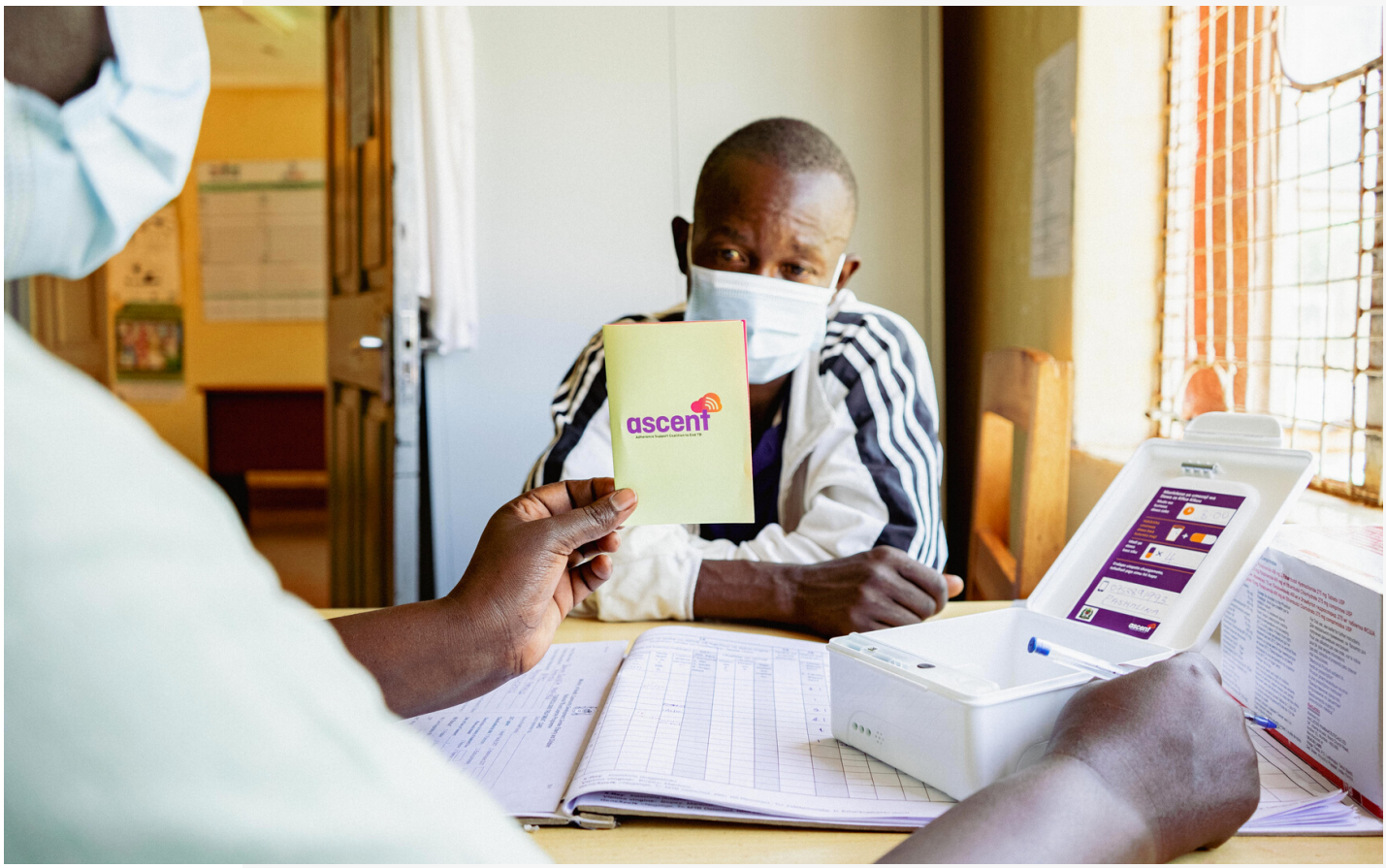
ascent
Adherence Support Coalition to End TB

TECHNICAL BRIEF

5 Country Experiences with **Digital Adherence Technologies**

MARCH 2023



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Introduction

Digital Adherence Technologies (DATs) are designed to support people infected with TB in taking their medication. Compared with the traditional directly observed treatment (DOT) approach, these tools allow people to take their medication at a place and time convenient to them while remaining connected to their healthcare provider. DATs provide real-time information to the healthcare provider, offering the opportunity for healthcare providers to follow-up and support the individual during treatment and identify people who need additional care and support.

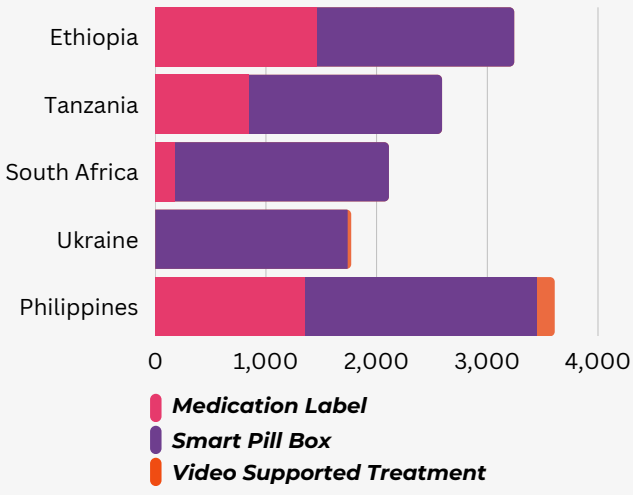
Image: A healthcare professional enrolling a person with TB onto the DAT technology.

Objective of Technical Brief

From January 2021 to December 2022, the Unitaid funded ASCENT (Adherence Support Coalition to End TB) project supported over 17,000 people during their TB treatment using digital adherence technologies in Tanzania, Ethiopia, South Africa, Ukraine, and the Philippines. Healthcare providers in more than 230 health facilities were trained on the use of 3 technologies as a tool to support their patients during the completion of treatment, namely the medication sleeve/label (99DOTS), the smart pill box (MERM) or video supported treatment (VST). These three DATs were linked to an online adherence platform (the Everwell Hub) which is accessible via tablet or computer by the healthcare provider to provide remote support and identify patients who may need additional support.

