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Viral suppression among persons in HIV care in the United States during 2009–2013: Sampling bias in Medical Monitoring Project (MMP) surveillance estimates

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Abstract

Purpose: To assess sampling bias in national viral suppression (VS) estimates derived from the Medical Monitoring Project (MMP) resulting from use of an abbreviated (four-month) annual sampling period. We aimed to improve VS estimates using cohort data from the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) and a novel cohort-adjustment method.

Methods: Using full calendar years of NA-ACCORD data, we assessed timing of HIV care attendance (inside versus exclusively outside MMP's four-month sampling period), VS status at last test (<200 vs. ≥200 copies/mL), and associated demographics. These external estimates were used to standardize MMP to NA-ACCORD data with multivariable regression models of care attendance andVS, yielding adjusted 2009–2013 VS estimates with 95% confidence intervals (CI).

Results: Weighted percentages of VS among persons in HIV care were 67% in 2009 and 77% in 2013. These estimates are slightly lower than previously published MMP estimates (72% and 80% in 2009 and 2013, respectively). The number of persons receiving HIV care was previously underestimated by 20%, because patients receiving care exclusively outside the MMP sampling period did not contribute toward the weighted population estimate.

Conclusions: Careful examination of national surveillance estimates using data triangulation and novel methodologies can improve the robustness of VS estimates.

Keywords

HIV viral suppression; HIV clinical care; surveillance; indirect standardization

Introduction

Sustained viral suppression (VS), which can beachieved through consistent use of antiretroviral therapy (ART), greatly improves health[1] and life expectancy[2] for persons living with HIV, while effectively eliminating HIV transmission risk[3,4]. Monitoring population-level VS is important for demonstrating progress toward reaching national goals of improving the health of persons living with HIV and reducing new infections[5]. The Centers for Disease Control and Prevention (CDC) has used two sources of surveillance data to measure VS. The Medical Monitoring Project (MMP) is a surveillance system that provides data to estimate VS among persons in HIV care, and the National HIV Surveillance

System (NHSS) provides data to measure VS among persons with diagnosed HIV in a subset of jurisdictions.

MMP collects behavioral and clinical data from annual, cross-sectional samples of persons living with diagnosed HIV using interviews and medical record abstraction[6]. During 2009–2015, MMP described U.S. adults in HIV clinical care by sampling U.S. jurisdictions and territories, followed by HIV clinical care facilities within those jurisdictions, then persons seeking care within those facilities during January – April of a given year. The January – April sampling period was used to expedite data collection for annual estimates, and at the time of MMP's inception, this sampling period captured 88% of adults in clinical care[7]. This coverage estimate has not been reassessed.

Surveillance estimates should be periodically revisited in light of temporal changes and methodological advances. One important temporal change over MMP's lifespan is that the recommended number of clinical visits to monitor virologic response for persons on ART has decreased over time[8]. As a result, persons engaged in HIV clinical care during a given year may be less likely to seek care during the four-month sampling period, and thus less likely to be sampled for MMP. The result of this sampling bias would be an underestimated weighted population size of persons receiving HIV clinical care and possibly biased estimates of the number and percentage of persons in HIV care with VS.

We previously published findings from MMP indicating VS among persons in HIV clinical care increased from 72% to 80% during 2009–2013[9]. A recent assessment of potential sampling bias in MMP indicates these estimates should be revisited[10]. Using 2012 data from a single clinical cohort, the HIV Outpatient Study (HOPS), in combination with a novel methodology to adjust for possible sampling bias, we demonstrated that MMP may have undercounted persons in HIV clinical care and that VS prevalence may have been differential among sampled versus un-sampled persons. Here, we assess the potential effect of sampling bias on MMP-derived VS estimates during 2009–2013 using data from a large, geographically diverse group of clinical cohorts from the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD).

Material and methods

NA-ACCORD is the largest multisite collaboration of clinical and interval cohorts in the United States and Canada, representing over 20 cohorts and 200 clinical care sites. Cohorts contribute data using standardized methods for patients ≥18 years including demographics, ART prescription, laboratory test results, and dates of primary HIV clinical visits. Participants are consented locally and all study activities have been approved by the local institutional review boards for each site and for Johns Hopkins University School of Medicine[11].

