Appendix

Table S1 Meta-analyses Of Observational Studies in Epidemiology (MOOSE) checklist

Item No.	Recommendation	Reported on Manuscript Page No.
Reporting of background should include		
1	Problem definition	1, 2
2	Hypothesis statement	Not applicable
3	Description of study outcome(s)	3, 4
4	Type of exposure or intervention used	Not applicable
5	Type of study designs used	4
6	Study population	1, 4
Reporting of search strategy should include		
7	Qualifications of searchers (eg, librarians and investigators)	5
8	Search strategy, including time period included in the synthesis and key words	3
9	Effort to include all available studies, including contact with authors	4
10	Databases and registries searched	3
11	Search software used, name and version, including special features used (eg, explosion)	Not applicable
12	Use of hand searching (eg, reference lists of obtained articles)	4
13	List of citations located and those excluded, including justification	Figure 1
14	Method of addressing articles published in languages other than English	4
15	Method of handling abstracts and unpublished studies	Not applicable
16	Description of any contact with authors	4
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	4
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	4, 5
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	Not applicable

Appendix: Impact of latent tuberculosis infection on health and well-being: a systematic review and meta-analysis

20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	Not applicable
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	Not applicable
22	Assessment of heterogeneity	5
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	5
24	Provision of appropriate tables and graphics	7, 8, figure 2-4 and appendix figure S1-S20

Reporting of results should include

25	Graphic summarizing individual study estimates and overall estimate	Figure 2-4
26	Table giving descriptive information for each study included	7, 8, Table 1
27	Results of sensitivity testing (eg, subgroup analysis)	Not applicable
28	Indication of statistical uncertainty of findings	5, 10-12

Reporting of discussion should include

29	Quantitative assessment of bias (eg, publication bias)	17
30	Justification for exclusion (eg, exclusion of non-English language citations)	Not reported
31	Assessment of quality of included studies	9

Reporting of conclusions should include

32	Consideration of alternative explanations for observed results	16
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	Not applicable
34	Guidelines for future research	13, 15, 16
35	Disclosure of funding source	18

Appendix: Impact of latent tuberculosis infection on health and well-being: a systematic review and meta-analysis

Table S2 Databases and search terms used

Database	Search terms
Pubmed	("latent tuberculosis" infection OR LTBI OR tuberculosis prevent* OR inactive tuber*) AND ("quality of life" OR "health related quality of life" OR well-being OR health status OR disability OR "health outcome" OR "patient reported outcome" OR "quality adjusted life year" OR "disability adjusted life year" OR anxiety OR stress OR depression OR mobility OR self-care OR usual activities OR pain OR discomfort OR physical health OR physical well-being OR physical HRQoL or physical functioning OR bodily pain OR general health OR vitality OR social functioning OR social health OR social well-being OR social HRQoL OR social relationship OR role emotion OR role physical OR "mental health" OR mental well-being OR mental HRQoL OR stigma OR psychosoc* OR psychological health OR fatigue OR emotional stress OR environmental health OR education OR employment OR income OR illness perception OR treatment perception OR morbidity OR mortality)
ProQuest	(latent tuberculosis infection OR LTBI OR tuberculosis prevent* OR inactive tuber*) AND ("quality of life" OR "health related quality of life" OR well-being OR health status OR disability OR "health outcome" OR "patient reported outcome" OR "quality adjusted life year" OR "disability adjusted life year" OR anxiety OR stress OR depression OR mobility OR self-care OR usual activities OR pain OR discomfort OR physical health OR physical well-being OR physical HRQoL or physical functioning OR bodily pain OR general health OR vitality OR social functioning OR social health OR social well-being OR social HRQoL OR social relationship OR role emotion OR role physical OR "mental health" OR mental well-being OR mental HRQoL OR stigma OR psychosoc* OR psychological health OR fatigue OR emotional stress OR environmental health OR education OR employment OR income OR illness perception OR treatment perception OR morbidity OR mortality)
EMBASE	('latent tuberculosis'/exp OR 'inactive tuberculosis') AND ('quality of life'/exp OR 'hrql' OR 'health related quality of life' OR 'life quality' OR 'quality of life' OR 'health related qualiy of life' OR 'wellbeing'/exp OR 'well being' OR 'wellbeing' OR 'wellness' OR 'health status'/exp OR 'clinical state' OR 'health state' OR 'health status' OR 'health outcome' OR 'patient-reported outcome'/exp OR 'patient reported outcome measures' OR 'patient-reported outcome' OR 'patient-reported treatment outcome' OR 'patientreported outcome' OR 'self-reported outcome' OR 'self-reported patient outcome' OR 'self-reported treatment outcome' OR 'selfreported outcome' OR 'anxiety'/exp OR 'anxiety' OR 'depression'/exp OR 'central depression' OR 'clinical depression' OR 'depression' OR 'depressive disease' OR 'depressive disorder' OR 'depressive episode' OR 'depressive illness' OR 'depressive personality disorder' OR 'depressive state' OR 'depressive symptom' OR 'depressive syndrome' OR 'mental depression' OR 'parental depression' OR mobility OR 'self care'/exp OR 'usual activities' OR 'pain'/exp OR 'acute pain' OR 'deep pain' OR 'lightning pain' OR 'nocturnal pain' OR 'pain' OR 'pain response' OR 'pain syndrome' OR 'treatment related pain' OR 'discomfort'/exp OR 'physical health score'/exp OR 'physical well-being'/exp OR 'physical well-being' OR 'physical wellbeing' OR 'physical hrqol' OR 'physical functioning'/exp OR 'bodily pain'/exp OR 'general health'/exp OR 'vitality'/exp OR 'social functioning scale'/exp OR 'social health'/exp OR 'social well being'/exp OR 'social hrqol' OR 'social interaction'/exp OR 'social functioning' OR 'social interaction' OR 'social relation' OR 'social relationship' OR 'role emotion' OR 'role physical' OR 'mental health'/exp OR 'condition, mental' OR 'health, mental' OR 'mental care' OR 'mental condition' OR 'mental factor' OR 'mental health' OR 'mental help' OR 'mental service' OR 'mental state' OR 'mental status' OR 'mental status schedule' OR 'psychic health' OR

'psychological well-being'/exp OR 'mental well-being' OR 'mental wellbeing' OR 'psychological well being' OR 'psychological well-being' OR 'psychological wellbeing' OR 'mental hrqol' OR 'psychological health'/exp OR 'stigma'/exp OR 'stigma' OR 'fatigue'/exp OR 'fatigue' OR 'tiredness' OR 'stress'/exp OR 'alarm reaction' OR 'stress' OR 'stress capacity' OR 'stress reaction' OR 'stress resistance' OR 'stress response' OR 'stress situation' OR 'stress tolerance' OR 'emotional stress'/exp OR 'emotional distress' OR 'emotional exhaustion' OR 'emotional pressure' OR 'emotional shock' OR 'emotional stress' OR 'emotional tension' OR 'stress, emotional' OR 'mental stress'/exp OR 'mental stress' OR 'mental stresses' OR 'mental tension' OR 'nervous stress' OR 'psychic stress' OR 'psychic tension' OR 'psycho-social stress' OR 'psycho-social stresses' OR 'psychologic stress' OR 'psychological stress' OR 'psychosocial stress' OR 'psychosocial stresses' OR 'stress, mental' OR 'stress, psychologic' OR 'stress, psychological' OR 'tension, mental' OR 'tension, psychic' OR 'environmental health'/exp OR 'environmental health' OR 'health, environmental' OR 'disability'/exp OR 'assessment, disability' OR 'chronic disability' OR 'disability' OR 'disability assessment' OR 'disability evaluation' OR 'disablement' OR 'disablement evaluation' OR 'evaluation, disability' OR 'handicap' OR 'quality adjusted life year'/exp OR 'qaly' OR 'quality adjusted life year' OR 'quality adjusted life years' OR 'quality-adjusted life years' OR 'disability-adjusted life year'/exp OR 'daly' OR 'dalys' OR 'disability-adjusted life year' OR 'disability-adjusted life years' OR 'morbidity'/exp OR 'disease frequency' OR 'disease incidence' OR 'disorder incidence' OR 'morbidity' OR 'morbidity pattern' OR 'morbidity rate' OR 'morbidity risk' OR 'rate, morbidity' OR 'mortality'/exp OR 'excess mortality' OR 'mortality' OR 'mortality model' OR 'education'/exp OR 'baccalaureate education' OR 'child education' OR 'college admission test' OR 'education' OR 'education service' OR 'education, distance' OR 'education, nonprofessional' OR 'education, pharmacy' OR 'education, pharmacy, continuing' OR 'education, pharmacy, graduate' OR 'education, special' OR 'education, veterinary' OR 'educational measurement' OR 'intellectual training' OR 'internship, nonmedical' OR 'perceptorship' OR 'pharmacy residencies' OR 'preceptorship' OR 'school admission criteria' OR 'self-evaluation programmes' OR 'self-evaluation programs' OR 'training support' OR 'employment'/exp OR 'employment' OR 'employment growth' OR 'income'/exp OR 'income' OR 'illness perception'/exp OR 'treatment perception')

