Why the FDA Must Discriminate Against Gay Blood: A (Gay) Activist's Perspective

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Abstract

Some AIDS and LGBT activists have advocated for the complete reversal of the United State's Food and Drug Administration's (FDA) ban on blood donation by sexually active men who have sex with men (MSM). In order to quantify the risk of such a policy change, we identify failure modes of the current blood screening protocol and construct a simple incidence dependent mathematical model of HIV screening and transmission in blood donation. Alas, the extraordinarily high rate of new HIV infections in MSM makes the probability of HIV transmission through the blood supply —even when screened with current antibody and pooled RNA based screening methods—non-trivial when sexually active MSM are allowed to donate. We estimate that at a (conservative) HIV incidence rate of 0.415 new infections per 100 persons-years in MSM, the expected number of HIV infected blood donations in the United States blood supply would be 22 per year. We are forced to conclude that a complete reversal of the current FDA policy would drastically increase the risk of HIV transmission in the blood supply. While a complete reversal of the MSM ban would be impractical, we believe that the FDA could shorten the deferment period to two months since last sexual contact in MSM without increasing risk of HIV transmission.

1 Introduction

"For a successful technology, reality must take precedence over public relations, for Nature cannot be fooled."- Richard P. Feynman

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The first probable case of HIV being transmitted through the blood supply was reported in December 1982, less than two years after the first case of AIDS was reported.[1] In September 1985, the FDA adopted a policy prohibiting the donation of blood by any man who has had sex with men since 1977—a sensible policy, considering the overwhelming epidemiological evidence that the causative agent of AIDS occurred with dramatically greater frequency in the MSM community compared to other population groups and the inability of testing technology at the time to detect recently acquired infections. On 21 December 2015, the FDA changed its MSM exclusion policy to only prohibit MSM who have had sex with men within 12 months of attempted donation.

While the new deferral policy was generally regarded as a "step in the right direction", many LGBT and AIDS activists continue to advocate for the complete abolition of policies excluding men who have sex with men from donating blood. The purpose of this short paper is to objectively analyze the implications of such a policy.

2 The Current Blood HIV Screening Protocol

Following the introduction of the first FDA approved enzyme linked immunosorbent assay (ELISA) based HIV antibody test in 1985, all donated blood products in the United States were required to be screened for HIV antibodies.[2] In 1999, the FDA began to require that blood products also be screened with a nucleic acid amplification test (NAAT) for HIV RNA, in order to increase the sensitivity of detection of HIV in donors who were recently infected.[3] Because performing an individual NAAT for every single blood donor is expensive, the FDA allows samples from each blood donor to be "pooled"—i.e. samples from multiple donors are mixed or "pooled" into one test—as long as the test is able to detect a single HIV positive donor who has a viral load of 5,000 RNA copies per mL or lower within a pool of HIV negative donors[4]. This quantity—i.e. the minimum viral load at which the test can detect a positive case—is known as the "limit of quantitation" or LoQ.

This testing protocol, while highly sensitive, is not a hundred percent accurate. Indeed, there have been four reported cases of HIV positive blood entering the blood supply in the United States, *despite* the use of both NAAT and serological screening and the FDA exclusion of MSM.[5]
There are two different ways in which the current screening protocol can fail, i.e. allow HIV positive blood to enter the blood supply, despite being tested. We call these "failure modes": [6]:

- **Test Failure** The test was performed improperly, resulting in a failure to detect a positive specimen. This is very improbable, the current literature estimates that only 0.05% (95% confidence interval 0-1.5%) of tests are performed improperly.

- **Window Period Failure** The donor is acutely infected and viremic, but has yet to reach a viral load at or above the limit of quantitation, so HIV

RNA is not detected within the pooled NAAT. Obviously, because the donor is so recently infected, the blood also has no detectable antibodies, and thus tests negative on the serological assay as well.

Because transfusing viremic blood from an HIV positive donor is associated with a nearly 100% probability of transmission to the recipient—even when the donors viral load is very low[7] we assume that a failure of the blood screening protocol results in (at least) one new transmission event.

