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Antiretroviral therapy adherence and use of an electronic shared medical record among people living with HIV

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Abstract

Electronic shared medical records (SMR) are emerging healthcare technologies that allow patients to engage in their healthcare by communicating with providers, refilling prescriptions, scheduling appointments, and viewing portions of medical records. We conducted a pre-post cohort study of HIV-positive adults who used and did not use SMR in two integrated healthcare systems. We compared the difference in antiretroviral refill adherence between SMR users and age- and sex-frequency matched non-users from the 12-month period prior to SMR use to the 12-month period starting six months after initiation of SMR use. High adherence was maintained among SMR users (change=−0.11%) but declined among non-users (change=−2.05%; p=0.003). Among SMR users, there was a steady improvement in adherence as monthly frequency of SMR use increased (p=0.009). SMR use, particularly more frequent use, is associated with maintaining high adherence and non-use is associated with declines in adherence over time among patients with access to these online services.

Keywords

HIV; electronic health records; medication adherence; antiretroviral therapy; integrated healthcare system

INTRODUCTION

The biggest threat to successful HIV treatment is non-adherence to antiretroviral therapy (ART), as non-adherence remains one of the strongest predictors of progression to AIDS and death[1–3]. Additionally, poor engagement in HIV care has been associated with delayed initiation of ART and non-adherence[4,5]. In the U.S., ART non-adherence is estimated to be

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in the 10% to 50% range[6,7] and has been reported to account for $1.8 billion in annual avoidable costs[8].

Prior research has shown that people living with HIV who used the internet for health-related purposes were significantly more likely to adhere to their ART regimen in the past week than those who did not use the internet for health-related purposes[9]. Additionally, self-care technology-based methods have the potential for improving engagement in care and enhanced adherence[10]. Therefore, healthcare systems that provide technology-based methods that enable patients to effectively and easily communicate with their healthcare providers, access laboratory test results, and request medication refills may result in improved engagement in care and adherence.

Patient websites or portals that provide secure access to sections of electronic medical records that are shared between patients and healthcare providers, also known as shared medical records (SMR), are emerging healthcare technologies. SMRs are a component of electronic medical records that allow patients to communicate with providers, refill medications, schedule appointments, and view portions of their medical record, including laboratory test results. An increasing number of healthplans are anticipated to offer SMR services in order to qualify for Stage 2 Meaningful Use Incentive Program under the Affordable Care Act[11]. Prior research has examined the efficiencies and positive impact of SMR in primary care[12,13] and other chronic conditions, including diabetes[14,15], hypertension[16], and depression[17]. Therefore, these online services may help meet ongoing healthcare needs of HIV-positive patients in many circumstances, such as when initiating a new ART regimen or experiencing adverse effects.SMR may ultimately improve engagement in HIV care and ART adherence and may be valuable in supporting disease management and self-care. Although the use of SMR by HIV-positive individuals has been previously described[18], the association between SMR use and HIV-related outcomes has not been examined. Thus, our objective was to determine whether SMR use (versus no use) and the frequency of SMR use were associated with changes in ART adherence in HIV-positive individuals.

METHODS

Design

We conducted a pre-post cohort study of HIV-positive adults who used SMR within two years of initial SMR rollout in two large integrated healthcare systems, Kaiser Permanente Northern California (KPNC) and Group Health Cooperative (GHC). We compared changes in ART refill adherence from the 12-month period prior to SMR use (pre-interval) to the 12-month period starting six months after initiation of SMR use (post-interval). The six-month period post-SMR rollout was considered a“confirmation stage in adoption”[19] of this emerging technology, and therefore excluded from adherence calculations. This helped to ensure that we were measuring adherence in the post-interval most likely to be influenced by SMR use, allowing enough time for SMR users to both gain confidence in use of the SMR features and to establish a personal SMR use routine.

Our primary objective was to compare refill adherence change between SMR users and age- and sex-frequency matched non-users pre- and post-SMR use (or a randomly assigned reference date in SMR non-users). Additionally, among SMR users, we evaluated the association between mean frequency of SMR use (i.e., mean number of days per month using any SMR service over a six-month period) and refill adherence change, as well as the factors associated with changes in adherence pre- and post-SMR use.