PscyInfo   (latent tuberculosis infection OR LTBI OR tuberculosis prevent* OR inactive tuber*) AND ("quality of life" OR "health related quality of life" OR well-being OR health status OR disability OR "health outcome" OR "patient reported outcome" OR "quality adjusted life year" OR "disability adjusted life year" OR anxiety OR stress OR depression OR mobility OR self-care OR usual activities OR pain OR discomfort OR physical health OR physical well-being OR physical HRQoL or physical functioning OR bodily pain OR general health OR vitality OR social functioning OR social health OR social well-being OR social HRQoL OR social relationship OR role emotion OR role physical OR "mental health" OR mental well-being OR mental HRQoL OR stigma OR psychosoc* OR psychological health OR fatigue OR emotional stress OR environmental health OR education OR employment OR income OR illness perception OR treatment perception OR morbidity OR mortality)

CINAHL Plus   (latent tuberculosis infection OR LTBI OR tuberculosis prevent* OR inactive tuber*) AND ("quality of life" OR "health related quality of life" OR well-being OR health status OR disability OR "health outcome" OR "patient reported outcome" OR "quality adjusted life year" OR "disability adjusted life year" OR anxiety OR stress OR depression OR mobility OR self-care OR usual activities OR pain OR discomfort OR physical health OR physical well-being OR physical HRQoL or physical functioning OR bodily pain OR general health OR vitality OR social functioning OR social health OR social well-being OR social HRQoL OR social

relationship OR role emotion OR role physical OR "mental health" OR mental well-being OR mental HRQoL OR stigma OR psychosoc* OR psychological health OR fatigue OR emotional stress OR environmental health OR education OR employment OR income OR illness perception OR treatment perception OR morbidity OR mortality)

Cochrane Central Register of Controlled Trials (CENTRAL)	(latent tuberculosis infection OR LTBI OR tuberculosis prevent* OR inactive tuber*) AND ("quality of life" OR "health related quality of life" OR well-being OR health status OR disability OR "health outcome" OR "patient reported outcome" OR "quality adjusted life year" OR "disability adjusted life year" OR anxiety OR stress OR depression OR mobility OR self-care OR usual activities OR pain OR discomfort OR physical health OR physical well-being OR physical HRQoL or physical functioning OR bodily pain OR general health OR vitality OR social functioning OR social health OR social well-being OR social HRQoL OR social relationship OR role emotion OR role physical OR "mental health" OR mental well-being OR mental HRQoL OR stigma OR psychosoc* OR psychological health OR fatigue OR emotional stress OR environmental health OR education OR employment OR income OR illness perception OR treatment perception OR morbidity OR mortality)
CHEST Journal	(latent tuberculosis) AND (quality of life OR health outcome OR well-being OR mental OR physical OR social OR perception OR stigma OR environment)
European Respiratory Journal (ERJ)	("latent tuberculosis") AND (quality of life OR health related quality of life OR well-being OR health status OR health outcome OR patient reported outcome)
International Journal of Tuberculosis and Lung Disease (IJTLD)	(latent tuberculosis) AND (quality of life OR health outcome OR well-being OR mental OR physical OR social OR perception OR stigma OR environment)

Table S3 Summary of health outcomes measures reported by studies

Instruments/ Indicators	Studies	Follow-up intervals	Scores[#]		Without TB infection	Outcomes
			LTBI	TB		
BDI	Marra et al., 2008 [1]	N/A	*Differences in scores between individuals with LTBI and patients with active TB disease:* Baseline- Mean difference: 3.98 (95% CI 224 to 5.71) 3 month- Mean difference: 2.60 (95% CI 1.04 to 4.16) 6 month- Mean difference: 1.22 (95% CI -0.54 to 2.98)		N/A	In individuals with LTBI, there was no difference in scores before and after treatment. In patients with active TB disease, the scores improved significantly after treatment.
	Unalan et al., 2008 [2]	N/A	17.4±12.3	17.5±11.5	9.1±5.4	Individuals with LTBI had comparable scores with patients having active TB disease, indicating similar risk of depression despite the asymptomatic manifestation of LTBI.

EMIC for TB in Haitian Populations	Coreil et al., 2010 [3]	N/A	25.1	N/A	N/A	Majority of individuals with LTBI were unwilling to disclose the medical condition to friends and family as an indication of stigma.
EQ-5D	Shedrawy et al., 2019* [4]	N/A	Median: 1 (IQR 0.79 to 1)	N/A	Median: 0.93 (IQR: 0.88 to 1)	Individuals with LTBI experienced stigma and fear of TB reactivation. HRQoL of individuals with LTBI was worse after treatment, hence the need to address psychosocial intervention.
	Dion et al., 2004 [5]	Baseline (Week 1)	Median: 84.8 (IQR 79.6 to 100)	Median: 79.6 (IQR 68.9 to 100)	N/A	Individuals with LTBI had better HRQoL at baseline than patients with active TB disease.
		Week 3	Median: 100 (IQR 79.6 to 100)	Median: 100 (IQR 72.5 to 100)	N/A	Patients with active TB disease had their HRQoL improved over time, comparable to individuals with LTBI, but results were not statistically significant.
HUI2	Guo et al., 2008* [6]	N/A	Mean: 0.93 (95% CI 0.90 to 0.95)	Mean: 0.85 (95% CI 0.80 to 0.89)	N/A	Individuals with LTBI had better health utilities than patients with active TB disease.

HUI3	Guo et al., 2008* [6]	N/A	Mean: 0.90 (95% CI 0.86 to 0.94)	Mean: 0.76 (95% C: 0.70 to 0.82)	N/A	Individuals with LTBI had better health utilities than patients with active TB disease.
RHS-15	Shedraway et al., 2019 [4]	N/A	N/A	N/A	N/A	38% of individuals with LTBI were screened positive with mental distress.
SF-36	Dion et al., 2004 [5]					
	PCS	Week 1 (Baseline)	Median: 56.0 (IQR 52.4 to 58.8)	Median: 49.8 (IQR 42.1 to 56.9)	N/A	Individuals with LTBI had better HRQoL than patients with active TB disease.
		Week 2	Median: 56.6 (IQR 51.2 to 58.3)	Median: 53.1 (IQR 45.0 to 57.4)	N/A	HRQoL of individuals with LTBI and patients with active TB disease became more comparable at subsequent interviews, with substantial improvement observed in patients with active TB disease
		Week 3	Median: 56.4 (IQR 54.3 to 58.4)	Median: 54.5 (IQR 43.3 to 55.7)	N/A	
	Marra et al., 2008 [1]; Guo et al., 2008 [6]					
	PCS	N/A	Mean: 54.7 (95% CI 53.2 to 56.1)	Mean: 44.8 (95% CI 42.1 to 47.5)	N/A	

MCS		Mean: 50.3 (95% CI 48.5 to 52.0)	Mean: 40.1 (95% CI 37.1 to 43.1)	N/A	Individuals with LTBI had better HRQoL than patients with active TB disease. Older individuals with LTBI had poorer HRQoL than younger individuals with LTBI.
Unalan et al., 2008 [2]					
PCS	N/A	43.6±9.9	41.8±10.1	48.7±6.2	Participants without TB infection had better HRQoL than individuals with LTBI and patients with active TB disease.
MCS	N/A	38.4±11.4	38.4±10.6	42.5±10.0	In individuals with LTBI, PCS scores deceased with co-morbidities (diabetes mellitus, hypertension, chronic obstructive pulmonary disease). In individuals with LTBI, lower PCS scores were observed in more elderly patients. In individuals with LTBI, MCS scores increased with longer duration of sleep.

