



## Original Article

# Advantage in privacy protection by using synchronous video observed treatment enhances treatment adherence among patients with latent tuberculosis infection

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## ABSTRACT

**Background:** Treatment of latent tuberculosis infection (LTBI) is an important strategy for active disease prevention. Conventional in-person DOT (CDOT) programs are challenged by patient dissatisfaction over problems of convenience and privacy. The present study assessed satisfaction to DOT program and treatment adherence of synchronous video observed treatment (SVOT) programs from patients' perspectives.

**Methods:** A two-part questionnaire was presented to 240 subjects with LTBI who received a 9-month isoniazid treatment regimen along with mandatory DOT monitoring during January 2014 to December 2017.

**Results:** Satisfactions with location arrangement ( $p < 0.001$ ), ensuring treatment adherence ( $p = 0.027$ ), and privacy issues ( $p = 0.005$ ) were superior in the SVOT group. The overall rate of LTBI treatment completion was 91.25%. One (1.25%) and 20 (12.50%) of the participants in the SVOT and CDOT groups, respectively, quit LTBI treatment ( $p = 0.008$ ). Development of adverse events [adjusted hazard ratio, aHR 8.01 (3.42–18.79)], and the concern of privacy infringement [aHR 5.86 (2.69–12.76)] by the DOT program independently increase the risk of withdrawal. SVOT program [aHR 0.21 (0.06–0.68)] and a belief in the importance of adherence on treatment efficacy [aHR 0.29 (0.08–0.98)] were independent predictors preventing patients from withdrawing from treatment.

**Conclusions:** A comprehensive patient-centered DOT program enables high treatment adherence for the 9-month isoniazid LTBI treatment. Furthermore, SVOT was associated with superior patients' satisfactions which translate into higher treatment completion rates. As treatment adherence is the key to the efficacy of LTBI treatment, SVOT should be a reasonable supplement for LTBI treatment.

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## Introduction

Tuberculosis (TB) remains a leading cause of morbidity and mortality from a single infectious agent, resulting in more than 1.6 million deaths annually and infecting more than 10 million people worldwide [1]. A quarter of the global population, approximately

1.7 billion individuals, were estimated to be latently infected with TB in 2014 [2]. Of those infected, 5–10% eventually develop active TB [3]. Management of those with LTBI is critical to halt TB transmission. The treatment efficacy of LTBI depends on adherence to therapy, while completion rates widely vary at 60–90% [4]. As such, a critical challenge in LTBI treatment is the therapy itself, composed of long treatment courses riddled with adverse events. Lack of or poor adherence to treatment raises concerns for the emergence of drug-resistant strains.

Directly observed treatment (DOT) programs are recommended as the most effective method to ensure adherence to treatment

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[5]. However, recent studies have questioned the effectiveness of DOT outcomes due to varying methods of implementation [6]. Stigmatization resulting in humiliation, loss of control, stress, and inconvenience with timing have been reported [7]. In addition, conventional in-person DOT (CDOT) programs often burden both patients and program personnel. At the program level, complicated logistics and labor-intensive demands often eclipse precious and limited public health resources [8].

To address these difficulties, electronic-based DOT to deliver health care to patients from a distance while maintaining patient security and privacy, was proposed as an alternative to CDOT methods [9,10]. Electronic-based remote monitoring allows for a more-flexible schedule for both healthcare workers and patients, eliminating travel time and costs, reducing privacy infringement, increasing safety from exposure to TB patients [11]. In populations that are more mobile, such as migrant contract workers or frequent movers, the inherent flexibility of the cloud-based service may also allow for a markedly more-consistent method of monitoring [10,12]. However, the main drawbacks reported for this method are difficulty in monitoring adverse effects and to some, less development of in-person rapport [10].

Although the burden of tuberculosis is steadily declining in Taiwan for the last decades, there were still 9179 TB patients in 2018, equivalent to an incidence of 38.9 per 10<sup>5</sup> person-year [13]. Retreated patients accounted for about 3.6% of all TB patients [14]. Programmatic treatment was provided free of charge to all patients diagnosed of tuberculosis and preventive treatment to all TB contacts with LTBI according to the treatment guidelines [15]. Directly observed treatment is mandatory throughout the course of anti-TB and LTBI treatment. The synchronous video-observed treatment (SVOT) program which allowed two-way video calls was introduced in Taipei City in 2014. Herein, we conducted a surveillance study among subjects receiving a 9-month isoniazid regimen to compare patients' satisfaction with the two DOT methods. The impact of satisfaction on the treatment adherence was also evaluated.

