had accessed HIV testing and been diagnosed. Nevertheless, important testing gaps remained. WHO and partners recommended the use of self-tests as an additional tool to overcome these gaps in December 2016.

Unitaid has funded the largest international HIV self-testing (HIVST) programme, covering six countries in southern Africa (Malawi, Zambia, Zimbabwe, South Africa, Eswatini and Lesotho). The HIV Self-Testing Africa (STAR) Initiative

Implementation and Research Project has been at the forefront of this development, catalysing a rapid transition from science to scale through research projects interlocked with public health programmes.

This case study first describes the global targets related to HIV and the evolution of HIVST. It then explores the design, development and implementation of HIVST, mainly in countries which are part of the STAR initiative where HIVST has been piloted and is in the process of being scaled up nationally. The case study will also provide insights into key enablers and challenges that were faced by these countries during design and implementation/scale-up as well as some cross-cutting enablers and challenges. The experiences of these countries could serve as a model for other countries or institutions interested in adopting and implementing HIVST.

2. Context

2.1 HIVST and the Sustainable Development Goals (SDGs)

The HIV epidemic prevails as one of the world's most relevant public health challenges, with SDG 3 focusing on aiming to end AIDS epidemics as one of its targets. An estimated 36.9 million people were living with HIV in 2017, and there are 1.8 million new cases yearly (STAR Initiative, Unitaid and WHO, 2018). Furthermore, more than 9 million people globally (25% of all people with HIV) do not know their HIV status (WHO, 2018a). While globally, most HIV testing services reach women during antenatal care, only 30% of all HIV tests are done with men (WHO, 2016).

Despite considerable scale-up of HIV testing services through facility-based and community-based HIV testing services, access to HIV regular testing services is not equitable. Several obstacles prevent people (particularly men, young women, and members of key populations,[6] which account for nearly half of new HIV infections each year globally) from knowing their HIV status. These obstacles include inconvenience, missed work, long distance to testing facilities, economic costs (STAR Initiative et al., 2018; Population Services International (PSI), 2017), and concerns about confidentiality, stigma, discrimination or criminalisation (STAR Initiative et al., 2018). Other studies have also identified that uptake of HIV testing remains low for other key sub-groups such as adolescents, people living in poverty, and those with less formal education (De Cock et al., 2019; Sande et al., 2018; Cowan et al., 2016).

To tackle the epidemic, ministries of health adopted the United Nations 90-90-90 targets to be achieved by 2020: 90% of people living with HIV will know their status, 90% of those people will be receiving treatment, and 90% of all people receiving antiretroviral therapy (ART) will have durable viral suppression (STAR Initiative et al., 2018; PSI, 2017). Progress towards the 90–90–90 testing and treatment targets has been strongest in eastern and southern Africa, Latin America and high-income countries (UNAIDS, 2018). However, the proportion of people not knowing their HIV status is higher in sub-Saharan Africa. For example, in Malawi, an estimated 35% of men and 18% of women have never tested for HIV and 60% of young people aged 15–19 years have never tested (d'Elbée et al., 2018). Similarly, in Zimbabwe, 39% of men versus 60% of women aged 15–49 had never tested (Cowan et al., 2016).

HIV self-testing, in which individuals perform the tests in private settings at their convenience and read the results by themselves, can play an important role in achieving the 90-90-90 goals, which is critical to the whole treatment cascade. Furthermore, according to UNAIDS (2018), an increase in resources for the expansion of HIVST and community-based testing could prevent almost 200,000 additional deaths between 2018 and 2030.

2.2 History and evolution

HIV testing was one of the first interventions in the international HIV strategy to tackle HIV/AIDS, with the first approved test in 1985 (STAR Initiative et al., 2018). Early testing programmes began in blood donation centres and special laboratory settings. Even as rapid testing (a finger-prick test that offers same-day diagnosis) became available and the possibility of self-testing was proposed, benefits of testing were limited due to the lack of available treatment as well as limited information and stigma against those who tested (ibid.).

Initial efforts focused on pre-test counselling, with protection against mandatory testing and requirement for informed consent necessary to access HIV testing (De Cock et al., 2019; Kojima and Klausner, 2018). Voluntary counselling and testing (VCT) expanded in the late 1980s and 1990s, providing HIV testing to individuals who requested it in confidential stand-alone sites and with strong requirements for pre- and post-test counselling to support newly diagnosed patients (STAR Initiative et al., 2018). Despite these efforts, implementation and uptake of testing was limited; with the VCT-only approach, in 2005, only 12% of people who wanted to test for HIV were able to do so (ibid.).

[6] The WHO (2018a) defines key populations as groups who, due to specific higher-risk behaviours and barriers that increase their vulnerability, are at an increased risk of HIV irrespective of the epidemic type or local context and often have legal and social issues related to their behaviours that increase their vulnerability to HIV. Key populations include men who have sex with men, people in prisons and other closed settings, people who inject drugs, sex workers, and transgender people.

Guidance on provider-initiated HIV testing and counselling (PITC) from the WHO and UNAIDS in 2007 recommended testing to all individuals attending health facilities in high HIV burden settings, as well as to key populations affected by HIV (De Cock et al., 2019). In 2007 and 2008, rapid HIV testing was scaled up through PITC and the number of HIV tests performed in low- and middle-income countries (LMICs) doubled, especially through antenatal care (STAR Initiative et al., 2018). In addition to VCT and PITC, other HIV testing approaches included door-to-door, mobile or workplace outreach, to further expand services. However, informal self-testing was also taking place and was not something new, as it was identified among health workers in sub-Saharan Africa between 2000 and 2010 (Mavedzenge et al., 2011), as explained by one study key informant:

> *For many years, healthcare workers have "borrowed" test kits to test themselves ... About 10 years ago we were involved in a survey in various countries in southern Africa and about 40% of healthcare workers said they had used one of these tests, which were not designed for self-testing but they tested themselves, because they wanted to do it in private. They often knew the person in the clinic so they would much rather do that test themselves. Then they would have the knowledge of their status and then with this could go to a health provider if they needed ... This gave us the idea that self-testing should be available more widely as additional way to provide access to HIVST testing.* (Coordinator, HIV prevention and testing, WHO)

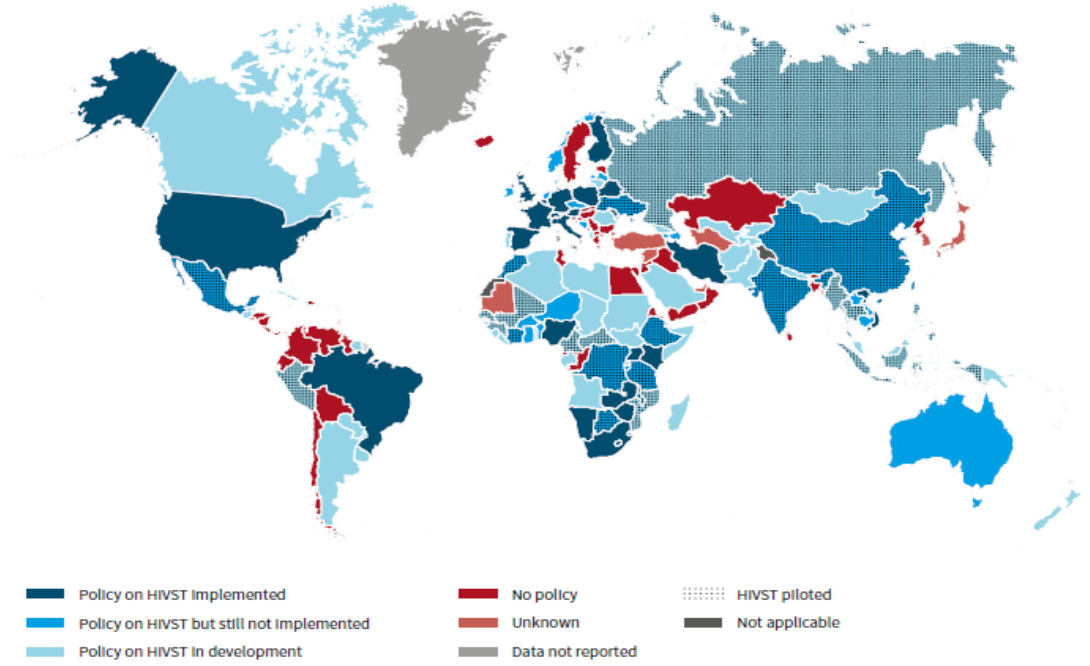
Even though discussions of the potential role of HIVST started early in the epidemic, it was a source of controversy and many policy-makers had reservations about its introduction (STAR Initiative et al., 2018). These were largely due to concerns about potential social harms[7] (e.g. increased domestic violence, marriage break-up, family members or sex workers being coerced into taking tests), lack of counselling, user errors and poor accuracy.

Increased availability and normalisation of HIV testing as well as evidence on the benefits of ART accentuated the need to increase HIV testing. Even with a large and increasing number of HIV tests performed each year, key populations such as men and young people were still being missed and testing services were not reaching those at higher HIV risk (STAR Initiative et al., 2018). A key advance came in 2012 when the US Food and Drug Administration (FDA) approved the OraQuick ADVANCE Rapid HIV-1/2 test, which is the first oral fluid HIVST product that does not require blood and gives a result within minutes. The next key step came in 2013, when interest in HIVST increased and experts from 14 different countries across the Americas, Europe, Africa and Asia congregated at the Brocher Foundation in Switzerland, to discuss the legal, ethical, gender, human rights and public health implications of HIVST scale-up (WHO, 2013) and to explore whether HIVST was 'even a priority', as one interviewee suggested.

In December 2016, HIVST became a testing option recommended by the WHO that can be used to reach undiagnosed populations. Following the WHO guidelines, 59 countries have adopted HIVST policies and, as of September 2019, 54 countries reported they were developing policies (Self-Testing and Policy Hub, 2019). Nine LMICs have also developed detailed operational guidelines (STAR Initiative et al., 2018). However, despite rapid uptake of the policy, implementation of HIVST is limited to 28 countries (see Figure 1).

[7] Social harm has been defined as 'any intended or unintended cause of physical, economic, emotional or psychosocial injury or hurt from one person to another, a person to themselves, or an institution to a person, occurring before, during or after testing for HIV' (Kumwenda et al., 2019: 54).

Figure 1 Map of countries according to HIVST policy and implementation situation (June, 2018)



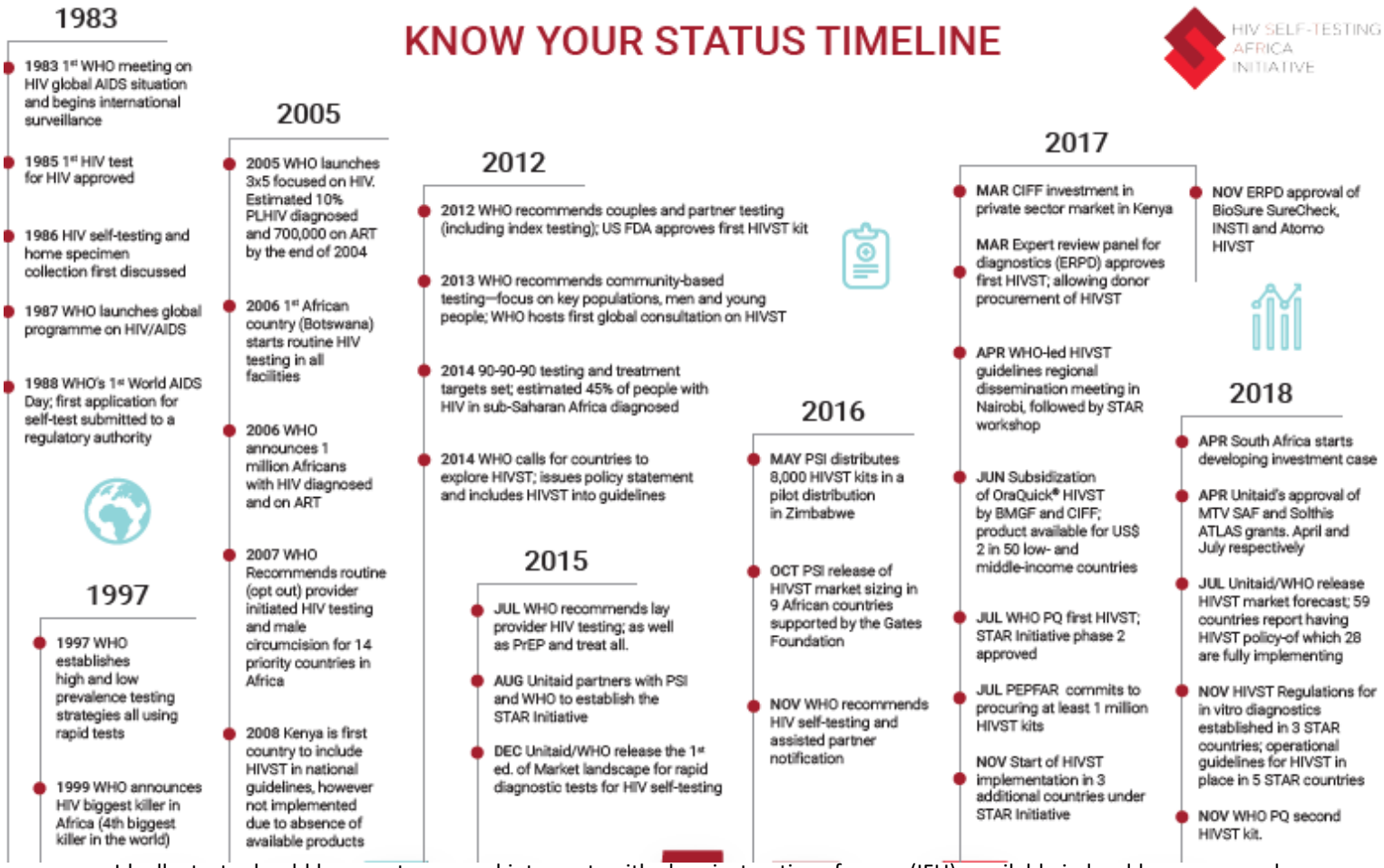
Source: Unitaid and WHO (2018)

As key informants mentioned, the gap between policy and implementation of HIVST at a national level reflects the time required for operationalising policies and regulation, including: establishing short, medium and long-term plans for HIVST; budgeting; developing distribution models; formal national registration of HIVST products; addressing human rights concerns; HIVST monitoring; and identification of target groups to avoid HIVST kits being used by low-risk groups. Similarly, the gap between policy and implementation is also due to a lack of evidence in some countries and a lack of national-level investment to guide implementation and scale-up. About two-thirds of these countries are considered upper middle-income or high-income countries. By 2018, STAR countries were still developing their HIVST operational frameworks, while only Kenya had released full operational guidelines.

In addition, only two HIVST kits have been prequalified by the WHO, although current guidance from the WHO encourages countries to pilot and explore how HIVST can be used to scale up HIV testing (STAR Initiative et al., 2018; The Global Fund, 2016). As a result, locally manufactured HIVST kits with national-level approval have emerged in Belarus, Brazil and Nigeria and other HIV self-tests have been under development (three use whole blood specimens, two use oral fluid specimens, and one uses urine specimens) (Unitaid and WHO, 2018).

A detailed timeline of HIV testing progress from 1983 until 2018 is provided in Figure 2.

Figure 2 Timeline of HIV testing progress, 1983 to 2018



Ideally, tests should be easy to use and interpret, with clear instructions for use (IFU), available in local languages and comprehensible at low literacy and education levels. The WHO also recommends that all positive results of self-tests are followed by further testing by a trained provider at an approved national testing centre (WHO, 2013; 2018b). It also recommends linkage to care following a positive HIV test as well as linkage to prevention and other follow-up services for those with positive and negative test results (WHO, 2013; 2018b).

There are several approaches to deliver HIVST, including facility-based or community-based distribution, secondary distribution through sexual or social networks, integration with related health programmes and interventions, workplace programmes, distribution through pharmacies, vending machines or kiosks, or the internet, and distribution through other public and private sector channels (Unitaid and WHO, 2018). Additionally, HIVST can be provided through assisted self-testing (direct assistance in the form of face-to-face demonstration and explanation by trained providers such as community-based distribution agents, pharmacists or health staff before, during and after self-testing) and unassisted self-testing (individuals only use the self-test kit following manufacturer provided IFUs) (UNAIDS, 2018). The price of HIVST with WHO prequalification or strict regulatory approval varies depending on the setting, market sector and product packaging presentation. In high-income countries, prices in the private sector fluctuate from $20 to $48 per test, while the price charged by public sector and non-governmental organisation (NGO) providers fluctuates from $7.5 to $15 per test. In LMICs, self-test prices fluctuate between $2 and $12 per test in the public sector and $7 and $12 in the private sector.

3.2 Stakeholder involvement

Key stakeholders have been involved at different stages of the adoption, implementation and scale-up of HIVST. This section outlines the role of these stakeholders at each stage, based on key informants' perspectives and the secondary literature.

The STAR Initiative

A key stakeholder involved in the implementation and scale-up of HIVST is the Unitaid-funded HIV Self-Testing Africa (STAR) Initiative. This five-year project aims to: address key market challenges that constrain access to HIVST; make a

quantifiable contribution to the achievement of the UN's 90-90-90 strategy; and reduce morbidity and mortality among people living with HIV (PSI, 2017). The origins of STAR were described by one key informant in the following way:

> *... We [the WHO] started working with the manufacturer who made an oral fluid test that was already used by health care workers for testing in clinics. The oral fuild HIV test was easy to use by just swabbing the gum ... very simple ... no blood. WHO worked with partners on some pilot studies in various places to see whether this could be used for self-testing in different settings. We then wrote a proposal with the London School of Hygiene & Tropical Medicine, the Liverpool School of Tropical Medicine and an international NGO implementer called PSI [Population Service International] for Unitaid. We were very lucky and this enabled a very large-scale project ... This project is called the STAR (Self-testing in Africa) project ... starting in Zambia, Zimbabwe and Malawi ...* (Coordinator, HIV prevention and testing, WHO)

The STAR Initiative is now being implemented in six sub-Saharan African countries (Zambia, Zimbabwe, South Africa, Malawi, Eswatini and Lesotho), working closely with the national ministries of health. The project is designed to reach people with limited access to HIV testing and low rates of testing uptake, particularly young people, men and key populations, including female sex workers and men who have sex with men (Choko et al., 2018). Phase I (from September 2015 to August 2017, including Malawi, Zambia and Zimbabwe) aimed to pilot and evaluate the acceptability and feasibility of HIVST among different target populations and to generate information about how products for HIVST can be distributed 'effectively, ethically, and efficiently' (Cambridge Economic Policy Associates (CEPA), 2018). Phase I also aimed to generate multi-country evidence to inform the WHO guidance and support national-level policy formulation in project countries as well as achieving a reduction in the price of the HIVST. Phase II (from August 2017 to July 2020, including the three initial countries plus South Africa, Eswatini and Lesotho) aims to support governments in establishing an enabling environment for HIVST scale-up and integration into national health systems by ensuring the adoption of cost-effective distribution models that reach their target population (ibid.).

International donors and partners

From 2010, the HIVST approach had been explored through different pilot studies mainly by using rapid diagnostic tests. Thus, there was a need to provide a body of evidence on HIVST (e.g. its impact, acceptability, feasibility, etc.) that would also support the WHO guidance and wider policy shaping. Likewise, for HIVST to succeed, it was important to create a market through providing demand and encouragement of supply (ibid.). In response to these needs, Unitaid approved the STAR Initiative in October 2014. STAR responded to Unitaid's funding scope and interests: projects that have global market and public health impacts from an 'innovation' perspective (Unitaid, 2019). According to one key informant, Unitaid does not fund national programmes but evaluations, so Unitaid is 'in-between' in terms of trials, developing of concepts, and establishing scale-up, which matched the outcomes of the STAR Initiative. With investment from Unitaid, three other projects are expanding access to HIVST, in collaboration with the STAR Initiative: 1) the ATLAS project, which will bring HIVST to West Africa; (2) mass media demand-creation campaigns in South Africa and Côte d'Ivoire developed by the MTV Staying Alive Foundation; and (3) the Fiotec ImPrEP project, implementing HIV self-testing as a strategy to increase demand for pre-exposure prophylaxis (PrEP) in Brazil, Mexico and Peru (UNAIDS, 2018).

Unitaid is scaling down its funding during STAR's phase II, while supporting the transition to adopt HIVST in the national health programmes. Now that the evidence of HIVST is established, donors like The Global Fund and the US President's Emergency Fund for AIDS Relief (PEPFAR) will continue funding scale-up in implementing countries. Similarly, LMICs with national HIVST policies have initiated funding applications and discussions with The Global Fund and PEPFAR (CEPA, 2018). One key informant from The Global Fund stated that the STAR Initiative was crucial to generate an interest for scaling up self-testing funded by The Global Fund in LMICs. The Global Fund also published a briefing note in 2016 to guide countries on how to include HIVST in their applications of reprogramming requests (ibid.).

National governments

The HIVST technical working groups mobilised government commitments. The working groups were established to facilitate national policy development in STAR countries during project implementation. They were chaired by ministries of health, including representatives from the project consortium, national regulatory bodies, WHO, in-country donors supporting national HIV programmes, and civil society organisations (CEPA, 2018). The technical working groups were established in Zimbabwe and Zambia during phase I, while in Malawi there were some challenges mainly due to changing Ministry leadership (ibid.). The working groups in these three countries were also an important space to discuss HIVST and issues around potential social harms, lack of counselling, user errors and other concerns. Other strategies shared by stakeholders to address government concerns and to secure sufficient 'buy-in' from policy-makers included offering technical support through different channels (e.g. providing additional research, producing policy recommendations) that could help countries to identify gaps within their existing HIV strategy that could be addressed by self-testing (e.g. reaching husbands of pregnant women, youths, key populations). Offering technical support and policy recommendations to governments on the type of HIVST delivery models more suited to their national context and needs

was also part of the strategy to address policy barriers, as key informants noted. Similarly, in phase II countries such as South Africa, technical working groups were also established in order to draft national guidelines, coordinate the activities of implementing partners, review research findings and advise on messaging on HIVST (WHO, 2018c).