Setting and Participants

GHC is an integrated healthcare delivery system with over half a million members in Washington and North Idaho. KPNC is a large integrated healthcare delivery system that provides comprehensive medical services to over three million members in Northern California. In total, these two organizations provide healthcare to more than 15,500 people living with HIV in the U.S. and maintain a similar confidential HIV registry of these individuals, as well as hospital, pharmacy, laboratory, and administrative databases. Over 90% of members obtain their prescription medications from KPNC and GHC pharmacies[20,21]. These healthcare systems have robust and comprehensive HIV care programs that have demonstrated previous success with high levels of ART adherence and viral suppression among their members[22,23]. Key elements of this successful care have been the multidisciplinary care team and electronic health records[22,24].

SMR became available to all patients at GHC (MyGroupHealth.org) and KPNC (KP.org) in August 2003 and November 2005, respectively. As these healthplans were early adopters of SMRs, they offer the ideal settings to evaluate the effectiveness of this emerging technology on health outcomes. SMR in these healthplans have seven common features, including: secure messaging with healthcare providers; requesting medication refills; scheduling appointments with healthcare providers; and viewing after-visit summaries, allergies, immunizations, and laboratory test results. The descriptions of these web services have previously been reported[18,25–27].

In our study, we first identified a cohort of SMR users consisting of HIV-positive adults (≥18 years) who had: 1) completed the enrollment process to use the online services at MyGroupHealth.org or KP.org; 2) used one or more of the seven SMR functions sometime during the first 24 months post-SMR rollout (8/1/2003 for GHC and 11/1/2005 for KPNC); 3) enrolled in the healthplan at least 12 months prior to the date of first SMR use and maintained enrollment for at least 18 months after the date of first SMR use (to ensure sufficient length of time for adherence calculation in the pre- and post-intervals); and 4) started ART at least 12 months prior to the first SMR use. We examined the association between mean frequency of SMR use and refill adherence change pre- and post-interval, as well as the factors associated with changes in adherence in this cohort of SMR users.

We first compared refill adherence change between SMR users and age- and sex-frequency matched non-users. SMR non-users were HIV-positive adults who met the abovementioned inclusion criteria, except for the fact that they had not registered for SMR during the first 36 months post-SMR rollout. The 36-month period was chosen to ensure a sufficient timeframe to establish SMR non-use. For this comparison, to ensure comparability with the extended 36-month timeframe of SMR non-use, we created a restricted SMR user group that included

members of the SMR user cohort with the additional inclusion criteria of at least 36 months healthplan membership post-SMR rollout. SMR non-users were frequency matched to the restricted SMR user group according to age group (i.e., 18–29, 30–39, 40–49, and ≥50 years), sex, and number of months since SMR rollout. We randomly assigned an index date for non-users within the month they were selected as a non-user, in order to compute pre- and post-interval adherence measurements, analogous to pre- and post-SMR adherence measurements for users.

Institutional Review Board approval including waivers of informed consent was obtained from both institutions.

Main Measures

The difference in refill adherence change pre- and post-SMR use (for users) or before and after a randomly assigned reference date (for non-users) constituted our primary outcome measure. The pharmacy databases provided refill dates for each antiretroviral medication. Our refill adherence measure was computed using previously described methods[28–30] and involved computing percent refill adherence for each antiretroviral during the specified 12-month pre- and post-intervals. Specifically, for individual antiretrovirals, we first computed the continuous measure of medication gaps[29] using a numerator of days' supply dispensed from first fill to end of interval, and a denominator of total days between first fill to end of interval. Such an approach assumes that any observed gap in medication coverage prior to the end of an interval (i.e., terminal gap) is due to non-adherence. Therefore, we looked for evidence to more accurately distinguish between terminal gaps that represented true non-adherence or a change in ART, similar to a validated approach previously described[30]. Briefly, if the original antiretroviral was re-prescribed within 60 days of the start of the terminal gap, we did not adjust the denominator and assumed that the terminal gap did represent non-adherence. However, if a new antiretroviral was prescribed, we assumed that there was a medication change, and adjusted the denominator to either: (a) the end of the last fill of the original antiretroviral if the new antiretroviral was prescribed within 60 days of the start of the terminal gap; or (b) the start of the new antiretroviral fill if the new antiretroviral was prescribed more than 60 days of the start of the terminal gap. Finally, we computed the overall refill adherence during an interval as the mean refill adherence across all individual antiretrovirals[31].

