“VIDEO DIRECTLY OBSERVED THERAPY FOR MONITORING ADHERENCE TO LTBI TREATMENT (VMALT)"

Richard S. Garfein, PhD, MPH

Union North American Region Meeting
Nursing Sponsored Session: Digital Health, Telemedicine and TB

February 25, 2021

UC San Diego
Herbert Wertheim
School of Public Health and
Human Longevity Science

UC San Diego
Herbert Wertheim
School of Public Health and
Human Longevity Science

DISCLOSURE

Dr. Garfein is a co-founder of SureAdhere Mobile Technology, Inc. (a VDOT service provider).
No funding, software or other resources were provided by SureAdhere for this study.
Dr. Garfein's contributions were reviewed and approved in accordance with UC San Diego conflict of interest policies.

BACKGROUND

Recommended LTBI Treatment

Drug(s)	Duration	Interval	Minimum Doses
Isoniazid	9 months	Daily	270
		Twice weekly	76
	6 months	Daily	180
		Twice weekly	52
Rifampin	4 months	Daily	120
Isoniazid & Rifapentine*	**3 months**	**Once weekly**	**12**

Source: CDC https://www.cdc.gov/tb/

*CDC required administration using directly observed therapy (DOT). *MMWR.* December 9, 2011 / 60(48);1650-1653.

In 2018, CDC updated recommendations removing DOT requirement. *MMWR.* June 29, 2018 / 67(25);723–726.

COVID-19

Barriers to DOT

- Cost

- Personnel

- Travel

- Privacy and Stigma

- Patient Autonomy

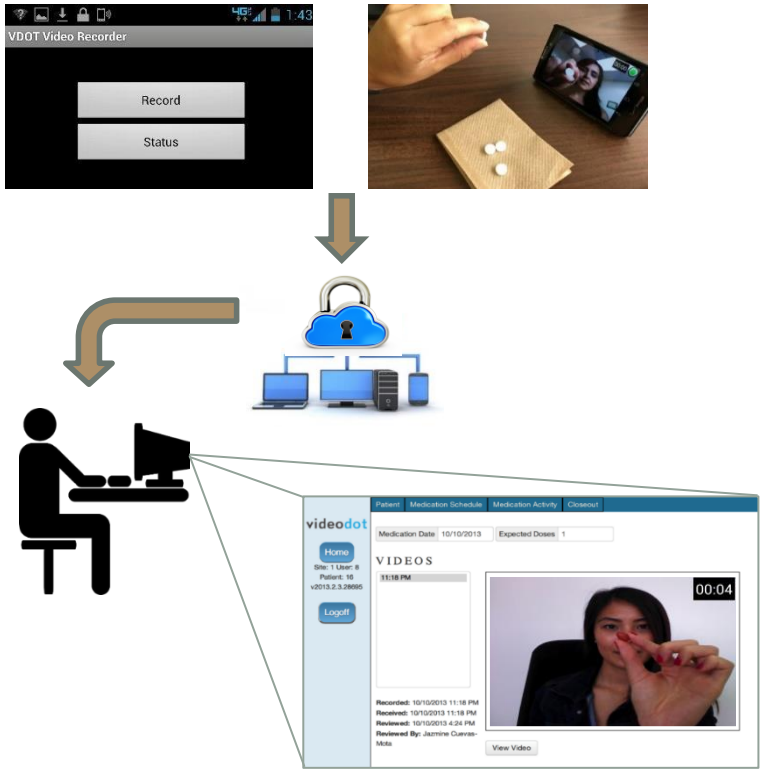
Video Directly Observed Therapy (VDOT)

Synchronous VDOT

- Videoconferencing
- "Real-time" or "Live"

