Tuberculosis among people living with HIV: can we prevent a million TB deaths by 2015?[1]

Abstract

In line with the TB targets for Millennium Development Goal 6 and the Global Plan to Stop TB, UNAIDS, WHO and the Stop TB Partnership have agreed on a target of reducing the number of TB deaths among HIV infected people by half between 2004 and 2015. Here we use a mathematical (cohort) model to investigate whether and how this target can be reached, or even exceeded, by implementing a combination of interventions against TB and HIV. We find that, by diagnosing and treating TB patients more effectively in clinics and in the community, and by providing wider access to TB preventive therapy, it is feasible to halve the number of HIV-related TB deaths by 2015. Indeed, given the high efficacy of present diagnostics and drugs when used in combination, as many as 80% of TB deaths could be prevented by 2015. This more intensive strategy would save more than a million lives that would otherwise be lost to TB between now and the end of 2015. Our analysis is conservative in that we have not yet included the additional benefits of co-trimoxazole preventive treatment offered to people living with HIV, antiretroviral therapy (ART) taken during the course of TB treatment, or reductions in TB transmission. However, while the present set of tools for control offers very substantial clinical and epidemiological benefits in principle, there are major financial and logistical challenges to their widespread implementation.

Methods

Because TB deaths among HIV-infected people are expected to respond quickly to improved interventions (within a year or two), and because the effects of these interventions on transmission are smaller and occur over a longer period (beyond 2015), we use a cohort-model to track the impact of control on a cohort of people assumed to be in a steady state (Appendices).

We start with a cohort of people assumed to be of age $a = 25$ years since this is the median age of people infected with HIV. We take as given the annual risk of TB infection, ARI, from which we calculate the proportion of people with and without a latent infection when they enter the cohort. We assume that they have all just been infected with HIV and we follow the cohort for 50 years. During this time we let their CD4$^+$ cell counts fall, as

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[1] Analysis carried out by Brian Williams and Christopher Dye for the Stop TB Partnership (STP) and the StopTB Department of the World Health Organization (STB), with advice from a steering group including Annabel Baddeley (STP), Lucica Ditiu (STP), Haileyesus Getahun (STB), Philippe Glaziou (STB), Reuben Granich (WHO/HIV), Judith Mandelbaum-Schmid (STP), Craig McClure (WHO/HIV), Tunga Namjilsuren (WHO/HIV), Alasdair Reid (UNAIDS), and Joel Spicer (STP).

described in more detail in the Appendices. Their risk of dying at any time after entering the cohort follows the standard Weibull distribution[1,2] and the risk of developing TB, if they already have a latent infection, increases exponentially as their CD4$^+$ cell count decreases.[3,4] They may be offered an HIV test at a predetermined rate; they may then be started on antiretroviral therapy (ART), isoniazid preventive therapy (IPT), cotrimoxazole preventive therapy (CPT) or some combination thereof. ART reduces AIDS related mortality and the likelihood that people will develop TB; isoniazid reduces the likelihood that they will develop TB. Full details of the model structure, transitions and parameter are given in Appendix 1. Details of the relationship between CD4$^+$ cell counts and time since seroconversion are given in Appendix 2, of the background mortality calculations and the impact of ART on mortality and TB incidence in Appendix 3, of the effect of CPT on TB mortality in Appendix 5, and of the effect on ART on TB case fatality rates in Appendix 6.

Interventions and outputs

The model permits us to set the testing interval for HIV, to introduce ART at any given CD4$^+$ cell count, to start people on IPT as soon as they are found to be HIV-positive, to treat people for TB when they present at clinics (passive case-finding) or when they are tested for TB because they have been tested for HIV (active case-finding).

We follow the cohort for 50 years, after which everyone has died, and determine the number of a) TB cases treated; b) people given IPT; c) person years on ART; d) TB deaths; e) AIDS deaths; f) deaths from other causes; g) average life-expectancy in the cohort. We can also estimate the cost of treating a person for TB, of giving them a course of IPT or maintaining them on ART, and can therefore determine the cost of any given combination of interventions and the cost per life year saved.

Results

We ran the model to explore the conditions under which we could reduce HIV-related TB deaths by 50% and by 80% by 2015 (as compared with 2004). We start with the base-line scenario in which we use an exponential fit to extrapolate the current number of TB deaths up to 2015 (based on WHO estimates). This is shown in Figure 1. Under the base-line scenario TB deaths will continue to decrease at a rate of 1.1% per year for the next five years.