Based on the experience of implementing digital adherence technologies at scale in five different contexts, this technical brief serves to highlight and summarize the ASCENT project implementation experiences with the technologies before the final research from the ASCENT project is published. The technical brief is structured around the following considerations:

- Ease for persons with TB to use the technology
- Ease for healthcare providers to use the technology
- Accessibility of the technology for people with TB
- Ease of technology implementation and continued management



Graph: Total DAT enrollments per country up to December 2022

Key Learnings and Considerations

When considering digital adherence technologies as a tool to support TB treatment, it is vital to delineate the key reasons to implement such an intervention for people infected with TB.

Primarily, TB treatment should be person centered. To define what this means in the framework of DATs, a person-centric implementation means that the level of burden for a patient to participate in the intervention (including ease of use; financial implications; time implications; additional actions; and risk of stigma), as well as technological prerequisites to enroll a person on DATs should be kept to a minimum. It also implies that people are empowered and given own agency and trusted to be an active participant in their healthcare and treatment.

Secondly, the intervention should ensure that the burden placed on the healthcare system is as low as possible and does not exceed the burden the healthcare system experiences with the standard of care. This includes the time investment by healthcare providers; cost implications; reliability and maintenance of the technology; and overall coordination.

Based on this, we summarize our key learnings as a project when comparing these three technologies within this framework, before taking a deeper look at each technology.

ACCESSIBILITY AND REACH FOR PATIENTS

Both the medication label and VST presented a major obstacle in ensuring accessibility to DATs. People with TB needed to have daily access to a mobile device, as well as data/airtime/network connectivity, which is not always a given in developing countries. The smart pill box on the other hand was provided to people with TB at no extra cost, without any further prerequisites. Therefore, this technology had the greatest reach of the 3 technologies implemented.

Ideally with a DAT intervention the reach and accessibility of the technology should be as wide as possible to ensure all patient groups are able to benefit from the tool.

When there is a prerequisite for a person to have access to certain technology in order to enroll on the intervention the reach is reduced per requirement placed on the patient. In other words, when relying on a person to provide their own mobile device, and/or mobile data, the percentage of TB infected people eligible to enroll will drop substantially.

TIME INVESTMENT BY A PERSON USING THE TECHNOLOGY

On average, the amount of effort required for a person to log their daily medication intake was perceived to be higher for the medication label and VST in comparison to using the smart pill box. For the pill box the only action required was opening the pill box to access the medication, whereas for the other two technologies an additional action was required to log their adherence and therefore increasing the burden for use. VST required the most effort and time investment. As a consequence of the technology selected, a person's engagement with the technology decreased over time when more effort was

required to engage with it.
This had a knock-on effect to healthcare providers, who are required to follow up with people when adherence had not been digitally recorded (digital adherence) on the adherence platform – creating an additional burden. In instances where people had taken their medication, but had not recorded their medication intake, the healthcare provider would need to mark a dose manually on the adherence platform (manual adherence).

BENEFITS AND BURDENS FOR HEALTHCARE PROVIDERS

Overall healthcare providers reported that digital adherence technologies were useful and easy to use, and they were positive about having real-time data to assist in tailoring support per patient to ensure their treatment completion. Healthcare providers also note that it provides more opportunity for engagement with patients, relationship building, and trust in patients for the ownership of their own treatment.
However, the extent to which the above was experienced varied per technology.
The smart pillbox provided the most consistent digital adherence data. It requires the least additional action from people and has mechanisms in place to send adherence data retrospectively in instances where there were connectivity issues. Therefore, it required the least follow up action by healthcare providers.
For the medication label technology, the data sending and retrieval from a patient's reports were often inconsistent and unreliable due to numerous infrastructural challenges. This placed additional burden on healthcare providers workload, as they would need to follow up on a person's adherence unnecessarily.
For VST a healthcare provider was required to review patient videos daily, which was viewed as a time drain. People did not always send videos of medication intake for various reasons, requiring an additional follow-up action by the healthcare provider.

TECHNOLOGY AS PERSON CENTRIC

DATs are a person-centric move away from directly observed treatment (DOT), with each technology meeting this objective to a greater or lesser extent. All DATs reduce the time and financial burden placed on people in comparison with daily facility visits for DOT. Video supported treatment (VST) is considered to be the digital version of DOT where a person can be directly observed taking their medication, however it removes the opportunity for building a trusting relationship between patients and their healthcare providers. It also increases the patient's risk of stigma and breach to privacy. With the smart pill box, one does not have a direct observation of a person taking their medication, however, it increases the level of trust and empowerment given to people on TB treatment where it is viewed as a tool rather than a management mechanism.

Image: A healthcare professional providing differentiated care to a TB infected person in Tanzania

TECHNICAL LITERACY OF HEALTHCARE PROVIDERS

Each technology requires a certain degree of technical understanding by healthcare providers. Often healthcare providers are the first point of call for patients when they experience technical challenges.
We observed a wide variety of challenges while implementing the medication label. With numerous links in the chain of implementation (including the adherence

platform, the telecom providers, the toll-free line rental, and the telecom aggregator) it was often impossible for healthcare providers to provide solutions to their patients for the challenges experienced, which required further support from the ASCENT project team and technology providers.

The pill box presented technical challenges from time to time, however, these were easier to pin-point and resolve by healthcare providers, such as disconnecting and reconnecting the battery from the module, or recommending the person locates an area with better network strength to upload the adherence data onto the platform. This technology required less support over time from the project team and technology providers, and with adequate training healthcare providers can resolve many basic technical challenges experienced by their patients.

It is clear from both instances that technical support and coordination is required to a degree, however, the intensity of this is less with the pill box.

IMPLEMENTATION AND CONTINUED MANAGEMENT

When comparing the implementation and continued management of the three technologies during the project, the medication label proved to be the most unpredictable and complex to setup, and it required the most support from the project team to maintain.

