Use of Health Information Technology to Improve Medication Adherence

William M. Vollmer, PhD; Adrianne Feldstein, MD; David H. Smith, PhD, MPH; Joan P. Dubanoski, PhD, MPH; Amy Waterbury, MPH; Jennifer L. Schneider, MPH; Shelley A. Clark, RN; and Cynthia Rand, PhD

Objectives: To evaluate the effectiveness of an intervention based on health information technology (HIT) that used speech recognition software to promote adherence to inhaled corticosteroids (ICS) among individuals with asthma who were members of a large health maintenance organization.

Study Design: Pragmatic randomized clinical trial.

Methods: Adults with asthma enrolled in a large managed care organization (N = 8517) were randomized to receive either usual care or an interactive voice recognition (IVR) intervention designed to prompt medication refills and improve ICS adherence. The primary outcome was ICS adherence as measured by modified medication possession ratio calculated from the electronic medical record (EMR). Secondary measures included survey- and EMR-based measures of asthma morbidity.

Results: Our primary analyses found that ICS adherence increased modestly but significantly for participants in the intervention group relative to those in the usual care group (Δ = 0.02, 95% confidence interval 0.01-0.03), with a baseline adherence of 0.42 in both groups. No difference was observed in asthma morbidity measures. In post hoc analyses of participants receiving 2 or more direct IVR contacts or detailed messages, the intervention effect was more marked. The overall effect was triple that observed in the primary analyses (0.06 vs 0.02), and significant differences were observed between groups in asthma control.

Conclusions: An HIT-based adherence intervention shows potential for supporting medication adherence in patients with chronic diseases such as asthma. However, additional research is needed to determine how best to enhance the reach and effectiveness of such interventions.

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For author information and disclosures, see end of text.

Despite the proven efficacy of anti-inflammatory therapy in the management of asthma, patient nonadherence is common.[1-4] The clinical implications of this nonadherence include treatment failure; unnecessary and dangerous intensification of therapy; and excess healthcare costs, hospitalizations, and deaths.[5]

Relatively few studies have examined strategies to improve adherence with respiratory medications.[6-9] A review of primarily adult-focused adherence interventions stressed the need for innovative approaches to assist patients in following chronic medication regimens,[10] while others have called for strategies that leverage health information technologies (HITs) to promote and sustain medication adherence.[11]

Interactive voice recognition (IVR) technology has been widely used to deliver automated health education via telephone and to remind patients about appointments or health screening activities.[12-14] Such applications have been shown to have a significant effect on both behavioral and clinical outcomes.[15,16] The use of speech recognition software can further enhance the acceptance and effectiveness of this form of telephone-based interaction.[17,18] Linking IVR applications with electronic medical records (EMRs) offers additional opportunities to provide personalized adherence messages triggered by a patient's own refill patterns. A low-cost, HIT-based adherence intervention, if successful, would have immediate application for improving chronic disease management across a wide range of medical conditions.

We report the main results of a randomized clinical trial designed to test the effectiveness of an HIT-based intervention using speech recognition software to promote adherence to inhaled corticosteroids (ICS) among adults with asthma.

METHODS

Study Design

We conducted a pragmatic clinical trial[19] among patients receiving care in a routine clinical setting in which 8517 adults with asthma were randomized to receive either usual care or an IVR intervention designed to improve ICS adherence. The study was approved by the institutional review boards of each participating institution.

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Research Setting

Kaiser Permanente (KP) is a group-model HMO that provides

Take-Away Points

An intervention based on health information technology (HIT) that utilized automated refill reminders resulted in a small but significant overall improvement in asthma medication adherence among managed care patients.

- For that subset of patients who accepted the reminder phone calls, the benefit for medication adherence was larger and resulted in an improvement in asthma control.
- Future HIT strategies that more fully integrate physicians, pharmacists, and other clinical staff into adherence promotion systems have the potential to address more complex barriers to adherence and assist patients in the successful long-term management of chronic disease.

comprehensive, prepaid healthcare service to about 450,000 members of the Northwest region (KPNW) and 230,000 members of the Hawaii region (KPH). KPNW serves a population that is largely Caucasian (≈91%), while the KPH population includes about 27% Caucasians, 33% Asians, 12% native Hawaiians or Pacific Islanders, and about 24% of mixed heritage. Both KPNW and KPH utilize an EMR that includes pharmacy dispensings.

