Cost effectiveness of testing HIV infected individuals for TB in a low TB/HIV setting

WEB APPENDIX

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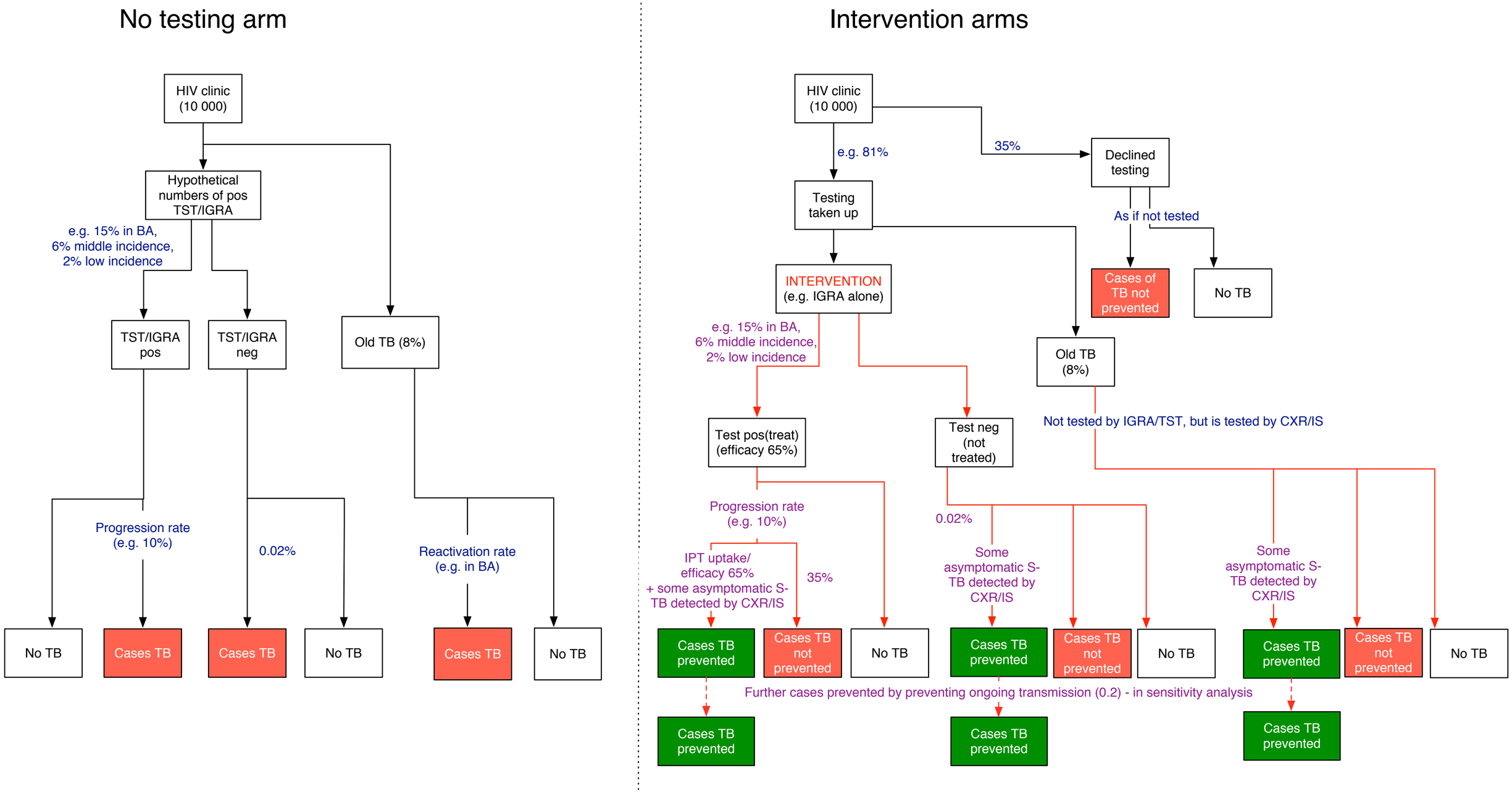
Appendix Figure 1: Model for cost-effectiveness analysis, no testing and intervention arms



BA: black African; CXR - chest X ray; IGRA - Interferon-gamma release assay; IS: induced sputum; S- : Smear negative, culture positive; TB - tuberculosis; TST - tuberculin skin test

Appendix Table 1: Assumptions used for relevant variables within cost-effectiveness analysis

Variable	Mean/ baseline	Sensitivity analysis lower	Sensitivity analysis upper	Std Dev	Alpha	Beta	Distribution	Source
TST	£18.51	£9.26	£37.02	4.72	15.37	1.20	Gamma	[1]
IGRA	£53.34	£26.67	£106.68	13.61	15.37	3.47	Gamma	[1]
CXR	£38.10	£19.05	£76.20	9.71	15.37	2.47	Gamma	[1]
Sputum induction	£100	£67	£150	16.84	35.28	2.83	Gamma	Estimate, local costs
Sputum induction and TB PCR	£160	£116.87	£200	22.01	52.86	3.03	Gamma	Estimate, local costs
LTBI	£666.04	£333.02	£1,332.08	169.91	15.37	43.2	Gamma	Local charges, [1,2]
Active TB	£9674.21	£4,837.11	£19,348.42	2467	15.37	629.56	Gamma	[2]
Cost of asymptomatic disease	£1,247.62	£623.81	£2,495.42	318.27	15.37	81.19	Gamma	Estimate, [1]
Proportion black African	25%	20%	30%	0.002	14938.78	45060.22	Beta	[4]
Proportion middle incidence	13.9%	4%	24%	0.049	6.69	41.3	Beta	Study

Appendix Table 1: Assumptions used for relevant variables within cost-effectiveness analysis

Variable	Mean/ baseline	Sensitivity analysis lower	Sensitivity analysis upper	Std Dev	Alpha	Beta	Distribution	Source
Asymptomatic disease in BA	0.17%	0%	0.41%	0.0012	2.09	1201.91	Beta	Study, [5]
Asymptomatic disease in MI	0.09%	0%	0.18%	0.00087	1.11	1202.89	Beta	Study, [5]
Asymptomatic disease in LI	0.04%	0%	0.1%	0.00057	0.48	1203.52	Beta	Study, [5]
Uptake LTBI	50%	35%	65%	0.05	49.5	49.5	Beta	Study
Efficacy LTBI	62%	59%	65%	0.05	1473.74	903.26	Beta	[6]
QALY loss LTBI	0.01	0	0.05	0.01	7.53	0	Gamma	[1]
QALY loss active TB	0.68	0.35	1	0	16.72	0.04	Gamma	[1]
QALY loss asymptomatic TB	0.2	0.01	0.3	0.17	7.31	0.03	Gamma	Estimate
Progression rate with pos TST alone	2%	1%	4%	0.07	7.68	0	Gamma	[7]

Appendix Table 1: Assumptions used for relevant variables within cost-effectiveness analysis

Variable	Mean/ baseline	Sensitivity analysis lower	Sensitivity analysis upper	Std Dev	Alpha	Beta	Distribution	Source
Progression rate with pos IGRA and TST	10%	3%	17%	0.01	7.84	0.01	Gamma	[8-10]
Progression rate with neg TST	0.2%	0%	0.5%	0.04	3.84	0	Gamma	[10-11]
Proportion old TB	7%	2.1%	12.6%	0.02	15.93	200.07	Beta	Study, local demographics
TST return rate for those having TSTs as well as IGRAs	53%	30%	90%	0.03	116.07	102.93	Beta	Study
Transmission (for transmission CEAC)	20%	10%	30%	0.004	1701.8	6807.2	Beta	[1]

CXR - Chest X Ray, IGRA - Interferon Gamma Release Assay, MI - Middle incidence, QALY - Quality Associated Life Year, TB - Tuberculosis, TST - Tuberculin skin test.

