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Do Persons Living with HIV Continue to Fill Prescriptions for Antiretroviral Drugs during a Gap in Care? Analysis of a Large Commercial Claims Database

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Abstract

The significance of a gap in HIV care depends, at least partially, on whether patients continue to fill prescriptions for antiretroviral (ARV) drugs during the gap in care. We used a billing claims database to determine the proportion of persons who filled 1 prescription for ARV drugs during a gap in care (no clinic visit in >6 months). Persons were stratified into 3 groups: “never” (prescriptions never filled), “sometimes” (prescriptions filled >0%-<100% of months), and “always” (prescriptions filled monthly). Logistic regression analyses were conducted to determine factors associated with “never” filling ARV drugs. Of 14 308 persons, 69% (n = 9817), 13% (n = 1928), and 18% (n = 2563) “never,” “sometimes,” and “always” filled ARV drugs during the gap in care. Persons aged 18 to 29 years (odds ratio [OR] = 1.56, 95% confidence interval [CI] 1.39–1.74), women (OR = 1.67, CI 1.52–1.83), and persons from the Northeast region of the United States (OR = 1.86, CI 1.69–2.03) were more likely to never fill ARV drugs than persons aged ≥30 years, men, and persons outside the Northeast, respectively. Efforts should be made to minimize gaps in care, emphasize importance of therapy, and provide adherence support.

Keywords

HIV; AIDS; antiretroviral therapy; adherence; health care

Introduction

Retention in HIV care is associated with initiation of antiretroviral (ARV) therapy (ART), viral suppression, reduced mortality, and transmission risk.[1–4] Despite the importance of being retained in care, in the United States, a substantial proportion of persons living with HIV experience gaps in HIV care (defined as no clinic visit in >6 months). In 2 recent studies in the United States of publicly and commercially insured persons with HIV, up to 30% experienced gaps in care.[5,6] Although persons who have gaps in care are considered to

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Authors’ Note

The findings and conclusions in this study are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

Declaration of Conflicting Interests

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be out of care, it is conceivable that some of these individuals continue to fill ARV drug prescriptions, during the gap, and could reach viral suppression.

In 2012, the US Department of Health Human Services recommended that all persons living with HIV be prescribed ART.[7] Because all persons living with HIV should be on ART, ARV drug prescription filling behavior can indicate that a person is engaged in care even if he or she has not recently been seen by a clinic provider. The significance of a gap in HIV care depends, at least partially, on whether patients continue to fill ARV drug prescriptions during the gap. Information on filling ARV drug prescriptions has seldom been evaluated in previous studies of gaps in HIV care because of the lack of available prescription data. We used a commercial claims database, which contains pharmacy and diagnosis claims data, to determine whether persons who experienced gaps in HIV care continued to fill ARV drug prescriptions during the gap. To our knowledge, this is the first analysis that examines filling of ARV drug prescriptions during a gap in care.

Methods

We used the 2012 to 2014 Truven Health Market Scan Commercial Claims and Encounters Databases (Truven Health) to determine the unweighted proportion of persons with HIV who experienced a gap in care and who filled ≥1 prescription for an ARV medication during each individual gap month.The data base contains paid, patient-level health care, procedure,and pharmacy billing claims from inpatient and outpatient services for active employees, their spouses and dependents, early retirees, and COBRA continuers insured by employer-sponsored plans in the United States.[8] The 2012 MarketScan Commercial Claims and Encounters Database included 53 131 420 unique enrollees.

Case Definition and Cohort Inclusion/Exclusion Criteria

Persons with HIV were identified using the 2012 Market Scan database. A person was defined as having HIV if he or she had an inpatient or outpatient service claim with 1 of the following *International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9 CM)* diagnosis codes: 042, V08, 079.53, and 795.71. An outpatient visit claim was defined using the following *Current Procedural Terminology (CPT)* codes: 99201, 99202, 99203, 99204, 99205, 99212, 99213, 99214, and 99215. Antiretroviral drugs were defined using National Drug Codes (http://www.accessdata.fda.gov/scripts/cder/ndc/default.cfm). A gap in care was defined as no outpatient visit claim with a physician, nurse practitioner, or physician assistant in more than 6 months.[9] Persons who were ≥18 years of age in 2012, who had ≥1 gap in care that was ≤6 months in length between 2012 and 2014, and who were continuously enrolled in employer-sponsored insurance for the entire duration of the gap were included in the analysis. Persons with gaps that were more than 6 months in length were excluded because they were few in number and the length of their gaps varied substantially. To evaluate individual months of the gap, persons with ARV drug prescriptions for more than a 30-day supply of medication were excluded. Finally, persons who filled an ARV drug prescription prior to the start of the gap, which covered part of the gap, were also excluded. The final study sample included 14 308 persons.

