

Gaps Up To 9 Months Between HIV Primary Care Visits Do Not Worsen Viral Load

Lytt I. Gardner, PhD,¹ Gary Marks, PhD,¹ Unnati Patel, MPH,² Edward Cachay, MD,³ Tracey E. Wilson, PhD,⁴ Michael Stirratt, PhD,⁵ Allan Rodriguez, MD,⁶ Meg Sullivan, MD,⁷ Jeanne C. Keruly, MS,⁸ and Thomas P. Giordano, MD⁹

Abstract

Current guidelines specify that visit intervals with viral monitoring should not exceed 6 months for HIV patients. Yet, gaps in care exceeding 6 months are common. In an observational cohort using US patients, we examined the association between gap length and changes in viral load status and sought to determine the length of the gap at which significant increases in viral load occur. We identified patients with gaps in care greater than 6 months from 6399 patients from six US HIV clinics. Gap strata were >6 to <7, 7 to <8, 8 to <9, 9 to <12, and ≥12 months, with viral load measurements matched to the opening and closing dates for the gaps. We examined visit gap lengths in association with two viral load measurements: continuous (log₁₀ viral load at gap opening and closing) and dichotomous (whether patients initially suppressed but lost viral suppression by close of the care gap). Viral load increases were nonsignificant or modest when gap length was <9 months, corresponding to 10% or fewer patients who lost viral suppression. For gaps ≥12 months, there was a significant increase in viral load as well as a much larger loss of viral suppression (in 23% of patients). Detrimental effects on viral load after a care gap were greater in young patients, black patients, and those without private health insurance. On average, shorter gaps in care were not detrimental to patient viral load status. HIV primary care visit intervals of 6 to 9 months for select patients may be appropriate.

Keywords: HIV, gaps in care, viral load, viral suppression

Introduction

ENTRY INTO HIV care provides access to antiretroviral therapy (ART), and retention in care provides opportunity for clinical management and assistance to patients with achieving and sustaining suppressed viral load, which has both personal¹ and public health^{2,3} benefits. Guidelines for clinical care of HIV patients recommend primary care visits every 3–4 months.⁴ Patients who are clinically stable with

sustained viral suppression may be able to extend the visit interval to 6 months, but intervals longer than 6 months for in-person care and viral load testing are not recommended.⁴

Patients who go beyond a 6-month interval have generally been considered to have a “gap” in care. Cohort studies have shown that gaps in care range from 27% to 63% in patients with a new HIV diagnosis^{5–9} and 24–35% in cohorts that contain a majority of established patients.^{10–16} These studies defined gaps as 6 or more months as well as 12 or more

¹Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia.

²Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention and ICF, Atlanta, Georgia.

³Department of Medicine, University of California School of Medicine, San Diego, California.

⁴Department of Community Health Sciences, School of Public Health, State University of New York, Downstate Medical Center, Brooklyn, New York.

⁵Division of AIDS Research, National Institute of Mental Health, Bethesda, Maryland.

⁶Division of Infectious Diseases, Miller School of Medicine, University of Miami, Miami, Florida.

⁷Department of Medicine, Boston University School of Medicine, Boston, Massachusetts.

⁸Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland.

⁹Department of Medicine, Baylor College of Medicine, Center for Innovations in Quality, Effectiveness, and Safety, Michael E. DeBakey VA Medical Center, Thomas Street Health Center and Harris Health System, Houston, Texas.

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months, used varying follow-up periods, and included completed and open-ended gaps. Altogether, these studies indicate the probability of experiencing a gap in care is substantial. However, it is an open question about just how harmful shorter gaps in care may be with respect to viral load status. The clinical significance of shorter gaps in particular must be carefully evaluated, because even though a patient may have visit intervals that extend beyond 6 months, the patient may be highly adherent to ART and have a suppressed viral load. Other patients with shorter gaps in care may not remain adherent, and their viral loads may increase during the gap.

