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Electronic inhaler monitoring and healthcare utilization in chronic obstructive pulmonary disease

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Abstract

Introduction: The effect of electronic inhaler monitoring (EIM) on healthcare utilization in chronic obstructive pulmonary disease (COPD) has not been studied. We hypothesized that the use of EIM in conjunction with a disease management program reduces healthcare utilization in patients with COPD.

Methods: This is a retrospective pre- and post-analysis of a quality improvement project. Patients with COPD and high healthcare utilization (≥one hospitalization or emergency room visit during the year prior to enrolment) were provided with electronic monitoring devices for monitoring controller and rescue inhaler utilization for one year. Patients were contacted when alerts were triggered, indicating suboptimal adherence to controller inhaler or increased use of rescue inhalers, potentially signalling an impending exacerbation. Healthcare utilization was assessed pre- and post-monitoring, with each subject serving as his/her own control.

Results: Patients with COPD and high healthcare utilization ($n = 39$) were recruited. Mean EIM duration was 280.5 (±120.6) days. The mean age was 68.6 (±9.9) years, FEV1 (mean forced expiratory volume in one second) was 1.1 (±0.4) L, and mean Charlson Comorbidity index was 5.6 (±2.7). Average adherence was 44.4% (28.4%). Compared with the year prior to enrolment, EIM was associated with a reduction in COPD-related healthcare utilization per year (2.2 (±2.3) versus 3.4 (±3.2), $p = 0.01$). Although there was a reduction in all-cause healthcare utilization, this was not statistically significant (3.4 (±2.6) versus 4.7 (±4.1), $p = 0.06$).

Discussion: EIM in conjunction with a disease management program may play a role in reducing healthcare utilization in COPD patients with a history of high healthcare utilization.

Keywords

COPD, adherence, inhaler, exacerbations

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Introduction

Electronic inhaler monitoring (EIM) is a technology that allows the assessment of adherence to inhaler therapy.[1,2] Modern commercial EIM systems include audiovisual (AV) reminders. Some systems offer interactive platforms allowing real-time monitoring and feedback to patients.[1–3] While older systems proved useful in assessing study drug compliance in clinical trials, newer-generation EIM systems have shown promise in improving clinical outcomes. Adherence to prescribed inhalers improved with the use of EIM-coupled AV reminders,[4–6] EIM-based automated feedback (text messages, interactive voice calls, etc.),[7,8] and EIM-based provider feedback[9–13] among patients with asthma. Combining provider feedback with AV reminders did not result in further improvement in adherence.[5] In a study of poorly controlled asthmatics, EIM was instrumental in

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improving asthma control, reducing hospitalizations and exacerbations.[14]

Consistent use of inhaled therapy reduces acute exacerbations of chronic obstructive pulmonary disease (AECOPD).[15–20] There is a gap, however, between adherence in clinical trials[21] and practice.[22–24] For instance, 79.8% of TOward a Revolution in COPD Health (TORCH) trial participants had >80% adherence to the study drug.[21] In contrast, only 19.8–30.6% of patients achieved that adherence in a Veterans Affairs Health System-based study.[24] Another population study in 55,076 Medicare patients reported an average adherence rate of 23–43% depending on the frequency of inhalers.[22] Hence, there is an unmet need for interventions that improve adherence to reap the full benefits of inhaled therapy. The use of EIM-coupled provider feedback to improve adherence in chronic obstructive pulmonary disease (COPD) patients is supported by clinical studies.[25,26] Monitoring the frequency of rescue inhaler use may help in the early prediction of AECOPD.[27] Nevertheless, the potential role of EIM in reducing COPD-related healthcare utilization remains unknown. We hypothesized that an EIM-coupled disease management program reduces healthcare utilization in a COPD cohort of high healthcare utilizers.

Methods

Study design, setting, and participants

This is a retrospective analysis of a quality improvement project conducted at the Cleveland Clinic (OH, USA) between October 2016 and June 2018. Patients with spirometry-proven COPD (post-bronchodilator forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) ratio <0.7) as defined by GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria[28] and high healthcare utilization (≥one ER visit or hospitalization in the year prior to enrolment) were enrolled. EIM devices were attached to one or both of the controller and the rescue inhalers (Propeller Health, Madison, WI, USA). Models with AV reminders were used when compatible with patients' inhalers. Patients were followed for one year and continued regular follow-ups with their pulmonologists. Platform-generated alerts were emailed to the study team when patients did not use their controller inhalers for four consecutive days or when their rescue inhaler use increased for a day by ≥1.64 times the standard deviation (SD) above their average. Patients were contacted when alerts were generated, and open-ended conversations were held aiming to foster adherence and detect exacerbations early. A unit of "24 hours" was used as a "possible exacerbation window" to calculate the accuracy of rescue alerts in detecting exacerbations within seven days. Patients who completed one year in the program by May 31, 2018 were included in this analysis.