3 Mathematical Model

In order to estimate the number of HIV positive blood donations that are *not* detected by the screening protocol and thus allowed to enter the blood supply, we need to know three things:

1. How long an acutely infected patient has a viral load that is below the limit. (We assume that this period does not vary between transmission categories.) We will call this period "time to detecability" and denote it with the Greek Letter τ (tau). This quantity has dimensions of time.

2. The rate that members of a population, on average, acquires HIV per unit time. This is known as the "incidence rate". This quantity has dimensions of infections per person-time. We denote this quantity with the letter J, and this obviously is dependent on whether that person is an MSM or a member of some other transmission category. (We will use a subscript, e.g. J_{MSM}, to denote the different incidence rates.)

3. Finally, we need to know how many people of each transmission category donate blood each year, we will denote this quantity with the letter n and use a subscript to denote different transmission categories.

The expected number or "lambda" (λ) of HIV positive blood samples passing through the screening protocol per unit time is simply[8]:

$$\lambda = \tau J n \tag{1}$$

Because this process occurs with a known rate and each contaminating event is independent of each other, the process is Poisson. Thus, the expected probability mass function (i.e. a function telling you what the probability that k contaminating events occurred is):

$$\Pr(k) = \frac{\lambda^k e^{-k}}{k!} = \exp\{k \ln \lambda - \lambda - \ln \Gamma(k+1)\} \quad k \in \mathbb{N} \tag{2}$$

3.1 Acute Viral Load Kinetics

We need to figure out how long it will take a donor who is acutely infected to reach a viral load at the *LoQ* (i.e. τ). In the earliest stages of acute HIV

infection, a relatively good first order approximation of viral load expansion kinetics is given by the following elementary exponential growth function (see Figure 1). [9]:

$$V(t) \simeq V_0 e^{rt} \tag{3}$$

Where V is the viral load (in copies per mL) at time t, V_0 is the initial viral load at $t = 0$ (note at $t = 0$, $e^{rt} = e^0 = 1$) and r is the viral expansion rate derived from patient data. The values for r will be taken from the patient cohort (n=50) analyzed by Alan Perelson's team at the Theoretical Biology and Biophysics (T-6) Department at the Los Alamos National Laboratory. Values for r were computed using a linear mixed effects model, with a mean of 1.09, an interquartile range of 0.15, a minimum value of 0.62 and a maximum value of 1.46.[9] It is important to note that the function in Equation 3 starts *after* the eclipse period—the period preceding acute HIV infection where there is no virus in systemic circulation, which can last up to 14 days after the exposure.

We want to know τ—the time at which the viral load is at the level of quantitation—which is solved via simple algebraic manipulation of equation 3 (See Figure 2):

$$\tau = \frac{1}{r} \ln \left(\frac{LoQ}{V_0} \right) \tag{4}$$

3.2 Number of Donors per Transmission Category

The CDC has estimated that 2.9% (95% CI: 2.63.2) of the U.S. population are men who have had sex with men in the last 12 months. [10] Therefore, we assume that the MSM population, if the deferral policy was lifted, would represent 2.9% of the blood donor population. Considering there are 9.2 million blood donors a year in the United States, we estimate that there would be 248,400 (95% CI: 239,200 to 294,200) blood donations made by MSM each year.

3.3 HIV Incidence

The next thing we need to figure out is what portion of blood donors are acutely infected *and* with a viral load under the LOQ at the time of donation. We first begin by transforming *yearly* incidence rates to *daily* rates. This is simply [11]:

$$J_d = \frac{1}{365.25} J_a \tag{5}$$

The CDC estimates, using the Prejean et al. modified Stratified Extrapolation Approach (SEA), that 29,800 MSM became infected in 2010. [12] assuming a baseline HIV prevalence of 0.2 in MSM and that 2.9% of the US population is MSM, this translates to a incidence rate of 0.415 per 100 persons-years. We note that this is lower than, other, published estimates. [13]

4 Results

At the current FDA mandated level of quantation (5,000 copies per mL), with 248,400 MSM donors and the estimated HIV incidence of 0.415 per 100 person-years and at a viral expansion rate of 1.09, we estimate that we would expect 22.0536 HIV positive blood samples from MSM donors to enter the blood supply. We simulated the number of MSM transmissions by varying the incidence and varying the viral expansion rate (r), see Figure 3.