Civil society organisations

Civil society organisations (CSOs) are another key stakeholder for the implementation of HIVST. CSOs are members of the technical working groups and are also able to advocate and achieve policy goals, mobilise investment, establish strong supply of HIVST, and assist with the design of marketing strategies and distribution models (PSI, 2017). For example, Zambart (the implementer in Zambia) has an established civil society group called the Community Partners Platform (CPP), drawn from organisations that represent people living with HIV such as the Network of ARV Users, HIV/AIDS and Malaria (CITAM) and AfroCAB, among others) who discussed the STAR study in their first meeting in 2016 (LSHTM, 2016). Similarly, non-governmental, community-based and faith-based organisations in sub-Saharan Africa have gained valuable and extended experience and expertise with integrating HIVST into outreach services, as well as in motivating individuals to access HIV treatment and prevention (WHO, 2018b). Community-based distribution (e.g. using door-to-door, workplace, or peer educators – trusted individuals by the local community, or representative of the community the outreach is intended for) has been especially beneficial to reach first-time testers (including men, adolescents, couples, key populations) and in rural areas, where literacy may be low (ibid.).

Private sector

Key informants highlighted that private sector distribution models were important. However, STAR focuses on public sector delivery models, and does not encompass private pharmacy-based distribution. Nevertheless, the private sector market is forecast to contribute 7.3 million (6.6 million–8.0 million) self-test sales in 2020. Indeed, the WHO (2018c) recommends the use of private sector resources for HIVST implementation (e.g. through pharmacies and other retail venues such as the internet and social media) as these channels might be important for scaling up. Although the sale of HIVST kits through the private sector in LMICs has been limited, forecasts suggest there will be significant market growth in middle-income settings from 2017 to 2020: from 0% to 21% in lower middle-income countries and from 0% to 64% in upper middle-income countries (Unitaid and WHO, 2018). To support financing for HIVST through the private sector, it will be important to increase the availability and affordability of quality products as well as to generate consumer awareness and demand for HIVST (WHO, 2018c).

4 Impacts/effects of the innovation

This section examines the overall effects of HIVST, focusing firstly on direct effects and then moving on to explore the indirect benefits. As mentioned in section 3.1, several models of distribution have been used during its piloting and implementation, which will be assessed at the end of the section.

4.1 Overall impact of the innovation

By November 2018, the STAR Initiative had distributed 2.3 million HIVST kits in the six countries through different modalities including open access (e.g. pharmacies, community-based outlets), community-based distribution (e.g. door-to-door, workplace, peer educators, resident volunteer-counsellors), and facility-based distribution (e.g. HIV testing clinics, public sector facilities). STAR has estimated that 81% of people with HIV in those six countries are now aware of their status as a result of the intervention, compared to only 45% before (STAR Initiative et al., 2018). The literature and key informants identified that HIVST has had positive overall effects, including acceptability (willingness to take the test) (Choko et al., 2019; Hatzold et al., 2019; Indravudh, Choko and Corbett, 2018; Figueroa et al., 2015); increased coverage among men, young people and first-time testers (STAR Initiative et al., 2018; UNAIDS, 2018); feelings of empowerment (Kumwenda et al., 2019; Choko et al., 2017); increased uptake (Mulubwa et al., 2018; STAR Initiative et al., 2018; Choko et al., 2017); and adequate performance from no or little support from health workers (Figueroa et al., 2018; Krause et al., 2013). Mixed evidence exists in relation to linkage to HIV treatment and prevention services (STAR Initiative et al., 2018; UNAIDS, 2018) and social and behavioural effects such as coercive testing among couples and among sex workers by clients or sex partners (Kumwenda et al., 2019; Mulubwa et al., 2018; STAR Initiative et al., 2018). These effects are summarised in the following section.

4.1.1 Direct and indirect (unintended) impacts/effects

Direct effects

Acceptability

HIVST has increased acceptability of testing (98% acceptance) among men and adolescents (Unitaid, 2018) and this finding is supported by evidence from Malawi (Choko et al., 2019; 2015), Zambia (Mulubwa et al., 2018) and Zimbabwe (Indravudh et al., 2018). Hatzold et al. (2019) found that acceptability indicators in these three countries were high in all age groups using several different models for delivery such as bus terminals, HIV testing services (HTS), workplace or truck stops. Likewise, the review conducted by Indravudh et al. (2018) in sub-Saharan Africa evaluating oral fluid tests

confirms a high willingness to self-test among men, young people, serodiscordant couples, and sex workers and their partners. Principal incentives include convenience related with time and cost savings, control over the testing process, privacy and confidentiality, ease of use, and painlessness of the oral fluid self-test version. The reviews conducted by Figueroa et al. (2015) and Krause et al. (2013) in low-, middle- and high-income countries also identified high acceptability using oral HIVST kits.

Coverage

HIVST is reaching more men, young people and first-time testers (Hatzold et al., 2019; Unitaid, 2018). The STAR Initiative distributed more than 750,000 HIVST kits during its first years of implementation (2015–2017) across Malawi, Zimbabwe and Zambia, increasing testing coverage by 21%–35% among men and 22%–28% among women (UNAIDS, 2018; PSI, 2017) and by 14%–27% among first-time testers (STAR Initiative et al., 2018). Indeed, Hatzold et al. (2019) identified that a higher proportion of male self-testers (22.3%) were first-time testers than women (17.1%) in all three countries. The same study also noted that the highest proportions of first-time testers were among young men (16–24 years) and older men (>50 years) (18.7%–35.9% and 13.8%–26.8% respectively) in all three countries.

Increased uptake

According to UNAIDS (2018), HIVST has been up to twice as effective at finding people who are HIV positive than conventional testing. The systematic review conducted by Johnson et al. (2017) looking at studies which offered free oral HIVST kits found that HIVST is associated with increased uptake and frequency of testing compared to standard testing services, and particularly among those at risk who may not otherwise test. There is evidence on this effect using different delivery mechanisms and among different groups of individuals. In Zambia, Mulubwa et al. (2018), using a cluster randomised trial (eligible participants were given the choice of HIV testing using HIV self-testing or routine door-to-door HIV testing services), provided evidence that a 3-month intervention of door-to-door distribution of HIVST kits increased knowledge of HIV status (defined as a participant self-reporting their HIV positive status to a community HIV care provider or accepting an offer of HIV self-testing and having the result recorded by the care provider). Knowledge of HIV status was slightly higher (68%) among the HIVST group, compared with 65% for those who were given routine door-to-door HIV testing services, particularly among men and adolescents aged 15–19 years who were not at home during household visits but who tested and reported their results. In Malawi, Choko et al. (2019) and Choko et al. (2017) found that high acceptability and uptake among men was also achieved under secondary distribution models such as women in antenatal care services who were given HIVST kits for their male partners. Also, in Malawi, trained resident volunteer-counsellors offered oral HIVST kits to adult residents, and uptake reached 83.8% of the population where the study was implemented (Choko et al., 2015).

Indirect effects

Empowerment

HIVST gives individuals control of when and where to test (Unitaid, 2018). For example, men in Malawi preferred HIVST (men were given the tests by their wives who had attended antenatal care services) compared with standard testing, as they found it convenient and offered them privacy as well as reducing stigma (Choko et al., 2017). Similarly, women in the study by Kumwenda et al. (2019) also reported HIVST to be empowering as it helped them to feel in control of the testing environment and allowed them to discuss testing with their partners. Youths in the study by Indravudh et al. (2017) in Malawi and Zimbabwe reported that HIVST provided them with autonomy, control, respect and confidentiality.

Linking people to care and prevention

Some studies have suggested concerns about linkage to HIV prevention and care services as well as treatment to maximise the benefits of HIVST (Indravudh et al., 2018). For example, some users have expressed concerns regarding the potential lack of counselling (Choko et al., 2017) or experienced inadequate counselling after a positive result (Krause et al., 2013). In Namibia, for instance, only 8% of those who were confirmed HIV negative after self-testing were linked to PrEP services through peer distributors who aimed to assist people to reach further treatment and prevention services, highlighting existing challenges to linkage (Unitaid and WHO, 2018).

However, other evidence suggests that more people are linked to HIV treatment and prevention services through HIVST than through other forms of testing (STAR Initiative et al., 2018; UNAIDS, 2018). The STAR Initiative has been evaluating the effects of HIVST on prevention, including saving health workers' time and facilitating uptake of PrEP. Evidence from Malawi (Choko et al., 2019) showed an increase in the proportion of male partners who were reported to have tested for HIV and linked into care or prevention within 28 days (through antenatal care partner-delivered HIVST kits) when they received a financial incentive. Randomisation was to either standard of care (SOC) through a clinic invitation letter to the male partner to attend the clinic for HIV testing and to receive post-test services, or one of five intervention arms that provided women with HIVST kits for their male partners and a conditional fixed financial incentive of different amounts to link to care. The study showed that male partner testing and linkage increased from 17% with SOC, to

between 87% and 95% with the oral HIVST kits, suggesting that additional interventions such as financial incentives might encourage linking to care and prevention services. Similarly, participants in the study by Choko et al. (2017) in Malawi considered that a fixed financial incentive of approximately $2 would increase linkage as it would help to cover transport and opportunity costs.

Similarly, some evidence suggests different preference for linkage into care services following a reactive HIV self-test in Zambia and Malawi. D'Elbée et al. (2018) in Malawi found that participants showed a strong preference for separate HIV services at health facilities, while in Zambia participants had a preference for inclusive services. Community-based confirmatory testing (at the participant's or counsellor's home) was preferred to facility-based confirmation. Thus, location for HIV care services matters, as well as how these are provided.

Social and behavioural effects

Literature reviews (Indravudh et al., 2018; Figueroa et al., 2015) and the STAR Initiative identified that the incidence of serious social harms related to HIVST has been consistently low, with no cases of suicide or adverse emotional reactions to positive tests, and few reports of intimate partner violence. These findings are confirmed by studies in Zambia (Mulubwa et al., 2018) and Malawi (STAR Initiative et al., 2018). Similarly, in Malawi, Kumwenda et al. (2019) identified very few cases of social harm events in their sample (0.011%); those they did find were mostly related to marriage break-ups. The same study also found that couples reported some benefits from HIVST, such as facilitating more discussion within the relationship, building trust, enhancing partner fidelity, and increasing efforts to reduce risky sexual behaviours.

Nevertheless, some coercive testing has been identified among couples who feel they should know each other's status (Indravudh et al., 2018). Likewise, coercive HIVST has been observed among men and individuals who self-tested with their partners (Choko et al., 2015), and among female sex workers who reported frequent coercion by employers, facility owners and peer HIVST distributors (Kumwenda et al., 2019).

Performance

Figueroa et al. (2018) conducted a systematic review to assess the reliability and performance of HIVST when assistance was provided (by a trained healthcare worker) or not in different country settings. Their review show that self-testers could reliably and accurately do an HIV self-test whether assistance was provided or not. Similarly, the literature review by Krause et al. (2013) identified that most individuals were able to perform HIVST accurately with little or no support from staff.

4.1.2 Impacts of different models of distribution

The literature suggests that the effects of HIVST are very context-specific across distribution models and groups of users.

Community-based

Community-based approaches to HIV self-testing involve distributing HIV self-testing kits to community members through volunteers or community health workers. This approach can involve receiving some supervision from the community provider before and/or after individuals test themselves for HIV in private. Pre-test support may include a demonstration of how to use the test and interpret the result, as well as information on where and how to seek additional support, further testing and services for HIV prevention, care and treatment. Post-test support may provide an opportunity for community members to disclose their result, and may also include face-to-face counselling, peer support and referrals for additional services for HIV prevention, treatment and care (UNAIDS, 2013). Community-based HIVST distribution has been recommended to contribute to activities such as national HIV testing campaigns and targeted campaigns in districts with low testing coverage, and as a way to provide ongoing testing access in remote communities (Hatzold et al., 2019; Mulubwa et al., 2018; Choko et al., 2015). However, community-based distribution is expensive. In the study conducted by Mangenah et al. (2019), the recurrent costs of door-to-door community-based HIVST distribution in 71 sites across Malawi, Zambia and Zimbabwe were between 70% and 92% of the total costs, and 20% to 62% higher than routine facility-initiated HIV testing services.

Clinic distribution

Clinic-based distribution has been used to reach individuals who have not been reached otherwise (Hatzold et al., 2019; STAR Initiative et al., 2018). Offering HIV self-testing through clinics increases testing coverage among patients (particularly seen among female sex workers in Zimbabwe) while saving health workers' time (STAR Initiative et al., 2018). Likewise, in Zimbabwe, HIVST was offered as another option to provider-delivered HIV testing services to patients accessing other health services at outpatient departments of 42 clinics. After the introduction of HIVST at these clinics, the number of patients tested for HIV almost doubled from 529 to 955, in six months (ibid.). In the same study, around 30% of all those tested at the clinic opted for self-testing over provider-initiated testing. Hatzold et al. (2019) observed

that integrating HIVST in clinical settings reached over 80% of men and women accepting HIVST when offered as an alternative to provider-delivered HIV testing. Thus, the authors of that study suggested that providing HIVST in clinical settings promises to contribute where testing capacity is limited or poorly implemented.

Workplace distribution

HIVST is distributed through work programmes of occupations traditionally taken up by men and other key or high-risk populations (lorry drivers, miners and fisherfolk) (CEPA, 2018). The WHO (2018a) recommends the use of HIVST by male workers in such industries as they might not have easy access to HIV testing services, and the workplace may be the best place to reach them. HIVST kits distributed in male-dominated workplaces in South Africa, where undiagnosed HIV burden is high, reached men previously untested or not re-tested in the past 12 months. Among participants, 4% who self-tested and shared their result were diagnosed with HIV, and more than half of these men started treatment (STAR Initiative et al., 2018).

Secondary distribution

Secondary distribution (primarily through the partners of people with HIV, high-risk populations and to postpartum women) has fostered high rates of uptake, particularly among high-risk men (ibid.). Choko et al. (2017) found that HIVST secondary distribution via antenatal care services was supported by male and female participants over facility-based HIV testing, given that it fits into men's lifestyles, particularly their working commitments. Likewise, in a cohort of 280 pregnant and postpartum women and sex workers, 75%–91% of participants across groups distributed kits to their partners and 90% of sex workers also distributed kits to clients (Thirumurthy et al., 2016).

Home-based and peer distribution

In Uganda, Choko et al. (2018) found that distribution mechanisms such as peer networks, among men offering HIVST kits to their peers in fishing communities, was a successful strategy to increase uptake, as 87% of participants reported having self-tested immediately upon receipt of the kit (including 25% of participants who had never been tested). Similarly, in Nigeria, self-identified gay men distributed kits to their peers, reaching 17.9% of participants who were first-time testers (UNAIDS, 2018). Regarding home-based distribution, young people in Malawi and Zambia preferred low-cost, home delivery HIVST as it offered greater discretion around their sexual debut (Indravudh et al., 2018).

5 Innovation enablers and barriers

This section explores the enablers and challenges faced during three phases of the HIVST cascade: (1) during design/R&D; (2) during implementation; and (3) cross-cutting factors. Although some of the challenges described still persist, the perspective of key informants shows how some other challenges were solved and decisions taken by different stakeholders to achieve better results during different stages.

5.1 Enablers of success

During design/R&D

Clear/easy local language instructions: Improvements in the design of HIVST kits were important for success of the initiative. For example, clear, easy and understandable instructions in local languages using multiple approaches that consider literacy levels (e.g. videos, animations, diagrams, in-person demonstrations) were key factors to achieve high acceptability and performance by users. For example, in Uganda, Choko et al. (2018) showed that improvements in the manufacture of HIVST kits were important. Most participants found the instructional leaflet that accompanied the kit useful, as it was clear and translated into the local language. Similarly, the systematic review by Figueroa et al. (2018) found that people were more likely to use the HIV self-tests correctly when they had received an in-person demonstration of how to do the test and interpret the result. Likewise, their ability to use the test correctly increased when they could access or receive assistance over the phone, through the internet or with additional visual instructions (videos, animations, diagrams), and when clear instructions were provided. These findings are confirmed by Choko et al. (2015) in Malawi where, in a context of low literacy, users were given a short video demonstration, which was identified as a key factor in maintaining high accuracy of use. Thus, using multiple approaches such as in-person demonstrations, visual tools for instructions or providing them over the phone were all important design characteristics that helped maximise reach to non-literate individuals.

Privacy and user-led focus: Users have reported their willingness to self-test due to greater convenience in terms of time and cost savings (Cambiano et al., 2015), control over the testing process (Indravudh et al., 2017), privacy and confidentiality (Krause et al., 2013; Mavedzenge et al., 2011), ease of use and painlessness of the oral fluid self-test version (Indravudh et al., 2018; 2017; UNAIDS, 2013).

During implementation/scale-up

Diversification of delivery models: Unitaid and WHO (2018) suggest that HIVST kit type (oral or fluid) does not seem to have a major influence on user choice; however, the report suggests that diversifying and offering the choice of available self-tests in national interventions will probably make testing accessible and appealing to more people. Thus, having various kinds of delivery models (e.g. community-based distribution; secondary distribution through antenatal care or people living with HIV; provider-initiated, clinic distribution, offered at men's workplace, integrated with HIV testing services for key populations) and using channels that can also be informal and spontaneous (e.g. peer distribution) as appropriate for different settings/contexts is another important consideration for successful implementation.

Cross-cutting factors

Funding from donors also allowing for low-cost tests: The funding from donors has been recognised as a critical enabler to implement HIVST and to offer tests at low cost, particularly in the countries where the STAR Initiative has been implemented. The core of HIVST planned procurement and donor funding that supports the 2017–2020 forecast was mainly provided by Unitaid, The Global Fund and PEPFAR, exceeding 1 million tests in 2017 and estimated to grow rapidly to 6.4 million (12.9 million – 19.3 million) by the end of 2020, driven largely by confirmed procurement of HIVST in five countries: Kenya, Malawi, South Africa, Zambia and Zimbabwe (Unitaid and WHO, 2018). The lowest price per test is $2, available in the public sector in 50 high HIV-burden settings through an agreement between the Bill & Melinda Gates Foundation and the manufacturer OraSure from mid-July 2017 covering the next four years. This is important as evidence shows that HIVST is highly accepted and increased uptake is observed when provided at no or very low cost in the case of youths in Malawi and Zimbabwe (STAR Initiative et al., 2018; Indravudh et al., 2017). In Malawi, this was seen to be particularly important for youths who were not working or financially dependent on their families (Indravudh et al., 2017).

Political support: As mentioned, although many policy-makers had reservations about the introduction of HIVST due to potential issues such as social harms or lack of counselling, nowadays more key stakeholders in developing countries, including policy-makers and government officials, have been supporting its introduction after evidence showing its effectiveness (STAR Initiative et al., 2018; Makusha et al., 2015). Similarly, greater evidence relevant to certain policy gaps – including social harm, usability, acceptability, preferences and user demand – supported the adoption of HIVST policies (CEPA, 2018). This positive evidence was supported by the WHO, which released guidance in 2016 recommending HIVST as an additional testing approach, as well as WHO prequalification of the first HIVST in 2017. Recently, implementation has been increasing, as shown in section 2.2. Indeed, by the end of 2018, several quality-assured HIVST products had been registered and four STAR Initiative countries drafted regulations related to in vitro diagnosis, including HIVST kits (STAR Initiative et al, 2018).

Other reasons that explain the adoption of policies are government's interest to know how HIVST could be used effectively and at scale, and the ongoing formal and informal dialogues that take place between project partners and governments (CEPA, 2018). These are illustrated by Zimbabwe, Zambia and Malawi. Before STAR, none of these countries had HIVST policies. However, official documents in Zimbabwe (e.g. the National Guidelines in HIVST Testing and Counselling, 2014) and Malawi (e.g. the National HIV Prevention Strategy, 2014) included HIVST as possible interventions to increase testing rates. Likewise, PSI and research partners had been conducting in-country research for several years prior to STAR and had established good relationships with policy-makers, as the STAR Research Director reported. This close relationship also allowed informal project interactions beyond the technical working groups that kept governments updated on STAR's findings (ibid.). In Zambia and Zimbabwe alike, government ownership is reflected in their current processes of developing the operational frameworks that will guide scale-up at the national level.

Close interactions and collaboration: Close and constant consultations between communities, researchers and manufacturers allowed for the improvement of the kits during the design phase, as one key informant noted:

> *When work manufacturers who design self-testing kits (there are lots of manufacturers who make HIV point of care tests that could potentially be adapted for self-tests) we consider the specifications that would make them a suitable product. For example a test kit which was not complicated to use and had a few number of steps, making sure that the product is stable in settings with high temperatures, that the packaging is robust, and importantly making sure that the instructions for use are very clear for the populations who will be using them... When developing instructions for use we coordinated work with various groups of communities, rural, urban, young, old, etc. This included observing how people could perform self-tests and asking them to comment on how easy the instructions were, what was clear and what was not clear ... With self-tests it is important to read the results after a specific time. This may vary from five to 30 minutes deending on the product. So, this information on the 'read time' has to be well communicated in the instructions for use, understanding how people can do this, by for example, using mobile phones. The instructions for use also have to be trabslated into appropriate languages. Checking back and forth with the communities to make*

sure that the instructions are understood and using pictorial instructions as much as possible. (Coordinator, HIV prevention and testing, WHO)

5.2 Challenges faced and solutions identified

During design/R&D

Technological limitations: Technological limitations of HIVST kits are noted in the literature and by key informants. Most kits are second-generation assays, which detect immunoglobin G antibodies (IgG) but not immunoglobin M antibodies (IgM) (third generation) nor viral antigens (four generation) and nucleic acids (Indravudh et al., 2018). Second-generation tests require a longer window period of 28 days between infection and test positivity. Third-generation tests can detect the acute phase of HIV, but this is still not possible with the oral HIVST products. An ideal situation, according to one key stakeholder, would be more availability of blood-based HIVST kits as well as third- or fourth-generation oral HIVST kits.