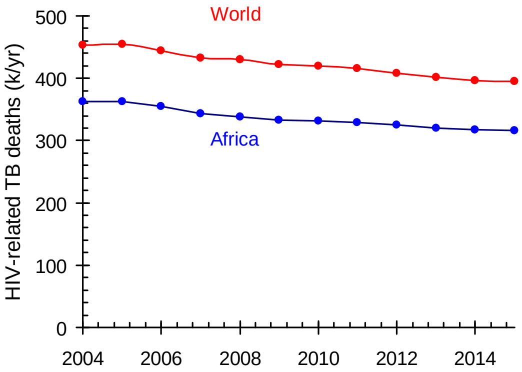

Figure 1. The base-line data for the number of HIV-associated TB deaths up to 2015. The data up to 2010 are WHO estimates and an exponential trend line is used to extrapolate the data up to 2015.

Reducing TB deaths by 50% by 2015

Figure 2 and Table 1 show a set of interventions that should reduce HIV-associated TB deaths by 50% by 2015. The figure shows the cumulative reduction in deaths as we progressively add additional interventions. The series of 8 bars in Figure 2 represent:

Status quo

Bar 1. Limited TB control and use of ART (started at CD4 100/µL on average, resembling South Africa)

In TB clinics

Bar 2. Increasing the proportion of HIV-positive TB patients that present (passive case detection, PCD) for diagnosis and treatment at clinics before dying of TB.
Bar 3. Increasing the cure rate of HIV-positive TB patients by improved use of current anti-TB drugs.
Bar 4. Increasing the sensitivity of diagnosis of active TB by introducing the latest molecular diagnostic tools (mainly Xpert MTB/RIF).

In the population of people living with HIV at large

Bar 5. Molecular diagnostics used to test for TB among those who test positive for HIV (active case detection, ACD), after offering HIV testing to the whole population at 5-yearly intervals. The higher the proportion of people who decline the offer of an HIV test, the lower the impact.
Bar 6. IPT for people living with HIV who do not have active TB (e.g. test negative on Xpert MTB/RIF).
Bars 7–8. ART provided for HIV-infected people who have CD4 cell counts of either <200/µL or <350/µL.

The 7 interventions beyond baseline are introduced at equal intervals (5/7 of a year) over the period 2011 to 2015.

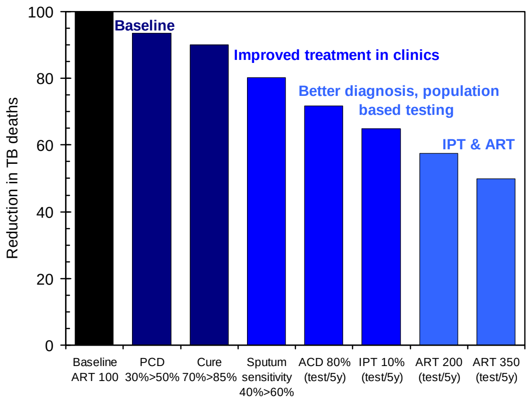

Figure 2. A set of interventions that could achieve a 50% reduction in HIV-associated TB deaths by 2015.

The order and coverage of interventions could vary, but the analysis in Figure 2 (with numbers in appendix 4) shows that cutting deaths by half is entirely feasible from the perspective of technical efficacy. It is important to note that the impact of successive interventions depends, in some cases, on what has gone before. For example, the impact of improving sputum sensitivity is greater if we assume that the case detection rate has already been increased.

Table 1. Cumulative reductions in the number of AIDS-related TB deaths under a scenario designed to reach a 50% reduction shown in Figure 2.

Baseline ART 100	100
PCD 30%>50%	93
Cure 70%>85%	90
Sputum sensitivity 40%>60%	80
ACD 80% (test/5y)	72
IPT 10% (test/5y)	65
ART 200 (test/5y)	57
ART 350 (test/5y)	50

The projected course of HIV-related TB mortality up to 2015 is shown in Figure 3, assuming that the interventions are rolled out in the order indicated in Figure 2 and Table 1 and that all are in place by 2015. Applied globally, this strategy saves more than half a million lives between 2011 and 2015 (587,000).