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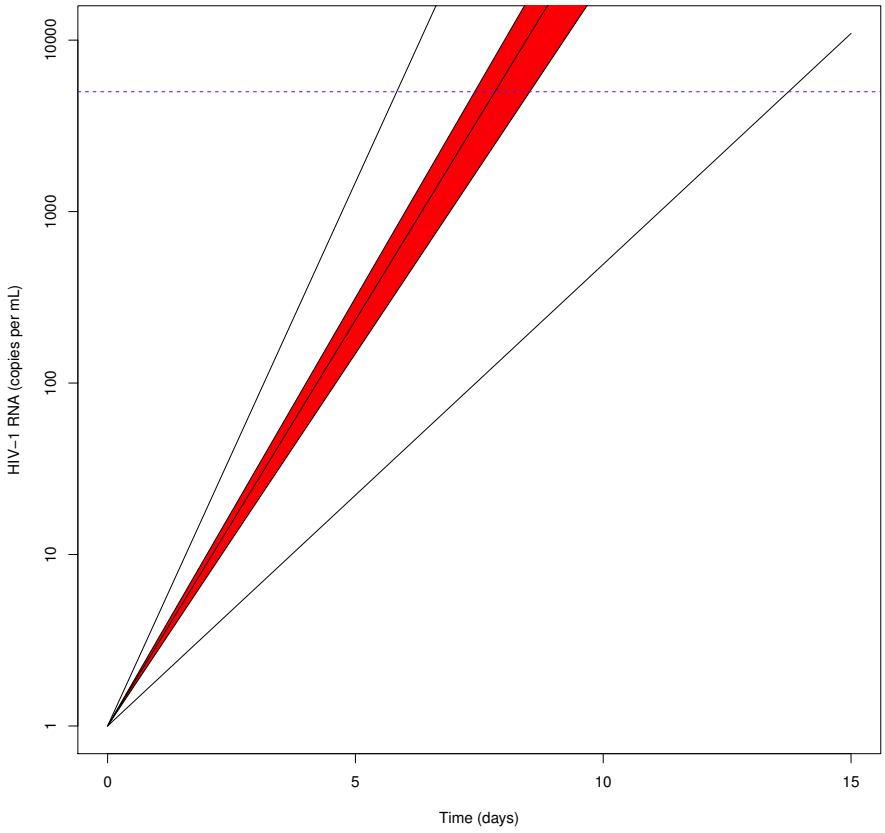

Figure 1: A semi-log plot of simulated viral load trajectories in Acute HIV Infection. (Calculated using Eq. 3) The leftmost line represents the maximum growth function (r=1.46), the red shaded areas represents growth values within the IQR and the rightmost line represents the slowest growth for the Los Alamos cohort (r=0.62). The blue line represents a viral load of 5,000 HIV-1 RNA copies per mL, the current FDA mandated LoQ.