During implementation/scale-up

Doubts at the community level: Community members raised concerns and doubts about potential social harms such as suicide, gender-based violence and coerced testing. Informal consultations with community members and organisations of people living with HIV were key to address these concerns and gain community support during the introduction of HIVST, as one key informant highlighted:

> *We have to listen to communities. We held a large workshop in Nairobi with about 20 or 25 countries to only talk about self-testing ... and someone from a community group in South Africa said, "I don't believe in this at all, I think self-testing is terrible, everyone is going to be committing suicide, you are really doing something very dangerous here". So I said "let's talk about it". So a couple of months later, WHO held a community consultation in South Africa and we asked people to come and meet with us. We asked groups from organisations of people living with HIV, women's groups, youth groups and organisations that support communities. We sat down and we discussed and we listened to all their concerns. This was incredibly helpful to understand concerns and gave us an opportunity to provide information to reassure them, but also to make sure that we really understand their concerns, particularly around the potential for coerced testing and unintended social harms. The community can support in not allowing this to happen , helping to report misuse of self-testing, considering the most acceptable and effective ways of distributing HIVST kits, providing information to communities about HIVST and the support service available – including where to go to get tests confirmed and access treatment and prevention services and the social and emotional support... Wherever we go and every step of the way, you are never going to succeed unless the community is really involved and you really listen to the community.* (Coordinator, HIV prevention and testing, WHO)

As a result of consultations with the communities and community organisations, the WHO released its 'key questions, answers and messages for community organizations' to continue addressing these kinds of concerns (WHO, 2018b) and the STAR Initiative also added information to its website (www.HIVST.org), to assist ministry officials, implementers, researchers, and others interested in HIVST.

Ongoing stigma and other behavioural challenges: Although confidentiality and privacy help to reduce issues around stigma, key informants observed unintended consequences when distributors are stigmatised by the community, especially by sex workers:

> *... when we were doing that community-based implementation in those three countries [Zimbabwe, Zambia and Malawi] and we saw the evaluation data, one of the things that came up with the sex workers implementation through a community-led approach is that sometimes the distributors themselves are stigmatised by the community and this is something that I don't think we really thought about. People were thinking "maybe this person is distributing self-tests because they have HIV". So maybe there are some challenges around the community and having this agreement in the communities about who should give the self-test and to understand this underlines values within communities that really start to come out ...* (WHO lead for the STAR Initiative)

Similarly, some key informants observed unnecessary re-testing among those who want to re-confirm their HIV status, or people testing more frequently than they need to. Sharing information and clear messages about what HIVST is and who it is for were mentioned as potential solutions to this issue.

Cross-cutting factors

Funding and price point: Based on data provided by Unitaid and WHO (2018), although donors have played a key role in funding 2.1 million (30%) of the 7 million tests that will be procured in 2019 (in addition to 2.2 million or 31% that were already planned for procurement), there were still 2.7 million tests (39%) with no known resources committed to their procurement by the end of 2018. Similarly, for 2020, 74% of projected self-test kits have not yet been funded, which presents a challenge to continuing scale-up. Furthermore, market competition is limited due to only two WHO prequalified tests, which dominate the donor-funded market. The price negotiation between the Bill & Melinda Gates Foundation and the manufacturer OraSure, which lowered the price of the OraQuick product to $2 per kit, has made market entry more difficult for manufacturers who cannot compete with that price at the volumes they produce. Manufacturers need more predictability related to advance information or forecasting of procurement so they can commit the investments required (CEPA, 2018). However, key informants also mentioned that awareness of HIVST is still low among target populations in many contexts, which could compromise procurement. Moreover, key informants also pointed out that barriers to affordability of HIVST kits are more persistent in middle-income countries because they cannot benefit from cheaper prices, as high-burden low-income economies do:

> *... In countries like China, India, Mexico, things are often more complicated because they can't always get the HIVST kits at cheaper prices, they don't have often access to the big donor funds that the low-income countries do. These large countries have a lot of [vulnerable] people who could benefit from self-testing. For example, in Mexico gay men, in India sex workers and gay men, in China gay men – they are at high risk of HIV and do need support for testing. Regulatory issues and costs are big barriers ... But hopefully there will be possibilities to negotiate with manufacturers because they [self-test kits] are not expensive to make and in high volumes manufacturers can reduce prices and give middle-income countries a lower price*. (Coordinator, HIV prevention and testing, WHO)

Legal barriers: For an HIVST kit to meet the rigorous regulatory standards of the International Medical Device Forum, it must demonstrate the required stability and accuracy, but also take into account mechanisms for ensuring that the kit performs optimally in the hands of intended users (Dacombe et al., 2019). Non-existent, time-consuming or unclear national registration and regulatory processes are a barrier to introducing and scaling up HIVST in public and private sector markets (Unitaid and WHO, 2018). Regulators of HIVST would usually consider HIVST kits as a higher-risk medical device due to the possible severe outcomes of an incorrect result and its use by non-professionals, thus HIVST would usually be under the greatest degree of regulation (ibid.). As such, regional and national regulatory systems for HIVST are generally poorly developed and for most countries planning to use HIVST as part of their strategy, it remains unregulated (ibid.).

This is illustrated by the context of sub-Saharan Africa, where unregulated and low-quality products are available for purchase in certain markets (Indravudh et al., 2018). In the study by Dacombe et al. (2019) in Malawi, Zambia and Zimbabwe, national-level key stakeholders indicated that they had a poor understanding of the process and requirements for HIVST regulations. Indeed, the lack of an effective regulation system and coordination approach (between health ministries, national reference laboratories and the regulators of tests on specimens taken from the body) was perceived as a concern for all respondents in all countries. Another key concern was the potential for entry of unregulated and poor-quality HIV self-tests sold by the private sector. Although this was not observed in Malawi and Zambia, most policy-makers in Zimbabwe considered that HIVST was already available in the private sector. Likewise, Unitaid and WHO (2018) noted that lack of clarity or lack of national regulations in some contexts is limiting market entry for new, quality products. One way to solve problems with the regulatory system in STAR phase I countries has been to organise workshops comprising regulators, laboratory technicians and policy-makers. These workshops have discussed plans towards a harmonised regulatory system in these countries and allowed participants to share lessons learned across all three countries (CEPA, 2018).

6. Key lessons/findings

The combined evidence from the literature review and key informant interviews suggests that HIVST is contributing to efforts to improve individuals' knowledge of their HIV status and is also a first step towards accessing HIV treatment and prevention. However, evidence on measurement and actual linkages to post-test services is mixed (Choko et al., 2019; D'Elbée et al., 2018; Kojima and Klausner, 2018). HIVST also addresses the costs and barriers to uptake of HIV testing services (STAR Initiative et al., 2018) that particularly affect adolescents and young people, men, and key populations (Choko et al., 2019; D'Elbée et al., 2018; Kojima and Klausner, 2018). HIVST also contributes to reaching people earlier and facilitates re-testing among individuals with ongoing HIV risk (De Cock et al., 2019). Important findings and lessons emerged during design/R&D, implementation/scale-up and other cross-cutting areas, and these are summarised below.

During design/R&D

- Before implementing HIVST, key informants recommended (particularly to implementing agencies) involving policy-makers in discussions as a first step to solve doubts about potential challenges (e.g. coercion, stigma), regulation steps, and to be clear about how HIVST will contribute to a government's broader HIV strategy.
- Key informants also recommended that implementers and agencies interested in investing in self-testing talk to key stakeholders such as the WHO, UNAIDS, PSI and others, which can provide lessons and recommendations, and to read the available documents such as the WHO strategic framework.
- Consultations with potential users and efforts to tailor HIVST kits to their needs is also critical for acceptability and to ensure adequate performance.

During implementation/scale-up

- Consultation with target communities, including groups from organisations of people living with HIV, gives an opportunity to provide information about what HIVST is, and to discuss any doubts or concerns as well as possible entry points.
- Continuing to increase awareness about when to test and who should test is important to avoid re-testing behaviour and to achieve rational use of HIVST kits.
- Delivering HIVST using several different models (e.g. home-delivery, workplace delivery, peer distribution, clinic-based, community-based, pharmacy, etc.) is more effective in reaching a higher proportion of men, young people and first-time testers, although preferred models by groups of users are context-specific.
- Ongoing studies and consultations with users of HIVST are needed to continue reaching people through different distribution models.
- It is vital to provide ongoing information to users to make sure that HIVST users know how to use the test and how to interpret it. Options include through telephone hotlines, package inserts, mobile phones, videos or computer-based programmes. For those who test positive, information on follow-up support and referral by a community health worker or home-based care is also important.
- Knowing the gap that HIVST could fill can contribute to reducing the burden on facilities from frequent re-testing or testing from low-target populations.

Cross-cutting issues

- There remain economic barriers to introducing HIVST, especially in middle-income countries such as India, China or Mexico, which do not benefit from donor funding. Donors should be involved in consultations with these countries as well as low-income countries in other regions of the world who have not benefited from a large initiative such as STAR.
- Regulation for HIVST can be a barrier to introducing it in public and private sector markets; governments need to re-examine their regulatory and market supervision system to protect consumers from ineffective devices and to increase the supply of quality kits available in the private sector, particularly pharmacies.
- Good/effective collaboration across ministries and between different sectors (regulators, ministries, reference laboratories, implementers) through working groups is critical to achieve adequate regulation and national HIVST policies.
- Support from the media is critical during design and implementation in disseminating information about what HIVST is, what it is not, and how it can help a national HIV strategy, as well as in supporting large-scale promotion campaigns needed to generate demand and facilitate market growth.
- Different models of linkage into prevention, treatment and care for self-testers will need to be explored as the evidence on linkage to services after self-testing is mixed.

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4.0 MDiabetes India case study

SUMMARY BOX

What is the innovation?

The mDiabetes programme in India, based on an mHealth model, sends text messages to large numbers of users to improve their lifestyle and health-seeking behaviour to prevent diabetes. Users are registered by dialling a given phone number (missed phone call) or through a website. Based on their response, participants are grouped into categories (e.g. persons with diabetes, pregnant/lactating women, high-risk individuals) and receive messages on healthy living for six months.

	Design/ R&D	Implementation / scale-up	Cross-cutting
Enablers	• Use of established information technology (IT) infrastructure that reduces costs and increases reach of users • Use of texts that can be sent to the most basic mobile phones in a practical, fast and convenient way, reaching users from different regions and socioeconomic status	• Text messages are short, simple and easy to understand, and are tailored for different groups of users according to their needs	• Collaboration of different partners at different levels (national, international, civil society, telecommunication partners, etc.) facilitated effective design and implementation of the programme • The Indian telecoms network is the second largest in the world • Well-established leadership/management structure among stakeholders involved in designing, improving and implementing the programme • Government ownership • Good reputation of mobile network providers
Challenges	• Language barriers make it difficult for users to understand the material • Challenges in confidentiality between users and other individuals with access to their phones and personal information • Exclusion of certain groups (e.g. older people, people with visual impairments, people with disabilities who cannot read and/or engage with text messages	• Registration costs at early implementation discouraged participation • Less interest from persons without diabetes • Limited physical activity among users due to unwillingness but also barriers to do outdoor exercise (e.g. weather, insecurity) • Lack of publicity strategies and a strong media campaign to promote enrolment	• Lack of access to a personal mobile phone • Lack of access to formal health facilities, particularly in rural areas • Other mDiabetes initiatives implemented in the country could lead to duplication of efforts and lack of coordination between these and the government programme • Ongoing need for funding for implementers such as non-government organisations (NGOs)
Lessons	• A needs assessment to collect key data is important to inform the development and implementation of mDiabetes programmes • Messages should be tailored to specific groups and	• A balance between mHealth modalities (e.g. texts, Skype, FaceTime, emails) can help to include different type of users (e.g. illiterate people, elderly people, people with disabilities)	• There is a need for ongoing evaluation of the content and relevance of messages, as well as identifying population groups who may be dropping out, etc.

	offered in a variety of languages • Framing and content of messages need to be context-specific	• Simple and cost-effective/free enrolment procedures are critical for success • Implementers need to evaluate whether the platform will allow a two-way interaction (e.g. users able to ask questions), and the possibility of stopping or changing the programme	• Partnerships between the government and NGOs can help to maximise results • Partnerships between the government and other implementers (including NGOs) can also strengthen coordination and build a centrally controlled mDiabetes programme

1. Introduction

The Indian government's Ministry of Health and Family Welfare (MoHFW) launched the mDiabetes programme in 2016. It involves sending tailored short text messages to registered users to encourage lifestyle changes that prevent or manage diabetes. The programme's main objectives are: to improve healthcare-seeking behaviour; to promote early diagnosis and treatment; and to promote lifestyle adherence. It is expected that the programme will open up avenues for implementation of similar large-scale interventions through mobile messaging to prevent and control lifestyle disorders.

India was selected as a case study for this series as it clearly illustrates the strengths of an innovation in a context of strong governmental and technical support during its design and implementation. In India, mDiabetes has been successful in terms of disseminating information and raising public awareness about the illness and how to prevent it. This outcome could not have been achieved without the use of mobile technology, which allows the dissemination of information to millions of users over short periods of time in an affordable way. Likewise, mDiabetes was successful due to strong cross-sectoral government collaboration and the support of international partners. However, the programme also illustrates the challenges faced by health innovations when implemented in a very diverse context in terms of language, urban/rural location, or population characteristics (age, gender, literacy levels, etc.). Adherence to the advice received over the long term also remains a challenge, as we discuss further below. As such, mDiabetes in India also provides important lessons to other countries or institutions interested in using mHealth interventions to provide information to prevent illnesses such as diabetes.

This case study first presents a brief overview of the global burden of diabetes followed by an overview of diabetes in India. It then explores the evolution and history of mDiabetes in India and describes the characteristics of the programme and the stakeholders involved at the national and international levels. In order to provide additional evidence of the programme's effects, they are presented alongside the results of other mHealth pilot interventions for diabetes, including those that informed the national programme before mDiabetes was launched. These other mHealth programmes also continue to provide evidence of what works and what does not work when implementing mDiabetes interventions in the country. After presenting the programme's effects, we examine the enablers and challenges faced by the national programme and the additional pilot studies. Finally, we present lessons learned. The case study is informed by the literature and by interviews with key informants involved in both the national mDiabetes programme and in the pilot studies.

2. Context

a. The global burden of diabetes

Diabetes is a major cause of blindness, kidney failure, heart attack, stroke and lower limb amputation as well as the seventh leading cause of death globally in 2016 according to the World Health Organization (WHO) (WHO, 2018). The number of people with diabetes has increased from 108 million in 1980 to 442 million in 2014 (WHO and International Telecommunication Union (ITU), 2016). Moreover, this number is expected to increase to over 640 million in 2040 (Fatehi et al., 2018). However, diabetes can be treated, and its negative consequences avoided or delayed, with a healthy diet, physical activity, avoidance of tobacco use, medication and regular screening, and treatment to evade complications (WHO, 2018). Likewise, it has been recognised in both the WHO Global Action Plan and the 2011 United Nations Political Declaration of Non-Communicable Diseases (NCDs) that although improvement of treatment and care are important, prevention through lifestyle changes is crucial and cost-effective (WHO and ITU, 2016). As such, several organisations such as the WHO have been at the forefront of promoting the use of text messages in disease management and disease prevention and to determine best practices for research and implementation to continue building the evidence base for mHealth (ibid.).

2.2 Diabetes in India

Despite its low rates of obesity and overweight, India has more than 60 million people diagnosed with diabetes among a population of 1.3 billion (Ramachandran et al., 2018). Due to the size of its population, India has the world's largest population living with diabetes after China (Yesudian et al., 2014). In 2015 alone, over 9000,000 deaths were caused by diabetes directly or indirectly, and the number of diabetic people in India is expected to reach 109 million by 2035 (Ramachandran et al., 2018). The increased prevalence of diabetes and other NCDs in the country is caused by a combination of factors such as sedentary lifestyle, unhealthy diet, increasing life expectancy, family history of diabetes, and ethnicity (Ramachandran et al., 2018; WHO, 2016a). Indeed, the Asian Indian phenotype is predisposed to a higher propensity of metabolic syndrome, diabetes mellitus and coronary artery disease (Ramachandran et al., 2018).

Regarding awareness of diabetes, the Indian Council of Medical Research, using data from 2008 to 2011 (WHO, 2016a), found that only 58.4% of urban residents and 36.8% of rural residents reported that they knew about a condition called diabetes, while only 65.7% of the urban residents and 51% of the rural residents were aware that diabetes could be prevented. Prevalence of diabetes varies from state to state and seems to be higher in the south than in northern and eastern parts (Yesudian et al., 2014). Likewise, self-reported prevalence is lower in rural than in urban areas, from 3.1% to 7.3% respectively (ibid.). Among the rural population, according to the National Institute of Nutrition (2012), 8.2% of adult men and 6.8% of adult women were diabetic in 2012, with higher prevalence in the states of Kerala, Tamil Nadu and Gujarat, among both genders from 8.2% to 16.4%. However, the lack of national studies on diabetes prevalence leads to a lack of complete and reliable nationwide data (Yesudian et al., 2014). While prevalence is lower in rural areas, people have more difficulties accessing diabetes care due to a lack of health facilities, so tend to have worse health outcomes (ibid.).

Many of those who know about their diabetes status do not access treatment for a range of reasons, including lack of availability, affordability or awareness about the need for adherence to treatment (WHO, 2016a). Likewise, people with diabetes need to cover direct costs related to hospitalisation, complications, and the costs of medication, which can often represent more than 50% of total direct costs for households (Yesudian et al., 2014). Diabetes can also incur additional non-direct costs such as productivity loss and disability (Ramachandran et al., 2018; WHO, 2016a; Yesudian et al., 2014). The relatively high costs of treatment (estimated at $45–$150 per year) influence lack of adherence, especially among lower socioeconomic groups (Ramachandran et al., 2018; WHO, 2016a). Likewise, lack of access to public health services forces people to seek care from the private sector. This is important in the Indian context, where estimates suggest that the economic costs of healthcare fall heavily on individuals, with the government contributing one-third of total health spending and out-of-pocket payments consisting of about 58% of total health spend in 2012 (Yesudian et al., 2014).

Aware of the challenges faced by diabetes and other NCDs, in 2009 the Indian government launched the National Programme for Prevention and Control of Cancers, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS), which aims to integrate NCD interventions into the National Health Mission framework to enhance scarce resources (Ramachandran et al., 2018). The government then adopted the National Action Plan and Monitoring Framework for prevention and control of NCDs (2017–2022), which aims to achieve a 25% reduction in mortality due to NCDs and to halt the rise in obesity and diabetes prevalence by 2050 (National Institute of Nutrition, 2012). Among other objectives, the Plan aims to prevent and control chronic NCDs, including diabetes, through promoting behavioural change and early diagnosis, treatment, surveillance, monitoring and evaluation (M&E) (MoHFW, 2017). In June 2016, the government of India launched the mDiabetes programme, whose evolution and components are described in the following sections.

2.3 Evolution and history of mDiabetes

The global increase in mobile phone use from 1 billion subscriptions in 2002 to more than 7 billion in 2015 made mHealth one of the most attractive areas of public health intervention due to its potential to reach large numbers of people at low cost (WHO and ITU, 2016). Since the expansion of information and communications technology (ICT) in the 2000s and its use to support health services, the WHO has emphasised that universal health coverage cannot be achieved without the support of ICT interventions such as telehealth, mobile health or digital health, among others (ibid.).

Text messaging is one option that has been used in developing countries to transmit health information as it is simple, fast and affordable (Fatehi et al., 2018). Text messaging has also been used to deliver information to diabetic patients in different settings, achieving positive results in terms of (for instance) increased knowledge about the illness. In Bangladesh, for example, a twice-weekly voice message intervention improved diabetes knowledge among participants in a randomised control trial (Fottrell et al., 2019). In Senegal, where the government introduced mDiabetes in 2014 to promote good health behaviours during and between fasting periods in the Ramadan season, an evaluation found that daily messages to diabetic users for three months improved their glycaemic control – an effect which persisted three

months after the end of the messaging period (Wargny et al., 2018). The positive outcomes observed in Senegal largely motivated the Indian government to create a similar intervention for diabetes that could be supported by the existing infrastructure created for the mCessation programme (designed to help tobacco users quit).

Several factors motivated the introduction of the mDiabetes programme at the national level in India. A few previous mHealth initiatives had achieved positive results in the country (Ramachandran et al., 2015; Kaufman et al., 2013; Shetty et al., 2011). Furthermore, the Indian telecommunications network is the second largest in the world, with close to 900 million mobile phone subscribers (Hameed et al., 2016). As the use of mobile phones in India has increased, including in rural areas, text messages are increasingly perceived as an effective tool to disseminate information and advice on health and healthy lifestyles to large numbers of people (Ramachandran et al., 2018; Pfammatter et al., 2016).

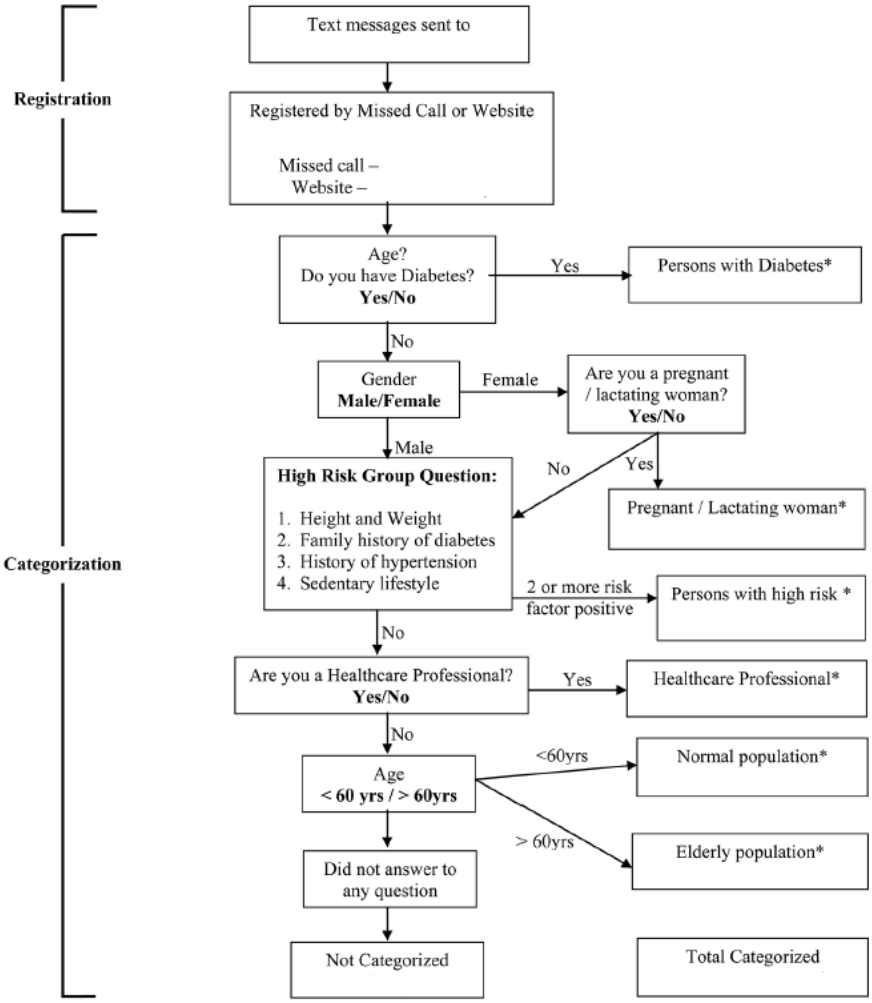
The high and increasing risk of diabetes among the Indian population created an urgent need for effective interventions with the potential to be scaled up across regions (Pfammatter et al., 2016). As a result of the positive outcomes of previous trials and the increased use of mobile phones, mDiabetes was launched in June 2016 by the MoHFW, with support from the WHO Country Office for India and the ITU (the UN agency for ICTs), targeting people with diabetes as well as the general population.