## Methods

In Taiwan, preventive treatment is provided to all TB contacts with LTBI, and DOT is mandatory throughout the course of LTBI treatment. The CDOT program in Taipei City was implemented in 2006 [16]. The program is highly systematic and allows for time and location arrangements for CDOT to be flexibly customized to meet subjects' preferences. The CDOT program can largely accommodate short notices in changes and quickly reschedule along with subjects due to the already established ease of transport within the city. The subjects taking 9-month isoniazid regimen can choose either the SVOT or CDOT program. LTBI treatment and the DOT service including the smartphones and data plans are provided free of charge to the participants. Both the CDOT and SVOT programs are administered by trained independent DOT providers. A nutritional allowance is provided to each subject according to their adherence to the DOT program.

The retrospective surveillance study invited subjects who completed or quit their 9-month isoniazid LTBI treatment regimen during January 2014 to December 2017 to describe their satisfaction with the DOT program and voice their opinions about LTBI treatment policies via a telephone interview. Participants included those aged 15 years and older who had received LTBI treatment for at least 30 days. Those who switched DOT methods during LTBI treatment were also excluded. The Joint Institutional Review Board of Taipei Medical University approved the study (TMU-JIRB: N201701076) and waived the need for written informed consent.

Participants were instructed to complete a two-part questionnaire of their opinions toward the LTBI treatment policy and their satisfaction with their experience under the DOT service. The satisfaction questionnaire was composed of five elements: convenience in (1) time scheduling and (2) location arrangement; efficacy of (3) monitoring and managing adverse events and (4) ensuring treatment adherence; and (5) efficacy of alleviating privacy concerns. Satisfaction to each element was graded into a four-point scale.

Intergroup differences were calculated using *Chi*-squared test or Fisher's exact test for categorical variables, if appropriate. DOT adherence was defined as the percentage of directly observed doses from the total doses prescribed. A multivariate logistic regression analysis and a Cox regression were performed to evaluate risk factors for premature termination of LTBI treatment. Inverse probability of treatment weighting was applied to the logistic regression and Cox regression. Age, sex, occupation, shift work or business trip required, comorbidities were used to calculate the propensity score (PS) grouped into SVOT, and then converted to weighted weights. The SVOT group weight is set to 1/PS, and the weight of the CDOT group is 1/(1-PS). Statistical significance was set to a two-sided  $p < 0.05$ . All analyses were performed using R statistical software (version 3.4.4, The R Foundation for Statistical Computing, Vienna, Austria).

## Results

During the study period, 1096 TB contacts were diagnosed with LTBI in Taipei City, and 887 received LTBI treatment. Among these, 465 subjects began the 9-month isoniazid regimen. Excluding 20 subjects who were still receiving ongoing LTBI treatment at the end of enrollment, 445 finished or discontinued LTBI treatment during the study period. Among them, 96 who selected SVOT and 349 who selected CDOT were screened for eligibility. Finally, 80 who selected SVOT and 160 who selected CDOT agreed to participate in surveillance and completed the questionnaire (Supplementary Figure S1).

The mean  $\pm$  SD age of the 240 subjects enrolled was 31.2  $\pm$  16.6 years (Table 1). Participants in the CDOT group were older and more likely to have comorbidities. The most prevalent comorbidities were hypertension (7.9%) and diabetes mellitus (5.8%). Students accounted for a larger proportion of participants in the SVOT group. Index cases in the SVOT group were most likely from campus contacts (71.25%). Campus and household contacts accounted for 38.75% and 28.75%, respectively, of the CDOT group. Participants in the SVOT group were more likely to have higher educational levels, more experience using video calls, and more-convenient access to the network.

During the LTBI treatment, 27.5% and 23.75% of participants in the SVOT and CDOT groups experienced adverse events, respectively ( $p = 0.635$ ) (Supplementary Table S1). The most common grade 1 adverse events were malaise (8.3%), hepatotoxicity (5.4%), and gastrointestinal upset (4.2%). The most important grade 3 adverse event was hepatotoxicity (1.6%). No participants reported life-threatening (grade 4) adverse events.