Study Population

The target patient population consisted of adult KPNW and KPH members with asthma who met the eligibility criteria in **Table 1**. To assure maximum generalizability, we did not exclude individuals with comorbid physical or mental health conditions.

For research-related logistical reasons (eg, to eliminate the need for multiple rounds of introductory mailings, to simplify the programming that would be required with a rolling enrollment) we "prerandomized" a patient pool who made up our potential sample. However, in keeping with how the intervention would be used in clinical practice, our analysis protocol prespecified an inclusion criterion that only those individuals who ever received (or for usual care participants, who would have qualified for) intervention calls were included in the analysis samples. Thus, while included in the randomization pool, patients who never qualified for a call did not receive an intervention and were not part of our primary (intention-to-treat) analysis; this design does not introduce bias because prerandomized control group patients were handled in the same way.

In order to be able to study adherence among both new ICS users and preexisting ICS users, we included in the target population members without an ICS dispensing prior to randomization. This article focuses on adherence among preexisting ICS users, who were the primary focus of the grant and were defined as having at least 1 ICS dispensing in the 12 months prior to their qualifying ICS dispensing or order. We also briefly describe findings for new ICS users.

Recruitment and Randomization

Of 15,164 individuals who were sent an invitation letter, 1100 (7.3%) opted out of the study and the remaining 14,064 were randomized to either the intervention or the usual-care arm, with randomization stratified by region and the clinic facility to which each patient was paneled. Over the 18 months of intervention calling, 8517 individuals qualified for 1 or more calls, of whom 6905 were preexisting ICS users and 1612 were new ICS users. The primary reasons for not qualifying for a call were the lack of a triggering ICS dispensing or order among potential new ICS users (52%) and perfect adherence to a monthly ICS regimen (33%). The **Figure** shows how the study sample was chosen.

Intervention

The intervention included 3 basic IVR call types, each of which typically lasted 2 to 3 minutes: a refill reminder call, a tardy refill call, and an initiator/restart call. Each month, we scanned the EMR to determine who was eligible for which type of call.

The refill reminder call went to participants whose last ICS dispensing was at least 1 month ago and who had fewer than 30 days of supply left, assuming appropriate use. The call reminded patients that they were due for a refill and offered a transfer to the automated pharmacy refill line and/or information about KP's online refill service. The tardy refill call went to individuals who were more than 1 month past their projected refill date. It not only reminded patients that they were due for an ICS refill, but also assessed asthma control, explored ICS adherence barriers, and provided tailored educational messages. Patients in poor control who declined to be transferred to the automated pharmacy refill line were offered the option to speak to a live pharmacist. Finally, the initiator/restart call was designed to provide support to patients who were either starting ICS for the first time (new users) or were lapsed users. These calls went to individuals with an ICS order or dispensing in the previous month and no other ICS dispensing in the previous 6 months, and were similar to the tardy refill calls in that they included probes for asthma control and adherence barriers and offered tailored educational messages.

When possible, the calling program left messages on answering machines or with another household member if the target participant was not at home. As part of the first direct contact with each participant, the scripted IVR call asked for permission to leave detailed messages that included the name of the target asthma medication. Lacking this, the phone messages simply noted it was the Breathe Easy Medication

Table 1. Eligibility Criteria

Inclusion Criteria
Treatment for asthma during the 12-month period prior to randomization.
One or more dispensings of a respiratory medication (corresponding to Generic Product Identifier class 44 [anti-asthma drugs including inhaled steroids, leukotriene antagonists, beta agonists, and ipratropium bromide]) at a Kaiser Permanente Northwest or Kaiser Permanente Hawaii outpatient pharmacy during the 12-month period prior to randomization.
Age 18 years or older as of the time of randomization.
Continuous Kaiser Permanente membership from the start of the baseline year until the time of randomization.
Willing to participate in the study.
Exclusion Criterion
Individuals meeting the above criteria were only included in the final analysis sample if they ever received (or for usual care participants, would have qualified for) an intervention call.

Reminder Program calling and asked the participant to call back on a toll-free number.