Given the fact that the medication label requires setup and configuration across multiple links in a chain (including the toll-free line integration with local Mobile Network Operators; and two-way messaging functionality between the adherence platform and the patients mobile device, with the mediation of a telecom aggregator) there were many unpredictable factors that derailed the start-up phase in the project, and the experience and/or success in one country was not always replicable in another.

The smart pill box and VST were far less troublesome to setup and maintain, and any issues encountered during the early phases of the project were ironed out, which makes any future roll-out in other countries predictable and reliable.

Image: The ASCENT project team in Ethiopia providing technical support to an implementing healthcare facility

COST CONSIDERATIONS

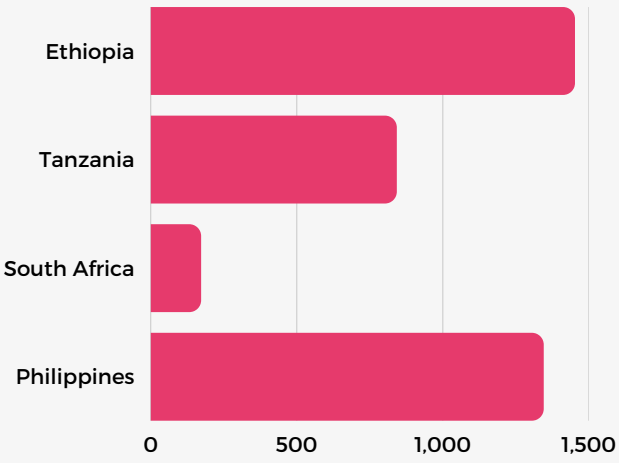
Lastly, when considering cost implications and accurate budgeting, the medication label has the most budget lines that need to be kept in account, and often presents with unpredictable costs only revealed during the implementation setup. Each country also varies in their requirements. In some countries there are contractual costs borne by the NTP for the toll-free line rental, which are not always easy to predict, and in other countries there were costs borne by patients to send their daily text message (although a project requirement was that the technology should not push any costs to the patient).

When budgeting for the smart pill box there was an initial investment to procure the box, and monthly contractual costs for the adherence platform (which is required for all technologies). Both budget lines were far more predictable for accurate budgeting. As the pill box was reused for multiple people on treatment, the per person cost of the pill box technology was reduced as it was reused. It can therefore be viewed as an investment over a three-year implementation period.

Medication Sleeve / Label (99DOTS)

The medication sleeve/label, also called 99DOTS, uses customized packaging such as printed sleeves or labels that fit Fixed Dose Combination (FDC) medication for drug-susceptible TB treatment. It was first piloted and used on a large scale in India. The person on TB treatment reports medication intake daily, either by calling a toll-free phone number or sending a free SMS message using a code found on the package. They can utilize any type of mobile phone to submit the code to the adherence platform.

In the ASCENT project Ethiopia, Tanzania, South Africa, and the Philippines implemented the medication label (although in South Africa it was discontinued early in the project). The medication label was an adaptation from the original 99DOTS medication sleeve approach used in India. The main reason to adapt to medication labels as customized packaging rather than using sleeves was the high variability of medication packaging (over 20 different FDC packages) in these countries. The procurement and supply chain processes were unpredictable which made forecasting and manufacturing at scale impossible, and therefore impeding the implementation of this technology.



Graph: Total medication label enrollments per country to December 2023

EASE FOR PEOPLE ON TB TREATMENT TO USE THE TECHNOLOGY

For people to use this technology, they need to be able to send a 3-digit code to a toll-free number by SMS with each daily dose ingested. They should have a basic degree of technological literacy to report their adherence correctly. For some patient groups sending the code required assistance from a treatment supporter more adept at using a mobile phone as the example from the Philippines illustrates below:

67-Year-old Estela Mariano (name has been changed for privacy), from Arayat Rural Health I, Pampanga, initially hesitated to use the medication sleeve. But with the nurse's assistance, she learned how to use it successfully and completed her treatment with 100% adherence rate (79.76% digital; 20.24% manual) and no missed dose. Her granddaughter served as her treatment supporter and sent the 3-digit code after every medication intake.

"After the nurse showed me how to use the medication sleeve and gave me step-by-step instructions in Kapampangan, our local dialect, I found that it was easy to use after all. Following the arrows and the simple illustrations on the sleeve enabled me to take my medication on my own. And the 3-digit numbers were written large enough for someone like me with poor eyesight. I tend to forget most things these days, so the reminder - to take my medication - I received daily on my phone was particularly useful."

Image: The medication label used in the Philippines

Similarly in Ethiopia, elderly and illiterate people experienced challenges sending their text message after taking their daily dose for adherence confirmation. As a solution, healthcare providers saved the short code number on the person's phone with an easy to remember name and provided instruction on sending the text message. These people were also encouraged to find a treatment supporter that could assist in sending text messages.

At the beginning of the project, the team in Tanzania anticipated that medication labels would be more viable in urban facilities rather than in rural facilities due to the differences in network coverage. Instead, the predominant factor influencing enrollment across the country was related to literacy level. Many elderly people in Tanzania have a lower level of literacy and some had poor eyesight. These people were therefore excluded from enrolling onto the medication label technology. Unexpectedly, several younger population groups were also not able to read or write, although many of them owned mobile phones. In South Africa, it was reported that numerous people were unable to send text messages due to their older age, illiteracy or being too sick. This created a burden for family members who assisted the person on TB treatment.

All countries observed that daily user engagement with the medication label technology - sending messages - decreased over time. Several people in South Africa withdrew from the intervention due to the burden of sending these daily messages. In Tanzania, an initial analysis of interaction trends showed that engagement of people on TB treatment slowly declined as their treatment progressed, whereas they began their treatment with a consistently high rate of digital reporting. When several people using the technology were asked to reflect on the reason for the decrease in technology engagement, there was a common theme that sending daily SMS messages caused technology fatigue. Other reasons mentioned included forgetting to send the daily SMS; depleted phone battery; and limited network coverage. In many of these cases non-engaging with the medication label technology was not representing non-adherence to medication.