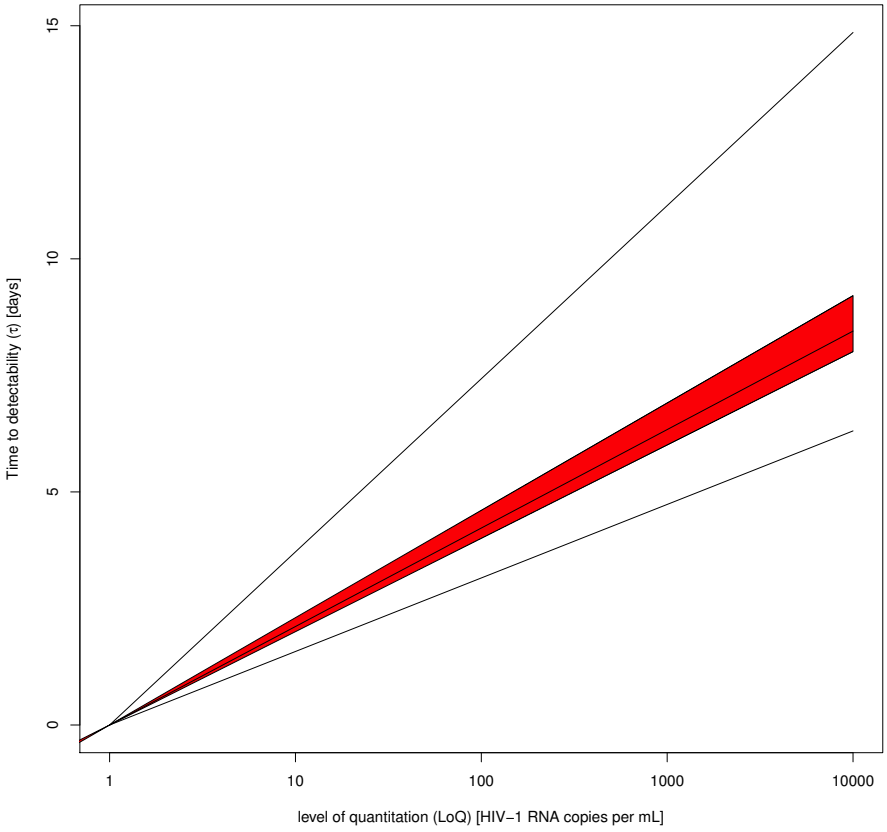

Figure 2: A semi-log plot of the dependence of τ on the Limit of Quantitation. (Calculated using Eq. 4)

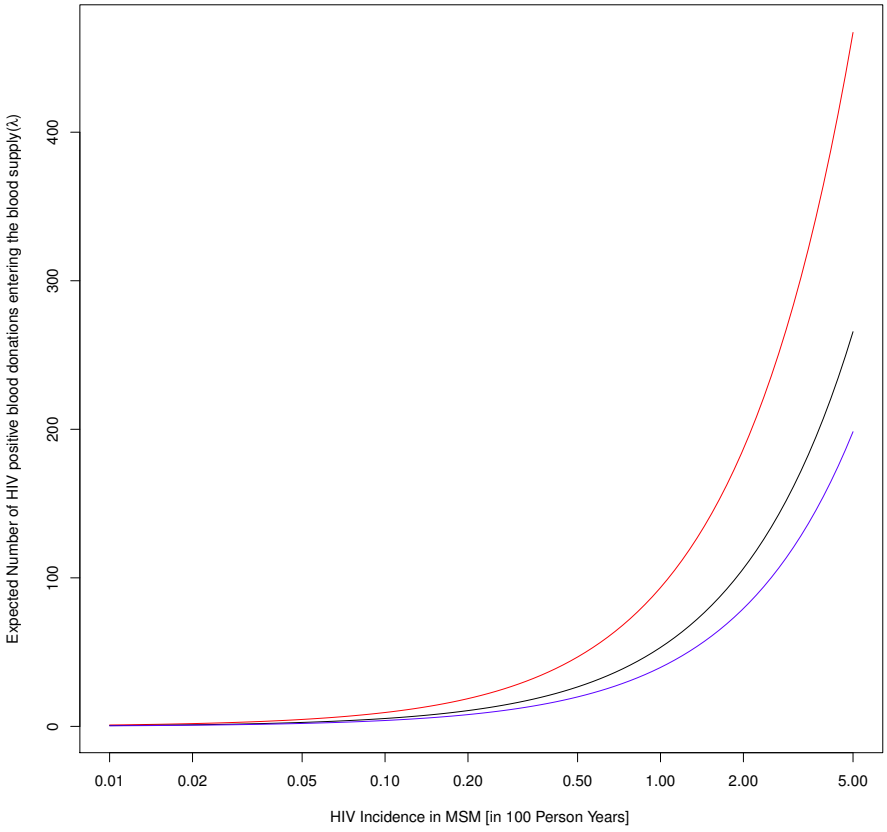

Figure 3: A semi-log plot of the number of transmissions in the blood supply (λ) with diffrent incidences and viral load growth rates.