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Bayesian Structural Equation Modeling to Identify Factors Influencing Tuberculosis Treatment Adherence

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Abstract

Adherence to anti-Tuberculosis (TB) treatment is vital for curing TB patients and avoids drug resistance TB. Structural Equation Model (SEM) is a powerful tool for modeling latent variables and to control measurement errors. Bayesian SEM (BSEM) gives better estimates of the latent variable compared to conventional frequentist approaches to SEM. To our knowledge the use of BSEM to identify the significant latent constructs influencing the TB patients' adherence to anti-TB treatment was not studied so far. A total of 725 pulmonary TB patients who were registered with Directly Observed Treatment Short course (DOTS) at Government health facilities in Tiruvallur district, south India under National Tuberculosis Elimination Programme were used for this analysis. In this study, a model of adherence to anti-TB treatment of TB patients using BSEM was explored which used to identify the relationship between adherence to anti-TB treatment and the latent variables "socio-economic", "habits", "problems" (problems in taking treatment) and "DOT" (treatment related variables). The latent variables "DOT" (0.199, p<0.005) and "problems" (-0.202 p<0.01) were significantly associated with adherence variable. The latent variable "DOT" had a positive effect while "problems" had a negative effect on adherence to anti-TB treatment. Hence reducing the patient's specific problems might encourage treatment regularity under guided supervision.

Keywords: Tuberculosis; Adherence; Structural equation model; Bayesian SEM; Latent variable

Abbreviation: TB: Tuberculosis; SEM: Structural Equation Model; DOTS: Directly Observed Treatment Short course; MDR: Multi Drug Resistant; NTEP: National Tuberculosis Elimination Programme; RNTCP: Revised National Tuberculosis Control Programme; PPPV: Posterior Predictive P-value CI: Credible Interval

Introduction

Although tuberculosis (TB) is a preventable and curable disease, it is still one of the leading causes of morbidity and mortality in spite of recent progress of drug development and management of anti-TB treatment regimen [1]. Globally, there were estimated 10 million new TB cases and 5,58,000 Resistant to Rifampicin (RR-TB). Out of this, 1,60,684 cases were diagnosed as Multi Drug Resistant TB (MDR-TB) [2]. The low adherence of TB treatment could lead to poor treatment outcome and multi drug resistant (MDR) TB. Consequently, this emphasizes TB patients should not miss any dose of anti-TB treatment. TB patients' adherence to anti-TB treatment is ensured through the significant component of DOTS (Directly Observed Treatment Short course) where every dose is given under direct observation [3]. Non-adherence to anti-TB treatment is the prime factor to drug resistant, relapse, treatment failure and death [4,5]. Numerous studies reported about the association of major components such as socio-economic character, lifestyle, treatment taking behaviour of the TB patients and health service centres etc. with patients' adherence to anti-TB treatment [3,5-7].

Treatment adherence is a multi-dimensional concept influenced by different latent variables which can be divided in to five dimension such as socio-economic, health care system, health condition of patient, treatment therapy and patients related factors [8]. The use of latent variables is relevant and popular when risk factors of interest can't be obtained with a single exact measurement. In most substantive research, it is important to establish an appropriate model to evaluate a series of simultaneous hypotheses about the impact of latent variables and manifest variables on the other variables and take the measurement errors into account. Structural equation modeling is a well-recognized technique in medical research for identifying complex relationship between latent variables and observed variables [9]. Latent variables are hypothesized to explain the co-variances in the observed indicators variables. In structural equation model (SEM), interest focuses on latent constructs, rather than on the observed indicator variables used to measure the constructs.

Meulemans et al. used SEM to identify the factors leading to non-compliance with DOT [10]. Nyamathi et al. assessed the predictors of latent TB infection treatment completion using SEM [11]. Bayesian SEM (BSEM) gives better estimates of the latent variable compared to conventional frequentist approaches to SEM [12]. The rationale and methodological details of BSEM are discussed in the literature [13-16]. BSEM with dichotomous variables was applied to study about non-adherence to medication of hypertensive patient [16]. To our knowledge the use of BSEM to identify the significant latent constructs influencing the TB patients' adherence to anti-TB treatment was not studied so far. In the current study, we hypothesized to identify the factors influencing adherence of anti-TB treatment using BSEM with dichotomous variables.