Appendix Table 2: Costs for all 30 strategies (discounted cost/case prevented and cost/QALY gained to no testing and last non-dominated) strategy (£)

Strategy	Total cost of strategy per 10,000 PLHIV 95% uncertainty ranges)	Cases TB prevented (discounted) (95% uncertainty ranges)	QALYs gained compared to no testing (95% uncertainty ranges)	Cost/case averted (95% uncertainty ranges)	Cost/QALY compared to no testing (95% uncertainty ranges)	Incremental cost/QALY compared to last strategy (95% uncertainty ranges)
No testing	£889,527 (£153,844-£3,310,891)	0	0	£0	£0	
BA TST	£922,744 (£172,160-£3,338,385)	3.9 (1.1-10.6)	2.1 (0.4-8.6)	£8,510 (£2,603-£16,120)	£15,868 (£3,254-£49,229)	£15,868
BA MI TST	£933,733 (£175,202-£3,353,942)	4.5 (1.1-15.3)	2.4 (0.4-12.4)	£9,837 (£2,831-£18,657)	£18,221 (£3,506-£56,938)	EXTENDEDLY DOMINATED
BHIVA 2011	£940,875 (£173,101-£3,389,891)	2.3 (0.2-11.1)	1.3 (0.1-9.2)	£22,552 (£7,126-£107,863)	£40,050 (£8,642-£303,159)	DOMINATED
BA TST&CXR	£970,468 (£215,217-£3,349,862)	7.3 (1.8-19.2)	3.7 (0.6-14.0)	£11,133 (£2,065-£34,518)	£21,900 (£2,843-£104,693)	£29,777 compared to BA TST
BHIVA strategy with CXR	£945,567 (£216,157-£3,400,455)	5.6 (0.8-19.6)	2.9 (0.3-14.7)	£17,554 (£4,634-£76,036)	£34,343 (£6,247-£224,611)	DOMINATED
BA IGRA	£997,509 (£221,671-£3,419,191)	6.8 (2.0-18.3)	3.8 (0.7-15.2)	£15,808 (£5,928-£34,016)	£28,074 (£7,189-£95,604)	EXTENDEDLY DOMINATED
NICE 2011	£999,136 (£208,110-£3,487,781)	1.1 (0.0-6.3)	0.6 (0.0-5.2)	£98,334 (£28,263-£1,822,488)	£174,631 (£34,274-£5,122,253)	DOMINATED
All TST	£1,000,540 (£212,273-£3,447,275)	5.6 (1.3-18.9)	2.9 (0.4-14.9)	£19,729 (£7,213-£43,819)	£38,801 (£9,211-£147,999)	DOMINATED
BA MI TST&CXR	£1,015,938 (£230,785-£3,408,667)	8.9 (1.8-28.9)	4.5 (0.6-21.1)	£14,265 (£3,411-£42,302)	£28,059 (£4,699-£128,225)	EXTENDEDLY DOMINATED
BA IGRA&TST	£1,043,042 (£244,113-£3,511,933)	7.1 (2.0-19.6)	3.9 (0.7-15.7)	£21,584 (£10,269-£44,695)	£39,358 (£12,879-£126,912)	DOMINATED

Strategy	Total cost of strategy per 10,000 PLHIV 95% uncertainty ranges)	Cases TB prevented (discounted) (95% uncertainty ranges)	QALYs gained compared to no testing (95% uncertainty ranges)	Cost/case averted (95% uncertainty ranges)	Cost/QALY compared to no testing (95% uncertainty ranges)	Incremental cost/QALY compared to last strategy (95% uncertainty ranges)
BA IGRA&CXR	£1,045,234 (£264,728-£3,430,668)	10.2 (2.6-26.8)	5.4 (0.9-20.6)	£15,269 (£4,487-£42,076)	£28,575 (£5,873-£120,072)	EXTENDEDLY DOMINATED
BA MI IGRA	£1,056,145 (£238,982-£3,524,589)	9.1 (2.1-31.6)	5.1 (0.8-26.3)	£18,391 (£6,769-£40,170)	£32,660 (£8,209-£112,902)	DOMINATED
BA TST&CXR&IS	£1,062,425 (£288,031-£3,441,094)	9.1 (2.1-23.8)	4.5 (0.7-17.0)	£19,094 (£5,496-£63,671)	£38,036 (£7,761-£192,748)	DOMINATED
BA MI IGRA&TST	£1,121,162 (£267,302-£3,663,453)	9.3 (2.1-32.9)	5.2 (0.8-26.8)	£24,796 (£10,720-£52,891)	£44,927 (£13,262-£150,095)	DOMINATED
BA IGRA&CXR&IS	£1,137,190 (£337,542-£3,521,900)	12.0 (3.0-31.5)	6.3 (1.0-23.6)	£20,668 (£6,723-£61,959)	£39,320 (£9,026-£177,753)	EXTENDEDLY DOMINATED
BA MI IGRA&CXR	£1,138,350 (£294,565-£3,579,314)	13.4 (2.8-45.2)	7.2 (1.0-34.9)	£18,530 (£5,954-£50,381)	£34,651 (£7,760-£143,751)	EXTENDEDLY DOMINATED
CXR in all	£1,095,328 (£338,835-£3,521,798)	6.3 (0.7-20.3)	3.0 (0.2-13.0)	£40,825 (£10,463-£271,789)	£85,768 (£16,502-£814,460)	DOMINATED
BA MI TST&CXR&IS	£1,163,467 (£323,904-£3,600,855)	11.2 (2.2-36.4)	5.6 (0.7-25.9)	£24,508 (£7,999-£78,550)	£48,853 (£11,312-£237,661)	DOMINATED
All TST&CXR	£1,256,188 (£397,265-£3,659,068)	11.9 (2.0-39.3)	5.8 (0.6-27.9)	£30,841 (£8,896-£120,827)	£62,765 (£12,603-£391,294)	DOMINATED
BA MI IGRA&CXR&IS	£1,285,879 (£387,684-£3,771,502)	15.7 (3.1-52.7)	8.3 (1.1-39.7)	£25,176 (£8,761-£74,487)	£47,851 (£11,707-£213,659)	EXTENDEDLY DOMINATED
All IGRA	£1,303,929 (£411,809-£3,816,372)	10.2 (2.2-36.0)	5.7 (0.8-29.9)	£40,767 (£14,047-£119,309)	£72,397 (£17,035-£335,329)	DOMINATED
NICE 2016	£1,407,200 (£505,335-£3,776,864)	10.2 (2.2-36.0)	5.7 (0.8-29.9)	£50,926 (£15,899-£182,142)	£90,439 (£19,435-£547,239)	DOMINATED