Finally, the unreliability of the toll-free messaging short-code infrastructure also led to problems for people when sending in their daily text message, which will be discussed in further detail below under technology accessibility for the person on TB treatment.

Image: A person enrolled on the medication sleeve technology in the Philippines sending their daily code.

EASE FOR HEALTHCARE PROVIDERS TO USE THE TECHNOLOGY

At start of treatment the healthcare provider sticks the label on the TB medication blister package provided to the person on TB treatment; registers the person's phone number on the adherence platform; and explains the procedure, and importance, of sending a daily SMS message with their unique code to the toll-free number listed on the label. Each time the person returns to the clinic for a refill, the healthcare provider places a label on the new medication blister package. In between a person's visit to the facility, healthcare providers should view the adherence calendar per patient or a grouped "task list" view of TB patients in their facility on a daily basis.

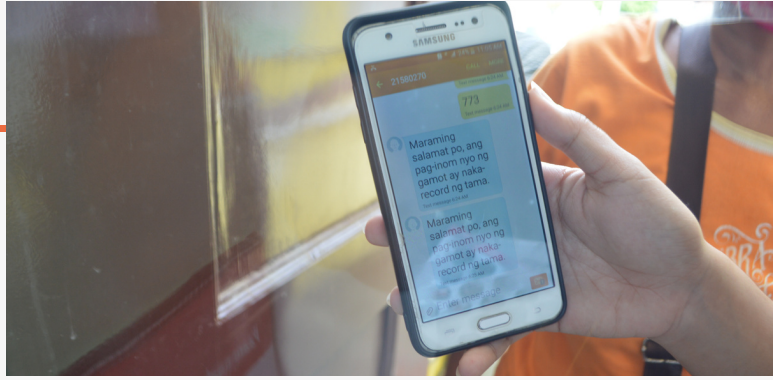


Image: Confirmation SMS to a person in the Philippines for daily dose taken

If no adherence was reported by the person on treatment, a follow-up action (e.g., phone call or home visit) would be performed.
Daily adherence of that person will be updated digitally only if the phone number from which the person sent their daily text message is registered on the adherence platform. Healthcare providers expressed that keeping this information up to date was seen as an additional burden which could not always be maintained. It often led to unnecessary phone calls to people on treatment to follow up on medication adherence and requiring healthcare providers to mark manual doses on the adherence platform, therefore increasing the workload on healthcare providers, leading to frustration for both healthcare providers and people on treatment.

Medication label facilities in South Africa experienced several technical barriers in setting up national technology infrastructure for the use of the medication label which could not be overcome, thus it became impossible to report adherence accurately and to make use of the adherence data in real-time. Errors with text messaging due to these technical barriers resulted in frustrations by healthcare providers as they needed to make unnecessary phone calls to patients and mark manual doses.
Since healthcare providers are the first point of contact for patients, they were often contacted to solve technical issues related to the medication label technology, increasing an already heavy workload, particularly exacerbated by the Covid-19 pandemic.

People enrolled on the medication label generally required more follow-up actions by healthcare providers when compared to people enrolled on the smart pill box technology.

ACCESSIBILITY OF THE TECHNOLOGY FOR PEOPLE WITH TB

The basic requirements for the medication label approach to be a viable option for people to report their daily medication intake is as follows: daily access to a mobile phone (owned or shared with a treatment support partner); a daily electricity supply to charge their mobile device; good network coverage to send SMS's; and toll-free short code integrations with local telecom providers that enable people to send free SMSs to log their adherence.

Amongst the most prevailing uptake barriers of the medication label experienced in Tanzania is the requirement for person on treatment to have daily access to a phone. Although the technology works with all types of phones (feature phone or smart phone) it is evident from the implementation experience that almost half of people enrolled on the adherence platform didn't have daily access to the phone registered in the adherence platform. Among people enrolled in medication label facilities, 689 (45%) were initiated on smart pillboxes instead of medication labels and this can be attributed to – in conjecture – not owning a phone; limited access to a shared phone; and poor network coverage at their place of residence. 94 (6%) patients from these facilities who were initiated on medication labels switched to smart pillboxes during their treatment for similar reasons. In theory more people could be enrolled on the medication label by utilizing a treatment supporter who owns a phone, however, based on experience, digital reporting is not optimal in these situations where phones are shared or owned by a third party. This then translates into follow-up actions required from the healthcare provider to log manual doses on the system, thus placing an extra burden on the healthcare system.

People on TB treatment in at least 5 of the 36 intervention facilities in Tanzania resided in areas with very poor network coverage. This became a hinderance in the optimal and real-time functioning of the technology as the text messages would not send to the adherence platform because there was no network coverage in these areas. These people were therefore enrolled on the smart pill box.

As stated earlier, the medication label approach was discontinued in South Africa due to multiple difficulties experienced during implementation. Many people on treatment had limited access to mobile phones, or an intermittent electricity supply and therefore sent their adherence text message sporadically. Numerous people also resided in areas with poor network connectivity, and therefore the text message would not be sent to the adherence platform, resulting in healthcare providers following up unnecessarily as the person's adherence calendar was not accurate, causing frustration for the healthcare providers and person on treatment due to a technology that was functioning sub-optimally. A major hurdle which eventually led to the discontinuation in South Africa was that people were not able to send free text messages to log their adherence as toll-free messaging integration was not possible for several South African Mobile Network Operators (MNOs).
Toll-free messaging integration issues were also experienced in the Philippines, where one of the MNOs required a minimum of 1 peso balance to enable free SMS messaging. This led to a decreased reach of the technology and did not fully meet the objective to provide the technology to people on TB treatment at no costs, independent of mobile phone provider used.

TECHNOLOGY IMPLEMENTATION AND CONTINUED MANAGEMENT

While the medication label technology seems to be a low-tech and low-cost way to ensure pill-in-hand adherence, our project experience has highlighted numerous hurdles in its implementation and continued management.
Our experiences conclude that the setup and management of toll-free SMS short-code infrastructure differ per country and requires substantial technical coordination and maintenance based on the country infrastructure and adaptations.

