Supplementary information

Supplementary 1: Key to calculations

Relative risk of tuberculosis calculated as

$$RR = \frac{TB\ incidence\ in\ key\ population}{TB\ incidence\ in\ general\ population}$$

Number to be screened to find one case calculated using the prevalence

$$NNS = \frac{1}{TB\ prevalence\ in\ key\ population}$$

Number of tuberculosis cases reported calculated from the absolute population and the incidence of tuberculosis per 100,000

$$Number\ of\ cases = \frac{TB\ incidence\ in\ key\ population}{100{,}000} * Size\ of\ key\ population$$

Overall contribution to tuberculosis epidemic calculated by the number of tuberculosis cases in each risk group over the cases in the general population

$$Overall\ contribution = \frac{Number\ of\ cases\ reported\ in\ key\ population}{Total\ number\ of\ cases\ reported\ in\ general\ population} * 100$$

Population attributable fraction calculated as a percentage from prevalence and relative risk

$$PAF = \left\{\left(prevalence * \left(\frac{RR-1}{1}\right)\right) + (prevalence * (RR-1))\right\} * 100$$

Supplementary 2: Summary of observational studies quality

		Scores				
Key population	Author and Year	Study duration	Study design	Diagnosis method	Sample size	Total
Prevalence						
Healthcare workers	Kranzer et al. (2010)	1	1	4	1	7
Healthcare workers	Naidoo and Jinabhai (2006)	4	1	4	2	11
Mineworkers	Lewis et al. (2013)	3	1	4	4	12
Inmates	Nyasulu et al. (2015)	2	1	3	2	8
Inmates	Telisinghe et al. (2014)	2	1	4	1	8
Inmates	Zishiri et al. (2015)	1	2	4	3	10
Inmates	Hanifa et al. (2015)	2	1	2	1	6
Informal settlements	Wood et al. (2007)	3	2	4	1	10
Informal settlements	Kranzer et al. (2012)	4	1	4	3	12
Informal settlements	Dawson et al. (2010)	1	1	2	1	5
Tuberculosis Contacts	Shapiro et al. (2012)	1	2	4	2	9
Tuberculosis Contacts	Thind et al. (2012)	3	2	4	2	11
Tuberculosis Contacts	Van Schalkwyk et al (2014)	1	1	4	1	7
Tuberculosis Contacts	Deery et al. (2014)	1	2	4	2	9
Children under-five	Bekker et al. (2012)	3	2	4	1	10
Children under-five	Seddon et al (2013)	2	1	4	1	8
Children under-five	Frigati et al. (2010)	4	3	4	1	12
Pregnant women	Hoffman et al. (2013)	3	1	2	2	8
Pregnant women	Bekker et al. (2016)	2	3	4	3	12
Pregnant women	Peters et al. (2015)	2	1	4	1	8
Pregnant women	Gounder et al. (2011)	2	1	4	2	9
HIV-infected	Naidoo et al. (2014)	4	3	3	1	11
HIV-infected	Goulab et al. (2009)	4	3	4	2	13
HIV-infected	Lawn et al. (2009)	4	3	4	1	12
HIV-infected	Hanifa et al. (2012)	2	1	4	1	7
Incidence						
Healthcare workers	Ayuk et al. (2013)	4	2	4	1	11
Healthcare workers	Tudor et al. (2014)	4	2	4	2	12
Mineworkers	Hermans et al. (2016)	4	3	4	4	15
Mineworkers	Sonnenberg et al. (2005)	4	3	4	4	15
HIV-infected	Naidoo et al. (2014)	4	3	3	1	11
HIV-infected	Goulab et al. (2009)	4	3	4	2	13
HIV-infected	Lawn et al. (2009)	4	3	4	1	12
Children under-five	Hesseling et al.	4	3	4	1	12
Children under-five	Zar et al. (2010)	4	3	4	1	12

Key					
	1	< 6months	Cross-sectional	None mentioned	<1000
	2	6-12months	Evaluation	Symptoms screening	1000-4999
	3	13-24months	Cohort	Microscopy/x-rays	5000-9999
	4	>24months	Trial	Culture/smear	≥10000

