Supplementary Material

In this supplement we derive the full form of the monetary and health costs of testing every T years, $g_c(T)$ and $g_h(T)$; we derive the approximation shown in (1); and we justify the baseline values of f_c and f_h and and those used in the sensitivity analysis.

Full form of $g_c(T)$ and $g_h(T)$

Let us define the following notation: $x \wedge y := \min\{x, y\}$ to denote the minimum of two numbers and $1\{\cdot\}$ to denote the indicator function. Let $X \sim Exp(h)$ be an exponential random variable with hazard rate h representing the time of an individual's infection since their last test. Thus $p := \Pr[X \leq T]$ is the probability that a test will detect an infection and the geometric random variable, $N \sim Geo(p)$, is the number of tests spaced T years apart until an infection is detected. We will only consider times T between tests that exactly divide a person's sexually active lifetime, τ. (This explains the staircase shape of Figure 1.) Hence over a person's sexually active lifetime, $N \wedge \tau/T$ tests will be administered. Thus the total discounted cost of testing is $\sum_{i=1}^{N \wedge \tau/T} Cr^{-iT}$. If a person tests positive, $X \leq T$, then the discounted cost of the delay is $F(T - X)r^{-NT}1\{NT \leq \tau\}$. Thus the total discounted expected monetary and health cost is

$$g_c(T) := C\mathbb{E}\left[\sum_{i=1}^{N \wedge \tau/T} (1+r)^{-iT}\right] + \mathbb{E}[F_c(T-X)|X \leq T]\mathbb{E}[(1+r)^{-NT}1\{NT \leq \tau\}],$$

$$g_h(T) := \mathbb{E}[F_h(T-X)|X \leq T]\mathbb{E}[(1+r)^{-NT}1\{NT \leq \tau\}.]$$

In the sensitivity analysis, we incorporate the probability, p, of an unsuccessful linkage to long-term HIV care, by multiplying the expected cost of delayed detection, $g_c(T)$ and $g_h(T)$, by p and adding to each expression $(1-p)K$, where K is the average societal monetary and health

cost for a newly diagnosed HIV positive patient unsuccessfully linked to long-term HIV care. However, since $(1-p)K$ does not depend on the testing frequency, we may remove from the modified expressions.

Deriving Approximation

Due to the assumption of linearity we can write, $F_c(t) = f_c t + F_c(0)$ and $F_h(t) = f_h t + F_h(0)$. To derive the approximation (1), we use the bound $\mathbb{E}\left[\sum_{i=1}^{N\wedge\tau/T} (1+r)^{-iT}\right] \leq \tau/T$, a conservative assumption that overestimates the cost of testing. Note that $p = Th + O(h^2)$, $\mathbb{E}[T - X | X \leq T] = T/2 + O(h)$, and $\mathbb{E}[(1+r)^{-NT} 1\{NT \leq \tau\}] = (\tau/T)p + O((p+r)^2)$. Substituting these approximations into (s.1), we obtain the approximation:

$$g_c(T) \approx C\frac{\tau}{T} + h\tau(f_c T/2 + F_c(0)), \qquad g_h(T) \approx h\tau(f_h T/2 + F_h(0)). \tag{1}$$

The $C\tau/T$ term approximates the lifetime cost of testing and the other terms are the product of the approximate lifetime probability of becoming infected, $h\tau$, and the monetary and health costs, $F_c(T/2)$ and $F_h(T/2)$, resulting from the expected lag, $T/2$, between infection and detection. Thus, the approximate incremental cost-effectiveness ratio (ICER) of testing every T_2 years instead of every T_1 years is

$$ICER = \frac{g_c(T_2) - g_c(T_1)}{g_h(T_1) - g_h(T_2)} \approx \frac{2C}{h f_h T_1 T_2} - \frac{f_c}{f_h}. \tag{2}$$

Calculating f_c and f_h

We now discuss the parameters in Supplementary Table 1 and then how they are combined to calculate f_c and f_h. As before, all costs are inflated to 2010 dollars.

Costs of HIV Treatment

Gebo et al. found the average annual expenditure on HIV care for 14,691 adults receiving treatment in 2006 at sites of the HIV Research Network to be $23,007 (1).

