Digital health for the End TB strategy: progress since 2015 and future perspectives

Meeting Report

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Quotes

"Programme managers, technical agencies and donors have shown increased interest in recent years to invest in innovative digital technologies as a way to enhance efforts to combat tuberculosis. Such bold action needs to be sustained into the future and backed by matching commitment at the highest political level."

Dr Mario Raviglione, Director, WHO Global TB Programme

"The European Respiratory Society is proud to be among the leading professional bodies in respiratory health to support WHO and countries to implement novel technologies and to improve the quality of research to the benefit of our patients"

Dr Guy Joos, President, European Respiratory Society

Background note

1. Why digital health for tuberculosis?

The End TB Strategy of the World Health Organization (WHO) aims to bring the global TB epidemic to an end in the 20 years post 2015(1),(2). Actions envisaged to achieve the targets of this Strategy are in three areas: patient-centred TB care and prevention; supportive policies and systems in which TB care operates; and research. All of these areas could benefit from measures which make current operations more effective or efficient, such as an improved deployment of electronic and mobile phone applications (eHealth / mHealth, collectively known as digital health) with which we are surrounded(3). Any progress within the first decade of the End TB Strategy will rely heavily upon the wider uptake by TB programmes of measures which can exploit "test and treat" approaches available today and which make no assumption about the large scale implementation of revolutionary breakthroughs (e.g. vaccines) in a near future.

Digital health continues to attract interest from programme managers, decision makers, donors and other key actors in TB care and prevention as a means to improve the quality, effectiveness or efficiency of their efforts. In 2015, WHO's Global TB Programme (WHO/GTB) and the European Respiratory Society (ERS) released a joint "agenda for action" to define how different digital technologies could be roped into efforts in achieving the different goals envisaged by the End TB Strategy following a major consultation of interested parties in February of that year (Figure 1)(3),(4). Target product profiles for priority digital health technologies were further elaborated in 2016(5). These events, including a number of associated symposia at major scientific conferences in recent years and parallel work supported by technical and funding partners, successfully advanced the discussion on several leading digital health products. This was particularly instrumental in achieving concrete progress in the areas of medication adherence (such as the development and country implementation of video-observed therapy), electronic recording and reporting (e.g. DHIS2), and diagnostic device connectivity for molecular and conventional platforms. They also led to the development of a collaborative effort to review the study evidence systematically and model the potential of digital technologies when applied at scale.

2. Objectives of the WHO/ERS consultation of 2017

This technical consultation cast a look back over the last two years since the start of the WHO/ERS collaboration, taking stock of progress made and considering future perspectives moving forwards (see agenda at Annex 1). The meeting brought together about 60 experts from a broad cross-section of technical expertise in TB and other major communicable and non-communicable disease programmes, digital health, evidence review, laboratory science, programme management, funding agencies and end-users with a stake in this subject (list of participants at Annex 2). The presentations[1] held over the two days drove the discussion along the four main themes of the meeting, namely:

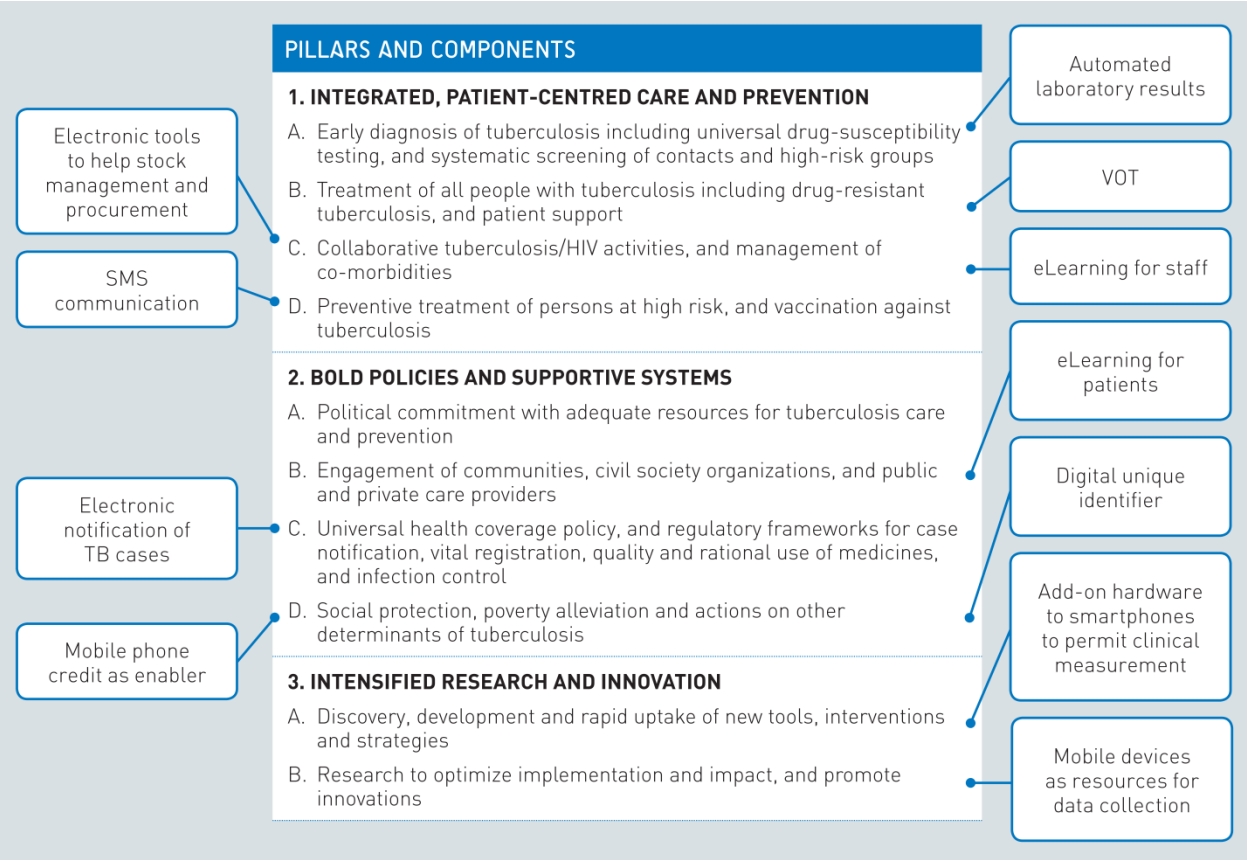
- the evidence for effectiveness and efficiency of digital health interventions in TB treatment adherence and their potential contribution to the End TB Strategy targets;
- the progress made in the development and implementation of technologies covered by the Target Product Profiles (TPP) created by WHO/ERS in 2015-2016;

[1] Accessible at https://www.dropbox.com/sh/1u6oedugmnwk3yo/AADjJkZOOC5MTSX1Wk4-M4zpa

- key novel concepts which could play a role in the future prevention and care of TB and how they could be included in the work plan of the WHO/ERS collaboration
- models for the future support of digital health technologies for TB and other health issues

Abbreviations & acronyms used in this report are explained at the end of this report (page 28)

Figure 1: *Schematic representation of common exemplars of digital health technologies and their potential entry points the End TB Strategy*(3)



3. Meeting sessions

3.1. Main messages from the leadership of the WHO Global TB Programme and the European Respiratory Society

(Mario Raviglione, WHO/GTB; Guy JOOS, Giovanni Battista Migliori, ERS)

