To the Editor—I wish to clarify the literature with regard to a recent publication by Anderson and Hanson [1]. They present a mathematical model for an imperfect preexposure HIV vaccine with therapeutic effects (see the flow diagram in figure 3 and the equations in the Appendix). However, this model has already been published by Blower et al. [2–5]. In 1993, McLean and Blower were the first to model the population-level impact of imperfect (i.e., those with an efficacy of <100%) preexposure HIV vaccines [6]. They assumed that vaccinated individuals would receive only partial protection against infection. Their model included 3 mechanisms by which vaccines could fail: (1) by generating a low “take” (e), (2) by providing a low degree of protection against infection (ψ), and/or (3) by waning (ω) (figure 1). Thus, the efficacy (e) of an imperfect vaccine could be understood as the product of take and degree of protection: e = eψ [3, 4, 6]. Furthermore, Blower and McLean showed that the population-level impact (Φ) of an imperfect preexposure HIV vaccine could be evaluated by multiplying e by the proportion of vaccinated individuals in whom the vaccine does not wane ([μ/(μ + ω)], where 1/μ specifies the average time spent selecting new sex partners and 1/ω specifies the average duration of vaccine-induced immunity) [2, 3, 6, 7]. Thus, Φ = eψ[μ/(μ + ω)], and, if vaccine-induced protection is lifelong, then Φ = e. Using their model [6, 7], Blower and McLean were the first to derive the expression for the critical vaccination coverage (ρc) necessary to achieve HIV eradication with an imperfect vaccine:

$$P_c = \left(\frac{1}{\phi}\right)\left(1 - \frac{1}{R_v}\right),$$

where $R_v$ is the average number of secondary infections caused by an infected individual.

Analysis of the model revealed that even imperfect vaccines could substantially decrease prevalence and incidence but that the rate of waning of vaccine-induced immunity is critical [3, 4, 6–8]. Blower and McLean also calculated the vaccine efficacy and vaccination coverage levels necessary to eradicate HIV in San Francisco [7]. They quantified the trade-off between coverage, efficacy, and potential changes in risky behaviors. They were the first to show that an imperfect preexposure vaccine could significantly curtail the HIV epidemic, provided that risky behaviors did not increase [7]. However, their analyses also indicated that it would be unlikely—unless risky behaviors were considerably reduced—that an imperfect vaccine could eradicate HIV in San Francisco. More importantly, they were the first to show that, if risky behaviors increased, mass vaccination with imperfect vaccines could have the perverse outcome of increasing the severity of the epidemic [7].

Blower et al. expanded their original model to develop a new one for predicting the impact of imperfect preexposure HIV vaccines that slow disease progression (i.e., disease-modifying, or therapeutic, vaccines) (figure 1B) [2–5]; this new model is the same as that which was recently presented by Anderson and Hanson [1]. The new model included a take, degree of protection, and duration effect. However, the key additional assumptions included were that the vaccine increases survival and reduces infectiousness (and, hence, decreases transmission) (figure 1B). An interactive Web-based version of this model can be found at: http://www .biomath.medsch.ucla.edu/faculty/sblower /applets/HIVVAC/hivvac.html. Blower et al. [4] derived the critical vaccination coverage necessary to achieve eradication with an imperfect preexposure disease-modifying vaccine:

$$P_c = \left(\frac{\mu + \omega}{\nu\mu}\right)\left(1 - \frac{R_v}{(1 - \psi)R_c - R_v}\right).$$

Smith and Blower further analyzed this model [5] and defined a new quantity, the fitness ratio (f), as defined by $f = R_v/R_w$, where $R_v$ and $R_w$ are the average number of secondary infections caused by a vaccinated-infected individual and an unvaccinated-infected individual, respectively. Disease-modifying vaccines will reduce transmission if they cause a reduction of 1.5 log_{10} copies/mL or more in viral load and if risky behaviors do not increase [5]. However, disease-modifying vaccines that provide only a low degree of protection against infection and/or generate high fitness ratios will increase transmission, even if risky behaviors do not increase [5]. High fitness ratios will be generated if the vaccine substantially increases survival times but does not substantially reduce infectiousness. Specifically, transmission will increase if $f > 1/(1 - \psi)$ [5]. Smith and Blower derived 3-dimensional threshold surfaces to identify critical boundaries at which disease-modifying vaccines switch from causing a beneficial to causing a detrimental effect at the population level if risky behaviors change [5]. These surfaces are determined by the value of the fitness ratio, the proportion of the population that is successfully vaccinated, and the degree of...
Figure 1. A, Flow diagram of an imperfect preexposure HIV vaccine model, designed by McLean and Blower (diagram is a modified version of that published in [6]). The population is divided into 4 states: susceptible individuals \((X)\), infected/infectious individuals \((Y)\), vaccinated individuals \((V)\), and individuals with AIDS \((A)\). The imperfect vaccine can produce a “take” effect, reduce susceptibility to a certain degree \((1 - \psi)\), and wane (at rate \(1/\omega\)). B, Flow diagram of an imperfect preexposure HIV vaccine model with therapeutic effects, designed by Blower et al. [2–4]. This model is an extension, by 1 state, of the 4-state model shown in panel A, which was designed in 1993. The population is now divided into 5 states: susceptible individuals \((X)\), infected/infectious individuals \((Y)\), vaccinated-uninfected individuals \((V)\), vaccinated-infected individuals \((V)\), and individuals with AIDS \((A)\). The imperfect vaccine can produce a take effect, reduce susceptibility to a certain degree \((1 - \psi)\), wane (at rate \(1/\omega\)), and both reduce infectivity and slow disease progression in vaccinated individuals who subsequently become infected.

change in risky behaviors in unvaccinated-infected individuals.

In summary, the model of an imperfect vaccine with therapeutic effects presented recently by Anderson and Hanson [1] was one that had been designed and analyzed previously by Blower et al. [2–5, 8].

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References