Relatively little is known about how the length of the gap is associated with changes in viral load status. Our PubMed-NLM literature search identified 15 HIV cohort publications since January 2012 that specifically included measures of gaps in care of 6 months or more,^{5–19} but none assessed the relationship between gap length and changes in viral load over the gap interval. We examined this association and sought to determine the length of the gap at which significant increases in viral load occur. We identified patients who fell into one of five gap-interval strata ranging from a short gap (>6 but <7 months between primary care visits) to a long gap (≥ 12 months between visits). Using patient viral loads closest to the beginning and closest to the end of care gaps, we looked at two outcomes: changes in mean \log_{10} viral load from the beginning to the end of the gap for patients in each gap-interval and the proportion of patients in each gap-interval who began with a suppressed viral load, but who did not maintain suppression at the end of the gap.

Methods

Study participants and analysis design

HIV-infected adults receiving care at six academically affiliated HIV clinics in the United States were included in the analysis. The clinics were located in Birmingham, AL; Boston, MA; Houston, TX; Miami, FL; San Diego, CA; and Seattle, WA. Patients with no gaps in primary care, defined as two primary care visits with an interval ≤ 6 months between them, were excluded from analysis. However, results from intervals of 3–6 months are presented to illustrate change in “normal” intervals. In addition, patients with care gaps needed to have viral load results close in time to the dates of the two clinic visits comprising the opening and closing of the gap. We selected for analysis the first gap opening that occurred during the observation period defined for the cohort. Given the relatively short observation period, we did not include any subsequent gaps because of limited follow-up time to document the closing of the gap. Thus, we examined one gap per patient, and the gap length could range from just over 6 months to over a year. Patients with open-ended gaps and no return to the clinic were excluded from analysis.

The analytic cohort of patients with gaps in primary care (from the CDC/NIMH “APTcare” project) consisted of patients from the general HIV clinic population, regardless of prior clinic attendance history or viral load status.²⁰ The APTcare cohort observation period for patients with a qualifying gap interval was January 1, 2013 through December 31, 2015. The first patient care visit had to occur between January 1, 2013 and June 30, 2014. The second visit closing the care interval gap had to occur by December 31, 2015. Institutional Review Board approval was obtained at each participating site.

Patients in the cohort were identified by unique study numbers generated by a computerized algorithm at the clinics.

Outcome variables

Two viral load outcomes were examined: (1) a continuous measure of \log_{10} viral load at the opening and the closing of the gap and (2) a dichotomous measure, whether patients initially virally suppressed did not maintain suppression at the closing of the gap. Each measure used a window of ± 90 days for capturing the viral load result closest to the dates of the primary care visits that defined the opening and closing of the care gap.

Gap-interval strata and correlate variables

We examined five gap-interval strata: >6 to <7 months, 7 to <8 months, 8 to <9 months, 9 to <12 months, and 12 or more months. Several demographic variables (sex/orientation [women, men who have sex with men (MSM), and heterosexual men], age, race/ethnicity, recency of HIV diagnosis, and type of health insurance or assistance) were examined for inclusion in the statistical models. Patient-level ART prescription/use data were not available as a routinely collected variable in the clinics’ databases. However, the clinics tracked aggregated ART use for other reporting requirements, and ~ 90 –95% of the clinics’ populations had been prescribed ART during the observation period.

In addition to examining the five gap-interval strata, we identified patients without care gaps who had routine intervals of 3–6 months between primary care visits. In this, we selected the first instance of a nongap interval during observation. Some of these patients may also have had a gap later on and are included in one of the gap categories. We present these data for descriptive comparisons only.

Statistical analysis

For the continuous outcome, we used a paired-observations linear model with normal errors to calculate the unadjusted mean \log_{10} viral load at the opening and closing of care gaps and the difference between the means in each gap-interval strata. For descriptive purposes, we calculated the geometric means of the viral loads at the opening and closing of the gaps and the difference. Model-based mean differences (closing minus opening \log_{10} viral load) within each gap-interval strata were calculated from univariate least square means of the paired values. For patients with undetectable viral load, we used the value reflecting the limit of detection of the assay in calculating the means. To calculate the multivariable-adjusted differences, we used least square means from all the factors that met criteria for inclusion in the model ($p < 0.20$), in addition to the gap-interval variable. Based on collinearity diagnostics, length of time since HIV diagnosis was removed from the model to improve stability and precision of model estimates. For the dichotomous outcome, we examined the proportion of patients in each gap-interval strata with suppressed viral load (<200 copies/mL) at gap opening and who did not maintain suppressed viral load at gap closing. We estimated adjusted risk ratios from all the factors that met criteria for inclusion in the model ($p < 0.20$), in addition to the gap-interval variable. We used a multivariable Poisson model with robust standard errors for generating the model-adjusted risk

ratios.²¹ For selected demographic variables, we tested for differences in average days in gap with an omnibus likelihood ratio test, and least square means tests between subgroups. Statistical analyses were performed using SAS software version 9.3 (PROC GENMOD, SAS Institute, Cary, NC).