In their introductory messages, the Director of WHO/GTB and President of the ERS thanked the numerous technical and funding agencies, national TB programme managers, developers and other stakeholders who have helped WHO to elaborate the digital health agenda for the End TB strategy, particularly in the last two years. The 2017 consultation comes two years after the first one held in February 2015, and highlights the progress made since. Evidence for the effectiveness and efficiency of some of the most common digital interventions applied to improve TB treatment adherence has been

increasingly consolidated in the last few years and while more studies will be needed to help understand the role these technologies can play at different points in patient pathways. Nonetheless, it is important to keep a close watch on the findings in order to help guide implementers on how best to use these technologies. The meeting also provides the first opportunity to assess the progress made in the development of some of the target product profiles (TPPs) and the implementation of technologies like video-supported therapy (VOT), connected diagnostics, and electronic surveillance in countries. It also discusses other concepts which could have an application in TB efforts, such as Massive Open Online Courses (MOOCs) for human resource development, support tools for programmatic implementation of LTBI and the potential for some novel concepts like artificial intelligence and nanotechnology in precision medicine, as well as "drones" as a means of delivering health care in remote settings. I believe that TB could act as a pathfinder for innovative mechanisms which can catalyse the further deployment of leading edge digital technologies for patient needs and large scale impact and which can be applied to other global health issues. The ERS remains deeply committed to supporting digital health interventions in respiratory health (such as eLearning) and has provided exemplary leadership for other professional bodies, and technical and funding agencies to follow, by playing a pivotal role in its support to WHO and to countries to invest in these technologies. This will be important to ensure maximal operationalization of efforts for the End TB Strategy. The outcome of this consultation could contribute importantly to the subjects and deliverables expected in a near future, particularly the Moscow ministerial conference in November and the UN General Assembly in 2018(6).

3.2. Digital health for the WHO End TB Strategy: meeting objectives & milestones since 2015

(Dennis FALZON, Hazim TIMIMI, Ernesto JARAMILLO, Karin WEYER, WHO/GTB)

The introductory presentations highlighted the structure and objectives of the technical consultation. There were three major processes which hallmarked the period 2015 to 2016, namely

- In April 2015 WHO/GTB convened a *Global task force for digital health and TB*(7) to advise it on:
    - the development of digital health products that are aligned to the challenges posed by TB to health care providers and patients;
    - the approach to the review of evidence and best practices for the effectiveness of digital health interventions in TB care and prevention; and
    - how to support WHO Member States to scale up digital health technologies for TB care and control based on existing knowledge

  The experts on the Task force are appointed for two years and the membership will be renewed in 2017.
- A conceptual framework for digital health & TB was used to organise the digital technologies applied to TB under 4 inter-related functions: patient care, surveillance, programme management and eLearning. Through 2015 this framework was further elaborated into an "agenda for action". The "agenda" highlights the strategic direction that WHO has mapped out to integrate digital health into activities to strengthen the preventive and care of different components of the End TB strategy. It also includes commentary on the evidence for the

different interventions and the rationale behind the priority digital products identified for profiling in TPPs

- The TPPs were elaborated and published in mid-2016(5) (Table 1). These TPPs are descriptions of key features and conditions required of the priority digital products in order for them to serve TB programmes in particular. A number of country projects were also started to document the use of the concepts profiled.

In addition to the processes set into motion through the WHO/ERS activities since 2015, the meeting also acknowledged the parallel processes on products not encompassed by the priority TPPs which had been taken forward through separate initiatives. For example electronic medication monitoring has been implemented at very large scale in high TB burden settings like India and China and was the subject of randomised controlled trials(8),(9). Moreover, WHO/GTB has also been involved for several years in the support to national programmes and technical agencies to strengthen patient recording and reporting in aggregated and disaggregated electronic systems for surveillance and logistics management(10). Most recently WHO/GTB has been collaborating with leading technical and funding agencies (the Global Fund to Fight AIDS, TB and Malaria, USAID) to help countries implement DHIS2(11) as a prototype open-source system for the management of aggregated or individual patient data. Its implementation fits within the scope of the surveillance TPPs. Such work opens opportunities to build upon the infrastructure created in order to develop other components, such as laboratory information systems within the ambit of "connected diagnostics" and mortality registries. These technologies can also support patient care, particularly adherence measures (e.g. link between video-supported therapy and electronic registration(12)).

Table 1: *Summary of priority digital technologies defined by TPPs*(5)

Function	***TPP : short description***
Patient care	1. Video-supported treatment (VOT) via mobiles
	2. eHealth portal
Surveillance & monitoring	3. Graphic dashboards
	4. eNotify
	5. eReporting of adverse events of treatment
Programme management	6. Diagnostic device connectivity
eLearning	7. Patient information platform
	8. Web-based training for health care professionals
	9. Clinical decision support systems

Presentations and the ensuing discussions held at the consultation fell into four themes: evidence, country experience, funders' perspectives and future concepts. Two main motifs ran through the meeting discussions, namely :

(1) what evidence exists for effectiveness and/or efficiency and how can it be strengthened ?

(2) what impact is expected at large scale ?

Introductory session 1. Digital health for TB: state of the evidence for adherence

(Richard LESTER, University of British Columbia, Canada)

Tuberculosis programme managers are increasingly taking advantage of the diffusion of affordable mobile electronic devices to address critical challenges in patient care. An updated literature review of studies of the effects on tuberculosis treatment outcome attributable to three digital technologies which can be implemented at large scale: short message service (SMS), video directly-observed therapy (VOT) and electronic medication monitors (e.g., digital pill dispensers). MEDLINE/PubMed, EMBASE, Cochrane Library, Web of Science, clinicaltrials.gov and Global Health were searched in July 2016 for the effect of digital health on cure or treatment completion of active tuberculosis. Given a dearth of published studies the search was extended to unpublished literature. Six geographically-diverse studies that included control groups and provided summary effect estimates were eligible for full review. Three randomized controlled SMS trials showed no statistically-significant effect on cure or treatment completion when compared with local standard TB care. Two observational studies of synchronous VOT reported risk ratios for treatment completion of 1.02 and 1.47 (neither statistically-significant)(13),(14). For medication monitors, one observational study reported an effect on cure (risk ratio=2.3, 95%CI: 1.6-3.4) and one randomized controlled trial reported no statistically-significant effect. Despite interest in applying digital technologies in tuberculosis care, effects have been variable and evidence from implementation studies remains sparse. However, evidence suggests that these technologies might be at least as effective as standard care. Data from ongoing and future research, including non-inferiority studies, are needed to promote practical approaches to optimizing interventions, such as using interactive SMS and blending technologies to achieve large-scale impact.

Introductory session 2. Modelling the potential impact of digital health on adherence measures of TB infection and disease

(Kevin SCHWARTZMAN, McGill University, Canada)

A decision analysis modelling study was conducted to project potential costs and impacts of four digital technologies in the management of active and latent TB. These were: two-way SMS messaging, video-observed therapy (VOT), and two types of electronic medication monitors (Wisepill® and 99DOTS®). Both drug-sensitive and MDR-TB were considered and Brazil was used as the setting for the simulation. For latent TB infection (LTBI), the modelling included both the close contacts and unselected individuals with LTBI. Model inputs reflected a systematic review, as well as published cost data, product specifications, and information provided by key informants. For active TB models, the simulation covered two treatment cycles i.e. initial treatment followed by retreatment if needed. For LTBI, the simulation spanned 20 years from the time of treatment initiation, using a Markov model with 3% annual discounting. The analysis was conducted from both societal and health system perspectives.

For the treatment of active TB, SMS could not replace in-person directly observed treatment (DOT). However, the substitution of DOT by VOT may lead to equivalent outcomes with substantial savings, particularly for drug-sensitive disease. Medication monitors are even cheaper; limited evidence suggests they may improve adherence compared with standard DOT. If confirmed, this would make them extremely attractive i.e. cheaper than DOT with better outcomes.

For LTBI treatment the current standard in many settings is self-administered treatment. Extrapolation from the experience with HIV treatment-support suggests that SMS could improve adherence and TB prevention in a highly cost-effective manner, particularly in persons at higher risk for progression to active TB. Again, confirmation in the TB context is required. For daily LTBI treatment support, VOT appears substantially more expensive and hence much less cost-effective. Medication monitors, while cheaper than VOT, also appear less cost-effective than SMS for the support of LTBI treatment.

