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Assessing the public health impact of HIV interventions: the critical role of demographics

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Human immunodeficiency virus (HIV) continues to spread and take the lives of millions around the world. Advances in antiretroviral therapy (ART) have substantially extended survivorship without completely removing the risk of transmission. Some preventive interventions have demonstrated efficacy in clinical trials [1,2] but their effectiveness remains to be confirmed at community levels where the optimized level of implementation may not be replicable.

In a recent analysis, Kato and colleagues estimated the potential impact of expanding ART and combination prevention in Vietnam [3]. Other mathematical models have also been used to project the public-health impact of HIV prevention into sexually-active populations [4-10]. Presented results in these modeling studies necessarily depend on various assumptions regarding population demographics, sexual behavior and HIV transmission. With focus on the impact of the interventions, the primary interest falls on the ability of the proposed preventive method to reduce transmission, its acceptability by the targeted groups, the willingness of potential users to follow prescribed regimen and the public health risks associated with the new product (such as the spread of drug resistance associated with antiretroviral products). However, insufficient evidence is presented to justify the way processes of: i) population recruitment, including immigration and sexual maturation, and ii) population departures, including emigration, age- and gender-specific mortality, infection-induced fatalities, and sexual inactivity are modeled. In this commentary, we discuss the merits of the demographic assumptions employed in Kato et al. [3], among other commonly used, and outline the need for their systematic reassessment.

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Recruitment assumptions

Most of the published models on intervention impact assume that the number of individuals joining the population per year is constant (constant recruitment) [3,6-8,10-12] or proportional to the total population size (proportional recruitment) [4,5,9,13,14]. In sexually-active population with no immigration, constant recruitment implies that the same number of people reach sexual maturity annually. That may be an acceptable approximation over short periods of time, but becomes troublesome when the simulation period increases. The progression of HIV infection from acquisition to full-blown AIDS and death is incredibly slow and delayed even further by ART. Therefore, a meaningful impact of prevention intervention should be expected over several decades which may explain why simulation periods of 20-50 years are used in mathematical models. Projections, presented in Kato et al [3], are over 40 years. If the population growth rate is 1% as currently estimated for Vietnam [15] the cumulative growth over 40 years will be 49%. In comparison, the population in Sub-Saharan Africa, which is impacted the most by the HIV epidemic, is growing at a rate of 2.2% per year [16] and is expected to more than double by 2050 [17]. It is not realistic to expect that the number of 15-year olds in these populations will remain the same over several decades. Proportional recruitment seems to address this issue but has the deficiency of connecting the current population size directly to the number of new recruits, i.e., any change in the population size affects the cohort that joins the community instantaneously. However, the cohort of 15-year-olds is more likely to depend on the population size when they were conceived, i.e., 16 years prior to their sexual maturation. A delayed proportional mechanism, which is certainly more appropriate when sexually-active populations are simulated, adds computational complexity and limits the analytical tools available to study the model behavior (see comparison between some recruitment mechanisms in Fig.1A).

Another popular modeling decision is to assume that the cohort joining the population consists entirely of susceptible individuals [3-12,14]. In sexually-active populations, the newcomers may be adolescents reaching sexual maturity or adults migrating into the community. We may agree that the prevalence of HIV among sexually inactive teenagers could be negligible due to the success of worldwide prevention strategies in mother-to-child transmission. However, that may not be the case for the migrating individuals. This is particularly important when analyzing populations with steady influx of people, such as the men-who-have-sex-with-men community in San Francisco or large metropolitan areas in Sub-Saharan Africa. Recent data from King County, Washington (including Seattle area) show that over a 5-year period, three times more HIV-positive individuals have moved in than left the county. Ignoring the immigration of infected individuals, one may draw an imprecise picture of the drivers of the HIV epidemic or overestimate the projected impact of prevention interventions which target uninfected young adults, by agglomerating all newcomers into that group (see Fig.1B).

Departure assumptions

Population departures are most often modeled assuming proportional rates of population losses per year due to sexual inactivity, HIV-related or -unrelated causes, etc. [3-10]. Problems with such assumptions arise in populations with strong gender imbalance in HIV-

unrelated deaths (“background mortality”). Data from South Africa suggests that the mortality among 15-49-year-old men is higher than among women even though the number of HIV-related deaths among women is larger [18]. The influence of this differential gender mortality on the dynamics of the HIV epidemic is unclear but it may partially compensate for the stronger HIV toll on women. Additionally, both HIV mortality and acquisition risk differ by age, which suggests the importance of the age structure to the epidemic dynamics. Unfortunately, stratification by age requires individual-based models or models with large number of compartments and sophisticated parameterization. However, some published studies have shown that the complexity is manageable and feasible [13]. In depth analyses are necessary to determine when differences in departure rates between population subgroups have to be taken into consideration.

Bridging recruitment and departures

Kato and colleagues [3], as well as other modelers [5,8,10,11], assume that recruitment and departures are balanced (equal in size) before the start of the HIV epidemic. Assuming that before the introduction of HIV the population size remains constant implies persistent population decline when HIV-related fatalities are added to the departures and may result in substantial population reduction over 20 to 50 years. This is inconsistent with observed demographic trends in Vietnam and even in countries with significantly higher HIV prevalence. Alternatively, modelers often assume that the population in presence of HIV is already at equilibrium when new prevention is introduced [4,6,12]. This is obtained by simulating the HIV epidemic for sufficiently long time until all compartments show negligible changes in size. Unfortunately, in the process of achieving “equilibrium”, all epidemic conditions including transmission rates and survival time of the infected individuals are kept unchanged for periods often longer than the time HIV has been circulating in the population. In reality, the introduction of various treatment options at different times has affected the transmission and mortality rates. Even if the epidemic parameters are selected “to fit” historic epidemic data (usually HIV prevalence) they will most likely represent the “average HIV epidemic” over the whole period toward dynamic stability rather than the state of the epidemic at the end of the period (the current time at which point the intervention will be initiated). However, no parameter adjustments can be made when equilibrium is reached because that will destabilize the population and lead to a new steady state.

Conclusions

The way we model demographic processes may have little impact on short lasting epidemics but shall not be neglected for simulations over extended time periods, typically used to evaluate HIV prevention interventions. Demographic assumptions affect the projected HIV epidemic by controlling the intake of new susceptible individuals and the removal of infected individuals from the population. They also alter the HIV prevalence in different subgroups and therefore play an important role in determining the forces of infection between different compartments. The influence of the demographic assumptions on the projected effectiveness of HIV interventions is rarely the focus of modeling analyses but

deserves the attention of the researchers who work in the field of HIV prevention, as the role of mathematical modeling to intervention evaluations increases.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

A) Effects of the choice of recruitment mechanism on the number of individuals joining the population of initial size of 100,000 assuming that 2% population growth is observed at the beginning of the simulations. B) Effects of the assumptions related to the HIV status of the individuals joining the population on the HIV epidemic over extended periods of time. The curves are obtained by fitting dynamic model to annual HIV prevalence data over 5-year period twice, under scenarios with 0% and 6% infected individuals among new recruits. Graphs show perfect alignment over the fitted period but diverge afterward. Model description is provided in the Supplemental Digital Content.