Data Collection

We surveyed 2000 randomly selected individuals prior to randomization and again at the end of the study. Additional data, including our primary adherence measures, were derived from the EMR

Study Measurements

Adherence. We used a modification of the medication possession ratio (MPR)[20-22] as our primary outcome measure. The MPR is computed as the days of supply of medication during a given time window divided by the time between the first dispensing in the window and the end of the window. Our modified MPR (mMPR) also accounted for medication that was on hand at the start of the window and ignored any days of supply that would extend beyond the end of the window. We also assumed that medications were used as directed and that a new ICS canister was not started until any medication on hand was exhausted.[22] Since all participants were prior ICS users or had an ICS order prior to randomization, we assumed they met criteria for persistent asthma and hence should have been taking ICS throughout their entire intervention period.[23] This enabled us to calculate an mMPR for everyone, not just for those with at least 1 dispensing. Finally, since the implied adherence associated with medication on hand at the start of randomization could not be related to intervention status, we ignored this initial period in our calculations. A baseline mMPR was computed for the 12 months prior to the start of call eligibility in a similar manner. In computing the mMPR, we treated all ICS medications, including combination agents containing an ICS, as equivalent. The mMPR was an indication of the proportion of days during our observation window that patients had ICS medication available. Thus, an mMPR of 1.0 suggests that a patient was dispensed enough medication to cover all the days during the window, while an mMPR of 0.5 suggests that a patient was dispensed enough ICS medication to cover half of the window of observation.

Other EMR–Based Measures. We used data from the EMR for the year prior to qualifying for calling (the baseline year) to capture the following information: age, race, sex, smoking status, comorbid chronic obstructive pulmonary disease (COPD; defined as either a visit coded 490, 491, 492, or 496 during the baseline year or the presence of 1 of these codes on the patient's problem list), acute asthma healthcare utilization (urgent care, emergency department care, or hospitalization), oral steroid use, short-acting beta agonist (SABA) use, and total number of distinct medications filled in the past 12 months. We classified smoking status based on the most recently available EMR data prior to the start of call eligibility.

Survey Measures. The baseline and follow-up surveys captured information related to race and asthma-specific health status (ie, the Juniper mini-Asthma Quality of Life Questionnaire [AQLQ]).[24] The follow-up survey also included the Asthma Therapy Assessment Questionnaire (ATAQ) asthma control index[25] and a series of questions (for those randomized to the active intervention arm) related to satisfaction with the intervention.