	Study	Time				Notes
	Bauer et al., 2015 [7]					
	PCS	Baseline	50.3±1.1	49.5±1.3	50.2±0.7	HRQoL of individuals with LTBI
		6-month	50.1±0.7	49.8±0.6	50.1±0.9	was comparable with participants
		12-month	50.3±0.9	49.7±0.7	49.9±0.7	without TB infection but better than
						patients with active TB disease.
	MCS	Baseline	50.6±4.7	47.2±6.5	51.7±4.3	
		6-month	51.5±3.9	51.5±5.8	51.9±4.1	
		12-month	51.3±4.5	54.3±2.9	52.9±4.1	
SF-6D	Bauer et al., 2015* [8]	Baseline	0.81±0.11	0.69±0.14	0.81±0.12	Individuals with LTBI had lower mean health utilities scores than
		6-month	0.80±0.12	0.81±0.14	0.83±0.13	patients with active TB disease
		12-month	0.82±0.12	0.86±0.11	0.84±0.12	over 12 months, but not statistically significant.
						LTBI treatment did not impose substantial impact on the health utilities.
	Guo et al., 2008* [6]	N/A	Mean: 0.82 (95% CI 0.80 to 0.85)	Mean: 0.68 (95% CI 0.65 to 0.72)	N/A	Individuals with LTBI had better health utilities than patients with active TB disease.
SG	Bauer et al., 2015* [8]	Baseline	0.91±0.21	0.64±0.34	0.96±0.09	Individuals with LTBI had lower mean SG utilities scores than
		6-month	0.90±0.17	0.83±0.23	0.95±0.11	

		12-month	0.91±0.16	0.89±0.21	0.97±0.06	patients with active TB disease, but not statistically significant.
	Dion et al., 2002 [9]	Baseline	Median: 97.5 (IQR 97.5 to 100)	Median: 92.5 (IQR 75.0 to 97.5)	N/A	Individuals with LTBI had higher self-rated scores than patients with active TB disease, implying better self-evaluated health status.
SGRQ	Pasipanodya et al., 2007 [10]; Miller et al., 2009 [11]	N/A	10.0±14.4	24.0±23.0	N/A	Individuals with LTBI had lower scores than patients with active TB disease, indicating better lung function in individuals with LTBI. Patients with active TB disease suffered from lung impairment even after treatment completion. Foreign-born participants had higher scores than local-born participants, indicating poorer lung function in foreign-born participants.
VAS	Guo et al., 2008* [6]	N/A	Mean: 0.87 (95% CI 0.84 to 0.90)	Mean: 0.66 (95% CI 0.61 to 0.71)	N/A	Individuals with LTBI had higher scores than patients with active TB disease.

	Dion et al., 2002 [9]	Baseline	Median: 90.0 (IQR 85.0 to 97.0)	Median: 80.0 (IQR 50.0 to 86.0)	N/A	Individuals with LTBI had higher self-rated scores than patients with TB disease, implying better self-evaluated health status.
Lifetime expected QALY	Miller et al., 2009 [11]	N/A	67.43 QALYs	64.68 QALYs	69.11 QALYs	QALY lost from TB (owing to illness, impairment and death) due to impairment after microbiologic cure. Preventive care on LTBI could yield better health quality.
Cox Regression-Adjusted Mortality per 1000 Person-Years	Miller et al., 2015 [12]	N/A	1.23 Person-Years (95% CI 0.72 to 1.74)	8.79 Person-Years (95% CI 4.94 to 12.64)	N/A	Preventive care targeting on LTBI management may be an important approach to reduce the risk and repercussion of TB.
Regression-Adjusted Duration of Survival HR	Miller et al., 2015 [12]	N/A	HR: 5.7 (95% CI 5.2 to 6.3)	HR: 4.1 (95% CI 3.3 to 4.9)	N/A	Preventive care targeting on LTBI management may be an important approach to reduce the risk and repercussion of TB.
Semi-structured interview	Jansson et al., 2020 [13]	N/A	N/A	N/A	N/A	Pregnant women with LTBI experienced panic and worries upon LTBI diagnosis due to

misperception and a lack of knowledge of LTBI. They were reluctant to reveal their status of diagnosis to friends and family due to stigma.

* Study data presented as health utilities value.

Scores are presented in mean±standard deviation, otherwise as stated.

LTBI: latent tuberculosis infection; TB: tuberculosis; N/A: not applicable; IQR: Inter-quartile range; CI: confidence interval; HRQoL: health-related quality of life; VAS: Visual Analogue Scale; HUI2: Health Utilities Index Mark 2; HUI3: Health Utilities Index Mark 3; SG: Standard gamble tasks; SF-36: Short Form (36) Health Survey; PCS: physical component summary; MCS: mental component summary; SF-6D: Short-Form Six-Dimension; EQ-5D: EuroQol-5 dimensions; SGRQ: St George Respiratory Questionnaire; BDI: Beck depression inventory; RHS-15: Refugee health screener-15; EMIC: Explanatory Model Interview Catalogue); HR: hazard ratio; QALY: quality-adjusted life year.

Table S4 Psychometric properties of health-related quality of life instruments and health utilities measures used in tuberculosis

Instrument	Reliability		Validity	
	Internal consistency	**Test-retest reliability**	**Content validity**	**Responsiveness**
BDI [2]	Excellent in individuals with LTBI and patients with active TB disease; good in participants without TB infection.	Not tested	BDI has strong correlation with SF-36 MCS; moderately strong correlation with SF-36 PCS; and moderate to strong correlation with the eight domains of SF-36.	Not tested
EQ-5D [5, 9]	Not tested	Good agreement	EQ-5D has moderately strong correlation with VAS, PCS and SF-36 MCS; poor correlation with SG.	Not tested
HUI2 [1]	Not tested	Not tested	HUI2 has strong correlation with SF-6D, HUI3 and SF-36 PCS; moderate correlation with VAS and SF-36 MCS.	Not tested
HUI3 [1]	Not tested	Not tested	HUI3 has strong correlation with HUI2, SF-36 PCS and SF-6D; moderate correlation with VAS and SF-36 MCS.	Not tested
SF-36 [2, 5, 7]	SF-36 domains: Acceptable to excellent in patients with active TB disease and individuals with LTBI; questionable to good in participants without TB infection [2]. Good to excellent for SF-36 summary components; acceptable to excellent for SF-36	Not tested Excellent agreement for MCS; moderate to good agreement in general [5].	SF-36 PCS has moderately strong correlation with BDI; SF-36 MCS has strong correlation with BDI; and the eight domains of SF-36 have moderate to strong correlation with BDI [2]. SF-36 PCS has moderately strong correlation with EQ-5D and VAS, poor correlation with SG [5]. SF-36 MCS has moderate correlation with EQ-5D and VAS; poor correlation with SG [5].	From the 2-to 4- month visits in HRQoL study, clinically meaningful improvement in mean PCS scores was observed (effect sizes ≥ 0.50). No significant change observed in LTBI cohorts [7].

	domains [5].			
SF-6D [6, 8]	Not tested	Not tested	SF-6D has strong correlation with VAS, HUI2/3, SF-36 PCS and MCS [6].	From the baseline to the 1-month evaluation in health utility study, clinically meaningful improvement in mean SF-6D health utility scores among participants treated for TB disease (effect size = 0.5) was observed, primarily among women (effect size = 0.7). No significant change observed in LTBI cohorts [8].
SG [9]	Not tested	Good to excellent	SG has poor correlation with EQ-5D, SF-36 PCS and MCS.	Not tested
SGRQ [10]	Excellent	Excellent agreement	SGRQ has significant correlation with MOS SF-36. SGRQ also correlates with pulmonary function test.	Not tested
VAS [6, 9]	Not tested	Not tested	VAS has stronger correlation with SF-6D and SF-36 PCS; moderate correlation with HUI2/3 and SF-36 MCS [6].	Not tested
	Not tested	Good to excellent [9]	VAS has moderate correlation with SF-36 PCS and EQ-5D; weak correlation with SF-36 MCS [9].	Not tested

HRQoL: health-related quality of life; VAS: Visual Analogue Scale; HUI2: Health Utilities Index Mark 2; HUI3: Health Utilities Index Mark 3; SG: Standard gamble tasks; SF-36: Short Form (36) Health Survey; PCS: physical component summary; MCS: mental component summary; SF-6D: Short-Form Six-Dimension; EQ-5D: EuroQol-5 dimensions; SGRQ: St George Respiratory Questionnaire; BDI: Beck depression inventory

Table S5 Risk of bias assessment of the observational studies using the Newcastle-Ottawa Scale

	Selection				Comparability	Outcome			Total scores
Question	1	2	3	4	1	1	2	3	9
Bauer et al. [7, 8]	1	1	1	1	2	1	1	0	8
Coreil et al [3]	1	1	1	1	2	1	NA	NA	7
Dion et al. [5, 9]	1	1	1	1	2	0	0	1	7
Guo et al. [1, 6]	1	1	1	1	1	0	1	1	7
Miller et al. [10, 11]	1	1	1	1	1	1	NA	NA	6
Miller et al. [12]	1	1	1	1	0	1	NA	NA	5
Shedrawy et al. [4]	1	0	1	1	1	0	NA	NA	4
Unalan et al. [2]	1	1	1	1	1	0	NA	NA	5

NA: not available

Table S6 Critical Appraisal Skills Programme (CASP) checklist for qualitative study

Qualitative study identified	No.	Study validity	Yes	Can't tell	No
Jansson et al. [13]	1	Was there a clear statement of the aims of the research?	/		
	2	Is a qualitative methodology appropriate?	/		
	3	Was the research design appropriate to address the aims of the research?	/		
	4	Was the recruitment strategy appropriate to the aims of the research?	/		
	5	Was the data collected in a way that addressed the research issue?	/		
	6	Has the relationship between researcher and participants been adequately considered?			/
		Findings			
	7	Have ethical issues been taken into consideration?	/		
	8	Was the data analysis sufficiently rigorous?	/		
	9	Is there a clear statement of findings?	/		
		Value of the study			
	10	How valuable is the research?	/		

Figure S1 to S20

Study or Subgroup	LTBI Mean	LTBI SD	LTBI Total	TB Mean	TB SD	TB Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	50.3	1.1	81	49.5	1.3	33	29.5%	0.80 [0.30, 1.30]
Dion 2004	55.73	5.031	25	49.6	11.96	17	18.0%	6.13 [0.11, 12.15]
Guo 2008	54.7	6.6529	78	44.8	12.4416	84	25.4%	9.90 [6.86, 12.94]
Unalan 2008	43.63	9.89	108	41.79	10.06	196	27.0%	1.84 [-0.50, 4.18]
Total (95% CI)			**292**			**330**	**100.0%**	**4.36 [0.29, 8.42]**

Heterogeneity: Tau² = 14.49; Chi² = 36.56, df = 3 (P < 0.00001); I² = 92%
Test for overall effect: Z = 2.10 (P = 0.04)

Figure S1 Mean difference for SF-36 PCS between individuals treated for LTBI compared to patients treated for active TB disease.

