Webappendix A

Table S1 Comparison of characteristics at screening for the 478 who were not randomised and the 1,369 that were randomised

Characteristic	1,369 Randomised	478Not randomised
Median age (IQR), years	34 (29-40)	34 (29-39)
Female	75.1%	71.4%
On-ART	65.9%	38.2%
Median CD4+ count (IQR), cells/mm^3		
Overall	232 (159-382)	198 (141-286)
	N=1362	N=470
Start-ART	171 (127-213)	177 (125-210)
	N=464	N=289
On-ART	303 (199-440)	302 (205-421)
	N=898	N=181
Previous TB	42.2%	34.5%
	N=1,367	N=475

Table S2 Reasons for stopping isoniazid or placebo during the active intervention phase, by study arm

Outcomes	667 Placebo[1]	662 Isoniazid[2]	1,329 Total
Completed study drug phase	550	550	1,100
Raised ALT ≥ grade 3[3]	10	19	29
Clinical Hepatitis	3	-	3
Peripheral neuropathy ≥ grade 2	1	3	4
Rash ≥grade 2	4	5	8
Tuberculosis	24	10	34
Hospitalization[4]	1	1	2
Death	6	5	11
Participant choice	28	23	51
Default study drug for ≥3months	41	46	87

[1]On ART alone; [2]On ART plus isoniazid; [3]Grade 3 alanine transaminase (ALT) elevation if ≥ 5 times upper limit of normal;

[4]Hospitalisation: cerebrovascular accident, acute psychosis.

Table S3 Effect by time period since randomisation

	Placebo			INH					
	n	**Cases / PY**	**Rate/ 100 PY**	**n**	**Cases / PY**	**Rate/ 100 PY**	****HRu**	**95% CI**	**¥P**
Period since randomisation									
0-11 months (active phase)	667	25/ 634.0	3.9	662	13/636.3	2.0	0.52	0.27 - 1.01	0.05
12-23 months	601	21/ 567.4	3.7	609	13/ 580.2	2.2	0.61	0.30 - 1.21	0.15
≥ 24* months	521	12/ 395.9	3.0	539	11/ 412.8	2.7	0.88	0.39 - 2.0	0.75

*Max time at risk=3.7 years **Hazard ratio unadjusted ¥P=Logrank test p-value for equality of survival functions. The likelihood ratio test p-value for interaction was 0.61 and for trend, P=0.34.

Table S4 Number needed to treat to benefit vs. harm

Endpoint	Non-cases	Cases	Absolute Risk	Absolute Risk Difference (95% CI)	Number needed to treat
All tuberculosis					
Placebo	609	58	0.10		
Isoniazid	625	37	0.06	0.04 0.03-0.06	*25
[§]Stopping drug for adverse events					
Placebo	649	18	0.03		
Isoniazid	635	27	0.04	0.01 0.004 - 0.04	**100

*Number needed to treat to benefit one individual and **Number needed to treat to harm one individual: [1 / Absolute Risk Difference]. [§]Stopping for any of grade 3/4 ALT, clinical hepatitis, new or worsening grade 2 or more rash or peripheral neuropathy

Table S5 Specific causes of death by study arm

Cause	Placebo	Isoniazid	Total
Tuberculosis	**6**	**2**	**8**
Non Tuberculosis	**7**	**6**	**13**
Epileptic seizure	-	1	
Renal failure	-	2	
Road traffic accident	1	1	
Suicide	-	1	
Complications following nosocomial infection	-	1	
Complications following gastric cancer	1	-	
Cerebro vascular accident	1	-	
Complications following emergency caesarean section	1	-	
Gun shot to the head	1	-	
Bacterial meningitis	1	-	
Upper GI bleed	1	-	
Unknown	**8**	**8**	**16**
Total	**21**	**16**	**37**