TPP Session 1: Connected diagnostics target product profile

(Chris ISAACS, FIND Geneva)

In the last few years connectivity software has been implemented widely to capture data direct from GeneXpert machines(15),(16),(17). In addition to the data extraction step which was the original scope of the connected diagnostics TPP(3), the implementation of these solutions has shown that the successive steps of data storage and transmission were inseparable and could be incorporated as part of the same TPP. Nonetheless, these solutions have up to now been focused on a single technology and do not yet address the crucial need to combine data from different diagnostic technologies used in the same laboratory or for the same individual. In 2016 FIND developed and implemented a Connected Diagnostics Platform (CDP) in one site in Viet Nam to test the convergence of automated data from Xpert MTB/RIF as well as microscopy results entered via a human interface. By 6 January 2017, the system had captured 3378 microscopy and 310 Xpert results. It also demonstrated the feasibility of transferring these results data directly into the two electronic medical records systems in use by the TB programme (VITIMES and eTB Manager; see also presentation below). This experience has provided valuable insights for the further enhancement and for a more comprehensive documentation of the connectivity TPP. The connected diagnostics TPP was originally meant to describe the first of three processes on a continuum (the other two being data storage and presentation of results) : it would be practical to have the current TPP extended to incorporate all the three elements into a single product. The speaker proposed that connected diagnostics be evaluated on four elements namely (i) Coverage of sites and tests; (ii) Quality of data in terms of timeliness, reliability and consistency; (iii) Impact on patient care and programmatic improvement; and (iv) Sustainability of the intervention with steady expansion.

TPP Session 2: Perspectives on video-observed therapy (VOT) for TB

(Richard GARFEIN, University of California San Diego, United States)

While the current WHO recommendation calling for patients with TB to be observed in-person taking each dose of medication through DOT has lowered TB mortality, prevented acquired drug resistance and reduced disease transmission, its use has been limited by the high cost and burden for TB programs and patients, particularly in high-burden countries. Rapidly increasing proliferation of smartphones globally

creates an opportunity to lower the costs and burden associated with traditional in-person DOT by allowing healthcare providers to remotely observe their patients' administration of medication. The arrival of video-conferencing software has allowed providers to employ VOT in situations in which patients could not be observed in person. Subsequently, mobile phone applications that could securely record, store and forward videos began to be developed in response to the limitations posed by "real-time" VOT, particularly the need for reliable network connectivity and conduct observations only during set business hours. Two VOT modalities utilizing mobile-devices have thus emerged. *Synchronous* VOT involves the use of live videoconferencing software for patients and providers to see and hear each other at the time that patients take their medications. *Asynchronous* VOT allows patients to record themselves ingesting their medications using a smartphone or a tablet computer and forward the video to their providers to be observed immediately or at a later time. A few completed and ongoing evaluations of VOT have shown that both forms produce high treatment adherence, increased patient and provider satisfaction, and lower programme costs compared to in-person DOT. VOT has also been found to be feasible under circumstances when in-person DOT was not. Despite the dearth of studies evaluating VOT's efficacy, TB providers in a number of countries have begun incorporating VOT into national programmes based on the perceived benefits of the technology and evidence from small pilot studies. Two RCTs of VOT for TB are ongoing(18),(19). More experimental and observational studies are needed to increase evidence and improve its quality, so that stronger recommendations can be made on how and when to best use VOT.

Country experience 1. VOT in London

(Alistair STORY, Find & Treat, United Kingdom)

The Find & Treat TB outreach service implemented a RCT on VOT for TB in London using a dedicated smartphone application developed by the University of California San Diego(18). The trial was open to all TB patients aged 16 years or older at participating sites who had at least two more months of treatment remaining and met national or local guidance for DOT were eligible for inclusion. The trial recruited 225 patients by the time it ended in 2016 (plus another 26 non-randomised patients who had MDR-TB or were children and were thus ineligible). Preliminary findings show that a much larger proportion of patients randomized to receive VOT started treatment and had outcome data for >1 week (84% vs. 54% respectively) and more patients in the VOT arm had all medications observed than those on DOT (68% vs 32% respectively in intention to treat analysis). These findings suggest that VOT is more feasible than in-person DOT in a highly urbanised setting such as London.

Country experience 2. VOT in Belarus

(Alena SKRAHINA, National TB Programme, Belarus)

DOT has been recommended to improve adherence to tuberculosis treatment, but the daily commitment over many months presents challenges for both patients and health-care staff. VOT can help bridge the gap between patients and health services and conceivably promote adherence. In 2015 the Ministry of Health of Belarus, with support from the World Health Organization (WHO), piloted VOT for TB patients in the capital, Minsk(12). The intervention was aligned to the digital health target product profiles developed by WHO/ERS in 2015. A smartphone application was created by a local systems developer and linked to the national electronic TB register. Patients were provided with

smartphones and internet time, and shown how to record and transmit video files to trained clinic staff. The pilot showed the feasibility of VOT and it was expanded countrywide with support from a Global Fund grant. Between 1 January 2016 and 1 February 2017, 105 patients were recruited: their median age was 32 years (range:18-67); 68% were male; and 62% had multidrug- or extensively-drug resistant TB. Of 4,797 VOT episodes registered, 94% were of good quality. No smartphone was lost during the period. The preliminary experience indicates a positive influence on adherence and good acceptability by staff and a diverse mix of TB patients located in all six regions of Belarus. The experience gained can promote this patient-centred approach for other diseases (e.g. ART for HIV) and in other countries.

TPP Session 3: Electronic case-based surveillance for TB

Country experience 1. Viet Nam

(Le Van HOI, National TB Programme, Viet Nam)

Viet Nam has had a long experience in electronic case-based recording of TB data. A TB disease prevalence survey in 2006-2007 revealed widespread under-reporting; this motivated the NTP to invest in digital patient records for surveillance and logistics. The first pilot project of a national TB notification system on an electronic platform (VITIMES) was undertaken in 2010. That same year, the NTP also started exploring a separate platform for the electronic registration of data from patients on treatment for multidrug-resistant TB (eTB Manager supported by the MSH SIAPS Program). It required about 5 years for both VITIMES and eTB Manager to be rolled out nationwide and they have now been adopted completely by the programme. A review of VITIMES data in 2015, the first year of countrywide implementation, showed that about 87% of aggregated reports were also registered in the VITIMES. The “connected diagnostics” platform introduced in 2016 by FIND Geneva has succeeded to “push” results data into VITIMES and eTB Manager from the laboratory system. While running two electronic systems in parallel for TB has inconveniences there are also some advantages: the two electronic systems have their own individual strengths and moreover the dataset needed for the management of MDR-TB is much bigger than the one needed for non MDR-TB patients and would therefore overburden VITIMES were the two to be merged. A firm bridge to interoperate connected diagnostics software with eTB Manager and VITIMES is envisaged for future. The other enhancements required are data quality assurance, the creation of dashboards, and worker skills in data analysis and utilization. The running of the electronic systems requires to collect a massive amount of data and the investment in terms of infrastructure and health care worker time are substantial (one comment in the discussion following the presentation is to make such systems more “health care worker centred”).