Asynchronous VDOT

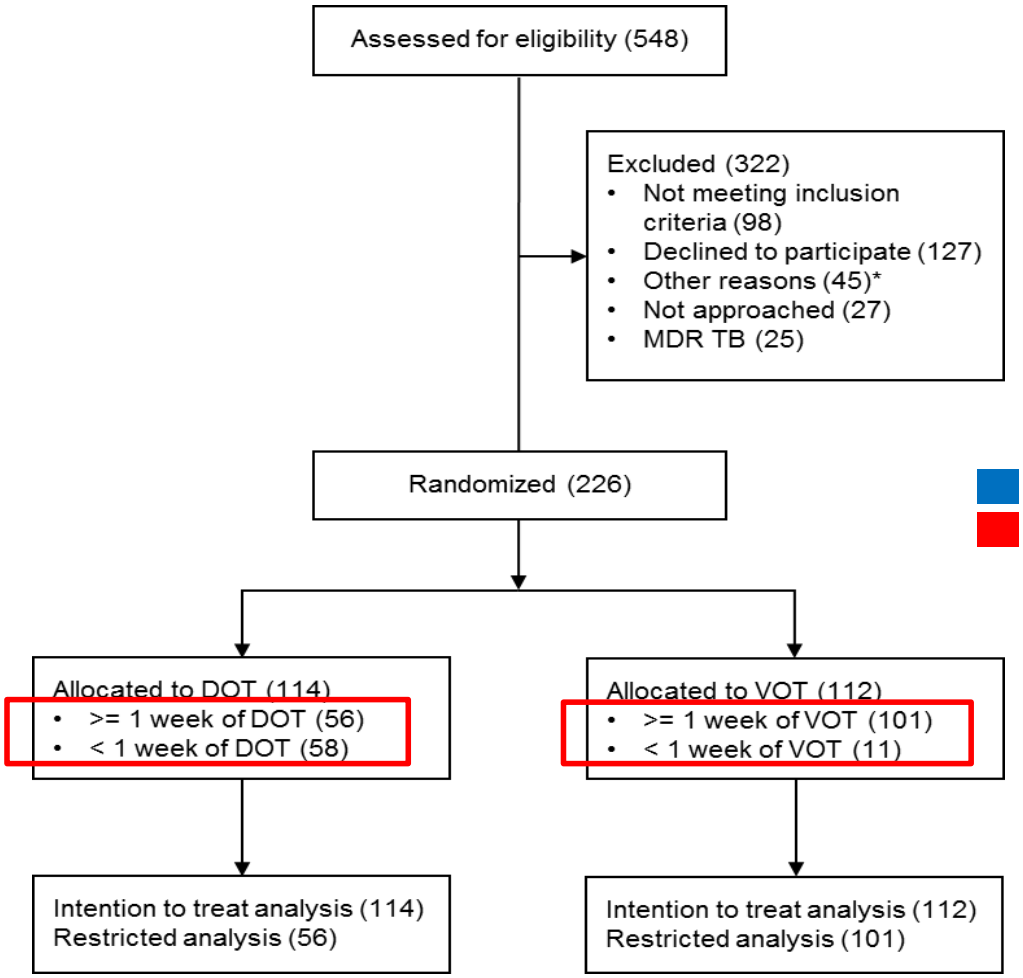
- Recorded videos
- "Store-and-forward"



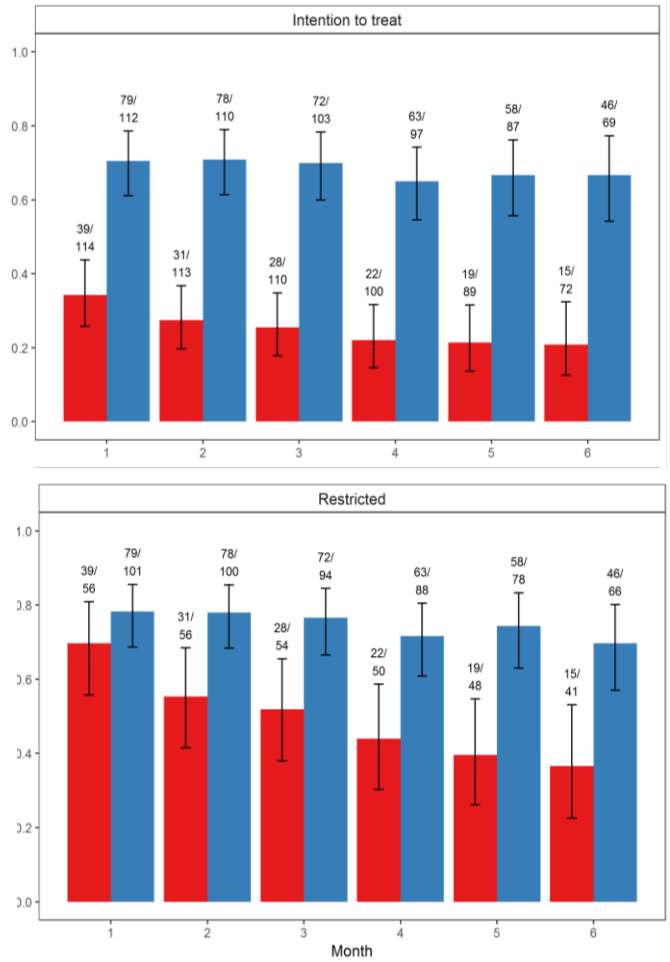
Smartphone-enabled video-observed versus directly observed treatment for tuberculosis: a multicentre, analyst-blinded, randomised, controlled superiority trial