3. Key elements of mDiabetes

3.1 Characteristics of the innovation

According to the WHO and ITU (2016), an mDiabetes intervention should provide information, promote prevention, encourage testing in people at risk, and deliver appropriate, culturally relevant guidance both for people with diabetes and for the population as a whole. Likewise, the importance of dietary habits, physical activity and access to healthcare must be considered as part of the intervention (ibid.). In India, registration for the mDiabetes programme starts either by dialling a 'missed call' phone number or by accessing the mDiabetes website. The system then calls back the user to invite them to register, and to respond to initial categorising questions by pressing buttons on their phone. For online users, these questions are captured during the online registration. Based on the responses, users are grouped into one of six categories: (1) persons with diabetes; (2) pregnant/lactating women; (3) high-risk individuals (who have two or more risk factors which, taking into account height and weight, include family history of diabetes, history of hypertension, and sedentary lifestyle); (4) healthcare professionals; (5) elderly people; and (6) 'normal population' (with less than two risk factors and under 60 years old). Figure 1 shows the process of registration and categorisation according to participants' answers. After categorisation, text messages on healthy diet, lifestyle behaviours, physical activity, adherence to medication, and the basics of diabetes/gestational diabetes are then sent to all participants in their preferred language. Each participant receives 90 text messages over six months on alternate days (Ramachandran et al., 2018).

Figure 1 Process of registration and categorisation of the mDiabetes programme in India

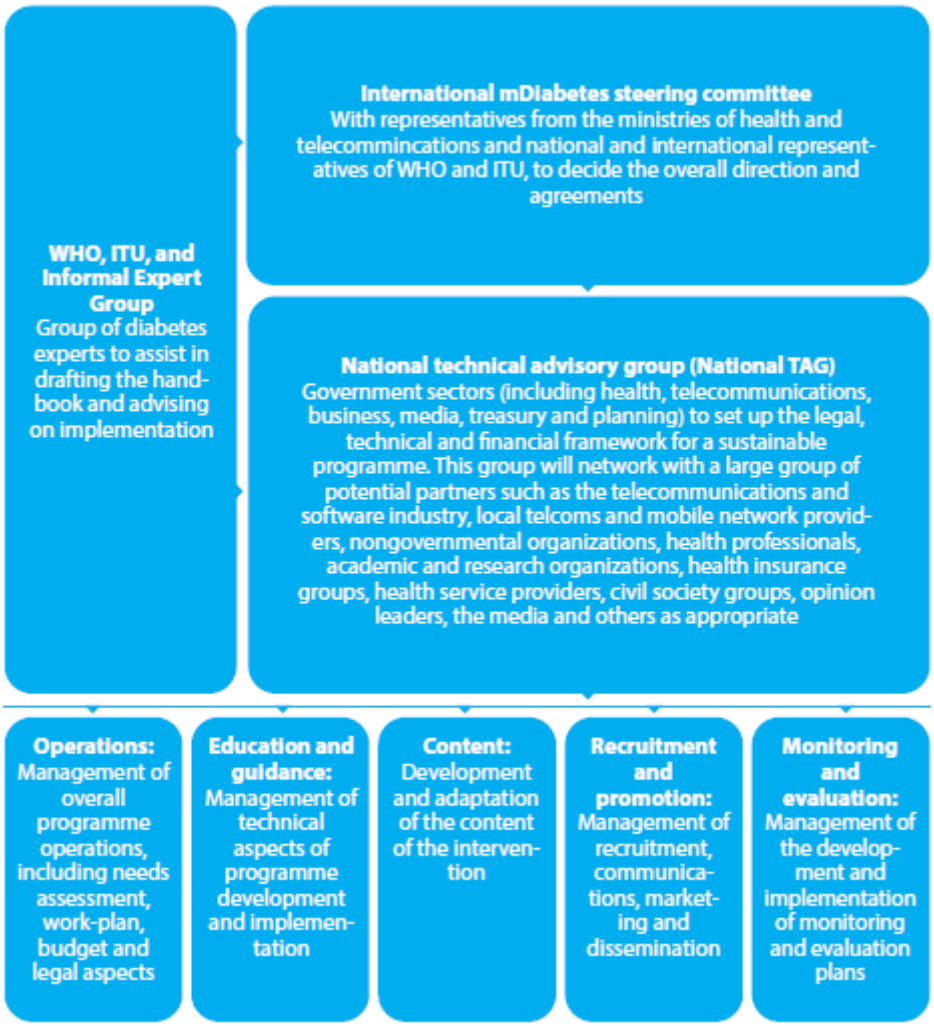


Note: Each asterisk refers to one of the six categories based on the answers provided by users
Source: Adapted from Ramachandran et al. (2018)

3.2 Stakeholder involvement

In the handbook designed to guide implementation of the mDiabetes programme, the WHO and ITU advise establishing a leadership team for the planning, implementation and monitoring of activities within the programme. This team should consist of a steering committee, an international advisory group of experts, and a national technical advisory group of in-country leaders (Figure 2). This structure is then adapted by the implementing countries, as in India, according to the relevant stakeholders at different levels (e.g. national ministries, civil society, academic/research institutes).

Figure 2 Proposed structure of an mDiabetes programme leadership team



Source: WHO and ITU (2016)

International mDiabetes steering committee

The WHO and ITU (2016) recommend that the steering committee provides overall direction and facilitates agreements for dealing with technical and other issues. In India, these agreements were established between the MoHFW and the Ministry of Electronics and Information Technology, and both were represented in the steering committee. The WHO was a key stakeholder promoting adoption of mDiabetes by the Indian government and was part of both the informal expert group and the steering committee. As some key informants mentioned, the WHO was initially interested in exploring the opportunities that digital health could provide, which motivated a partnership with the ITU to launch the Be He@lthy, Be Mobile global initiative to help combat NCDs such as diabetes by using mobile technology, particularly text messages and mobile applications. Based on a request from the Indian government, the WHO supported implementation of the programme by offering technical support to adapt it to the national context.

WHO, ITU and informal expert group

Within this group, key informants mentioned the role of international NGOs such as the NCD Alliance and the Diabetes Federation, which provided overall advice to the WHO, including about bringing users on board. The WHO and ITU (2016) also recommend including in the expert group stakeholders from international IT organisations to advise on legal issues, choice of platforms and feasibility, as well as health economists and business development experts to advise on models for sustainability.

National technical advisory group

The WHO and ITU (2016) recommend this group be formed by in-country stakeholders to manage operations, technical specifications, content development and adaptation, recruitment and promotion, and M&E. In India, technical support for the programme is provided by the Ministry of Electronics and Information Technology as well as academic and research institutions. The WHO and the India Diabetes Research Foundation (IDRF), in Chennai, are both part of the

national technical advisory group (Ramachandran et al., 2018). This group was established to finalise the algorithm. Text messages were drafted by the IDRF and further revised by the MoHFW (ibid.).

Arogya World

Although not part of the national mDiabetes leadership team in India, another mDiabetes campaign has been implemented in the country since 2013 (before the government campaign started). That campaign is led by the global NGO, Arogya World, and aims to examine the feasibility of, and create initial evidence on the use of, mDiabetes. During the 2013 implementation, Arogya World partnered with Nokia Life and recruited 1,052,633 users who opted in to receive mDiabetes text messages provided free to consumers across India, twice a week for six months, in one of 12 languages (Pfammatter et al., 2016). Arogya World also partnered with the US-based Rollins School of Public Health at Emory University to develop the messages, which were also reviewed for cultural relevance and technical accuracy with health and communications experts in India. According to key stakeholders from Arogya World, the NGO influenced the mDiabetes national programme as Arogya World was being implemented when the WHO and ITU were developing their Be He@lthy, Be Mobile campaign, with the accompanying manual reporting on the experience of Arogya World as well as the messages that were used.

4.0 Impacts/effects of the innovation

This section examines the impacts of mDiabetes in India, and presents the results of the first evaluation of the programme. It then focuses on studies that have examined the effects of other pilots on diabetes that have also used text messages in interventions implemented in India.

4.1 Overall impact

The first evaluation of the mDiabetes programme, carried out between 2016 and 2017 with 4,954 participants, assessed the impact of text messages on behavioural changes related to diet, physical activity, medication adherence, and health-seeking behaviour (screening for diabetes/gestational diabetes) at the third and sixth months. Results showed behavioural changes after the third month and/or sixth month: 57% of participants followed healthy dietary advice, 72% practised physical activity, 51% went for screening for diabetes, and 67% checked their glycaemic status. These outcomes are explained by participants' increased awareness and adoption of healthy lifestyle practices as well as their motivation to screen for diabetes after receiving text messages through the programme (Ramachandran et al., 2018). At the end of year 1, the evaluation assessed participants' interest in and acceptability of the programme, its feasibility, scope for improvement and behavioural changes in a subsample of 855 participants. Results are shown in Table 1.

Table 1 Outcomes of mDiabetes programme at the end of year 1 (unless otherwise stated)

Interest	• All participants expressed an interest in the programme • 72.9% were interested in knowing more about diabetes and 16.8% wanted details of healthy lifestyle • 75% understood and tried to follow a healthy lifestyle behaviour • 64% of participants shared text messages with parents, relatives and friends		
Acceptability	• Text messages sent for registration were found acceptable to 97.3% of participants and encouraged them to participate • 80% were motivated to participate to improve their knowledge about diabetes and healthy lifestyle. Content of messages was understood and appreciated by 83.5% • 57.2% were satisfied with the frequency of the messages • 16.5% preferred increased frequency of the messages		
Feasibility	• Registration into the programme was found to be easy and feasible by 85% of participants • 32.5% found that the text messages at the third and sixth months were difficult to understand and respond to due to language barriers • 36.4% missed the evaluation text messages (the study does not explain why) • 26.1% did not respond since they had to pay to do so		
Behavioural changes		At third-month and/or sixth-month follow-up (%)*	At 1-year follow-up (%)**
	Diet habits	57.2	41.2

	Physical activity	72.3	54.6
	Screening for diabetes	51.9	11.3
	Checked glycaemic control	67.3	N/A

* From the 4,954 participants, 2,022 responded after the third-month follow-up, 2,354 responded after the sixth-month follow-up and 578 responded both times

** Responses were obtained from 855 participants after 1-year follow-up

Source: Ramachandran et al. (2018)

As Table 1 shows, behavioural changes were seen to have declined at the 1-year follow-up, particularly those related to following advice on a healthy diet and physical activity. Although mDiabetes cannot control whether users follow the advice given, it still succeeded in generating awareness and sensitised users on diabetes prevention and management.

4.1.2 Other mDiabetes pilot studies in India

Incidence

The first trial to show the benefit of mobile phone technology in the prevention of diabetes in India was that of Ramachandran et al. (2013). The two-year trial was conducted among 271 Asian Indian pre-diabetic people who received frequent text messages on lifestyle modification, compared to 266 individuals in the control group who only received messages at baseline. The study found a 36% reduction in the cumulative incidence of diabetes compared to the control group over the two years. It also found that mobile phone messaging was an acceptable method for delivering advice and support for lifestyle modification to prevent diabetes.

Healthy dietary advice

An evaluation of the mDiabetes programme implemented by Arogya World, at the end of a six-month period, found that participants improved their consumption of fruit and vegetables. Respondents taking 2–3 servings of fruit a day in the treatment group increased from 34% to 49%, while the control group only increased from 32% to 33%. Similarly, there was an 8% increase in the intake of 2–3 servings of vegetables a day in the experimental/treatment cohort (from 62% to 70%), while the control group remained at 53% at the pre and post stages (Pfammatter et al., 2016).

Stress reduction

Patnaik et al. (2015) developed an intervention to reduce stress among diabetic patients who were sent text messages once a week containing some educational tips to decrease stress, while they also received lifestyle education (using printed materials and computers) and were contacted by the investigator every three weeks for three months (to receive counselling if required). The control group only received printed educational materials. The study found that after three months, the average stress scores reduced to 17.05 for the treatment group but increased to 20.7 for the control group from a baseline of 18.9 for both groups, which shows that talking with health professionals and getting some health messages can reduce stress among diabetic patients.

Quality of life

Jha et al.'s (2016) study evaluated the effectiveness of an mDiabetes platform compared to providing conventional care. While the control group saw their physician and received diabetes education/counselling as normal, the treatment group received educational videos and daily advice on managing diabetes, via email or text. Participants in the treatment group not only increased their knowledge scores but also achieved better quality of life indices (88.5 ± 7.8 for the treatment group compared to 83.5 ± 10.7 for the control group, p value = 0.015). This was explained by their greater sense of empowerment to take control of their disease, which in turn improved their satisfaction/quality of life.

Sharing of messages

Arogya World (2013) also found that those receiving the intervention were sharing the information received via text message with relatives. This had been identified from the testimonies of users who reported having shared messages with their parents, preparing their meals, following guidance from the programme, as well as increasing their knowledge on diabetes and its complications. Likewise, key informants from Arogya World also reported that those receiving the intervention were not only diabetic people but also relatives or carers interested to transmit such messages to their diabetic relatives.

Reduction of fasting blood glucose

Another pilot study using mobile text messages to reduce mean fasting blood glucose recruited a total of 955 patients with type 2 diabetes from primary and secondary healthcare facilities to participate in the mHealth intervention. Patients received mobile messages twice a month for a year with information on how to maintain the desired fasting blood glucose (FBG) levels. Messages were tailored to the personal situation of the patient as they included their name, current and ideal FBG value (along with the next date of FBG assessment), current and ideal weight based on body mass

index (BMI), salt restriction and advice for a brisk walk in case of high blood pressure, and to avoid butter/oil-rich food items. After the intervention, there was a higher decline in FBG levels among the treatment group: average FBG declined from 163.7 to 152.8md/dl (P=0.019) in the intervention group and from 150.5 to 149.2 mg/dl (P=0.859) in the control group (Kumar et al., 2018).

Adherence to medication

Prabhakaran et al. (2019) assessed the effectiveness of mWellcare, an mHealth system that consists of electronic health record storage and electronic decision support for the integrated management of five chronic conditions (hypertension, diabetes mellitus, current tobacco and alcohol use, and depression) versus enhanced usual care among patients with hypertension and diabetes mellitus. The system was in part equipped to send short text message reminders to patients about taking their medication and attending follow-up visits. The study found no statistical difference between the treatment group and the control group in outcomes including FBG, total cholesterol, predicted 10-year risk of cardiovascular disease, BMI, and tobacco and alcohol use. However, the study found that patients in the treatment group reported greater adherence to medications explained by the text message reminders.

5 Innovation enablers and barriers

This section presents the enablers and challenges of both the mDiabetes national programme and the additional pilot studies, which offer insights on the use of text messages to share information on diabetes in the Indian context.

5.1 Enablers of success

During design/research and development (R&D)

Use of established IT infrastructure that reduces costs and increases reach among users: The government is using the same IT infrastructure for mDiabetes that was used previously by the mCessation programme, implemented in 2015. As one key informant mentioned, the Indian government's use of the same platform for both programmes has reduced the costs of delivery of messages and increased reach among users. Likewise, the government reduced the number of questions asked to users to simplify the categorisation stage and reduce costs.

Use of text messages that can be sent to the most basic mobile phones in a practical, fast and convenient way, reaching users from different regions and socioeconomic groups: Although in developed countries studies have focused on mobile health for diabetes using more advanced smartphone features (WHO, 2016b), mDiabetes relies on basic mobile phone text messaging, which is simple, fast and efficient. Texts can be sent to the most basic mobile phones without requiring internet connection, reaching people from different socioeconomic groups and geographic regions. This is important, as other pilot interventions that have used mHealth with more advanced modalities that may require a smartphone (e.g. Skype, FaceTime or sending an email) have observed a link between people's level of education and socioeconomic status and their interest in participating in the programme, compared to those with lower education/socioeconomic status (Jha et al., 2016).

During implementation/scale-up

Text messages are short, simple and easy for everyone to understand, and are tailored to different groups of users according to their needs: Text messages are short, simple and easy to understand. This was achieved through consultation with users and civil society groups before implementation. For example, key informants from Arogya World mentioned that the NGO collected feedback on messages among 750 users as well as holding focus group discussions with consumers from the north and south of India. Although this consultation process took around six months, Arogya observed good outcomes in terms of users reporting messages being culturally acceptable and actionable (Pfammatter et al., 2016). Messages are also tailored to the specific needs of groups of users (Ramachandran et al., 2018; Pfammatter et al., 2016). Likewise, when users' information is included (such as name, next date of assessment, and goals to achieve – for example, ideal weight or FBG values), positive outcomes have been observed (Kaufman et al., 2013).

Cross-cutting

Collaboration among partners at different levels (national, international, civil society, telecommunication partners, etc.) facilitated effective programme design and implementation: The core of the design and implementation of mDiabetes rested on effective collaboration between partners at different levels, including experts in government, academics, civil society organisations (CSOs), the WHO and ITU, telecommunications partners and other stakeholders who all shared their expertise and advice during the process. This collaboration was important to provide the overall direction of the programme, and discuss technical issues such as availability of technology options, negotiation with telecoms regulators, technology pre-testing or scale-up plans.

Widespread use of mobile phones: The use of mobile phones has become widespread in India, even in rural areas. Thus, text messages are an effective tool to reach people and disseminate information on a large scale.

Well-established leadership/management structure of the stakeholders involved in designing, running and improving the programme: The mDiabetes leadership and management team is clearly structured and organised, with a well-established division of tasks for the different phases of the programme: operations, guidance, content, recruitment, M&E, etc. This partnership enabled constant feedback during the process and meant that the programme was able to respond to challenges (e.g. including more languages, reducing the number of the categorisation questions, etc.) quickly and effectively.

Government ownership: The government implements and pays for the programme and has recently integrated it into the screening phase of diabetes, such that all those diagnosed with diabetes are automatically enrolled in the programme. Key informants also reported the government's commitment to continue expanding and improving mDiabetes.

Good reputation of mobile network providers: Key informants from Arogya World mentioned that one important enabler was working with mobile network providers with a good reputation. Nokia was the ideal partner as it was a renowned company that people could trust, which also motivated users to enrol in the programme and to follow the advice received through it.

5.2 Challenges faced and solutions identified

During design/R&D

Lack of publicity strategies: Although mDiabetes messages were sent to 130 million people, response for registration was obtained only from 107,000 individuals (Ramachandran et al., 2018). This was in part because promotional messages were sent only once, and some users may not have noticed them or had doubts about the registration process. There was also no strong media campaign to accompany the programme's launch.

Language barriers making it difficult for users to understand the information sent: Of those who registered, 70% did not respond to the initial categorisation questions, probably because messages were sent only in English and Hindi. Similarly, some people dropped out because they could not understand the messages. Now, mDiabetes is available in 17 languages (for enrolment and to receive messages).

Challenges in confidentiality between users and other individuals with access to their phones and personal information: If messages with patients' private information are sent to a mobile phone that anyone can have access to, this could potentially raise issues of confidentiality. This has been considered by one mHealth intervention in India, which integrated security features in the platform to ensure confidentiality (Jindal et al., 2018).

Exclusion of certain groups who cannot read and/or engage with text messages: Certain groups of people may not be able to read text messages sent to their phones or to engage with them due to physical challenges (e.g. poor eyesight, visual impairments, or arthritis). During the evaluation of the mDiabetes programme, these users expressed their preference for the use of voice calls rather than text messages to access health information – something that still needs to be considered (Ramachandran et al., 2018). At the moment, Arogya World is scaling up its mDiabetes programme using voice messages in order to include those population groups. Similarly, key informants suggested that the use of smartphones might enable messages that use video or photos, which would enable the intervention to reach those who may otherwise be excluded.

During implementation/scale-up

Registration costs: Initially, mDiabetes users had to pay when replying to text messages. This also partly explains the high proportion of users who did not enrol or who were not categorised by the system. As a solution, users can now enrol online or respond to questions pressing numbers in their mobile after a miscall to the server – all for free.

Less interest from persons without diabetes: mDiabetes has generated more interest from persons with diabetes than those from other categories. This was reflected in the evaluation, which showed that a higher proportion of persons with diabetes completed the programme than those without diabetes (ibid.).

Limited physical activity among users due to unwillingness but also barriers to do outdoor exercise: Key informants mentioned the programme's limited results in encouraging participants to do more physical activity. For example, Ramachandran et al. (2013) found that the proportion of participants following a healthy diet was high (95%) but adherence to physical activity advice did not differ between the control and treatment groups. Likewise, Arogya World

found that six months after implementing its mDiabetes programme, there was no differential change in exercise between the control and treatment groups. Key informants noted that it can be difficult for users to follow physical activity advice due to lack of motivation, lack of infrastructure (e.g. lack of pedestrian walkways) and security concerns (especially for women) to do outdoor exercise. It is also the case that high temperatures and high pollution levels during certain months in big cities such as Delhi (especially from October to December) do not allow people to do outdoor exercise. Furthermore, not all people can afford a gym, which further constrains some mDiabetes users from following the advice to do more physical activity.