Strategy	Total cost of strategy per 10,000 PLHIV 95% uncertainty ranges)	Cases TB prevented (discounted) (95% uncertainty ranges)	QALYs gained compared to no testing (95% uncertainty ranges)	Cost/case averted (95% uncertainty ranges)	Cost/QALY compared to no testing (95% uncertainty ranges)	Incremental cost/QALY compared to last strategy (95% uncertainty ranges)
All IGRA&TST	£1,475,296 (£504,165-£4,115,667)	11.0 (2.3-38.9)	5.9 (0.8-31.1)	£53,282 (£20,654-£152,474)	£99,566 (£26,060-£449,728)	DOMINATED
All IGRA&CXR	£1,559,576 (£596,801-£4,028,165)	16.4 (2.8-56.4)	8.7 (1.0-42.9)	£40,789 (£12,753-£155,815)	£76,975 (£16,874-£444,539)	EXTENDEDLY DOMINATED
All TST&CXR&IS	£1,659,430 (£698,297-£4,112,155)	15.2 (2.4-50.4)	7.4 (0.7-35.0)	£50,623 (£15,927-£230,250)	£103,732 (£23,081-£736,873)	DOMINATED
All IGRA&TST&CXR	£1,730,943 (£689,157-£4,327,460)	17.3 (3.0-59.3)	8.9 (1.0-44.1)	£48,761 (£17,157-£179,740)	£94,926 (£23,243-£532,060)	EXTENDEDLY DOMINATED
All IGRA&CXR&IS	£1,962,818 (£897,833-£4,481,252)	19.7 (3.2-67.5)	10.3 (1.1-50.0)	£54,352 (£17,370-£233,027)	£104,356 (£23,609-£668,330)	EXTENDEDLY DOMINATED
All IGRA&TST&CXR&IS	£2,134,185 (£990,189-£4,780,547)	20.6 (3.3-70.4)	10.4 (1.1-51.2)	£60,492 (£20,885-£251,295)	£119,173 (£28,938-£744,827)	EXTENDEDLY DOMINATED
All IGRA&TST&CXR&IS inc PCR	£2,393,679 (£1,201,286-£5,093,885)	20.6 (3.3-70.4)	10.4 (1.1-51.2)	£73,104 (£25,333-£314,679)	£144,019 (£35,100-£932,694)	EXTENDEDLY DOMINATED

ART - antiretroviral therapy, BA - Black African, BHIVA - British HIV Association, CD4 - blood CD4 cell count in cells/μL, CXR - chest X ray, IGRA - Interferon-gamma release assay, IS - induced sputum, LI - low [TB] incidence countries, MI - middle [TB] incidence countries, NICE - National Institute of Health and Care Excellence, PCR - Xpert MTB/RIF *M. tuberculosis* polymerase chain reaction, PLHIV - People living with HIV, QALY - Quality adjusted life year, TB - tuberculosis (includes active disease and subclinical tuberculosis cases), TST - tuberculin skin test.

Strategies are either named (e.g. BHIVA 2011), or consist of the group tested followed by the test(s) - (e.g. BA TST is Testing black Africans with a tuberculin skin test only).
BHIVA 2011: IGRA only in BA with any CD4 on ART < 2 years; MI with CD4 <500 on ART < 2 years; LI with CD4 <350 on ART < 6 months.
NICE 2011: IGRA + TST if blood CD4 <200 and IGRA alone if blood CD4 200-500.
NICE 2016: IGRA + TST if blood CD4 <200 and IGRA alone if blood CD4 ≥200.
Uptake was 82% for IGRA and CXR, 41% for TST and induced sputum.

Appendix Table 3: Univariate sensitivity analyses Cost/case prevented (in £'000)

Variable and baseline		Cost TST (£18.51)		Cost IGRA (£53.34)		Cost CXR (£38.10)		Cost Sputum induction (£100)		Cost LTBI (£666)		Cost asymptomatic TB (£1,247)		Cost Active TB (£9674)		Proportion BA (24%)		Uptake LTBI (50%)			
Min/Max variable	Base	9.2	37	26.7	106.68	19	76	67	150	333	1,332	624	2495	4837	19348	20%	30%	35%	65%	80%	100%
BA TST	8.5	6.1	13.2	8.5	8.5	8.5	8.5	8.5	8.5	1.6	22.4	8.5	8.5	13.6	CS	8.5	8.5	10.5	7.4	6.7	6.1
BA MI TST	9.8	6.6	16.2	9.8	9.8	9.8	9.8	9.8	9.8	3.1	23.4	9.8	9.8	14.9	CS	10.1	9.6	12.6	8.4	7.4	6.6
BHIVA 2011	22.6	22.6	22.6	11.8	44.0	22.6	22.6	22.6	22.6	16.9	33.8	22.6	22.6	27.6	12.4	24.8	21.0	31.7	17.6	14.5	11.8
BA TST&CXR	11.1	9.9	13.7	11.1	11.1	5.8	21.8	11.1	11.1	7.4	18.6	10.8	11.7	16.2	1.0	11.1	11.1	12.5	10.1	9.3	8.6
BHIVA strategy with CXR	17.6	17.6	17.6	13.2	26.2	10.7	31.3	17.6	17.6	15.3	22.1	17.2	18.3	22.6	7.4	18.5	16.9	19.8	15.8	14.4	12.8
BA IGRA	15.8	15.8	15.8	8.5	30.5	15.8	15.8	15.8	15.8	10.2	27.0	15.8	15.8	20.9	5.7	15.8	15.8	22.1	12.4	10.3	8.5
NICE 2011	98.3	97.4	100.2	50.7	193.7	98.3	98.3	98.3	98.3	92.7	109.6	98.3	98.3	103.4	88.2	98.3	98.3	140.0	75.9	61.9	49.7
All TST	19.7	13.1	32.9	19.7	19.7	19.7	19.7	19.7	19.7	11.4	36.4	19.7	19.7	24.8	9.6	22.2	17.7	25.4	16.7	14.8	13.1
BA MI TST&CXR	14.3	12.6	17.5	14.3	14.3	7.5	27.9	14.3	14.3	10.8	21.1	13.9	14.9	19.3	4.2	14.9	13.8	16.2	12.8	11.7	10.6
BA IGRA&TST	21.6	19.1	26.5	14.5	35.7	21.6	21.6	21.6	21.6	15.2	34.3	21.6	21.6	26.6	11.5	21.6	21.6	29.7	17.2	14.5	12.1
BA IGRA&CXR	15.3	15.3	15.3	10.4	25.1	11.5	22.9	15.3	15.3	11.5	22.8	15.1	15.7	20.3	5.2	15.3	15.3	18.8	12.9	11.2	9.6
BA MI IGRA	18.4	18.4	18.4	9.8	35.7	18.4	18.4	18.4	18.4	12.8	29.6	18.4	18.4	23.4	8.3	18.8	18.0	25.8	14.4	11.9	9.8
BA TST&CXR&IS	19.1	18.1	21.1	19.1	19.1	14.8	27.6	15.2	25.0	16.1	25.1	18.7	19.8	24.2	9.0	19.1	19.1	21.4	17.3	15.9	14.5
BA MI IGRA&TST	24.8	21.9	30.6	16.4	41.5	24.8	24.8	24.8	24.8	18.6	37.1	24.8	24.8	29.9	14.7	25.4	24.4	34.5	19.6	16.3	13.5
BA IGRA&CXR&IS	20.7	20.7	20.7	16.5	29.0	17.4	27.1	17.7	25.2	17.5	27.1	20.4	21.2	25.7	10.6	20.7	20.7	24.7	17.8	15.7	13.6
BA MI IGRA&CXR	18.5	18.5	18.5	12.7	30.2	14.0	27.5	18.5	18.5	14.7	26.1	18.3	19.0	23.6	8.4	19.1	18.1	22.9	15.6	13.5	11.5
All CXR	40.8	40.8	40.8	40.8	40.8	16.0	90.5	40.8	40.8	40.8	40.8	40.2	42.1	45.9	30.7	45.2	36.9	40.8	40.8	40.8	40.8
BA MI TST&CXR&IS	24.5	23.2	27.1	24.5	24.5	19.1	35.3	19.6	32.0	21.8	30.0	24.1	25.3	29.6	14.4	25.5	23.7	27.4	22.2	20.4	18.5
All TST&CXR	30.8	27.7	37.1	30.8	30.8	17.8	57.0	30.8	30.8	26.9	38.7	30.5	31.5	35.9	20.7	34.6	27.7	34.9	27.8	25.5	23.0
BA MI IGRA&CXR&IS	25.2	25.2	25.2	20.2	35.1	21.3	32.8	21.7	30.5	21.9	31.6	24.9	25.7	30.2	15.1	26.0	24.6	30.2	21.6	19.0	16.4
All IGRA	40.8	40.8	40.8	21.0	80.4	40.8	40.8	40.8	40.8	35.2	52.0	40.8	40.8	45.8	30.7	46.4	36.2	57.8	31.6	25.9	20.9
NICE 2016	51.0	44.9	63.1	33.4	86.0	51.0	51.0	51.0	51.0	44.3	64.4	51.0	51.0	55.8	41.3	57.4	45.6	71.2	40.1	33.2	27.3
All IGRA&TST	53.3	46.9	66.0	35.0	89.9	53.3	53.3	53.3	53.3	46.3	67.3	53.3	53.3	58.3	43.2	60.0	47.7	74.4	41.9	34.8	28.6
All IGRA&CXR	40.8	40.8	40.8	28.5	65.3	31.3	59.7	40.8	40.8	37.3	47.7	40.5	41.3	45.8	30.7	45.9	36.5	49.8	34.6	30.0	25.6
All TST&CXR&IS	50.6	48.2	55.5	50.6	50.6	40.4	71.1	41.2	64.8	47.5	56.8	50.2	51.4	55.7	40.5	56.4	45.7	56.1	46.2	42.6	38.7
All IGRA&TST&CXR	48.8	44.7	56.9	37.1	72.1	39.8	66.8	48.8	48.8	44.3	57.7	48.5	49.2	53.8	38.6	54.5	43.9	59.4	41.6	36.4	31.3
All IGRA&CXR&IS	54.4	54.4	54.4	44.2	74.8	46.5	70.1	47.1	65.3	51.5	60.1	54.0	55.0	59.4	44.2	60.9	48.8	64.1	47.2	41.8	36.3
All IGRA&TST&CXR&IS	60.5	57.1	67.3	50.7	80.1	52.9	75.6	53.6	71.0	56.7	68.0	60.2	61.1	65.5	50.4	67.5	54.6	71.3	52.7	46.8	40.8
All IGRA&TST&CXR & IS&PCR	73.1	69.7	79.9	63.3	92.7	65.6	88.2	73.1	73.1	69.4	80.6	72.8	73.7	78.2	63.0	81.5	66.0	86.3	63.5	56.3	49.0