Study or Subgroup	LTBI Mean	LTBI SD	LTBI Total	TB Mean	TB SD	TB Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	50.6	4.7	81	47.2	6.5	33	34.2%	3.40 [0.96, 5.84]
Guo 2008	50.3	7.9835	78	40.1	13.824	84	31.9%	10.20 [6.75, 13.65]
Unalan 2008	38.43	11.42	108	38.35	10.6	196	33.9%	0.08 [-2.54, 2.70]
Total (95% CI)			**267**			**313**	**100.0%**	**4.44 [-0.81, 9.69]**

Heterogeneity: Tau² = 19.40; Chi² = 21.07, df = 2 (P < 0.0001); I² = 91%
Test for overall effect: Z = 1.66 (P = 0.10)
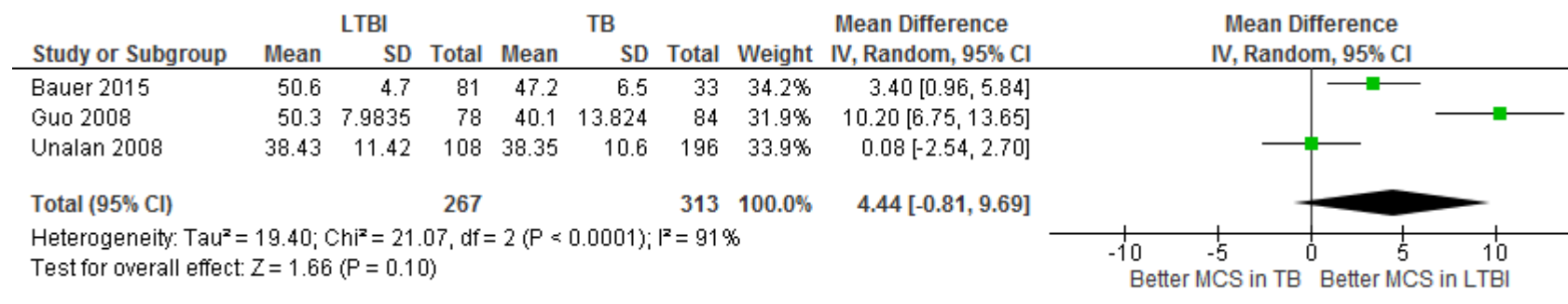
Figure S2 Mean difference for SF-36 MCS between individuals treated for LTBI compared to patients treated for active TB disease.

Study or Subgroup	LTBI Mean	LTBI SD	LTBI Total	TB Mean	TB SD	TB Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	94.8	11.8	103	76.6	23.8	47	23.7%	18.20 [11.02, 25.38]
Guo 2008	54.3	7.0964	78	41.2	14.2848	84	45.9%	13.10 [9.66, 16.54]
Unalan 2008	75.37	23.52	108	66.7	26.52	196	30.4%	8.67 [2.89, 14.45]
Total (95% CI)			289			327	100.0%	12.96 [8.56, 17.37]

Heterogeneity: Tau² = 7.93; Chi² = 4.16, df = 2 (P = 0.12); I² = 52%
Test for overall effect: Z = 5.77 (P < 0.00001)

Mean Difference IV, Random, 95% CI
−20 −10 0 10 20
Better PF in TB   Better PF in LTBI

Figure S3 Mean difference between SF-36 Physical Function (PF) domain for individuals treated for LTBI compared to patients treated for active TB disease.

Study or Subgroup	LTBI Mean	LTBI SD	LTBI Total	TB Mean	TB SD	TB Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	91.8	13.6	103	62.6	33.4	46	29.7%	29.20 [19.20, 39.20]
Guo 2008	51.9	8.8706	78	38.1	15.6672	84	40.0%	13.80 [9.91, 17.69]
Unalan 2008	42.59	41.62	108	33.93	40.07	196	30.3%	8.66 [-0.99, 18.31]
Total (95% CI)			289			326	100.0%	16.81 [6.95, 26.68]

Heterogeneity: Tau² = 59.36; Chi² = 9.77, df = 2 (P = 0.008); I² = 80%
Test for overall effect: Z = 3.34 (P = 0.0008)

Mean Difference IV, Random, 95% CI
−20 −10 0 10 20
Better RP in TB   Better RP in LTBI

Figure S4 Mean difference for SF-36 Role Physical (RP) domain between individuals treated for LTBI compared to patients treated for active TB disease.

Study or Subgroup	LTBI Mean	SD	Total	TB Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	87.8	21.4	86	71.7	29	38	24.7%	16.10 [5.83, 26.37]
Guo 2008	55.7	10.2011	78	50.1	12.9024	84	43.0%	5.60 [2.03, 9.17]
Unalan 2008	57.84	31.42	108	58.74	31.52	196	32.2%	-0.90 [-8.29, 6.49]
Total (95% CI)			272			318	100.0%	6.10 [-1.24, 13.43]

Heterogeneity: Tau² = 29.22; Chi² = 6.97, df = 2 (P = 0.03); I² = 71%
Test for overall effect: Z = 1.63 (P = 0.10)

Figure S5 Mean difference for SF-36 Bodily Pain (BP) domain between individuals treated for LTBI compared to patients treated for active TB disease.

Study or Subgroup	LTBI Mean	SD	Total	TB Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	79.4	16.2	102	69.7	18.9	47	30.4%	9.70 [3.45, 15.95]
Guo 2008	52.5	7.9835	78	44.5	10.1376	84	38.5%	8.00 [5.20, 10.80]
Unalan 2008	47.85	26.21	108	50.45	23.32	196	31.2%	-2.60 [-8.52, 3.32]
Total (95% CI)			288			327	100.0%	5.21 [-1.50, 11.92]

Heterogeneity: Tau² = 28.42; Chi² = 11.17, df = 2 (P = 0.004); I² = 82%
Test for overall effect: Z = 1.52 (P = 0.13)

Figure S6 Mean difference for SF-36 General Health (GH) domain between individuals treated for LTBI compared to patients treated for active TB disease.

Study or Subgroup	LTBI Mean	SD	Total	TB Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	71.6	15	100	59	22.3	45	29.5%	12.60 [5.45, 19.75]
Guo 2008	52.7	8.8706	78	44	13.824	84	38.1%	8.70 [5.15, 12.25]
Unalan 2008	44.07	25.47	108	45.03	25.13	196	32.4%	-0.96 [-6.91, 4.99]
Total (95% CI)			286			325	100.0%	6.71 [-0.35, 13.78]

Heterogeneity: Tau² = 30.83; Chi² = 10.09, df = 2 (P = 0.006); I² = 80%
Test for overall effect: Z = 1.86 (P = 0.06)
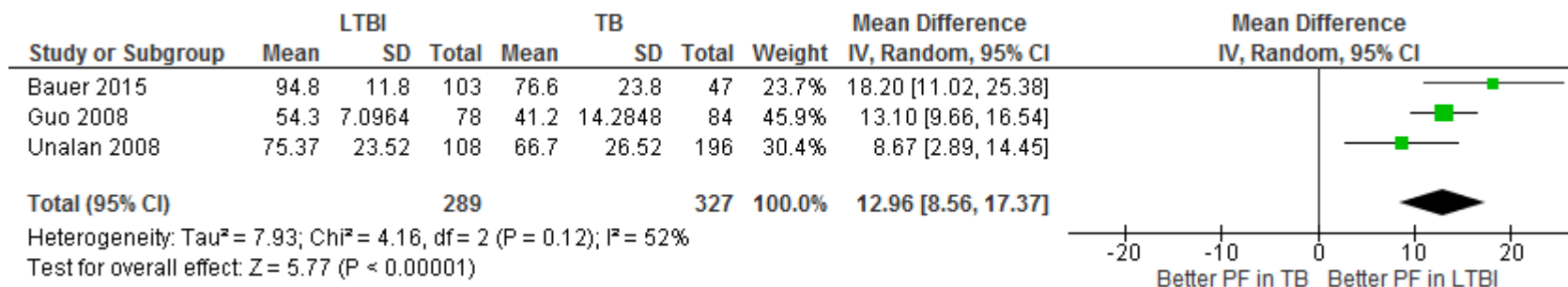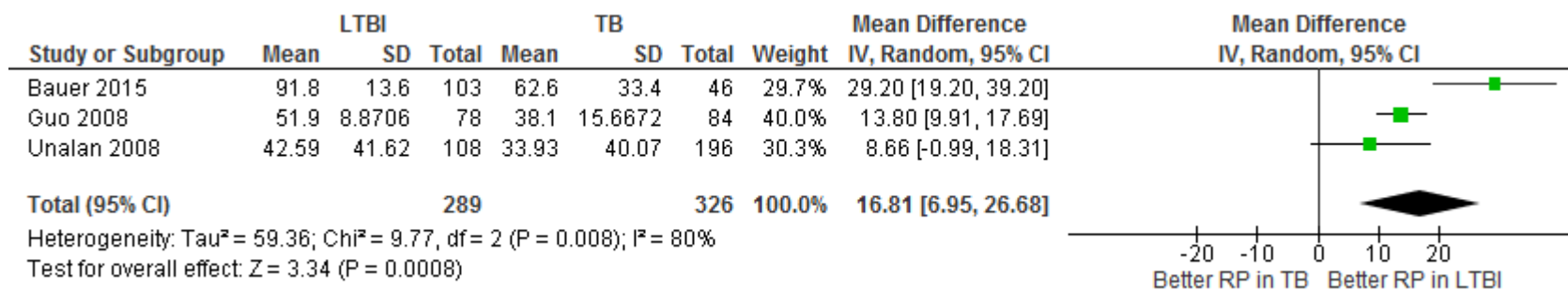
Better VT in TB   Better VT in LTBI