Cross-cutting

Lack of access to a mobile phone: Although there is increased ownership of mobile phones in rural areas, some studies have observed that mobile phone ownership among rural patients was relatively low, and many would depend on a family member to access health information. For example, Ramachandran et al. (2015), in a study of patients attending an NCD clinic in a rural area, found that only 38% had access to a personal mobile phone and 43.5% had access through a family member. Likewise, some rural inhabitants still lack a predictable electricity supply and rely on phones with short battery life.

Lack of access to formal health facilities: In rural areas, evidence from diabetic patients who could benefit from mHealth interventions to manage their disease showed that many were mostly consulting unskilled informal medical practitioners, while the formal health sector (public and private) was absent or avoided. While 70% of India's population lives in rural areas, only about 40% of health workers are working in rural areas (WHO, 2016a). These challenges limit the ability of patients to screen for diabetes and/or to manage the disease as advised by mDiabetes.

Other mDiabetes initiatives implemented in the country that could lead to duplication of efforts and lack of coordination between these and the government programme: As already noted, there are other mDiabetes initiatives being implemented in India, such as that by Arogya World. This can be challenging due to a lack of coordination and collaboration between the government and organisations implementing other initiatives, as some key informants from Arogya World noted. Multiple campaigns could also lead to duplication of effort if initiatives are implemented at the same time in the same settings.

Funding: Implementers, such as NGOs, need access to more funding to scale up successful activities. Key informants from Arogya World reported their constant need to search for funding opportunities, specially to bear the costs of the text messages sent to users.

6. Key lessons/findings

During design/R&D

- During the design phase, there should be a comprehensive needs assessment (e.g. visiting, observing, interviewing key informants and members of the target population, documenting existing resources) to collect key data (e.g. diabetes burden, perceptions of diabetes, existing prevention and control programmes, the state of mobile communications, target group, cultural and contextual factors) to inform the development and implementation of a national mDiabetes programme.
- The needs assessment should investigate any legal or regulatory requirements regarding mHealth or the mobile network environment. If these are not addressed during the design phase, implementers risk delaying or even abandoning the programme.
- Constant interaction and feedback from consumers before implementation is crucial to produce culturally tailored messages that are accepted by different groups of users (e.g. rural/urban residents, young people and older people, men and women, people with diabetes and those without, different ethnic groups, etc.). Consultations with consumers are also important to establish the frequency and number of messages and duration of the intervention.
- Messages should be tailored to specific groups (e.g. diabetic and healthy populations, rural and urban residents, people from different socioeconomic groups, and of different ages, gender and ethnicity).
- Messages offered in a variety of languages (to match users' choices) are more accepted and actionable by the population.
- Framing and content of messages need to be context-specific. For example, key informants mentioned that in some contexts (such as the USA), messages that encourage self-advocacy (e.g. the user making their own choice to follow a healthy lifestyle) work well. However, in the Indian context, messages that were more direct and told users what to do worked better and were better received, as users wanted to know what to do to prevent/manage diabetes.

- Stakeholders interested in implementing mDiabetes should not draft messages from scratch but instead adapt existing health messages, as recommended by key informants. Messages used by different implementers (e.g. mDiabetes in India and Senegal, and Arogya World) are widely available and have gone through a rigorous review process by expert groups.

During implementation/scale-up

- Key informants considered it important to scale-up mDiabetes using other modalities than text messaging, such as mobile applications (apps) that could allow users to ask questions or receive information through videos, pictures, voice or other modalities that could allow illiterate people or people with disabilities to access and understand the messages. eHealth platforms that allow patients to use modalities such as Skype, FaceTime or emails as well as to receive advice via email or text have been tested in India with positive results (Jindal et al., 2018; Jha et al., 2016).
- However, cost is a factor, as smartphones with these features can be more expensive and might not be the preferred modality for low-income or less-educated individuals (Jha et al., 2016).
- Simple and cost-effective/free enrolment procedures – including free message, free phone number and local contact at point of care – are critical to motivate consumers to enrol and thereby maximise reach.
- Promotion of the mDiabetes programme is crucial for maximum success. Repeated and brief promotional messages in local languages as well as a media and promotional campaigns (e.g. advertising on local radio and buses, leaflets distributed at points of care) can improve participation and motivate people to enrol. The target population can also play a crucial role in advising on the media and channels to be used. Similarly, key informants also advise that influential and respected stakeholders (such as doctors and nurses) can motivate people to sign up during healthcare delivery.
- Implementers need to evaluate whether the platform will allow a two-way interaction (e.g. users being able to ask questions), the possibility of stopping or changing the programme, and the potential interaction that users can have with health professionals or the national health system.

Cross-cutting

- Adaptation of messages also needs to consider the reputation of the sender. In India, messages shared by respected providers (e.g. Nokia) or authorities (e.g. health professionals) were well received by the population.
- There is a need for ongoing evaluation of the content of messages, their relevance, and any population groups that might be dropping out, and to develop strategies to adapt the model accordingly. It is essential to involve local experts (e.g. through a national technical advisory group) for a successful design and adaptation process.
- Partnerships between the government and NGOs can help to increase the number of people who sign up to mHealth initiatives, maximising results at scale-up.
- Partnership between the government and other implementers such as NGOs can also lead to stronger coordination and a centrally controlled mDiabetes programme. Among other benefits, this would allow NGOs to access funds provided by government and allow the government to benefit from the experience of NGOs. This kind of partnership could also increase programme reach among users through multiple fronts.

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5.0 MenAfriVac Meningitis A case study

SUMMARY BOX

What is the innovation?

This case study explores the development and implementation of the MenAfriVac Meningitis A conjugate vaccine. This refers to both the partnership that led to its development, known as the Meningitis Vaccine Project, and the rollout of vaccine in the meningitis belt of sub-Saharan Africa. Considering the combination of these efforts as one innovation, we explore this novel approach and capture learning for the global health and development community. The table below summaries the enablers, challenges and lessons learnt from this innovation.

	Design/ research and development (R&D)	Implementation / scale-up	Cross-cutting
Enablers	• Clear science and available technology to support the innovation	• In-country political support for rollout of the innovation	• Community support from relevant local and international stakeholders • The innovation and its rollout were context-specific • R&D integrated with implementation of the product • International funding with flexibility and a long-term view • Coordinated partnership between international bodies, government, industry and local community
Challenges	• Intellectual property frameworks create difficult and technically complex barriers to overcome • Legal frameworks and regulation create complexities and slow development of new pharmaceutical products	• Inclusion of all targeted beneficiaries was sometimes challenging • Adverse events creating negative public perception to impact the scale-up • Economic limitations and infrastructure may hinder delivery of the innovation	
Lessons	• Overcome the limits of industry through product development partnerships		• Innovate with a clear prospect for success, with a clearly defined purpose and attainable deliverables • Consider context first and ensure that innovation is country-driven • Ensure long-term flexible funding through the innovation cycle and rollout

1 Introduction

MenAfriVac® is a conjugate vaccine that induces a long-term immune response against Group A *Neisseria meningitidis* meningitis A (MenA), the strain of bacterial meningitis responsible for the vast majority of epidemics in the meningitis belt of sub-Saharan Africa. This vaccine was developed through a product development partnership (PDP) called **the Meningitis Vaccine Project (MVP**), which existed from 2001 to 2014 and was created in response to repeated and severe MenA epidemics during the 1990s. The project brought together scientists, regulators, African governments, international agencies, public health institutes, non-governmental organisations (NGOs), civil society groups, funders and industry. MVP developed two formulations of a vaccine (MenAfriVac®) that were prequalified by the World Health

Organization (WHO): a PsA-TT 10-µg vaccine for use in mass vaccination campaigns among 1- to 29-year-olds, and a 5-µg vaccine for use in routine immunisation programmes among children below 2 years of age.

The vaccination was introduced through a coordinated, phased campaign that targeted people aged 1–29 years (~70% of total population) and was rolled out in 15 priority countries between 2010 and 2014. By the end of 2017, more than 280 million people had been vaccinated in 21 countries (WHO, 2018). The vaccine has now been integrated into routine immunisation services in 10 of the 16 countries planned. According to the WHO: 'the use of the MenAfriVac® vaccine to prevent meningitis A epidemics in the African Region is one of the greatest vaccination success stories in public health history and highlights what partners can accomplish when unified by a compelling cause' (ibid.).

We consider the innovation to be the combination of elements related to the development of the vaccine, its scaling and rollout; it is in the unique orchestration of these efforts that we find the novel approach and learning for the global health and development community. The aim of this case study is to review these elements around the development and rollout of MenAfriVac, to explore enablers and obstacles to its success, and to reflect on how this achievement could serve as a model for future innovation in support of Sustainable Development Goal (SDG) 3 ('ensure healthy lives and promote wellbeing for all at all ages).

2 Context

2.1 Meningitis A

Since the late 1800s, epidemics of bacterial meningitis have been recorded throughout a region of sub-Saharan Africa known as the meningitis belt, comprising 26 contiguous states[8] ranging from Senegal to Ethiopia and home to up to 400 million people. Historically, the majority of these epidemics were due to serogroup A (MenA) (Mohammed, Iliyasu and Habib, 2017). Before 2010 and the MenAfriVac mass preventive immunisation campaigns, MenA accounted for an estimated 80%–85% of all cases in the meningitis belt, with large epidemics occurring at intervals of 7–14 years (WHO, 2018).

Meningococci, the meningitis bacteria, reside in the nose or throat of carriers – people who do not themselves fall sick because they have a measure of natural or acquired immunity, but who can spread the organism to others. If the meningococcus falls on a susceptible host, it can invade the tissues of the nose and throat, spreading into the bloodstream and up to the brain. Disseminated meningococcal infection causes a toxic effect, including shock and bleeding into the skin, producing a characteristic rash. The case fatality rate for untreated meningococcal meningitis approaches can be as high as 50%, and even those people who survive may have subsequent brain damage causing disabilities such as paralysis or deafness, as well as limb amputations and other long-term disabilities resulting from co-existing sepsis. Even when treated aggressively with appropriate antibiotics, s early and appropriately, the case fatality rate ranges from 10% to 30% (Médecins Sans Frontières (MSF), 2000).

Prior to the development of MenAfriVac, the polysaccharide meningitis vaccines deployed in epidemics did not stem the recurrence of large outbreaks. This is because the polysaccharide vaccines do not provoke an immune response in young children, induce a long-term immune response, or reduce carriage of the bacteria in healthy people; therefore, they do not lower transmission. They were thus unsuitable for broader prevention campaigns and could not generate herd immunity – when a sufficiently high proportion of individuals are immune to the disease so that there is less disease transmission and the population is protected (Mohammed et al., 2017). In 2006, the direct costs of emergency mass vaccination campaigns in Burkina Faso alone were evaluated at $3.5 million (5% of the country's annual health expenditures) (Meningitis Vaccine Project, n.d.).

Although reoccurring, MenA outbreaks were unpredictable and this lack of predictability limited market demand to have the vaccine on hand in affected countries. Instead, the International Coordinating Group on vaccine provision for meningitis (ICG, hosted by the WHO) held a stockpile of polysaccharide vaccines to be deployed, but only as a reactive measure to diminish the spread. Due to the absence of a long-term immunological response and effect on carriage, these vaccines had no sustained public health benefit. One hundred million doses of the meningococcal polysaccharide vaccine were used from 1999 to 2003, yet epidemics still occurred (Kulkarni et al., 2015). As opposed to polysaccharide vaccines – in which only the capsular sugar part of the bacteria is included as the antigen to stimulate a short-term immune response – when the capsular sugar is linked to a carrier protein, the resultant conjugate vaccines elicits a much stronger, longer-term immunological response against disease and carriage (Medical Republic, 2017). In a conjugate

[8] Benin, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Côte D'Ivoire, Democratic Republic of Congo, Ethiopia, Eritrea, Ghana, Guinea, Guinea Bissau, Kenya, Mali, Mauritania, Niger, Nigeria, Rwanda, Senegal, South Sudan, Tanzania, The Gambia, Togo, Uganda.

vaccine, the weak antigen is covalently attached to a strong antigen, creating a more robust response to the weak antigen (ibid.).

At the time the MVP emerged, large Western pharmaceutical manufacturers were working to develop a serogroup C and possible polyvalent (combined MenA and C) conjugate vaccine for use in the United Kingdom (UK) (Aguado et al., 2015). However, in the end, only the MenC conjugate vaccine was developed, as this was the priority for UK and other Western markets where MenA was not an issue (ibid.). With the benefit of hindsight, the efforts to develop a C meningococcal conjugate vaccine rather than a bivalent meningococcal AC conjugate vaccine were a missed opportunity. This is demonstrative of how the pharmaceuticals industry does not prioritise innovation within the safety of a defined commercial market such as the UK, or public health benefit where profitability is unlikely – i.e. where a disease (like MenA) impacts only poor people. In order to develop a conjugate MenA vaccine, a new model was therefore required. Innovation was needed to facilitate equity-led R&D that could overcome the limits of Pharma business models, models that lead to prioritisation of profits over public health, and risk leaving many millions behind from scientific and SDG progress.

2.2 Meningitis and the SDGs

To achieve SDG 3, there is a need to accelerate R&D around diseases like MenA that lie beyond the limits of Pharma business models. The story and lessons around the successful development of MenAfriVac therefore has great significance for those working towards SDG 3 targets and the wider Agenda 2030 pledge to 'leave no one behind'. Specifically, MenAfriVac relevance falls under target 3.3 (end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases). Persistence of such epidemics is a clear barrier to accomplishing this target. Tackling meningitis would also reduce mortality among children under 5 and contribute towards target 3.2 (end preventable deaths of newborns and children under 5 years of age).[9] Vaccinations and other forms of preventive health services are a key part of target 3.8 (to achieve universal health coverage).[10] The development of MenAfriVac also resonates with target 3.b[11] (to support R&D and access to affordable vaccines).

Beyond SDG 3, this innovation has relevance for SDG 1 (end poverty in all its forms everywhere), as meningitis affects the world's poorest countries, and those least on track to meet SDG 1. It is estimated that at least 14 million survivors of meningitis are disabled or impaired (WHO, 2018). The economic impact on households and communities through loss of earnings (the highest attack rates are among young adults at the peak of their economic potential) and cost of support and healthcare for people with sequelae and their families also threatens progress towards SDG 1. Finally, the partnership model of the MVP – a public–private partnership (PPP) – has relevance for SDG 17: those working on targets 17.7 on technology transfer,[12] 17.9 on capacity-building,[13] 17.16 on multi-stakeholder partnerships,[14] and 17.17 on PPPs[15] can all learn from this innovation.

2.3 History and evolution

[9] Target 3.2: End preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under-5 mortality to at least as low as 25 per 1,000 live births.

[10] Target 3.8: Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all.

[11] Target 3.b: Support the research and development of vaccines and medicines for the communicable and non-communicable diseases that primarily affect developing countries, provide access to affordable essential medicines and vaccines, in accordance with the Doha Declaration on the TRIPS Agreement and Public Health, which affirms the right of developing countries to use to the full the provisions in the Agreement on Trade-Related Aspects of Intellectual Property Rights regarding flexibilities to protect public health, and, in particular, provide access to medicines for all.

[12] Target 17.7 Promote the development, transfer, dissemination and diffusion of environmentally sound technologies to developing countries on favourable terms, including on concessional and preferential terms, as mutually agreed.

[13] Target 17.9 Enhance international support for implementing effective and targeted capacity-building in developing countries to support national plans to implement all the sustainable development goals, including through North-South, South-South and triangular cooperation.

[14] Target 17.16 Enhance the global partnership for sustainable development, complemented by multi-stakeholder partnerships that mobilize and share knowledge, expertise, technology and financial resources, to support the achievement of the sustainable development goals in all countries, in particular developing countries.

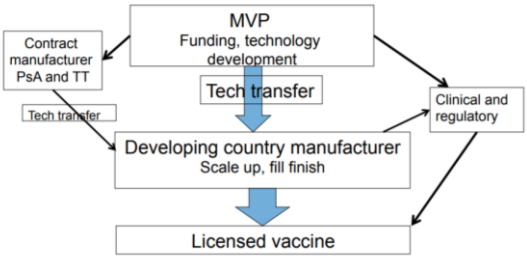
[15] Target 17.17 Encourage and promote effective public, public-private and civil society partnerships, building on the experience and resourcing strategies of partnerships.

Before MenAfriVac, MenA epidemics devastated countries across the meningitis belt, causing mortality, morbidity and negatively impacting health sector development. Responding to MenA epidemics drained resources, capacity and morale in ministries of health, as well as leaving many households to cope with disabled members who needed services that were often unavailable or unaffordable. After the especially deadly epidemic of 1995–96, government health officials in the region came together to ask the WHO to help them address the problem. During a 1996 meeting of ministers from 16 African countries, epidemic meningitis was recognised as a high priority. Country representatives met with WHO staff in April 2000 and, following the evaluation of a number of proposals, endorsed the goal of the immediate development of an affordable conjugate vaccine for Africa (WHO, n.d.). An informal collaboration between PATH (a Seattle-based NGO), WHO and the Centers for Disease Control and Prevention (CDC) Atlanta further assessed the issues. In June 2001, the MVP was created as a 10-year partnership between PATH and WHO to put an end to MenA epidemics in Africa.

The MVP was created with the support of the Bill & Melinda Gates Foundation (BMGF), designed as a partnership around a specific and singular goal: developing, testing, licensing and introducing an affordable MenA conjugate vaccine for Africa. MVP discussions with African public health officials and WHO/AFRO (in Zimbabwe (WHO Regional Office for Africa at the time), Niger, Burkina Faso and Nigeria) yielded consistent information. First and foremost, cost was the most important limiting factor to the introduction of new vaccines; success of the MVP (widespread use of a conjugate meningococcal vaccine in mass campaigns) would not be possible unless vaccines were priced at less than $0.50 per dose (Tiffay et al., 2015). Discussions with Pharma began, with the general expectation that the MVP would negotiate a contract with a multinational for the development of a combined MenA and MenC conjugate vaccine. Key issues for Pharma consulted (Chiron, Baxter and GSK) included vaccine price, guaranteed purchase (and effect of volume on price), investments to increase manufacturing capacity, and creating a 'no risk' model (LaForce, 2016). In this scenario, a small MVP team at WHO and PATH would focus on managing this partnership while working to improve meningitis surveillance in Africa and planning for the vaccine's introduction in meningitis belt countries (Tiffay et al., 2015). Yet 18 months after the project's starting date, no agreement could be reached; it would not be possible for Pharma companies to produce the vaccine at the price required by African governments.

Hence the MVP evolved into an innovative 'virtual company': a new model for public sector vaccine development that linked a network of partners with unique roles and responsibilities, and sought to transfer technology and know-how for all aspects of vaccine production to a developing country vaccine manufacturer (ibid.). Three critical elements facilitated the decision: (1) inputs from African public health officials on the importance of vaccine price; (2) the availability of a detailed business plan that had been commissioned by WHO, which indicated that the 'cost of goods' for making 25–50 million doses of a Group A meningococcal conjugate vaccine could be as low as $0.18 per dose; and (3) expert input from key consultants with strong experience in conjugate vaccine development (LaForce, 2016). Figure 1 illustrates the key components of the model.

Figure 1 MVP product development plan



Source: LaForce (2016).

The MVP faced scrutiny from the global health community about the feasibility of the approach and fears that the possibility of working with a developing country vaccine manufacturer would result in a lower-quality vaccine.

The Serum Institute of India Pvt. Ltd (SIIPL) – a respected vaccine manufacturer already producing and selling several WHO prequalified[16] vaccines – was chosen as MVP's manufacturing partner. SIIPL had a strong performance record for meeting timelines, a robust management structure, financial health, excellent physical facilities, a skilled technical team, and a strong interest in MVP's public health vision and guiding principles (Tiffay et al., 2015). SIIPL agreed to develop a

[16] Prequalification is a process that guarantees that vaccines meet international standards of quality, safety and efficacy.

MenA conjugate vaccine at less than $0.50 per dose, and to provide the necessary tetanus toxoid carrier protein (TT component of the vaccine). With support from PATH, pharmaceutical consultants, public health institutes, regulatory agencies, the Center for Biologics Evaluation and Research (CBER) and WHO, the preclinical and clinical trial work R&D was completed in record time. The timeline below (figure 2) outlines the key milestones in the project.

Figure 2 Timeline of the Meningitis Vaccine Project

2000 Delegates from African and Eastern Mediterranean countries, multilateral organisations, vaccine manufacturers, and the scientific community agree that development of a meningitis conjugate vaccine for Africa is a high priority. Plans are drawn up for the Meningitis Vaccine Project (MVP).

2001 BMGF awards PATH and WHO $70 million. Discussions are held with African public health officials who clarify that a cost of more than $0.50 per dose would be unsustainable. Enhanced surveillance activities begin, and pharmaceutical companies are approached.

2002 When it becomes clear that no manufacturer in the developed world can produce a MenA conjugate vaccine at less than $0.50 per dose, MVP starts exploring alternative strategies.

2003 MVP supported the work to develop a supply of vaccine grade MenA polysaccharide (SynCoBioPartners, Amsterdam) and facilitated two suppliers in improving their purification methods, and MVP leads the transfer of an innovative conjugation technology from the US Center for Biologics Evaluation and Research (CBER).

2004 PATH enters into a long-term sub-license and supply agreement with the Serum Institute of India Limited (SIIPL) to develop, test and produce clinical and commercial lots of vaccine at target price. SIIPL prepares test lots and the first batches of the MenA conjugate vaccine. Partnerships are established with laboratories at the US Centers for Disease Control and Prevention (CDC) and the UK Health Protection Agency (HPA) for clinical trials.

2005 Partnerships are established with clinical research sites and organisations in India. The first human clinical trial is launched, which evaluates the safety and immunogenicity of the MenA conjugate vaccine in 74 healthy adults in India. SIIPL prepares additional batches of MenA conjugate for phase 2 clinical trials and stability studies. Standard operating procedures are finalised for enhanced meningitis surveillance in belt countries.

2006 One-year follow-up data from the phase 1 trial show the vaccine to be safe and immunogenic. Partnerships are established with clinical research sites and organisations in Africa (Ghana, The Gambia, Mali, Senegal). The MVP pivotal phase 2 trial is launched.