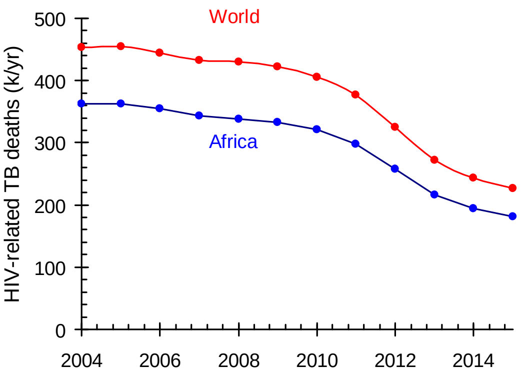

Figure 3. The expected reduction in HIV-related TB deaths between 2011 and 2105 under the interventions indicated in Figure 2.

Reducing TB deaths by 80% by 2015

Figure 4 and Table 2 show a set of interventions that should reduce HIV-associated TB deaths by 80% by 2015. The figure shows the cumulative reduction in deaths as we progressively add additional interventions.

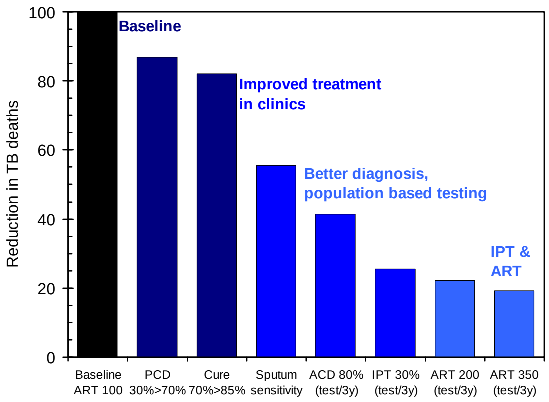

Figure 4. A set of interventions that could achieve an 80% reduction in HIV-associated TB deaths by 2015.

Table 2. Cumulative reductions in the number of AIDS-related TB deaths under a scenario designed to reach a 80% reduction shown in Figure 4.

Baseline ART 100	100
PCD 30%>70%	87
Cure 70%>85%	82
Sputum sensitivity 40%>80%	55
ACD 80% (test/3y)	41
IPT 30% (test/3y)	26
ART 200 (test/3y)	22
ART 350 (test/3y)	19

The projected course of HIV-related TB mortality up to 2015 is shown in Figure 5, assuming that the interventions are rolled out in the order indicated in Figure 4 and Table 2 and that all are in place by 2015. Applied globally, this strategy saves more than a million lives between 2011 and 2015 (1,064,000).

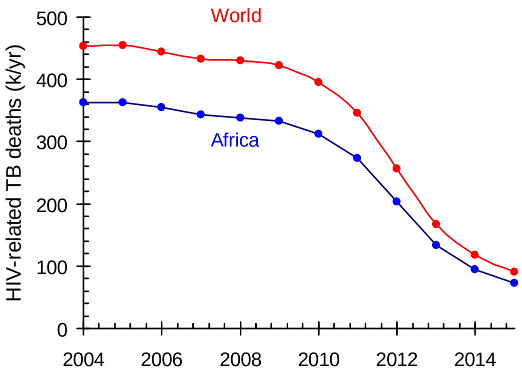

Figure 5. The expected reduction in HIV-related TB deaths between 2011 and 2105 under the interventions indicated in Figure 4.

TB mortality and life expectancy

The cumulative increase in life-expectancy under the scenario intended to reduce TB deaths by 80% by 2015 is shown in Figure 6. This shows that while TB treatment reduces the number of TB deaths the danger is that people cured of TB will die of other causes if they are not started on ART and the earlier they start on ART the greater will be the increase in life expectancy.

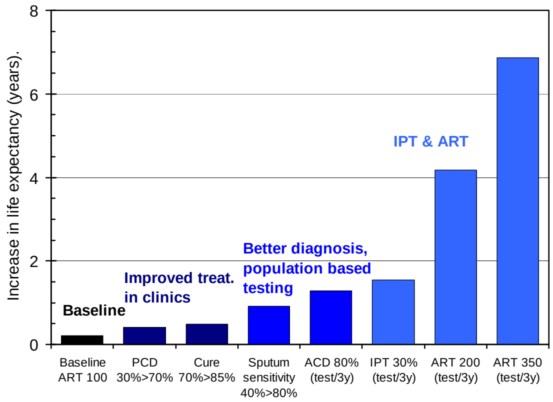

Figure 6. Cumulative increase in life-expectancy under the set of interventions that reduces TB deaths by 80% by 2015.