Our predictors of interest included: (1) SMR use versus no use and (2) frequency of SMR use (mean SMR use <0.5, 0.5 to <1, 1 to <2, or ≥2 times per month over a six-month period). Potential confounders considered in analyses included age (18–39, 40–49, 50–59, and ≥60 years of age), sex (women versus men), race/ethnicity (Asian/Pacific Islander, Black, Hispanic, White, and other/unknown), baseline CD_4^+ cell count (<200, 200–499, and ≥500 cells/mm^3), baseline plasma HIV RNA (≤500, 501–9,999, and ≥10,000 copies/mL), and healthplan membership (GHC versus KPNC).

Analysis

Initially, we used descriptive statistics to characterize demographics of SMR user sandnon-users. Next, we estimated "refill adherence change" for the restricted SMR user group and

SMR non-users, calculated by subtracting refill adherence pre-interval from refill adherence post-interval in each group. A linear regression model was then used to estimate the unadjusted "difference" in refill adherence change between SMR users and non-users, interpreted as refill adherence change of the restricted SMR user group minus refill adherence change of SMR non-users. We then employed multivariable linear regression, adjusted for potential confounders, to compute an adjusted difference in refill adherence comparing users and non-users. Next, among the SMR users and non-users, we estimated refill adherence change and the difference in refill adherence change stratified by baseline CD^{4+} cell count (≥200 versus <200 cells/mm^3) and plasma HIV RNA (<500 versus ≥500 copies/mL). Lastly, among SMR users only, using linear regression, we evaluated factors associated with refill adherence changes, including mean frequency of SMR use, age, sex, race/ethnicity, baseline CD4 and HIV RNA, and healthplan.

For all analyses, a p-value <0.05 was deemed statistically significant. We used SAS software version 9.3 (SAS Institute Inc., Cary, NC).

RESULTS

We identified 1,638 HIV-positive patients in the SMR user cohort, who had a mean age of 49 years and were primarily men (94%) and White (76%). At baseline, mean ART refill adherence was 90% (standard deviation [SD]= 13%), mean CD_4^+ cell count was 524 cells/mm^3, and 91% had plasma HIV RNA below the limit of quantification. Ninety percent were enrolled in KPNC and 10% at GHC. In the restricted SMR user group, we included 1,453 individuals with at least 36 months membership post SMR-rollout, and identified 1,014 age- and sex-frequency matched SMR non-users (Table 1). Baseline adherence was slightly lower among non-users compared with users (88% versus 90%; P<0.001). Race/ethnicity, healthplan, and baseline CD_4^+ cell count were also significantly different between the two groups.

Table 2 displays the refill adherence changes and differences in refill adherence change between the pre- and post-intervals for the restricted SMR user group and SMR non-users, both overall and stratified by CD_4^+ cell counts and plasma HIV RNA. Between the pre- and post-intervals, high adherence was maintained among the restricted group of SMR users (refill adherence change= −0.11%; 95% CI= −0.83, 0.62); however, mean adherence declined among SMR non-users (refill adherence change = −2.05%; 95% CI = −2.92, −1.18). The corresponding difference in refill adherence change when comparing SMR users and nonusers was 1.94% (95% CI = 0.81, 3.07; p<0.001) in unadjusted models and 1.80% (95% CI = 0.62, 2.98; p = 0.003) with adjustment for potential confounders. Among those with CD_4^+ cell count ≥200 cells/mm^3, SMR users maintained high levels of adherence (refill adherence change = −0.22%; 95% CI = −0.94, 0.50) but SMR non-users had a reduction in refill adherence (refill adherence change = −2.31%; 95% CI = −3.20, −1.42). This reduction corresponds to an unadjusted refill adherence change of 2.09% (95% CI = 0.95, 3.23; p<0.001) and adjusted refill adherence change of 1.91% (95% CI = 0.72, 3.10; p = 0.002). Similarly, among those with plasma HIV RNA <500 copies/mL, SMR users maintained high levels of adherence (refill adherence change = −0.36%; 95% CI = −1.08, 0.35) but SMR non-users had a decline in refill adherence (refill adherence change = −2.30%; 95% CI