2007 SIIPL and MVP develop a strategic plan for vaccine licensure and production. SIIPL prepares the clinical lot for the infant study and starts compiling data for the regulatory file to be submitted to the Drugs Controller General of India (DCGI) for Indian licensure**.** Results from PsA-TT-002, the pivotal phase 2 clinical study, show that the MenA conjugate vaccine is safe and highly immunogenic. As a result, phase 2/3 studies are launched.

2008 The phase 2 infant study is launched in Ghana.

2009 SIIPL submits the regulatory file to the DCGI for Indian licensure and to WHO for prequalification.

2010 Phase 3 trials launched in India and Mali. The Maharashtra state Food and Drug Administration grants SIIPL the marketing authorisation enabling the vaccine to be exported and used in Africa. WHO prequalifies MenAfriVac. MenAfriVac is introduced at pilot scale in September in Burkina Faso, Mali and Niger, protecting more than 1 million people. On 6 December MenAfriVac is introduced at large scale in Burkina Faso, Mali and Niger.

2011 Cameroon, Chad and Nigeria become the next countries to introduce MenAfriVac at large scale. Burkina Faso, Mali and Niger report no cases among the nearly 20 million people who received one dose of MenAfriVac during 2010 mass vaccination campaigns.

2012 Cameroon and Chad complete their vaccination campaigns while Nigeria continues to roll out MenAfriVac. The vaccine is introduced in four new countries: Benin, Ghana, Senegal and Sudan. By the end of 2012 more than 100 million people are vaccinated against meningitis. MenAfriVac receives regulatory approval to be kept outside the cold chain for up to four days at up to 40°C, in a controlled temperature chain (CTC). A pilot project using the CTC approach is conducted in Benin in November as part of the mass vaccination campaign. Phase 3 infant study launched in Mali.

2013 Sudan completes the second phase of the MenAfriVac campaign while Nigeria completes its third campaign. MenAfriVac is further deployed in The Gambia, which vaccinates the whole of its target population in one go; and in Ethiopia. Countries organise mop-up vaccination campaigns for nomadic populations and people who live in refugee camps.

2014 WHO grants approval of MenAfriVac for use in infants and formulates the related policy. This decision opens the door to use of MenAfriVac in routine immunisation programmes in sub-Saharan Africa. Ethiopia completes the second phase of the campaign; Nigeria completes its last vaccination campaign. Côte d'Ivoire, Mauritania, and Togo introduce MenAfriVac using CTC. Indian regulatory authorities approve use of the MenAfriVac vaccine in children younger than 12 months.

3 Key elements of the innovation

This section outlines the key elements of the MVP and implementation of MenAfriVac.

3.1 Features

Affordable price: As stated, the affordability of the product for African countries affected by MenA was critical. By partnering with a developing country manufacturer, the vaccine was developed and manufactured and priced at $0.40 per dose – well under the $0.50 required.

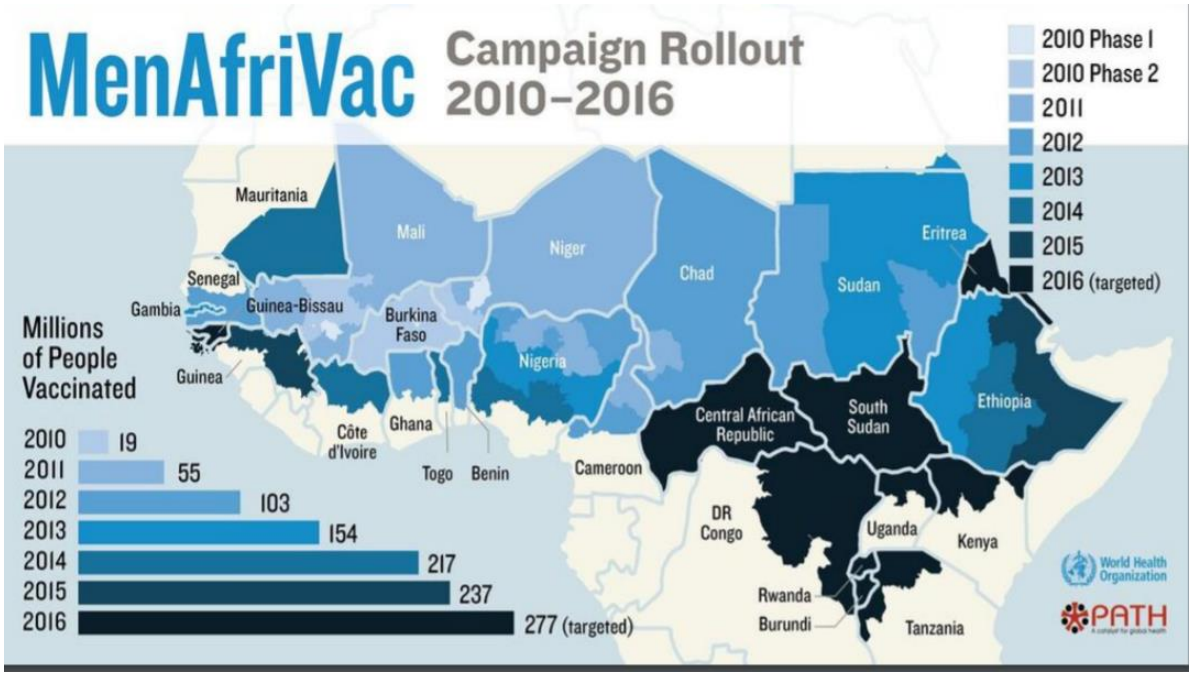
Context-specific design: The vaccine was designed for the context in which it would be used. Cold chain logistics are among the most difficult obstacles to overcome in conducting mass vaccination campaigns in the meningitis belt, particularly in remote areas with scant resources and infrastructure. The thermal stability was studied in detail by SIIPL, with the help of PATH's Optimize Project and the regulatory help of Health Canada. Permission was granted that the conjugate vaccine could be safely exposed to temperatures as high as 40°C for up to four days without affecting its efficacy (Djingarey et al., 2015).

Innovation and implementation as one: The rollout of this innovation cannot be delinked from its development (see timeline). The phased rollout also considered the production capability of industry and offered an accurate production target by coordinating with SIIPL to produce the required quantities of the vaccine on an annual basis to avoid any potential shortages of supplies.

Phased public health-driven scale-up: With coordination and technical support from WHO's Regional Office for Africa, the rollout of the vaccine began in 2010 in Burkina Faso. The campaign had strong backing from state institutions, with local delivery actors supported by international agencies.

The public health-led approach to scale-up considered disease burden and incidence as primary criteria where countries were ranked into five categories, from those with high epidemic risk and high disease burden to those with low risk and burden. Specifically, the selection criteria for priority countries to be among the first to introduce MenAfriVac were as follows: (1) presence of epidemic risk indicators; (2) presence of case burden indicators; (3) size of the target population; (4) expected annual vaccine supply; and (5) participation of population in clinical trials (Diomandé et al., 2015).

Figure 3 MenAfriVac campaign rollout, 2010–2016



Source: Levine (n.d.), 'Vaccine delivery', Bill & Melinda Gates Foundation

Within countries, the district prioritisation tool was developed. This evidence-based tool allows countries to take into account their epidemiological situation, their capacity to organise a mass campaign, and the vaccine supply situation. It proposes a framework for national discussions and decisions on the progressive introduction of vaccine in different districts and regions (WHO, n.d.).

Capacity-building: The MVP aspired to leave behind increased knowledge, experience and capacity among its network of partners. Whenever possible, it selected partners based in Africa and India, and capacity-building was sometimes required to ensure that partners had the requisite skills and knowledge to complete project activities in accordance with national and international regulatory requirements (Tiffay et al., 2015).

Strength of partnership: The foundation of the MVP structure was the PATH/WHO partnership. Each organisation brought different and complementary strengths to the project, and by defining clear roles and responsibilities, established a solid partnership. PATH's capabilities in product development, partnership with the private sector, and project management, finance and administration, along with WHO's knowledge of vaccine introduction, strong presence in meningitis belt countries, and expertise in disease surveillance, evolved into a strong working group. To avoid differences in organisational culture undermining the project, team-building efforts focused on understanding each organisation's unique characteristics to avoid frustrations and instead take advantage of these differences. Robust project management based on clear contractual arrangements, as well as strong shared leadership, were key to coordination and success.

A final element of the innovation worth noting is the sheer number and range of stakeholders involved (Figure 4) (see also Figure 5, on stakeholders).

Figure 4 Stakeholders in the Meningitis Vaccine Project

Source: The Meningitis Vaccine Project Closure Conference, Addis Ababa, Ethiopia: 22–23 February 2016

Figure 5 Stakeholders in the Meningitis Vaccine Project

Lead partners

- **WHO**: Provided overall project guidance and technical advice; coordinated the clinical development; supported enhanced disease surveillance in target countries; assisted countries in preparatory activities for vaccine trials authorisation and oversight, licensure and introduction, in particular the strengthening of national ethics committees and regulatory authorities, set-up of pharmacovigilance systems, logistics frameworks and financial sustainability mechanisms; and fostered training opportunities as well as political and community engagement.
- **PATH**: Provided overall project management and contributed expertise in business development, communications, vaccine development and testing. PATH identified the commercial partners for vaccine development and manufacturing, negotiated agreements, and led the pharmaceutical, clinical, and regulatory development work.
- **Ministries of health across the African meningitis belt**: Health officials in key target countries worked in partnership with WHO and PATH throughout the project. MVP partners have learnt much about the specific needs and opportunities in each country, and target countries have been able to strengthen systems for disease surveillance, clinical development, pharmacovigilance, ethics, vaccine regulation and vaccine logistics.

R&D

- **Serum Institute of India Ltd (SIIPL):** A major supplier of quality vaccines, SIIPL was chosen as the manufacturer. Its agreement to accept technology transfer and its willingness to sell the vaccine for less than $0.50 per dose were determining factors.
- **Aérial**: A French company, Aérial–Technology Resource Center provided expertise in the formulation and lyophilisation of the meningococcal A conjugate vaccine.
- **Synco Bio Partners B.V**: The company was the original supplier of meningococcal group A polysaccharide (MenA PS), one of the two main components of MenAfriVac.
- **Center for Biologics Evaluation and Research (CBER)**: Part of the US Food and Drug Administration, the CBER developed the MenA PS-TT conjugation technology before its transfer to SIIPL.
- **National Institute of Biological Standards and Control (NIBSC)**: The UK-based NIBSC was responsible for the independent analytical testing of intermediate and final products to ensure that product specifications were met.
- **Centers for Disease Control and Prevention (CDC), Atlanta.** CDC was a key partner in strengthening regional meningitis surveillance and intensified laboratory and surveillance in Burkina Faso while serving as an essential component in the post-introduction Burkina Faso carriage studies.
- **National Institutes of Health**: The US-based National Institutes of Health licensed the conjugation technology to SIIPL.
- **Norwegian Institute of Public Health:** Provided financial and technical support for the post-introduction carriage studies while serving as a site for the genomic study of meningococcal isolates.
- **African Meningococcal Carriage Consortium (MenAfriCar):** Coordinated by the London School of Hygiene & Tropical Medicine, MenAfriCar documented the vaccine's impact on transmission of the infection.
- Multiple clinical trials partners in Ethiopia, Ghana, Senegal, the Gambia, Mali, as well as India and Europe.
- Public Health England was in charge of serological testing.

Implementation

- MSF and UNICEF provided in-country expertise and support.
- **Agence de Médecine Préventive (AMP)**: A France-based non-profit organisation, AMP undertook the original research and wrote the socioeconomic study that provided the basis for the meningitis investment case that was submitted to the Gavi Alliance.
- **GAVI Alliance**: Made a critical contribution, spending US$ 29.5 million for the introduction of MenAfriVac in Burkina Faso, Mali, and Niger. This money covered vaccine purchase, planning, equipment, mass campaigns, training, and evaluation. The Alliance also spent a

4. Impact

The project is about public health impact and not simply making vaccines available. (MVP guiding principle)

This section outlines both the direct and indirect impacts of the MVP and rollout of MenAfriVac.

4.1 Direct impacts

The first mass vaccination campaign took place in Burkina Faso in 2010. Burkina Faso is known as the 'buckle' of the meningitis belt, as it has endured higher rates of meningococcal disease than other countries in the region. Data from Burkina Faso demonstrated a substantial and remarkable effect: from 2010 to 2014, there was not one case of MenA meningitis among vaccinated individuals (CDC, 2018). Carriage studies documented the disappearance of group A meningococci in immunised populations. Between 2010 and 2014, MenAfriVac was rolled out in 20 more countries through an innovative phased campaign (see Figure 5 and Key Elements).

Over a seven-year period (2010–2017) more than 280 million Africans between the ages of 1 and 29 years received a dose of MenAfriVac in large vaccination campaigns that were well-received by local populations. The direct impacts can be observed in the public health benefit to the target population, resulting in the complete cessation of epidemics related to MenA. Not only was the population protected through a long-term immune response (herd immunity), but there was also a dramatic reduction in carriage of the bacteria.

The WHO's Inter-Country Support Team for West Africa and partners led evaluations to understand the public health impacts in countries participating in the vaccination campaigns in order to generate an evidence base on outcomes. In Chad, for example, over a two-year period during which MenA epidemics were rife, the regions wherein the vaccine was introduced had immediate and dramatic drops in incidence, while those where the vaccine was not yet introduced did not (Trotter et al., 2017). The epidemic completely stopped once the entire population had been vaccinated. In Burkina Faso, the percentage of positive specimens dropped to 0 (see Table 1). A review of surveillance data proved that there was a 99% reduction of incidence in vaccinated countries (ibid.).

Table 1 Impact of MenAfriVac on isolation of group A Neisseria meningitidis from spinal fluid specimens (2005–2017) in Burkina Faso

Year	Reported meningitis cases	CSF specimens sent to laboratory	% Group A in positive CSF specimens
2005 (wk 18)	3,626	118	27.1
2006	19,134	1997	84.6
2007	26,878	417	91.1
2008	10,401	241	79.2
2009	4,723	275	30.1
2010	6,732	469	24.9
	Introduction of MenAfriVac in December 2010		
2011	3,875	3125	0.1
2012	6,797	3297	0.0
2013	2,512	1104	0.0
2014	3,476	2391	0.0
2015	2,927	1781	0.5
2016	2,645	1857	0.0
2017 (wk 23)	1,729	945	0.0

*data from WHO/IST-WA, Meningitis Weekly Bulletin. 2005-2017.

Source: LaForce et al. 2018.

Effectively, the mass vaccination campaigns conducted throughout the meningitis belt have eliminated MenA epidemics. In 2017, only two cases of MenA were recorded for the population of the entire meningitis belt (estimated

at 350 million to 400 million people); an estimated 250,000 to 500,000 cases of MenA have been prevented (LaForce et al., 2018). With a fatality rate of 50% if left untreated and case fatality rate of 5%–15% for patients receiving care, this implies that tens of thousands, if not hundreds of thousands of deaths have been prevented. Beyond this, debilitating conditions for people living with sequelae (including loss of limbs, paralysis or deafness) have been prevented en masse.

4.2 Indirect benefits

Cost-saving

For national health systems, the burden of MenA cases would have been significant. The reduced burden of disabilities (thanks to fewer cases) also saved thousands of families from loss of earnings (MenA predominately affects people in their most economically productive years), and protected households from potential catastrophic health expenditures associated with caring for survivors. Economic analysis has found that, after initial investment in the preventive strategy, $1 invested in routine immunisation with MenAfriVac saves an additional $1.3 compared to a reactive strategy of only deploying during outbreaks (Colombini et al., 2015).

Public health

The successful rollout of a controlled temperature chain (CTC) approach in mass vaccine demonstrates the utility of this approach in hot climates/low-resource contexts. The reduced costs and higher coverage rates observed indicate that additional testing should be conducted for other vaccines (such as yellow fever, measles, cholera and hepatitis) frequently used in mass vaccination campaigns or remote birth settings in similar hot and resource-poor contexts (Lydon et al., 2014). However, according to MSF, although considerable data is already available on the heat stability of most vaccines, companies are reluctant to seek re-licensing (a time-consuming and costly regulatory process) of their vaccines for use in extended temperature conditions, and MenAfriVac remains the only successful rollout to date (MSF, n.d.). The conjugate MenA vaccine used a carrier protein from tetanus toxoid (TT). This was shown to generate a robust tetanus serologic response in 1- to 29-year-olds, similar to those expected after a booster dose of TT – an unintended but additional positive public health impact. Also of note is that neonatal cases of tetanus have fallen by 25% in countries that completed vaccination campaigns for 1- to 29-year-olds (Okwo-Bele et al., 2015).

Capacity-building

Many indirect benefits were conferred to project partners. For example, the reputation of SIIPL as a global player was enhanced. As the main vaccine development partner for the project, SIIPL benefited from capacity-building in all phases of vaccine development. The SIIPL clinical team worked closely with the MVP for the clinical development plan and study design, implementation, and monitoring of clinical studies, and in the preparation of a regulatory strategy and file meeting the highest international regulatory requirements to obtain vaccine licensure.

In contrast to Pharma-led R&D, skills and expertise were strategically strengthened by the MVP's investment in capacity-building. National regulatory authorities in several meningitis belt countries were trained by the WHO Quality, Safety, and Standards team and MVP staff. Meningitis belt country laboratories gained capacity in advanced testing methods for detecting infecting organisms. Their surveillance teams benefited from MVP investments in surveillance and data collection training. The investments in capacity-building and technical support not only resulted in sustainable public health impact, but also returned benefits to the project as the vaccine was expeditiously licensed. Clinical sites became more autonomous as the project evolved, and the improved surveillance data yielded sound information before and after the introduction of MenAfriVac; some sites were also able to support additional vaccine trials related to other projects (Tiffay et al., 2015).

5. Enablers and barriers

One of the key features of MenAfriVac was the anticipation and successful navigation of the many barriers that R&D innovations face. These barriers include: funding; regulation related to qualification and clinical trials of introducing a novel pharmaceutical product; technical issues related to public health and surveillance; social barriers related to health messaging and the acceptance of vaccination campaigns; lack of political support; and limited logistical capabilities. The orchestration of enablers required for MenAfriVac's successful development should be viewed as a model to follow for future innovation in vaccine development and rollout.

5.1 Enablers

During design/R&D

Clear science and available technology: The existence and successful deployment of technology for a MenC conjugate vaccine meant that it would be possible to do the same for MenA. Unlike other diseases (malaria, HIV), there was scientific certainty that the problem was solvable. For WHO, MenAfriVac's 'unprecedented achievement is due to the overall availability, safety and effectiveness of the vaccine' (WHO, 2018). Global scientific and technical expertise ensured that the MenA conjugate vaccine met all international safety and efficacy standards (Tiffay et al., 2015).

International buy-in: The MVP invested significant resources in due diligence and consultations while compiling detailed plans and information to help convince stakeholders of the viability of the proposed vaccine development model; 10 international meetings in Africa, Europe and the United States were held during 2002 to gain international support and buy-in (ibid.). The high-profile nature of the project and global reputation of its leaders attracted international and local experts, and the scientific advisory committee benefited from significant pro bono expertise (more enablers, linked to overcoming barriers, are captured in the next section).

During implementation/scale-up

Community support: At community level, discussion groups (to explain the vaccination process, answer questions, and respond to concerns) included tribal elders and local administrators, while local social mobilisers were hired to promote the campaigns (Mohammed et al., 2017). Led by specialists from UNICEF, communication and mobilisation experts employed evidence-based techniques to promote maximum uptake of public health messaging, which created broader participation and acceptance of the campaigns.

Context-specificity: The design of the vaccine was highly context-specific, and the circumstances of implementation and end users were considered from inception. As high temperatures and low levels of infrastructure are a feature of the context, the CTC approach (as opposed to classic cold chain management) enabled the vaccine to remain effective at temperatures of up to 40°C for four days. It is estimated that this approach reduced costs by 50% and helped achieve greater coverage (WHO, 2018).

R&D integrated with implementation: Innovation and implementation were considered as one. For example: as early as 2006 and while the phase 1 study results were being finalised, planning for introduction of the MenA conjugate vaccine began. With most vaccines, this work is not usually begun until phase 2 or 3 results indicate that the product will be licensed (Kulkarni et al., 2015). The phased rollout enabled coordination with SIIPL to produce the required quantities of the vaccine on an annual basis to avoid any potential shortages of supplies, allowing almost uninterrupted scale-up.

Cross-cutting

***International funding*:** Doing new things in new ways can be expensive, and always involves trial and error: 'Solid upfront project funding allowed for judicious but important risk-taking, particularly in the early years of the project' (Tiffay et al., 2015). The project would not have been possible without the initial $70 million grant from the Bill & Melinda Gates Foundation or, indeed, the financial support of other donors, including the United States Agency for International Development (USAID), the Michael & Susan Dell Foundation, the CDC, the Research Council of Norway and the Fondation Mérieux (WHO, n.d.). The 10-year one-off grant from BMGF enabled long-term planning, capacity-building and relief from fundraising pressure. Furthermore, BMGF was invested in the project, offering opinions but ultimately respecting the MVP's decisions, allowing flexibility, and providing additional funding. For implementation, Gavi, the Vaccine Alliance funding enabled the rollout of the mass vaccination, while Gavi co-financing arrangements are enabling MenAfriVac's inclusion in routine immunisations.

Coordinated and complementary partnership: Excellent commercialisation agreements and contracts facilitated effective management by clarifying responsibilities and accountability (Tiffay et al., 2015). The MVP is an example of a well-coordinated multi-stakeholder partnership built on mutual trust and a sound and inclusive strategy. Although there were an extraordinary number of partners involved (see Figure 4), the partnership was successful thanks to its single

focus and complementarity of partners. For example, at the start, PATH's expertise in catalysing innovation and navigating the private sector enabled the project to overcome legal issues related to commerce and intellectual property; WHO's expertise in the international regulatory environment led to successful pre-qualification and effective collaboration with developing country policy-makers; while later, WHO and Gavi's experience at country level supported rollout in partnership with governments and implementing agencies.

