Could we – should we – calculate a risk exposure score for an HIV-negative individual in a serodiscordant couple?

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The Bernoulli risk equation has long been used within HIV transmission models to calculate population-level incidence rates [1–3]. In an article in this issue, Fox et al. [4] use the Bernoulli risk equation to quantify the degree to which an uninfected individual in a discordant couple has been exposed to HIV, based on their past sexual practices. Consequently, Fox et al. describe the Bernoulli risk equation as a risk exposure score; notably, it is a measure of past and not future risk. They calculate risk exposure scores for heterosexual women, heterosexual men, and MSM based on four risk factors. Two risk factors are based on characteristics of the HIV-positive partner: viral load and HIV stage (primary, chronic, or late). The other two risk factors, genital ulcer disease (GUD) and genital herpes (herpes simplex virus-2; HSV-2), either increase susceptibility of the HIV-negative partner and/or increase infectivity of the HIV-positive partner. Notably, the presence of bacterial sexually transmitted infections is not included as a risk factor in the proposed risk exposure score. However, pregnancy is included as an additional risk factor for women and it is assumed to increase risk by 116% [confidence interval (CI) 39–237%] based on results from one study [5]. Circumcision is included, for heterosexual men, as a factor that reduces the risk of acquiring HIV. The HIV risk exposure score is determined for any individual by calculating their cumulative exposure risk from their specific risk factors and is based on the number of unprotected acts they engaged in during the sexual relationship. To simplify the calculations, Fox et al. assume that condoms are 100% effective and that the HIV-positive partner is not on treatment. In addition, they assume that all of the risk factors are independent. However, clearly, the viral load of the HIV-infected partner and their stage of infection are not independent and neither are GUD and HSV-2. By assuming independence, the authors are overestimating the risk of exposure to HIV.

It is straightforward to calculate a risk exposure score for a ‘theoretical’ HIV-negative individual in a discordant couple. However, it is not clear that the proposed risk exposure score could be so easily calculated for an HIV-negative individual in a discordant couple in the ‘real-world’. In the ‘real-world’, in general, it would only be possible to calculate a risk exposure score for an individual who had been of low risk of acquiring HIV. It is rather unlikely that an HIV-negative individual in a discordant couple who had a high ‘theoretical’ risk exposure score would have remained uninfected; consequently, individuals with high-risk exposure scores would be hard to find in the ‘real-world’. For example, if an individual had a ‘theoretical’ risk exposure score of 0.8, only eight (on average) out of 10 HIV-negative individuals in serodiscordant couples would have remained uninfected in the ‘real-world’. Consequently, it would be rare to find an

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individual in a discordant couple with a high-risk exposure score. It is also not clear that it would be feasible to calculate the proposed risk exposure score in the ‘real-world’ as it would be necessary to have accurate information on all of the risk factors included in the risk equation, as well as an accurate assessment of the total number of sex acts that occurred since the beginning of the sexual relationship. The two most important risk factors needed to calculate the risk exposure score for the HIV-negative individual are the viral load and the stage of infection for the HIV-positive partner. However, it is unlikely that many individuals in discordant relationships would know the viral load, or even the stage of infection, of their HIV-positive partner.

Fox et al. suggest that their proposed risk exposure score should be used to quantify and compare true exposure in individuals termed ‘exposed uninfected’ within clinical trials and provide a means for constructing evidence-based risk reduction practices for individuals. To evaluate the practicality of these suggestions, we calculated ‘theoretical’ risk exposure scores using the approach described by Fox et al. [4]. Figure 1 shows the estimates for these scores for eight scenarios; the variation resulting from using the limits of the 95% CIs for each of the included risk factors is plotted. The wide variability in the estimates of the HIV risk exposure scores is due to the considerable heterogeneity in the estimates of risk obtained from empirical studies [6,7]. For example, the risk exposure score for an HIV-negative pregnant woman with HSV-2 infection who has unprotected vaginal intercourse 50 times with a man who is in the chronic stage of HIV infection and has GUD is between 0.1 and approximately 1 (scenario 1); a score of 1 signifies that an individual would have had such high-risk exposure to HIV that it would be almost 100% certain that the individual would have become infected. The risk exposure score shows that even if the woman had unprotected vaginal intercourse only 30 times, her risk of acquiring HIV would have been extremely high (scenario 2). Wide variation in risk exposure scores can also be observed for heterosexual men. Scenario 3 shows the score for an HIV-negative man who has unprotected vaginal intercourse 50 times with a woman who is in the late stage of infection with a high viral load (log viral load > 4.7 copies/ml). Scenario 4 is the same as scenario 3, although in this case, the man only has unprotected vaginal intercourse 30 times. Notably, the risk exposure score indicates that MSMs can engage in high-risk behaviors and remain at low risk of acquiring HIV. In scenario 5, the HIV-negative man is infected with HSV-2 and the HIV-positive man is in the chronic infection stage; it is assumed that the HIV-negative man is engaged in 50 unprotected acts of insertive anal intercourse. Scenario 6 is the same as scenario 5, although in this case, the HIV-negative man has engaged in 30 unprotected acts of insertive anal intercourse. The risk exposure score for MSM increases substantially if the uninfected partner engages in receptive anal sex and the HIV-positive partner has GUD (scenarios 7 and 8).

Using the risk exposure score proposed by Fox et al., we find that, due to heterogeneity in the data, it is unlikely to be possible to quantify risks – with an appropriate degree of accuracy – for any specific individual in the ‘real-world’. Furthermore, the calculated score for risk exposure could be misleading; it can indicate high-risk individuals are at low risk of acquiring HIV (MSM scenarios) and, conversely, low-risk individuals are at high risk of acquiring HIV (pregnant women scenarios). We caution against, as the authors suggest, using the risk exposure score to decide who is eligible for postexposure prophylaxis (PEP); any individual who has recently been exposed to HIV should be offered PEP. Furthermore, many evidence-based risk reduction practices have already been firmly established; for example, reducing...
numbers of sexual partners, increasing condom usage, and PEP. All discordant couples should be provided with appropriate information on prevention and counseled about risk reduction, regardless of whether their past exposure risk is estimated to have been high or low. The Bernoulli risk equation has been exceptionally useful in modeling the transmission dynamics of HIV [1,2]; however, it is too simple to capture the complexity of reality. Therefore, it is not clear that it could – or should – be used in the ‘real-world’ for quantifying risk exposure for HIV-negative individuals in serodiscordant couples.

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References