In Tanzania, South Africa, and the Philippines, to enable toll-free messaging, integrations among multiple Mobile Network Operators (MNOs) had to be managed and supported by a telecom aggregator. Various challenges with this were experienced.
In Tanzania the costs to register, integrate and sustain a short code are high, and not all MNOs could be integrated.
In the Philippines, the two MNOs had differing requirements for integration (for example the Smart telecom provider requires a minimum 1 peso to send a text message), and in South Africa the toll-free infrastructure could not be setup as their MNO's also had differing requirements for free SMS messaging.
In Ethiopia, where only one MNO exists (Ethio Telecom), the integration was also more complicated than expected. During the run-in phase, there were long down times of SMS services of the Ethio telecom server and eventually a backup SMS server was setup as not all incoming messages were received, and therefore adherence data was not being logged on the adherence platform.
The initial successful setup of toll-free messaging was not an indicator that the infrastructure continued to work as required, even with the technical oversight that the ASCENT project was able to provide. There were numerous instances where people were unable to send their SMS messages or they were not forwarded by the MNO to the aggregator, leading to the data not uploading to the adherence platform. These errors, therefore, appear as non-adherence on the adherence platform which then required (unnecessary) manual actions by the healthcare provider.

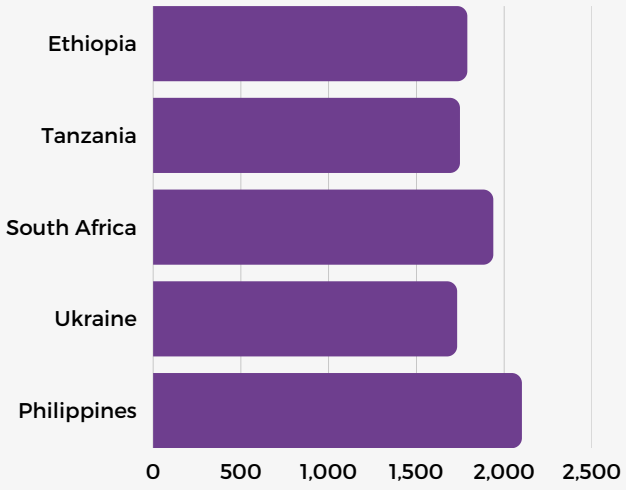
Smart Pill Box

With the use of a plastic medication container, a battery powered, re-usable module and a mobile data connection, the smart pill box automatically logs medication intake each time the person on TB treatment opens the box to take medication by sending a signal to the adherence platform.

The smart pill box features include:

- A battery that lasts up to 6 months before it requires a recharge.
- Global mobile data subscription for 36 months.
- LED and speaker to enable visual/audible reminders for daily dosing and clinic appointments.

All ASCENT project countries (Ethiopia, Tanzania, South Africa, Ukraine and the Philippines) implemented the smart pill box for the duration of the project.



Graph: Total smart pill box enrollments per country to date

EASE FOR PEOPLE ON TB TREATMENT TO USE THE TECHNOLOGY

The smart pill box requires the least amount of effort for people to record daily adherence. It was experienced by all five countries as the easiest technology for people on treatment to use. All TB medication is stored in the box and when the person opens the box to take medication a signal is automatically sent to the adherence platform to log the adherence. No additional actions are required by the person on treatment. Depending on personal preference, a daily medication intake alarm and/or a clinic visit reminder can be configured through the adherence platform by the healthcare provider.

In all five countries the feedback from people on treatment and healthcare providers acknowledged that the pill box was the easiest technology to use and store medication for safe keeping. Generally, the reminder alarms were viewed as helpful and an effective means of reminding people to take their daily dose and visit the facility for a refill.

While most people enjoyed the alarm reminder and phone calls that formed a part of the pill box treatment support, some raised the concern that the alarm could draw attention to them at work and increase the risk of stigmatization. It would be beneficial to include the functionality for people using the technology to manually adjust the volume or switch off the alarm directly on the box.

Overall, the smart pill box is easily portable when travelling to the healthcare facility for a medication refill. However, there were a few

observations noted with regards to the size: Some people on larger treatment doses struggled to fit all medications in the plastic container and thus stored some of their medication outside the box. Some people enrolled on the technology noted that travelling with the pill box is cumbersome. They would remove medication from the box and leave the box at home while travelling and resume using the box when they returned. A suggestion is to design smart pill bags or cases that are more suitable for travel purposes, and that make provision for larger treatment doses.

There were reports from the Ukraine of people who stopped using the smart pill box for a few days for fear of stigma, specifically when they visited their relatives whom they had not disclosed their TB status to or if they had to undergo a security check at the entrance of the enterprises where they worked. Several people in Tanzania who worked in mines were not permitted to enter their workplace with the pill box.

In Ethiopia, people were pleased to use the smart pill box as a treatment support, and they found it user friendly. They experienced the daily dose alarm and refill reminder light on the box as helpful. In general people with TB reported that the pill box technology saved them time and transportation fees; they could get to work on time; and it decreased the risk of stigma and COVID -19 infection because of the reduced frequency of travel to a health facility for directly observed treatment (DOT).

In the Ukraine people generally found the pill box easy to use. Healthcare providers set up the smart pill box for the person on treatment and provided basic training on how to use it. People who were technologically literate were also trained by the healthcare providers on plugging / un-plugging the battery of the device to reset it since it was needed in some cases when basic troubleshooting for the device could be done remotely.
A few people did not receive sufficient training

Image: A healthcare provider preparing the corrugated pill box for distribution to a DR-TB patient

on the use of the pill box and therefore didn't understand the importance of opening the box every day, so they removed their medication from the box. In such cases, the project team worked with the healthcare providers to ensure the provision of sufficient training and explanation to their patients.

For people on DR-TB treatment the plastic box is too small to store all the medication. Therefore, the larger corrugated box was used. However, the corrugated box did not always close properly, and at times it opened on its own as it is not secured by a clip to keep the lid of the box down.
For this reason, people on treatment and healthcare providers often preferred the use of the plastic boxes over the corrugated boxes.