Results

A flowchart describing the steps in selecting the analytic cohort is presented in Fig. 1. The cohort included 6399 patients who had viral loads within the ± 90 -day windows; 83% of the viral loads were within ± 30 days of the opening and closing of the care gap. The patients in this cohort were overwhelmingly (91%) those diagnosed for more than 2 years, according to the length of time since HIV diagnosis variable.

As seen in Table 1, the mean \log_{10} viral loads at the beginning of the gap interval increased as the length of that interval increased. The unadjusted changes in viral load by the end of the gap also exhibited a dose-response pattern; however, the changes in viral levels were significant only when the gap length was 9 to <12 months and ≥ 12 months. For 9 to <12 months gaps, the geometric mean was 98 copies at opening of gap and 137 copies at closing of gap, a difference of 39 copies/mL on average; for 12 or more months, the geometric mean was 150 copies at opening and 259 copies at closing, a difference of 109 copies/mL on average. Adjusted results showed the same pattern—change in viral loads were significant only when the gap length was 9 to <12 months or ≥ 12 months. Unadjusted results indicated that all three age groups had a significantly higher end of gap viral load; in the adjusted result, the mid-aged (40–49 years) patients' change was significant. Patients with nonprivate health insurance had significantly higher end-of-gap viral loads in contrast to private health insurance, in both adjusted and unadjusted results. Non-Hispanic black patients had the highest \log_{10} viral loads at the beginning and end of gaps, and significant increases in \log_{10} viral load in both unadjusted and adjusted results.

In the dichotomous analysis (Table 2) that conditioned on patients having been suppressed at the start of the gap, 5242 or 82% of the 6399 patients in the cohort had a viral load <200 copies/mL at the opening of the care gap. Length of gap in

care showed a clear dose-response relationship, with increasing percentages of patients not maintaining their suppression as the gap length increased. Fewer patients became unsuppressed when the gap length was <12 months than ≥ 12 months. When the gap was ≥ 12 months, 23% of patients became unsuppressed. Black patients were significantly more likely than white patients to not maintain a suppressed viral load by the end of a care gap. The percentage who did not maintain suppression was higher among younger (18–39 years and 40–49 years) than older (50 years and older) patients, and among those who did not have private health insurance (vs. those who did). Also, fewer MSM than heterosexual men did not maintain suppression.

To explore further why these patient factors (age, health insurance, race/ethnicity) had distinct patterns of association with not maintaining a suppressed viral load after a gap in care, we evaluated in Table 3 the distribution of length of gap in care between and among levels of these three factors. This was done because if one of the factor subcategories had a significantly higher average gap length than others, that factor subcategory would be more likely not to maintain a suppressed viral load at the end of the gap in care. The age-group variable revealed that relative to patients aged 50 and older, patients aged 18–39 had the longest gap, about two-thirds of a month longer; and patients aged 40–49 years had average gaps about one-third of a month longer (both comparisons $p < 0.01$). In addition, patients aged 18–39 had the longest average gaps of all 13 factor levels in Table 2. Relative to patients with private insurance, patients with nonprivate health insurance had average gaps about one-half month longer ($p < 0.01$). Relative to non-Hispanic white patients, non-Hispanic black patients had average gaps about one-half month longer, and Hispanic patients had average gaps about one-third of a month longer (both comparisons $p < 0.01$).