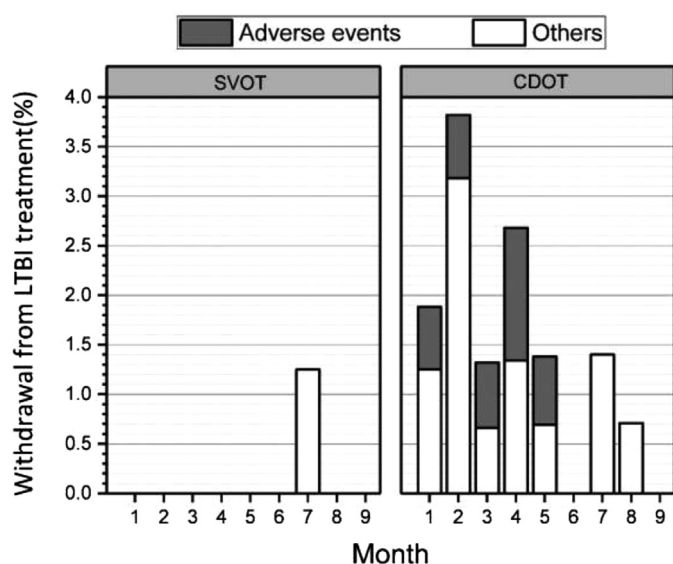
The overall rate of LTBI treatment completion was 91.25%. Proportions of withdrawals from the DOT programs were 5% and 26.88% from the SVOT and CDOT groups ( $p < 0.001$ ), respectively. Adherence to the DOT program was higher among participants in the SVOT group (66.60%) than in the CDOT group (61.42%,  $p = 0.001$ ). Eventually, one (1.25%) and 20 (12.50%) of the participants in the SVOT and CDOT groups, respectively, quit LTBI treatment before completion ( $p = 0.008$ , Fig. 1). Compared to the SVOT method, subjects in the CDOT group were more likely to have withdrawn from LTBI treatment unrelated to an adverse event ( $p = 0.023$ ). The Kaplan Meier analysis similarly revealed a significantly higher

**Table 1**  
Clinical characteristics of 240 participants who underwent directly observed treatment (DOT) for latent tuberculosis infection.

	SVOT( n= 80)	CDOT(n= 160)	DF	p Value
<b>Age (years)</b>				<0.001 <sup>a</sup>
15–29	75 (93.75%)	109 (68.13%)		
30–59	4 (5.00%)	26 (16.25%)		
≥60	1 (1.25%)	25 (15.63%)		
<b>Sex</b>			1	0.068 <sup>b</sup>
Male	47 (58.75%)	74 (46.25%)		
Female	33 (41.25%)	86 (53.75%)		
<b>Comorbidities</b>			1	0.079 <sup>b</sup>
Hypertension	10 (12.50%)	35 (21.88%)		
Hypertension	2 (2.50%)	17 (10.63%)		0.040 <sup>a</sup>
Diabetes mellitus	2 (2.50%)	12 (7.50%)		0.151 <sup>a</sup>
Asthma	2 (2.50%)	6 (3.75%)		0.722 <sup>a</sup>
Arrhythmia	2 (2.50%)	7 (4.38%)		0.722 <sup>a</sup>
Chronic viral hepatitis	3 (3.75%)	5 (3.13%)		1 <sup>a</sup>
<b>Relationship to the index case</b>				<0.001 <sup>a</sup>
Classmate	57 (71.25%)	62 (38.75%)		
Colleague	4 (5.00%)	5 (3.13%)		
Household member	11 (13.75%)	46 (28.75%)		
Roommate	1 (1.25%)	4 (2.50%)		
Other	7 (8.75%)	43 (26.88%)		
<b>Educational level</b>			4	<0.001 <sup>b</sup>
Graduate school	30 (37.50%)	16 (10.00%)		
College/university	34 (42.50%)	85 (53.13%)		
Senior high school	15 (18.75%)	31 (19.38%)		
Junior high school	1 (1.25%)	18 (11.25%)		
Elementary school	0 (0.00%)	10 (6.25%)		
<b>Occupation</b>				<0.001 <sup>a</sup>
Student	59 (73.75%)	68 (42.50%)		
Office staff	6 (7.50%)	18 (11.25%)		
Service industry	13 (16.25%)	18 (11.25%)		
Military service	0 (0.00%)	7 (4.38%)		
Others	1 (1.25%)	9 (5.63%)		
Nil	1 (1.25%)	40 (25.00%)		
<b>Shift work or business trip required</b>			1	1.000 <sup>b</sup>
No	69 (86.25%)	138 (86.25%)		
Yes	11 (13.75%)	22 (13.75%)		
<b>Convenient access to network</b>			2	<0.001 <sup>b</sup>
Mobile network	62 (77.50%)	112 (70.00%)		
Landline network	18 (22.50%)	22 (13.75%)		
Nil	0 (0.00%)	26 (16.25%)		
<b>Experience using video calls</b>				<0.001 <sup>a</sup>
No	0 (0.00%)	50 (31.25%)		
Yes	80 (100.00%)	110 (68.75%)		

