1 Appendix 1

The RITA proposed in this paper (RITA3) classifies all diagnosed and low viral load individuals as non-recent. Previous studies have used RITAs that classify treated individuals as non-recent using viral load and ARV biomarkers (RITA2). This is operationalized as a screening step where individuals are screened out of recency if any of the following conditions hold:

1. The subject is HIV negative.
2. The subject tests positive for ARV biomarkers.
3. The subject is virally suppressed (viral load $< 1{,}000$).

This relaxed RITA fits nicely into our framework. The only difference is that instead of diagnosis and assay recency combining to screen individuals out, treatment and assay recency are combined. Thus, our methods and formulas can be applied to this RITA provided we have an estimate of the probability that an individual infected t time units ago is on treatment. This may be available from an external source, but alternatively we can use the distribution of time from diagnosis to treatment in combination with the distribution of the time from infection to diagnosis. Time from diagnosis to treatment may be available from medical or administrative records, and time from seroconversion to diagnosis can be estimated using the methods in the main paper.

Let S_{Tr} be the event where an individual passes RITA2 screening and $w(t)$ be the probability that an individual is receiving treatment t time units after diagnosis. The probability an individual received their diagnosis at time x and is on treatment at time t is

$$w(t-x)\frac{d}{dx}(1-\hat{P}(S|T=x,H)) = -w(t-x)\frac{d}{dx}\hat{P}(S|T=x,H)$$

The estimated probability an HIV+ individual has not been screened out at time t is one minus the probability that they have been diagnosed at some point in the past and are on treatment

$$\hat{P}(S_{\text{Tr}}|T=t,H) = 1 + \int_0^t w(t-x)\frac{d}{dx}\hat{P}(S|T=x,H)dx.$$

This probability can then be used to calculate mean duration of screening as

$$\hat{\Omega}_s^{\text{Tr}} = \int_0^\tau \hat{P}(S_{\text{Tr}}|T=t,H)dt$$

and mean duration of recency as

$$\hat{\Omega}_{r,s}^{\text{Tr}} = \int_0^\tau q(t)\hat{P}(S_{\text{Tr}}|T=t,H)dt.$$

The incidence equation then becomes

$$\hat{\lambda}_{\text{RITA2}} = \frac{\big(\hat{P}(R|S_{\text{Tr}}) - \beta\big)\hat{P}(S_{\text{Tr}})}{(1-\hat{P}(H))(\hat{\Omega}_{r,s}^{\text{Tr}} - \beta\hat{\Omega}_s^{\text{Tr}})}. \tag{1}$$

2 Appendix 2

The RITA aware estimators show strong agreement with the Historical estimator in the PHIA studies, except perhaps for the two countries with the highest estimated incidence (Eswatini and Lesotho). To better visualize this agreement, it is useful to compare a plot of the RITA estimates with the historical and Naïve estimates.

Figure 1 provides this comparison. Here we see that there is very little deviation from the perfect agreement line (denoted in blue) between the RITA and Historical estimates for all but two estimates. The Naïve estimate on the other hand shows large departures, with the larger incidence estimates showing the least agreement.