Figure S7 Mean difference for SF-36 Vitality (VT) domain between individuals treated for LTBI compared to patients treated for active TB disease.

Study or Subgroup	LTBI Mean	SD	Total	TB Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	90.1	16.7	102	49.5	38.2	46	29.6%	40.60 [29.10, 52.10]
Guo 2008	52.7	9.3141	78	39.5	14.7456	84	36.2%	13.20 [9.43, 16.97]
Unalan 2008	67.36	29.34	108	60.43	28.68	196	34.1%	6.93 [0.09, 13.77]
Total (95% CI)			288			326	100.0%	19.18 [5.33, 33.03]

Heterogeneity: Tau² = 134.14; Chi² = 24.81, df = 2 (P < 0.00001); I² = 92%
Test for overall effect: Z = 2.71 (P = 0.007)

Better SF in TB   Better SF in LTBI
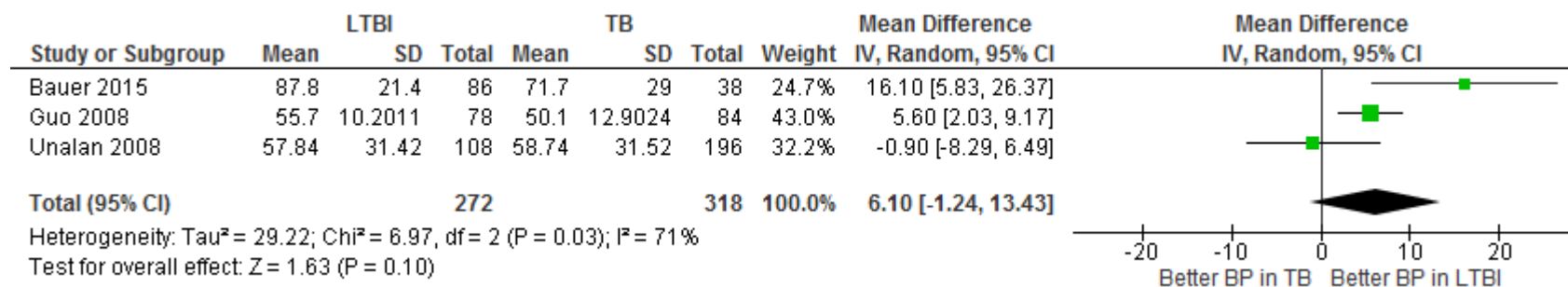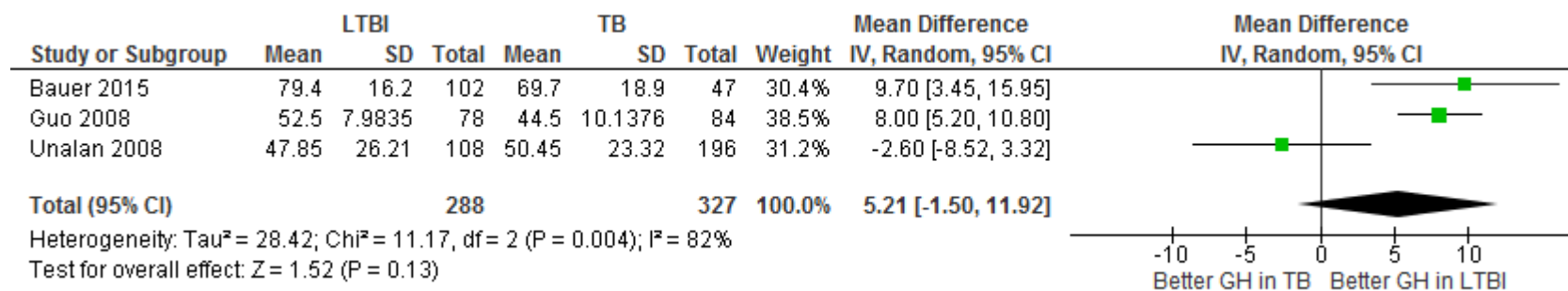
Figure S8 Mean difference for SF-36 Social Function (SF) domain between individuals treated for LTBI compared to patients treated for active TB disease.

Study or Subgroup	LTBI Mean	SD	Total	TB Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	88.4	16.9	104	70.5	31.6	46	29.4%	17.90 [8.21, 27.59]
Guo 2008	50.7	9.3141	78	35	18.8929	84	40.5%	15.70 [11.16, 20.24]
Unalan 2008	42.21	40.06	108	40.65	39.91	196	30.1%	1.56 [-7.84, 10.96]
Total (95% CI)			**290**			**326**	**100.0%**	**12.10 [3.21, 20.99]**

Heterogeneity: Tau² = 45.45; Chi² = 7.88, df = 2 (P = 0.02); I² = 75%
Test for overall effect: Z = 2.67 (P = 0.008)

Mean Difference IV, Random, 95% CI
-50 -25 0 25 50
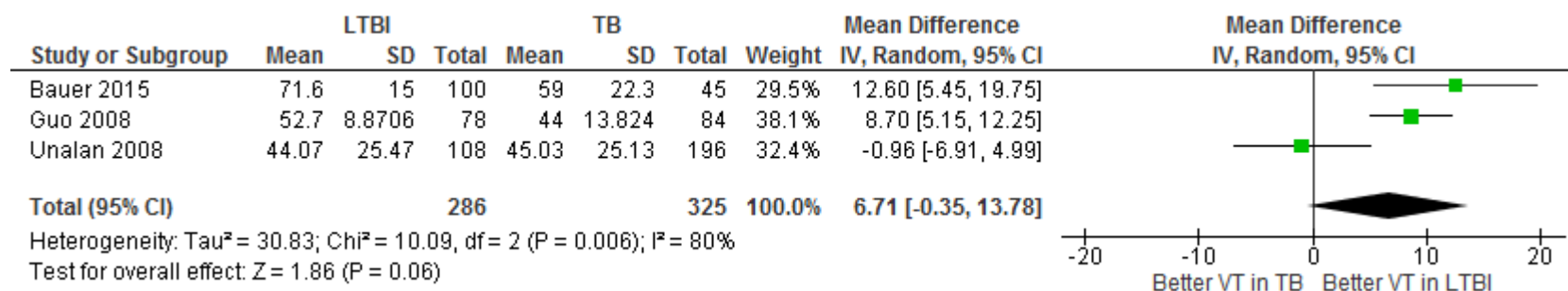Better RE in TB   Better RE in LTBI

Figure S9 Mean difference for SF-36 Role Emotion (RE) domain between individuals treated for LTBI compared to patients treated for active TB disease.