= −3.16, −1.44), corresponding with an unadjusted difference in refill adherence change of 1.94% (95% CI = 0.82, 3.05; p<0.001), and adjusted refill adherence change of 1.78% (95% CI = 0.62, 2.95; p = 0.003). There was no difference in refill adherence change between the restricted group of SMR users and non-users who had a baseline CD_4^+ cell count <200 cells/mm^3 or plasma HIV RNA ≥500 cells/mL.

When comparing refill adherence in the pre- and post-intervals in the SMR user cohort, those who used SMR at a mean frequency of <0.5 times, 0.5 to <1 time, 1 to <2 times, and ≥2 times per month had a −1.58%, −0.15%, 0.31%, and 0.98% mean refill adherence change, respectively, as seen in the Figure (unadjusted overall p = 0.009). These changes correspond to a difference in refill adherence change of 1.43% (95% CI = 0.40, 3.26; p = 0.12), 1.89% (95% CI= 0.18, 3.60; p = 0.03), and 2.56% (95% CI = 0.52, 4.60; p = 0.01) for mean SMR use of 0.5 to <1 time, 1 to <2 times, and ≥2 times, respectively, compared to <0.5 times. After adjustment for potential confounders, these changes across categories remained statistically significant (adjusted overall p = 0.007), with corresponding differences in refill adherence change of 1.39% (95% CI = −0.43, 3.22), 2.03% (95% CI = 0.32, 3.74), and 2.60% (95% CI = 0.54, 4.66), respectively (Table 3).

In addition to higher mean frequency of SMR use per month, female sex was the only other factor associated with improved refill adherence among the SMR user cohort, with a difference in refill adherence change of 2.90% (95% CI = 0.14, 5.67; Table 3) compared to male sex. Age, healthplan, race/ethnicity, CD_4^+ cell count, and plasma HIV RNA were not associated with difference in refill adherence change among SMR users.

DISCUSSION

Our research demonstrates that SMR use is associated with maintenance of high levels of ART adherence and SMR non-use is associated with declines in adherence over time among HIV-positive patients enrolled in integrated healthcare systems with access to SMR. The benefits of SMR use versus no use were particularly evident in those with better controlled HIV disease (i.e., CD_4^+ cell count ≥200 cells/mm^3 and those with plasma HIV RNA <500 copies/mL). Among SMR users, we noted a positive “dose-response” relationship between frequency of SMR use per month and ART adherence. However, changes in mean refill adherence between the pre- and post-intervals were similar among SMR users regardless of age, race/ethnicity, CD_4^+ cell count, and plasma HIV RNA.

HIV adherence research is increasingly supporting the use of bidirectional communication between patients and healthcare providers[10,32], personalized message content[32], and the use of tools that are practical and can be used in patients’ daily lives[10]. Additionally, according to an internet-based survey of HIV-positive online social media users, the use of the internet for healthcare engagement purposes (including emailing providers, refilling medications online, or making medical appointments online) was significantly associated with higher odds of self-reported ART adherence and maximal virologic control even after controlling for potential confounders[33]. Internet use for health-related purpose has been associated with significantly lower likelihood of non-adherence[9] and greater patient self-confidence in adhering to ART[34]. Correspondingly, SMR allows for the use of the internet for direct and

personal communication between patients and healthcare providers, refilling medications, and making medical appointments. These SMR functions may support better ART adherence among SMR users compared to non-users. However, it is unclear whether SMR use results in a higher level of engagement in care, which in turn is related to ART adherence[4,5], or if those who are already more engaged in their HIV care are more likely to become SMR users.

We have previously described our cohort of HIV-positive patients at KPNC and GHC who are web-based SMR users[18]. During the first 36 months following the implementation of SMR, more than half of HIV-positive patients studied used SMR, primarily the SMR's medication refill function, secure messaging of healthcare providers, viewing medical test results, and requesting appointments. Initial SMR users were more likely to identify as non-Latino and White. In our study, we did not note any racial/ethnic disparities in changes in refill adherence pre- and post-intervals among SMR users. This may be due to the fact that among individuals with similar access to care[35], the association between SMR use and adherence is not modified by race/ethnicity.