SVOT, synchronous video observed treatment; CDOT, conventional in-person DOT; DF, degree of freedom.

p value calculated by using (a) Fisher's exact or (b) Chi-squared test



**Fig. 1.** Trends of adverse event-related (grey) and adverse event-unrelated (white) withdrawals from a 9-month isoniazid regimen among subjects with latent tuberculosis infection supported with either synchronous video observed treatment (SVOT) or conventional in-person DOT (CDOT).

probability of remaining in the anti-TB treatment in SVOT group participants ( $p = 0.0038$ ) (Supplementary Figure S2).

Proportion of participants who voiced satisfaction to flexibility of time scheduling, location arrangement, and efficacy in ensuring treatment adherence and monitoring adverse events were 81.3%, 96.7%, 88.8%, and 98.3%, respectively. However, 7.5% of all participants were concerned over privacy infringement. Compared to participants who finished the whole course of the LTBI treatment (Fig. 2A), those who quit the LTBI treatment voiced markedly lower levels of satisfaction with time scheduling ( $p < 0.001$ ), location arrangement ( $p = 0.039$ ), efficacy in ensuring treatment adherence ( $p = 0.024$ ), and privacy issue ( $p = 0.007$ ). Regarding the methods of DOT delivery, participants in the SVOT group had higher satisfaction rates with convenience in location arrangement and efficacy for ensuring treatment adherence and were concerned less about the infringement of privacy by the DOT service (Fig. 2B).

Supplementary Table S2 summarizes insights into LTBI treatment by the 240 participants. Compared to participants who completed LTBI treatment, the 21 participants who quit LTBI treatment agreed less on the risk of LTBI transforming to active TB and the importance of LTBI treatment adherence on treatment efficacy. Those who completed LTBI treatment were less aware that LTBI does not spread TB infection.

The propensity score-weighted Cox regression analysis revealed that development of adverse events and concern over privacy

**Table 2**

Univariate logistic regression, multivariate logistic regression with propensity score weighting, and multivariate cox regression with propensity score weighting of risk factors for withdrawing from latent tuberculosis infection (LTBI) treatment among 240 participants who underwent directly observed treatment for LTBI.