Data Analysis

Analyses were restricted to each person's first gapin care. Median length of the gap was determined and stratified by age, sex, and region of country. The Kruskal-Wallis test was used to determine the difference between median gap length by characteristic. The. For each month (30-day period) after day 187, we calculated the unweighted proportion of persons who filled a pre scripti on for at least1 ARV. West ratified persons in to 3 groups based on how of ten they filled an ARV drug prescription during the length of the gap: "never" for persons who never filled an ARV drug prescription in any month of the gap, "sometimes" for persons who filled a prescription in >0% to <100% of the months, and "always" for persons who filled an ARV drug prescription in every month of the gap. Because 13% of persons who didn't have a clinic visit in >6 months (180 days) returned for a clinic visit by day 186, a grace period of 7 days was given and the gap was calculated from day 187 from the last clinic visit.

The proportion of persons who never, sometimes, or always filled an ARV drug prescription were stratified by the length of the gap. To determine whether the proportion of persons who filled an ARV drug prescription changed as the length of the gap increased, we conducted a χ^2 test for trend in each category. Because there were only 2 possible categories (never and always) for filling an ARV drug prescription for persons with gaps 1 month in length, we excluded persons with 1-month gap when calculating the test for trend to keep all trends consistent. The proportion of persons who never, sometimes, or always filled an ARV drug prescription during their gap months was also stratified by age, sex, and region of country; Pearson's χ^2 test was used to test for differences between groups. Race/ ethnicity data were not available in the Market Scan Commercial Claims and Encounters Database.

Univariate and multivariable logistic regression analyses were conducted to determine factors associated with increased odds of never filling an ARV drug prescription in any gap month; the outcome was never filling an ARV drug prescription versus filling an ARV drug prescription sometimes or always. We calculated odds ratios with 95% confidence intervals (CIs), using age, sex, and region of country as explanatory variables in the model. Backward selection was used for the multivariable model.[10] All analyses were performed using SAS 9.3 (SAS Institute Inc).

Results

There were a total of 70 854 persons with HIV identified in the 2012 Market Scan Commercial Claims and Encounters Database. Between 2012 and 2014, a total of 22 089 persons had a gap in care, of whom 2774 had a gap >6 months in length. After excluding persons with ARV drug prescriptions for >30-day supply of medication (n = 1783) and those with an ARV drug prescription that overlapped the start of the gap (n = 3224), a total of 14 308 people were included in the study. The median age was 44 years (interquartile range [IQR]: 36–50). Persons aged 40 to 49 years made up the largest proportion of the sample (38%). Seventy-eight percent of the sample was male and 40% resided in the Southern United States (Table 1).

Characteristics of Gaps in Care

The median length of the first gap was 43 days (IQR: 20–85; Table 1). Persons aged 18 to 29 years had the longest median gap length at 54 (IQR: 25–101) days compared to each of the older age-groups. Women had longer median gap length at 50 (IQR: 23–93) days than men; persons residing in the northeast region had longer median gap length at 49 (IQR: 23–92) days compared to persons residing in each of the other geographical regions. Persons who sometimes filled an ARV drug prescription had longer median gap length at 84 days (IQR: 16–78) than persons who always (33 days [IQR: 21–65]) and never (36 days [IQR: 16–78]) filled an ARV drug prescription.

Proportion of Persons Who Filled an ARV Drug Prescription during the First Gap in Care

Overall,69% (n= 9,817),13% (n= 1,928),and18% (n= 2,563) of persons never, sometimes, and always filled an ARV drug prescription during the gap (Table 2). Over 70% of persons who sometimes filled an ARV drug prescription filled a prescription in at least 50% of their gap months (data not shown). Between 17% and 28% of the entire sample filled an ARV drug prescription during any given gap month (data not shown).

Between 60% and 78% of persons never filled an ARV drug prescription in any gap month depending on the gap length. After excluding gaps that lasted for ≤1 month, there was no significant difference in the proportion of persons who never filled an ARV drug prescription, as the length of the gap increased. Between 20% and 33% of persons filled an ARV drug prescription in some but not all months of the gap. The proportion of persons who sometimes filled an ARV drug prescription increased as the length of the gap increased (P for trend ≤.001). Between 7% and 22% of persons filled an ARV drug prescription in every month. Forty-four percent of the sample's first gap was short at 7 to 30 days in length. After excluding gaps that lasted for ≤1 month, the proportion of persons who filled a prescription each month, throughout the entire length of their gap, decreased as the gap length increased (P for trend ≤.001; Table 2).