Costs, effects and cost-effectiveness

The data in Figure 6 also allow us to calculate the cumulative cost and the marginal costs per life year gained. As expected, the costs of providing ART are considerably greater than the costs of TB treatment, bearing in mind that everyone in the cohort is assumed to be HIV-positive (Figure 6, left). However, the number of life-years gained by providing ART is greater than the number gained through treating TB so that the marginal costs per life year gained by providing ART are only about double those of treating people for TB (Figure 6, right).

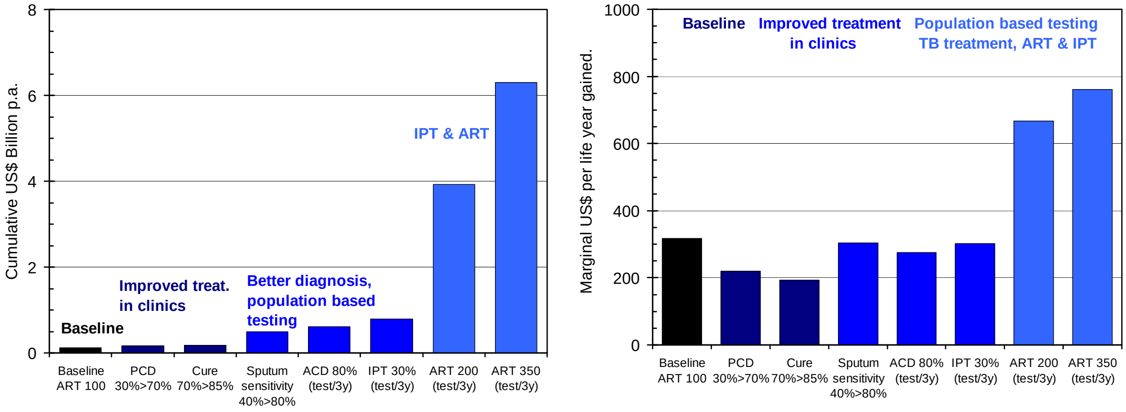

Figure 7. Cumulative (left) and incremental (right) cost per life year saved under the set of interventions that reduces TB deaths by 80% by 2015.

The costs of taking each successive step towards 50% and 80% reduction in deaths in 2015 are given in the following two tables.

For a 50% reduction in mortality in 2015

6 intervention steps in 5 years	Cost $bn/step	Deaths averted	Cumulative deaths averted	Cumulative costs ($bn)	Cumulative cost/death averted
0	0.01	0	0	0.01	
1	0.03	41	34	0.04	1037
2	0.12	44	71	0.14	1974
3	0.16	71	130	0.27	2075
4	0.16	85	200	0.40	2006
5	0.45	125	305	0.77	2535
6	0.36	171	448	1.08	2406
7	0.42	198	613	1.42	2323

Deaths averted = 198 thousand

Total costs = US$ 1.4 billion (US$ 280M/year)

Cost per death averted = US$ 2323

For a 80% reduction in mortality in 2015

6 intervention steps in 5 years	Cost $bn/step	Deaths averted	Cumulative deaths averted	Cumulative costs ($bn)	Cumulative cost/death averted
0	0.01	0	0	0.01	
1	0.03	41	35	0.04	1029
2	0.12	44	71	0.14	1955
3	0.17	98	153	0.28	1813
4	0.17	118	252	0.42	1674
5	0.49	230	443	0.83	1881
6	0.61	282	678	1.34	1975
7	0.79	345	966	2.00	2071

Deaths averted = 967 thousand (approx. 1 million)

Total costs = US$ 2 billion (US$ 400M/year)

Cost per death averted = US$ 2071

Discussion

With the technology and interventions that are now available, it is technically feasible to reduce HIV-associated TB deaths by 50% by 2015 and, with further modest improvements to TB treatment and testing people more frequently for HIV, to reduce HIV-associated deaths by 80% by 2015. TB treatment averts HIV-associated TB deaths and is more cost-effective in this regard than starting people on ART. However, the benefits of averting TB deaths are much reduced if people then die of other causes because their immune systems are severely compromised. Many more life-years can be gained by also starting people on ART and for this reason the costs per life year gained through the provision of ART are only about double the costs per life year gained by finding, diagnosing and treating people for TB more effectively.

