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The HIV Care Cascade: Simple Concept, Complex Realization

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Introduced in 2009 to represent the status of the HIV epidemic in Washington, DC, the HIV care cascade has become a critical metric for program assessment.[1] The cascade has been embraced in the United States National HIV/AIDS Strategy and by the WHO.[2] With guidance from the Centers for Disease Control and Prevention, most state and large urban health departments use routinely collected surveillance data to provide estimates of the number of HIV-infected persons living in their jurisdiction and the proportion at each stage of the cascade, including diagnosed, linked to care, retained in care, on antiretroviral therapy (ART), and virally suppressed. Given the variable potential for transmission by HIV-infected persons depending on their position in (or outside of) the cascade, this stepped framework is appealing.[3]

In the United States, HIV/AIDS surveillance data are captured in the expanded HIV/AIDS reporting system (eHARS). This system includes physician, laboratory, and hospital reports of HIV and AIDS diagnoses for persons living in a given jurisdiction; data for persons living with HIV (PLWH) who in-migrate to the jurisdiction; and deaths for HIV-infected persons. In many locations, laboratory reporting of CD4 count and HIV RNA concentration (viral loads) is mandated and recorded in eHARS. In estimating the cascade, reported CD4 or viral loads are used as a proxy for active engagement in HIV care. Similarly, the viral load measures provide direct evidence of viral suppression.

Although intuitively appealing, in practice, the cascade is difficult to estimate accurately. Furthermore, the cascade may oversimplify the complexity of HIV care in the US and globally. In this issue of *Sexually Transmitted Diseases*, Buskin, et al. describe one major source of error in the estimation of the cascade – migration (4). Here, we discuss migration and other challenges in estimating the cascade.

The fundamental observations of Buskin, et al., are that the number of PLWH in King County, Washington and the proportion of persons out of care were overestimated with routine surveillance estimates due to migration of residents (4). The number of PLWH varied from a low of 6018 if in- and out-migration were addressed to 8120 if only in-

migration was considered. The proportion out of care varied from a low of 16% of PLWH when out-migrants were removed from the denominator to 31% if out-migration was ignored. These observations clearly show the significant impact of migration on the estimates of the cascade.

The procedures used to determine the residence status of PLWH were not simple, but are within the capabilities of many jurisdictions. Deaths were identified by periodic linkage to death databases, such as the Social Security Death Index. PLWH who were in care but who did not have CD4/VL tests reported were identified by matching surveillance data to Medical Monitoring Project data and Ryan White Care Act quality assurance data. A partnership with a large public health hospital allowed identification of additional PLWH who were in care but had no reported laboratories. Finally, residence information in Accurant, a for-profit data warehouse of residential information was used to identify PLWH who had moved out of the jurisdiction. These activities were followed by attempts to contact the last medical provider and the individual, if the status remained uncertain after all matching activities. With these procedures, the King County staff classified 47% of investigated persons as relocated, 7% as deaths, and 8% with unknown disposition; the remaining 38% continued to be King County residents. Although not discussed in the paper, accurate identification of individual matches in multiple databases is not straightforward, and further work addressing the performance of matching algorithms is necessary to assess accuracy.

Migration is only one problem in estimating the cascade. Each cascade stage presents its own challenges for estimation and potential sources of error.

The first cascade estimate, number of persons infected with HIV, is one of the most challenging to estimate accurately, especially in the United States. Current estimates of the total number of PLWH are based on diagnosed and reported HIV cases and assumptions about the number of persons who remain undiagnosed. Reported HIV cases are likely an underestimate of diagnosed cases, due to underreporting. More accurate estimation of both the number of PLWH and diagnosed cases would require population-based surveys, as well as alternative sampling methods that would identify hard-to-reach populations. Unfortunately, such surveys are expensive, infrequently performed, and may be biased because people with known HIV infection may be less likely to participate, at least in some settings.[5]