A group of patients with routine visit intervals of 3–6 months contained 11,186 patients. The results for this group were not compared with the five gap-interval groups, as many of the patients had routine visit intervals before or after a gap in care and are thus not independent. For these 11,186 patients, there was a mean difference of -0.099 (signifying small improvement) for the closing minus opening \log_{10} viral

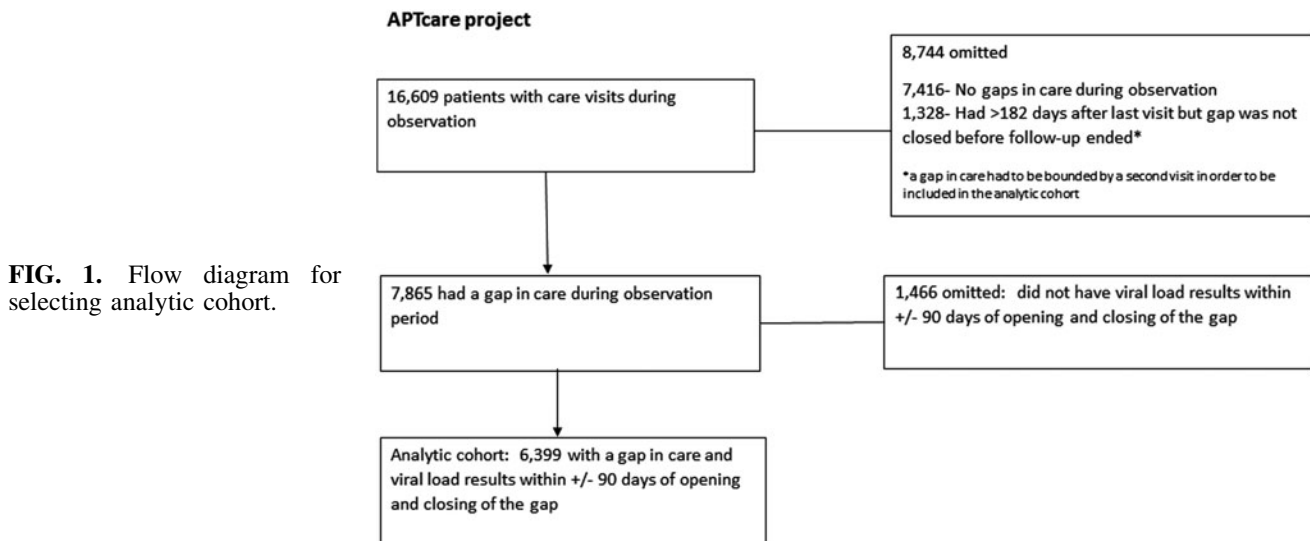


FIG. 1. Flow diagram for selecting analytic cohort.

TABLE 1. MEAN LOG₁₀ VIRAL LOADS AT BEGINNING AND END OF GAP IN PRIMARY CARE BY LENGTH OF THE GAP, APTCARE PROJECT (2013–2015)