For this analysis, we included nine United States clinical cohorts: Fenway Community Center (MA), the HIV Outpatient Study, the HIV Research Network (multi-state), Johns Hopkins HIV Clinical Cohort (MD), Retrovirus Research Center (PR), University of Alabama at Birmingham 1917 Clinical Cohort (AL), University of Washington HIV Cohort

(WA), Veterans Aging Cohort Study (multi-state), and Vanderbilt Comprehensive Care Clinic HIV Cohort (TN). We chose these cohorts based on the following criteria: being observational in nature, being located in the United States, and being willing to participate in this analytic activity. For each of the years 2009–2013, we considered adult patients who had ≥1 CD4 test, viral load measurement, or HIV clinical care visit during January 1 – December 31 as having received HIV care during that year, yielding approximately 30,000 patients annually. Within each year, we categorized patients as receiving care within the MMP sampling period (January 1 – April 30) or exclusively outside the sampling period. We used individual data on age (categorized as 18–24, 25–34, 35–44, 45–54, and 55+ years) and race/ethnicity (categorized as non-Hispanic white, non-Hispanic black, Hispanic, and other) as predictors of clinical care receipt exclusively outside the MMP sampling period. Sex at birth was not associated with care receipt exclusively outside the sampling period.

We applied our previously described cohort-adjustment method[10], which uses principles of indirect standardization[12] and synthetic estimation[13] to adjust MMP-derived estimates of VS among persons in HIV care using 2009–2013 NA-ACCORD data. First, separately for each year of NA-ACCORD data, we fit a logistic model regressing receipt of care exclusively outside the sampling period on age group, race/ethnicity, and the interaction term age group*race/ethnicity. This model yields estimated odds of care receipt exclusively outside the sampling period, among all persons receiving care during the year, within each age group*race/ethnicity stratum. These odds, multiplied by the MMP-derived weighted estimate for number of persons receiving HIV medical care during the sampling period, yielded adjusted estimates for the number of persons who would not have been included in the MMP sample despite receiving care during the year.

Next, for each year of NA-ACCORD data, we fit a logistic model regressing VS (viral load <200 copies/mL or undetectable) at most recent test (last in calendar year) on care receipt exclusively outside the sampling period, age, race/ethnicity, and the interaction term age*race/ethnicity. We estimated the predicted marginal prevalence ratios of VS among those receiving care exclusively outside versus inside the sampling period, within each age*race/ethnicity stratum[14]. Multiplying these prevalence ratios by MMP-derived VS estimates yielded VS estimates for persons who would not have been sampled.

We combined these estimates with the original MMP weighted population size estimates for VS, yielding revised estimates for the total number of persons receiving care and VS, and the percent VS among persons in care. Point estimates for all outcomes and the 95% confidence intervals for the percent VS were obtained from the 50^{th} (point estimates), 2.5^{th}, and 97.5^{th} percentiles (confidence intervals) of Monte Carlo bootstrap simulations. Simulations were based on 100,000 runs in which we jointly sampled normal distributions with means and standard deviations, respectively, defined by the point estimates and the standard errors for all regression model parameter estimates and MMP weighted frequency estimates.

Results

The cohort-adjustment method yielded weighted population estimates of 355,156 persons VS and 526,850 in care in 2009 and 441,619 persons VS and 595,807 in care in 2013 (Table 1). Therefore, weighted percentages of VS among persons in HIV care in the United States were 67% in 2009 and 77% in 2013. The estimated number of persons in HIV care using the MMP data alone was approximately 20% lower in each year than the estimate yielded by the cohort-adjustment method and the two data sources together. Similarly, the estimated number of persons who were VS using the MMP data alone was 15–17% lower in each year than the estimate yielded by the two data sources together. This pattern held across age and race categories, although the percent differences for weighted estimates of the numbers of persons in HIV care and virally suppressed were larger in each year among younger versus older age groups (Supplemental table).

In 2009, VS among persons in HIV care ranged from 60% among non-Hispanic blacks to 70% among Hispanic/Latinos and 75% among non-Hispanic whites (Table 2). In 2013, VS ranged from 72% among non-Hispanic blacks to 78% among Hispanic/Latinos and 84% among non-Hispanic whites. The VS percentages generally increased with increasing age group in each year. In 2009, 54% of 18–24 year olds in HIV care were VS compared to 79% of persons aged 55 years or older. In 2013, 58% of 18–24 year olds in HIV care were VS compared to 84% of persons aged 55 years or older. The largest percentage increases in VS from 2009 to 2013 were observed among non-Hispanic blacks and among persons aged 25–34 years, while only modest increases were observed among the youngest and oldest age groups.

Discussion

Using two large, geographically diverse data sources and a novel methodology, we estimated that the percentage of persons in HIV clinical care who were VS increased from 67% in 2009 to 77% in 2013. These estimates are similar to, but lower than, previously published MMP-derived estimates, which indicated VS in this population increased from 72% (95% confidence interval [CI]: 69–74) in 2009 to 80% (95% CI: 78–83) in 2013[9]. Conversely, weighted population sizes presented here suggest that the *numbers* of persons in HIV care and the number VS were previously underestimated.