Alistair Story, Robert W Aldridge, Catherine M Smith, Elizabeth Garber, Joe Hall, Gloria Ferenando, Lucia Possas, Sara Hemming, Fatima Wurie, Serena Luchenski, Ibrahim Abubakar, Timothy D McHugh, Peter J White, John M Watson, Marc Lipman, Richard Garfein, Andrew C Hayward

Lancet. 2019;S0140-6736(18):32993-3.



% with ≥80% of Scheduled Doses Observed



Cost to Monitor 6 Months of Treatment, U.K.

- DOT
  - $7,771 per patient @ five doses/week
  - $4,663 per patient @ three doses/week
- VDOT
  - $2,243 per patient @ seven doses/week

Story, et al., *Lancet*. 2019;S0140-6736(18):32993-3.

Video DOT for Monitoring Adherence to LTBI Treatment (V-MALT) Study – Aims

Funded by the National Institutes of Health (U01-AI116392)

- To determine whether completion of LTBI treatment with 3HP is greater among patients using VDOT versus clinic-based DOT
- To compare 3HP treatment satisfaction among patients using VDOT versus clinic-based DOT
- To measure the cost-effectiveness of VDOT compared to clinic-based DOT

METHODS

Study Design & Eligibility

Design

- Two-arm, parallel design, randomized controlled trial
- VDOT versus in-person clinic-based DOT (target n=155 per arm)