In our study, women who used SMR had a larger improvement in mean ART adherence in comparison to men; however, in our prior descriptive study, women were about half as likely to use SMR compared to men[18]. Women are reported to have worse HIV-related health outcomes, lower rates of ART initiation and adherence, and higher likelihood of discontinuing ART[23,36–38]. Although further research is warranted, it is possible that targeted campaigns to increase SMR use among HIV-positive women may result in improved HIV clinical outcomes in this group.

Our study has several limitations. First, while timely refill of ART has been associated with plasma HIV RNA[39], this adherence measure only represents receipt of medication and not actual medication ingestion. However, using pharmacy refill to calculate adherence also has a number of advantages; these data can easily be collected, are not influenced by patients' ability to recall, are relatively inexpensive to acquire, and are readily obtainable from computerized records. Additionally, because we calculated mean adherence over a 12-month time-frame, short periods of ART non-adherence may have been masked, leading to a potential overestimation of ART adherence.

A second important limitation is that we conducted an observational study with which we cannot establish causality. Although randomized trials would allow causal evaluation of SMR use on adherence, the feasibility of these trials is limited due to the implementation of federal meaningful use criteria for electronic health records[40]. These criteria include some of the functions of the SMR studied here such as secure messaging with healthcare providers and viewing portions of the medical record. Third, we evaluated SMR use in HIV-positive patients in two integrated healthcare delivery systems; therefore, the generalizability of results to uninsured HIV-positive individuals or those not enrolled in an integrated healthcare system may be limited. Fourth, we were unable to assess internet access among our study population which has previously been shown to be a key barrier for the use of patient portals among HIV-infected populations[41].

A final limitation was our use of a pre-post cohort design was that it could not account for secular changes in adherence occurring concurrently with the rollout of SMR. To account for possible secular trends, we conducted a two-group pre-post within-person longitudinal design comparing changes in adherence among SMR users and non-users. We acknowledge that potential selection biases may still exist and we were unable to account for unmeasured variables such as participants' personality traits and level of proactivity and vigilance in their own health care. However, it is noteworthy that our finding of maintenance of adherence with SMR use was observed in both the analysis of the restricted group of SMR users versus non-users and in the analysis of SMR use frequency among the complete cohort of SMR users. Given little data regarding this important area of research and clinical care for HIV patients, future studies should evaluate the benefits of specific features of SMR prospectively or in randomized clinical trials and examine its cost-effectiveness.

In summary, in two healthplans which were early adopters of SMRs, we observed stable adherence over time among SMR users, compared with small declines among non-users. This difference is likely to have significant health impact, given prior research indicating that ART adherence typically declines over time and that even small reductions in adherence are associated with increased mortality risk[42]. In addition, an increasing number of healthplans are anticipated to provide SMRs with implementation of the Affordable Care Act. Thus, based on our data and other studies demonstrating the relationship between HIV clinical outcomes and use of online services for healthcare engagement[33], we believe that healthcare systems should adopt and promote access to SMR use for all HIV-positive patients in order to improve communication between patients and providers and increase patients' engagement in their HIV care.