Study or Subgroup	LTBI Mean	SD	Total	TB Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	76.6	16.5	101	68.3	20.6	46	28.7%	8.30 [1.53, 15.07]
Guo 2008	50.9	9.7576	78	44.4	11.9808	84	38.1%	6.50 [3.15, 9.85]
Unalan 2008	53.11	22.33	108	55.65	21.17	196	33.3%	-2.54 [-7.69, 2.61]
Total (95% CI)			**287**			**326**	**100.0%**	**4.01 [-2.32, 10.34]**

Heterogeneity: Tau² = 24.50; Chi² = 9.76, df = 2 (P = 0.008); I² = 79%
Test for overall effect: Z = 1.24 (P = 0.21)

Mean Difference IV, Random, 95% CI
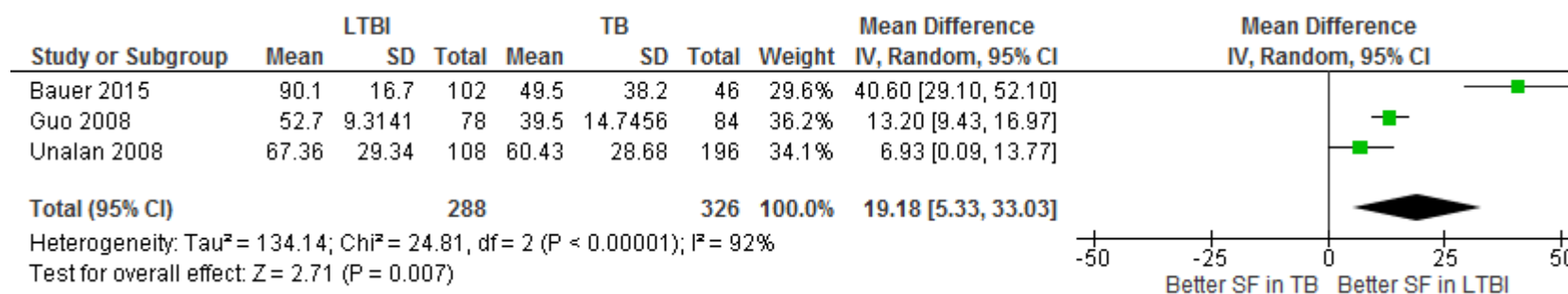-10 -5 0 5 10
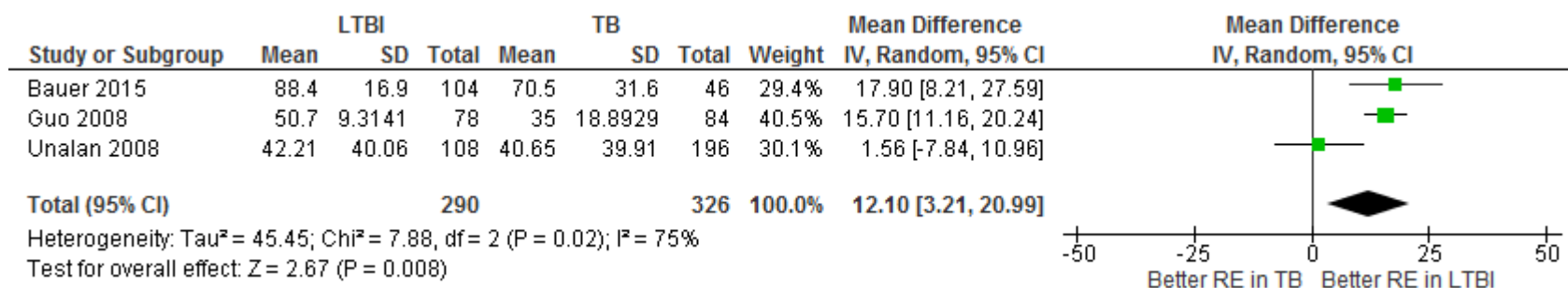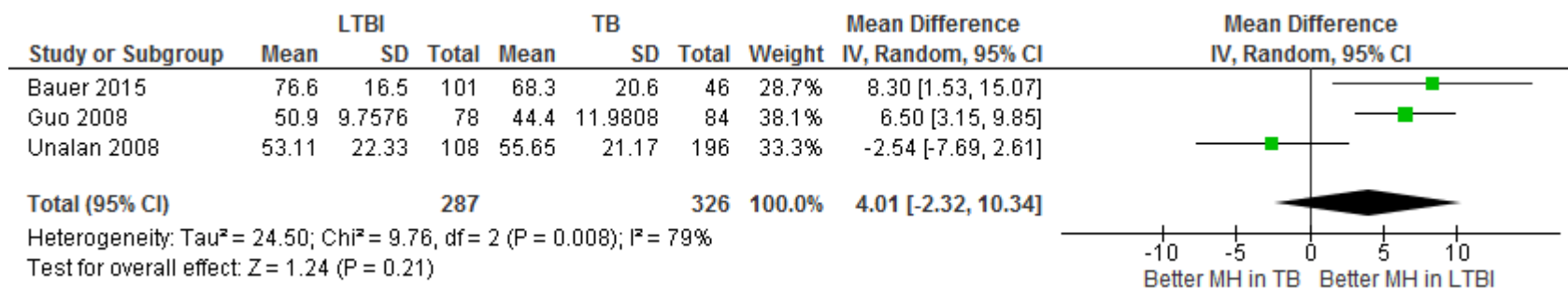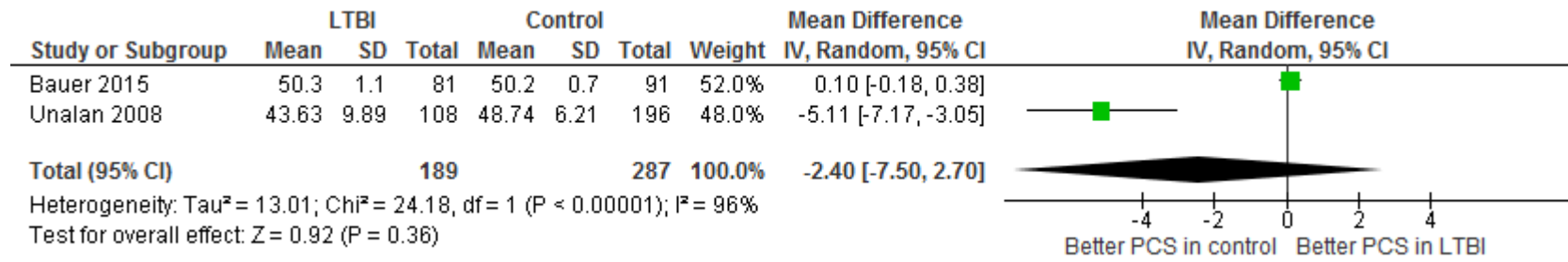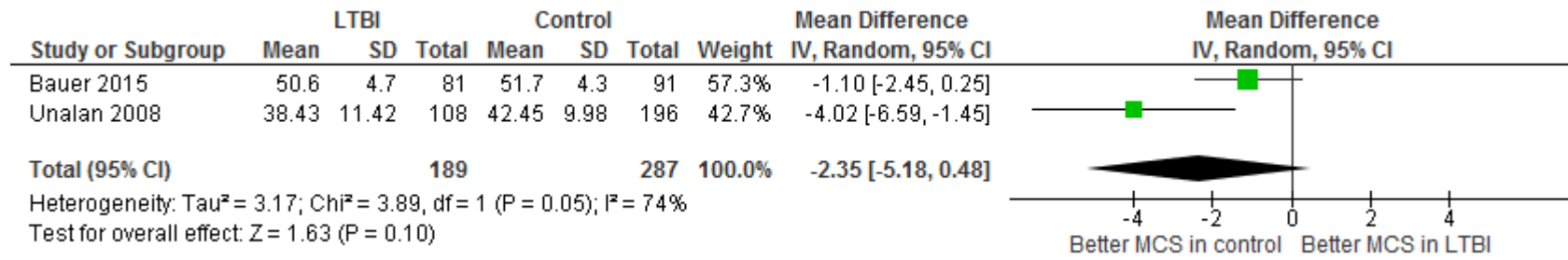Better MH in TB   Better MH in LTBI

Figure S10 Mean difference for SF-36 Mental Health (MH) domain between individuals treated for LTBI compared to patients treated for active TB disease.

Study or Subgroup	LTBI Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	50.3	1.1	81	50.2	0.7	91	52.0%	0.10 [-0.18, 0.38]
Unalan 2008	43.63	9.89	108	48.74	6.21	196	48.0%	-5.11 [-7.17, -3.05]
Total (95% CI)			189			287	100.0%	-2.40 [-7.50, 2.70]

Heterogeneity: Tau² = 13.01; Chi² = 24.18, df = 1 (P < 0.00001); I² = 96%
Test for overall effect: Z = 0.92 (P = 0.36)

Figure S11 Mean difference for SF-36 Physical Component Scores (PCS) between individuals treated for LTBI compared to individuals without TB infection.