Life Expectancy

There are no cohort studies estimating the life expectancy of HIV positive individuals who initiated treatment at a CD4 count of 350/µl or above. Thus, we turn to the recent Antiretroviral Therapy Cohort Collaboration study (2). Aggregating 43,355 patients in high-income countries, they estimated a life expectancy of 37 years for an HIV positive 35-year-old initiating treatment above a CD4 count of 200/µl. This contrasts with an average remaining life expectancy for a 35-year-old of 45 years (3). In 2008, Braithwaite et al. estimated a life expectancy of 18 years for an HIV positive 30-year-old in the Veterans Aging Cohort Study who is starting therapy with a CD4 count of 500/µl and a viral load of 30,000. Due to its larger size, we use the figure from the Antiretroviral Therapy Cohort Collaboration study as our baseline estimate of the life expectancy of an average HIV positive individual initiating HAART immediately after infection, and we substitute the Braithwaite et al. figure in our sensitivity analysis.

Loss of QALYs

Braithwaite et al. provide a direct estimate for the loss in QALYs and unadjusted life years resulting from withholding comprehensive HIV treatment at an early stage in the progression of HIV in their model (4). For a 30-year-old HIV-positive patient with a

viral load of 30,000 starting treatment with a CD4 count of 350/µl, instead of 500/µl results in a loss of 0.7 QALYs and 0.7 unadjusted life years. Recent published estimates of the yearly decline in CD4 count range vary from 109/µl in (5), 66/µl in (6), 61/µl in (7) and 53/µl in (8). Thus, in the above scenario, waiting until the person's CD4 count drops to 350/µl will likely take roughly two years at a loss of 0.35 QALYs and 0.35 unadjusted life years per year. In the sensitivity analysis we consider a loss of 0.2 QALYs and 0.2 unadjusted life years per year.

Quality Multiplier for HAART

Recent estimates of the quality of life multiplier for HIV-positive individuals on highly-active antiretroviral treatment range from 0.73 to 0.83 (9-11). We use the intermediate value of 0.78.

Secondary Infections

We assume that each infected individual not on treatment causes 0.04 secondary infections per year. Following Sanders et al. we rely on three studies of heterosexual couples that find rates of 0.036 (12), 0.054 (13), and 0.048 (14). In addition, Cohen et al. find a transmission rate of 0.017 (15). Another way to estimate the rate of secondary transmissions is to divide the population level incidence (0.02% in the US (16, 17)) by the population level prevalence (0.6% (18)), giving a 3.3% rate of secondary infections. We consider a rate of 2% in the sensitivity analysis.

[Insert Supplementary Table 1 Here]

Calculating f_c

Delaying treatment for one year saves one year's worth of treatment at the beginning and 0.35 year's worth at the end (in 37 years). Thus the discounted monetary cost to the patient of delaying treatment for one year is $-\$1{,}007(1 + 1.03^{-37}) \approx -\$25{,}704$. In addition to the cost to the patient, delaying treatment one year causes 0.04 additional secondary infections each costing $\$1{,}007$ annually for 37 years, or $0.04 \sum_{t=1}^{37} \frac{\$1{,}007}{1.03^t} \approx \$20{,}400$. Adding the patient and societal costs yields $f_c \approx \$20{,}400 - \$25{,}704 = -\$5{,}304$.

Calculating f_h

Delaying treatment for one year results in a loss of 0.35 QALYs at the end of the patient's treatment in 37 years, or $\frac{0.35}{1.03^{37}} \approx 0.117$ discounted QALYs. In addition, delaying treatment infects 0.04 individuals who's life expectancy drops from 45 years at full health to 37 years with a quality multiplier of 0.78, or $0.04 \left[\sum_{t=1}^{45} 1.03^{-t} - \sum_{t=1}^{37} \frac{0.78}{1.03^t}\right] \approx 0.289$ discounted QALYs. This underestimates the QALYs lost because we assume that the secondary infections are immediately treated. Adding the patient and societal costs yields $f_h \approx 0.117 + 0.289 \approx 0.41$.

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Tables

Supplementary Table 1. Extended Set of Parameter Values*

Parameter	Value
Annual cost of HIV care ($) (1)	23,007
Life expectancy of HIV+ individual initiating treatment immediately (years) (2)	37
QALYs lost by delaying HAART by one year (4)	0.35
Life years lost by delaying HAART by one year (4)	0.35
QALY multiplier, on HAART (9-11)	0.78
Rate of secondary cases per year (%) (12-15)	4

* All costs are in 2010 dollars.