Country experience 2. India

(Kirankumar RADE, Revised National TB Programme, India)

From the early days of DOTS implementation in 1998, India espoused electronic TB recording. The first system (EPI-CENTRE) was initially DOS-based and later (2007+) run on Windows. EPI-CENTRE captured aggregated information from the TB units at sub-district level; it only covered the public sector operating in the Revised National TB Control Programme (RNTCP) while the huge private sector was excluded. In 2012, TB notification became mandatory in India. To facilitate notification by both public and private providers a new electronic case-based surveillance system - Nikshay - was introduced and

scaled-up countrywide within 6 months. Since its launch in 2012, Nikshay has cumulated >7 million patient notifications from the public sector. With the exception of a few States, Nikshay is the standard tool now in use for recording and reporting of TB patients in India, and EPI-CENTRE has now been discontinued. It now has an option for notification via a mobile application (in Android), and >30% of patients are now notified through this application. In 2015, Nikshay was enhanced to include modules for contact tracing, adherence support, drug-susceptibility testing, follow-up and outcome reporting alongside the original notification functionality. Online directories also allowed the electronic platform to improve communication with all staff and facilitate the referral and transfer of patients across the country. In 2017 it is expected that the patient's unique AADHAAR number(20), which is registered on Nikshay, will provide the authentication needed for secure payments of enablers to be made to both patients and providers.

Nikshay also covers notification from the private sector. Most private providers polled in 2013 preferred electronic reporting over paper-based systems. When private practitioners notify a case they are issued with a voucher number, which entitles patients for TB medicines free-of-charge. This incentive has improved private sector notification. More than 0.1 million private providers are now registered with Nikshay and have notified 0.8 million patients to date. Nikshay has made it possible for the RNTCP to calculate treatment outcomes in the private sector for the first time. It also provides crucial insights into how care is dispensed and presents opportunities to reinforce positive behaviour or fix incorrect practice.

Nikshay is now providing a reliable evidence base to guide programmatic action. For example, the direct measurement of TB patient body weight is used for more precise drug forecasting and for advocacy on nutritional support to TB patients. The database represents another data source for inventory studies. The notification patterns by different age-group and sex bands help prioritise different interventions. The granular information on site of disease, microbiological confirmation, and drug-resistance patterns was previously unavailable and is starting to allow better planning of diagnosis and treatment support.
Alongside the reinforced electronic surveillance, India has made progress in other areas of digital health. For instance, VOT, medication electronic monitoring system (MEMS), SMS, and voice calls – including 99DOTS[2] - are all being evaluated for their role in improving patient medication adherence.

Panel discussion: perspectives for the operationalization of fast-moving digital technologies while evidence is strengthened

Chairs: Mario RAVIGLIONE, Giovanni Battista MIGLIORI

The funding agencies were requested to present their perspectives on digital health in TB work, addressing topical questions such as the following:

- What models of engagement have worked out for your agencies to help countries scale up digital health interventions in a situation of incomplete evidence or uncertainty of impact?

[2] 99DOTS is an intervention which monitors daily TB treatment adherence through a series of Freephone numbers; the unique number for a patient to call each day is disclosed when medication is removed from its blister pack(21).

- Under which conditions will a TPP approach be best suited to steward the development of a given technology?
- Which key actors should be engaged to convert an emergent concept in digital technology into a fully-fledged product which can be scaled up?
- In your opinion are there products where the benefit is so clear that they should be implemented without waiting for further evidence of effect? If so what are their attributes?
- In addition to steering the TPP process, how do you see WHO's role complement the efforts of donors to help countries implement promising technologies?
- In your opinions, could a body independent of WHO, with its own separate funding, catalyze the uptake of existing technologies for TB control while enhancing their performance? Is there a "critical mass" of products, demand and potential suppliers which would justify devoting such a facility to TB (in contrast to a multi-disease mechanism)?

BMGF (Daniel CHIN)

The model of engagement for BMGF has typically started with a country assessment of needs and demands. BMGF has been particularly active in this domain in China and India. In China in 2007, in-person DOT presented challenges and experiments were started with medication electronic monitoring system (MEMS). China has since rolled out MEMS at a large scale and its impact is evaluated by trials supported by the Foundation(8),(9). These studies help optimise the interventions, finding how they can be most effective and/or efficient, and identify implementation weaknesses as well as opportunities (e.g. FDC implementation). The results of these RCTs will be important for the funders (for the national programme they were less crucial given that the conviction that in-person DOT was not feasible). In the opinion of the donor an RCT is not needed for all technology innovations. In India, one of the main issues has been the low coverage of TB care in the private sector. The introduction of 99DOTS(21) was one of the scalable approaches for BMGF/USAID to support the RNTCP improve patient medication adherence. Data are being collected to assess the effectiveness of 99DOTS in India, including usability testing and validation against urine testing. This information can measure performance at both the individual and programme and is expected to inform approaches to 'differentiated care' and to guide overall case management. The "backend" of 99DOT is open source and its linkage to Nikshay is being tested out in India. MEMS and 99DOTS could not replace DOT but are much more scalable. Adherence monitoring is needed over the whole course of TB treatment, during which different methods may be applied for this purpose. The monitoring system would thus need to comply with different technologies employed.

ERS (Werner BILL)

The ERS is primarily a European professional body, but with a global perspective. It is more of a medical society specialised in lung health than a traditional funding agency. Even if the funding for the Global TB Programme to work on digital health is relatively recent, the technical collaboration with WHO has a much longer history. It also extends to non-communicable diseases (e.g. ERS is on the Global Alliance against Chronic Respiratory Diseases (GARD)(22)). TB is one of the "big five" priority conditions for the ERS although funding for TB is much less when compared with COPD. The ERS is interested to promote the whole domain of digital health and online services. For instance it has been on the forefront of

leading-edge debates on how digital health and a fuller use of patient data can help personalise respiratory care(23). The TB *consilium* is a collaborative intervention with the WHO Regional Office for Europe which ERS has supported in order to provide expert advice to clinicians treating difficult cases(24). The ERS has also been very active on eLearning(25). The ERS views its joint initiative with WHO/GTB on digital health as an early investment in an emergent area of work which overlaps with its own efforts. The ERS leadership is pleased with the achievements to date, and always favours of initiatives which promote research and disseminate knowledge. It believes that WHO should retain a leading role, even if an independent "facility" is created in future to promote the concept of digital technologies for the TB care.

Global Fund to fight AIDS, TB and Malaria (Mohammed YASSIN)

The Global Fund investment in innovations like digital health for TB is primarily driven by the request from a country within the framework of an approved or proposed funding grant and the evidence of impact of a particular intervention, be it data from local experience or evidence from published studies. Country allocations are typically for 3 years and therefore these are not similar to project-funding operated by other funding or technical partners. Another mechanism for funding such interventions would be via "catalytic" funding (e.g. for expansion of DHIS2). Communication of information/evidence about digital technologies (e.g. to country-coordinating mechanisms (CCM)) would be important in order to evoke appropriate initiatives for GF investment. The discussion and engagement should start at country level and is not a headquarters-level decision. GF promotes broad discussion about such interventions between local partners. It also encourages country-level partners and civil society to accept some level of risk associated with novel interventions. Such was the case with the GF support provided to several national TB programmes and technical agencies like UNION and Action Damien to implement shorter MDR-TB regimens in recent years. This allowed critical data on the effect of these regimens to be collected and analysed within a few years, and as a consequence WHO could update its MDR-TB treatment policy swiftly after(26). Continued monitoring is important to limit risks and to collect more information useful for implementation. Such a model could equally apply to digital technologies. One clear example of bold action was described by Belarus earlier in the day, where GF seed funding allowed a VOT project to be tested out for feasibility ahead of nationwide expansion. Apart from electronic surveillance another recent example of continued investment in digital technologies has been the support to "connected diagnostics". Finally, with respect to having a "facility" which would champion the development and scale-up of digital technologies for TB, this is *a priori* a positive move which could strengthen the profile of these interventions as well generate evidence. However, independence is needed and therefore potential conflict of interest needs to be managed well.