Supplementary 3: Summary of experimental studies quality

Section	Item No	Item Checklist	Lebina et al 2016	Churchyard et al 2014	Zar et al 2006
Title and abstract	1a	Identification as a randomised trial in the title	0	1	1
	1b	Structured summary of trial design, methods, results, and conclusions	1	1	1
Introduction					
Background	2a	Scientific background and explanation of rationale	1	1	1
Objectives	2b	Specific objectives or hypotheses	0	1	1
Methods					
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	1	1	1
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	1	0	1
Participants	4a	Eligibility criteria for participants	1	1	1
	4b	Settings and locations where the data were collected	1	1	1
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	1	1	1
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	0	1	1
	6b	Any changes to trial outcomes after the trial commenced, with reasons			1
Sample size	7a	How sample size was determined	0	0	1
	7b	When applicable, explanation of any interim analyses and stopping guidelines	0	0	1
Randomisation					
Sequence generation	8a	Method used to generate the random allocation sequence	1	0	1
	8b	Type of randomisation; details of any restriction (such as blocking and block size)		0	1
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	1	0	1
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	1	0	1
Blinding	11a	If done, who was blinded after assignment to interventions and how	0	0	1
	11b	If relevant, description of the similarity of interventions		0	1
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	1	1	1
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	1	1	1
Results					
Participant flow diagram	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	0	1	1

Section	Item No	Item Checklist	Lebina et al 2016	Churchyard et al 2014	Zar et al 2006
	13b	For each group, losses and exclusions after randomisation, together with reasons	0	1	1
Recruitment	14a	Dates defining the periods of recruitment and follow-up	1	1	1
	14b	Why the trial ended or was stopped	0	0	1
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	1	1	1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	1	1	1
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	1	1	1
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	0	1	1
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	1	1	1
Harms	19	All-important harms or unintended effects in each group	0	0	1
Discussion					
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	0	1	0
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	0	1	1
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	1	1	1
Other information					
Registration	23	Registration number and name of trial registry	0	1	1
Protocol	24	Where the full trial protocol can be accessed, if available	0	1	0
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	0	1	1
Total score			18	25	35

Supplementary 4: Estimated size of key population and data sources

Risk group	Key population	Size of risk group as an absolute number	Risk group as % of the general population	Data Source
People with increased risk of tuberculosis due to occupational or community exposure	Healthcare workers	231,111	0.4%	Evidence to Inform South African Tuberculosis policies (EVISAT) Review 2014 on Health Care workers
	Miners	510,000	0.9%	Chamber of Mines Annual Report 2015 EVISAT Review 2014 on Miners
	Inmates	162,000	0.3%	Annual Report Department of Correctional Services 2015 EVISAT Review 2014 on Inmates
	Informal settlements	3,306,697	6.1%	Housing Development Authority report on the status of informal settlements in South Africa 2013 EVISAT Review 2014 on Informal settlements
	Tuberculosis contacts†	1,621,296	3.0%	2011 Census 2016 WHO tuberculosis report
People with limited access to tuberculosis services	Children under 5 years	5,900,000	10.6%	EVISAT Review 2014 on Children 2015 Mid-year estimates 2011 National Census
	Elderly	3,000,000	5.6%	2015 Mid-year estimates 2011 National Census
	Migrants and refugees	1,458,000	2.7%	United Nations High Commission for Refugees (UNHCR) report 2014
	Women	24,635,900	51.2%	2015 Mid-year estimates 2011 National Census
People at increased risk of tuberculosis due to biological or behavioural factors that compromise immune function	HIV infected	5,510,000	10.2%	EVISAT Review 2014 on HIV infected UNAIDS Global AIDS update 2016
	Diabetics	2,300,000	4.3%	Global Diabetes Score Card 2014
	Pregnant women	1,200,000	2.2%	2015 Mid-year estimates
	Smokers	9,504,000	17.6%	The National Health and Nutrition Examination Survey 2013
	Chronic alcohol users	8,300,000	15.4%	The National Health and Nutrition Examination Survey 2013 The Global Alcohol Report 2014

† Population size of household contacts was determined by the number of TUBERCULOSIS cases reported in 2016 multiplied by the average household size reported in the last census (437 000*3.6≈1.6M)