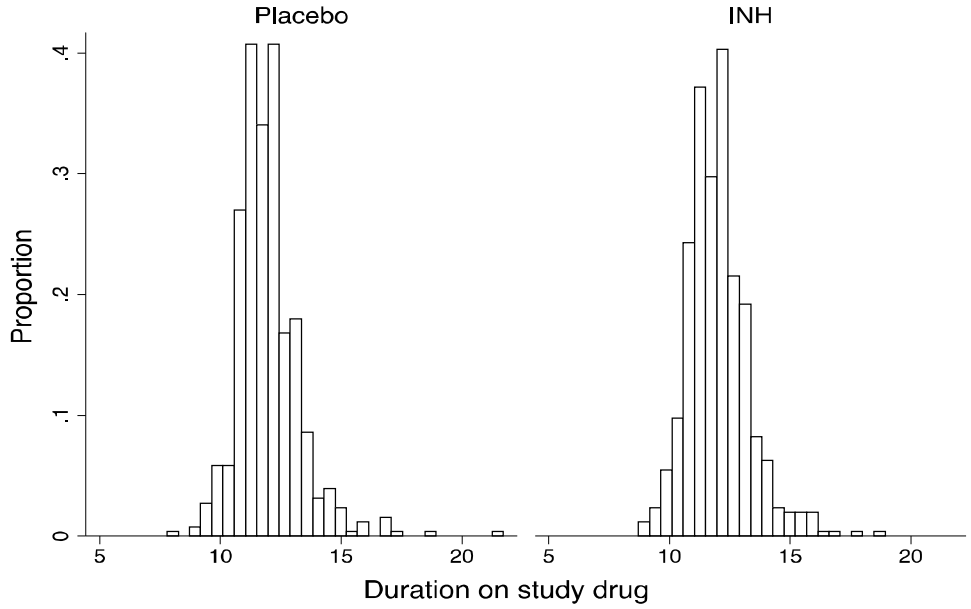
Tests of tuberculosis infection

Tuberculin skin tests (TST; 2TU RT23 PPD, Statens Serum Institut, Denmark) and interferon gamma release assays (IGRA; QuantiFERON Gold In-Tube, Cellestis, Australia) were performed as part of a nested study.(13) TST and IGRA were performed at the baseline screening visit, prior to application of RCT-specific inclusion/exclusion criteria, in persons who indicated willingness to return for TST results. Manufacturer's criteria for IGRA positivity were used (≥ 0.35 IU/ml); TST induration of ≥ 5 mm was deemed positive. 77% (1,027) of the cohort at analysis had TST and IGRA tests performed. 998 of 1,027 had IGRA results available, 93% of those had valid results. 944 of 1,027 had TST results available. Those who did not accept TST/IGRA testing did not differ from those who did with respect to age, gender, CD4+ count, previous history or ART status (see table below).

Table S6 Summary of enrolment characteristics of those who did not accept TST/IGRA and those who did

Characteristic	302 Not accepted	1027 Accepted
Median age (IQR), years	34 (30-41)	34(29-39)
Female	68.9% (208)	76.9% (790)
Established on ART	73.5% (222)	71.1% (730)
Median CD4+ count (IQR), cells/mm^3	225 (159-396)	214 (150-350)
	N=269	N=918
Previous TB	43.4% (129)	42.6% (431)
	N=297	N=1,012

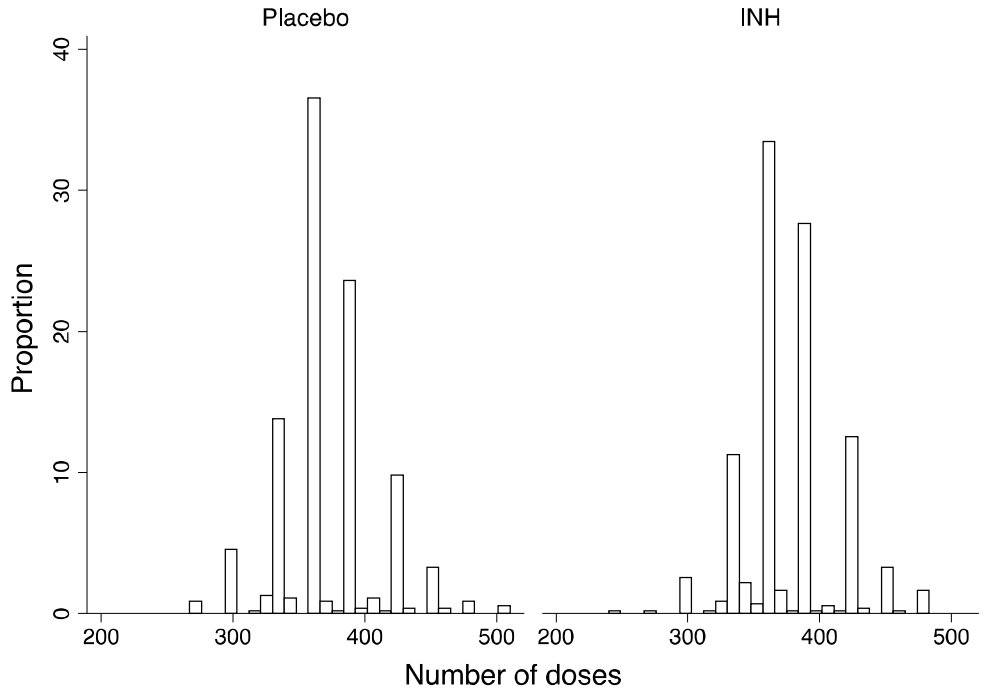
Figure S1a. Frequency histogram of study drug duration for those registered as completed the active phase (N=1,100)



Placebo: range 8-22months; median 12 (IQR: 11-13)

INH: range 9-19 months; median 12 (IQR: 11-13)

Figure S1b. Actual number of doses prescribed, for those registered as completed the active phase (N=1,100)



Placebo: range 268-510 doses; median 360 doses (IQR: 360-390)

INH: range 240-480 doses; median 360 doses (IQR: 360-390)

Tests of tuberculosis infection

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Table S5 Comparison of characteristics at screening for the 478 who were not randomized and the 1,369 that were randomized

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