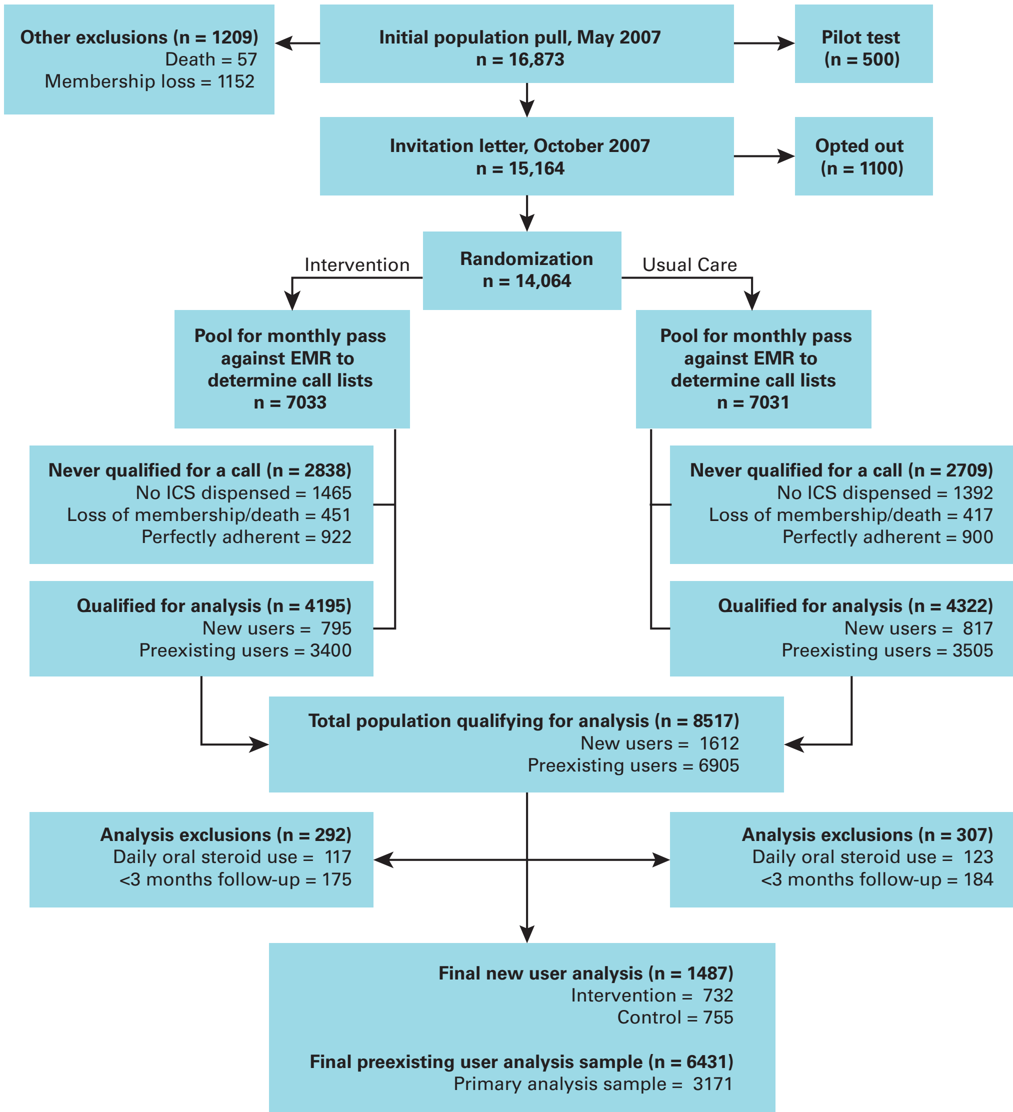
Intervention Process Data. For each call we captured the date and type of the call, participant responses during the call, and information on transfers.

Composite and Other Measures. We used self-reported race from the surveys if available, and otherwise relied on EMR-based race information where available. We used geocoding to map zip code information to block-level income data as a proxy for household income.

Statistical Analysis

For our primary analysis, we excluded 474 preexisting users (6.9% of those who qualified for calls) who either appeared to be daily users of oral steroids (n = 215) or had fewer than 3

■ **Figure.** Derivation of Study Sample



EMR indicates electronic medical record; ICS, inhaled corticosteroid.

months of follow-up data (n = 259). We excluded users with daily oral steroid use because these individuals would be unlikely to gain additional benefit from ICS for preventive purposes and users with fewer than 3 months of follow-up because we thought that the mMPR would be too unreliable in this group.[20] The proportions excluded were very similar in the 2 intervention groups (7.0% vs 6.7%, P = .68). A sensitivity analysis that included these individuals gave similar results.

For the analysis of mMPR scores we used a general linear model (with assumed normal errors) that adjusted for performance site (KPH vs KPNW), sex, age (18-45, 46-60, ≥61 years), baseline SABA use (0, 1-2, 3+ canisters), comorbid COPD status (any diagnosis with code 492/496, any diagnosis with code 490/491 but not code 492/496, or no COPD), and approximate tertiles of baseline mMPR (<0.20, 0.20-0.55, ≥0.55). We used duration of follow-up as a weighting variable to reflect the fact that these adherence measures become more accurate and reliable with longer follow-up. Results are also expressed for subgroups defined by age, sex, tertiles of baseline mMPR, baseline SABA usage, and comorbid COPD status. Appropriate subgroup-by-treatment interaction terms were used to formally test whether treatment effects differed across subgroups. We also conducted logistic regression analyses of the proportion of individuals with good adherence (defined as mMPR ≥0.8).

For the analysis of SABA use and acute asthma healthcare utilization, we used overdispersed Poisson regression analysis to analyze the rate of use (canisters per year and acute visits per year, respectively) while adjusting for the same set of baseline covariates. However, we restricted analysis of SABA use to those patients without comorbid COPD because SABA use is very common in this latter group and hence might not be affected by the intervention.

To assess the impact of the intervention on asthma-related quality of life and self-reported asthma control, we utilized data from the 1535 individuals who completed the follow-up survey. The analytic model for these analyses was similar to that for the mMPR data.