Appendix Table 3: Univariate sensitivity analyses Cost/case prevented (in £'000)

Variable and baseline		Efficacy LTBI 62%)		Efficacy &Uptake	Progression rate TST + IGRA - (2%)		Progression rate IGRA + (10%)		TST return rate (53%)		Proportion asympt disease BA (0.17%)		Proportion asympt disease MI (0.09%)		Proportion asympt disease LI (0.04%)		Worst case	Best case	With onward transmission prevented (R)			
Min/Max variable	Bas	40%	100%	100%	1%	4%	3%	17%	30%	90%	0%	0.4	0%	0.2	0%	0.1			0.2	0.4	1.0	2.0
BA TST	8.5	18.8	1.4	0.0	9.1	7.6	43.0	1.2	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5	38.6	CS	7.1	6.0	4.2	0.0
BA MI TST	9.8	20.8	2.3	0.3	10.4	9.0	47.9	1.9	9.8	9.8	9.8	9.8	9.8	9.8	9.8	9.8	44.0	CS	8.2	7.0	4.9	2.8
BHIVA 2011	22.6	40.5	10.1	3.5	22.6	22.6	98.8	9.1	22.6	22.6	22.6	22.6	22.6	22.6	22.6	22.6	93.6	CS	18.7	16.0	11.1	3.2
BA TST&CXR	11.1	16.1	5.9	3.0	11.5	10.6	22.5	5.6	11.1	11.1	28.3	3.6	11.1	11.1	11.1	11.1	19.9	CS	9.2	7.9	5.5	7.4
BHIVA strategy with CX	17.6	22.2	12.1	6.9	17.6	17.6	28.4	11.5	17.6	17.6	56.5	6.0	17.6	17.6	17.6	17.6	26.4	CS	17.6	17.6	17.6	3.7
BA IGRA	15.8	30.1	6.0	1.4	15.8	15.8	76.3	5.1	15.8	15.8	15.8	15.8	15.8	15.8	15.8	15.8	68.8	CS	13.1	11.2	7.8	17.6
NICE 2011	98.3	158.0	57.1	27.0	98.3	98.3	351.4	53.7	98.3	98.3	98.3	98.3	98.3	98.3	98.3	98.3	372.3	CS	81.6	69.8	48.6	5.2
All TST	19.7	36.1	8.4	4.3	21.7	16.9	63.9	8.6	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	77.6	CS	16.4	14.0	9.8	32.3
BA MI TST&CXR	14.3	19.6	8.5	4.6	14.6	13.7	26.4	8.2	14.3	14.3	28.4	6.6	17.2	11.6	14.3	14.3	24.2	CS	11.8	10.1	7.1	6.5
BA IGRA&TST	21.6	39.0	9.5	3.6	22.1	20.7	86.6	8.8	21.3	22.0	21.6	21.6	21.6	21.6	21.6	21.6	88.6	CS	17.9	15.3	10.7	4.7
BA IGRA&CXR	15.3	23.2	7.9	3.1	15.3	15.3	37.7	7.2	15.3	15.3	27.1	8.0	15.3	15.3	15.3	15.3	33.5	CS	12.7	10.8	7.5	7.1
BA MI IGRA	18.4	34.1	7.6	2.2	18.4	18.4	84.9	6.7	18.4	18.4	18.4	18.4	18.4	18.4	18.4	18.4	78.3	CS	15.3	13.0	9.1	5.0
BA TST&CXR&IS	19.1	24.4	13.0	7.8	19.5	18.5	30.4	12.7	19.1	19.1	35.6	10.0	19.1	19.1	19.1	19.1	29.0	CS	15.9	13.5	9.4	6.0
BA MI IGRA&TST	24.8	44.0	11.5	4.5	25.3	24.1	98.6	10.7	24.6	25.1	24.8	24.8	24.8	24.8	24.8	24.8	100.8	CS	20.6	17.6	12.3	6.3
BA IGRA&CXR&IS	20.7	28.5	12.7	6.3	20.7	20.7	41.1	11.9	20.7	20.7	32.2	12.7	20.7	20.7	20.7	20.7	38.1	CS	17.2	14.7	10.2	8.1
BA MI IGRA&CXR	18.5	27.5	10.2	4.4	18.5	18.5	44.2	9.3	18.5	18.5	27.7	11.8	20.7	16.3	18.5	18.5	40.2	CS	15.4	13.1	9.2	6.8
All CXR	40.8	40.8	40.8	40.8	40.8	40.8	40.8	40.8	40.8	40.8	98.6	20.3	50.3	33.0	62.3	25.2	40.7	40.7	40.8	40.8	40.8	6.1
BA MI TST&CXR&IS	24.5	30.3	17.7	11.0	24.9	23.9	36.9	17.3	24.5	24.5	38.9	15.1	27.8	21.3	24.5	24.5	35.8	CS	20.3	17.4	12.1	40.8
All TST&CXR	30.8	39.1	21.6	13.7	32.1	28.9	47.0	21.8	30.8	30.8	46.5	20.1	34.5	27.3	38.4	23.1	47.8	CS	25.6	21.9	15.2	8.0
BA MI IGRA&CXR&IS	25.2	34.2	16.0	8.2	25.2	25.2	49.0	15.0	25.2	25.2	34.4	17.7	27.5	22.8	25.2	25.2	46.1	CS	20.9	17.9	12.4	10.1
All IGRA	40.8	68.8	21.4	9.1	40.8	40.8	159.5	19.8	40.8	40.8	40.8	40.8	40.8	40.8	40.8	40.8	160.6	CS	33.8	28.9	20.1	8.3
NICE 2016	51.0	84.3	27.9	13.3	53.0	47.9	162.2	27.1	51.5	50.2	51.0	51.0	51.0	51.0	51.0	51.0	201.7	CS	42.5	36.3	25.3	13.4
All IGRA&TST	53.3	88.1	29.2	13.9	55.4	50.0	169.6	28.4	53.8	52.5	53.3	53.3	53.3	53.3	53.3	53.3	205.5	CS	44.2	37.8	26.3	16.8
All IGRA&CXR	40.8	55.1	26.8	14.2	40.8	40.8	79.7	25.4	40.8	40.8	53.6	30.3	44.0	37.5	47.3	33.4	77.3	CS	33.9	28.9	20.2	17.5
All TST&CXR&IS	50.6	59.8	39.4	26.6	52.1	48.3	67.8	39.6	50.6	50.6	67.5	37.3	54.8	46.4	59.1	41.2	69.9	CS	42.0	35.9	25.0	13.4
All IGRA&TST&CXR	48.8	66.0	32.2	17.9	50.0	46.8	90.1	31.6	49.0	48.4	62.7	37.1	52.3	45.1	55.9	40.5	93.3	CS	40.5	34.6	24.1	16.6
All IGRA&CXR&IS	54.4	68.8	38.9	22.6	54.4	54.4	90.7	37.3	54.4	54.4	67.3	42.8	57.7	50.8	61.1	46.3	89.2	CS	45.1	38.6	26.9	16.0
All IGRA&TST&CXR&IS	60.5	77.0	43.1	25.6	61.7	58.5	97.8	42.3	60.9	59.9	74.1	48.3	64.0	56.8	67.5	52.0	100.8	CS	50.2	42.9	29.9	17.8
All IGRA&TST&CXR & IS&PCR	73.1	92.6	52.6	31.3	74.6	70.8	117.1	51.7	73.7	72.1	89.1	58.7	77.3	68.7	81.4	63.0	121.5	CS	60.7	51.9	36.1	19.9

