

ADHERENCE TECHNOLOGY -- TO SUPPORT PATIENT-CENTRIC OBSERVATION AND DOSE HISTORY-DRIVEN DIFFERENTIATED CARE

Bruce V. Thomas, Founder & Managing Director, The Arcady Group, LLC



YES! Poor medication adherence may have the following impacts on health outcomes:

 Lower treatment completion and higher loss to follow-up



Poor adherence is associated with increased rates of discontinuation of treatment.

Source: Vrijens et al, BMJ. 2008;336 (7653):1114-7.1



YES! Poor medication adherence may have the following impact on health outcomes:

- Lower treatment completion and higher loss to follow-up
- Increased disease relapse
 - Low adherence increased TB relapse in recent clinical trials³



TB patients taking HRZE with <90% adherence had 5.6 times increased risk of TB recurrence in a meta-analysis of the OFLOTUB, REMox, and Rifaquin trials.

Source: TB ReFLECT Consortium, unpublished data³



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Severity of non- adherence	TB recurrence rate, 18 months after completing treatment
"Regular" adherence	9%
"Irregular" adherence	15%
"Very irregular" adherence	25%

Study of 534 smear + patients in India found a strong relationship between adherence and post-treatment TB recurrence.

Source: Thomas et al. Int J TB Lung Dis 2005; 9(5): 556-61⁴



YES! Poor medication adherence may have the following impact on health outcomes:

- Lower treatment completion and higher loss to follow-up
- Increased disease relapse
- Increased acquired drug resistance
 - Modeling study found adherence to be the strongest predictor for the emergence of MDR TB in retreatment patients⁸

PLOS COMPUTATIONAL

RESEARCH ARTICLE

The Role of Adherence and Retreatment in De Novo Emergence of MDR-TB

Dominique Cadosch¹, Pia Abel zur Wiesch^{3,3}, Roger Kouyos⁴, Sebastian Bonhoeffer¹⁺

1 Institute for Importune Biology, CH & Zunch, Bactarena, 3 Divesor of "potentiagy of Miccosal Bessess, Yee Biolecul Public Health American Control Links (Medi Belles of Humans, 3 Department of Pharmage, Faculty of Health Biolocula, Norwegia Andol University (JUT), Tomas, Norwey, 4 Divesor of Interbusic Diseases of Hospita Egolomous, University Hospita Zunch, University 2 Zunch, Stratbarted & Institute of Habitatis (Sectional Center for Networkee, University of Zunch, Zunche), Stratbarted



* sebastian bonhoeffer@env.athz.ch

Abstract

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Obation: Galaxie D. Alor zer Wesch P. Kaupa R. Barhadfer 1,020(). The Nam of Adverses and Retractives to Prove Simergence at MON 19. PLoS CompatiBiol 12(3), w1004196. doi:10.1011/ journal.pdb.1004199

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Equiplipit: 0-2018 Celevit-414. This is an oper access article distributed under the terms of the Constant Common Mithado License, which germits unwahicked vas, darbballor, and reproduction is any medium, provided the original softer and source are unabled. Treatment failure after therapy of pulmonary tuberoulosis (TB) infections is an important challenge, especially when it coincides with de novo emergence of multi-drup-resistant TB (MOR-T8). We seek to explore possible causes why MDR-T8 has been found to occur much more often in patients with a history of previous treatment. We develop a mathemati cal model of the replication of Mycobacterium tuberculosis within a patient reflecting the compartments of macrophages, granulomas, and open cavities as well as parameterizing the effects of drugs on the pathogen dynamics in these compartments. We use this model to study the influence of patient adherence to therapy and of common retreatment regimens. on treatment outcome. As expected, the simulations show that treatment success increases with increasing adherence. However, treatment occasionally fails even under perfect adherence due to interpatient variability in pharmacological parameters. The risk of generating MDR de novo is highest between 40% and 80% adherence. Importantly, our simulations highlight the double-edged effect of retreatment. On the one hand, the recommended retreatment regimen increases the overall success rate compared to re-treating with the initial regimen. On the other hand, it increases the probability to accumulate more resistant genotypes. We conclude that treatment adherence is a key factor for a positive outcome, and that screening for resistant strains is advisable after treatment failure or relapse.

"[P]robably the cheapest and most effective way to ensure a positive treatment outcome while minimizing the risk for the emergence of MDR-TB is to maintain proper patient compliance with the treatment."⁸

Source: Cadosch et al. Plos Comp Bio 2016;12:e10047498



BARRIERS RELATED TO ADHERENCE GENERALLY





RECENT WHO ACTION ON ADHERENCE

TREATMENT OF TUBERCULOSIS

Guidelines for treatment of drug-susceptible tuberculosis and patient care

2017 UPDATE

World Health Organization As treatment supervision alone is not likely to be sufficient to ensure good TB treatment outcomes, additional treatment adherence interventions need to be provided."

⁶⁶ The evidence also showed that when patients receiving treatment adherence interventions (e.g. different combinations of patient education, staff education, material support, psychological support, tracer and use of medication monitor) in conjunction with DOT or SAT, the treatment outcomes were significantly improved compared to DOT or SAT alone."

Recommendations

ions²⁵

- 2.1.1 Health education and counselling on the disease and treatment adherence should be provided to patients on TB treatment (Strong recommendation, moderate certainty in the evidence)
- 2.1.2 A package of treatment adherence interventions²⁵ may be offered to patients on TB treatment in conjunction with the selection of a suitable treatment administration option²⁶ (Conditional recommendation, low certainty in the evidence)
- 2.1.3 One or more of the following treatment adherence interventions (complementary and not mutually exclusive) may be offered to patients on TB treatment or to health-care providers:
 - a) tracers²⁷ and/or digital medication monitor²⁸ (Conditional recommendation, very low certainty in the evidence)
 - b) material support²⁹ to patient (Conditional recommendation, moderate certainty in the evidence)
 - c) psychological support³⁰ to patient (Conditional recommendation, low certainty in the evidence)
 - d) staff education³¹ (Conditional recommendation, low certainty in the evidence).