We have developed a separate model for TB in people who are HIV-negative and we have not included any benefits of the interventions described here on TB among HIV-negative people (e.g. community-based testing for HIV infection potentially has benefits for those who test negative for HIV and TB through access to IPT; efforts to recruit more HIV-positive TB patients to clinics will also draw in people who are HIV-negative, etc). Neither have we included the impact of TB control programmes in cutting TB transmission from HIV-negative to HIV-positive people.

Because TB disease duration varies more or less inversely with the TB incidence when people are HIV-positive[4] the effect of HIV is to drive up the incidence, but not the prevalence, of TB as first demonstrated by Corbett *et al.*[5-7] As a result, the incidence of TB in HIV-negative people is only marginally affected by the much higher incidence in HIV-positive people. The prevention packages suggested here, excluding of course those relating to HIV, should reduce TB mortality by 80% or more but the increase in overall life expectancy will not be substantial because TB incidence is low in HIV-negative people. Details of these calculations will be made available elsewhere.

We have not explicitly included the effect of CPT, which appears to reduce the mortality rate of HIV-positive people on ART by about 5% in year one after the start of treatment and only among those with a $CD4^+$ cell count below about 200/µL (Appendix 5). This is an order of magnitude less than the reduction due to ART. From the perspective of individual patients CPT is very cheap, will benefit those with very low $CD4^+$ cell counts, and will reduce the likelihood that they develop other opportunistic infections. For these reasons CPT should be given but the population level effect will be small.

It is clearly better for the individual TB patients to start ART as soon as they start TB treatment,[8] especially for patients with low CD4 cell counts. Under trial conditions immediate ART for TB patients reduced the TB case fatality rate from 6% to 3% (Appendix 6). Our present calculations do not include this extra benefit for TB patients. Thus far we have simply assumed that the cure rate for HIV-positive TB patients is 85%, and that all those that are not cured will die within one year.

While this cohort model demonstrates what can be achieved in principle in the short term, the actual impact by MDG target date 2015 will depend on the extent to which these interventions can be implemented. What can be achieved beyond 2015 depends on whether coverage can be maintained, and the effect this has in reducing transmission. Evaluating these longer-term impacts – for specific countries, for regions and globally – is the subject of continuing analysis.

Appendix 1. Model, parameters and initial conditions

Model structure

The model is illustrated schematically in Figure 8 for a given time after the start of the cohort and is repeated at annual intervals. The model includes people with and without latent TB infection, (L^+ and L^-), on and off ART (A^+ and A^-) and with TB disease (T).

During the course of each year t ($t = 0$ to 50) the following transitions take place:[2]

1. People who are not on ART die at a rate

$$\mu^-(t) = \frac{1}{W(t)}\frac{dW(t)}{dt} \qquad 1$$

where $W(t)$ is a Weibull survival function so that

$$\mu^-(t) = \ln(2)s\left(\frac{t}{m}\right)^{s-1}. \qquad 2$$

The median survival is typically $m = 11$ years and the shape parameter is usually taken to be $s = 2.25$.[2]

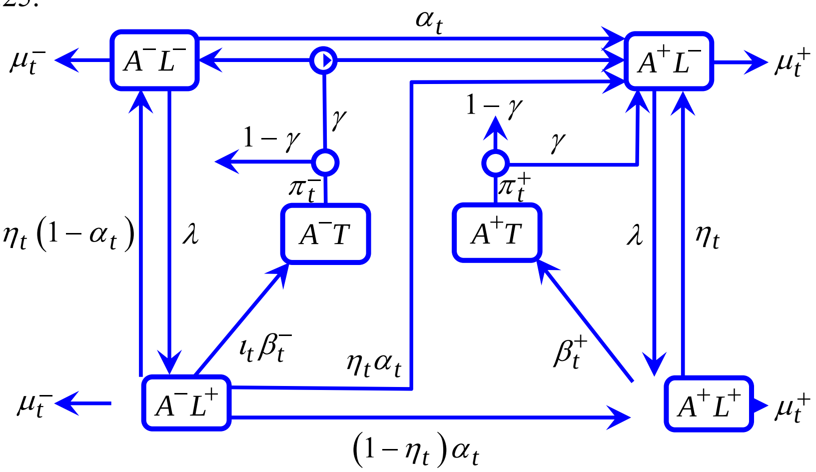

Figure 8. Schematic diagram of the HIV-TB model. A^+ and A^- for those on ART and not on ART, and L^+ and L^- for those with and without a latent TB infection, respectively. T those with TB disease. Rate parameters given in the text.

