

Rapid, Affordable, Scalable Product Innovation and Implementation: Beginning With The End In Mind

Bruce Thomas June 2, 2021



- An Illustrative Case Study: Digital Adherence Technology to Transform TB Care
- Facilitating Implementation, By:
 - 1. Adopting a "commercial" perspective
 - 2. Innovating with the end (scaled uptake) in mind,
 - 3. Pushing for simultaneous rather than sequential,
 - 4. Segmenting target markets to identify trail-blazers, fast followers, and the rest of the pack
 - 5. Building broad-based collaboration and collaborators
- Your Questions

Illustrative Case Study: Digital Adherence Technology to Transform TB Care



PROBLEM STATEMENT

- Current TB regimens are complicated and confusing from a dosing perspective (weight-banded, high pill burden).
- Current TB regimens are unforgiving to poor adherence (< 90 percent adherence = 5.6 times increased risk of relapse).
- *Directly observed therapy* form of patient management highly burdensome on patients and very resource intensive.
- Significant adherence challenges exist in resource-limited settings.
- Baseline adherence for selfadministering patients appears to be sub-optimal/poor.



Typical DS-TB medication: weight-banded; no dosing or other patient instructions



One month of MDR-TB medication: high pill burden and dosing complexity



1708, Marjorie Z. Imperial, Rada M. Savic, et al.)

Treatment outcome	Descriptive statistics		Univariable findings	
	Proportio n of overall sample in given category ^b	Proportion with suboptimal adherence ⁴	Odds ratio (95% confidence interval)	p-value
	n (%)	n (%)		
Treatment success	513 (90.8)	72 (14.0)	Ref	
(cure or treatment				
completion)				
Died	18 (3.2)	7 (38.9)	3.9 (1.5-10.4)	0.0065*
Lost to follow-up	34 (6.0)	13 (38.2)	3.8 (1.8-7.9)	0.0004*

TB patients with sub-optimal adherence had nearly 4 times increased risk of poor outcome in pragmatic trial involving 650 patients in India. Participants spending 30+ minutes collecting medications were at significantly higher odds of being sub-optimally adherent (medRxiv 2021.01.12.21249655 Beena Thomas, Ramnath Subbaraman et al.)



OUR THEORY OF CHANGE

Can we empower patients, assist HCWs, and improve current regimen performance globally by closing gaps in the treatment-half of the cascade of care through the use of digital adherence technologies and digital adherence technologyenabled care?



All While Reducing The Patient Burden and Inconvenience of Traditional Facility-Based Care

OUR VISION: DAT AND DAT-ENABLED CARE



- Help with dosing confusion: pictograms of other graphical cues
- Reminder: via SMS, ringing / glowing light on electronic pillboxes
 - *Verification:* via video observation, SMS response, unique phone number, opening/closing of pillbox

Dosing history compilation: usually to a website or smartphone interface

- *Healthcare provider interface:* direct video communication with patients, phone calls to patients, etc.
- Triage: into high- or low-risk patients

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Differentiated care: unique screening and intervention approaches for patients with different levels of risk

These Tools and This Patient Management Approach Has Been Proven Effective Across A Wide Range of Disease States In High Income Settings.

Our Question: Can They Be Implemented With Similar Impact in TB and In LMIC?



WHAT EVIDENCE, WHAT SCALE, WHAT PER PATIENT COST?

Evaluative criteria	Current state		
Feasibility	 Formal usability assessment conducted (432 patients) in 2012. Published – Chin J Antituberculosis. 2012; 34:419–424. 		
Acceptance	 Formal usability study (50 patients, 10 providers) conducted in 2016. Manuscript in review (Terry Blaschke, Sabina deGeest. 		
Accuracy	 432 patient study in china compared monitor records with random urine tests. 97.1% accurate. Published – China J Antituberculosis. 2012;34:419–424. 		
Effectiveness: Adherence	 Adherence effect (improvement of 40%) demonstrated in 4500 patient RCT. Published Liu et al, PLoS Medicine (2015) 		
Effectiveness: Health Outcomes	 Health outcomes-oriented RCT in process. Xiaoqiu Liu (China CDC) Principal investigator. 3800 patients, 24 clusters. <i>Trial Registry http://www.isrctn.com/ISRCTN35812455</i> 		
Cost-Effectiveness	 In Process: Anna Vassal (LSH&TM) Principal Investigator. In connection with Current RCT. Trial Registry http://www.isrctn.com/ISRCTN35812455 		



Over 300,000 Patients At Present – In 13 Countries. Emerging Standard of Care in China and India Total Intervention Cost – Monitoring Devices, Data, Platform Access (Automated Task Lists Based on Algorithms) – Roughly \$25 Per Patient for Entire Period of Treatment.