Appendix Table 3: Univariate sensitivity analyses Cost/case prevented (in £'000)

ART - antiretroviral therapy, BHIVA - British HIV Association, CD4 - blood CD4 cell count in cells/μL, CS - Cost saving, CXR - chest X ray, IGRA - Interferon-gamma release assay, LI - low [TB] incidence countries, MI - middle [TB] incidence countries, NICE - National Institute of Health and Care Excellence, PLHIV - People living with HIV, QALY - Quality adjusted life year, TB - tuberculosis, TST - tuberculin skin test.

BHIVA 2011: IGRA only in subSaharan Africa with any CD4 on ART < 2 years, MI with CD4 <500 on ART < 2 years, LI with CD4 <350 on ART < 6 months.

NICE 2011: IGRA + TST if blood CD4 <200 and IGRA alone if blood CD4 <500.
NICE 2016: IGRA + TST if blood CD4 <200 and IGRA alone in all others.

These univariate and multivariate analyses assume no onward transmission, except in transmission column, where R stands for the number of subsequent cases of active TB prevented by stopping transmission from each active case of TB.

Worse case uses most expensive TST, IGRA, CXR, sputum induction, latent TB treatment; lowest uptake for tests and lowest efficacy; cheapest cost of treatment of active TB. Best case uses least expensive TST, IGRA, CXR, sputum induction, latent TB treatment; highest uptake for tests and highest efficacy; most expensive cost of treatment of active TB. These do not include transmission.

Appendix Table 4: Univariate sensitivity analyses Cost/QALY gained (in £'000)

