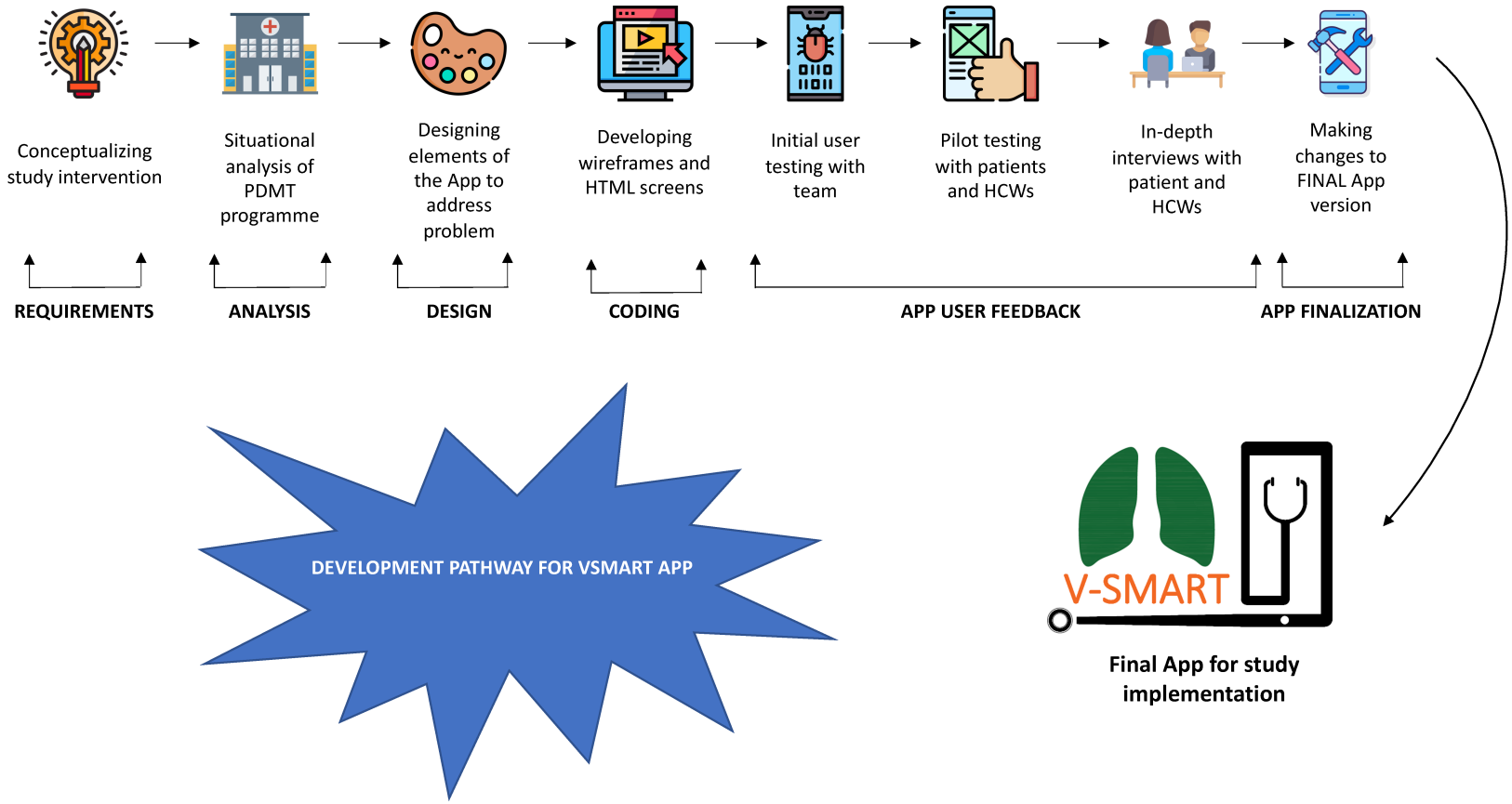
Supplementary Appendix

eFigure 1. mHealth application development cascade using 'Waterfall' framework



eMethods 1. Summary of mHealth training workshop activities

Patients randomized to the intervention group will be asked to attend a baseline mHealth training workshop. During this workshop:

(a) Evaluation of patients' existing smartphones

Patients will be asked to bring their smartphone to the start-up workshop. The model number and performance characteristics of the smartphone will be compared to a pre-determined list of valid phones. If a patient owns a smartphone on this list (i.e. capable of installing the mHealth application), then this phone will be used throughout the study.

Patients without their own smart phone will be loaned a low-cost smartphone for the study period, funded by the study. Patients unable to operate a smartphone, despite training, will be offered a low-cost non-smart phone still capable of running the application.

Queries about the suitability of smartphones will be referred to a study Data Manager.

(b) Installation of the mHealth Application

Patients with a smartphone will have the mHealth application installed by research staff. The operation of the App will be demonstrated during a group session run by research staff, independent of the PMDT program.

Training will be provided to participants in the intervention arm to ensure they are able to use the mHealth application; basic functionality testing will be conducted with each patient before they leave the health facility.

Patients will receive monthly credit to their phones to cover data cost. In the event that a patient in the intervention group loses his/her smartphone, he/she will be requested to report this to the study team for a replacement device to be provided; such incidents will be documented by the study team.

Patients will be reminded to use the mHealth application to obtain information about adverse events, and if necessary, telephonically contact PMDT health workers working at their health facility directly. Staff will respond to individual patients with Grade 1 and 2 adverse events through the mHealth application and organize urgent assessment of participants with severe adverse events (Grade 3 and 4), or hospitalisations.

