The HIV prevention cascade: more smoke than thunder?

See Articles pages e289, e297, and e307

See Personal View pages e318 and e323

"All happy families are alike; each unhappy family is unhappy in its own way."

Leo Tolstoy, Anna Karenina

The need for a call to action for HIV prevention is clear. The UNAIDS global estimates of the burden of HIV released on May 31, 2016, show continuing extraordinary progress in rolling out antiretroviral therapy to people living with HIV. Around 17 million of the 36·7 million people living with HIV are now accessing treatment leading to substantial reductions in mortality.[1] By contrast, despite the steady rise in the proportion of people living with HIV on treatment, the number of new infections among adults has remained stubbornly high, with a modest 4% fall in east and southern Africa over the past 5 years, and an alarming increase of over 50% in eastern Europe and central Asia. So the HIV Prevention 2020 Framework, laid out in this issue[2] by the Global Prevention Focal Point Group is welcome.

The 90-90-90 target set by UNAIDS in 2014[3] and subsequently incorporated into the planning of many countries has been a major advocacy success in pushing governments and programmes to respond to the clear evidence that all people should be offered treatment.[4–6] The target consists of three sequentially linked goals that, if achieved, would lead to 73% of individuals living with HIV being effectively treated so that their virus was supressed. This is good for people living with HIV and also renders them no longer infectious. Such a simple, clear strategy to find as many people living with HIV as possible, to treat as many of them as possible, and to ensure that the treatment is as effective as possible lends itself well to monitoring through an approach known as cascade analysis.

Peter Godfrey-Faussett

Two of the papers in this issue[7,8] are based around the concept of the HIV Prevention cascade and another[9] uses prevention cascades for each of several interventions. The cascade presented is from demand to supply to adherence, which is a useful framework for analysing bottlenecks and programmatic ways to improve outcomes. The cascade approach makes perfect sense when considering a set of (public health) actions that are consequent one upon another. This approach was probably first popularised in the Piot model proposed by Maurice Piot at WHO in the 1960s to describe the likely effect of tuberculosis control programmes and the importance of each of the transitions from symptoms through health-seeking behaviour to accurate diagnosis and effective treatment.[10] Similar models have been used for sexually transmitted infections (the Piot-Fransen model, no relation to Maurice)[11] and malaria.[12] However, HIV prevention, with the exception of preventing mothers living with HIV from passing infection to their infant, does not lend itself to the same linear processes making the cascade concept harder to define, to explain, and to measure. Every one of the 37 million people living with HIV needs essentially the same thing (diagnosis, linkage to care, the offer of treatment and support to maintain viral suppression). Both the denominator and the numerator for each step in the cascade are intuitive and (at least in principle) measureable. However the prevention needs of the approximately 4 billion sexually active adults who are currently uninfected are highly varied and dependent on local context and individual behaviour. Recent advances in HIV prevention have aimed to expand the range of effective approaches and to promote individuals' autonomy and choice. The notion of combination prevention,[13] emphasises the same multisectoral view described by Hargreaves and colleagues[8] linking prevention to structural, behavioural, and biomedical interventions. Although

the HIV prevention cascade is described as being "similar to the HIV treatment cascade", we are also advised to avoid confusion because "our use of the term cascade is different to the HIV treatment cascade" and not to "oversimplify HIV prevention".[8] Within a single key population, there is, of course, enormous heterogeneity, and by implication, there are different prevention needs.[14] Even the value of a condom to prevent HIV is entirely conditional on the likelihood of a sexual partner being infected and the likelihood that an infected partner is taking treatment and taking it effectively. One of the strengths of Smith and colleagues' model in this issue is that the different HIV prevention modalities interact.[15] The cascade begins to feel less like a cascade and more like a web. Garnett and colleagues,[9] begin with individual cascades for each of several core HIV prevention interventions and then suggest merging sequential cascades. They too acknowledge the challenges of denominators that are hard to define and measure and may change as people come in and out of "seasons of risk".[16] They talk of "a population at risk of acquiring infection over a given period of time", but even within easily identifiable populations, the actual risk may vary enormously and "risk perception" a key element in the demand step of the cascade may or may not be close to this actual risk. For example, the recorded incidence in the subset of men having sex with men who returned for more than one HIV test at a Barcelona clinic averaged 2·5 per 100 person-years, but a few questions about partnerships, sexually transmitted infections, and sexual behaviour disaggregated the population into groups with incidence of less than 1 per 100 person-years up to 25 per 100 person years.[17] Men who seek out services or trials that offer pre-exposure prophylaxis have substantially higher risk than other men from the same community, but they are hard to count for a cascade denominator.[18]

HIV prevention interventions are situated within a broader context, and structural interventions, such as keeping girls in school for more years, can lead to important reductions in HIV risk.[19] However, the benefits of longer education or improved gender relationships go far beyond HIV control. These externalities are hard to capture in a framework based on linear transitions towards a single objective. Likewise the benefits of apparently narrowly focused HIV prevention interventions may extend to broader sexual and reproductive health benefits and to linking previously undiagnosed individuals into HIV treatment programmes.