	Logistic Regression						Cox Regression					
	Unweighted			IPTW <sup>a</sup> Weighted			IPTW <sup>a</sup> Weighted			IPTW <sup>a</sup> Weighted		
	Crude OR (95% CI)	Adjusted OR (95% CI)		Adjusted OR (95% CI)			Adjusted HR (95% CI)			Adjusted HR (95% CI)		
<b>DOTS</b>												
CDOT (ref.)												
SVOT	0.09*	(0.01 ~ 0.70)	0.18	(0.02 ~ 1.48)	0.21*	(0.06 ~ 0.70)	0.21*	(0.06 ~ 0.68)	0.21*	(0.06 ~ 0.68)	0.21*	(0.06 ~ 0.68)
<b>Age</b>												
15–29 (ref.)												
30–59	0.89	(0.20 ~ 3.94)	0.92	(0.19 ~ 4.41)								
60~	2.65	(0.95 ~ 7.35)	2.36	(0.69 ~ 8.13)								
<b>Sex</b>												
Male (ref.)												
Female	0.91	(0.39 ~ 2.15)	0.57	(0.21 ~ 1.54)								
<b>Occupation</b>												
Nil (ref.)												
Student	0.41	(0.14 ~ 1.19)										
Other	0.64	(0.22 ~ 1.91)										
<b>Shift work or business trip required</b>												
No (ref.)												
Yes	1.97	(0.72 ~ 5.38)	3.97	(1.31 ~ 12.07)								
<b>Comorbidities</b>												
No (ref.)												
Yes	0.71	(0.21 ~ 2.40)										
<b>Adverse events</b>												
Nil/Grade 1 (ref.)												
Grade 2/3	7.41*	(2.87 ~ 19.16)	7.87*	(2.54 ~ 24.46)	13.40*	(4.07 ~ 44.12)	8.01*	(3.42 ~ 18.79)				
<b>Do you agree that subjects with latent infection of TB are associated with an increased risk of development of active TB?</b>												
Disagreed (ref.)												
Agreed	0.26*	(0.10 ~ 0.64)	0.32*	(0.11 ~ 0.94)	0.31*	(0.11 ~ 0.89)	0.47	(0.20 ~ 1.12)				
<b>Do you agree that LTBI does not spread infection to others?</b>												
Disagreed (ref.)												
Agreed	1.63	(0.55 ~ 4.85)										
<b>Do you agree that adherence to the LTBI regimen is important for the efficacy of eliminating dormant pathogens?</b>												
Disagreed (ref.)												
Agreed	0.10*	(0.03 ~ 0.35)	0.33	(0.060 ~ 1.79)	0.17	(0.020 ~ 1.53)	0.29*	(0.080 ~ 0.98)				
<b>Do you agree that interruption or inadequate dosage of LTBI treatment can predispose the emergence of resistant strains?</b>												
Disagreed (ref.)												
Agreed	0.39	(0.13 ~ 1.17)										
<b>Flexibility in time scheduling</b>												
Unappreciated (ref.)												
Appreciated	0.28*	(0.12 ~ 0.67)	0.39	(0.14 ~ 1.10)	0.44	(0.17 ~ 1.12)	0.50	(0.23 ~ 1.07)				
<b>Convenience in location arrangement</b>												
Unappreciated (ref.)												
Appreciated	0.17*	(0.05 ~ 0.58)										
<b>Efficacy to ensure treatment adherence</b>												
Unappreciated (ref.)												
Appreciated	0.13*	(0.03 ~ 0.55)										
<b>Privacy infringement</b>												
Unconcerned (ref.)												
Concerned	9.78*	(4.05 ~ 23.63)	7.90*	(2.62 ~ 23.85)	12.08*	(4.20 ~ 34.74)	5.86*	(2.69 ~ 12.76)				

OR, odds ratio; HR, hazard ratio; CI, confidence interval; CDOT, conventional in-person directly observed treatment; SVOT, synchronous video-observed treatment.

<sup>a</sup> IPTW, Inverse Probability of Treatment Weighting: age, sex, occupation, shift work or business trip required, comorbidities are used to calculate the propensity score grouped into SVOT.

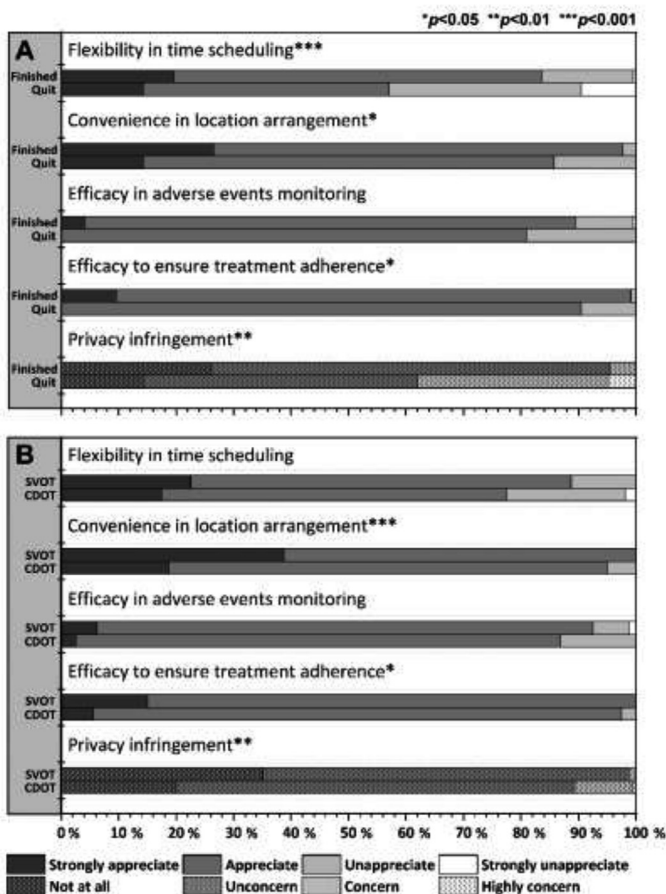
\* Significant ( $p$  value < 0.05).