UNITAID (Sara PADIDAR)

The UNITAID mission is to maximize the effectiveness of global health response by catalyzing equitable access to better health products. The model of engagement is typically project-based and follows a call for proposals (e.g. for LTBI, childhood TB, MDR-TB). Implementation of innovative technologies is challenging, especially with solid evidence so frequently in short supply, therefore it is often necessary to take measured risk. The objective of some projects is focused on generating evidence; in others it is

more about achieving a threshold of implementation to catalyse further implementation. Funded projects need to have a clear pathway to global health impact and longer-term plans for sustainability. UNITAID also assess if the innovation is expected to be a radical game-changer or if the expected gain is incremental. For digital health interventions, amongst the constituencies which would be essential, civil society and mobile network providers would also need to be engaged. Other important ones would be the prospective users, laboratories, suppliers, manufacturers, national authorities and donor agencies. Insofar as an independent "facility" to further the goals of the End TB strategy through digital health, it would probably make more sense not to have it specialised on TB (TB might however be a pathfinder). By keeping it broader in scope it would promote integrated action on other related health issues which the same patients and providers need to address and also interface with other technologies.

USAID (Kaiser SHEN)

The USAID investment model in digital health is driven primarily by country work-plans, even if USAID has core funding and a strong institutional support for IT in health care(27). USAID looks at digital health as a cross-cutting utility and engages beyond the technology to help in its implementation. Taking GenXpert by analogy - which is relatively straightforward to install and operate, is endorsed by WHO and other technical and funding partners, and for which there is solid evidence of superior performance compared with other diagnostics - what stands in the way of wider scale-up seems to be country buy-in. Likewise for other innovations in digital health, for which there is often less evidence and common thinking on a single product. It thus requires the concerted effort of partners on the ground to come up with workable solutions for scaling up. Creating a facility focused exclusively on TB may work against greater integration of disease-diagnostic technologies. It is likely that action would be more convincing if it targets more than a single disease and also bridges different platforms. For instance the interoperability of electronic medical or health records (EMR/HER) with laboratory information systems remains very often a weak link, a situation that is not restricted to TB. Funding cycles are not long enough to pilot technologies or undertake operational research. The role of WHO could complement the efforts of donors to help implement promising technologies by providing countries with standards and policies for decision making.

Discussion points

The main points raised by the participants following the presentation included:

- Monitoring adherence needs to take into account the patient viewpoint to avoid replicating similar problems inherent to in-person DOT. The importance of monitoring adherence was highlighted given that poor treatment compliance in TB is so consequential, which may be less important for other diseases (and thus motivation may be lower). If cost-effective approaches which add value to the patient's treatment experience could be effectively scaled up, then other disease programmes could also become interested.
- Improving the evidence base is key. Even if RCTs are expensive and may risk underreporting benefit they have proven to be informative, even when they revealed negative findings (e.g. unidirectional SMS used as a TB treatment reminder). So continued donor support for trials and for other studies, particularly cost-effectiveness modelling, is very much needed.

- More sustainable sources to fund the scale-up and maintenance of digital products remain critical. The practicalities of scaling up following the completion of a pilot and adequate support for the maintenance phase are still a challenge. IT companies and pharmaceutical companies are among those who benefit from digital health and they could contribute to digital expansion. Likewise mobile network providers could discount the SMS subscription services. Mobile network providers, which may be interested in large scale implementation but less so at the pilot phase.
- Funders seemed in general to take a cautious approach towards investment in the initial, exploratory stages, with a preference for less risky implementation of developed tools. Having a "facility" dedicated to the development of digital technologies for major diseases like TB and which directs some of its resources to help develop technologies at the start-up phase could be a workable model.

TPP Session 4: An application for the implementation of LTBI

(Haile GETAHUN, Yohhei HAMADA, WHO/GTB)

With about one fourth of the world's population estimated to have latent tuberculosis infection (LTBI)(28), its treatment is critical to reduce the disease burden to the levels envisaged by the WHO End TB targets. Nonetheless, uptake of LTBI treatment on a programmatic level is still suboptimal and its systematic monitoring and evaluation (M&E) remains weak in many countries. A global consultation on LTBI convened by WHO in 2016 identified digital health as an important opportunity to facilitate the implementation of programmatic LTBI management and to generate the standardized indicators for the M&E framework. We searched the literature for research on LTBI digital health tools and found two ongoing randomized controlled trials(29),(30), and another unpublished one(31), which evaluate the use of SMS or VOT to support LTBI treatment adherence. Tools designed to strengthen areas of LTBI management other than patient adherence are in contrast limited. With the support of the ERS grant 2016-2017, WHO/GTB started developing a mobile phone application focused on improving the registration of details on patients enrolled on LTBI treatment. The tool aims to help health care workers to collect patient-level variables (demographic, clinical, outcomes) on-site which are required for the standardized, aggregated LTBI indicators. Moreover, the dashboard allows users to access geo-location data and track indicators in real-time at the national, sub-national levels, and facility levels. These two functions align to two TPPs which were primarily conceived to improve notification of active TB and presentation of findings in TB patient databases (see TPPs 2.1 and 2.2 in (5)). The concept is still under development and there is space for customization to different user demands and possibly other infectious diseases (e.g. different indicator sets and target populations identified in a national policy; high and low burden settings). Further evidence will be required to validate the application under different settings (feasibility and acceptability), and to explore if adherence support with the LTBI digital tool improves registration, treatment coverage and completion, and cost effectiveness.

TPP Session 5: Clinical decision support tools for precision medicine

(Zelalem TEMESGEN, Mayo Clinic, United States)

Precision medicine is a concept of disease prevention and treatment that classifies individuals into subpopulations based on their variable characteristics and tailor treatment or prevention interventions accordingly. For this concept to be realized there needs to be the capability to generate and analyse a wide range of biomedical information, including molecular, genomic, cellular, clinical, behavioural, physiological, and environmental data, resulting in an improved understanding of disease risk and disease mechanisms. This capability is provided by technology, which not only enables research into disease mechanisms and risk but also provides the platform for communication between diagnostics and patient care. Thus both advancement in the science of medicine and technology are obligatory components of precision medicine.

Clinical decision-support systems (CDSS) are computer systems designed to interpret and filter clinical, laboratory, and other patient-specific information through a structured protocol and present it to the clinician at appropriate times in the care of the patient. Clinical decision support systems have been shown to enhance healthcare delivery and promote efficiency in a variety of disease states and settings. The management of tuberculosis (TB) involves the coordination of a variety of clinical, public health, and psychosocial activities over a prolonged period of engagement with individual patients and lends itself to benefit from the application of clinical decision support systems. A TPP for CDSS for the management of TB has already been proposed under the eLearning function(5); the presentation went into more detail on the desirable elements of such a product and challenges expected in its development and deployment.

In the discussions that followed, it was highlighted that tools available today serving a CDSS function in TB tend to be narrow in focus (e.g. the McGill tool to interpret LTBI test results(32)) and thus the area still needs to develop. Some applications for mobile devices are helping to guide health workers who have a minimum level of training to work through decision-making, acting somehow midway between clinician and textbook. So the eLearning attributes of CDSS are important given that they are destined to improve the users' knowledge. In addition to their educational properties, CDSS can help in patient triage. There may be resistance by users to adopt such tools, one point being their reliability and boundaries for liability in case something goes wrong. As other software applications the products will come with a disclaimer which indemnifies the developer from liabilities in case of error; clinicians will need to apply their judgement when using them and they are not expected to replace clinical expertise (tool *versus* an end-to-end solution).