Study or Subgroup	LTBI Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	50.6	4.7	81	51.7	4.3	91	57.3%	-1.10 [-2.45, 0.25]
Unalan 2008	38.43	11.42	108	42.45	9.98	196	42.7%	-4.02 [-6.59, -1.45]
Total (95% CI)			189			287	100.0%	-2.35 [-5.18, 0.48]

Heterogeneity: Tau² = 3.17; Chi² = 3.89, df = 1 (P = 0.05); I² = 74%
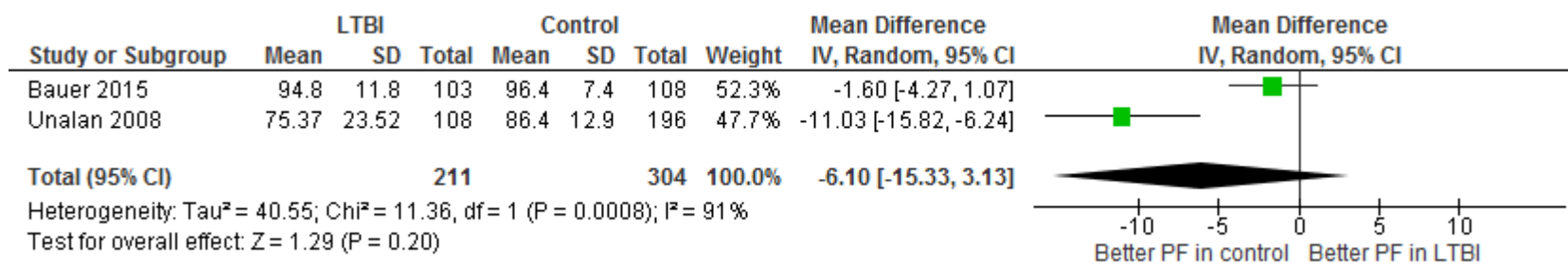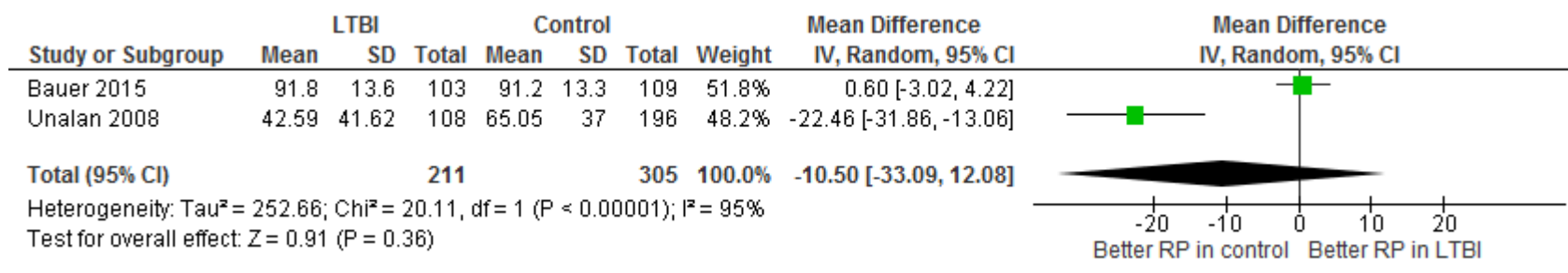Test for overall effect: Z = 1.63 (P = 0.10)

Figure S12 Mean difference for SF-36 Mental Component Scores (MCS) between individuals treated for LTBI compared to individuals without TB infection.

Study or Subgroup	LTBI Mean	LTBI SD	LTBI Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	94.8	11.8	103	96.4	7.4	108	52.3%	-1.60 [-4.27, 1.07]
Unalan 2008	75.37	23.52	108	86.4	12.9	196	47.7%	-11.03 [-15.82, -6.24]
Total (95% CI)			211			304	100.0%	-6.10 [-15.33, 3.13]

Heterogeneity: Tau² = 40.55; Chi² = 11.36, df = 1 (P = 0.0008); I² = 91%
Test for overall effect: Z = 1.29 (P = 0.20)

Mean Difference IV, Random, 95% CI — Better PF in control / Better PF in LTBI
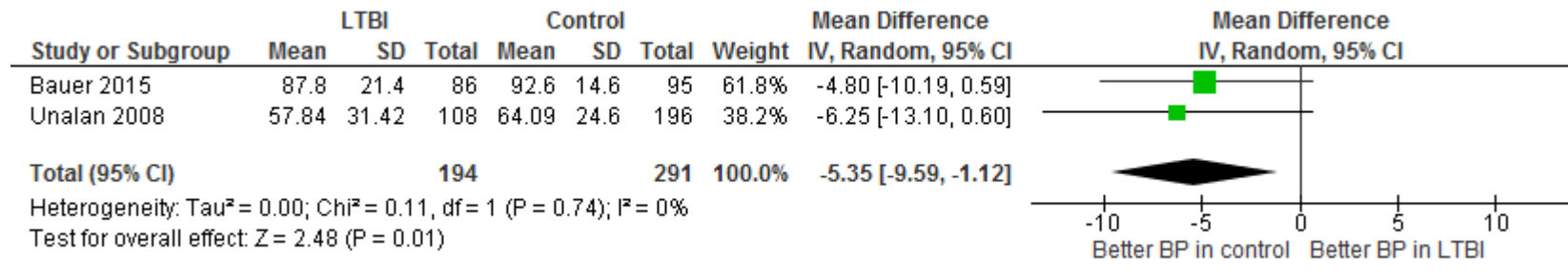
Figure S13 Mean difference for SF-36 Physical Function (PF) domain between individuals treated for LTBI compared to individuals without TB infection.

Study or Subgroup	LTBI Mean	LTBI SD	LTBI Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	91.8	13.6	103	91.2	13.3	109	51.8%	0.60 [-3.02, 4.22]
Unalan 2008	42.59	41.62	108	65.05	37	196	48.2%	-22.46 [-31.86, -13.06]
Total (95% CI)			211			305	100.0%	-10.50 [-33.09, 12.08]

Heterogeneity: Tau² = 252.66; Chi² = 20.11, df = 1 (P < 0.00001); I² = 95%
Test for overall effect: Z = 0.91 (P = 0.36)

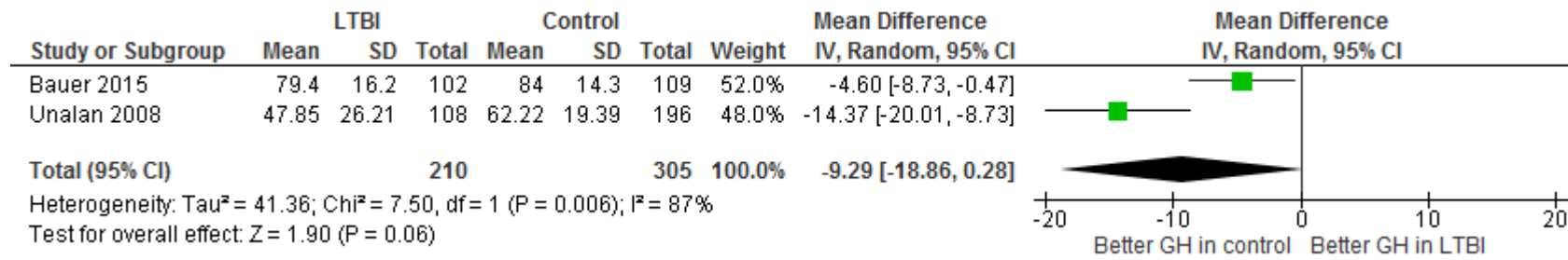Mean Difference IV, Random, 95% CI — Better RP in control / Better RP in LTBI

Figure S14 Mean difference for SF-36 Role Physical (RP) domain between individuals treated for LTBI compared to individuals without TB infection.
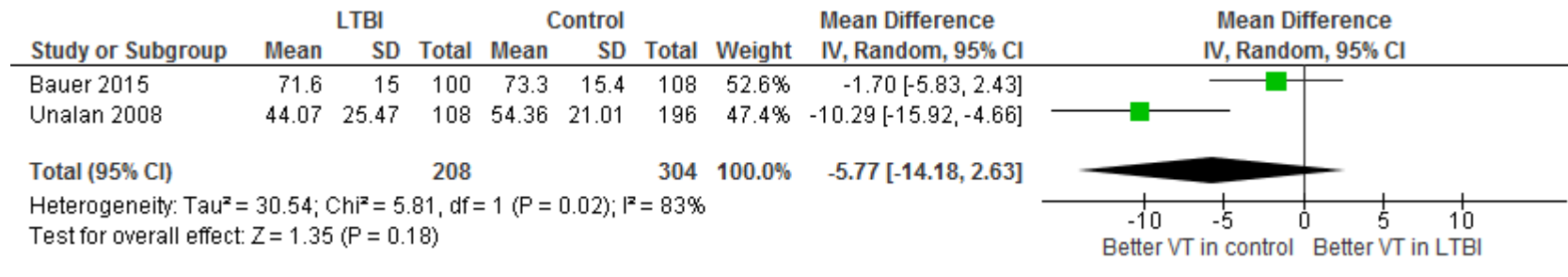
Figure S15 Mean difference for SF-36 Bodily Pain (BP) domain between individuals treated for LTBI compared to individuals without TB infection.
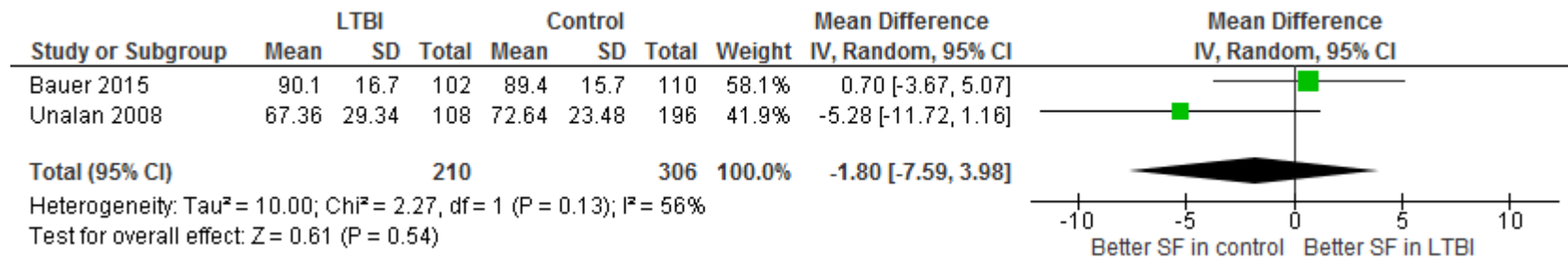

Figure S16 Mean difference for SF-36 General Health (GH) domain between individuals treated for LTBI compared to individuals without TB infection.