infringement were independent predictors for withdrawal from LTBI treatment (Table 2). SVOT program and a belief in the importance of adherence on treatment efficacy were independent predictors preventing patients from withdrawing from treatment. Satisfaction over the convenience in time scheduling was associated with a marginally lower risk of premature withdrawal from LTBI treatment. Multivariate logistic regression analyses with or without propensity score weighting showed consistent findings in the independent predictors for withdrawal from LTBI treatment. The standardized absolute differences of variables used to calculate the propensity score between the CDOT and SVOT groups were listed in Supplementary Table S4. Including these variables for calculating the propensity score showed similar results in the multivariate Cox regression (Supplementary Table S3). The impact of the SVOT program, development of adverse events, and concern of privacy infringement remained significant by including

these variables. The belief in the importance of adherence on treatment efficacy had a wider 95% confidence interval after including these variables and became statistically insignificant. The subpopulation analysis among the 160 participants in the CDOT group also revealed consistent predictors for LTBI treatment withdrawal (Supplementary Table S5).

## Discussion

The present study demonstrated that the satisfactions on DOT program have strong impact on LTBI treatment completion rate among subjects undergoing 9 months of isoniazid LTBI treatment. The concern with privacy infringement by DOT program is especially a strong impediment refrains the participants from adhering to LTBI treatment. Since subjects supported by SVOT voiced higher satisfaction over convenience in time scheduling and privacy pro-



**Fig. 2.** (A) Satisfaction toward directly observed treatment (DOT) program stratified by either the participants finished or quit the latent tuberculosis infection treatment. (B) Satisfaction toward synchronous video observed treatment (SVOT) and conventional in-person DOT (CDOT) program.

tection, the higher treatment completion rate for SVOT over CDOT was not surprising from the patients' perspectives.

DOT programs establish bonds between healthcare providers and patients to promote treatment adherence [10]. However completion rates of conventional DOT programs are challenged by patients' dissatisfaction with lack of convenience and privacy infringement [17]. With the advance in smartphone and growing coverage of network, video-observed treatment has been established as more cost effective and more customizable to better suit subjects' individual needs [18]. Asynchronous video-observed treatment was demonstrated to achieve a better adherence to DOT program as compared to CDOT [19]. Reported drawbacks of asynchronous video-observed treatment monitoring methods are mainly a lack of face-to-face interpersonal feedback, especially regarding monitoring of adverse events, as provided by traditional methods [17]. With advances in telecommunications, DOT supporters can provide real-time feedback through the SVOT video-conference applications which largely overcomes this problem. As shown here, this study found no difference in satisfaction rates over the monitoring of adverse events. If anything, the SVOT group found adverse reaction monitoring to be marginally more satisfactory than the CDOT group.

The superior satisfaction and subsequently better adherence to DOT programs with the SVOT method echoes a previously reported surveillance study which assessed the continuing benefits of SVOT over CDOT in TB treatment [10,20]. A greater percentage of the SVOT group reported being strongly appreciative of the location arrangements compared to the CDOT group. The SVOT group had a

greater percentage of patients reporting being completely unconcerned with privacy issue while the CDOT group did have a higher percentage of concerned patients. High concern was only voiced in the CDOT group. From our results, withdrawals unrelated to adverse events were higher in the CDOT group. The higher LTBI treatment completion rate with SVOT is likely a consequence of higher satisfaction among patients, stemming from increased flexibility in timing scheduling and maintenance of privacy to avoid stigmatization from the community.