| <i>Factors</i> | <i>Mean log₁₀ viral load at beginning of the gap (and SEM)</i> | <i>Mean log₁₀ viral load at end of the gap (and SEM)</i> | <i>Unadjusted change score and SEM (time 2 logVL–time 1 logVL)</i> | <i>Adjusted^a change score and SEM (time 2 logVL–time 1 logVL)</i> |
|-----------------------------------|---|---|--|--|
| APTCare project (N=6399) | | | | |
| Length of gap in care | | | | |
| >6 to <7 months (n=2084) | 1.71 (0.019) | 1.69 (0.019) | –0.017 (0.017) | –0.056 (0.028) |
| 7 to <8 months (n=1173) | 1.78 (0.028) | 1.81 (0.030) | +0.034 (0.028) | –0.006 (0.034) |
| 8 to <9 months (n=833) | 1.94 (0.039) | 1.99 (0.042) | +0.049 (0.037) | +0.007 (0.043) |
| 9 to <12 months (n=1242) | 1.99 (0.033) | 2.14 (0.038) | +0.147 (0.031)** | +0.104 (0.037)** |
| 12 or more months (n=1067) | 2.17 (0.040) | 2.41 (0.044) | +0.238 (0.042)** | +0.193 (0.048)** |
| Age (years) | | | | |
| 18–39 (n=1830) | 2.09 (0.029) | 2.16 (0.031) | +0.060 (0.027)** | +0.018 (0.034) |
| 40–49 (n=2029) | 1.89 (0.024) | 1.98 (0.026) | +0.093 (0.023)** | +0.070 (0.031)* |
| 50-plus (n=2540) | 1.73 (0.018) | 1.80 (0.020) | +0.072 (0.019)** | +0.056 (0.031) |
| Health insurance | | | | |
| Not private ^b (n=4758) | 1.95 (0.016) | 2.05 (0.018) | +0.097 (0.016)** | +0.092 (0.024)** |
| Missing data ^c (n=247) | 1.96 (0.0580) | 2.00 (0.063) | +0.037 (0.050) | +0.042 (0.052) |
| Private (n=1394) | 1.65 (0.021) | 1.65 (0.022) | +0.001 (0.021) | +0.011 (0.029) |
| Race/ethnicity | | | | |
| N-H black (n=2754) | 1.97 (0.022) | 2.09 (0.024) | +0.114 (0.021)** | +0.097 (0.026)** |
| Hispanic (n=1317) | 1.85 (0.029) | 1.90 (0.031) | +0.050 (0.029) | +0.033 (0.036) |
| Other ^d (n=211) | 1.81 (0.058) | 1.82 (0.067) | +0.010 (0.066) | +0.015 (0.068) |
| N-H white (n=2117) | 1.80 (0.021) | 1.85 (0.023) | +0.046 (0.021)* | +0.048 (0.028) |
| Sex/orientation | | | | |
| Women (n=1647) | 1.96 (0.028) | 2.06 (0.031) | +0.100 (0.027)** | +0.059 (0.036) |
| MSM (n=3051) | 1.81 (0.017) | 1.86 (0.019) | +0.054 (0.017)** | +0.043 (0.026) |
| Heterosexual men (n=1701) | 1.94 (0.028) | 2.03 (0.030) | +0.089 (0.027)** | +0.042 (0.035) |

The change score is the end of gap log₁₀VL minus the start of gap log₁₀VL.

^aThe multivariable repeated measures regression model used a normal distribution and included variables that were significant at $p \leq 0.20$ in a preliminary model that entered all candidate variables in the equation simultaneously. Length of time since HIV diagnosis was removed to improve stability and precision of model estimates.

^bThe category “not private” included Medicaid, Medicare, Ryan White CARE Act, charity, and uninsured patients.

^cA missing data category was included to retain cohort patients in the multivariable analysis.

^dThe category “other” included Asian, Pacific Islander, Alaskan Native, and Native American heritage.

SEM, standard error of the mean; MSM, men who have sex with men.

* $p < 0.05$; ** $p < 0.01$.

load (least square means difference, $p < 0.001$). The dichotomous results indicated that 9276/11,186 (82.9%) were virally suppressed at the opening of the 3- to 6-month interval, and 5.2% of the 9276 failed to remain suppressed.

Discussion

Analysis of viral load changes in a cohort of patients from six clinics shows that gaps in HIV primary care of less than 9 months had little effect on viral load. In fact, viral load changes for these shorter gaps look a lot like the viral load changes during the time of routine care visits. Viral load significantly increased during the gap when the care gap reached 9 months. There was a small but significant increase (0.10 log increase; 98–137 copies/mL on average) in viral load for gaps 9 to <12 months. When the gap was ≥ 12 months, the increase in viral load was nearly twice as large (0.19 log increase; 109–259 copies/mL on average).

We observed a similar pattern of results when we focused on patients who had a suppressed viral load at the opening of the gap and examined how many of these patients did not maintain a suppressed viral load at the closing of the gap. Most virally

suppressed patients with shorter gaps (90–95%) remained suppressed. The largest effect was seen when the care gap was 12 months or more: 23% of suppressed patients became unsuppressed. It appears that many of the patients with shorter gaps in primary care were continuing to adhere to their ART regimens and thus maintaining their suppressed status. Patients with longer gaps may not have been adhering as well, and part of the nonadherence may have stemmed from lack of availability of ART prescriptions for refilling medications given the long interval between primary care visits. A recent analysis of a large billing claims database found that the proportion of persons who filled a prescription each month, throughout the entire length of gaps of more than 6 months, significantly decreased as the gap length increased.²² This finding suggests that longer gaps do contribute more failures to refill medications than shorter gaps.