Finally, we conducted post hoc analyses comparing usual care participants with those intervention participants whom we reached directly or for whom we left detailed messages at least 2 times.

Our a priori power calculations showed near-100% power to detect differences of 0.04 in adherence and 85% power to detect differences of 0.5 on the 7-point mini-AQLQ score; we did not perform power calculations for other secondary outcomes. All analyses were done with Stata version 10 (Stata Corporation LP, College Station, Texas).

RESULTS

Sample Characteristics

Baseline characteristics of the intervention and usual care groups were very similar (**Table 2**). Overall, 34% of participants in the primary analysis sample were male, with a mean age of 54 years (range 18-98 years). One-third had comorbid COPD, 14% had an emergency department visit or hospitalization for asthma, almost half had some oral steroid dispensing, and 23% received 3 or more SABA canisters during the baseline year. The mean baseline ICS mMPR was 0.42.

Intervention Process Data

A total of 11,714 IVR calls were delivered to 3171 different individuals in the active intervention arm. Of these, 27% were simple refill reminder calls, 61% were tardy refill calls, and 12% were initiator/restart calls. Overall, 91% of intervention participants received at least 1 tardy refill call, 38% received at least 1 refill reminder call, and 44% received an initiator/restart call. Of the calls we attempted, we successfully reached the target participant 39% of the time, left a detailed message 15% of the time, and left a nondetailed message 30% of the time. Thus, 84% of all calls resulted in some sort of message being left for the participant, and more than half were specifically able to mention the reason for the call. On an individual basis, 55% of intervention participants were reached directly or received a detailed message on 2 or more occasions.

Primary Analyses: Preexisting Inhaled Corticosteroid Users

Adherence with ICS increased significantly after randomization for participants in the intervention group compared with those in usual care (**Table 3**), although the magnitude of the difference (Δ = 0.02, 95% confidence interval 0.01-0.03) was small. Baseline adherence was 0.42 in both groups. The drops in mean mMPR from baseline to follow-up that were observed in both treatment groups likely reflect an upward bias in the baseline mMPR, because all participants were required to have at least 1 ICS dispensing during baseline. The intervention effects did not differ significantly by baseline mMPR, age, sex, baseline SABA use, or baseline COPD status. We observed no significant intervention effects on the proportion of good adherers (defined as mMPR $\geq$0.8), either overall or separately in those with and without good adherence at baseline (data not shown). We also observed no significant intervention effects on reliever medication (SABA) use, quality of life, asthma control, or the rate of acute asthma healthcare utilization.

Post Hoc Analyses: Preexisting Inhaled Corticosteroid Users

In post hoc analyses limiting intervention participants to those reached directly or with detailed messages 2 or more times (55% of intervention participants), the apparent effects of the intervention were much more pronounced (**Table 4**). The overall effect was 3 times greater than that shown in Table 3 (0.06 vs 0.02), and highly significant effects were seen in all subgroups studied. We also observed a significant improvement in the proportion of individuals with good control: 23% versus 17% overall and 10% versus 7% among those not in good control initially (both P <.007 based on multivariate logistic regression analyses). We did not see corresponding improvements in our other outcomes, and in fact the rate of acute asthma healthcare utilization increased significantly in this subset of intervention participants (relative risk =1.06, P = .038).

Postintervention Survey Results: Preexisting Inhaled Corticosteroid Users

A total of 559 intervention participants (56% of those completing the follow-up survey) remembered receiving the intervention calls and provided feedback on the intervention. Of these, roughly 50% indicated that the calls were helpful and that the service should be continued in the future; one-third reported they felt their asthma was in better control as a result of receiving the calls.