The estimated percentage of persons in HIV care who were VS was overestimated due to lower VS prevalence among persons un-sampled by MMP. NA-ACCORD cohort data indicated persons not receiving care during the sampling period had lower VS prevalence than those receiving care in the sampling period, which may be explained by a lower frequency of visits, thus a lower probability of receiving care during the sampling period and sub-optimal engagement in care. The finding likely reflects a higher likelihood of any care receipt during the four-month sampling period due to a higher overall number of care visits during a given year, which is associated with a higher probability of VS.[15] In other words, the more frequently a patient seeks care during the year, the more likely they are to be seen during a defined period, regardless of the period used. After making adjustments for these biases, the 2013 estimate of VS prevalence among persons in HIV care was 77.3%, which is

nearly identical to the 77.2% among persons in NHSS with an indication of HIV care during 2013 (as indicated by ≥1 reported CD4 or viral load test).[6]

The weighted population size for the total number of persons in HIV care in the United States was previously estimated to be 421,186 in 2009,[16] which is 20% lower than the 526,850 estimated using the cohort-adjustment method to account for un-sampled persons. Similarly, the weighted population size for the total number of persons in HIV care in the United States who were VS was previously estimated at 301,403 in 2009 (Medical Monitoring Project, unpublished data), which was 15% lower than the 355,156 presented here. These are substantially higher weighted population estimates for persons who are in HIV care and VS than those previously published. If used together with the number of persons living with diagnosed HIV during this period, this refinement of the weighted population estimates may also provide additional information about how many persons with diagnosed HIV were receiving care and VS at this time.[17]

In 2015, MMP expanded to represent all persons living with diagnosed HIV and now samples directly from the NHSS register of all persons with diagnosed HIV. The four-month sampling period is no longer used, and HIV care and treatment outcomes are now estimated for all diagnosed persons. Despite this change, examining bias in pre-2015 estimates is important for accurate interpretation of current estimates in their historical context. Historical estimates are used routinely in transmission models and for projecting goals and feasibility of change in clinical outcomes over time. Additionally, periodic quantitative evaluation of HIV surveillance estimates in light of temporal changes in population characteristics, clinical practices, and other external factors is good scientific practice and may help to increase the perceived (and real) reliability of estimates derived from imperfect data systems with inexact methods.

This analysis has limitations. First, data adjustments can only be applied reliably within strata defined by at most two factors due to stratum-specific sample sizes[10]. We chose age group and race/ethnicity for stratification because, of the variables we could measure in both NA-ACCORD and MMP, these characteristics were most strongly associated with both care receipt exclusively outside the sampling period and VS. Notably, sex at birth was not associated with care receipt exclusively outside the sampling period. Second, we used slightly different age groups for this analysis compared to age groups used for the previously published MMP VS estimates, which limits comparability by age between previous and current estimates. However, the age groups used for the present analysis are nearly identical to those in other national HIV surveillance reports using NHSS data, so this may facilitate comparisons to, and joint use with, national case surveillance data. Last, while annual estimates of VS among persons in HIV care from the cohort-adjustment method overlap with confidence intervals for the previously published MMP estimates, statistical tests cannot be used to compare previous and current estimates because they rely on data from the same MMP participants.

VS among persons in HIV care is an important indicator of quality of clinical care and of the need for non-clinical care services that may help close the gap between the number of people in HIV clinical care and the number VS. These findings are an improvement upon

previously published estimates[9] and likely bring them closer to truth. VS increased during 2009–2013, but more work is needed for further gains, particularly among racial/ethnic minority groups and young people. Careful examination of national surveillance estimates using data triangulation and novel methodologies can improve the robustness of VS estimates and help to identify groups for which focused interventions are needed for sustained health improvements and prevention of new infections.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Weighted estimates for persons receiving HIV medical care and virally suppressed using Medical Monitoring Project data alone versus Medical Monitoring Project and North American AIDS Cohort Collaboration on Research and Design data and cohort adjustment method