Methodology

Study design

This is a modeling study of treatment adherence using BSEM approach for secondary data

Source of data

This is a secondary data analysis of a total of 725 new smear positive pulmonary TB patients who were registered with DOTS programme in Tiruvallur district, south India under National Tuberculosis Elimination Programme (NTEP) formerly known as Revised National Tuberculosis Control Programme (RNTCP) were used for this analysis [3]. All these patients were treated under the direct observation of a DOT provider.

Tool used for data collection

ICMR-National Institute for Research in Tuberculosis, Chennai, India developed patient information form which is the semi-structured interview schedule. This tool includes information on socio economic demographic characteristics of patients, lifestyle characteristics, patient related problems, treatment related factors and whether the patients took treatment under supervision. This tool was used by trained field staff at patients' residence and collected information. The written consent was obtained from TB patients aged more than 18 years. The study was approved by the Institutional Ethics Committee of the ICMR-NIRT. We used this data for the current study purpose.

Model specification

In this study, there were eleven independent variables which formed four independent latent variables. This includes eight dichotomous variables such as tobacco smoking, drinking alcohol, substance abuse, DOT interfering daily activities, problems in taking drugs, difficulty in accessing health facility, loosing wages and DOT provider living in the patients' area. Further, the patients were given treatment at various DOT centres and these centres were grouped into a binary variable as government and non-government DOT centres. The variable "education" was classified into literate and illiterate as a binary variable and the variable "occupation" was classified into employed and unemployed as binary variable. The socio-economic variables such as education and occupation were intended to measure the latent variable "socio-economic".

The variables smoking, drinking and substance abuse were selected as indicators for the latent variable "habits". The four variables DOT interfering daily activities, problems in taking drugs, difficulty in accessing health facility and loosing wages formed the latent variable as "problems". The two variables type of DOT center and DOT provider living in the patients' area were chosen as indicators for the latent variable "DOT". Body weights at the time of initiation of treatment and age in years were taken as covariates. (Figure 1) depicts path diagram and SEM with the outcome variable adherence predicted by the four latent variables socio-economic, habits, problems, and DOT. In this study, it was hypothesized that the latent variables socio-economic, habits, problems, and DOT which were influencing factors for adherence to TB treatment.

BSEM model

The BSEM models with dichotomous variables using Markov Chain Monte Carlo algorithms were constructed for analyzing the influencing latent variables for adherence to TB treatment using Mplus version 7.1. The non-informative prior which is default in Mplus was used for BSEM. For BSEM, the model convergence was assessed by the trace plots and estimated potential scale reduction (EPSR). Convergence of the sequence has been achieved where the ESPR values are less than 1.2. A Posterior predictive p-value (PPPV) is used to test the goodness of fit of the posited model.

Results

Profile

The base line characteristics of the TB patients are given in (Table 1). At the initiation of treatment, socio demographic profiles of the 725 patients were: 190 (26.2) were females; 401 (55.3%) were ≤42 years old; 289 (39.9%) were illiterates; 202 (27.9%) were unemployed; 343 (47.3%) were smokers and 270 (37.2%) were alcohol users.