Variable and baseline		Cost TST (£18.51)		Cost IGRA (£53.34)		Cost CXR (£38.10)		Cost Sputum induction (£100)		Cost LTBI (£666)		Cost asymptomatic TB (£1,247)		Cost Active TB (£9674)		Proportion BA (24%)	
Min/Max variable	Base	9.2	37	26.7	106.68	19	76	67	150	333	1,332	624	2495	4837	19348	20%	30%
BA TST	15.9	11.5	24.7	15.9	15.9	15.9	15.9	15.9	15.9	2.9	41.8	15.9	15.9	25.3	CS	15.9	15.9
BA MI TST	18.2	12.3	30.1	18.2	18.2	18.2	18.2	18.2	18.2	5.7	43.3	18.2	18.2	27.6	CS	18.7	17.9
BHIVA 2011	40.0	40.0	40.0	21.0	78.1	40.0	40.0	40.0	40.0	30.1	60.0	40.0	40.0	49.0	22.1	44.1	37.2
BA TST&CXR	21.9	19.4	26.9	21.9	21.9	11.4	42.8	21.9	21.9	14.6	36.6	21.3	23.1	31.8	2.0	21.9	21.9
BHIVA strategy with CXR	34.3	34.3	34.3	25.9	51.3	20.9	61.2	34.3	34.3	29.9	43.2	33.6	35.9	44.2	14.6	36.2	33.1
BA IGRA	28.1	28.1	28.1	15.0	54.2	28.1	28.1	28.1	28.1	18.1	48.0	28.1	28.1	37.1	10.1	28.1	28.1
NICE 2011	174.6	173.0	178.0	90.1	344.0	174.6	174.6	174.6	174.6	164.7	194.6	174.6	174.6	183.6	156.7	174.6	174.6
All TST	38.8	25.8	64.7	38.8	38.8	38.8	38.8	38.8	38.8	22.4	71.6	38.8	38.8	48.7	18.9	44.2	34.5
BA MI TST&CXR	28.1	24.9	34.4	28.1	28.1	14.7	54.8	28.1	28.1	21.3	41.6	27.4	29.3	38.0	8.2	29.2	27.2
BA IGRA&TST	39.4	34.9	48.3	26.5	65.1	39.4	39.4	39.4	39.4	27.8	62.5	39.4	39.4	48.6	20.9	39.4	39.4
BA IGRA&CXR	28.6	28.6	28.6	19.4	47.0	21.5	42.8	28.6	28.6	21.5	42.7	28.2	29.4	38.0	9.6	28.6	28.6
BA MI IGRA	32.7	32.7	32.7	17.3	63.3	32.7	32.7	32.7	32.7	22.7	52.6	32.7	32.7	41.6	14.7	33.5	32.0
BA TST&CXR&IS	38.0	36.0	42.1	38.0	38.0	29.5	55.1	30.2	49.9	32.1	50.0	37.3	39.5	48.1	17.9	38.0	38.0
BA MI IGRA&TST	44.9	39.7	55.5	29.8	75.3	44.9	44.9	44.9	44.9	33.7	67.3	44.9	44.9	54.1	26.6	45.9	44.2
BA IGRA&CXR&IS	39.3	39.3	39.3	31.4	55.3	33.2	51.6	33.7	47.9	33.2	51.5	38.8	40.4	48.9	20.1	39.3	39.3
BA MI IGRA&CXR	34.7	34.7	34.7	23.8	56.4	26.2	51.5	34.7	34.7	27.6	48.8	34.3	35.4	44.1	15.7	35.7	33.8
All CXR	85.8	85.8	85.8	85.8	85.8	33.6	190.0	85.8	85.8	85.8	85.8	84.4	88.5	96.4	64.5	95.0	77.6
BA MI TST&CXR&IS	48.9	46.3	54.0	48.9	48.9	38.1	70.4	39.0	63.8	43.4	59.7	48.1	50.4	58.9	28.7	50.9	47.3
All TST&CXR	62.8	56.4	75.5	62.8	62.8	36.2	116.0	62.8	62.8	54.7	78.8	62.1	64.2	73.1	42.2	70.9	56.0
BA MI IGRA&CXR&IS	47.9	47.9	47.9	38.4	66.7	40.6	62.4	41.2	58.0	41.7	60.1	47.3	48.9	57.5	28.6	49.4	46.7
All IGRA	72.4	72.4	72.4	37.2	142.8	72.4	72.4	72.4	72.4	62.4	92.3	72.4	72.4	81.4	54.4	82.3	64.4
BHIVA 2016	90.5	79.7	112.1	59.4	152.8	90.5	90.5	90.5	90.5	78.6	114.3	90.5	90.5	99.1	73.3	102.6	80.7
All IGRA&TST	99.6	87.7	123.3	65.4	168.1	99.6	99.6	99.6	99.6	86.5	125.8	99.6	99.6	109.0	80.7	112.9	88.8
All IGRA&CXR	77.0	77.0	77.0	53.9	123.3	59.1	112.7	77.0	77.0	70.4	90.1	76.5	77.9	86.5	57.9	86.8	68.8
All TST&CXR&IS	103.7	98.7	113.7	103.7	103.7	82.8	145.6	84.5	132.9	97.4	116.4	102.9	105.4	114.1	83.0	116.2	93.1
All IGRA&TST&CXR	94.9	87.0	110.7	72.2	140.4	77.4	130.0	94.9	94.9	86.2	112.3	94.5	95.8	104.8	75.2	106.7	85.1
All IGRA&CXR&IS	104.4	104.4	104.4	84.8	143.5	89.2	134.6	90.5	125.4	98.8	115.5	103.7	105.6	114.1	84.9	117.2	93.6
All IGRA&TST&CXR&IS	119.2	112.5	132.6	99.9	157.8	104.3	148.9	105.5	139.9	111.8	133.9	118.6	120.4	129.1	99.2	133.5	107.1
All IGRA&TST&CXR & IS&PCR	144.0	137.3	157.4	124.7	182.6	129.1	173.8	144.0	144.0	136.6	158.8	143.4	145.2	154.0	124.1	161.2	129.5

Appendix Table 4: Univariate sensitivity analyses Cost/QALY gained (in £'000)