We observed a number of disparities in outcomes that are consistent with the results of other research. More younger patients failed to maintain a suppressed viral load at the end of a gap, consistent with other adverse HIV care findings for young persons.²³ Non-Hispanic black patients had significantly higher log₁₀ viral loads than Hispanic and non-Hispanic

TABLE 2. UNIVARIABLE AND MULTIVARIABLE ANALYSIS OF FACTORS ASSOCIATED WITH SUPPRESSED PATIENTS NOT MAINTAINING SUPPRESSED VIRAL LOAD AFTER GAPS IN CARE, APTCARE PROJECT (2013–2015)

| <i>APTCare project (N=5242 patients with suppressed viral load at beginning of gap)[†]</i> | <i>Patients who did not maintain suppressed viral load after gaps in care % (n)</i> | <i>Univariable analysis, unadjusted risk ratios (95% CI)</i> | <i>Multivariable analysis, adjusted risk ratios (95% CI)</i> |
|---|---|--|--|
| <i>Factors</i> | | | |
| Length of gap in care | | | |
| >6 to <7 months (n=1832) | 5.4 (98) | Referent | Referent |
| 7 to <8 months (n=1003) | 9.6 (96) | 1.79 (1.36–2.35)** | 1.74 (1.33–2.29)** |
| 8 to <9 months (n=667) | 10.3 (69) | 1.93 (1.44–2.60)** | 1.88 (1.40–2.51)** |
| 9 to <12 months (n=969) | 14.3 (139) | 2.68 (2.09–3.43)** | 2.52 (1.97–3.21)** |
| 12 or more months (n=771) | 23.2 (179) | 4.34 (3.44–5.47)** | 3.97 (3.14–5.01)** |
| Age (years) | | | |
| 18–39 (n=1369) | 14.2 (194) | 1.62 (1.34–1.95)** | 1.56 (1.28–1.90)** |
| 40–49 (n=1671) | 11.6 (194) | 1.32 (1.09–1.60)** | 1.30 (1.08–1.56)* |
| 50 and older (n=2202) | 8.8 (193) | Referent | Referent |
| Health insurance | | | |
| Not private ^a (n=3783) | 13.0 (491) | 2.06 (1.63–2.59)** | 1.91 (1.51–2.41)** |
| Missing data ^b (n=206) | 5.3 (11) | 0.85 (0.46–1.56) | 0.90 (0.49–1.66) |
| Private (n=1253) | 6.3 (79) | Referent | Referent |
| Sex/sex orientation | | | |
| Women (n=1283) | 13.5 (173) | 1.07 (0.88–1.30) | 1.03 (0.85–1.25) |
| MSM (n=2603) | 9.1 (237) | 0.72 (0.60–0.87)** | 0.80 (0.67–0.97)* |
| Heterosexual men (n=1356) | 12.6 (171) | Referent | Referent |
| Race/ethnicity | | | |
| Non-Hispanic black (n=2161) | 13.5 (292) | 1.55 (1.29–1.87)** | 1.22 (1.01–1.48)* |
| Hispanic (n=1101) | 10.9 (120) | 1.25 (1.00–1.57)* | 0.97 (0.77–1.23) |
| Other ^c (n=184) | 7.1 (13) | 0.81 (0.47–1.40) | 0.76 (0.44–1.30) |
| Non-Hispanic white (n=1796) | 8.7 (156) | Referent | Referent |
| Length of time since HIV diagnosis ^d | | | |
| <1 to 24 months (n=406) | 13.6 (55) | Referent | Referent |
| >24 to 72 months (n=1053) | 10.3 (108) | 0.76 (0.56–1.03) | 0.78 (0.58–1.04) |
| >72 months (n=3539) | 11.3 (398) | 0.83 (0.63–1.08) | 0.97 (0.75–1.26) |
| Missing data ^b (n=244) | 8.2 (20) | 0.61 (0.37–0.98)* | 0.68 (0.42–1.10) |

[†]A suppressed viral load is <200 copies/mL.

Poisson regression model used robust standard errors (sandwich variance estimates) for generating model-adjusted risk ratios.