THE 99DOTS SOLUTION

Chosen By India's CTD To Facilitate The Shift To Daily-Dosed FDCs at ART Centers

99D 5 Affordable, scalable ICT-based adherence monitoring





DESIGNED TO ENSURE ACCURACY OF SELF-REPORTING







VIDEO OBSERVED THERAPY



Recommendations

- 2.1.4 The following treatment administration options may be offered to patients on TB treatment:
 - a) Community- or home-based DOT is recommended over health facilitybased DOT or unsupervised treatment (Conditional recommendation, moderate certainty in the evidence).
 - b) DOT administered by trained lay providers or health-care workers is recommended over DOT administered by family members or unsupervised treatment (Conditional recommendation, very low certainty in the evidence).
 - c) Video observed treatment (VOT) may replace DOT when the video communication technology is available and it can be appropriately organized and operated by health-care providers and patients (Conditional recommendation, very low certainty in the evidence).



🧶 🙆 🔒 SEND MESSAGE

SureADHERE: A ROBUST V-DOT SOLUTION

SureAdhere Mobile Technology, Inc.

Mobile platform; Evidence-based; Data analytics



The Platform

- Patient records drug ingestion using a mobile phone or tablet
- Provider monitors patient on secure web platform, ensuring compliance



Scientific Evidence

- SureAdhere's platform has been evaluated through years of rigorous academic and clinical research
- The platform was designed for, and by, healthcare providers



Analytics

- SureAdhere captures anonymous macro data
- Allows real-time visualization of patients' treatment progress and analytics for research and surveillance



SureAdhere[™] VOT Provider Dashboard shows daily adherence by patient and aggregated by site. Missed doses are easily identified in red.

Patient Dashboard helps providers visualize how each dose was taken, and immediately identify missed doses.

sureAdhere

sureAdhere



EVRIMED[™] – AFFORDABLE, LOW PATIENT BURDEN VERSION THE "GOLD STANDARDS IN MONITORING

MEMS/Wisepill Evidence base:

- Used in 1000+ clinical trials (500,000 patients)
- 700+ published
- Rigorously assessed accuracy of "pill in hand" versus pill ingestion
- Recognized by WHO as "gold standards" in clinical trials

evriMED™

- Matches MEMS-CAP technical performance
- Significantly more affordable (Basic ≈\$7 per patient, Real-time (≈\$10 per patient, with 2X re-use) versus: \$100+
- Modular design: standard electronics but varied containers (DS, MDR)

TECHNICAL SPECIFICATION	MEMS-CAP	evriMED
Data capture method	Date/time captured on container open/close	Date/time captured on container open/close
Data accuracy	99% accuracy in event capture	99% accuracy in event capture
Number of events stored	3000	10,000
Clock precision	+/- 90 seconds per month	+/- 90 seconds per month
Medication accommodation	Loose fill, SOD only	Blistered medications – up to 6 separate medications
Container Form Factors	Single	Multiple substrates and multiple form factors
Battery charging required	No	No
Data retention post loss of power	Yes	Yes



KEY FEATURES OF THE EVRIMED[™] DEVICES

- Generates accurate detailed dosing histories.
- Two versions "real time" or store data for periodic download.
- Modular design mass-produced "modules" and customized, inexpensive (plastic or corrugated) containers.
- Powered by standard, disposable batteries (6 month battery life) or rechargeable lithium batteries.
- □ Fits wide range of blistered medications. Large "**billboard**" for patient instructions.
- Separate audible and visible reminders of **both dosing and refil**.
- □ Daily "heartbeat" confirming operational status in absence of dosing event.
- Affordable: Basic (≈\$7 per patient), Real-time (≈\$10 per patient) with 2X re-use.







ADHERENCE TECHNOLOGIES



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

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



HOWEVER, SOME UNANSWERED QUESTIONS



Video DOT Flow Diagram





Questions

- What percentage of patients have regular access to their own mobile phone, a shared mobile phone or land line?
- Will patients continue calling with every dose, especially after they become asymptomatic and/or establish good medication taking habits? Borrowed phones and related access issues
- Is there sufficient standardization of medication format (blister size) and sufficient printing capability/capacity to support 99DOTS scaled deployment?
- How will this technology roll out in areas where smart phone penetration and data connectivity are not universal?
- Will patients continue filming themselves/transmitting videos as they begin to feel better and their treatment adherence is well established?
- Will patients, particularly adolescent girls and women, be willing to film their faces in areas where TB stigma is commonplace?
- In areas of high TB stigma, will patients be willing to use a medication monitor box?
- Particularly with MDR TB/TB-HIV, how accurate is the medication monitor in determining whether patients did in fact take their doses?
- Will patients who travel frequently be willing to use the medication monitor and, if so, will they be willing to carry it with them during travel?

What Is The Health Outcomes Impact Of Deployment and Use Of Adherence Technologies IN HIGH BURDEN REGIONS?



CONCLUSION

- Proposals utilizing and evaluating adherence technologies and technology-enhanced patient management are invited/encouraged.
- Although 99DOTS, V-DOT, and evriMED are of particular interest, proposals involving other technologies/ approaches also are invited.
- It is desirable to have work done in, and have strong involvement from, high burden country programs.

Desired Outcomes

Country programs gain experience with, and insights about, the acceptability and impact of these adherence technologies.

We answer many/most of the remaining implementation and impact questions about these technologies.