TPP Session 6: MOOCs in Global Health: Opportunities and challenges for innovative education in the digital era

(Rafael Luis RUIZ DE CASTAÑEDA, University of Geneva, Switzerland)

The presenter explained the essential features of a MOOC (a **m**assive **o**pen **o**nline **c**ourse) in the context of improving global health. As its name implies a MOOC provides online learning to anyone who has internet access, and some of the platforms most often used in the health care area strive to match top-level quality content with no user charges (e.g.(33),(34),(35)). MOOCs could address TPPs 4.1 and 4.2 in particular(5). Despite their popularity and visibility, the evidence of impact for MOOCs in health care remains limited. The presenter concluded that a window of opportunity for TB in MOOCs exists at this

point, with thematic content on TB being low on leading platforms dedicated to eLearning in the health care field. Development of a MOOC entails a substantial investment in time and funding, and would require a dedicated source of funding and alliance with agencies which share a common experience and interest in these tools (e.g. ERS itself).

Introductory session 3. Differentiated care for TB patients: novel technologies, evidence and implementation

(Bruce V THOMAS, The Arcady Group Ltd, United States)

Medication adherence during the long months of TB treatment is important to avoid disease relapse and acquisition of resistance. New adherence monitoring technologies have been developed that generate detailed, accurate dosing histories in support of patient-centred, differentiated care. A number of these technologies are now being evaluated in high TB burden, resource-limited settings at large-scale. The presentation reviewed the approaches to differentiated TB patient care which are informed by the dose-history, and discussed the approaches to scale-up and the monitoring needed. The speaker also proposed 7 criteria to evaluate the evidence from the different approaches and compared existing and forthcoming digital products (including AI and ingestible technologies) against these criteria (Table 2).

Table 2: *Criteria to evaluate the evidence for digital technology interventions for TB treatment adherence*

Criteria	*Description*
Feasibility	• Relative ease of implementation and operation of the technology within existing health systems, technology infrastructure, and supply chains.
Acceptance / Burden	• Relative satisfaction of patients and providers with the technology • To include an understanding of (i) cultural or other barriers to uptake (ii) how this relative satisfaction changes over time, and (iii) how this burden affects both uptake and persistence with respect to the technology.
Accuracy	• For monitoring technologies, the extent to which the technology is validated (e.g., self-reported administration of medication versus independent proof of ingestion).
Effectiveness	• Extent to which the technology is able to generate or elicit the intended action, behaviour, or event (e.g., improvement in average adherence). • Should include information on the extent to which the effect persists over time. • Ultimate “effect” to be evaluated would be actual health outcomes
Affordability	• The total cost of the technology as implemented and used by patients/providers – in relation to (i) cost of treatment regimens, and (ii) total cost of treatment.
Cost Effectiveness	• An assessment of cost-effectiveness/comparative cost-effectiveness (mean and incremental costs per death and DALY averted) of the proposed technology-enabled intervention versus standard of care in the relevant context, i.e., disease burden, budget/costs of the resource-limited setting.
Available TPP	• Availability of a WHO TPP for the product/device.

Future perspectives session 1. Drone-supported TB care

(Peter SMALL, Stony Brook University, United States)

Drones have been tested out for TB care in places like Rwanda, Madagascar and Papua New Guinea in recent years (e.g.(36)). The speaker described contexts where drones could overcome logistic and geographical barriers to support TB care, such as reaching far-flung communities where the road network is undeveloped to collect samples, deliver medication and electronic devices which could monitor patient adherence (such as electronic medication monitors) and improve opportunities to communicate to patients and develop health workforce resource (via smartphones preloaded with eLearning apps). A funding proposal to support such an expanded role of drones has been developed. A number of challenges stand in the way of its implementation. These include uncertainties of its feasibility given that it is an emergent approach; unknowns about whether users will accept the technology and if regulatory/cultural/economic barriers will work against it; whether it would effectively deliver the expected services or if breakdowns in the conveyance would compromise its dependability; if it can improve services already delivered (e.g. provision of medication, transferring samples, improving communication with patients for adherence and reporting of drug-related harms); its affordability and cost-effectiveness. These would be areas for early implementation research if the drone-supported TB care idea takes off.

Future perspectives session 2: Nanotechnology in delivery & monitoring TB medicines

(Irina FELKER, Novosibirsk TB Research Institute; Oleg ABDIEV, Siberian Branch of Russian Academy of Sciences - Novosibirsk, Russian Federation)

The presenters described the experimental use of nanotechnology by the Novosibirsk TB Research Institute to deliver several TB medicines using inhaled aerosols and the monitoring of medication levels via exhaled air. The system has been developed by institutions associated with the Siberian Branch of Russian Academy of Sciences and is currently undergoing preclinical, animal studies. The approach has the advantage of lowering the dose of medicines required - and the associated toxicity, including need for parenteral administration of certain agents - while permitting the precise, “real-time” measurement of tissue drug levels to establish if the therapeutic thresholds are reached. If the validation studies prove the approach to be effective it would be offered for hospital, clinic and home settings using stationary or portable instruments operated with software which can adjust the delivery dose according to the tissue levels of drug achieved. This could contribute to the development of the field of personalised & precision medicine.

Future perspectives session 3: Application of artificial intelligence in patient support

(Adam HANINA, AI Cure, United States)

The presentation focused on the use of an artificial intelligence (AI) platform for mobile electronic devices to measure and support TB medication adherence. AI Cure is a marketed product which has been clinically-validated for use and is being deployed by the Los Angeles County Department of Public Health to monitor adherence to treatment in patients with active TB and latent TB infection. The pilot has a target enrolment of 500 patients. The primary endpoint is to demonstrate equivalence between automated monitoring of treatment and real-time observation. A secondary aim is to evaluate the

platform's cost-effectiveness compared with other monitoring methods. To date, data indicate that automated treatment monitoring using artificial intelligence platforms is safe and feasible for active TB and LTBI patients. Outside of tuberculosis, the AI platform is being used in clinical research and high-risk patient monitoring across different therapeutic areas. The technology has been validated against drug concentration levels. In conclusion, effective and accurate monitoring on a global scale requires scalable solutions that can benefit from being interactive, operating in real-time, and automated as much as possible.

The makings of a successful digital platform for large scale impact on TB treatment adherence

(Richard LESTER, discussant)

Although in-person DOT is widely held up as a standard of care for TB treatment programmes, only few patients receive it throughout their treatment, either as a result of perceived lack of need or because of limited resources to provide it consistently on a daily basis for months on end. The presenter proposed an "adaptive digital health solution" which would present the patient and the care provider with flexibility of digital options to support TB medication adherence on the same mobile device platform. A stepwise approach to support TB care would include applications ranging from text (SMS) to VOT to voice, with the option to interact with other technologies (e.g. medication monitors) and free-phone services (e.g. 99DOTS(3)). Communications and reporting, particularly for VOT, can be synchronous (real-time two-way communications) or asynchronous (messages are saved and reviewed at a later time). The development of the tool will be informed by documented evidence for the separate component technologies (e.g. SMS, VOT), as well as user and machine data collected in the course of its operation.

The adaptive nature is intended to offer choice of approaches to address predisposing factors for poor adherence, such as geographical barriers, poor communication, the emergence of adverse drug reactions and comorbidities. It could help reduce on the need for physical encounters and thus lower cost and inconvenience to patients. It would also, conceivably, open up new opportunities to engage in health promotion for risky behaviours (e.g. substance use). The product subscribes to the principles of patient-centred care and the fact that 'one size does not fit all'. Apart from the likelihood that different patients may differ in their needs for support and monitoring, both the intensity and the modality of support may differ in the same individual in the course of the same treatment episode. The conditions which prevail in a real world setting would support different levels of technology. Conceivably, SMS, voice and 99DOTS(3) would occupy the lowest level of a "pyramid" in which the sophistication of devices and internet access increases as one moves from its base to the peak. In contrast real-time video support would be at the highest tier of such a scale.