Seventy-six percent of persons aged 18 to 29 years (compared with 65%−69% for all other age-groups, all P values <.001), 77% of women (compared with 66% of men, $P < .001$), and 78% of persons from the Northeast region (compared with 63%−67% for all other regions, all P values <.001) never filled an ARV drug prescription in any month of the gap (Table 3). The proportion of persons who sometimes and always filled an ARV drug prescription during the gap is presented, by characteristic, in Table 3.

Factors Associated with Never Filling an ARV Drug Prescription during the First Gap in Care

The results of the univariate and multivariable logistic regression analyses are presented in Table 4. On multivariable analysis, persons aged 18 to 29 years (OR =1.56, 95% CI 1.391.74), women (OR =1.67, CI 1.52–1.83), and persons from the Northeast region (OR =1.86, 1.69–2.03) were more likely to never fill an ARV drug prescription during the gap than persons aged ≥30 years, men, and persons from outside the Northeast region, respectively (Table 4).

Discussion

Using a commercial claims database, we found that a substantial proportion (69%) of persons living with HIV who had a gap in HIV care failed to fill any ARV drug prescription throughout the duration of the gap. Women, persons aged 18 to 29 years, and persons residing in the Northeast region all had longer gap duration and were all more likely to never fill an ARV drug prescription compared to men, persons ≥30 years of age, and persons residing in all other regions. While the proportion who never filled an ARV drug prescription, during the gap, remained stable regardless of the length of the gap, the proportion of persons who always filled an ARV drug prescription decreased as the length of the gap increased.

Studies found poor ART adherence to be associated with low self-efficacy, current substance use, concerns about ART safety, mistrust of the prescriber, stigma, poor health literacy, and family responsibilities.[11–15] These factors may all play a role in failing to fill ARV drug prescriptions during overly long intervals between clinic visits. While nonadherence factors may be important, a less recognized reason for failing to fill ARV drug prescriptions, during a gap in care, might be a lack of access. Although the Department of Health and Human Services recommends that all persons living with HIV be prescribed ART, it is possible that some individuals in this study were never prescribed ART.[7] If true, the failure of such an individual to fill an ARV drug prescription is an issue of access rather that compliance. Another issue is the prescription interval. Because a gap in care in this study starts at least 6 months after the last clinic visit, some in this study population may not have had an active ARV drug prescription during their gap and been unable to refill. The pattern of filling prescriptions seen among the always group in this study suggests this; the proportion of those who always filled a prescription decreased as gap length increased. This pattern may also represent treatment fatigue.[16]

Women and younger persons were more likely to never fill an ARV drug prescription during the gap in care. This finding is congruent with the findings from several studies of lower ART adherence among younger persons and women.[17–20] This finding also follows a frequently reported trend of poorer retention in care and viral suppression among younger persons.[5,17,21–23] Studies, however, have also shown that younger persons are less likely to be prescribed ART, which may account for some of the difference seen in our study.[24–27] Studies have shown mixed results regarding the proportion of persons prescribed ARV drugs, by sex.[2,24,25,27] Both younger persons and women had longer median gap length than older persons and men which may amplify the failure to fill ARV drug prescriptions during these gaps. Persons from the Northeast region also were more likely to never fill an ARV drug prescription during the gap. The reason for this finding is unknown.

The definition of a gap in care used in this analysis was based on the Department of Health and Human Services' longest recommended intervisit interval of 6 months.[7] Some providers, however, might intentionally prolong the period between scheduled appointments for patients who are stably virally suppressed. Regardless of a person's clinic visit schedule, filling ARV drugs between visits might be considered a measure of continued care. However, only 18% of persons, within this analysis, filled ARV drug prescriptions

consistently between visits suggesting that a gap in care may be an indicator of potential poor adherence.