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eMethods 2. Definitions and criteria for adverse event classifications

An ***adverse event*** is defined as any untoward medical occurrence in a patient administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not related to this medicinal product.

A ***serious adverse event*** (SAE) is defined as any untoward medical occurrence that, at any dose:

- Results in death;
- Requires hospitalization or prolongation of hospitalization
- Results in persistent or significant disability/incapacity
- Is life-threatening
- Is a congenital anomaly or a birth defect
- Is otherwise medically significant

Severe adverse events (Grade 3, 4 or death) will be defined individually in a Manual of Procedures, applying the following approach.

General definitions of severity for grading of adverse events [3]

Grade 1	Grade 2	Grade 3	Grade 4
MILD	**MODERATE**	**SEVERE**	
- Transient or mild discomfort (<48 hours) - No medical intervention/therapy required	- Mild to moderate limitation in activity* - Some assistance may be needed - No or minimal medical intervention/ therapy required	- Marked limitation in activity* - Some assistance usually required - Medical intervention/therapy required - Hospitalizations possible	- Extreme limitation in activity* - Significant assistance required - Significant medical intervention/therapy required - Hospitalization or hospice care probable

eMethod 3. Cost-effectiveness data collection

Cost data collection will follow guidance by the Global Health Cost Consortium Reference Case for Estimating the Costs of Global Health Services and Interventions.[5] Patient and household costs will include direct costs (out-of-pocket medical and non-medical costs) and indirect costs (opportunity cost of patient and caregiver time spent seeking care and/or any lost productivity due to TB diagnosis), collected using patient cost diaries which will be reviewed by the research team during scheduled clinic visits and at the end of treatment. Provider costs will be collected through interviews with healthcare workers, retrospective review of project and government records, measurement of building space and observation of service delivery.[4] A micro costing or ingredients approach will be taken, where each quantity of resource used for the intervention will be multiplied by its unit cost or price for staff salaries, building space, training, supplies, drugs, equipment and overheads. Costs related to adverse events will also be estimated using an ingredients approach based on treatment protocols. Research costs will be excluded.

eMethod 4. Evaluating acceptance of mHealth application for support MDR-TB treatment

Overall objective

1. To evaluate what factors included in classic Technology Acceptance Models (TAMs), are important for understanding acceptance of an mHealth application supporting RR/MDR-TB patient treatment

We will evaluate potential barriers to scale-up ***during implementation*** through monitoring pre-defined process indicators using a dashboard interface to identify any potential gaps to implementation which could be overcome. We will also have at least one monthly meeting with sites where the proportion of patients reporting at least one adverse event is in the fourth quartile, to identify and overcome possible barriers to implementation.

A maximum of two PMDT staff and five MDR-TB patients per study facility will be interviewed at least three months ***after implementation*** of the intervention. Criteria for selecting PMDT staff include those who were (i) involved in implementing the mHealth application at the facility; (ii) responsible for follow-up of patients identified with adverse events; or (iii) responsible for facility management. In-depth interviews and focus group discussions will be held to determine the challenges and motivators for PMDT staff to implement the mHealth intervention, as well as patient experiences (including barriers) associated with using the mHealth application.

In-depth interviews

After written consent, in-depth interviews will be conducted in a quiet and private area to maintain privacy and confidentiality of participants using interview guides. The in-depth interview will be approximately an hour-long per session. All participants will be requested to provide written informed consent to digitally-record the session. The in-depth interview will take place in English or Vietnamese depending on participant preference.

Audio-recordings and process notes will be transcribed and where necessary translated prior to analysis. Process of translations and transcriptions will start within 7 days of the discussion. In-depth interviews conducted in English will be transcribed verbatim. Each session will first be transcribed verbatim into the local language then transcribed into English. For quality control purposes, random checks between the audio-recordings and transcriptions will take place by an independent staff member. Interview guides will be used to assist interviewers to address key topics. These will include:

- Patients' social relations within their neighbourhoods, households and between intimate partners
- Patients' experience of taking MDR-TB treatment, including barriers and facilitators to taking pills
- The meanings that patients ascribe to their medications in relation to notions of sickness and health, cure and treatment
- The corporeal aspects of their medication including side effects, psychological effects, and responses to these, for example dosing strategies, and timing of medication taking, manipulation of tablets

- Patients' understandings and responses to the use of an mHealth application and commentary on changes that have taken place in response to using the application, specifically with regard to treatment adherence
- Facility staff experience of implementing the mHealth intervention
- Key stakeholder perceptions of the feasibility of implementing the mHealth application and its sustainability

Analysis of in-depth interviews

Interview data will be analysed using QSR NVIVO 10 qualitative analysis software and manual reviewing. A grounded theory approach using content analysis will be used to describe the themes.[1 2] A codebook will be created using the deductive themes and any new themes that emerge. Steps to develop the codebook will include word frequency tabulation, text searches, highlighting statements that entail the frequently occurring words, linking statements to the deductive themes, further inductive review of the text, associating sub-themes to main themes and coding to index the transcript. Coding will progress from broad coding to focussed coding. For reliability, the original transcript and codebook will be sent to two independent reviewers. During a round-table discussion, the reviewers will categorise the original transcripts according to the codebook and suggest new codes as needed. The codebook will be revised and the themes finalised which will be displayed as direct quotes in the results.

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eReferences

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