EASE FOR HEALTHCARE PROVIDERS TO USE THE TECHNOLOGY

At start of treatment, the healthcare provider places the person's medication in the pill box and provides information about the use of the box and correct storage. Often two to four weeks of medication is provided. The unique identification number of the box module links the specific box to the person on the adherence platform. Based on personal preference, a daily intake alarm can be configured as well as an appointment reminder.

Before distributing the pill box to people on treatment, the healthcare provider ensures that the smart pill box battery is fully charged; and a label is stuck on the inside of the pill box showing dosing instructions and healthcare provider contact details.
Upon treatment completion, people are requested to return the smart pill box to the facility so that it can be cleaned and redistributed to a new person on TB treatment.

Image: The smart pill box with dosing instructions for people being treated for DR-TB

In between the patient's facility visits, healthcare providers should view the adherence calendar daily per patient or a grouped "task list" view of TB patients in their facility.
If no adherence was reported by the person on treatment, a follow-up action (e.g., phone call or home visit) would be performed. Generally, a healthcare provider can view a person's adherence on the adherence platform within 15 minutes of the smart pill box having been opened and closed.

Although the smart pill box technology raises the concern that a healthcare provider does not have complete certainty that the person on TB treatment takes their medication after they have opened the pill box, when considering that TB treatment should focus on person-centric treatment, the pill box provides the opportunity to empower people on treatment in their own healthcare and for healthcare providers to trust patients in their own agency towards health and treatment.
Tanzania notes that it has been viewed as a reliable tool for fostering close interrelationships between providers and their clients which is vital for case retention and reducing initial lost to follow-up cases.
The smart pill box technology was well received by healthcare providers in Ethiopia. They noticed a reduction in the daily facility queues with the introduction of DATs. This created the opportunity to dedicate their time to other department activities.
Healthcare providers in the Philippines consider the technology easy to use, and easy to educate and distribute to people on treatment.

In Tanzania, the burden placed on the healthcare provider is experienced as far less when comparing the box preparation and distribution, and reviewing adherence data, to the workload associated with manually following up with people not supported by DATs who miss refill appointments.
Many healthcare providers in facilities that implemented the smart pill box in the Ukraine agree that it is an easy and convenient tool to organize remote TB treatment adherence support. Follow-up to non-adherence was generally easy for healthcare providers in health facilities with previously organized good practices of interaction with patients.
The clinic appointment alarm on the pill box was highlighted as particularly helpful in South Africa for hard-to-reach people as it provided a reminder to return to the facility for a medication refill.

Image: Healthcare providers in South Africa reviewing a person's adherence calendar on the platform

In Ethiopia, out of the 1022 pill boxes that had been distributed up to the end of June 2022 only 75 pill boxes had not been returned. Out of the returned boxes up to June 30th, 2022, the healthcare facilities mentioned that 95% of the boxes were returned in a good condition, and the module could be reused by other people on TB treatment.

In the Philippines it was noted that the retrieval of the smart pill box was more troublesome. Although people who were enrolled on the technology signed a commitment form to return the pillbox after treatment completion, they often failed to comply. The healthcare provider workload prevented them from following up on the people to return the pillbox. As a solution, community health volunteers were mobilized to retrieve the device and charger.

In South Africa, the retrieval of the smart pill boxes is done on the last day of the person's treatment and generally has been an easy process. In instances where people had moved to a different region without collecting a transfer letter from the healthcare facility, the retrieval of the box was more troublesome. However, with the support of community healthcare workers, some people had been found, and the pill boxes collected from their new home address. Overall, approximately 13% of pill boxes in South Africa were not returned.

In Tanzania, about 7% of patients did not return their smart pill box after treatment completion.

In Ukraine, only limited issues were experienced with pill box returns. According to the standard of care, persons on treatment visited heath facilities for a final check-up and returned the smart pill box during this visit. Smart pill box returns were only challenging in cases when the person was lost to follow-up.

To reduce the workload on the healthcare providers in Tanzania, most of the initial technical preparations when boxes were received in country (such as battery charging, switching the module from shipping mode to active mode, activating the module with the pill box manufacturer; and sticking the medication instruction labels on the pill box) were done by the ASCENT project team. However, once the pill boxes were returned to healthcare facilities by patients, the healthcare providers needed to prepare boxes for redistribution by cleaning and disinfecting them; removing old medication dosage stickers; and charging the module battery. In the Ukraine, several TB doctors mentioned that the DAT intervention placed an additional burden on them due to the need to dedicate additional time to setup the pill box and resolve technical issues.

Therefore, it is our recommendation for future implementations to ensure provision for coordination of the preparation of pill boxes at a central level.

Image: Preparations of the smart pill box module and battery.

Viktoriia Semivolos, a TB doctor in Ukraine and Head of Dispensary Department of Donetska Oblast Clinical TB Dispensary in Sloviansk, mentioned: "We really like smart pill boxes (our doctors and nurses). In the very beginning of the introduction of the platform and boxes we were nervous about how this approach will work. But in reality, it was very easy and convenient for us and patients. The use of the platform helped us to save a lot of time, receive more reliable data, ensure timely intake of drugs by patients (sometimes patients forgot, so we could remind them over the phone). The platform is very easy, simple, reliable. Although, sometimes technical issues happened, but they were not major events."

ACCESSIBILITY OF THE TECHNOLOGY FOR PEOPLE WITH TB

The smart pill box is provided by the healthcare facility at no cost to the person on treatment, implying that a person on treatment does not require any additional technology to be able to record his or her adherence. All five countries noted that the smart pill box technology is suitable for almost all people, and ideal for people who do not have access to a mobile phone. In South Africa, for example, the project team noted that even people who do not have a cellphone and are homeless can be supported with this technology.

The smart pill box module uses a global SIM card to send daily adherence data to the adherence platform. It can make use of the network of any reachable Mobile Network Operator (MNO) using the widely available 2G network. In instances where mobile network coverage is not available, pill box opening events are stored in the module memory and uploaded automatically when mobile connectivity is available again.