Variables included in this analysis were those significant at $p \leq 0.20$ in a screening step that entered all candidate variables in the equation simultaneously. For comparison purposes, we then calculated unadjusted risk ratios (col. 3, each variable in the model by itself) and adjusted risk ratios for each factor in the model (col. 4).

^aThe category “not private” included Medicaid, Medicare, Ryan White CARE Act, charity, and uninsured patients.

^bA missing data category was included to retain cohort patients in the multivariable analysis.

^cThe category “other” included Asian, Pacific Islander, Alaskan Native, and Native American heritage.

^dMeasured from diagnosis date to the date of the opening of the first gap in primary care during the observation period.

* $p < 0.05$; ** $p < 0.01$.

MSM, men who have sex with men.

white patients, as well as a higher rate of not maintaining a suppressed viral load during the gap than white patients. Previous research has shown that black patients have worse retention in care,²³ and that retention in care partially mediates the relationship between race/ethnicity and lower rates of virologic suppression.²⁴ Having health insurance/assistance that was not private (i.e., Medicaid, Medicare, Ryan White coverage, or no insurance) also was associated with adverse effects on viral load during a gap in care.

We also found that younger patients, non-Hispanic blacks, and publicly insured patients had longer gaps in care compared with older, white, and privately insured patients. These longer gaps may be contributing to deficiencies in ART adherence as these three subgroups have also been shown in previous studies to be independently associated with ART nonadherence.^{25,26}

Younger patients, aged 18–39 in these data, had the longest average gaps in care and the highest percentage not maintaining a suppressed viral load after a gap in care; this subgroup of patients may benefit from more frequent viral load monitoring, as suggested recently by others.²⁷

The analysis has a number of potential limitations. Our findings are from six clinics and should not be generalized to the larger US population of patients in care. We only looked at the first completed gap among patients who had a gap during the observation period. Some patients had multiple gaps, but we do not believe that selecting the first gap during observation caused a systematic bias because patients' viral loads were not considered in selecting the gap, and it is reasonable to assume that viral load status was not artificially restricted by our method.

TABLE 3. DIFFERENCES IN AVERAGE LENGTH OF GAP IN CARE BY LEVELS OF SELECTED STUDY CHARACTERISTICS AMONG PATIENTS WITH A SUPPRESSED VIRAL LOAD AT BEGINNING OF THE GAP, APTCARE PROJECT (2013–2015)

| <i>APTcare project (N=5242 patients with suppressed viral load at beginning of gap)</i> | | | |
|---|-----------------------------------|---|--|
| <i>Factors</i> | <i>Mean days in gap (and SEM)</i> | <i>Likelihood ratio chi-square (df)</i> | <i>Differences in mean days in gap, with p</i> |
| Age (years) | | 28.6 (2 df)** | |
| 18–39 (n = 1369) | 284.37 (3.00) | | 20.35** |
| 40–49 (n = 1671) | 273.62 (2.72) | | 9.60** |
| 50 and older (n = 2202) | 264.02 (2.37) | | Referent |
| Health insurance | | 22.2 (1 df)** | |
| Not private ^a (n = 3783) | 277.22 (1.82) | | 17.21** |
| Private (n = 1253) | 260.02 (3.17) | | Referent |
| Race/ethnicity | | 16.7 (2 df)** | |
| Non-Hispanic black (n = 2161) | 278.56 (2.40) | | 14.39** |
| Hispanic (n = 1101) | 274.41 (3.36) | | 10.24* |
| Non-Hispanic white (n = 1796) | 264.17 (2.63) | | Referent |

^aThe category “not private” included Medicaid, Medicare, Ryan White CARE Act, charity, and uninsured patients. Cells with small numbers of patients (missing health insurance and “Other” race-ethnicity) omitted.

* $p < 0.05$; ** $p < 0.01$.

df, degrees of freedom; SEM, standard error of the mean.