For those prescribed ARV drugs, the failure to fill ARV drug prescriptions during a gap in care is concerning because suboptimal adherence can lead to inadequate viral suppression, increased transmission risk, and poor clinical outcomes including increased morbidity and mortality.[28–32] An adherence level of 70% to 95% is estimated to be necessary for viral suppression, and studies have shown that even short treatment interruptions can increase the risk of viral rebound.[31–38] A study by Haberer et al found that the odds of viral rebound increased by a factor of 1.25 for each day after 48 hours off medication.[37] A study by Parienti et al found that the number of treatment interruptions was associated with higher odds of viral rebound.[36] While the majority of persons in our study failed to ever fill a prescription during the gap, 13% filled ARV drug prescriptions intermittently (ie, the "sometimes" people), which may also put them at risk of viral rebound. However, 44% of persons within our study had a gap that lasted for ≤1 month; some of these individuals may have had extra medication from a previous prescription that could be used to cover the gap.

Failure to fill ARV drug prescriptions can be detected at multiple steps before the prescribing provider is aware of the situation, including by the filling pharmacies, insurers, and pharmacy benefit managers. Using pharmacy filling data to identify persons who fail to fill prescriptions and then to intervene has been demonstrated with other chronic diseases. For example, a study conducted by Lawrence et al used pharmacy claims data to identify persons who were 60 days late filling prescriptions for a variety of cardiovascular and diabetes medications. Identified persons received a telephone intervention by care managers who counseled patients on medication adherence. They found improved rates of medication reinitiation (59% versus 42% in the control group) and a shorter time to reinitiation (59 versus 107 days) postintervention.[39] Another study used prescription fill data to determine persons who never filled an initial prescription and followed up these individuals with telephone reminders to fill their prescriptions. Persons who received the intervention had improved primary adherence (risk ratio 1.6, 95% CI 1.5–1.8) compared to the control group.[40] Real-time monitoring of pharmacy claims data could be used to intervene upon people who are no longer filling their ARV drug prescriptions and to offer adherence and other support.[41]

This study is not without limitations. We restricted the analysis to the first gap in care; filling behavior may have changed during subsequent gaps. However, the median number of gaps for persons included in the study was 1. No HIV viral load data were available and, therefore, we were unable to determine whether failing to fill ARV drug prescriptions led to poor viral suppression. It is possible that persons filled ARV drug prescriptions using a second insurer (eg, spousal insurance benefit), which would not be accounted for in this analysis. We were unable to determine whether persons had active prescriptions for ARV drugs during the gap and, therefore, were unable to determine whether failure to fill was due to an access issue. Finally, all persons within the sample were privately insured; the results, therefore, may not be generalizable to all persons with HIV, particularly to uninsured persons or to persons who use alternative avenues to fill prescriptions such as drug assistance programs.

The majority of persons who experienced a gap in HIV care failed to fill an ARV drug prescription during the gap. The failure to fill ARV drug prescriptions during a gap in care emphasizes the importance of retention in HIV care, where patients can receive adherence support and the importance of treatment can be emphasized.

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Table 1.

Sample Demographics and Median Length of the First Gap in Care.

	n (%)	Median Gap Length, Days (IQR)[a]
Total	14308 (100)	43 (20–85)
Age (years)		
18–29 (referent)	1978 (14)	54 (25–101)
30–39	2871 (20)	48 (23–89)[b]
40–49	5368 (38)	41 (19–82)[b]
≥50	4091 (29)	37 (17–78)[b]
Sex		
Male (referent)	11224 (78)	42 (19–83)
Female	3084 (22)	50 (23–93)[b]
Region		
Northeast (referent)	3488 (24)	49 (23–92)
North Central	2076 (15)	41 (20–81)[b]
South	5785 (40)	40 (18–79)[b]
West	2959 (21)	44 (20–91)[c]

Abbreviation: IQR, interquartile range.

[a] A gap in care was defined as no outpatient visit claim with a physician, nurse practitioner, or physician assistant in more than 6 months. Length of the gap was measured from 187 days after the last clinic visit to the date of the next clinic visit.

[b] Kruskal-Wallis test P value of < .001.

[c] Kruskal-Wallis test P value of .015 comparing median gap length of the referent to the West region.

Table 2.

Proportion of Persons Who Filled 1 ARV during the First Gap in Care, by Length of the Gap and Frequency of the Action.[a]

		How often an ARV Was Filled during the Gap		
		"Never"[c] (n = 9817)	"Sometimes"[c] (n = 1928)	"Always"[c] (n = 2563)
Length of First Gap in Days[b]	**n**	**n (%)**	**n (%)**	**n (%)**
7–30	6325	4937 (78)	n/a	1,388 (22)
31–60	3194	1968 (62)	638 (20) [d]	588 (18) [d]
61–90	1878	140 (61)	451 (24)	287 (15)
91–120	1304	811 (62)	344 (26)	149 (11)
121–150	991	594 (60)	292 (29)	105 (11)
151–180	616	367 (60)	203 (33)	46 (7)

Abbreviations: ARV, antiretroviral; n/a, not available.