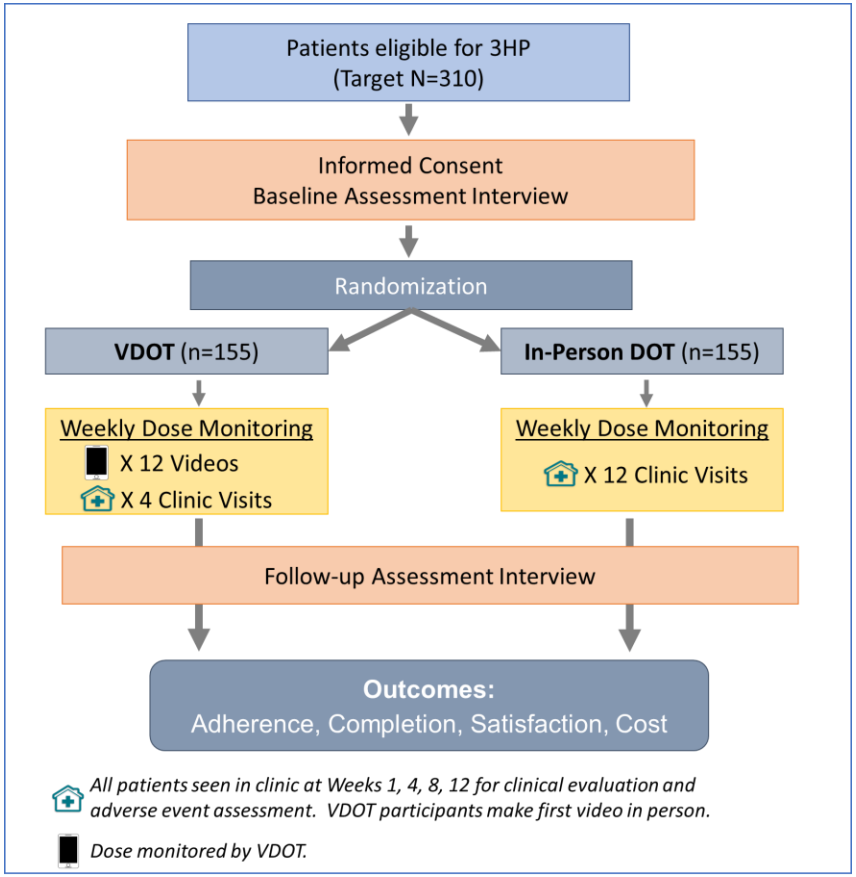
Eligibility Criteria

- LTBI and candidate for 3HP (per San Diego County TB program guidelines)
- Age ≥13 years
- Planned to reside in San Diego area for next 4 months
- Willing to follow study procedures and provide informed consent
- No physical or cognitive disabilities that preclude VDOT
    - Unless household member available to assist
- Not participating in a court ordered alcohol/drug treatment program

Recruitment Sites

- 7 San Diego County regional LTBI clinics
- UCSD Student Health Services clinic
- San Ysidro Health Center

Trial Flow Diagram



- 1st dose taken after randomization
- Both arms took 1st dose in-person
- Monthly clinic visits in both arms
- Participant data collection:
  - Baseline and follow-up interviews
  - Adherence record
  - Medical record review

Outcome Measures

- Proportion of participants completing treatment
  - 12 doses within 16 weeks
  - 11 doses accepted as “complete” by HHSA
- Proportion of participants completing treatment on-schedule (12 doses in 12 weeks)
- Proportion of participants taking medication doses off-schedule and mean number of doses taken off-schedule
- Participant treatment experience
- Cost to monitor participants by VDOT versus DOT

Cost Analysis

Approach:

- Ingredients-based micro-costing approach to estimate the 12-week treatment delivery cost for VDOT compared to in-person DOT

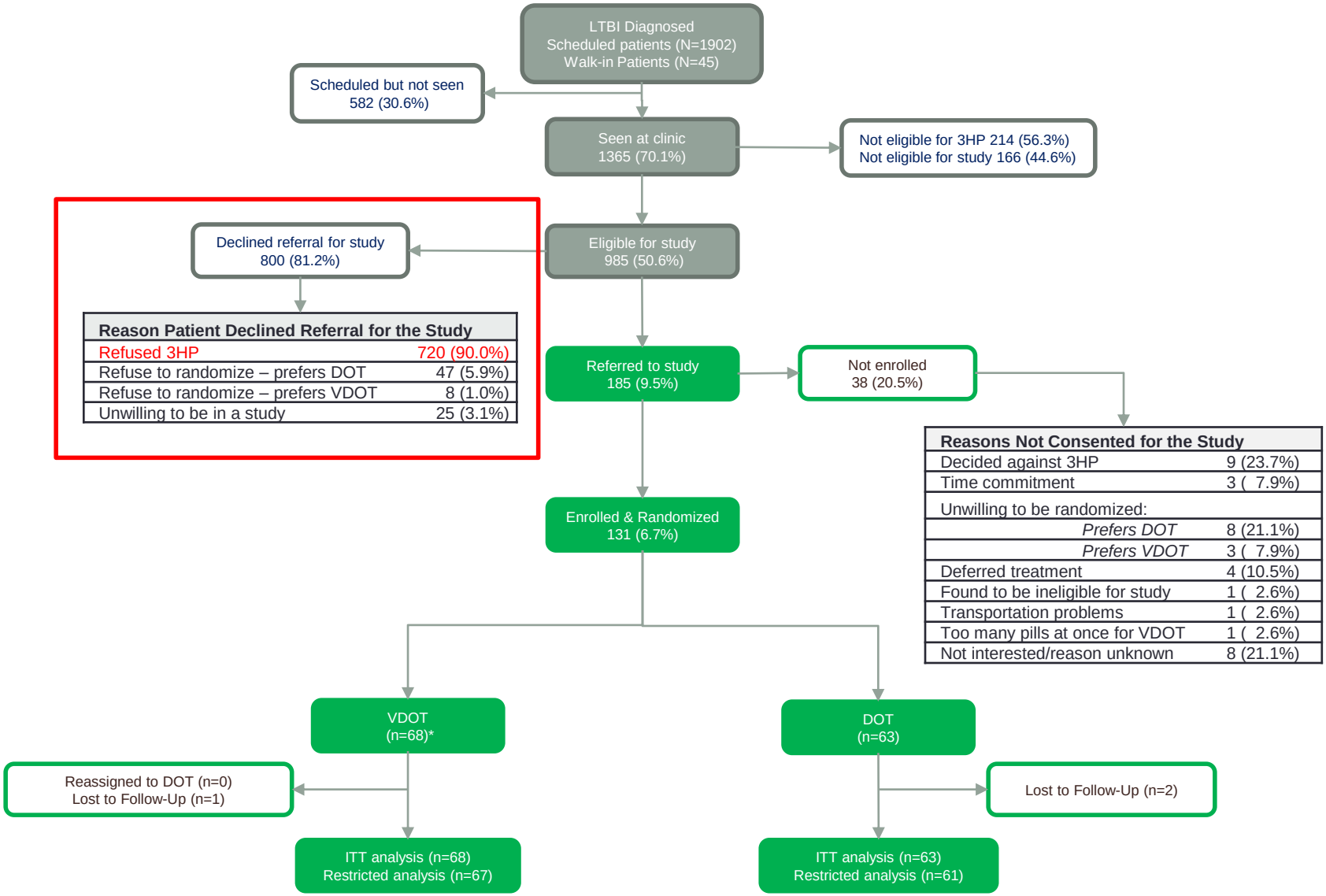
Data Collection:

- Provider questionnaire: personnel completing each task, percent effort and time in minutes (mode, min, max) required to complete each task
  - Consensus call to harmonize estimates
- Participant follow-up interview: Patient costs estimated based on self-reported transportation costs and lost wages

- Excluded costs for medications, laboratory tests and clinical exams (assumed to be equivalent in both arms)

RESULTS

Recruitment Flow Diagram (3/2016 - 3/2020)

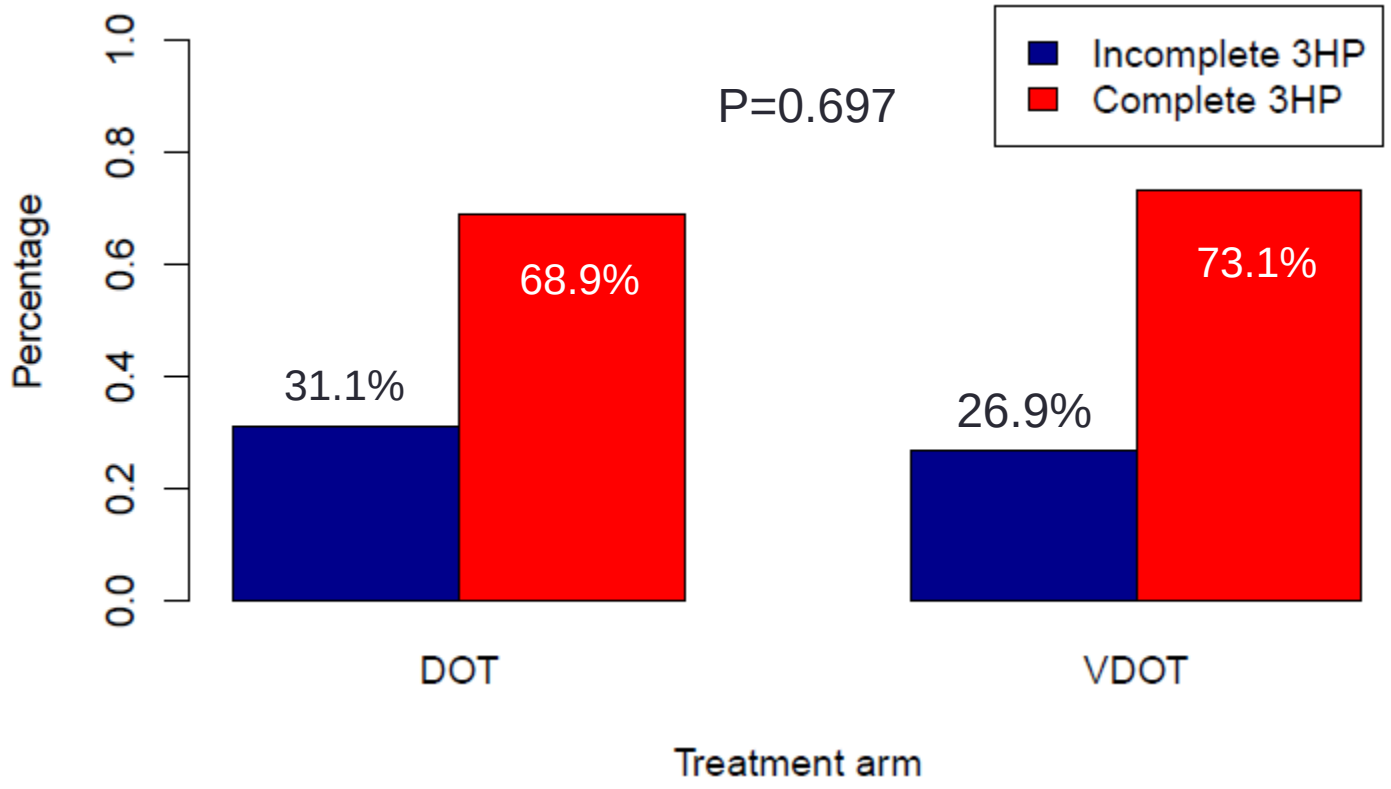


*The first 5 participants were assigned to VDOT prior to starting random assignment.

Baseline Participant Characteristics

Characteristic	VDOT	DOT
Trial arm: n (%)	68 (51.9)	63 (48.1)
Age – years: mean (range)	33.8 (13-75)	34.2 (14-57)
Sex – Female: n (%)	43 (63.2)	37 (58.7)
Race/ethnicity: n (%)		
- *Asian*	18 (26.5)	12 (20.6)
- *White*	2 (2.9)	4 (6.3)
- *Hispanic/Latino*	46 (67.6)	41 (65.1)
- *Other*	2 (2.9)	5 (7.9)
Foreign born – Yes: n (%)	52 (76.5)	48 (76.2)
Owned smartphone at baseline – Yes: n (%)	64 (97.0)	61 (96.8)
Typical mode of travel to TB clinic (check all that apply)		
- *Car (includes ride from family/friend)*	55 (80.9)	46 (73)
- *Public transportation or taxi*	18 (26.5)	16 (25.4)
- *Walk/bike/other*	10 (14.7)	9 (14.3)
Usual travel time to the clinic (minutes): mean (SD)	27.0 (24.3)	25.3 (23.7)
How it feels knowing someone will watch you take your meds?: n (%)		
- *Embarrassed / patronized / not trustworthy*	2 (2.9)	4 (6.3)
- *Cared for / I don't mind it*	54 (79.4)	52 (82.5)

3HP Completion* by Trial Arm



*Completion is defined as 12 ingested doses observed within 16 weeks.

Participant Satisfaction with Treatment

	DOT N (%)	VDOT N (%)	P-value
Satisfaction with clinical care overall			
- *Neutral or very dissatisfied* - *Somewhat or very satisfied*	1 (1.7) 52 (98.3)	0 (0.0) 63 (100)	0.488
Satisfaction with method of adherence monitoring			
- *Neutral or very dissatisfied* - *Somewhat or very satisfied*	8 (13.3) 52 (86.7)	5 (7.9) 58 (92.1)	0.330
Preferred method if had to redo Tx			
- *VDOT* - *DOT* - *No preference*	30 (50.0) 17 (28.3) 13 (21.7)	58 (92.1) 1 (1.6) 4 (6.3)	<0.0001
Would recommend my Tx to others			
- *No* - *Yes*	10 (16.3) 50 (83.3)	1 (1.6)* 62 (98.4)	0.003

*Response was “no preference”.