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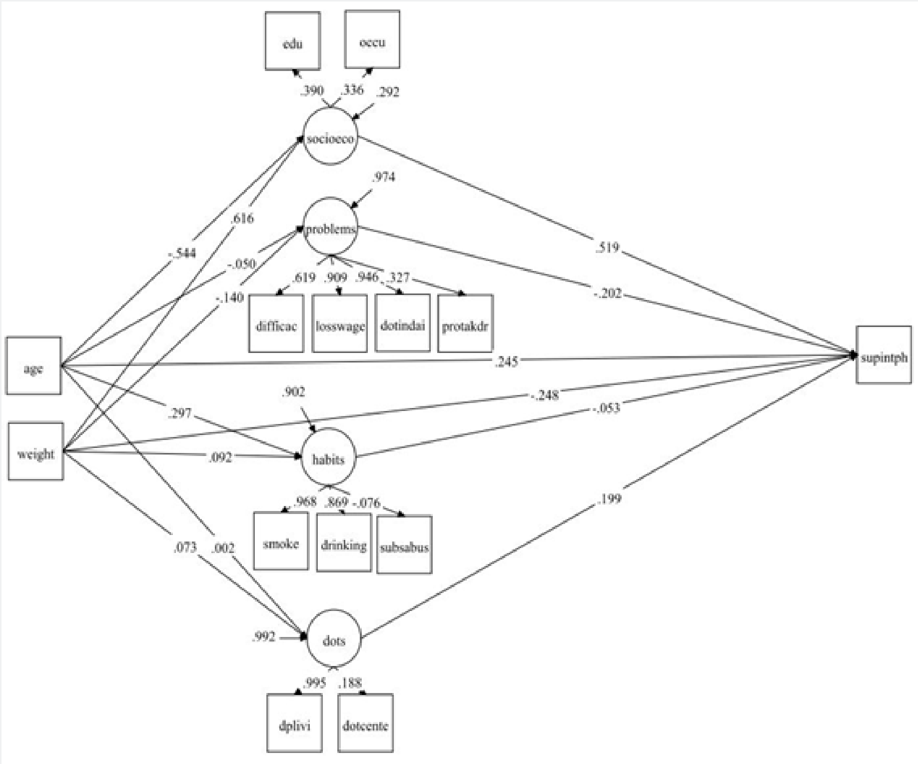

Figure 1: Standardized Bayesian estimate of structural equation model for adherence to anti-TB treatment.
Legend: socioeco=socioeconomic; edu=education; occu=occupation; subabus=substance abuse; dplivi=DOT provider living in the patients' area; dotcente=DOT centre; difficac=Difficulties in accessing health facility; losswage= Loosing wages; dotindai=DOTS interfering daily activities; protakdr=Problems in taking drugs; supintph = adherence to anti-TB treatment

Table 1: Basic characteristic of study population according to adherence and non-adherence to anti-TB treatment.

Variables	Non- adherence (N=249)		Adherence (N = 476)'		Total (N = 725)	
	n	%	n	%	n	%
Female	59	23.7	131	27.5	190	26.2
Age ≤ 42 years	132	53	269	56.5	401	55.3
Weight <=42 kgs	158	63.5	269	56.5	427	58.9
Illiterate	111	44.6	178	37.4	289	39.9
Unemployed	74	29.7	128	26.9	202	27.9
Smoking	127	51	216	45.4	343	47.3
Alcoholism	94	37.8	176	37	270	37.2
Substance abuse	6	2.2	26	5.5	32	4.4
Government DOT centre	101	40.6	285	59.9	386	53.2
DOT provider living in patients' area	164	65.9	374	78.6	538	74.2
DOT interfering daily activities	22	8.8	27	5.7	49	6.8
Problems in taking drugs	144	57.8	243	51.1	387	53.4
Difficulties in accessing health facility	36	14.5	22	4.6	58	8
Loosing wages	10	4	24	7.2	34	4.7

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BSEM Results

To obtain the Bayesian estimates, 57,000 observations were collected after discarding the first 57,000 burn-in iterations. The Bayesian estimates that were obtained by using 57,000 observations after convergence are reported in (Table 2 and 3). The posterior estimates of the parameters for measurement and structural models and their 95% posterior credible intervals (CI) are presented in (Table 2 and 3). PPPV for the model fit assessment was 0.058. The PPPV was reasonably close to the nominal 5% level. ESPR values are less than 1.2 after 55,950 iterations. Trace plots were also examined to verify convergence of the sampler. The trace plots are shown in (Figure 2) and it gives convergence plots which show a tight horizontal band for the parameter presented. The tight band indicates the parameters likely converged properly.