Several people in Tanzania experienced a delay in their adherence data being sent to the adherence platform due to limited network coverage. However, these technological limitations were not considered a disadvantage to people as the boxes would retrospectively update the adherence calendar whenever there was better mobile signal. As a result of the global SIM card, which works with any network provider, people that lived near the country borders in Tanzania would at times travel across the border with their pill box, and their adherence data would be sent to the platform using the neighboring country's network provider.

South Africa experienced frequent power outages (loadshedding) which impacted network signal, resulting in delays in updating the adherence data on the platform. But with the pill box opening events stored on the pill box, this was updated as soon as the network connection was back.

In Ethiopia, where only one mobile phone provider exists (Ethio Telecom), there was no 2G mobile network coverage within the region surrounding the Woliso health facility, influencing the sending of real-time adherence data. As an alternative approach, healthcare providers would connect the patients smart pill box module to their tablet or mobile phone during refill or home visits. Their tablets would use 3G or 4G network to synchronize the persons adherence data onto the platform.

Image: A person on TB treatment in Tanzania receiving their smart pill box

In the Ukraine issues to send daily adherence events were noted when the smart pill box was used inside buildings with thick walls or located on the lowest floor of the building (underground). In such cases, it was recommended to find a location where the mobile signal was better. There were also cases in Ukraine where the device could not connect to the network for unknown reasons. The general recommendation in such cases was to reset the device (disconnect and reconnect the battery), and if the problem was not resolved, to visit the healthcare provider to replace the device.

The smart pill box module battery should last for at least 6 months. If necessary, people who lived in regions where there was no electricity supply in Ethiopia would charge their smart pill box at the facility when they had a

medication refill appointment.

TECHNOLOGY IMPLEMENTATION AND CONTINUED MANAGEMENT

The smart pill box can be ordered through the Stop TB Partnership Global Drug Facility (GDF) at $53,75 for a complete kit that includes a plastic container, the smart pill box module, a global SIM with 36 months of mobile data and a USB charging cable for the device. It takes about 3-4 months from order submission to receiving the smart pill boxes, excluding time allocated for importation procedures. The ASCENT project countries mentioned that the ordering process is simple but that importation levies increase costs, and the importation process can be lengthy.

In light of these cost and logistical considerations, local manufacturing of goods was explored, however, local manufacturers were not able to produce the pill boxes at a competitive price in comparison to procurement through GDF as economies of scale would not be reached with a local manufacturer.

Image: Smart pill box kit as procured through the Global Drug Facility

Prior to distributing the smart pill boxes to healthcare facilities, the smart pill box batteries needed to be fully charged and their SIM card activated.

In South Africa, the project team mentioned that it is favorable that these activities are performed by a coordinating person or entity to reduce workload for healthcare providers. In Ukraine, some hurdles were experienced at the start of the project where the pill boxes did not log adherence as the module batteries had not been connected by healthcare providers prior to distribution. These issues were resolved quickly with sufficient training for healthcare providers.

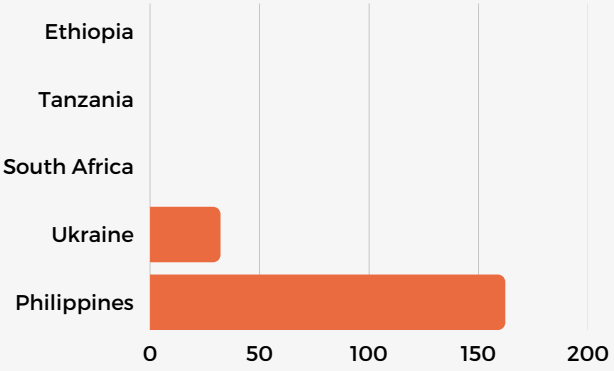
After the charging and distribution of the smart pill boxes to the facilities the technology required little to no technical oversight to ensure the smart pill boxes continued to work as expected. Almost all technical support could be performed remotely, but the management of stock and box returns did need continual oversight at the facility level.

An important consideration when comparing the pill box to the medication label is that no contractual obligations with MNOs or other partners in country are required for the successful implementation and continuation of the technology.

Image: A person in Tanzania receiving the pill box as a support tool for his TB treatment

Video Supported Treatment (VST)

Video Supported Treatment (VST) requires the person on treatment to video record their medication intake which the healthcare provider can watch at a later stage. Every day, the person on treatment is guided through a secured mobile application to record videos of themselves ingesting their daily medication. This is then uploaded to a secured server that can be accessed by the healthcare provider to review medication intake. The mobile application used for the ASCENT project is SureAdhere. In Ukraine and Philippines DR-TB patients were offered the option to use VST as an alternative to directly observed therapy (DOT).



Graph: Total video supported treatment (VST) enrollments per country to date

EASE FOR PEOPLE ON TB TREATMENT TO USE THE TECHNOLOGY

To record daily adherence, the person opens the app on their mobile device, enters their pin-code and records a video of their medication intake. When there is mobile data or a Wi-Fi connection the video is uploaded to the adherence platform for review. For a person on treatment to be able to use this technology, they need to be technologically literate, with experience of using a smart phone. When compared to the previous technologies (medication label and smart pill box) VST requires the most effort and time for a person to log daily adherence.

In Ukraine it was mentioned that the app minimized effort for the person on TB treatment, and increased data security, when compared to other video supported treatment approaches using instant messaging apps such as Viber, WhatsApp or Skype. This is attributed to the fact that people don't have to manually store videos on their device, send the video, and delete them after sending to the healthcare provider, as this is done automatically through the VST app.

On the contrary, the Philippines project team noted that some people found it cumbersome to upload videos through the VST app when compared with uploading through Facebook Messenger, primarily because people were more familiar with the use of Facebook Messenger. It was reported that people experienced difficulties in uploading videos onto the app. To overcome this, healthcare providers offered additional training to people enrolled on VST about the functionalities of the app, and basic troubleshooting.

Image: A person on treatment preparing to record their medication intake

EASE FOR HEALTHCARE PROVIDERS TO USE THE TECHNOLOGY

At the initiation of the VST intervention, the healthcare provider needs to assist the person on treatment with installing the app on their mobile device; load the persons details onto the adherence platform; and provide initial training on the use of the technology to record their daily medication intake.