The number of PLWH who have been diagnosed is taken to be equal to the number of diagnoses reported, although sometimes a correction for reporting delays is incorporated. Although reporting of HIV diagnoses is thought to be acceptably complete with minimal duplication,[6] the diagnosis date used to anchor PLWH to a particular cross-section of the HIV-infected population is often inaccurate.[7] As with the King County study, most jurisdictions rely on reported laboratory data to derive estimates of persons linked to and engaged in care. However, the accuracy and timeliness of such reports is undetermined. Estimates of engagement in HIV care may be biased downward due to underreporting of lab results. Some laboratories may not report results due to lack of technological capacity, time constraints, or concerns about HIPPA violations. Laboratories that are reporting may

omit results if laboratory test codes change and results are missed in automated queries. Laboratory results collected as part of research studies are exempt from reporting in some states. Additionally, as HIV treatment has become more successful and less toxic, some physicians have reduced the frequency of testing,[8] potentially leading to misclassification of disengagement from care. Without appointment data, persons who have remained in care but have not had CD4 and viral load tests will be classified as being out of care.

The number of persons initiated on antiretroviral therapy cannot be estimated without access to prescription information or medical records. In some jurisdictions, such data are captured in Ryan White administrative data or by the Medical Monitoring Project, but cannot be accurately assessed from eHARS. However, given that the Ryan White program reflects predominantly resource-poor settings and the MMP likely oversamples large providers or patients who seek care more frequently, estimates derived from these populations are likely biased. But, the magnitude of this bias is unknown.

The proportion of PLWH with suppressed viral load also presents challenges to estimation. Laboratory data are likely to be underreported as outlined above, in part, because persons with undetectable viral loads (i.e. negative assays) may not be reportable in some jurisdictions. Furthermore, clarifying the denominator can be challenging, as persons engage and disengage from care. Additionally, some persons will have multiple assays within the evaluation period, which may be undetectable at one time but detectable at others. These detectable events may reflect true viral failure or simply a detectable “blip”. Finally, the extent to which the estimated proportion of PLWH who are virally suppressed affects the HIV force of infection in the community is highly dependent on the HIV prevalence and the viral load of PLWH with no laboratory results reported.[9]

Movement through the cascade is typically presented as a linear process, but in reality, it is cyclical. Persons may be diagnosed but delay seeking care until symptoms develop, entering the cascade through a “side door” and initiate treatment immediately, spending essentially no time in the intermediate cascade stages.[10] In addition, persons may drop out of care and re-engage at a later point. Cyclical engagement/disengagement in care, referred to as “churn,” appears to be quite common: Buskin et al. found about 20% of persons in the King County area appeared to have dropped out of care for at least 12 months during the five year study period (4).

Given the challenges in estimating the cascade, what can be done to improve its accuracy? Buskin, et al. have made a significant contribution to improving its measurement by addressing the critical issue of migration (4). Next steps include careful evaluation of the strengths and weaknesses of surveillance data, coupled with consideration of the population that each data source represents. Triangulation of data sources with these considerations in mind is likely to result in a more nuanced understanding of each cascade stage, especially if investigators and public health officials provide a range of estimates for each cascade stage, rather than an artificially precise single numerical estimate. Uncertainty of surveillance estimates can be informative, guiding efforts to improve imprecise estimates. In addition, coordination across jurisdictions will improve estimates by facilitating monitoring of both migration and care across political boundaries. Finally, best practices should be established

for applying surveillance data to estimation of the cascade, such as the approach to identify the current residence of “missing persons.”

The HIV care cascade is undoubtedly a critical tool for conceptualizing and monitoring the HIV epidemic in the United States and globally. However, the challenges to enumerating the cascade accurately have been largely overlooked. Given the importance of the cascade in monitoring our efforts to control the epidemic and improve the lives of PLWH, considerable efforts should be devoted to improving its accuracy. The laudable work of Buskin, et al. is an important contribution to these efforts (4).

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