Rethinking the population attributable fraction for infectious diseases

The population attributable fraction (PAF) is commonly used in public health to signal the contribution, or importance, of a risk factor to a health outcome. The PAF poses the counterfactual: what would happen if the considered risk factor was entirely absent from the population? In The Lancet Infectious Diseases, Katharine Looker and colleagues estimated that globally, in 2016, 29·6% (95% uncertainty interval 22·9–37·1) of new HIV infections acquired via sexual transmission were attributable to herpes simplex virus type 2 (HSV-2) infection. To examine the public health relevance of these findings, a key limitation of the classic PAF must first be considered, as noted by Looker and colleagues.

To estimate the classic PAF from observational data, the relative risk of a given exposure for the health outcome is multiplied by the prevalence of the risk factor in the entire population (appendix). Thus, a small relative risk of a high-prevalence risk factor can drive the classic PAF, the public health implication being to prioritise resources to eliminate a small risk among many. For example, in a setting in which 30% of all individuals have risk factors associated with a small relative risk of HIV acquisition (eg, sex without condom with few partners) and 2% have risk factors associated with a large relative risk of HIV acquisition (eg, transactional sex without condom with many partners), the classic PAF would suggest programmes prioritise the larger subset of the population. However, such an approach runs counter to the propagation of infectious diseases, especially HIV and other sexually transmitted infections, as risk factors among the relatively few can sustain even generalised epidemics of these infections.

This disconnect derives from the fact that the classic PAF does not consider onward transmission: it is a static measure restricted to acquisition risks and ignores what happens within a sexual or drug-injection network after acquisition. When a risk factor, such as HSV-2 infection, increases susceptibility to HIV infection in one person, it might start a chain of HIV transmission events at the population level—ie, an HSV-2 infection in one person could indirectly, over time, lead to several HIV infections even among individuals without HSV-2. Therefore, the classic PAF probably underestimates the number of HIV infections in the total population that stem directly and indirectly from HSV-2 infection. This bias is largest when HSV-2 leads to HIV acquisition in a small subset of the population with disproportionately higher risks of onward HIV transmission (eg, individuals engaged in sex work whose HIV prevention and treatment needs have not been met) and when a static measure is used to predict long-term effects. For example, Looker and colleagues found that the contribution of HSV-2 infection to HIV acquisition within key risk populations (female sex workers and men who have sex with men) was lower than the contribution in the general population. But key populations are part of the wider sexual network, and in the long term, the downstream effects on HIV prevention of suppressing or preventing HSV-2 infection in such populations are likely to be larger than those of HSV-2 suppression or prevention in the wider population.

To address the limitations of the classic PAF, the transmission PAF (tPAF) can be estimated with mathematical models of onward transmission. As with the classic PAF, the tPAF generated from a transmission model is informed by observed relative risks, but it differentiates risks of onward transmission by simulating the sexual network. With a transmission model, the counterfactual can be simulated explicitly and projections of cumulative incidence with and without the risk factor can be compared (appendix). Consequently, the tPAF of a given risk factor can be interpreted—under the epidemic conditions of the modelled system—as the maximum fraction of infections that could be averted if that risk factor was absent or partially removed.

Using the tPAF to prioritise resources on the basis of potential long-term gains would have substantial policy and programmatic implications, including more specific strategies focused on comprehensively addressing the needs of the few to prevent infections among the many. Ultimately, the findings from Looker and colleagues’ study might underestimate the potential, population-level effects on HIV prevention of eliminating HSV-2. The magnitude of the underestimation will depend on the subset of the population prioritised for HSV-2 interventions and the time frame considered for anticipated effects.
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We declare no competing interests.

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