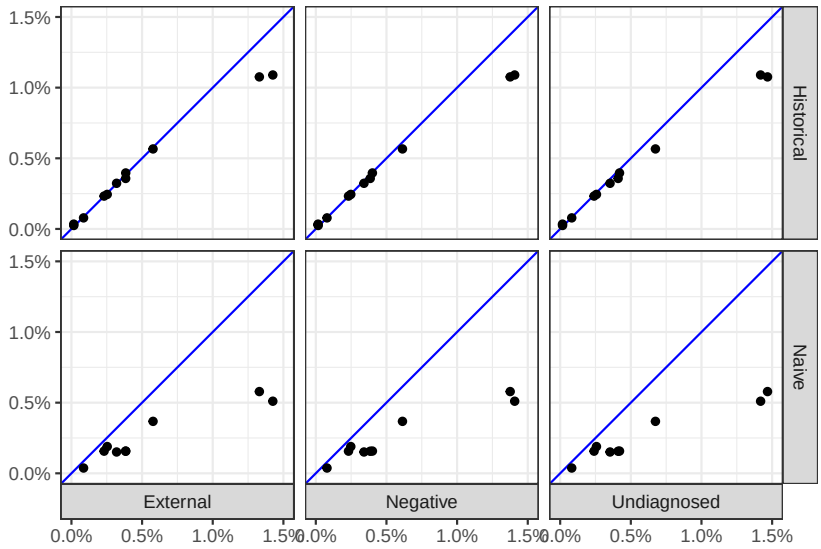

Figure 1: A comparison of the RITA incidence estimates in the PHIA studies to the Naive and Historical estimates. The perfect agreement line is denoted in blue.

3 Appendix 3

Below is an alternate derivation of Equation 7 plugging in Equation 6 into Equation 5

$$\begin{aligned}
\lambda &= \frac{\big(P(R \ \& \ S|H) - P(R \ \& \ S|T \geq \tau, H)\big)P(H)}{(1-P(H))(\Omega_{r,s} - P(R \ \& \ S|T \geq \tau, H)\tau)} \\
\lambda(1-P(H))(\Omega_{r,s} - P(R \ \& \ S|T \geq \tau, H)\tau) &= \big(P(R \ \& \ S|H) - P(R \ \& \ S|T \geq \tau, H)\big)P(H) \\
\lambda(1-P(H))\Omega_{r,s} - P(R \ \& \ S|H)P(H) &= \big(\lambda(1-P(H))\tau - P(H)\big)P(R \ \& \ S|T \geq \tau, H) \\
\lambda(1-P(H))\Omega_{r,s} - P(R \ \& \ S|H)P(H) &= \beta\big(\lambda\Omega_s(1-P(H)) - P(S|H)P(H)\big) \\
\lambda(1-P(H))(\Omega_{r,s} - \beta\Omega_s) &= (P(R|S) - \beta)P(S) \\
\lambda &= \frac{(P(R|S) - \beta)P(S)}{(1-P(H))(\Omega_{r,s} - \beta\Omega_s)}.
\end{aligned}$$

4 Appendix 4

Consider a population of individuals who engage in HIV testing over time and that the time between subsequent tests follows a renewal process. Let X be a random variable representing the time between subsequent tests and $F(X)$ to be a density function for the time between tests, which itself is a random variable. The support of F is assumed to be bounded such that $F(x) = 0 \quad \forall \quad x > m$. The renewal process is assumed to be at equilibrium at the time of an instantaneous cross-sectional survey, which, without loss of generality, occurs at time 0. Let B be the time between the last test and the survey, and A be the time from the survey to the next test.

We assume that the testing renewal process is independent of HIV seroconversion such that the probability of HIV infection is uniform in the period leading up to the survey

$$p(T = t \mid V, F) = V \qquad \forall \quad t \in [0, m],$$

where T is the time since HIV seroconversion and V is the probability the individual seroconverts during the period divided by m. After the first positive test, individuals generally do not get retested, so the renewal process post first positive is considered hypothetical had the individual not been infected. The population of interest is composed of at risk individuals, so those infected prior to $-m$ are excluded from consideration.

Heterogeneity of both HIV risk and testing frequency is to be expected. We express a general model for this as

$$V, F \sim \nu(V, F),$$

so the conditional probability density for time between tests is

$$p(X = x \mid F) = F(x)$$

and the marginal distribution is

$$p(X = x) = \int\int F(x)\nu(V, F)dV\,dF = E_\nu(F(x)).$$

ν is required to generate valid probabilities and densities over the relevant supports (i.e. $0 \leq V \leq m$, $\int F(x)dx = 0$, $F(x) \geq 0$ and $F(x) = 0 \quad \forall x > m$). While no additional direct restriction is put on ν, we do assume ν is such that the marginal distribution for the time between an incident infection at time 0 and the next test is well approximated by an exponential distribution with rate λ_a

$$p(A = x \mid T = 0) = \lambda_a e^{-\lambda_a x}.$$

We wish to investigate how and under what conditions the time since last test at the time of the survey can be used to estimate λ_a and hence the time from infection to diagnosis distribution.