Cascade analysis is one of the many tools that now populate the ever growing field of a range of overlapping disciplines such as implementation science or operations research or health systems research. Its power is in highlighting the gaps in implementation along a particular well characterised pathway. Value chain analysis, originally conceived for maximising profits within businesses may allow for a wider perspective.[20] As Garnett and colleagues[9] point out, "each intervention can be separated out". In the new era of the sustainable development goals, the emphasis is on integration and universal coverage. Attempting to measure the drop out along the process of each component of a prevention approach may be a strong way to improve performance but may not be the best overarching framework for prevention. The management framework and the core results for HIV Prevention by 2020[2] make prevention cascades just one element of quality improvement.

When David Livingstone stumbled upon the largest cascade in Africa, he learned that it was called Mosi-oa-tunya, the smoke that thunders. It would be a shame if the power of cascade analysis was hidden by attempts to shoehorn prevention frameworks into a linear model.

Peter Godfrey-Faussett
UNAIDS, Avenue Appia 20, Geneva, Switzerland; and Faculty of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, Keppel Street, London, UK
godfreyp@unaids.org

I declare no competing interests.

1 UNAIDS. Global AIDS Update 2016. http://www.unaids.org/sites/default/files/media_asset/global-AIDS-update-2016_en.pdf (accessed June 10, 2016)
2 Dehne KL, Dallabetta G, Wilson D, et al. HIV Prevention 2020: a framework for delivery and a call for action. *Lancet HIV* 2016; **3:** e323–32.
3 UNAIDS. 90–90–90 — an ambitious treatment target to help end the AIDS epidemic. http://www.unaids.org/en/resources/documents/2014/90-90-90 (accessed June 11, 2016).
4 INSIGHT START Study Group. Initiation of antiretroviral therapy in early asymptomatic HIV infection. *N Engl J Med* 2015; **373:** 795–807.
5 TEMPRANO ANRS 12136 Study Group. A trial of early antiretrovirals and isoniazid preventive therapy in Africa. *N Engl J Med* 2015; **373:** 808–22
6 WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. http://www.who.int/hiv/pub/arv/arv-2016/en/ (accessed June 11, 2016).
7 Krishnaratne S, Hensen B, Cordes J, Enstone J, Hargreaves JR. Interventions to strengthen the HIV prevention cascade: a systematic review of reviews. *Lancet HIV* 2016; **3:** e307–17.
8 Hargreaves JR, Delany-Moretlwe S, Hallett TB, et al. The HIV prevention cascade: integrating theories of epidemiological, behavioural, and social science into programme design and monitoring. *Lancet HIV* 2016; **3:** e318–22.

9 Garnett GP, Hallett TB, Takaruza A, et al. Providing a conceptual framework for HIV prevention cascades and assessing feasibility of empirical measurement with data from east Zimbabwe: a case study. *Lancet HIV* 2016; **3:** e297–306.

10 Waaler H, Piot M. The use of an epidemiological model for estimating the effectiveness of tuberculosis control measures. *Bull World Health Organ* 1969; **41:** 75–93.

11 Hayes R, Wawer M, Gray R, Whitworth J, Grosskurth H, Mabey D. Randomised trials of STD treatment for HIV prevention: report of an international workshop. HIV/STD Trials Workshop Group. *Genitourin Med* 1997; **73:** 432–43.

12 Mumba M, Visschedijk J, van Cleeff M, Hausman B. A Piot model to analyse case management in malaria control programmes. *Trop Med Int Health* 2003; **8:** 544–51.

13 UNAIDS. Fast-tracking combination prevention. http://www.unaids.org/sites/default/files/media_asset/20151019_JC2766_Fast-tracking_combination_prevention.pdf (accessed June 11, 2016).

14 Bauer GR, Travers R, Scanlon K, Coleman TA. High heterogeneity of HIV-related sexual risk among transgender people in Ontario, Canada: a province-wide respondent-driven sampling survey. *BMC Public Health* 2012; **12:** 292.

15 Smith JA, Anderson S-J, Harris KL, et al. Maximising HIV prevention by balancing the opportunities of today with the promises of tomorrow: a modelling study. *Lancet HIV* 2016; **3:** e289–96.

16 Namey E, Agot K, Ahmed K, et al. When and why women might suspend PrEP use according to perceived seasons of risk: implications for PrEP-specific risk-reduction counselling. *Cult Health Sex* 2016; published online April 19. DOI:10.1080/13691058.2016.1164899.

17 Ferrer L, Loureiro E, Meulbroek M, et al. High HIV incidence among men who have sex with men attending a community-based voluntary counselling and testing service in Barcelona, Spain: results from the ITACA cohort. *Sex Transm Infect* 2016; **92:** 70–75.

18 McCormack S, Dunn DT, Desai M, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. *Lancet* 2016; **387:** 53–60.

19 De Neve JW, Fink G, Subramanian SV, et al. Length of secondary schooling and risk of HIV infection in Botswana: evidence from a natural experiment. *Lancet Glob Health* 2015; **3:** e470–77.

20 Kim JY, Rhatigan J, Jain SH, Weintraub R, Porter ME. From a declaration of values to the creation of value in global health: a report from Harvard University's Global Health Delivery Project. *Glob Public Health* 2010; **5:** 181–88.