Variable and baseline		Uptake LTBI (50%)				Efficacy LTBI 62%)		Efficacy &Up	Progression rate TST + IGRA - (2%)		Progression rate IGRA + (10%)		TST return rate (53%)		Proportion asympt disease BA (0.17%)		Proportion asympt disease MI (0.09%)		Proportion asympt disease LI (0.04%)	
Min/Max variable	Base	35%	65%	80%	100%	40%	100%	100%	1%	4%	3%	17%	30%	90%	0%	0.4%	0%	0.2%	0%	0.1%
BA TST	15.9	19.6	13.8	12.6	11.5	40.8	2.4	CS	17.1	14.0	155.0	2.0	15.9	15.9	15.9	15.9	15.9	15.9	15.9	15.9
BA MI TST	18.2	23.3	15.5	13.8	12.3	44.8	3.8	0.5	19.4	16.5	171.1	3.3	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2
BHIVA 2011	40.0	56.4	31.3	25.8	21.0	80.9	16.7	5.8	40.0	40.0	329.6	14.9	40.0	40.0	40.0	40.0	40.0	40.0	40.0	40.0
BA TST&CXR	21.9	24.9	19.7	18.1	16.5	34.4	10.7	5.2	22.7	20.6	53.8	10.2	21.9	21.9	52.8	7.3	21.9	21.9	21.9	21.9
BHIVA strategy with CXR	34.3	39.3	30.5	27.5	24.4	45.9	22.2	12.1	34.3	34.3	63.7	20.9	34.3	34.3	100.4	12.1	34.3	34.3	34.3	34.3
BA IGRA	28.1	39.3	22.1	18.3	15.0	60.0	9.8	2.3	28.1	28.1	254.6	8.4	28.1	28.1	28.1	28.1	28.1	28.1	28.1	28.1
NICE 2011	174.6	248.6	134.8	109.9	88.3	315.3	94.3	44.5	174.6	174.6	1,172.6	88.1	174.6	174.6	174.6	174.6	174.6	174.6	174.6	174.6
All TST	38.8	49.9	32.8	29.1	25.8	86.8	14.7	7.5	43.7	32.2	245.5	15.0	38.8	38.8	38.8	38.8	38.8	38.8	38.8	38.8
BA MI TST&CXR	28.1	32.2	25.0	22.8	20.5	41.6	15.5	8.1	28.9	26.8	62.2	14.9	28.1	28.1	53.8	13.3	33.6	22.9	28.1	28.1
BA IGRA&TST	39.4	54.2	31.4	26.4	22.0	81.6	16.0	6.1	40.5	37.5	302.1	14.7	38.4	40.9	39.4	39.4	39.4	39.4	39.4	39.4
BA IGRA&CXR	28.6	35.7	23.9	20.7	17.6	47.3	13.7	5.3	28.6	28.6	92.1	12.4	28.6	28.6	48.2	15.5	28.6	28.6	28.6	28.6
BA MI IGRA	32.7	45.8	25.6	21.2	17.3	68.0	12.5	3.6	32.7	32.7	283.3	10.9	32.7	32.7	32.7	32.7	32.7	32.7	32.7	32.7
BA TST&CXR&IS	38.0	43.0	34.3	31.3	28.3	51.8	24.1	14.1	39.0	36.5	70.1	23.5	38.0	38.0	68.8	20.2	38.0	38.0	38.0	38.0
BA MI IGRA&TST	44.9	62.5	35.5	29.6	24.5	91.0	19.2	7.6	45.9	43.4	340.5	17.7	44.2	46.0	44.9	44.9	44.9	44.9	44.9	44.9
BA IGRA&CXR&IS	39.3	47.7	33.5	29.3	25.2	58.4	22.5	10.8	39.3	39.3	96.5	20.9	39.3	39.3	59.1	24.9	39.3	39.3	39.3	39.3
BA MI IGRA&CXR	34.7	43.5	28.9	24.9	21.1	56.2	17.6	7.4	34.7	34.7	108.2	16.1	34.7	34.7	49.9	22.6	38.4	30.8	34.7	34.7
All CXR	85.8	85.8	85.8	85.8	85.8	85.8	85.8	85.8	85.8	85.8	85.8	85.8	85.8	85.8	207.0	42.7	105.6	69.3	131.0	52.9
BA MI TST&CXR&IS	48.9	55.2	44.0	40.1	36.0	64.0	32.9	19.9	49.8	47.3	84.0	32.1	48.9	48.9	75.8	30.5	55.1	42.8	48.9	48.9
All TST&CXR	62.8	71.4	56.4	51.4	46.4	86.1	40.6	25.0	66.1	57.8	112.2	41.0	62.8	62.8	93.5	41.3	70.0	55.7	77.6	47.3
BA MI IGRA&CXR&IS	47.9	58.2	40.7	35.5	30.4	70.2	28.3	14.1	47.9	47.9	115.2	26.4	47.9	47.9	63.8	34.4	51.9	43.7	47.9	47.9
All IGRA	72.4	102.6	56.1	46.0	37.2	137.2	35.4	15.1	72.4	72.4	532.2	32.5	72.4	72.4	72.4	72.4	72.4	72.4	72.4	72.4
BHIVA 2016	90.5	126.4	71.1	59.0	48.6	175.1	45.1	21.4	94.9	83.9	557.1	43.7	89.4	92.2	90.5	90.5	90.5	90.5	90.5	90.5
All IGRA&TST	99.6	139.1	78.3	65.0	53.4	192.6	49.6	23.6	104.5	92.3	613.0	48.0	98.4	101.4	99.6	99.6	99.6	99.6	99.6	99.6
All IGRA&CXR	77.0	95.4	64.6	55.8	47.2	112.7	47.0	24.3	77.0	77.0	190.5	44.3	77.0	77.0	98.5	58.4	82.5	71.2	88.0	64.0
All TST&CXR&IS	103.7	115.6	94.3	86.7	78.5	130.1	75.4	49.3	107.7	97.7	156.0	75.9	103.7	103.7	137.4	76.8	112.1	95.2	120.6	84.7
All IGRA&TST&CXR	94.9	116.7	80.4	70.0	60.0	141.5	57.6	31.4	98.0	90.2	225.3	56.3	94.1	96.2	120.0	73.2	101.4	88.2	107.8	79.7
All IGRA&CXR&IS	104.4	124.9	89.7	78.7	67.8	141.4	69.7	39.2	104.4	104.4	209.2	66.3	104.4	104.4	127.0	83.6	110.3	98.0	116.2	89.9
All IGRA&TST&CXR&IS	119.2	141.9	103.0	90.9	78.9	164.5	78.4	45.3	122.3	114.2	233.7	76.9	118.6	120.0	144.1	96.2	125.8	112.2	132.2	103.2
All IGRA&TST&CXR & IS&PCR	144.0	171.8	124.3	109.5	94.7	197.7	95.7	55.5	147.8	138.2	279.8	93.9	143.7	144.6	173.5	116.9	151.8	135.8	159.4	125.2

Appendix Table 4: Univariate sensitivity analyses Cost/QALY gained (in £'000)

Variable and baseline		QALY loss LTBI (0.007)		QALY loss active (0.676)		QALY loss subclinical (0.2)		Worst case	Best case	With onward transmission prevented (R)			
Min/Max variable	Base	0	0.05	0.352	1	0.01	0.3			0.2	0.4	1.0	2.0
BA TST	15.9	12.6	D	40.1	9.9	15.9	15.9	D	CS	12.6	10.5	6.9	4.4
BA MI TST	18.2	14.6	D	45.6	11.4	18.2	18.2	D	CS	14.5	12.0	8.0	5.1
BHIVA 2011	40.0	33.4	D	94.3	25.4	40.0	40.0	D	CS	32.2	26.9	18.0	11.6
BA TST&CXR	21.9	19.1	233.1	60.4	13.4	18.7	24.1	D	CS	17.2	14.2	9.3	5.9
BHIVA strategy with (	34.3	31.5	75.9	93.8	21.0	28.1	38.9	394.5	CS	34.3	34.3	34.3	34.3
BA IGRA	28.1	23.4	D	66.1	17.8	28.1	28.1	D	CS	22.5	18.8	12.6	8.1
NICE 2011	174.6	145.5	D	411.3	110.8	174.6	174.6	D	CS	140.2	117.1	78.4	50.5
All TST	38.8	29.2	D	107.0	23.7	38.8	38.8	D	CS	30.5	25.1	16.4	10.4
BA MI TST&CXR	28.1	24.7	169.3	77.4	17.1	23.7	31.1	D	CS	22.1	18.2	11.9	7.5
BA IGRA&TST	39.4	31.9	D	96.2	24.7	39.4	39.4	D	CS	31.4	26.2	17.4	11.2
BA IGRA&CXR	28.6	25.0	218.8	72.6	17.8	25.6	30.5	D	CS	22.7	18.8	12.5	8.0
BA MI IGRA	32.7	27.2	D	76.9	20.7	32.7	32.7	D	CS	26.2	21.9	14.7	9.4
BA TST&CXR&IS	38.0	34.0	144.5	107.3	23.1	31.3	42.9	D	CS	29.8	24.5	16.0	10.1
BA MI IGRA&TST	44.9	36.7	D	108.8	28.3	44.9	44.9	D	CS	35.9	29.9	19.9	12.8
BA IGRA&CXR&IS	39.3	35.0	158.6	102.5	24.3	34.0	42.8	D	CS	31.1	25.8	17.0	10.8
BA MI IGRA&CXR	34.7	30.3	277.3	87.9	21.6	31.1	36.9	D	CS	27.5	22.8	15.1	9.7
All CXR	85.8	85.8	85.8	268.6	51.0	61.3	108.6	119.0	58.1	85.8	85.8	85.8	85.8
BA MI TST&CXR&IS	48.9	44.0	148.2	137.9	29.7	39.8	55.5	3,243.1	CS	38.3	31.5	20.5	13.0
All TST&CXR	62.8	54.0	7,165.3	184.3	37.8	52.1	70.3	D	CS	49.0	40.2	26.1	16.4
BA MI IGRA&CXR&I	47.9	42.6	198.2	124.6	29.6	41.5	52.1	D	CS	37.9	31.4	20.7	13.2
All IGRA	72.4	60.3	D	170.5	46.0	72.4	72.4	D	CS	58.1	48.5	32.5	20.9
BHIVA 2016	90.5	71.6	D	229.4	56.4	90.5	90.5	D	CS	74.5	62.2	41.7	26.9
All IGRA&TST	99.6	78.8	D	252.4	62.0	99.6	99.6	D	CS	79.1	65.6	43.4	27.8
All IGRA&CXR	77.0	68.0	405.0	198.1	47.8	67.7	82.9	D	CS	61.0	50.6	33.4	21.3
All TST&CXR&IS	103.7	92.0	471.9	308.7	62.3	83.3	119.1	D	CS	80.8	66.2	42.9	27.0
All IGRA&TST&CXR	94.9	80.8	D	257.1	58.2	83.7	102.1	D	CS	74.8	61.7	40.5	25.7
All IGRA&CXR&IS	104.4	93.9	331.8	276.1	64.3	88.7	115.1	D	CS	82.5	68.2	44.8	28.5
All IGRA&TST&CXR	119.2	103.8	1,336.5	329.5	72.7	101.5	131.2	D	CS	93.6	77.1	50.4	32.0
All IGRA&TST&CXR & IS&PCR	144.0	125.4	1,615.2	398.2	87.9	122.6	158.6	D	CS	113.2	93.2	61.0	38.7