For inclusion in the analysis, patients had to have a completed gap and a viral load within the window period of the opening and closing of the gap. We used a fairly wide window (± 90 days) for selecting the closest viral load to balance two concerns: to obtain viral load results that were in close temporal proximity to the opening and closing of the gap without being so overly restrictive (in how close) that we would omit a lot of patients from the analysis. As mentioned in Results, only 17% of patients with a gap were excluded because they did not have viral loads within the window period. Given that our intent was to examine changes in viral load by length of a gap in primary care, we were not able to include patients who had “open-ended” gaps (more than 182 days had elapsed after their last visit by the time follow-up had ended). Some of these patients may have moved and were receiving care elsewhere, whereas other patients may have disengaged from care. One might expect stronger increases in viral load in disengaged patients than what was observed in this study among patients with completed gaps.

Our results are averages across large numbers of patients and do not represent viral load changes that may be observed for an individual patient. Our results should not be construed as suggesting anything about optimal spacing of clinic appointments for an individual patient. Our results do suggest, however, that for some patients, wider intervals between in-person clinic visits may not be detrimental to clinical status. This result is supported by the previous research showing that in cases where providers schedule visits at 3, 4, or 6 months intervals and care visits are attended, 6-month intervals are as safe as visits scheduled at shorter intervals.²⁸ Increasing viral load (starting at 9 months and doubling by the 12-month mark) may stem from refill difficulty and difficulty maintaining long-term adherence without the motivational boost that may come from a care visit and interaction with a provider.

Our results have an important implication for patient reengagement efforts. One approach is to begin reengagement activity when the interval exceeds 6 months between care visits. This is supported by data demonstrating that there is a

decreasing probability of locating an out-of-care patient the longer they have been out of care.²⁹ Our results should not be viewed as suggesting that the reengagement process ought to be delayed, because it may take several weeks or longer to contact a patient. However, resources for reengagement must be taken into account, and decisions on whom to prioritize must take into account those resources. The resource issue was empirically verified in a recent report: even with the assistance of surveillance data to avert investigations of patients who had changed providers, moved, or died, fully twice as many reengagement case investigations (1600 cases) were required for a gap interval of 8 months as for a gap interval of 12 months (800 cases).¹⁴ Assuming resource constraints, the patients who are out of care for 9 months or longer might be a higher priority. In the absence of resource constraints, patients with all gap lengths could be pursued with equal urgency. The trade-off is that patients out of care for a long time may be inherently more difficult to contact and reengage than patients who have been out of care just over 6 months. Our results do provide some comfort in that many patients with short (less than 9 month) gaps do not have appreciable spikes in viral load, and thus, if reengagement activity does not commence shortly after a 6-month gap, the patient’s health status and transmission risk may not be overly concerning.

Long-term maintenance of viral suppression is important to achieving eventual elimination of HIV, and a recent report and editorial on the SEARCH intervention^{30,31} suggest that the United States faces the same challenges as sub-Saharan Africa. The World Health Organization and the International AIDS Society are moving to make finer distinctions among HIV patients in care (“differentiated care”) by coupling 12-month clinic visit intervals with greater use of community health workers for stable patients.^{32,33} The WHO strategy is an attempt to achieve higher levels of long-term VL suppression, the most difficult to attain the 90-90-90 goals. With safety-net HIV clinics in the United States being squeezed for resources from expanding patient populations and flat funding, new clinic strategies seem necessary, and a change to the visit interval for some patients ought to be considered as a

component of new strategies. Data presented in this study from predominantly publicly insured patients in the United States suggest that visit intervals of 6–9 months for select patients may be appropriate without endangering the health of patients or the public.

In summary, we observed very small changes in viral load among patients who had gaps in primary care that exceeded 6 months but were less than 9 months in duration. Significant increases in mean viral load and in percentage of virally suppressed patients who became unsuppressed were observed when the gap in care reached 9 months, and increases were larger still when the gap reached or exceeded 12 months. Younger patients, non-Hispanic black patients, and patients with nonprivate sources of health insurance were less likely to maintain a suppressed viral load during a gap compared with their counterparts. Interventions among these subpopulations to increase long-term ART adherence may increase the number of patients with durably suppressed viral loads.

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Address correspondence to:
Lytt I. Gardner, PhD
Division of HIV/AIDS Prevention
Centers for Disease Control and Prevention
Mailstop E-45
Atlanta, GA 30333

E-mail: marialytt@gmail.com