

**Falling through the cracks and dying: missed clinic visits and mortality among HIV-infected patients in care**

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Although necessary to improve individual health and maximally reduce HIV transmission, complete virologic suppression is only achieved by a minority of HIV infected persons in the US, a reality that has been highlighted repeatedly since the initial description of the HIV care cascade by Gardner et al in 2011 (1). The HIV care cascade, detailing patients diagnosed, linked and retained in care, and finally virologically suppressed, is a powerful graphic that demonstrates how patients fail to reach the next milestone of the care continuum at a variety of critical points, each representing a focus for intervention. The desire to utilize the care continuum for the monitoring and evaluation of HIV care has led to the development of clear definitions for each column by the Institute of Medicine, the Department of Health and Human Services and the Ryan White Program (2-4). Retention in care has proven to be difficult to define as there is no clear gold standard (5). Achieving retention in care also poses unique challenges and suffers from a paucity of proven effective interventions. Unlike many of the earlier steps on the cascade, improving retention requires a significant longitudinal effort while diagnosis and linkage can be seen as “point in time” interventions. Any discussion of retention in care must acknowledge that ultimately the most important outcome to limit AIDS-associated deaths is viral suppression. Appropriate re-evaluation of the continuum has highlighted that patients not retained in care may still be virally suppressed leading newer versions of the continuum to show the columns independent of achieving the prior milestone (6,7).

Given that the number of patients suppressed but not retained is relatively small, this study by Mugavero et al with the CFAR Network of Integrated Clinical Systems (CNICS) investigators highlights the importance of finding meaningful measures that are associated with outcomes (8). The authors show a dose-response relationship between missed visits and all-cause mortality and propose that the “missed visit metric” may add to existing definitions designed to describe

retention. Importantly, this focus on predicting mortality leads to four critical questions that need to be answered in order to determine how best to use these data and other measures that predict mortality outcomes.

***When do patients die?*** Although the “leakage” in the care continuum is well-described, little has been done to elucidate the contribution of mortality to patients not reaching the final milestone of virologic suppression. Do patients die between diagnosis and linkage to care? Or between linkage and retention in care but before starting antiretroviral therapy (ART)? Or it is after ART has been started? The design of the study by Mugavero et al excluded from analysis over one hundred patients (24% of all deaths in this cohort) who died early in the cascade; the remainder died after 24 months. This proportion of early deaths may vary considerably by geographic location, stage at diagnosis and percentage of women and racial minorities. One could imagine a “cascade of death” akin to the “cascade of care” where deaths are plotted as occurring at different stages in the cascade. In such an analysis, late diagnosis may be a more significant driver of increased mortality than missed visits.

***Why are missed visits associated with mortality and what are the causes of death?*** Because there is no gold standard definition of retention in care and little is known about interventions to improve retention, this study reporting on increased mortality in a dose response fashion for those with missed visits is an important contribution to the literature. Missed visits are not uncommon and have been found to be associated with poor outcomes in chronic diseases other than HIV (9,10) but, despite that, in 2012 when the Institute of Medicine published the report entitled “*Monitoring HIV Care in the United States: Indicators and Data Systems*” (2), missed visits were not included in the list of core indicators recommended to monitor HIV care. As a result, neither DHHS nor HRSA have included measuring missed visits in its reporting

requirements. While the association between missed visits and death intuitively seems to be associated with loss of virologic control of HIV, this has not been established. Were deaths in patients with controlled viremia and/or due to non-AIDS related causes? Were missed visits a surrogate for poor preventive care for other health issues like heart disease and hypertension? Or is the inability to keep visits associated with other life stressors and/or an increased risk of violent or accidental deaths? Or were these deaths AIDS-associated? Understanding the causes of death is critical to understanding if these deaths might be averted with interventions to improve retention and decrease the numbers of missed visits.

***Are there effective actionable interventions to improve visit adherence and would such an intervention change mortality?*** How should this information be used? Should clinics and clinicians monitor for missed visits and should this be an actionable event? While focusing on missed visits seems appealing, in fact two-thirds of the study patients had at least one missed visit and fully a quarter of the patients missed more than 2 visits over a 24 month period. An intervention designed to improve visit adherence for this population would need to target a significant proportion of a clinic's population. This would argue for further efforts to identify the subpopulation of those with missed visits at highest risk for mortality. A single isolated indicator is not likely to be as powerful as a predictive rule which combines additional variables, which may include last viral load, baseline CD4 count, age, black/African-American race or other factors associated with poorer outcomes. In the face of a possible decline in resources for non-billable services, identification of a subgroup in need of intensive intervention will be more cost-effective and therefore more accessible to clinics with limited monetary resources. Further research is needed to ensure not only efficacy but effectiveness of interventions and those that are studied must be scalable. Prospective studies looking at interventions that target missed

visits are clearly needed and these must evaluate meaningful outcomes such as mortality to ensure that improved visit adherence correlates with improved mortality.

The authors make a critical point of advocating for integration of data with regional public health surveillance. Accurately defining who is out of care or lost to care is vital and will also limit using scarce resources to track patients who have transferred care elsewhere or have died. The current shift in insurance status due to the Affordable Care Act complicates this picture as patients are more likely to change care providers than ever before. Combining state or municipality data with clinic level data by building close collaborations with Departments of Public Health (DPHs) will improve the ability to correctly classify patients who appear non-adherent to visits at the clinic level. Because some states have legal statutes which limit two-way sharing of data between DPHs and providers, updating of this legislation needs to be actively pursued and has been successfully revised in Georgia. Legal barriers to cooperation between the public health sector and care providers limit the ability to respond to the epidemic in the US.

***Should funding decisions be based on this information and how does this apply to the US epidemic?*** The use of core indicators (with or without the addition of missed visits) has been proposed as a measure of quality on which to base funding decisions for clinics. A nuanced understanding of clinic-level challenges and the population served will be required in order to not inadvertently penalize those clinics that may need the most resources. Currently, those clinics with larger socioeconomically disadvantaged populations or those in regions where stigma continues to be a significant deterrent to clinic attendance are more likely to have poorer retention in care by any measure. Interventions to improve retention are costly and these clinics may in fact need proportionally greater resources to improve the care continuum. These factors

are more likely to be present in the heavily impacted Southeastern United States where additional efforts are sorely needed to reduce community viral load and transmission in an effort to curb the current epidemic.

In summary, a number of obstacles prevent people with HIV from experiencing optimal health. Among these are late diagnosis, delayed access to care, breaks in care, delayed prescription and intermittent use of antiretroviral therapy, untreated mental health and substance use disorders and unmet basic needs. An improved understanding of factors that lead to poor retention in care and increased mortality is needed, and studies to develop interventions that impact retention and improve mortality are critical. The current study adds an additional measurable factor to our armamentarium to track patients and shows a significant correlation with mortality. Learning to optimally use these data requires additional answers and enhanced collaborations with the public health sector.

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