Results for New Inhaled Corticosteroid Users

An intention-to-treat analysis for the secondary analysis sample of new ICS users failed to show a significant inter-

Table 2. Characteristics of the Primary Analysis Sample: Preexisting Users of Inhaled Corticosteroids[a]

	Percentage[b]		
Electronic Medical Record Data	**Intervention Group (n = 3171)**	**Usual Care Group (n = 3260)**	**Total (n = 6431)**
Age, mean (SD), y	53.7 (15.3)	53.5 (15.3)	53.6 (15.3)
18-45	30.2	30.8	30.5
46-60	36.4	37.6	37.0
≥61	33.4	31.6	32.5
Male	32.2	35.3	33.8
Race			
White	51.5	48.4	50.0
African American	1.6	1.6	1.6
Asian	10.8	11.9	11.4
Native Hawaiian/Pacific Islander	4.6	4.0	4.3
American Indian/Alaskan Native	0.5	0.6	0.5
Mixed	6.2	7.2	6.7
Unknown	24.9	26.3	25.6
Estimated household income, $			
<40,000	26.9	26.7	26.8
40,000-59,999	44.9	45.3	45.1
≥60,000	27.4	27.1	27.2
Unknown	0.8	0.9	0.8
Smoking status			
Current	8.4	7.9	8.2
Former	9.5	8.7	9.1
Never	43.1	43.6	43.3
Unknown	39.1	39.9	39.5
Comorbid COPD[c]	33.3	33.3	33.3
ED visit or hospitalization for asthma[d]	13.9	13.4	13.7
Any oral steroid use (burst pack)	46.5	45.8	46.1
Beta agonist use (canisters)			
0	44.1	43.5	43.8
1	22.0	21.4	21.7
2	11.6	12.5	12.0
≥3	22.4	22.7	22.5
Total number of different medications dispensed[e]			
0-5	31.6	31.2	31.4
6-12	31.2	30.4	30.8
≥13	37.2	38.5	37.9
ICS mMPR, mean (SD)	0.42 (0.30)	0.42 (0.31)	0.42 (0.31)

COPD indicates chronic obstructive pulmonary disease; ED, emergency department; ICS, inhaled corticosteroid; mMPR, modified medication possession ratio.
[a]Based on chart information for the 12 months prior to call eligibility.
[b]Values are percentages unless indicated otherwise.
[c]Includes visit or problem list entry for *International Classification of Diseases, Ninth Revision* codes 490, 491, 492, and/or 496 in baseline year.
[d]Any listed diagnosis for ED or primary discharge diagnosis for hospitalization in baseline year.
[e]Number of unique generic medication names dispensed during the baseline year.

vention effect. Post hoc analyses were not conducted in this group.

DISCUSSION

The results from this large, pragmatic clinical trial suggest that the use of IVR phone calls had a modest but significant effect on overall ICS adherence. However, no outcome difference was observed between treatment groups for SABA use, quality of life, asthma control, or the rate of acute asthma healthcare utilization.

The magnitude of the observed intervention effect, although small, may still have important public health implications. For instance, it is well known that a 2 mm Hg drop

Table 3. Primary Analysis of Modified Medication Possession Ratio for Preexisting Users of Inhaled Corticosteroids

Analysis	Intervention Group (n = 3171)	Usual Care Group (n = 3260)	Mean Change (95% CI)[a]	*P*[b]
Overall				
Baseline[b]	0.42 ± 0.30	0.42 ± 0.30		
Follow-up	0.40 ± 0.32	0.38 ± 0.32		
Change	−0.02 ± 0.24	−0.04 ± 0.24	0.02 (0.01-0.03)	.002
Change in mMPR by tertiles of baseline mMPR[c]				
<0.20	0.07 ± 0.19	0.07 ± 0.20	0.01 (−0.01 to 0.03)	.39
0.20-0.54	−0.03 ± 0.23	−0.06 ± 0.22	0.03 (0.01-0.04)	.007
0.55-1.00	−0.11 ± 0.26	−0.12 ± 0.25	0.02 (−0.00 to 0.04)	.12
Change in mMPR by sex				
Male	−0.01 ± 0.24	−0.04 ± 0.24	0.03 (0.01-0.05)	.001
Female	−0.03 ± 0.24	−0.04 ± 0.23	0.01 (−0.00 to 0.03)	.15
Change in mMPR by age				
≤45 y	−0.04 ± 0.22	−0.05 ± 0.23	0.01 (−0.01 to 0.03)	.26
46-60 y	−0.03 ± 0.24	−0.05 ± 0.23	0.02 (0.00-0.04)	.045
≥61 y	0.00 ± 0.25	−0.02 ± 0.25	0.02 (0.00-0.04)	.036
Change in mMPR by baseline SABA use				
0 canisters	−0.03 ± 0.23	−0.05 ± 0.22	0.02 (0.00-0.04)	.039
1-2 canisters	−0.02 ± 0.23	−0.03 ± 0.23	0.01 (−0.02 to 0.03)	.62
3+ canisters	0.00 ± 0.27	−0.04 ± 0.27	0.04 (0.01-0.06)	.003
Change in mMPR by comorbid COPD status				
No COPD	0.00 ± 0.29	−0.04 ± 0.26	0.02 (0.00-0.03)	.022
Codes 490/491 only	−0.02 ± 0.24	−0.04 ± 0.23	0.01 (−0.01 to 0.04)	.29
Codes 492/496	−0.03 ± 0.23	−0.04 ± 0.23	0.04 (0.00-0.08)	.033