In the discussion following the presentation the point was raised that such a tool once more run the risk of entrenching conventional views on the need for the surveillance of patients taking treatment, at the risk of diminishing the patient's views in any decision taken by the programme about the monitoring of treatment. In such a situation how would the acceptability of monitoring, use of informed consent and the right for a patient to opt out of in-person DOT be guaranteed? The point was made that TB

treatment is long and subject to interruption, while adherence is needed to ensure successful patient outcome and also to protect public health. This may however risk an infringement of individual liberties in support of the public health argument. While attendance to clinics for DOT was inconvenient for the patient, home outreach may also be intrusive and may lead to inadvertent disclosure of a patient's condition within a neighbourhood. It was also mentioned that not all patients have negative views about DOT and some may appreciate adherence monitoring as an added measure of care (e.g. VOT in Belarus and London). At times the rationale behind DOT is not clear to the patient.

Participants also debated if a new TPP is needed to define a modality that offers a combination of distinct technologies which include some for which a TPP as a TB intervention has already been developed by the WHO/ERS process (VOT) or by another process (e.g. MEMS). Would it would be more productive to develop a TPP for processes which are not yet so-defined, particularly SMS and 99DOTS? Another discussion centred on whether the monitoring of dose patterns was a valid method to assess adherence and how much it was correlated with the final outcomes (e.g. using by analogy the relationship between doses of ARVs and viral loads). It was argued that feedback from the provider to the patient on the observance of expected doses could help communication and it would be useful to make adherence aids available more widely to build more knowledge about their use. When evaluating a multimodal intervention such as this it may prove difficult to adjust for an observer-induced ("Hawthorne") effect. Discussion touched upon the unique strengths and weaknesses of certain technologies, such as that synchronous VOT permits a direct dialogue, but is less feasible where internet is weak and in paediatric patients. It is becoming clearer from trials that the deployment of SMS as a one-way reminder is not effective, but this does not necessarily mean that it cannot support other points on the behaviour change pathway. Implementation of digital technologies needs to be adaptable and they should not be considered as a complete solution.

Creating a facility to promote digital health for TB

(Dennis FALZON, discussant)

The presenter proposed a concept whereby a specialist facility external to WHO is tasked to take forward a selection of digital products and see them through their further development into tools to help TB control. In a model of engagement analogous to those pioneered by agencies like FIND and the TB Alliance to develop innovative diagnostics and treatment regimens for tuberculosis, a new structure would steward promising innovations to fruition in various domains of digital health. The subject matter of digital health is no less technical in nature than diagnostics and medication, and in fact it bears strong parallels and often converges (e.g. diagnostic connectivity, novel treatment delivery/monitoring). The staff involved in this facility would be composed primarily of experts in information technology, would have the skill-set and expertise needed to contribute significantly to thought leadership in the technological debate, inspire traditional and new donors to mobilise appropriate levels of funding, convince implementers to take up new approaches under situations of imperfect evidence, and provide creative and pragmatic solutions in the design of implementation research. Through effective advocacy, marketing and communication, a small nucleus of dedicated professionals would convert concepts into concrete products. The activities envisaged to achieve this end would include technical consultations of system developers, implementers, scientists, funders, network providers, and other key stakeholders;

negotiation to swiftly translate success stories and research findings into large-scale, country-level interventions; the promotion of research and communication of findings. Within this new construct, WHO's role would be focused on providing the support needed to hatch the facility and eventually to occupy an oversight role. In the longer term WHO would focus on the review of evidence to inform its policies, evaluating country experience in implementation and participating in decisions on the strategic direction of the work of the facility, advising countries on the implementation of emergent technologies, and promoting the rapid scale-up of evidence-based interventions. TB could act as a pathfinder for other major diseases and the scope of the facility could be widened to deal also with other health issues (e.g. HIV or tobacco). Top level political commitment will be required for this facility to be realised; the Ministerial meeting in Moscow in November 2017 and the UN General Assembly session in 2018 during which TB will be discussed could be appropriate events to work towards and to help launch the facility concept(6),(37). Targeted funding by a group of committed donors with a longer term vision would be critical for the facility to be created.

In the discussion around this topic, it was generally agreed that there are currently many fragmented initiatives in development and implementation of digital technologies for TB which are driven either by national programmes or international technical agencies or, very often, both. Many of these initiatives lack a clear or transparent vision and have a history of remaining in the pilot stage, at times for a long time, and those that make it beyond often miss out on economies of scale. The landscape could thus benefit from a more unitary solution. It was highlighted that at present there are no other agencies with global reach which combine (i) a strategic engagement on digital health expansion and (ii) with a specific focus or relative advantage to combat major diseases like TB. This is where a single specialist facility could add value by identifying solutions which are more likely to address a given challenge, evaluate it, support its implementation and track its impact. This would conceivably take the burden of developing a technology off the shoulder of a national programme and allow it to focus more on creating the right atmosphere to support its implementation. In support of this, governments need to adopt eHealth strategies (38) and ministries of health need to maintain a digital health focal point. Another point discussed is that the SDG framework strengthens the position of connectivity (Target 9c: "...significantly increase access to ICT and strive to provide universal and affordable access to Internet in LDCs by 2020"(39) and thus adds legitimacy to the facility concept and a "right to connectivity". Another discussion centred on how to ensure that a country has the capacity needed for a technology to be taken up and to thrive. Very often the "last mile" is the weak link that stands between success and failure. The work of the facility thus needs to be matched with country-level technology "champions" who can shepherd the operationalization. The facility's potential to uphold equity and serve all layers of society was mentioned, and to avoid being too technology-focused. It could be an advantageous position to deal with suppliers and negotiate pricing strategies. GeneXpert is one clear example of the development of a product through a facility: its implementation has proven to be more difficult. Digital products may be more adaptable to programme conditions than a new drug or diagnostic. However, lack of human resources is a major barrier and could defy efforts to introduce new digital tools. The facility could serve as a clearinghouse for best practices and an "incubator" for evidence, keeping tabs on where and what is being developed and how such interventions can be applied more widely. The facility perspective needs to stay broad and vigilant for developments in other relevant areas.

The downsides of having a single agency to exercise this role were also debated. One view is that it could create a situation similar to a "corporate trust", which could negatively affect fairness and the entry of new providers. Opinions on having WHO lead the process of creation and maintenance of a facility ranged from views that WHO would add to "product appeal" and the likelihood of donor support to others that this may delay its launch and activities, and thus risk forfeiting opportunities. The financing for such a facility could come from a diversified portfolio of funding sources (see also Panel discussion from Day 1 regarding the views of donors). For the concept to materialise much will depend on whether a willing organisation to host the function can be matched with an appropriate funding source with the required vision.

Conclusions, next steps, proposed changes to the TPPs and perspectives for the WHO/ERS project in 2017/2018

(Giovanni Battista Migliori, ERS)

In conclusion, the participants agreed that the meeting took stock of important developments since the first WHO/ERS technical consultation of February 2015.

1) The group acknowledged that there are three technologies amongst the nine on the original list of TPPs which have advanced significantly since the first consultation, namely: VOT, connected diagnostics and electronic notification.

1. In the area of VOT, this has included the completion of one RCT(18). Additionally, and with the support of ERS and the Global Fund, VOT was pretested and started being implemented countrywide in Belarus(12);
2. In connected diagnostics, ERS support has made it possible for new functionalities to be developed and implemented in countries like Viet Nam;
3. Electronic notification has seen important developments in the last two years, and the large scale roll-out of systems in India and Viet Nam during this meeting attest to its feasibility. The continued adoption of DHIS2 as an open-source platform for both aggregated and individual TB patient data management in different settings presents a different approach which is being implemented in numerous countries with a high TB caseload.

2) In addition to these three fast-moving areas of progress, in the area of eLearning, the WHO/ERS process has also made it possible to develop prototype tools on respiratory and TB care for use on mobile platforms by health professionals in the Republic of Moldova and Belarus. The concept of clinical decision support tools is now also being developed further through an initiative driven by the Mayo Clinic Center for Tuberculosis. Since the first consultation, the WHO/ERS has also embraced an application for LTBI. Other changes are expected to the original set of TPPs (e.g. updating established ones as the evidence progresses) and will be the subject of discussion for the *Global Task Force on digital health* through 2017/2018.