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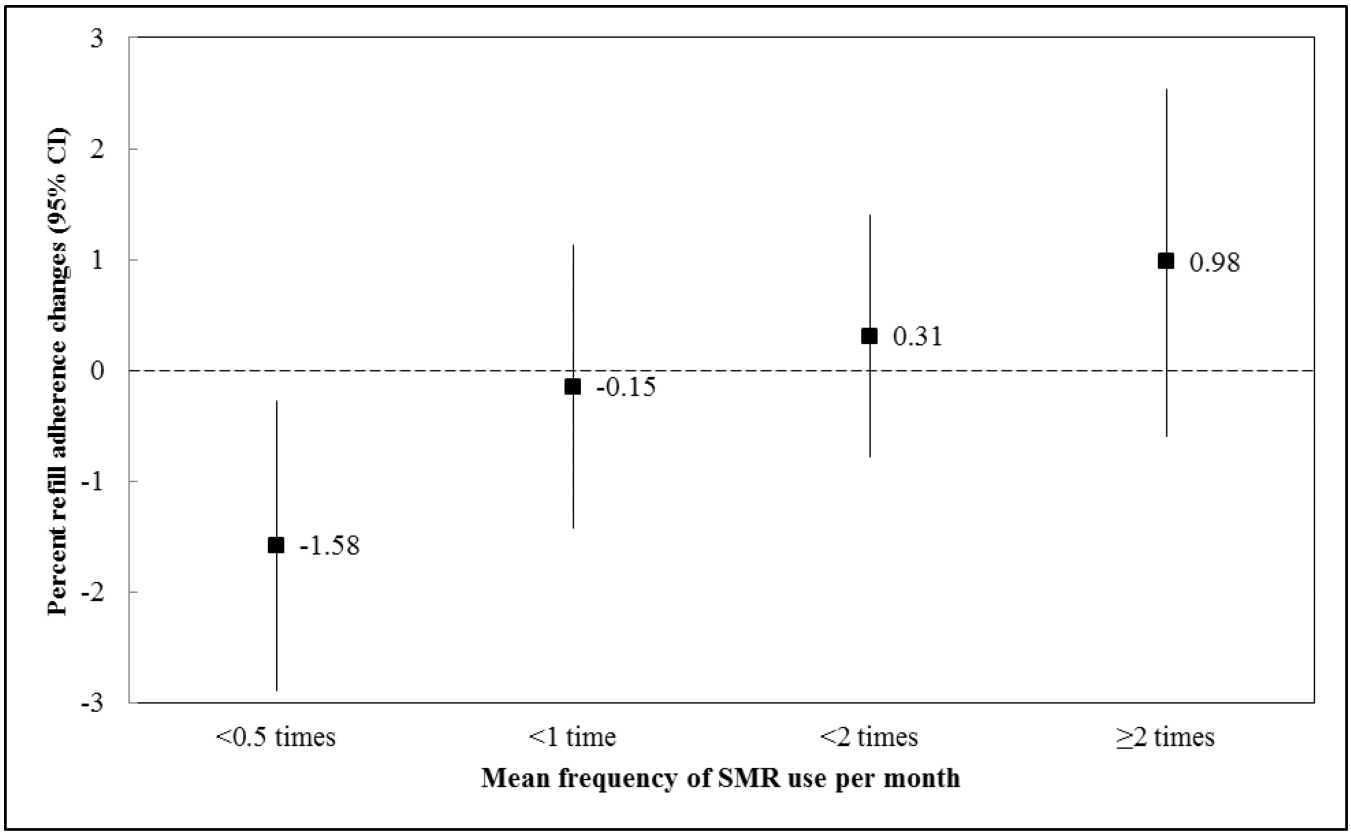

Figure 1.

Unadjusted[1] pre- to post-interval percent refill adherence changes based on mean frequency of SMR use among the SMR user cohort[2]

[1]Unadjusted p-value= 0.009

[2]Includes all SMR users, not limited to those with ≥36 months of healthplan enrollment following SMR rollout

▪ Represents the unadjusted point estimate of post-interval minus pre-interval ART refill adherence

| Represents the 95% confidence interval (CI) for the unadjusted change in ART refill adherence

… Represents no change in ART refill adherence from pre-interval to post-interval

Table 1

Baseline characteristics comparing the restricted SMR user group* and SMR non-users

Characteristic	SMR non-users (N = 1,014)	Restricted SMR user group (N = 1,453)	p-value
Age, mean years (SD)	49 (10)	49 (9)	0.38
Men, %	94	94	0.83
KPNC/GHC, %	96/4	91/9	<0.001
Race/ethnicity, %			<0.001
Asian/Pacific Islander	5	3	
Black	21	8	
Latino	19	10	
White	52	76	
Other	3	3	
ART refill adherence, mean % (SD)	88 (15)	90 (13)	<0.001
CD_4^+ cell count, mean cells/mm^3 (SD)	493 (267)	525 (261)	0.003
Plasma HIV RNA <75 copies/mL, %	90	91	0.74