CI indicates confidence interval; COPD, chronic obstructive pulmonary disease; mMPR, modified medication possession ratio; SABA, short-acting beta agonist.
[a]Net intervention effect.
[b]Two-tailed significance level for overall treatment effect based on linear regression analysis, adjusting for site and (as appropriate) age, sex, comorbid COPD status, baseline SABA use, and baseline mMPR categories.
[c]Baseline defined as 12 months prior to start of (eligibility for) calls for each participant.

in blood pressure, on a population basis, has important public health implications in terms of long-term cardiovascular risk reduction. Williams et al[5] found that each 25% increase in the proportion of time without an ICS medication resulted in a doubling of the rate of prednisone use and asthma-related hospitalization. In this trial we failed to see a reduction in either SABA use (a short-term measure of morbidity) or urgent asthma healthcare utilization. This suggests that the clinical benefit of small improvements in adherence may be negligible for most patients. Future interventions are likely to have more impact if accompanied by more intensive and targeted strategies for higher-risk patients. These strategies might include other, perhaps coordinated, HIT activities like e-mail and text messaging. One potential way forward is to obtain information about patients' preferences for HIT reminders and test whether incorporating those preferred methods yields favorable results.

Nonadherence with asthma controller therapy is common,[3-5,26] and the current study similarly found that at baseline 65% of existing ICS users used less than 50% of the prescribed therapy and only 16% of patients used 80% or more of the prescribed therapy. The causes of nonadherence with asthma therapy are multiple, including patients' beliefs about their asthma and therapy (eg, not needing as much medication, concerns about steroids), failure to understand the regimen, structural barriers to adherence (cost, transportation), and factors that contribute to erratic adherence such as regimen complexity and forgetting. The limited effect of the intervention may be attributable to the fact that the current study was primarily designed to address only 1 of these factors—forgetting—by serving as a reminder and prompt to refill prescriptions. Because of this limitation, our intervention's results for ICS use in patients with asthma may not be directly generalizable to other medications or diseases. The transferability of our findings to new conditions and treatments may largely depend on how similar those conditions are to asthma with regard to forgetting as a reason for nonadherence.

■ **Table 4.** Post Hoc Analysis of Modified Medication Possession Ratio for Primary Analysis Sample (Preexisting Users of Inhaled Corticosteroids), Limited to Intervention Participants With 2 or More Direct Contacts or Detailed Messages