In-country political support: One of the most critical elements of the development and introduction of MenAfriVac has been the commitment of national ministries of health (WHO, n.d.). During a WHO Regional Committee for Africa meeting in 2008, the health ministers of the countries of the meningitis belt signed a declaration committing themselves to introducing the new vaccine candidate when it became available. The project's success was underpinned by ongoing political support in all countries involved. The then president of Burkina Faso, Blaise Compaoré, helped create the local support required for a successful pilot vaccination campaign, and increased regional state-level adoption of the project (Berlier et al., 2015). African countries and public health leaders were priority project 'customers' as well as engaged partners. Progressive ownership of the MVP was experienced by African governments, health systems and communities (Tiffay et al., 2015).

5.2 Overcoming challenges

During design/R&D

Challenges negotiating legal and regulatory frameworks: PDPs are independent legal entities that must adhere to the legal and regulatory environment of their host countries. In the case of the MVP, this meant a range of countries involved in the project, including France, the United States and India. Negotiating the commercialisation agreements required was complex and time-consuming. Closing the agreement between PATH and SIIPL was a major legal and administrative challenge, and the process took two years before it was finalised. Thanks to the expertise of PATH's legal arm, overcoming these obstacles was possible, albeit a lengthy process (Kulkarni et al., 2015).

Intellectual property (IP) creating potential barriers to innovation: IP laws produce a barrier to innovation in that other companies cannot develop novel, even life-saving products on the back of existing technology – even when such developments are possible and relatively straightforward. The various components needed to create MenAfriVac had existed for decades but required a technology transfer (of the IP) to SIIPL to enable their use to develop this product. PATH's role here was pivotal to overcoming challenges. PATH was able to take technology that had been created for other vaccines and offer their use to SIIPL to create MenAfriVac. However, without high-level political support and the engagement of high-profile philanthropists such as Bill and Melinda Gates, these crucial technology transfers may not have been possible (or certainly not in such a relatively short time).

During implementation/scale-up

Low uptake among young men: Poor uptake of the vaccination among males aged 16–29 years was a challenge. Reasons why this group may not have attended the vaccination opportunities (whether in clinics or community settings) may include the belief that, based on their experience with polio campaigns, vaccines were only for children under 5 years. In other settings such as Burkina Faso, Mali and Niger, reasons may include the seasonal migration of young men from Sahel countries to southern countries and sociocultural beliefs that men should not attend the same activities at the same time as women and children (Djingarey et al., 2015). Successful efforts to overcome this challenge included peer education, targeted social mobilisation messages, the participation of celebrities known by young people, and the selection of launch sites for the campaigns taking place in universities and schools, which themselves would help promote MenAfriVac (Berlier et al., 2015).

Adverse events creating negative public perceptions: Adverse events in the campaign were countered by swift reactions at national and local levels. For example, in 2010, a crisis developed in Burkina Faso with the death of a child on day 8 of the planned 10-day vaccination campaign; news of the death was published on the front page of a national daily newspaper that erroneously linked the child's death to the vaccination. In response, a national-level press conference was held and an envoy was sent to address this in the affected community (ibid.). In 2013, in an isolated settlement in northern Chad, a wave of anti-MenAfriVac stories emerged: a Chadian journalist (subsequently identified

as a regime opponent) posted a story that described 40 children who had become severely ill (some with paralysis) after being vaccinated. The story was picked up by European and US anti-vaccination activists, who accused the MVP and its partners of deliberately committing genocide among Africa's poorest and most fragile populations. A WHO-supported rapid investigation led to understanding that there was no connection between the vaccine and the 'mass psychogenic illness' reported (ibid.). Support was offered to populations affected by this illness at local level and the press were contacted at national level and international level. Continued engagement with the press across the region was key to prevent misinformation from spreading further.

Cross-cutting

Limitations in economic (financial) resources: The single largest economic barrier to innovation of a new vaccine is financial; the development of a new vaccine is estimated to cost between $500 million and $750 million when working within the usual paradigm. The flexible BMGF grant covered all R&D activities, while contracting SIIPL ensured the cost of the vaccine. Although some countries reported the cost of campaigns as a challenge, use of the CTC brought implementation costs down. When additional funding was required to take on the development of the new formulation second form of the vaccine for use in routine immunisations, BMGF provided it, as budget decisions could be authorised with minimal bureaucracy. In the resource-poor countries of the meningitis belt, Gavi funding overcame financial restraints within local health systems.

6. Key lessons

During design/R&D

Innovate with a clear prospect for success: The MVP benefited from a specific purpose, with a clearly defined deliverable at an affordable price. MenAfriVac was known to have a clear potential to succeed from the development of a MenC vaccine in the UK. The prospect of success helped focus global efforts and align stakeholders around a clear mission and vision for the innovation.

Overcoming the limits of industry: The MVP reveals the limits of the pharmaceuticals industry with regards to public health of marginalised communities – and provides a model to overcome them. The PDP model helped bring stakeholders together under a not-for-profit framework to enable innovation for communities in sub-Saharan Africa often excluded from R&D innovation. The MVP also demonstrated the role and effectiveness of middle-income country-based industry partners in innovation and scaling health technologies. The lesson here is that 'Big Pharma' alone will not innovate the products that we need to accomplish the SDGs. Different operational modalities are required to attain those goals.

During implementation/scale-up

Context comes first: Not only was the product itself a request from the affected contexts, additional testing was conducted to develop the CTC approach (an innovation within an innovation). This context-led approach saved time and money and helped ensure success. State sponsorship, ownership and engagement helped connect the needs of marginalised populations with the highest levels of government.

Cross-cutting

Long-term flexible funding is key: Flexible multi-annual funding, including for technical support and capacity-building, were available in adequate supply from the onset of the project thanks to BMGF. Resources from Gavi were also essential for implementation of the mass vaccination campaign (where they covered all direct costs) and will also be required for the routine immunisation (although this second phase will also require countries to co-finance as per Gavi's rules). Flexibility of sufficient funds to cover a broad range of activities is also key for swift progress. With the current shift to shorter funding periods and incremental funding based on frequent detailed progress reports, the MVP story is an important reminder that major public health projects – especially those that involve innovation – rely on sufficient funds over a longer timeframe plus donor tolerance of risks that are part and parcel of innovation (Tiffay et al., 2015).

Success is possible: The MVP proves that the global community is capable of accomplishing remarkable achievements in a short time, when a variety of enabling factors are present: when the technology is possible, when planning is strategic and thorough, when the regulatory environment is clearly understood and addressed in advance, when the implementation is considered as an element within the innovation itself, when an inclusive approach is taken with international partners and governments, when adequate resources are available, and when cross-sector collaboration is genuine and not disrupted by other interests (Berlier et al., 2015). The MVP should be considered as a model par excellence in the development of future vaccines or essential medicines for use in contexts outside of the standard pharmaceutical paradigm, where public health needs are not in phase with profitability, and where progress towards SDG 3 is threatened.

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6.0 HITAP Case study

SUMMARY BOX

What is the innovation?

- The Health Intervention and Technology Assessment Programme (HITAP) is a non-profit, semi-autonomous research unit under Thailand's Ministry of Public Health (MoPH).
- HITAP uses the tools of health technology assessment (HTA) to evaluate evidence and inform policy and priority-setting.
- HITAP also builds capacity for HTA evidence generation, and serves as a convergence point for all HTA activities in Thailand.
- HITAP began with a domestic mandate but has increasingly been working with global and regional partners under the International Unit (HIU).

What were the enablers?

- Political commitment and public sector funding for public health and universal health coverage (UHC).
- Country demand, technical resources and capacity.
- Key individuals and champions to develop the programme and a network of allies.
- Independence from government and industry.
- HIU specific: international funding and partnerships between international institutions and countries.

What were the challenges?

- Overcoming a range of political and technical issues when setting up the programme.
- Relative lack of international support from global health agencies.
- Push back from industry when the programme may challenge pricing.
- Domestic politics may impede evidence-based policy-making.
- HIU specific: lack of domestic resources in counties reliant on official development assistance (ODA) to fund the health sector.

What are the lessons learnt?

- Success does not rely on international expertise, but is generated locally and regionally.
- HTA capacity development should be demand-driven, informed by local policy agendas.
- South–South collaboration builds context-specific support and shared learning.
- There may be international ambivalence towards projects promoting country-led policy prioritisation.
- The potential of country-owned 'market places' for evidence to help set priorities for locally appropriate country-designed benefit packages is not yet realised.

1 Introduction

The Health Intervention and Technology Assessment Programme (HITAP) is a non-profit, semi-autonomous research unit under Thailand's Ministry of Public Health (MoPH), created in 2007. HITAP uses the tools of health technology assessment (HTA) to evaluate evidence and inform policy and priority-setting. It also builds capacity for HTA evidence generation and serves as a convergence point for all HTA activities in Thailand. HITAP began with a domestic mandate but has increasingly been working with global and regional partners under the International Unit (HIU).

HITAP in Thailand has played a key role helping the MoPH refine and develop its benefits package for universal health coverage (UHC), which considers the introduction of novel technology into Thailand's specific social, health and economic context. Areas where HITAP has been effective include the negotiation of drug and vaccine prices, prioritising reforms in domestic health policy, and helping review performance and the impact of health sector interventions.

In the context of UHC, HITAP is recognised as an important innovation to facilitate resource allocation and to ensure equitable access to technologies. Although HITAP is the product of a specific time and place, its novel approach to HTA and promotion of country-led priority-setting resonates widely in the era of the Sustainable Development Goals (SDGs). Understanding more about HITAP's success in Thailand and beyond offers lessons for global health actors working towards SDG 3 targets, especially UHC. This case study explores HITAP and its use of HTA as an innovation, documenting the enablers, obstacles, successes and impacts of this country-demanded and driven programme.

2 Context

2.1 Thailand

Thailand's long-standing commitment to public health began in the 19th century. Prince Mahidol (born 1892) is considered the father of modern medicine and public health in Thailand, teaching citizens to 'put public interests first and self-interest second' (Prince Mahidol Award Foundation). Health professionals still learn his teachings by heart and the Thai health sector is characterised by a strong commitment to public good and equity; for example, newly qualified doctors are posted to rural deprived areas to begin their careers (Wibulpolprasert and Fleck, 2014). Equity is a fundamental principle in the Thai health system. The royal origins of the country's health system, combined with strong state governance of the sector, have created a political environment where long-term planning (especially important for preventive health interventions) is possible. As a result, remarkable progress has been made, and all within the context of a developing economy. According to the World Bank: 'Thailand is one of the great development success stories'. The country's adoption of smart economic policies led to it achieving upper middle-income status in 2011 (World Bank, n.d.).

Alongside only a handful of high-income countries, Thailand has achieved almost 100% universal coverage of health services (currently at 99.87%) and has made good progress across all health indicators. For instance, maternal and neonatal mortality rates are well below global targets and the proportion of undernourished population has fallen markedly from 34.6% to 7.5% (SDG platform, n.d.). In 2016, the World Health Organization (WHO) certified that Thailand had eliminated mother-to-child transmission of HIV and syphilis, becoming only the second non-OECD (Organisation for Economic Co-operation and Development) country to achieve this (Sidibé and Singh, 2106).

The success of Thailand's health sector is thus a source of inspiration for many low- and middle-income countries (LMICs). However, compared to other LMICs, Thailand has never been colonised, and the health sector has developed largely outside of the conventional ODA model. Thailand is not, and never has been, dependent on ODA that places conditionalities on prioritising and policy-making. While development partners have supported Thailand in many areas of the health sector, prioritisation (especially around the design of the UHC benefit package) has been country-led. For global health actors, Thailand's success is also an inspirational story. However, the lessons emerging must be caveated by the country's unique historical and political experience.

2.2 Global, regional and SDG context

Considering Thailand's experience, and in line with SDG 3.8, many countries are aspiring to UHC. Many of these countries are also growing economies, with increasing numbers of middle-class citizens, and with associated growing (potentially very expensive) burdens of non-communicable diseases (NCDs). A WHO consultation has found that policy-makers across LMICs have concerns about the financial sustainability of healthcare services and there is a growing demand for evidence-based prioritisation of tools to aid decision-making, especially around the benefit package (WHO, 2014). Yet in most LMICs in Asia and beyond, there is limited capacity for HTA, especially in making links between evidence and policy (Singer, 2008). In African countries, research has found that little attention has been paid to developing the capacity of individuals, institutions and networks to apply economic evaluation in support of HTA and effective priority-setting (Doherty et al., 2017).

UHC is a political project requiring country leadership and domestic resources. While there are offers of international support for UHC (especially around domestic resource mobilisation), global health agencies have been less forthcoming in supporting decision-making processes – for example, by helping to create a domestic market for evidence, or capacity building for HTA. In order to achieve UHC, countries need tools to help them generate, assess and translate evidence into policy. HITAP has enabled such tools in Thailand.

HTA is an important tool to help design equitable benefit packages for UHC (SDG target 3.8). As an increasing number of LMICs in Asia and elsewhere attempt to operationalise UHC commitments and increase investments in the scale-up of essential health services, HITAP's innovative approach to HTA for UHC is highly relevant, linked to the achievement of target 3.8 but also related health outcome targets (3.1, 3.2, 3.3 and 3.4).

Beyond SDG 3, HITAP-informed policy aims to increase access to affordable healthcare through UHC, reducing out-of-pocket expenditures, which are a major cause and perpetuator of poverty (SDG 1). HITAP's work also helps reduce inequality (SDG 10) by helping secure access to medicines for all. Partnerships and capacity-building are central to HITAP's approach; thus the innovation also contributes to SDG 17, especially target 17.9.

2.3 History and evolution

Linked to long-standing UHC ambitions, an interest in HTA existed in Thailand at least two decades before HITAP's creation in 2007; however, apart from universities and research institutions that carried out basic research mainly for academic purposes, there were only a few units within a handful of public organisations conducting health technology appraisal in ways that would support public policy-making. Before HITAP, three attempts to bring together HTA in Thailand were unsuccessful due to the limited expertise available in health economics, inadequate institutional support capacity, and a lack of any long-term commitment. The 1997 economic crisis, combined with increasing public expenditures from the introduction of new public health insurance schemes, provided the window in which to catalyse the development of HITAP (Culyer, Podhisita and Santatiwongchai, 2016).

HITAP emerged in Thailand from the existing International Health Policy Programme – a research project on health financing and economics in the Health Systems Research Institute (HSRI). Although many people contributed to HITAP's development, the key champions were Dr Suwit Wibulpolprasert, Dr Viroj Tangcharoensathien, Dr Yot Teerawattananon and Dr Sripen Tantivess.[17] In 2005, a proposal was submitted to Harvard University to initiate a national programme for HTA that would assist decision-making in the provision and utilisation of pharmaceuticals, medical devices, procedures, and health prevention and promotion in Thailand. When the grant application proved unsuccessful, funding was sought from four domestic sources instead: the Thai Health Promotion Foundation (ThaiHealth), the HSRI, the National Health Security Office, and the Bureau of Policy and Strategy in the Ministry of Public Health. The proposal was approved in January 2007 and approximately 30 million *baht* made available, mostly from the ThaiHealth, for running the first three years of what was to become HITAP (Culyer et al., 2016).

In 2010, the goal of HITAP was articulated as: 'to provide policymakers, health professionals, health providers and the public with scientific evidence about the costs and benefits of introducing of health products, procedures and programmes'. HITAP's vision is: 'a state of the world in which the only health interventions and technologies available at public expense are all demonstrably effective and available for all'. Its specific aims are:

- to appraise efficiently, using transparent processes, health interventions and technologies by using methodologies of a high international standard;
- to develop systems and mechanisms that will promote the optimal selection, procurement and management of health technologies and contribute to the effective policy design of the healthcare system;
- to disseminate research findings and elevate public understanding to enable the best use of the results of health interventions and technology assessment.

Building on the first international project with WHO in Myanmar[18] in 2010/11, HITAP began receiving requests for experience-sharing and technical support from countries in the Southeast Asia region. Demand has centred on support for analysing cost-effectiveness, with work ranging from technical assistance to support for specific projects. In 2013, the International Unit (HIU) was created. Although this is legally a separate entity from HITAP Thailand, there are close working relationships between the two. The HIU's strategy covers international relations (for example, collaboration with WHO), HTA capacity-building (e.g. through internship programmes, and study visits for policy-makers) and collaborative research (ibid.). The vision is to build HTA capacity in developing countries, through the mission: (1) to foster collaborations with international and regional organisations, HTA units, and other respective institutes in other countries; and (2) to coordinate technical support and policy advice from relevant institutes in Thailand (HITAP, n.d.).

> *HIU draws upon the experiences of its experts to match the growing demand for evidence-informed policy at the global level. Under HIU, dedicated professionals collaborate to provide our partners in different countries the means with which to build institutions for HTA and priority setting at the local, national and global levels. In this effort, HIU draws upon its experiences locally and various countries to become a regional hub for HTA and enable South-South collaboration. To this end, HIU works with international organizations, non-profits, and overseas governments to develop evidence-based priority setting practices globally.* (HITAP, n.d.)

[17] Dr Suwit, Dr Viroj and Dr Yot are all medical doctors. After graduation from medical school in Thailand, they worked in rural poor areas before moving to the Ministry of Public Health in Bangkok. Dr Sripen's first degree is in pharmaceutical science and her PhD is in public policy from the United Kingdom; she had more than 10 years' experience at the Food and Drug Administration (Culyer et al., 2016).

[18] In 2010, with financial support from the Global Alliance for Vaccine and Immunization's Health System Strengthening programme, the Government of Myanmar established a scheme to improve coverage of maternal and child health (MCH) services. Collaborative research was conducted by Myanmar's Ministry of Health, the WHO and HITAP, which led to proposals for a voucher scheme to be considered by Ministry of Health decision-makers (Teerawattananon et al., 2017).

HIU has worked directly in nine countries in Asia (Bhutan, India, Indonesia, Myanmar, Nepal, the Philippines, Sri Lanka, Timor-Leste and Viet Nam) and is now working in Kenya too. The international Decision Support Initiative (iDSI) was central to this scale-up.

> *The international Decision Support Initiative is a practitioner-led partnership that facilitates priority-setting. Its mission is to guide decision-makers towards effective and efficient healthcare resource allocation strategies for improving people's health. It aims to achieve this by providing a combination of practical support (hands-on technical assistance and institutional strengthening) and knowledge products (high-quality, policy relevant research and tools).* (Li et al., 2017)

Also launched in 2013, led by NICE International, iDSI brought together the Center for Global Development, NICE International, HITAP, several major UK universities, the US-based Johns Hopkins University, the Office of Health Economics, Meteos, and Priority Cost-Effective Lessons for System Strengthening South Africa (PRICELESS SA) (Culyer et al., 2016). HITAP's experience made it a natural partner for iDSI. Through iDSI, HITAP also participates in projects in South America (Chile, Colombia) and Africa (South Africa, Ghana). Criteria for country selection include the goal to move towards UHC and a policy demand for HTA capacity-building, a focal point committed to absorb capacity-building, and local partners to work on policy-relevant case studies or pilot projects in a participatory and transparent manner (Tantivess et al., 2017).

3 Key elements

In Thailand, HITAP itself conducts HTA-related activities (generating research, assessing evidence, capacity-building, training); in other contexts, HITAP supports local HTA agencies to conduct activities, using adapted elements of the HITAP model in Thailand. There is no one innovation that is scaled up or replicated; key elements vary across contexts. This section thus aims to capture the key aspects of HITAP Thailand's model/approach, as well as common (but not universal) elements elsewhere. Across different contexts, HITAP emphasises **systematic and transparent work**, aiming to cultivate public interest and encourage participation from all sectors to efficiently distribute and allocate resources to fulfil public objectives (HITAP, 2016).

3.1 HITAP Thailand

Capacity-building for HTA is central to HITAP's vision and there has been considerable investment in individual capacity in Thailand. Initially, domestic funding enabled young Thai researchers to undertake fellowships in leading US and UK universities. Over the past 12 years, HITAP has funded and supervised more than 40 scholars, most of whom are working in the public sector in Thailand. A new programme with leading universities in the region will offer an 'on-the-job' HTA Master's. HTA training helps to sensitise health professionals to the importance and process of HTA as a prerequisite to UHC.

Generating and appraising evidence. Unlike some HTA agencies (for example, the National Institute for Health and Care Excellence (NICE) in England), HITAP's research is mostly conducted 'in-house' by local researchers. Between 2007 and 2016, there were 124 technology assessment projects on drugs, medical devices and procedures, disease prevention and health promotion measures, packages of care and other public health policies (Culyer et al., 2016). HITAP researchers also appraise evidence from other sources, particularly that generated by manufacturers and other private sector actors that may be seeking to influence decision-making around priority-setting.

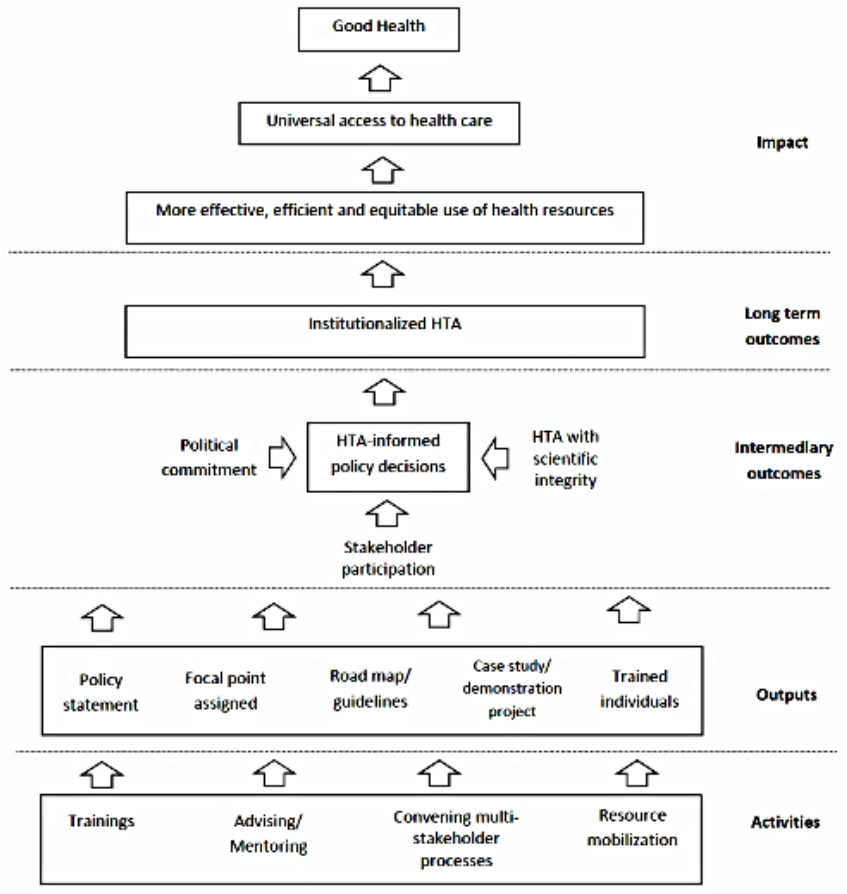
Stakeholder engagement. The key stakeholders for HTA in Thailand are civil society/patient groups, policy-makers, health professionals, academics and researchers, and private sector representatives. These groups are invited to participate in HITAP's workshops at different stages in the process – from prioritising research topics to reviewing results; involving stakeholders at all stages is one of the key strategies to enhance the quality, transparency and accountability of HTA (ibid.). To aid engagement in the dissemination of research results, diverse channels are used, including meetings, seminars, press releases, blogs, Twitter and Facebook. The aim is to create dialogue between researchers and users (including patients and the general public) (ibid.).