One-fourth of the global population was estimated to be latently infected with TB [2]. The use of chemoprophylaxis in TB contacts with evidence of LTBI was shown to reduce the risk of developing active TB disease by 94% [21]. However, low adherence remains the main obstacle to LTBI treatment efficacy [22,23]. As such, intervention programs have been developed to ensure success, largely in the form of DOT programs. However, regular supervision may impose unwanted stress on patients due to conflicts with patients' working hours and fears of stigmatization [24]. SVOT programs were developed to overcome drawbacks of CDOT ones [11]. As demonstrated in the present study, the satisfaction to SVOT as compared to CDOT is likely to main cause for better treatment completion rates for LTBI treatment. It should be noted that the beneficial effect of the SVOT method was exhibited with an already highly optimized CDOT program which had a high completion rate of 87.5%.

Although the DOT is not an universal standard practice for 9 month isoniazid LTBI treatment across the world, completion rates for both methods were high in this study compared to previous reports regarding 9-month isoniazid treatment with general completion rates ranging from 51.3% to 69.0% [22,23,25,26]. The high LTBI treatment completion rate could be attributed to the unique flexibility of Taiwan's DOT program. A comprehensive and patient-centered implementation of DOT service supports the patients to safely complete the long course of LTBI treatment. Development of the program was largely optimized to maximize convenience in an urban setting to accommodate patient needs and concerns by immediately and smoothly adjusting to requests for changes and accommodation. Travel within the city using any public transport or personal vehicles is reasonably efficient at most hours as well. Based on the survey, most participants were already highly satisfied with the location arrangement, leaving fewer factors of the program arrangement to dissuade patients from adhering to the program. As such, less of a difference in satisfaction rates between the two DOT programs is expected. Should the program be enacted in challenging geographical settings allowing telecommunication and technological familiarities, we expect that SVOT may serve as a potential strategy for DOT program with proved superior satisfaction and completion rates.

Belief in treatment efficacy and disease impressions play significant roles in determining completion rates among patients. Among the opinions surveyed, the completion rate of LTBI treatment was significantly correlated with a belief that treatment adherence has important impact on treatment efficacy. Fewer patients who withdraw from the program held this belief. Concern over wane in efficacy acts as a motivating factor to adhere to the treatment regimen. A strong belief in risk of transforming from latent to active disease was another opinion that significantly identified patients who continued with the program. Although the effect was statistically insignificant after adjustment of other predictors because the collinearity of this opinion with the belief in association between treatment adherence and efficacy. Adherence to anti-TB medication was shown to be significantly improved by appropriate education [27]. Promoting a better understanding of the disease and treatments through health education may be beneficial in raising completion rates [28,29].

There were several limitations of the study. First, the study was not a randomized controlled trail and the age and occupation dis-

tributions differed between the two groups. However, the impact of age and occupation on completion rates was insignificant in both the univariate and multivariate logistic regression analyses. Propensity score weighting was applied to address potential imbalance raised in preference-selection. Second, as the program was based in a metropolitan setting, the convenience of travel of residents in this location, leading to a possibly higher than usual CDOT completion and satisfaction baseline, would be difficult to replicate in a more rural or even suburban setting. With the possibility of decreased convenience in a suburban to rural setting, there would likely be greater, more-significant differences in satisfaction and completion rates between the two methods. Thus, there would be more reasons to favor use of SVOT over CDOT. Also, as the number of participants quitting treatment was notably low in the SVOT arm ( $n = 1$ ), the result of subpopulation analysis for SVOT is therefore omitted.

In conclusion, with the support of a patient-centered DOT program, high treatment adherence rates can be achieved for the 9-month isoniazid LTBI treatment. Furthermore, SVOT was associated with superior patients' satisfaction over CDOT which translates into higher treatment adherence and completion rates. As treatment adherence is the key to the efficacy of LTBI treatment, SVOT should be a reasonable alternative or supplement for CDOT programs.

**Data Share Statements:** Individual participant data that underlie the results reported in this article after deidentification will be available on request beginning 3 months and ending 36 months following article publication for researchers who provide a methodologically sound proposal. Proposals should be directed to chleew@tmu.edu.tw to sign a data access agreement.

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## Competing interests

None declared.

## Ethical approval

The Joint Institutional Review Board of Taipei Medical University approved the study (TMU-JIRB: N201701076) and waived the need for written informed consent.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.jiph.2020.03.013>.

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