Study or Subgroup	LTBI Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	71.6	15	100	73.3	15.4	108	52.6%	-1.70 [-5.83, 2.43]
Unalan 2008	44.07	25.47	108	54.36	21.01	196	47.4%	-10.29 [-15.92, -4.66]
Total (95% CI)			208			304	100.0%	-5.77 [-14.18, 2.63]

Heterogeneity: Tau² = 30.54; Chi² = 5.81, df = 1 (P = 0.02); I² = 83%
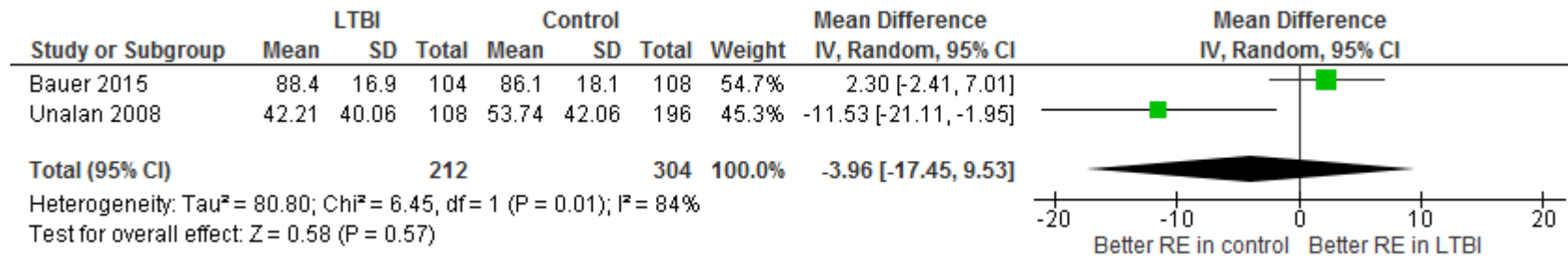Test for overall effect: Z = 1.35 (P = 0.18)

Figure S17 Mean difference for SF-36 Vitality (VT) domain between individuals treated for LTBI compared to individuals without TB infection.

Study or Subgroup	LTBI Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	90.1	16.7	102	89.4	15.7	110	58.1%	0.70 [-3.67, 5.07]
Unalan 2008	67.36	29.34	108	72.64	23.48	196	41.9%	-5.28 [-11.72, 1.16]
Total (95% CI)			210			306	100.0%	-1.80 [-7.59, 3.98]

Heterogeneity: Tau² = 10.00; Chi² = 2.27, df = 1 (P = 0.13); I² = 56%
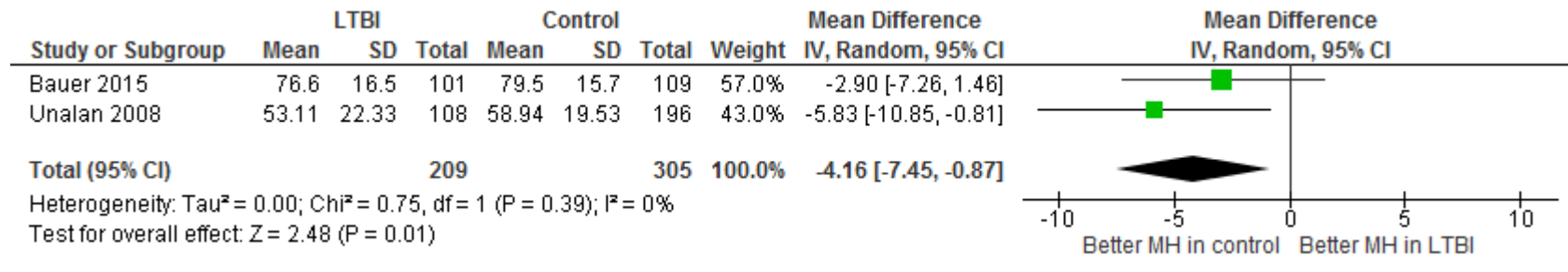Test for overall effect: Z = 0.61 (P = 0.54)

Figure S18 Mean difference for SF-36 Social Function (SF) domain between individuals treated for LTBI compared to individuals without TB infection.

Study or Subgroup	LTBI Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	88.4	16.9	104	86.1	18.1	108	54.7%	2.30 [-2.41, 7.01]
Unalan 2008	42.21	40.06	108	53.74	42.06	196	45.3%	-11.53 [-21.11, -1.95]
Total (95% CI)			212			304	100.0%	-3.96 [-17.45, 9.53]

Heterogeneity: Tau² = 80.80; Chi² = 6.45, df = 1 (P = 0.01); I² = 84%
Test for overall effect: Z = 0.58 (P = 0.57)

Mean Difference IV, Random, 95% CI
Better RE in control   Better RE in LTBI

Figure S19 Mean difference for SF-36 Role Emotion (RE) domain between individuals treated for LTBI compared to individuals without TB infection.

Study or Subgroup	LTBI Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Bauer 2015	76.6	16.5	101	79.5	15.7	109	57.0%	-2.90 [-7.26, 1.46]
Unalan 2008	53.11	22.33	108	58.94	19.53	196	43.0%	-5.83 [-10.85, -0.81]
Total (95% CI)			209			305	100.0%	-4.16 [-7.45, -0.87]

Heterogeneity: Tau² = 0.00; Chi² = 0.75, df = 1 (P = 0.39); I² = 0%
Test for overall effect: Z = 2.48 (P = 0.01)

Mean Difference IV, Random, 95% CI
Better MH in control   Better MH in LTBI

Figure S20 Mean difference for SF-36 Mental Health (MH) domain between individuals treated for LTBI compared to individuals without TB infection.

Appendix: Impact of latent tuberculosis infection on health and well-being: a systematic review and meta-analysis

References

1. Marra CA, Marra F, Colley L, et al. Health-related quality of life trajectories among adults with tuberculosis: differences between latent and active infection. Chest 2008; 133(2): p. 396-403.

2. Unalan D, Soyuer F, Ceyhan O, et al. Is the quality of life different in patients with active and inactive tuberculosis? Int J Infect Dis 2008; 55: p. 127-37.

3. Coreil J, Lauzardo M, Clayton H. Stigma and Therapy Completion for Latent Tuberculosis among Haitian-origin Patients. Fla Public Health Rev 2010; 7: 32–38.

4. Shedrawy J, Jansson L, Röhl I, et al. Quality of life of patients on treatment for latent tuberculosis infection: a mixed-method study in Stockholm, Sweden. Health Qual Life Outcomes 2019; 17(1): p. 158.

5. Dion M, Tousignant P, Bourbeau J, et al. Feasibility and reliability of health-related quality of life measurements among tuberculosis patients. Qual Life Res 2004; 13(3): p. 653-65.

6. Guo N, Marra C, Marra F, et al. Health state utilities in latent and active tuberculosis. Value Health 2008; 11(7): p. 1154-61.

7. Bauer M, Ahmed S, Benedetti A, et al. Health-related quality of life and tuberculosis: a longitudinal cohort study. Health Qual Life Outcomes 2015; 13: p. 65.

8. Bauer M, Ahmed S, Benedetti A, et al. The impact of tuberculosis on health utility: a longitudinal cohort study. Qual Life Res 2015; 24(6): p. 1337-49.

9. Dion M, Tousignant P, Bourbeau J, et al. Measurement of health preferences among patients with tuberculous infection and disease. Special Issue: Public health decision making 2002; 22(Suppl5): p. S102-S114.

10. Pasipanodya JG, Miller TL, Vecino M, et al. Using the St. George respiratory questionnaire to ascertain health quality in persons with treated pulmonary tuberculosis. Chest 2007; 132(5): p. 1591-8.

11. Miller TL, McNabb SJN, Hilsenrath P, et al. Personal and societal health quality lost to tuberculosis. PLoS One 2009; 4(4): p. e5080.

12. Miller TL, Wilson FA, Pang JW, et al. Mortality Hazard and Survival After Tuberculosis Treatment. Am J Public Health 2015; 105(5): p. 930-937.

13. Jansson L, Shedrawy J, Lönnroth K, Bruchfeld J, Kulane A. Latent tuberculosis in pregnant women: a patient perspective. Int J Tuberc Lung Dis 2020; 24(3):310-315.