*SMR users restricted to those with ≥36 months of health plan enrollment following SMR rollout

Table 2

Adjusted[1] and unadjusted pre- to post-interval percent refill adherence changes[2] and differences in percent refill adherence change[3] among the restricted SMR user group[4] and non-users overall and stratified by baseline CD_4^+ cell count and plasma HIV RNA

	Unadjusted			
	Percent Refill Adherence Change[2] (95% CI)	**Differences in Percent Refill Adherence Change[3] (95% CI)**	**p-value**	**Differences Refill**
Overall				
SMR non-users (N = 1,014)	−2.05 (−2.92, −1.18)	Reference		Reference
SMR users (N = 1,453)	−0.11 (−0.83, 0.62)	1.94 (0.81, 3.07)	<0.001	1.80
Baseline CD_4^+ <200 cells/mm^3				
SMR non-users (N = 116)	−0.01 (−3.51, 3.49)	Reference		Reference
SMR users (N = 101)	1.40 (−2.35, 5.15)	1.42 (−3.68, 6.51)	0.59	1.33
Baseline CD_4^+ cell count ≥200 cells/mm^3				
SMR non-users (N = 898)	−2.31 (−3.20, −1.42)	Reference		Reference
SMR users (N = 1,352)	−0.22 (−0.94, 0.50)	2.09 (0.95, 3.23)	0.0003	1.91
Baseline plasma HIV RNA <500 copies/mL				
SMR non-users (N = 915)	−2.30 (−3.16, −1.44)	Reference		Reference
SMR users (N = 1,317)	−0.36 (−1.08, 0.35)	1.94 (0.82, 3.05)	<0.001	1.78
Baseline plasma HIV RNA ≥500 copies/mL				
SMR non-users (N = 99)	0.31 (−3.80, 4.41)	Reference		Reference
SMR users (N = 136)	2.38 (−1.12, 5.88)	2.07 (−3.30, 7.44)	0.45	1.50

[1] Adjusted for age, sex, health plan, and race/ethnicity, baseline CD_4^+ cell count (excluding CD_4^+ cell count stratified), and plasma HIV RNA (excluding plasma HIV RNA stratified)

[2] Refill adherence changes calculated based on post-interval adherence minus pre-interval adherence

[3] Differences in refill adherence change calculated based on comparison of the pre- and post-interval adherence changes between SMR users and non-users

[4] SMR users restricted to those with ≥36 months of health plan enrollment following SMR rollout

Table 3

Factors[1] associated with the difference in percent refill adherence change[2] among the SMR user cohort (N=1,638)[3]

Factors	Difference in Percent Refill Adherence Change[2]	95% CI	p-value
Mean frequency of SMR use per month			
<0.5 times	Reference	-	-
0.5 to <1 time	1.39	−0.43, 3.22	0.14
1 to <2 times	2.03	0.32, 3.74	0.02
≥2 times	2.60	0.54, 4.66	0.01
Age, years			
18−39	Reference	-	-
40−49	−0.66	−2.61, 1.28	0.51
50−59	0.74	−1.31, 2.79	0.48
≥60	−0.34	−2.94, 2.26	0.80
Sex			
Men	Reference	-	-
Women	2.90	0.14, 5.67	0.04
Race/ethnicity			
White	Reference	-	-
Asian/Pacific Islander	1.40	−2.36, 5.16	0.47
Black	−1.52	−4.01, 0.96	0.23
Hispanic	0.27	−1.94, 2.48	0.81
Other\unknown	−2.96	−6.51, 0.59	0.10
Baseline CD_4^+ cell count, cells\mm^3			
<200	Reference	-	-
200–499	−2.04	−4.72,0.64	0.14
≥500	−0.53	−3.23, 2.18	0.70
Baseline plasma HIV RNA, copies/mL			
≥10,000	Reference	-	-
501–9,999	0.34	−4.03, 4.71	0.88
≤500	−2.36	−5.78, 1.06	0.18

[1] Model adjusted for all confounders in table and health plan

[2] Refill adherence changes calculated based on post-interval adherence minus pre-interval adherence

[3] Includes all SMR users, not limited to those with ≥36 months of health plan enrollment following SMR rollout