2. People acquire latent infection at a rate λ which we will take to be the annual risk of infection, ARI, calculated as $\lambda = 20I_{\text{TB}}$, where I_{TB} is the incidence of TB among HIV-negative people (pre-HIV).
3. People are offered an HIV test at random but on average once every τ years so that the probability of being tested in each year is $1/\tau$.[3]
4. People with a latent infection develop TB at a rate β_t^- if they are not on ART. We assume that

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[2] Note that any of the parameter values can be changed in the model.

[3] We explored the effect of testing at regular fixed intervals rather than randomly. The impact of treatment is greater under regular testing since under random testing some people are tested more often than is needed while some are never tested. However the difference is not great and random testing will always be conservative with regard to the impact of treatment.

$$\beta_0 = \beta I^{-} \tag{3}$$

so that the incidence of TB immediately after seroconversion is β times the incidence of TB in HIV-negative people, typically taken to be about 2, and

$$\beta_t^{-} = \beta_0 \, \mathrm{e}^{\varepsilon t} \tag{4}$$

so that the incidence of TB increases exponentially with time after sero-conversion. Typically the incidence is thought to increase at a rate of about 36% for each drop of 100 CD4^{+} cells.[3,4] If we assume that people lose 75 CD4^{+} cells per year then $\varepsilon = 0.36 \times 75 = 0.27$/year.

5. People start ART at a rate $\alpha_t = a_t / \tau$ where a_t will depend on whether or not people are eligible to start ART, if they are not $a_t = 0$, the coverage of HIV-testing and the sensitivity of the HIV test.
6. ART reduces mortality by a factor of about 2, so that people who are on ART die at a rate
$$\mu^{+}(t) = 0.5\mu^{-}(t)\,. \tag{5}$$
7. ART also reduces the incidence of TB by about 60% so that 0.4 so that
$$\beta_t^{-} = \beta_0 \, \mathrm{e}^{\varepsilon t}\,. \tag{6}$$
8. We assume that the proportional reduction in mortality and TB incidence are both independent of time since sero-conversion.
9. If people who test positive for HIV, are not on ART and do not have TB, they may be started on isoniazid preventive therapy (IPT) which further reduces the incidence of TB disease by a factor ι_t, which we take to be about 0.4.
10. The effect of CPT is to reduce mortality by a factor m_η, which we take to be about 0.7, and which we take to be independent of time since sero-conversion.
11. A proportion of those that have TB will present themselves to the TB services where a proportion γ will be treated and cured. We assume that this proportion is independent of the time since sero-conversion and whether or not the person is on ART. While these assumptions may not hold we do not have data to suggest otherwise. Those that are not cured will die in that year. The value of γ will depend on the likelihood that HIV-positive people with TB present to the health services before they die, the sensitivity of the TB test and the TB cure rate.
12. The duration-incidence parameter determines the relationship between the incidence of TB, *I*, (as CD4^{+} cell counts decline) and the duration of disease, *D*. The assumed relationship is
$$\frac{D_1}{D_0} = \left(\frac{I_0}{D_1}\right)^{\delta} \tag{7}$$
so that when $\delta = 0$ the disease duration is independent of the incidence (and is therefore the same for HIV-positive and HIV-negative people) while if $\delta = 1$ the disease duration is inversely proportional to the incidence so that the prevalence, *DI* is independent of incidence.[4] This in turn determines the rates, π_t^{+} π_t^{-} , and at which people progress from the disease class to cure, natural cure or death.

13. People in all categories experience a background mortality rate, not shown in Figure 8, assuming that the survival is also Weibull but with a shape parameter of 10 and a median survival of a further 45 years from infection at age 20 years.

Costs

We set the cost of treating one case of TB at US$100; the cost of providing one person with IPT at US$100; the cost of maintaining one person on ART at US$500 per year; the cost of one HIV test at US$5; the cost of examining one person for TB at US$300.