3) Alongside the products described by the WHO/ERS TPPs, the group also acknowledges that other digital technologies supported through other initiatives have advanced substantially in the TB landscape. Notable amongst these are the MEMS. Some of these technologies already possess a detailed TPP (e.g.

electronic pill boxes), while others are being implemented in high volumes ahead of the full elaboration of a TPP (e.g. 99DOTS), a step which could help steward their further development.

4) The role that a TPP can have to reassure prospective users on the value of a particular product diminishes as the formal evidence base for that intervention increases and the technology becomes embedded in policy. The new TB treatment guidelines released by the WHO Global TB Programme at the end of April 2017 contain its first-ever evidence-informed recommendations on how the digital technologies most frequently used and studied – namely cell-phone text or voice, VOT and MEMS - can support medication adherence(40).

5) It is envisaged that demand for technical assistance to implement policies on digital technologies for TB will increase in the coming years. The support of donors to ensure the most advantageous implementation of innovative technologies remains critical to their future deployment. At this early stage in evidence building, some of the funding will also need to be channelled towards the collection of evidence on implementation (feasibility, cost, acceptability and impact).

6) An appropriate source of funding would also be needed to finance the creation of a dedicated facility to champion the further promotion of digital concepts in TB and global health. This is very much needed to incentivise IT developers to address the needs of the TB community. If agreement is achieved on this idea, the concept can be launched at the Moscow ministerial conference in November 2017 and featured further at the session of the 2018 UN General Assembly focused on TB

7) Finally, it is planned for the ERS support in 2017/2018 to be focused on the continued development of ongoing activities and the implementation of further country case studies. A number of papers are expected to be published in the European Respiratory Journal (ERJ) and other peer-reviewed journals to communicate the result of the work embarked upon through the WHO/ERS collaboration. Among these are the systematic review of evidence and modelling work on the large-scale impact of digital technologies on medication adherence, the detailed documentation of the connected diagnostics TPPs, and other papers on the potential impact of digital health on the SDGs and the perspectives of artificial intelligence on the new generation of digital technologies that we expect to become available to TB programmes and patients.

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Abbreviations & Acronyms

(as used in this report)

ART	Antiretroviral treatment
BMGF	Bill & Melinda Gates Foundation
CCM	Country-coordinating mechanisms
COPD	Chronic obstructive pulmonary diseases
ERJ	European Respiratory Journal
ERS	European Respiratory Society
FDC	Fixed-dose combination
ICT (or IT)	Information & communication technology(ies)
DALY	Disability-adjusted life year
DOT	Directly observed treatment
EHR (or EMR)	Electronic health (medical) record
FIND	Foundation for innovative and new diagnostics, Geneva
GARD	Global Alliance against Chronic Respiratory Diseases
GFATM	Global Fund to Fight AIDS, TB and Malaria
GTB	WHO's Global TB Programme
LTBI	Latent tuberculosis infection
MDR-TB	Multidrug-resistant tuberculosis
M&E	Monitoring and evaluation
MEMS	Medication electronic monitoring system
NTP	National TB Programme
RCT	Randomised controlled trial
RNTCP	Revised National TB Control Programme, India
SDG	Sustainable Development Goals
SMS	Short message service
TB	Tuberculosis
TPP	Target product profile
USAID	United States agency for international development
VOT	Video-supported therapy for TB (originally an acronym for video-observed therapy)
WHO	World Health Organization

Annex 1 - Meeting agenda

"Digital health for the End TB strategy : progress since 2015 and future perspectives"

7-8 February 2017 (Global TB Programme (D Building), World Health Organization, Geneva)

Day 1. Chairs: Alistair STORY, Dennis FALZON

Time	Topic	Speaker/Facilitator
9:00 - 9:15	Welcome remarks & Introductions	Mario RAVIGLIONE, WHO/GTB Giovanni Battista MIGLIORI, ERS
9:15 - 9:25	Objectives and declarations of interest	Karin WEYER, WHO/GTB
9:25 - 9:40	Digital health for WHO's End TB Strategy: milestones since 2015	Dennis FALZON, Hazim TIMIMI, WHO/GTB
9:40 - 10:00	Introductory session 1. Digital health for TB : state of the evidence for adherence	Richard LESTER, University of British Columbia, Canada
10:00 - 10:30	Introductory session 2. Modelling the potential impact of digital health on adherence measures of TB infection and disease	Kevin SCHWARTZMAN, McGill University, Canada
10:30 - 10:45	Break	
10:45 – 11:20	TPP Session 1: Connected diagnostics target product profile	Chris ISAACS, FIND Geneva
11:20 - 12:00	TPP Session 2: Perspectives on video-observed therapy for TB (VOT)	Richard GARFEIN, University of California San Diego, US
	Country experience	Alistair STORY, Find & Treat, UK Alena SKRAHINA, NTP Belarus
12:00 - 12:30	TPP Session 3: Electronic case-based surveillance for TB	Le Van HOI, NTP Viet Nam), Kirankumar RADE, RNTCP India
12:30 – 13:30	Lunch	
13:30 - 14:45	Panel discussion : perspectives for the operationalization of fast-moving digital technologies while evidence is strengthened	*facilitated by Mario RAVIGLIONE & Giovanni Battista MIGLIORI* BMGF - Daniel CHIN ERS - Werner BILL GFATM - Mohammed YASSIN UNITAID - Sara PADIDAR USAID - Kaiser SHEN
14:45 – 15:15	TPP Session 4: Digital health to support programmatic management of LTBI	Haile GETAHUN, Yohhei HAMADA, WHO/GTB
15:15 – 15:45	Break	
15:45-16:15	TPP Session 5: MOOCs in global health: Opportunities and challenges for innovative education in the digital era	Rafael Luis RUIZ DE CASTAÑEDA, University of Geneva, Switzerland
16:15 – 16:45	TPP Session 6: Clinical decision support tools for precision medicine	Zelalem TEMESGEN, Mayo Clinic, US
16:45 - 17:00	Conclusions; plan for Day 2	Chairs

Day 2. *Chairs: Zelalem TEMESGEN, Kristian VAN KALMTHOUT*

Time	Topic	Speakers
8:45-9:00	ERS welcome message	Guy JOOS, President ERS
9:00 - 9:30	Introductory session 3. Differentiated care for TB patients : novel technologies, evidence and implementation	Bruce THOMAS, The Arcady Group, US
9:30 - 9:50	Future perspectives session 1: Drone-supported TB care	Peter SMALL, Stony Brook University, US
9:50 - 10:10	Future perspectives session 2: Nanotechnology in delivery & monitoring of TB medicines	Irina FELKER, Novosibirsk TB Research Institute; Oleg ABDIEV, Siberian Branch of Russian Academy of Sciences, Novosibirsk, Russian Federation
10:10 - 10:30	Future perspectives session 3: Application of artificial intelligence in patient support	Adam HANINA, AI Cure, US
10:30-10:45	Break	
10:45 - 11:15	The makings of a successful digital platform for large scale impact on TB treatment adherence	Richard LESTER, University of British Columbia, Canada
11:15 - 12:00	Creating a facility to promote digital health for major diseases	Dennis FALZON, WHO/GTB
12:00 - 12:30	Conclusions, next steps, proposed changes to the TPPs and perspectives for the WHO/ERS project in 2017/2018	Giovanni Battista MIGLIORI, ERS
12:30 – 13:30	Lunch	
13:30 - 15:00	Meeting of the "Global Task Force on digital health for TB"	Chair: Giovanni Battista MIGLIORI, ERS

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