3.2 HITAP International Unit

***Capacity-building towards institutionalising* HTA.** HITAP and iDSI capacity-building programmes provide training and mentorship on research and policy development, convene stakeholder processes, and help mobilise resources for HTA (financial, material and information). Initial stages of capacity development generate road maps, demonstration projects and case studies as well as trained human resources to sustain the work (Tantivess et al., 2017). Figure 1 outlines the framework being used in the target countries for institutionalising HTA (India, Indonesia, Kenya, the

Philippines and Viet Nam). In contexts where health sector resources are especially constrained (for example, Myanmar and Timor-Leste), the goal of capacity development is not to institutionalise HTA but to expose decision-makers and technical officers to evidence-informed policy-making concept and practice (ibid.).

Figure 1 iDSI conceptual framework for HTA capacity development programmes in LMICs



Source: Tantivess et al. (2017)

Technical assistance for HTA projects. Since 2013, the experience and expertise in HTA that has been built in Thailand is being shared internationally, mainly through the partnership with iDSI. However, Thai HITAP experts are also requested bilaterally by international partners (WHO, UNICEF and the United Nations Development Programme (UNDP)) to provide expertise on country missions. As well as longer-term capacity-building programmes, at the request of countries and/or international actors, HIU provides technical assistance for specific projects. For example, following the closure of the Gavi health system strengthening programme in Myanmar, the WHO, on behalf of the Ministry of Health and Sports, requested HITAP to provide technical support to conduct a study to help understand the impact of the programme, especially the health financing schemes implemented (Dabak, Teerawattananon and Win, 2019). In Timor-Leste, HITAP was commissioned by UNICEF to assess a new monitoring and evaluation (M&E) tool and conduct training to ensure that local staff could use it effectively (HITAP, 2018a). In Bhutan, an economic evaluation on the pneumococcal conjugate vaccine recommended its introduction into routine immunisation services (Dorji et al., 2018). The WHO's Southeast Asia Regional Office (SEARO) has appointed the HIU to conduct projects in Sri Lanka, Nepal and Bhutan.

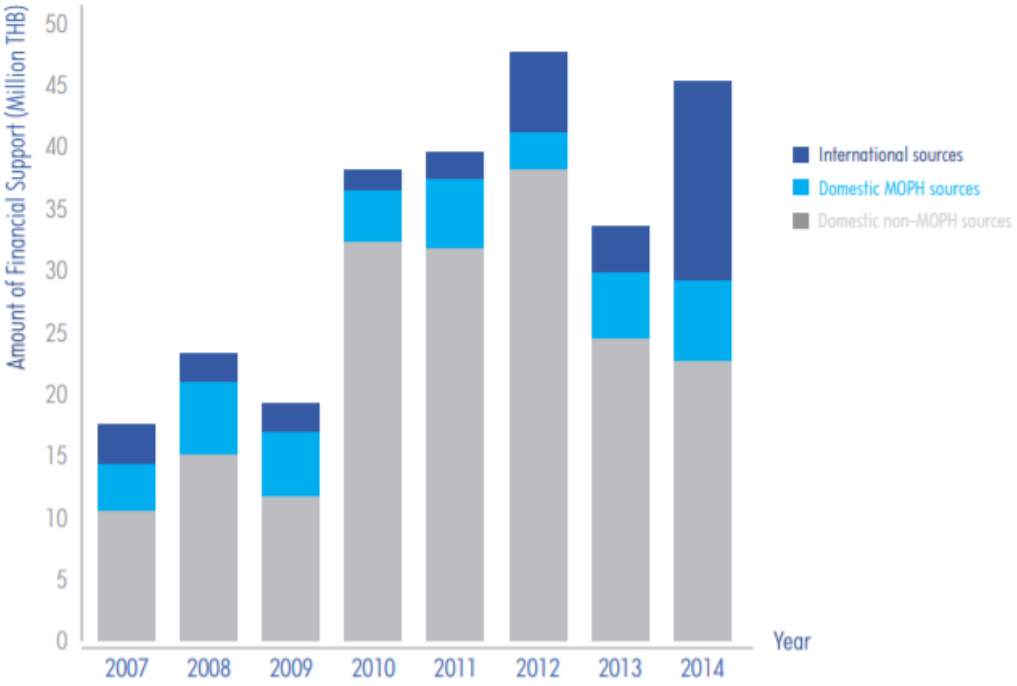
South–South collaboration. HITAP's capacity-building work is a two-way process building partnerships based on common challenges as well as a shared commitment to the UHC goal. As well as the Asian countries, Kenya has now signed a memorandum of understanding with Thailand to support its UHC work, in which HITAP is closely involved, and a study visit has been conducted (HITAP, 2018b). The Ministry of Health in Chhattisgarh state, India, has also benefited from a study visit (Eames and Kim, 2019). HITAP is a founding member of HTAsiaLink, a network established in 2010 by countries in the Asia-Pacific region to strengthen collaboration between HTA agencies. Currently, it has 34 members from 17 countries, as well as two associate members from HTA agencies from two countries outside of the region. Since its formation, HTAsiaLink has become a forum for engaging in academic activities, research, and information/knowledge

exchange relevant to HTAs. The network functions as a platform for HTA capacity-building (peer-to-peer knowledge exchange in HTA best practice and experience-sharing) and fosters new HTA research collaboration (Teerawattananon et al., 2018).

3.3 Funding

In the first three years of its existence, about 80% of HITAP's funding came from four national sources: ThaiHealth, the HSRI, the National Health Security Office, and the Bureau of Policy and Strategy (the latter being the only organisation sitting within the Ministry of Public Health). Relatively little support came from international sources. Over the years, the number and variety of funding sources has increased; most striking is the large share of funding taken up by international sources in more recent years, reflecting both HITAP's effectiveness as an international networking organisation and its growing reputation and international standing (see below) (Culyer et al., 2016). Figure 2 shows the changing balance of funding – a trend which has continued.

Figure 2 HITAP's income, 2007–2014



Source: Culyer et al. (2016)

4 Impact

> *"The greatest merit that HITAP has on health care practices and the national health system is that it acts as a key mechanism to facilitate justifiable and evidence-based allocation of the limited public resources, in preference to the practice of arbitrary budget allocation (by some authority) or in favour of certain advocacy groups."* (Professor Vicharn Panich, Thai health leader, cited in Culyer et al., 2016)

The impact of a complex and multi-faceted innovation like HITAP is hard to measure. HITAP has innovated health research so that the emphasis is on country-led decision-making, based on domestic priorities and criteria (as opposed to academic or global health trends).

Since 2007, HITAP has succeeded in:

- building local capacity for HTA
- building domestic demand for economic evaluation
- generating country-owned policy-relevant research

- creating an indigenous and international community of producers and users of HTA
- raising awareness around the indispensability of local evidence in policy-making.

There is now more training and research capacity for HTA in Thailand and regional capacity has been built via the HIU's work and HTAsiaLink. It is estimated that most of the 150 or more studies in Thailand have been fed into national policy-making processes, and HITAP-supported research has been formally embedded as part of coverage decisions elsewhere. HITAP has contributed towards the institutionalisation of HTA across the region, developing guidelines, tools, databases and knowledge management (for example, the GEAR database) (Tantivess et al., 2017).

4.1 Influencing policy and pricing nationally

HITAP's own estimate of domestic policy impact is that around one-third of its publications have resulted directly in policy action while at least 70% have generated public discussion. In Thailand, HITAP has considered more than 120 topics nominated by stakeholders for prioritisation and selected more than 50 for further assessment; informed by this process, 20 new interventions were included in the benefit package based on value for money, budget impact, feasibility and impact on equity (Culyer et al., 2016).

An example of this impact is how HITAP's analysis of two possible drugs for age-related macular degeneration found that Bevacizumab and Ranibizumab were equally effective, but the former was much cheaper; Bevacizumab was subsequently recommended to be included in the national list as a result (the WHO also later supported the use of the drug for treating this condition). HITAP has also empowered and incentivised the government to negotiate domestically for reduced vaccine prices (Teerawattananon and Tritasavit, 2015).

Influencing HPV vaccine introduction (Culyer et al., 2016) In 2007, when two companies were applying for human papillomavirus (HPV) vaccine licensing in Thailand, HITAP was asked to conduct an economic evaluation and budget impact analysis. The findings showed that at the price of $450 per course (three doses), HPV did not represent good value for money for public investment. The price of the vaccine needed to be reduced by approximately 60% for the vaccine to become cost-effective. The results were made publicly available and the government decided not to include the vaccine, preferring prevention through screening. Furthermore, the two companies examined the report and agreed with the findings, three months later reducing the price of the vaccine in line with the report's recommendations.

Informing antiretroviral treatment (ART) policy (Culyer et al., 2016) In 2013, HITAP was asked by the National Health Security Office to assess the feasibility of the national AIDS committee 'end AIDS' policy to provide ART regardless to all patients. Upon examination of the report (which had been produced with international AIDS experts), HITAP identified two issues: (1) the report provided an over-optimistic estimate of the effectiveness of HIV screening, which contrasted with the empirical evidence in Thailand; and (2) the total cost estimated by economists from the United States Agency for International Development (USAID) had been misinterpreted – HITAP's estimate was that the actual total cash flows over the period were almost four times the $10 million suggested. The review results were presented in a stakeholder consultation meeting and stimulated important debate about the policy.

4.2 Influencing policy and pricing internationally

Examples of influencing policy and pricing internationally emerge from iDSI and HITAP's work in the region. For example, in Indonesia, several years of technical assistance and support from HITAP has helped the government to acknowledge the importance of evidence-informed decision-making; two cancer drugs regarded as 'budget-burners' were delisted from the national drug formulary (Stewart, Sharma and Li, 2018). In the Philippines, as part of the capacity-building programme, assessments of pneumococcal conjugate virus (PCV) and HPV vaccines for the national Expanded Programme on Immunization (EPI) were conducted, aiming at transferring HITAP's experience on vaccine assessment; the results suggested that both vaccines were cost-effective, but that a countrywide HPV immunisation programme might be unaffordable. The government thus decided to scale up PCV vaccine coverage, while requesting reanalysis of HPV vaccination (Tantivess et al., 2017). A final example comes from Viet Nam, where in 2016 the Ministry of Health commissioned HITAP to provide support to its research institute for the revision of the Vietnamese benefits package, which led to the reform of a benefit package of high-cost medicines and medical devices under the Viet Nam Social Security Scheme, leading to nearly $150 million of savings per year (ibid.). Under the Thai delegation, HITAP also helped secure the 2014 World Health Assembly resolution: 'Health intervention and technology assessment in support of UHC' (Culyer et al., 2016).

5 Enablers of HITAP's success in Thailand

The following is a summary of enablers that allowed HITAP in Thailand to succeed. The same factors are likely to be important in other countries aspiring to replicate the HITAP model.

Political commitment to public health and UHC: Public health is a priority in Thailand and public expenditure reflects this. The historical commitment is underpinned by royal, political and societal support for achieving equity in health. State and societal support for equity in health have been essential to help institutionalise HTA and the work of HITAP in government and among the public.

Public funding*:* The allocation of budget – ultimately from Thailand's progressive use of the 'sin tax' on alcohol and tobacco to fund health equity-related activities – was essential to start HITAP in Thailand. The HIU will only commit to long-term capacity-building in countries where the government is willing to pay.

Country demand: HITAP in Thailand was a ***demand-driven innovation*** and this factor is crucial in other contexts. Linked to the above point, country demand drives buy-in across the range of stakeholders involved in HITAP and helps to ensure ongoing political commitment (e.g. through political cycles) and sustainability.

Domestic capacity for HTA: Under the HITAP model, health research priorities are set in-country and studies are conducted by local researchers/institutions. Capacity-building has been a strong focus to ensure that Thai researchers are equipped with skills to conduct HTA studies that contribute to policy-making. HITAP's strategy to build domestic capacity is a key enabler to develop its expertise and help retain independence.

Key individuals: These same individuals, most notably Dr Suwit Wibulpolprasert, Dr Viroj Tangcharoensathien, Dr Yot Teerawattananon and Dr Sripen Tantivess, have remained ***champions***, using their political capital where necessary. Finding high-level HTA champions is important elsewhere. HTAsiaLink is building a network of HTA allies to help support individuals.

Independence from government and industry: As a governmental programme, HITAP has a formal link with the MoPH. However, it also has other accountabilities and income sources to enable its 'arm's length' relationship. HITAP's funding principle is that no contracts or financial support of any kind are accepted from for-profit sources, ensuring independence from industry. Maintaining an independent advisory role, with distance between HITAP and decision-makers, together with the visible involvement of other researchers and stakeholders, means that it is largely immune to political and commercial pressures (Culyer et al., 2016).

5.1 Enablers for scale-up internationally

International funding and partnerships have been key to scaling up the work beyond Thailand. The scale-up of the HIU has been organic in that, as HITAP's reputation and visibility have grown, it has attracted more funding in a process that was not planned. HITAP has received funding for research, capacity-building and technical assistance in other contexts directly from a range of sources to enable its work internationally. HITAP was a founding member of the iDSI and this partnership and funding through iDSI were key to the formation of the International Unit and regional scale-up.

In 2007 and 2008, modest contributions were received from international funders but the majority of HITAP's work in Thailand has been funded through public money (see Figure 2). Since 2013, international funding and partnerships have enabled HITAP to work in other countries. However, it is important to note that – following the HITAP/iDSI model – the majority of costs for HTA development in countries must be borne domestically; international funding is not currently a key enabler of HTA in general (see final lesson below), but it is important for HITAP and partners to work beyond Thailand.

Table 1 HITAP scale-up from 2007 to 2017

Year/s	Country/ies	Project	International partners/funders (not including in-country partners)
2007	Thailand	HITAP Thailand	World Bank, Global Development Network
2008	Thailand	HITAP Thailand	Global Development Network
2009	Thailand	HITAP Thailand	WHO

2010	Thailand	HITAP Thailand	n/a
2010	Myanmar	Maternal and child voucher scheme	WHO
2011	Thailand	HITAP Thailand	n/a
2012	Thailand	HITAP Thailand	n/a
2013	Thailand*	Motherhood in childhood	United Nations Population Fund (UNFPA)
2013/14	Bangladesh, India, Viet Nam	Assessing Decision Maker Needs and the Transferability of Information across Countries and Regions	Bill & Melinda Gates Foundation (BMGF)
2014/15	Philippines	HTA capacity-building	iDSI**, Nice International, Department for International Development (DFID)
2014/15	Indonesia	HTA capacity-building	BMGF, DFID, Nice International, iDSI
2014/15	Viet Nam	HTA capacity-building	iDSI, Nice International
2014/15	Chile, Colombia, Ghana, Philippines, Thailand	The Groundworks Project	DFID, METEOS, NICE International
2015/16	Indonesia	Package of Essential Non-communicable (PEN) Disease Intervention evaluation	WHO
2015/16	Nepal	Reviewing the free drugs list	WHO
2015/16	Sri Lanka	Evaluating the social cost of tobacco	WHO
from 2016	India	HTA capacity-building	iDSI
2016/17	Bhutan	Introduction of PCV in Bhutan I	
2016/17	Myanmar	Gavi Health Systems Strengthening study	WHO

* domestic work continues until present
**iDSI is funded by BMGF, DFID and the Rockefeller Foundation
Source: HITAP website, 2016 report

6 Challenges for scaling up the HITAP model globally

This section focuses on the challenges for HITAP's international work, and its aim to support the institutionalisation of HTA in other countries. Reflecting on their experience within HITAP and NICE International, Tantivess et al. (2017) identify the following challenges:

***Lack of capacity*:** The range of infrastructure and resources required for HTA technical capacity – data, expertise, guidelines, money – is often absent in the health sector in LMICs. Therefore, in such contexts as Myanmar, the goal is not full institutionalisation of HTA, but rather to strengthen evidence-based policy-making capacity. However, for this capacity-building to have sustained impact, it needs buy-in from development partners (who drive the majority of health spending) in the country, as well as their continual technical and financial support (ibid.). Institutionalising HTA requires the capacity to connect the research community with the complex policy-making sphere, which remains a difficult task even in high-income settings (Lehoux and Blume, 2000).

Lack of domestic resources: Domestic resources are a prerequisite for HITAP's work in partner countries. However, the ability to fund HITAP collaboration through domestic health sector budgets may be a barrier for less economically developed contexts exploring the model; for example, in Laos, a country accustomed to donor-funded programmes, it has been a challenge to fund HITAP staff time. Investing in 'invisible' innovations like HTA that only indirectly impact health outcomes is not always the most attractive (or politically viable) option to policy-makers.

Lack of international support: The work on HTA capacity-building within countries requires long-term effort and flexibility. iDSI reports that it has been difficult to secure funding for the kind of work it does, as it does not offer clear, measurable and certain deliverables: 'We are constantly faced with uncertainty and are subject to local champions and to political priorities guiding each country's agenda'. As Table 1 shows,

Resistance from global health agencies: The fact that donors often control valuable resources for buying commodities (whereas Ministry of Health resources tend to be committed to infrastructure and salaries) and tend to have needed technical resources makes them the ideal conduit for HTA. However, their work concentrates on specific diseases (The Global Fund) and technologies (Gavi, the Vaccine Alliance), making allocative efficiency considerations less applicable. With more countries interested in merging vertical programmes with their own basic packages and with donor support declining, HTA is likely to become increasingly important.

Resistance from industry: A final challenge is the role of the private sector in the process of building institutional, data and technical capacity for HTA. Within a transparent framework where interests can be managed on all sides and participation is encouraged, HTA can serve as an ideal platform for healthcare products as well as the private insurance industry, reducing uncertainty regarding market access and helping set standards for managing providers: 'Experience has been that HTA is an engagement tool that can benefit private players, many of whom still see it as a cost-containment measure'.

In some settings, there may be strict controls on research dissemination, which means that research outcomes that are unfavourable to decision-makers tend not to be used in policy-making. However, as demonstrated in Thailand, this can be overcome through strategic communication with the public, organising multi-stakeholder fora, and training stakeholders in HTA. The fact that respect for expert (senior) opinions or authorities is held in higher regard than evidence-based research may be a barrier for using HTA in policy decisions (Chootipongchaivat et al., 2016).

7 Lessons and conclusions

Success does not rely on international expertise. HITAP's work involves a range of stakeholders but success does not depend on expertise from the 'Global North', nor technical assistance from international health agencies – quite the opposite. In scaling up its international work, ***HITAP has been an equal partner*** within the iDSI. In implementing capacity-building and technical assistance, HITAP experts from Thailand undertake the role historically reserved for expatriates from high-income countries. The HIU's technical assistance work for WHO-SEARO has not involved international global health actors.

HTA capacity development should be demand-driven*, informed by the local policy agenda* in order to link HTA to policy decisions and also help build trust. In countries without demand for use of evidence in certain policy areas, long-term capacity development to encourage evidence-informed priority-setting may not be worth the effort. ***Buy-in for HTA is needed,*** from all senior decision-makers, including not only politicians but also health officers. This can be achieved by building on the reputation of local as well as international partners. HITAP shows how public programmes can lead policy discussions surrounding priority-setting and the political economy of health domestically. HITAP emerged from a unique historic and political context and stemmed from a country-identified need – it is a demand-driven innovation. When Harvard University rejected the original proposal, funding was instead successfully sought from domestic sources. (Until 2013, public funding covered most activities.)

The strength of South–South collaboration: HITAP and its South–South collaborations have created a strong regional network to enable progress towards UHC, with minimal support or funding from international agencies. The capacity and experience HITAP has built in Thailand provides valuable lessons for international actors seeking to support HTA and UHC in Asia and beyond. Working internationally comes with its own challenges. However, it has generated much learning around the political economy of priority-setting (for example, collusion with industry) and cultural factors that influence policy-making (for example, how respect for hierarchy may override respect for evidence).

There is international ambivalence towards HITAP: HITAP has succeeded in creating its identity in the past decade, both domestically and overseas. However, while international interest is growing, it does not reconcile with the success of the innovation thus far. This lack of interest may be attributed to a potential aversion towards country-led policy prioritisation tools and processes that may undermine the goals of some (disease-focused) global health actors, for whom making allocative efficiency considerations may be problematic if the disease/issue they support is no longer considered a domestic priority. This reflects a wider picture where **global health is less supportive of domestic institutional building** than other initiatives, likely due to the explicit trade-off decisions that HTA forces, which may see vertical programmes deprioritised. HITAP has been unsuccessful in securing Gavi funding, for example. Despite this, HITAP has explored engagement with international actors, showing that prioritisation tools and processes are useful even within their specific areas of work.

There is unrealised potential: The role of international agencies in creating country-owned 'market places' for evidence, and institutionalising HTA as a technical and political tool to set priorities, has not been fully realised. There remains an asymmetrical situation whereby research and evidence generated does not always match local needs or priorities to increase access to essential health services. As more countries seek to merge vertical programmes with country-designed benefit packages towards sustainable health sector development, HTA is likely to become increasingly important. Global health agencies can learn from HITAP and adapt approaches to focus on country capacities and prioritisation processes, essential for sustainable development in health.

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