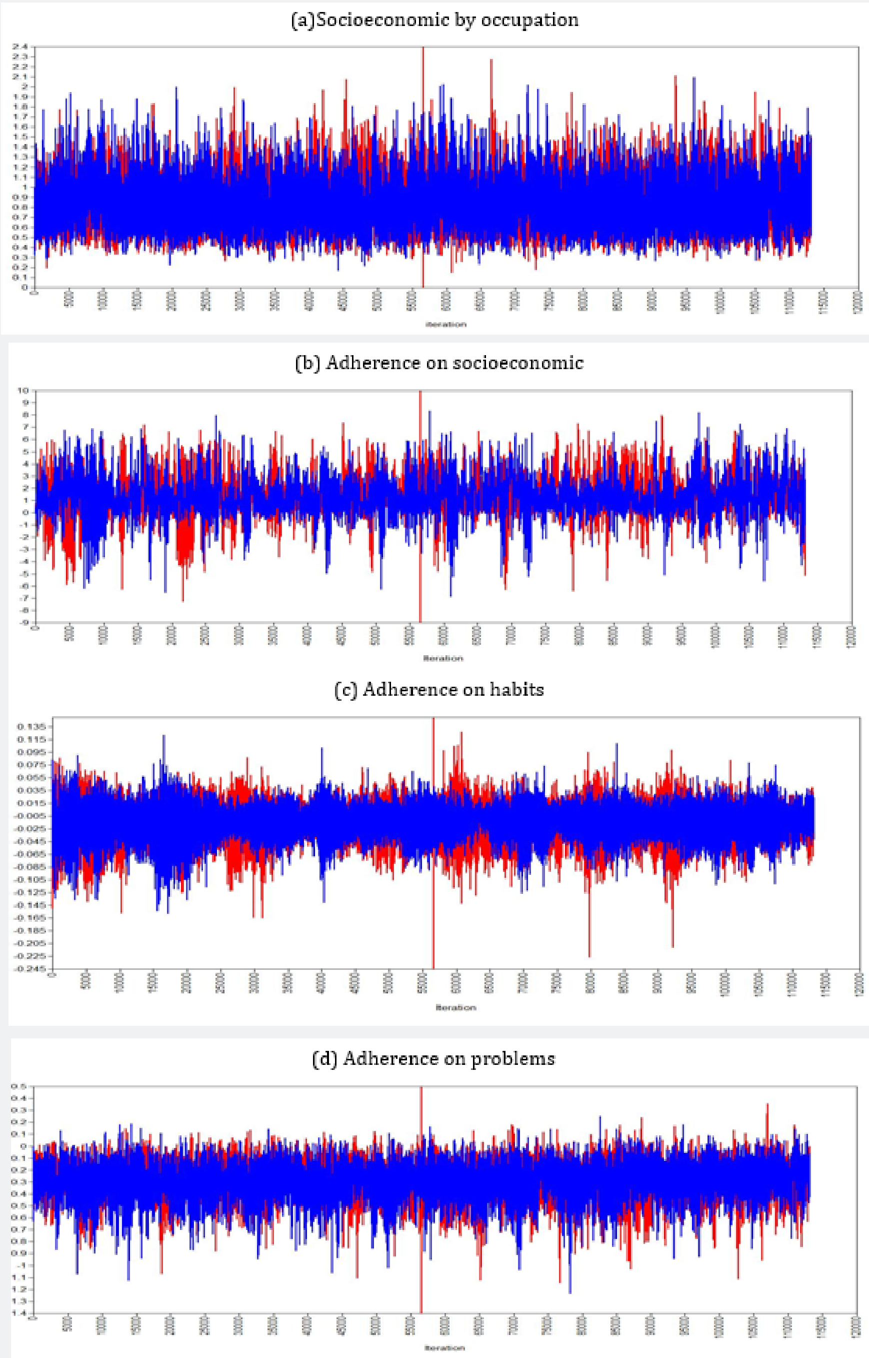

Figure 2: Bayesian posterior parameter trace plots for different iterations.

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Table 2: Bayesian estimates of measurement model for adherence to anti-TB treatment.