Analysis	Intervention Group (n = 1758)	Usual Care Group (n = 3260)	Mean Change (95% CI)[a]	*P*[b]
Overall				
Baseline[b]	0.46 ± 0.31	0.42 ± 0.30		
Follow-up	0.47 ± 0.33	0.38 ± 0.32		
Change	0.00 ± 0.24	−0.04 ± 0.24	0.06 (0.04-0.07)	<.001
Change in mMPR by tertiles of baseline mMPR[c]				
<0.20	0.11 ± 0.20	0.07 ± 0.20	0.04 (0.01-0.07)	.004
0.20-0.54	0.01 ± 0.23	−0.06 ± 0.22	0.07 (0.04-0.09)	<.001
0.55-1.00	−0.08 ± 0.24	−0.12 ± 0.25	0.06 (0.03-0.08)	<.001
Change in mMPR by sex				
Male	0.02 ± 0.24	−0.04 ± 0.24	0.08 (0.05-0.10)	<.001
Female	−0.00 ± 0.24	−0.04 ± 0.23	0.05 (0.03-0.06)	<.001
Change in mMPR by age				
≤45 y	−0.00 ± 0.20	−0.05 ± 0.23	0.07 (0.04-0.10)	<.001
46-60 y	−0.00 ± 0.25	−0.05 ± 0.23	0.06 (0.04-0.08)	<.001
≥61 y	0.01 ± 0.25	−0.02 ± 0.25	0.04 (0.02-0.07)	<.001
Change in mMPR by baseline SABA use				
0 canisters	−0.01 ± 0.23	−0.05 ± 0.22	0.05 (0.033-0.07)	<.001
1-2 canisters	0.00 ± 0.22	−0.03 ± 0.23	0.04 (0.013-0.06)	.003
3+ canisters	0.04 ± 0.27	−0.04 ± 0.27	0.08 (0.055-0.11)	<.001
Change in mMPR by comorbid COPD status				
No COPD	−0.00 ± 0.23	−0.04 ± 0.26	0.05 (0.04-0.07)	<.001
Codes 490/491 only	0.01 ± 0.24	−0.04 ± 0.23	0.06 (0.03-0.08)	<.001
Codes 492/496	0.02 ± 0.29	−0.04 ± 0.23	0.07 (0.03-0.11)	.001

CI indicates confidence interval; COPD, chronic obstructive pulmonary disease; mMPR, modified medication possession ratio; SABA, short-acting beta agonist.
[a]Net intervention effect.
[b]Two-tailed significance level for overall treatment effect based on linear regression analysis, adjusting for site and (as appropriate) age, sex, comorbid COPD status, baseline SABA use, and baseline mMPR categories.
[c]Baseline defined as 12 months prior to start of (eligibility for) calls for each participant.

The absence of a larger intervention effect also could have been due to the fact that many individuals in the intervention group actually received little or no real intervention. In only 54% of our IVR calls did we either speak with the participant or leave a detailed message. When we limited the analyses to those individuals whom we contacted directly or for whom we left detailed messages 2 or more times (55% of intervention participants), we found much stronger effects in both adherence and improved asthma morbidity that persisted across a wide range of subgroups. While we acknowledge the limitations of such post hoc analyses and recognize that this subset of intervention participants had much higher levels of baseline adherence than did those who were excluded from this analysis (mMPR score of 0.46 vs 0.36, *P* <.0001), these results nonetheless suggest that the calls, if received, were useful.

The large sample size, randomized design, and pragmatic nature of the trial (with limited exclusion criteria) are strengths of the study and support the generalizability of the findings. While we had to rely on pharmacy dispensing records to infer adherence, such measures have become increasingly more common and have been shown to correlate with patient outcomes.[3,27] In addition, such measures have high face validity when measured over long periods of time because high levels of adherence can only be achieved by persistently refilling medications, which in turn is strongly suggestive of ongoing use of those medications. Also, while our databases do not capture dispensing from non-KP pharmacies, the majority of KP members have some form of prescription benefit and previous studies have shown that most of them fill their prescriptions at KP pharmacies. Furthermore, the use of non-KP pharmacies should be distributed evenly across the 2 treatment groups and hence not bias our treatment comparisons. Reassuringly, although the specifics of the methods and populations differ, our adherence findings are broadly similar to those of other studies that have examined adherence with ICS using pharmacy refill patterns in adults.[27,28]

In summary, the impact of this HIT-based IVR adherence intervention may have been limited by participants' willingness to take the calls. Our qualitative data suggest that continuing to find ways to make the calls personalized, streamlined, nonredundant, and actionable may further increase utility and participation. In the future, inclusion of mail, e-mail, or Internet-based platforms may be necessary to reach the broadest populations. In addition, HIT strategies that more fully integrate physicians, pharmacists, and other clinical staff into adherence promotion systems have the potential to address more complex barriers to adherence than could be addressed by this intervention.

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Author Affiliations: Kaiser Permanente Center for Health Research (WMV, AF, DHS, AW, JLS), Portland, OR; Kaiser Permanente Center for Health Research (JPD, SAC), Honolulu, HI; Johns Hopkins University (CR), Baltimore, MD.

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Address correspondence to: William M. Vollmer, PhD, Center for Health Research, 3800 N Interstate Ave, Portland, OR 97227-1110. E-mail: william.vollmer@kpchr.org.

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