Once the person has been enrolled, the healthcare provider needs to review the videos sent by their patients on a daily basis, and approve their video, or follow up with the person (by means of a phone call or home visit) if there were ambiguities in the video or if they did not send their daily video.

Only once the daily video review has been performed can healthcare providers view the adherence calendar per patient or a grouped "task list" view of TB patients in their facility.

There is a heavy burden placed on the healthcare providers workload to ensure the effective implementation of VST as daily reviewing of videos per person enrolled on the treatment support approach is necessary to ensure there are no discrepancies in medication intake.

The Philippines team noted that due to the healthcare provider's workload, which was further exacerbated by the COVID-19 pandemic, DAT-trained healthcare providers were not able to conduct daily monitoring and patient follow up, particularly given the length of time associated with reviewing each patient video.

The team in Ukraine reported that VST could easily be incorporated into the standard of care as the country had experience implementing VST with the use of Viber or WhatsApp. A challenge raised by healthcare providers in the Ukraine was setting up the VST app on different models of smartphones. Some models required adjusting the mobile device settings (e.g., Xiaomi smartphones) which was challenging for healthcare providers who were not very confident users of smartphones.

We conclude, based on the ASCENT project experience, that VST is time consuming, especially when compared to the other technologies, from both a patient as well as a healthcare provider perspective.

ACCESSIBILITY OF THE TECHNOLOGY FOR PEOPLE WITH TB

For people on treatment to make use of VST they need daily access to a smart phone (iOS or Android), as well as daily access to an internet connection (mobile data or Wi-Fi). It is also required that people enrolled on VST are technologically literate with a basic knowledge of using a smart phone.

In the Ukraine, the internet connectivity in urban areas was usually covered by 3G or 4G network from mobile operators, however, in rural areas the connection strength was weaker.

Monthly data packages cost between $4 and $7 per month, limiting the reach of this technology for people with a low income. The ASCENT project did not provide smart phones or data packages for people enrolled on the technology.

The Philippines project team noted that people enrolled on VST had difficulty accessing their SureAdhere account in cases where they did not have access to their registered mobile device and instead used a different mobile device to log their daily adherence.

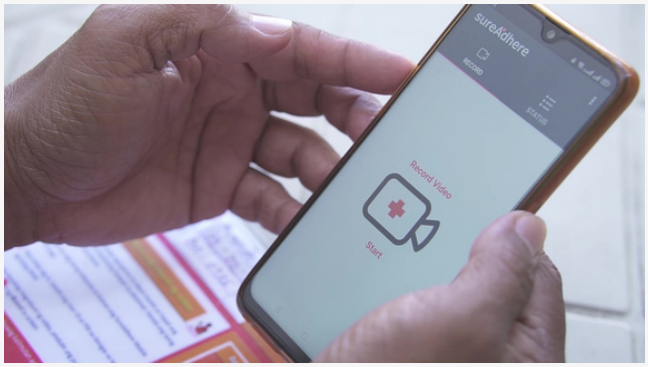
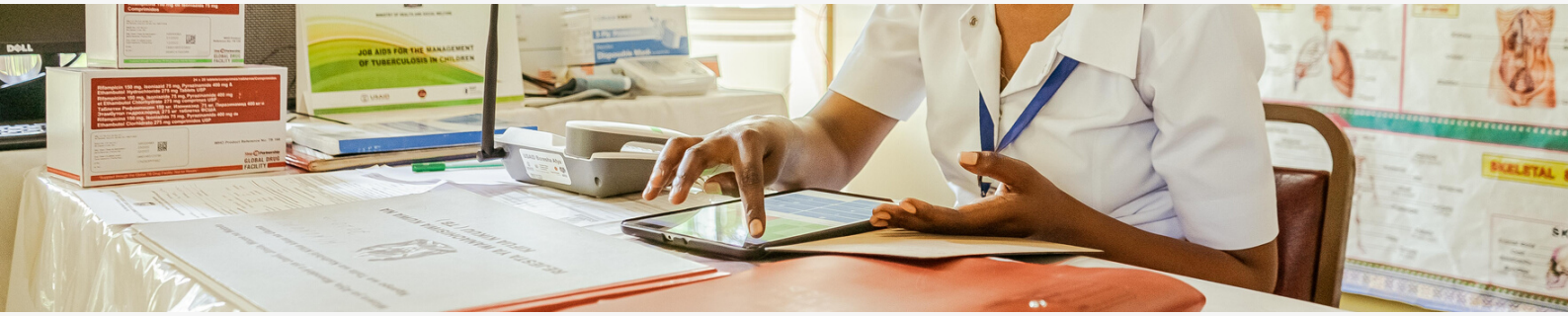


Image: A person on treatment needs to have daily access to a smart device in order to record their medication intake

TECHNOLOGY IMPLEMENTATION AND CONTINUED MANAGEMENT

Data privacy policies impact how to setup VST technologies. For instance, in Ukraine healthcare providers implementing VST should adhere to the requirements of the Ukrainian legislation on the protection of personal data and compliance with the norms of ethics and deontology. Namely, video recordings of each person should be archived and kept until the end of the course of treatment; videos must be encrypted to ensure maximum confidentiality (using a password and using a separate encryption channel); only authorized users should have access to video recordings; access to confidential information by unauthorized persons is strictly prohibited and the VST curator needs to discuss confidentiality procedures with the patient, such as privacy while conducting VST and storing video files on the device, etc.

In the Philippines, the Data Privacy Act (RA 10173) provides that all processing of an individual's sensitive and personal information, which includes health among others, is prohibited except when it is needed for medical treatment, or it is necessary to protect the life or health of a person.



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"I REALLY LIKE THE SYSTEM; IT HAS EVEN CREATED FRIENDSHIP BETWEEN ME AND THE HEALTHCARE PROVIDER HERE. HE SHOWS ME MY CALENDAR (ADHERENCE) WHEN I COME FOR DRUGS AT THE FACILITY. IT IS ALL GREEN AND I WOULD LIKE TO KEEP IT UP".

- A person from Tanzania enrolled on DATs as a TB treatment support tool