4.1 Time to Diagnosis From Time Since Last Test

From renewal theory, the time since last test and the time to next test have the same distribution

$$p(A = x \mid F) = p(B = x \mid F) = \frac{P(X > x \mid F)}{E(X \mid F)}.$$

The marginal time-to-diagnosis density can be expressed as

$$\begin{aligned} p(A = x \mid T = 0) &= \frac{p(A = x, T = 0)}{p(T = 0)} \\ &= \frac{\int\int p(A = x, T = 0 \mid F, V)\nu(V, F)dV\,dF}{\int\int p(T = 0 \mid V)\nu(V, F)dV\,dF} \\ &= \frac{E_\nu\Big(p(A = x, T = 0 \mid F, V)\Big)}{E_\nu(V)} \\ &= \frac{E_\nu\Big(V\frac{P(X>x \mid F)}{E(X \mid F)}\Big)}{E_\nu(V)}. \end{aligned} \tag{2}$$

The density of time since last test in the HIV negative population is estimable from a cross-sectional survey based on self-reported testing history and lab verified HIV status. If infection risk is independent of testing frequency ($\nu(V, F) = \nu_1(V)\nu_2(F)$) then this density is the same as the time-to-diagnosis density. Explicitly, the time-to-diagnosis density is

$$p(A = x \mid T = 0) = \frac{\int\Big(\int V\nu_1(V)dV\Big)\frac{P(X>x \mid F)}{E(X \mid F)}\nu_2(F)dF}{E_\nu(V)} = E_\nu\Big(\frac{P(X > x \mid F)}{E(X \mid F)}\Big),$$

which is the same as the time-since-last-test density conditional upon HIV negativity

$$p(B = x|T < 0) = \frac{E_\nu\Big(p(B = x, T < 0 \mid F, V)\Big)}{E_\nu(P(T < 0))} = \frac{E_\nu\Big(p(B = x \mid F)\Big)E_\nu\Big(P(T < 0 \mid V)\Big)}{E_\nu(P(T < 0))} = E_\nu\Big(\frac{P(X > x \mid F)}{E(X \mid F)}\Big).$$

If the independence condition does not hold, then we may look at the time since last test among the undiagnosed population

$$\begin{aligned} p(B = x \mid \ 0 \leq T < B) &\propto E_\nu\Big(P(0 \leq T < x \mid B = x, V)P(B = x \mid F)\Big) \\ &= xE_\nu\Big(V\frac{P(X > x \mid F)}{E(X \mid F)}\Big). \end{aligned}$$

Noting that the expectation is proportional to the time-to-diagnosis density (Equation 1) and then applying the marginal exponential assumption, we have that

$$p(B = x \mid 0 \leq T < B) = \lambda_a^2 x e^{-\lambda_a x}.$$

The expected time to diagnosis among incident cases is then half of the expected time since last test among undiagnosed

$$E(A \mid T = 0) = \frac{1}{\lambda_a} = \frac{1}{2} E(B \mid 0 \leq T < B).$$

Alternatively, the median, which is robust to outliers, may be used as a basis for inference on λ_a. Let Q_2 be the median of $p(B = x \mid 0 \leq T < B)$, then

$$\begin{aligned} .5 &= \int_0^{Q_2} \lambda_a^2 x e^{-\lambda_a x} \\ .5 &= e^{-\lambda_a x}(\lambda_a Q_2 + 1) \end{aligned}$$

Thus, λ_a may be calculated from the median by solving the above equation.

4.2 Including Non-Testers

In the above we have posited a population that engages in regular testing. If instead only a certain proportion of the population engages in regular testing, then the time from infection to diagnosis must be adjusted for this. Let U be the event that an individual is a non-tester and assume that the probability of an incident case being a non-tester is uniform across T, then we define $\omega = P(U \mid T = 0)$ be the probability that an incident case is a non-tester.

$$d(x) = P(A > x \mid T = 0) = 1 - p(A \leq x \mid T = 0)(1 - \omega)$$