Cost by Trial Arm

	VDOT Median (range)	In-person DOT Median (range)
Personnel	$205 ($170 – $340)	$236 ($211 – $368)
Device charge*	$96	$0
Patient costs	$27 ($20 – $71)	$82 ($60 – $212)
Total	$328 ($285 – $506)	$318 ($272 – $580)
Total (excl. device charge)	**$240 ($198 – $418)**	**$318 ($272 – $580)**

*Device charges include loaned smartphone and phone service, which could be avoided if patients use their own phones.

LTBI Patients Declined Study Referral (n=800)

Reason Patient Declined Referral to the Study	
Patient refused 3HP	720 (90.0%)
Scheduling for DOT	231
Transportation for DOT	186
Treatment monitoring reasons:	
Not interested in coming to clinic for in-person DOT	*10*
Does not feel comfortable/ trusted being observed	*1*
Need to delay treatment	*32*
Does not want to wait to start 3HP due to travel	*1*
In-person DOT will be difficult due to travel	*2*
Prefers same treatment as family member	*16*
Conflict with drug treatment program rules	*11*
Will be treated through private provider	*1*
Medication-related reasons:	
Too many pills at once	*13*
Prefers daily treatment	*6*
Does not want to change birth control method	*5*
Prefers other regimen based on past treatment	*7*
Concerns about side effects	*2*
Mother's decision for minor	*2*
Not interested in 3HP - reason unknown	194
Prefers in-person DOT arm	47 (5.9%)
Too many pills for VDOT	*6*
Does not want to record videos	*8*
Other/Unknown	*33*
Prefers VDOT – refuse to randomize	8 (1.0%)
Unwilling to be in a study	25 (3.1%)

DISCUSSION

Problems with Recruitment

- Change in U.S. immigration policies during the study reduced access to potential participants
- Self-administered 4R was preferred over 3HP with DOT
- Academic schedules for 3HP among UCSD students
- 3HP new to San Diego and offered judiciously

VMALT Trial Recruitment Lessons Learned: Acceptability of 3HP Regimen

Conflict with in-person DOT

- Transportation
- Time/scheduling
- Prefers not going to clinic

Unwilling to be randomized

- Refused to accept in-person DOT
- Refused to accept VDOT

Treatment regimen concerns

- Too many pills in each dose
- Potential side effects
- Contraindications with other medications

Strengths & Limitations

- **Strengths:**
  - Rigorous trial design
  - Implemented by TB program staff in natural setting
- **Limitations:**
  - Small sample size
  - Volunteer bias reduced differences in treatment completion and patient costs
  - Lack of effect precluded cost-benefit analysis

Conclusions

- Uptake of 3HP was low overall in San Diego County
- No difference was observed in 3HP completion or treatment satisfaction by trial arm
  - Volunteer bias might have contributed to null findings
- Preference for VDOT was greater than DOT in BOTH arms
- Per patient cost was lower for VDOT than for DOT when patients could use their own smartphone

Collaborators

Richard S. Garfein[1], Ankita Kadakia[2*], Stacie San Miguel[3], Lin Liu[1], Antonette Antonio[2], Jazmine Cuevas-Mota[1], Valerie Mercer[1], Donald G. Catanzaro[4], Timothy Rodwell[1], Phillip Rios[5], Ryan Moran[1], McKayla Smith[1], Constance Benson[1]

[1]School of Medicine, University of California San Diego, La Jolla, CA
[2]County of San Diego, Health and Human Services Agency, San Diego, CA
[3]Student Health Services, University of California, San Diego, La Jolla, CA
[4]University of Arkansas, Department of Biological Sciences, Fayetteville, AR
[5]Qualcomm Institute, University of California San Diego, La Jolla, CA
*Kathleen Moser and Susannah Graves contributed while serving as Branch Chief

Funded by the National Institutes of Health (U01-AI116392)

THANK YOU