Appendix Table 4: Univariate sensitivity analyses Cost/QALY gained (in £'000)

ART - antiretroviral therapy, BHIVA - British HIV Association, CD4 - blood CD4 cell count in cells/μL, CS - cost saving, D - dominated (lose more QALYs than no testing) CXR - chest X ray,
IGRA - Interferon-gamma release assay, LI - low [TB] incidence countries, MI - middle [TB] incidence countries, NICE - National Institute of Health and Care Excellence, PLHIV - People living with HIV, QALY - Quality adjusted life year, TB - tuberculosis, TST - tuberculin skin test.

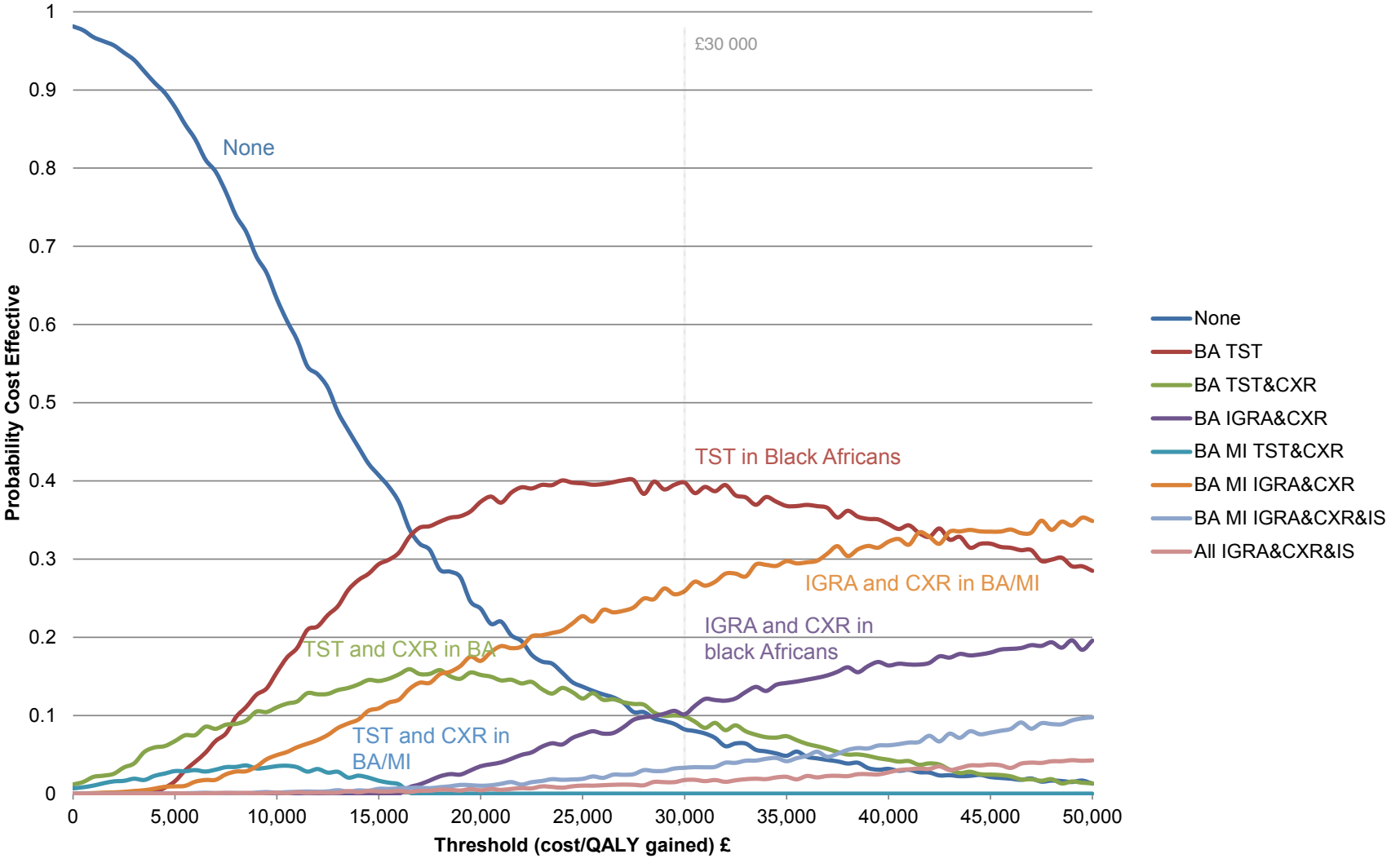
BHIVA 2011: IGRA only in subSaharan Africa with any CD4 on ART < 2 years, MI with CD4 <500 on ART < 2 years, LI with CD4 <350 on ART < 6 months.

NICE 2011: IGRA + TST if blood CD4 <200 and IGRA alone if blood CD4 <500.
NICE 2016: IGRA + TST if blood CD4 <200 and IGRA alone in all others.

These univariate and multivariate analyses assume no onward transmission, except in transmission column, where R stands for the number of subsequent cases of active TB prevented by stopping transmission from each active case of TB.

Worse case uses most expensive TST, IGRA, CXR, sputum induction, latent TB treatment; lowest uptake for tests and lowest efficacy; cheapest cost of treatment of active TB. Best case uses least expensive TST, IGRA, CXR, sputum induction, latent TB treatment; highest uptake for tests and highest efficacy; most expensive cost of treatment of active TB. These do not include transmission.

Appendix Figure 2: Cost effectiveness acceptability curve for TB testing strategies inc transmission



Exclusion criteria from the study:

Already undergoing treatment or active or latent TB
Inability to undergo sputum induction (e.g. pneumothorax, rib fracture, hypotensive, severe airways disease)
Pregnancy
Use of immunosuppressive medications
Active solid organ or haematological malignancy
Extensive eczema
Unable to give informed consent

Definition of positive and borderline T.SPOT-TB tests [16]
(from Oxford Immunotec. T-Spot.TB package insert. Abingdon, Oxford, United Kingdom.)

A positive T-Spot.TB result was defined a difference of ≥6 spots between either CFP10 or ESAT6 antigen panels and the nil control panel , <6 spots defined as a negative result. Where the difference between the higher of both panels and nil control was 5,6, or 7 spots, the result was considered borderline. A positive control of <20 spots in the context of a negative sample or nil control >10 spots was considered indeterminate. Borderline and indeterminate results were retested two weeks later.

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