Factors	Unstandardized			Standardized			p-value
	Estimate	Posterior SD	95% CI	Estimate	Posterior SD	95% CI	
Socio-economic By							
Education	1			0.39	0.059	(0.280, 0.516)	<0.001
Occupation	0.845	0.207	(0.510, 0.324)	0.336	0.062	(0.222, 0.466)	<0.001
Habits By							
Smoking	1			0.968	0.019	(0.914, 0.988)	<0.001
Alcoholism	0.455	0.207	(0.243, 0.987)	0.869	0.029	(0.812, 0.925)	<0.001
Substance abuse	-0.019	0.029	(-0.083, 0.033)	-0.076	0.099	(-0.267, 0.118)	0.225
DOT By							
DP living area	1			0.995	0.022	(0.945, 0.998)	<0.001
DOT centre	0.019	0.028	(0.006, 0.071)	0.188	0.064	(0.062, 0.313)	<0.005
Problems By							
Difficulties in accessing health facility	1			0.619	0.064	(0.477, 0.729)	<0.001
Loosing wages	2.776	0.8	(1.635, 4.730)	0.909	0.038	(0.814, 0.962)	<0.001
DOT interfering daily activities	3.756	0.955	(2.147, 5.859)	0.946	0.029	(0.864, 0.975)	<0.001
Problems in taking drugs	0.439	0.144	(0.204, 0.775)	0.327	0.078	(0.165, 0.472)	<0.001
Socio-economic on							
Age	-0.463	0.09	(-0.646, -0.296)	-0.544	0.09	(-0.724, -0.373)	<0.001
Weight	0.53	0.091	(0.352, 0.707)	0.616	0.092	(0.437, 0.785)	<0.001
Habits on							
Age	2.315	0.642	(1.255, 3.722)	0.297	0.041	(0.213, 0.376)	<0.001
Weight	0.689	0.368	(-0.011, 1.454)	0.092	0.046	(-0.001, 0.179)	<0.05
DOT on							
Age	0.033	0.901	(-1.535, 2.078)	0.002	0.046	(-0.093, 0.088)	0.484
Weight	1.405	1.131	(-0.284, 3.999)	0.073	0.047	(-0.022, 0.160)	0.064
Problems on							
Age	-0.078	0.093	(-0.265, 0.104)	-0.05	0.058	(-0.162, 0.066)	0.199
Weight	-0.219	0.103	(-0.443, 0.037)	-0.14	0.058	(-0.251, -0.025)	<0.01

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Table 3: Bayesian estimates of structural model for adherence to anti-TB treatment.

Factors	Unstandardized		Standardized		p-value
	Estimate, Posterior SD	95% CI	Estimate, Posterior SD	95% CI	
Adherence on					
Socio-economic	1.341, 1.431	(-1.244, 4.631)	0.519, 0.433	(-0.423, 1.324)	0.1
Habits	-0.015, 0.021	(-0.061, 0.023)	-0.053, 0.063	(-0.177, 0.072)	0.202
DOT	0.023, 0.023	(0.007, 0.085)	0.199, 0.066	(0.068, 0.323)	<0.005
Problems	-0.290, 0.134	(-0.590, -0.063)	-0.202, 0.079	(-0.353, -0.044)	<0.01
Adherence on					
Age	0.555, 0.679	(-0.625, 2.150)	0.245, 0.265	(-0.290, 0.797)	0.131
Weight	-0.567, 0.739	(-2.267, 0.767)	-0.248, 0.291	(-0.835, 0.351)	0.149

Bayesian Structural Model

The standardized estimate of structural equation for adherence of anti-TB treatment of the patients is

$$\eta = 0.519\xi_1 - 0.0535\ \xi_2 + 0.199\xi_3 - 0.202\xi \quad (1)$$

The latent variables "DOT" and "problems" were significantly associated with adherence variable. The standardized estimate of the latent variable "DOT" on adherence is 0.199; 95% CI: (0.068 - 0.323); p<0.005 and the estimate of the latent variable "problem" on adherence is -0.202; 95% CI: (-0.353 - -0.044); p<0.01. The latent variable "DOT" had a positive effect while the latent variable "problems" had negative effect on adherence to anti-TB treatment. From the above structural equation, it was understood that TB patients with lesser problems were more likely to adhere to the anti-TB treatment. Hence reducing the patient's specific problems might encourage treatment regularity under guided supervision (Table 3).