[a] N = 14 308.

[b] Represents 30-day periods past 180 days from the last clinic visit. Because 13% of persons who didn't have a clinic visit in >6 months (180 days) returned for a clinic visit by day 186, a grace period of 7 days was given and the gap started on day 187 from the last clinic visit. The first, 30-day period, therefore, represents days 7 to 30 after the start of the gap.

[c] The frequency of having filled an ARV drug prescription during the gap was stratified into 3 groups: "never," for persons who never filled an ARV drug prescription in any month of the gap; "sometimes," for persons who filled an ARV drug prescription in >0% to <100% of the months; and "always," for persons who filled an ARV drug prescription in every month of the gap.

[d] After excluding gaps of ≤1 month in length, χ^2 test for trend P value of <.001.

Table 3.

Proportion of Persons Who Filled ≥1 ARV Drug Prescription during the First Gap in Care, by Characteristic and Frequency of the Action.[a]

		How often an ARV Was Filled during the Gap		
	n	**"Never"[b] (Total n = 9817)**	**"Sometimes"[b] (Total n = 1928)**	**"Always"[b] (Total n = 2563)**
Characteristic		n (%)	n (%)	n (%)
Age, years				
18–29 (referent)	1978	1499 (76)[c]	227 (11)	252 (13)[c]
30–39	2871	1971 (69)	414 (14)[d]	486 (17)
40–49	5368	3507 (65)	790 (15)[e]	1071 (20)
50	4091	2840 (69)	497 (12)	754 (18)
Sex				
Male (referent)	11224	7443 (66)[c]	1,951 (14)[c]	2190 (20)[c]
Female	3084	2374 (77)	337 (11)	373 (12)
Region				
Northeast (referent)	3488	2719 (78)[c]	347 (10)	422 (12)[c]
North Central	2076	1397 (67)	278 (13)[f]	401 (19)
South	5,785	3822 (66)	833 (14)[e]	1130 (20)
West	2959	1879 (63)	470 (16)[g]	610 (21)

Abbreviation: ARV, antiretroviral.

[a] N = 14 308.

[b] The frequency of having filled an ARV drug prescription during the gap was stratified into 3 groups: "never," for persons who never filled an ARV drug prescription in any month of the gap; "sometimes," for persons who filled an ARV drug prescription in >0% to <100% of the months; and "always," for persons who filled an ARV drug prescription in every month of the gap.

[c] Pearson χ^2 test P value of <.001 comparing the referent to each characteristic within the "never," "sometimes," and "always" categories.

[d] Pearson χ^2 test P value of .003 comparing persons aged 18 to 29 years to persons aged 30 to 39 years within the "sometimes" category.

[e] Pearson χ^2 test P value of <.001 comparing persons aged 18 to 29 years to persons aged 40 to 49 years within the "sometimes" category.

[f] Pearson χ^2 test P value of <.001 comparing persons from the Northeast region to persons residing each in the North central and South regions within the "sometimes" category.

[g] Pearson χ^2 test P value of .005 comparing persons from the Northeast region to persons residing in the West region.

Table 4.

Factors Associated with Increased Odds of Never versus Ever Filling ≥ARV Drug Prescription during a First Gap in Care.[a,b]

		Univariate	Multivariable[c]
Characteristic	**n, (total N = 14 308)**	**Odds ratio (95% CI)**	**Odds ratio (95% CI)**
Age, years			
18–29	1978	Referent	1.56 (1.39–1.74)
30–39	2871	1.03 (0.94–1.13)	
40–49	5368	0.76 (0.71–0.82)	
≥50	4091	1.01 (0.94–1.10)	
Sex			
Male	11224	Referent	
Female	3084	1.80 (1.64–1.98)	1.67 (1.52–1.83)
Region			
Northeast	3488	Referent	1.86 (1.69–2.03)
North Central	2076	0.91 (0.83–1.01)	
South	5785	0.79 (0.73–0.85)	
West	2959	0.76 (0.69–0.82)	

Abbreviations: ARV, antiretroviral; CI, confidence interval.

[a] N = 14 308.

[b] The outcome of the logistic regression analyses was “never” filling an ARV drug prescription versus filling an ARV “sometimes” or “always.”

[c] Multivariable logistic regression analysis comparing 18–29 years to persons ≥30 years, females to males and persons residing in the Northeast region to all other regions combined.