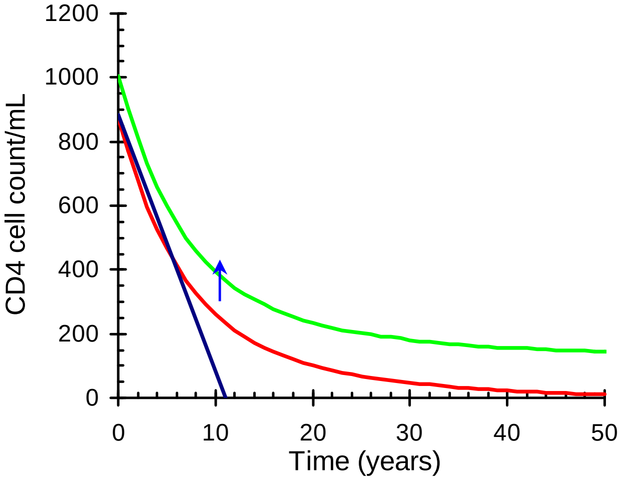

Figure 9. CD4$^+$ cell count as a function of time since infection. Red line: Not on ART; green line: on ART. If, for example, people are started on ART 10 years after infection, then their CD4$^+$ cell count will be, on average 250/µL. If they start ART their CD4$^+$ cell count will increase to 554/µL. They will then progress down the green line rather than the red line.

Appendix 2. CD4$^+$ cell counts and time since seroconversion

Since we follow a cohort of incident cases with each stage lasting for one year we need to determine the mean CD4$^+$ cell count as a function of time since seroconversion since the ART interventions will depend on CD4$^+$ cell counts rather than time since sero-conversion. To do this we assume that survival is independent of initial CD4$^+$ cell counts[9] and use the distribution of CD4$^+$ cell counts in HIV-negative people from South Africa.[9] For other countries we will assume that the shape of the distribution is the same but the whole distribution is scaled to give the best estimate of the mean CD4$^+$ cell count for that country. Using a Monte-Carlo integration the relationship, for South Africa, is given by the red line in Figure 9. The usual approach assumes that everyone starts at the mean CD4$^+$ cell count of about 900/µL, allowing for the initial 25% drop and dies after 11 years as shown by the dark blue line in Figure 9. For the first five years after sero-conversion the mean CD4$^+$ cell as a function of time is quite similar with the two approaches. After that they diverge because although fewer and fewer people are still alive, among those that are alive the CD4$^+$ cell count is, of course, greater than zero.

In this model we proceed as follows. If people in the cohort are tested at a given number of years after sero-conversion we use the relationship in Figure 9 to determine their mean CD4$^+$ cell count and if it is below the threshold for treatment they all become eligible for treatment. We could carry this one step further and work out the proportion of people whose CD4$^+$ cell count is below the threshold at any given time after sero-conversion and then let this proportion be eligible for treatment. I do not think that this would change the result significantly.

Appendix 3. Mortality calculations and effect of ART on TB incidence

Background mortality

We also need to make assumptions about the background mortality. Although it is generally much lower than the AIDS related mortality we want to avoid long exponential tails on the survival curves to facilitate convergence. We therefore use a Weibull survival function with a large value of the shape parameter which allows us to fit the background mortality to population level data if we so choose. With a median survival of 65 years and a shape parameter of 10 we get the survival curve shown in Figure 10. We assume that the average age at infection is 30 year so that the mean survival without ART from the age at which the cohort starts would be 45 years.

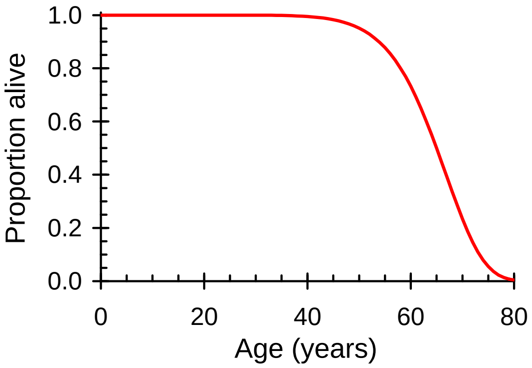

Figure 10. The background survival curve with a median of 65 years and a shape parameter of 10.

Mortality on ART

We assume that the effect of starting people on ART is to reduce their mortality, from that point onwards, by a fixed factor (Note 27). For a Weibull survival the functional form of the survival curve is

$$S(t) = 2^{-(t/m)^k}, \tag{8}$$

where m is the median survival and k is the shape parameter, so that the mortality at time t is

$$\frac{dS(t)}{S(t)dt} = -\ln(2)\frac{k}{m}\left(\frac{t}{m}\right)^{k-1}. \tag{9}$$

To reduce the mortality at any time by a factor of ρ, say, we increase the value of m in Equation 9 by a factor of m^k which, from Equation 8 will also increase the median survival by the same factor.