Bayesian Measurement Model

Among the factor loadings of variables, excluding substance abuse were significantly associated with their respective latent variables. The estimate of factor loading for education and occupation on the latent variable "socio-economic" (socio-economic status) were 0.390; 95% CI: (0.280-0.516); p<0.001 and 0.336; 95% CI: (0.222-0.466); p<0.001 respectively. It was found to be statistically significant in measuring the latent variable "socioeconomic". The estimate of smoking and drinking on the latent variable "habits" were as 0.968; 95% CI: (0.914-0.988); p<0.001 and 0.869; 95% CI: (0.812-0.925); p<0.001 respectively. It was found to be significant with the latent variable habit. The factor loading of DOT provider living in the patients' area and DOT center were statistically significant in measuring the latent variable DOT.

The estimate of DOT provider living in the patients' area and DOT center on the latent variable "DOT" were 0.995; 95% CI: (0.945-0.998); p<0.001 and 0.188; 95% CI: (0.062-0.313); p<0.005. The estimate of difficulties in accessing health facility, loosing wages, DOT interfering daily activities, and problems in taking drugs on the latent variable "problems" were 0.619; 95% CI: (0.477-0.729); p<0.001, 0.909; 95% CI: (0.814-0.962); p<0.001, 0.946; 95% CI: (0.864-0.975); p<0.001 and 0.327; 95% CI: (0.165-0.472); p<0.001 respectively and found to be significantly influencing the latent variable problems (Table 2). The variables age and weight were significantly associated with the latent variables socio-economic and habits.

Discussion

The study is the first of its kind to apply latent variable modeling using Bayesian approach to explore for adherence of TB patients to anti-TB treatment. The finding of this study supports our theoretical model as conceptual framework for the prediction of medication adherence. The main finding of our study is that the latent variables "DOT" and "problems" were significantly influencing the adherence of anti-TB treatment. The structural and measurement equations obtained from this study were valuable statistical models to identify the latent variables influencing adherence of TB patients to anti-TB treatment. Though, the percent-

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age of adherence was 66% in this study, TB patients with problems failed to adhere the anti-TB treatment. Hence reducing the patient's specific problems might encourage treatment regularity under guided supervision.

Our findings corroborate with the previous studies done in India and parts of the world using SEM model for latent TB treatment reported that nurse case managed program, older age, less heroin and cocaine use, and TB knowledge were significantly associated with treatment adherence [11]. Another study for TB treatment reported that the latent constructs of stigmatization are associated with treatment adherence [10]. The current study results were corroborated with the findings from similar other studies using traditional statistical methods [17-20]. A study from China, 2009 found that Heavy financial burdens, lack of social support, adverse drug reactions and personal factors were related with non-adherence to anti-TB treatment [17]. According to an Indonesian study, the TB patients' reasons for non-adherence to treatment were lack of money to pay for consultation fees and transportation charges, feeling better during treatment, and not gratified with the behavior of the health care staff [18].

Ershova et al. reported that the patients who did not complete treatment successfully and pervious history of defaulting from TB treatment were associated with poor treatment outcome [19]. Utilization of community health workers improved TB treatment adherence in both urban and rural areas whereas it was best in urban compared to rural area [20]. The two limitations of this study: First, the prior used for analyses was non-informative that is default in Mplus software which may impact our results. Secondly the percentage of missed drug was not able to assess from this data.

Conclusion

The Novel approach of the study was that from our knowledge we used first time BSEM to identify the latent constructs which influence the TB treatment adherence. BSEM is a powerful statistical computing tool for more accurate analysis of more complex data. The latent variable "DOT" had a positive effect while "problems" had a negative effect on adherence to anti-TB treatment. There is a need to take action on reducing the patient's specific problems. This might encourage treatment regularity under direct supervision. This will provide strong scientific evidence to the policy makers to take appropriate action.

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