Approach We Used To Fast Track Implementation



1. ADOPT A COMMERCIAL PERSPECTIVE

- Too often, we think of global health as unique in terms of product introduction
- This thinking effectively discards decades of lessons learned and proven effective approaches to introduce new products in the places and to the people in whom we are most interested



- Our approach was NOT to create new product implementation pathways for global health, but to translate commercial innovation and product implementation best practices into global health
- Finally, we adopted "commercial" timelines innovation to global scale in 5 years!



2. INNOVATING WITH THE END IN MIND

Our Approach

- 1. Adapt AND invent.
- 2. Develop detailed target product profiles that truly will enable access/generate demand and stick to them.
- 3. Make sure that TPPs include ALL supply chain considerations think backwards from what current supply chains can do.
- 4. Pursue all open innovation channels in (e.g., Gates Grand Challenges) and beyond global health
- 5. Think differently about suppliers to gain new insights on key problems (e.g., battery life and reliability)

For Example, In Our TB Work

Constraints

Cost constraints – entire TB regimen (6 months) costs less than \$25

Internet access constraints – smart phones and data not commonplace

Technical literacy constraints – patient usage of SMS and IVR low

Medications/medication format constraints -- cannot be changed

Ability/willingness to recharge devices is low – long battery life required

THE POWER OF TPPs – DRIVING ADAPTATION

Available Technology (High Level)	Our Target Product Profile (High Level)	
Design limited: available in only one design, package format	Modular : A single, removable electronics module across multiple containers	
Loose fill, solid oral dose only	Blisters as well as loose fill	
Not "real-time" – periodic download of dosing data	" Real-time " and "a utomatic " (no patient involvement)	
Expensive: \$60+ (excluding data)	Affordable: \$20 per unit (including data)	
Battery life: Regular charging required	Battery life: No charge required for the entire length of therapy (6 months)	
No dosing instructions or cues	Both reminders (of dosing and refill) and some type of dosing assistance	
Relatively sensitive to drops, vibration, heat/cold	Highly robust – vibration resistant, designed to last > 5 years	

This ultimately led us to a supplier highly experienced **in automotive tracking technology**... with an interest in TB and HIV

Grand THE POWER OF TPPs – DRIVING INVENTION Challenges **Target Product Profile** (High Level) EVERY DAY, TAKE 2 PILLS AND SEND FREE CALL TO HIDDEN NUMBER Ultra Affordable: Less than \$5 per patient (including data) for 6-month treatment Supply Chain Friendly: immediately deployable AND manufacturable within India's TB supply chain Based on pragmatic technology: "feature phone" compatible Accurate: more than mere self-reporting: Dose instructive: contains features to help with dosing confusion **Discrete and portable**: appropriate for young, mobile populations and in high stigma regions



3. PUSH FOR SIMULTANEOUS RATHER THAN SEQUENTIAL

• As we planned, we mapped activities along this pathway to implementation

for Synergies





4. SEGMENT THE MARKET FOR IMPLEMENTATION

- Too often, markets are segmented by size, attractiveness, impact, etc.
- For rapid implementation/scale-up, markets should be segmented as follows:
 - Trail blazers (especially those willing to adopt BEFORE regulatory/policy guidance)
 - Fast followers (especially those readily paired with trail blazers)
 - The rest of the pack
- Efforts should be focused ENTIRELY on trail blazers until they begin to act
- Extra focus should be placed on trail blazers that are seen as persuasive for regulators and policy authorities (e.g., WHO)
- For us: our trail blazers were





5. DON'T GO IT ALONE



CONCLUSION

- In about 5 years, we are providing precision medicine-style patient management to 250,000 TB patients in more than 13 high burden countries
- None of the technologies being used existed before all are new innovations or radical adaptations of older technologies
- During this time, these technologies were rigorously evaluated in large scale, pragmatic RCTs and approved for use by the WHO
- What we've learned:
 - 1. A good make-ready is essential (Robust Market/Access Insights, Detailed TPPs, etc.)
 - 2. Simultaneously pursue radical adaptation and innovation
 - 3. Aggressively seek out highly non-traditional suppliers
 - 4. Think backwards from what current supply chains and supply bases can do well/at scale
 - 5. Work simultaneously, not sequentially
 - 6. Segment markets by readiness/receptivity regardless of size or attractiveness
 - 7. Build a coalition of willing collaborators and help them "find their lane"



QUESTIONS?