Effect of ART on TB incidence

We need to know the extent to which ART restores CD4$^+$ cells. For want of a better model we will assume that ART reduces the incidence of TB by 60% from the level that they are at and which increases as peoples CD4$^+$ cell count declines. This is equivalent to assuming that the effect of ART is to restore a persons CD4$^+$ cell count by an amount

$$\Delta C = -\frac{\ln(0.4)}{\alpha}. \qquad 10$$

With $\alpha = 0.0036/\mu\text{L}$ we get $\Delta C = 255/\mu\text{L}$. This is illustrated by the green line in Figure 9.

Appendix 4. Numbers associated with figures in the text

Table 1. Numbers corresponding to the data in Figure 1.

Year	AFRO	World
2004	363	454
2005	362	455
2006	355	444
2007	344	433
2008	338	430
2009	333	422
2010	332	420
2011	329	416
2012	325	408
2013	320	401
2014	317	397
2015	316	395

Table 2. Numbers corresponding to the data in Figure 3.

Year	AFRO	World
2004	363	454
2005	362	455
2006	355	444
2007	344	433
2008	338	430
2009	333	422
2010	321	406
2011	298	377
2012	257	325
2013	217	272
2014	194	243
2015	182	227

Table 3. Numbers corresponding to the data in Figure 5.

Year	AFRO	World
2004	363	454
2005	362	455
2006	355	444
2007	344	433
2008	338	430
2009	333	422
2010	312	395
2011	273	346
2012	203	256
2013	133	167
2014	94	118
2015	73	91

Appendix 5. Cotrimoxazole Preventive Therapy

Two key studies present data on the way in which the benefit of CPT varies over time since the start of ART. The first shows that CPT reduces 12 month mortality in those starting ART as shown in Table 4[10]

Table 4. One year mortality with and without CPT as a function of $CD4^+$ cell counts. Weibull is the mortality derived from the standard Weibull survival curve.

CD4/µL	Without CPT	With CPT	Weibull
< 200	0.17	0.09	0.16
200 to 350	0.06	0.03	0.10
> 350	0.04	0.03	0.06

Table 4 shows that our survival estimates using the Weibull function are about right and that for the first year CPT roughly halves the mortality at least at low $CD4^+$ cell counts. The relative risks of dying are: 0.52 (0.40 to 0.68) for CD4 < 200/µL; 0.92 (0.42 to 2.0) for $200/\mu L < CD4^+ < 350/\mu L$; 1.7 (0.5 to 5.2) $350/\mu L < CD4^+$.

The results of the DART trial[11] (Table 5) suggest that the effect of CPT in people starting ART is in the initial drop during the first year which is half as great if people are on CPT in both cases. For the next four years the slopes are the same suggesting that CPT gives no further benefit. These data seem optimistic especially for those starting ART at a CD4+ cell count of 15/micro-litre, but imply the result shown in Table 2.

Table 5. Mortality in year one and annual mortality in years 2 to 4 for people starting ART at $CD4^+$ counts of 15/µL and at 150/µL, with and without CPT Weibull is the mortality derived from the standard Weibull survival curve.

	Mortality in year 1		Mortality in years 2 to 5 (per yr)		
CD4/µL	Without CPT	With CPT	Without CPT	With CPT	Weibull
150	0.045	0.025	0.006	0.007	0.16
15	0.110	0.052	0.018	0.018	0.84

These results also suggest that adding CPT to ART halves mortality in year one but has no further benefit beyond that. The survival in years 2 to 5, on ART and with or without CPT, seems remarkably low. For those that start at 150/µL ART appears to reduce mortality in years 2 to 4 by about 26 times and for those that start at 15/µL by about 4 times.

For the purposes of this model we will assume that in year one after the start of CPT mortality falls from about 10% to about 5%. While this will be important for individuals and is very cheap to administer, the overall benefits will be much less than the long term benefits of providing ART and curing TB.

Appendix 6. ART and TB case-fatality rates

We need to know the effect of ART on TB treatment outcomes. A study has been carried out comparing the mortality among TB patients who start ART as soon as they start TB treatment, at the end of the intensive phase or after the end of treatment.[8] When people started treatment at the end of treatment (i.e. six months) the case fatality rate was 6%; when they started ART and TB treatment at the same time this was reduced to 3%.

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