	2009			2010			2011			2012			2013		
	N (95% CI) suppressed	N (95% CI) in care	% (95% CI) suppressed	N (95% CI) suppressed	N (95% CI) in care	% (95% CI) suppressed	N (95% CI) suppressed	N (95% CI) in care	% (95% CI) suppressed	N (95% CI) suppressed	N (95% CI) in care	% (95% CI) suppressed	N (95% CI) suppressed	N (95% CI) in care	% (95% CI) suppressed
MMP alone															
	301,296	421,119	71.6	327,108	442,601	73.9	361,421	478,380	75.6	368,161	476,197	77.3	393,282	490,960	80.1
	(274,737, 328,394)	(385,236, 457,196)	(69.8, 73.4)	(298,103, 356,461)	(405,023, 480,182)	(72.2, 75.6)	(328,679, 394,540)	(436,439, 520,172)	(73.9, 77.2)	(333,445, 403,092)	(433,418, 519,143)	(75.8, 78.8)	(360,540, 426,466)	(451,338, 530,855)	(78.7, 81.5)
MMP + NA-ACCORD															
	355,156	526,850	67.4	387,856	556,645	69.7	441,107	613,220	71.9	441,619	595,807	74.1	473,693	612,966	77.3
	(323,770, 387,092)	(482,009, 571,878)	(65.6, 69.2)	(353,344, 422,753)	(509,706, 603,665)	(68.0, 71.4)	(401,342, 481,295)	(559,998, 666,365)	(70.3, 73.6)	(400,008, 483,485)	(542,731, 649,090)	(72.5, 75.7)	(434,227, 513,686)	(563,724, 662,608)	(75.8, 78.7)

Ns represent weighted population totals.

Percentages are weighted percentages.

Table 2.

Cohort-adjusted viral suppression estimates among persons receiving HIV medical care, United States and Puerto Rico, 2009–2013: Medical Monitoring Project and North American AIDS Cohort Collaboration on Research and Design

	2009			2010			2011			2012			2013		
	N suppressed	**N in care**	**% (95% CI) suppressed**	**N suppressed**	**N in care**	**% (95% CI) suppressed**	**N suppressed**	**N in care**	**% (95% CI) suppressed**	**N suppressed**	**N in care**	**% (95% CI) suppressed**	**N suppressed**	**N in care**	**% (95% CI) suppressed**
Race/ethnicity															
White	137,190	181,928	75.4 (72.7, 78.1)	147,245	190,151	77.5 (74.9, 79.9)	161,464	208,454	77.5 (74.8, 80.1)	171,466	211,872	80.9 (78.8, 83.0)	165,290	197,123	83.9 (81.8, 85.9)
Black	132,492	220,821	60.0 (57.2, 62.8)	147,231	233,428	63.1 (60.5, 65.7)	164,573	248,071	66.4 (63.8, 68.9)	171,650	249,698	68.8 (66.2, 71.3)	191,412	265,507	72.1 (69.6, 74.6)
Hispanic	68,369	97,748	70.0 (66.6, 73.3)	73,636	105,819	69.6 (66.0, 73.2)	90,427	123,223	73.4 (70.0, 76.9)	78,052	106,466	73.3 (70.0, 76.7)	96,585	123,170	78.4 (75.7, 81.1)
Other	16,922	26,313	64.4 (56.3, 73.2)	19,616	27,279	72.0 (65.5, 78.7)	24,481	33,501	73.2 (66.1, 80.1)	20,280	27,721	73.3 (66.4, 79.9)	20,221	27,108	74.7 (68.4, 81.0)
Age (yrs)															
18 – 24	9,714	17,943	54.3 (44.9, 66.0)	10,140	23,771	42.8 (33.7, 52.8)	10,273	22,363	46.1 (38.9, 53.7)	12,435	22,734	54.8 (47.8, 61.9)	12,915	22,264	58.2 (50.5, 66.3)
25 – 34	34,979	68,551	51.2 (46.2, 56.0)	39,430	69,442	56.9 (52.0, 61.8)	48,734	78,994	61.8 (57.1, 66.5)	50,745	79,855	63.6 (59.8, 67.4)	51,822	77,742	66.7 (62.7, 70.7)
35 – 44	89,008	141,034	63.2 (59.7, 66.6)	102,186	146,161	69.9 (66.9, 72.9)	96,515	140,894	68.6 (65.0, 72.1)	88,767	124,973	71.1 (68.2, 73.9)	94,616	126,617	74.8 (71.2, 78.3)
45 – 54	142,810	200,129	71.4 (68.8, 74.0)	146,172	202,630	72.2 (69.4, 74.8)	175,179	232,568	75.3 (73.0, 77.8)	166,162	218,258	76.2 (73.3, 78.9)	175,380	221,196	79.3 (77.0, 81.6)
55+	78,359	99,202	79.0 (75.7, 82.2)	89,818	114,704	78.3 (75.5, 81.0)	110,175	138,471	79.6 (76.6, 82.6)	123,318	149,926	82.3 (79.8, 84.7)	138,784	165,199	84.0 (81.8, 86.2)
Total	355,156	526,850	67.4 (65.6, 69.2)	387,856	556,645	69.7 (68.0, 71.4)	441,107	613,220	71.9 (70.3, 73.6)	441,619	595,807	74.1 (72.5, 75.7)	473,693	612,966	77.3 (75.8, 78.7)

Ns represent weighted population totals.

Percentages are weighted percentages.