The study was approved by the Cleveland Clinic Institutional Review Board (IRB# 18-138). The informed consent was waived as the study was a retrospective analysis of a quality improvement project.

Study outcomes

The primary outcome was all-cause healthcare utilization. Secondary outcomes included COPD-related healthcare utilization, number of pulmonary and/or primary care clinic visits, outpatient antibiotic and/or steroid courses, adherence, adherence determinants, adherence and healthcare utilization correlation, adherence pattern over time, and accuracy of rescue alerts in predicting moderate-to-severe exacerbations. A subgroup analysis of the primary outcome was performed in the AV reminders group.

Study variables

"All-cause healthcare utilization" was defined as the number of emergency room (ER) visits and hospitalizations. "COPD-related healthcare utilization" was determined based on the treating provider's documentation in the electronic health records (EHRs). "Adherence" to controller inhalers was defined as (number of taken doses/number of prescribed doses) × 100%, truncated at 100% for each day. Patients were deemed to be adherent if they took the full number of inhalations prescribed at the specific time. If the patient's took more than the prescribed dosing, we did not count these additional doses for calculating adherence (i.e. truncated at prescribed dose). In essence, patients needed to take the dose at the right time and (at least) at the full prescribed dose to be considered adherent. We calculated "adjusted adherence" after deducting days of hospitalizations or ER visits, during which patients did not have access to their EIM-capable inhalers. Healthcare utilization was obtained by review of electronic medical records. Healthcare utilization was obtained for the entire year of monitoring, regardless of patient compliance status or use of EIM devices. "Moderate COPD exacerbations" were those requiring outpatient courses of antibiotics and/or corticosteroids. "Severe COPD exacerbations" were those requiring ER visits or hospitalizations. A voluntary end-of-study survey was conducted. It explored barriers to adherence, devices technical difficulties, and overall satisfaction with the program.

Our analysis excluded those who died so as to not skew the healthcare utilization of the cohort, as

extensive use of healthcare resources is common in the final months of life for COPD patients.[29]

Statistical analysis

Statistical analysis was conducted using SAS software (version 9.4, SAS Institute, Inc., Cary, NC, USA) and R version 3.5.0 (The R Foundation for Statistical Computing, Vienna, Austria). Descriptive analyses were presented as mean (SD) for continuous variables and counts (percentage) for categorical variables. To compare pre- and post-intervention healthcare utilization, a paired *t*-test was utilized. The Pearson correlation coefficient was used to explore associations between adherence and healthcare utilization. Linear regression analysis was performed to seek determinants of adherence. Linear mixed-effects regression analysis was performed to characterize adherence pattern over time. A two-sided *p*-value <0.05 was considered statistically significant.

Results

Forty-five patients were recruited between October 1, 2016 and May 31, 2017. Thirty-nine patients were included in the analysis. Among the six patients excluded, four died during the study, one had stage 4 sarcoidosis, and one had idiopathic pulmonary arterial hypertension requiring parenteral therapy. COPD was not a driver of healthcare utilization in the latter two patients. Thirty patients (76.9%) received devices with AV reminders. Twenty-one patients (53.8%) achieved 100% syncing with the platform throughout the study (Figure 1).

Mean monitoring duration was 280.5 (120.6) days. The baseline characteristics of the 39 subjects are summarized in Table 1.

Healthcare utilization

There was a significant reduction in COPD-related healthcare utilization compared with the year prior to enrolment (2.2 (2.3) versus 3.4 (3.2), $p=0.01$). All-cause healthcare utilization was reduced, although the difference was not statistically significant (3.4 (2.6) versus 4.7 (4.1), $p=0.06$). All-cause healthcare utilization in the AV reminders subgroup was significantly reduced (3.1 (2.6) versus 5.4 (4.3), $p=0.005$). Pre- and post-monitoring healthcare utilization data are summarized in Table 2.

We found no significant difference in the number of outpatient corticosteroid or antibiotic courses, pulmonary or primary care clinic visits. These findings are shown in Table 3.

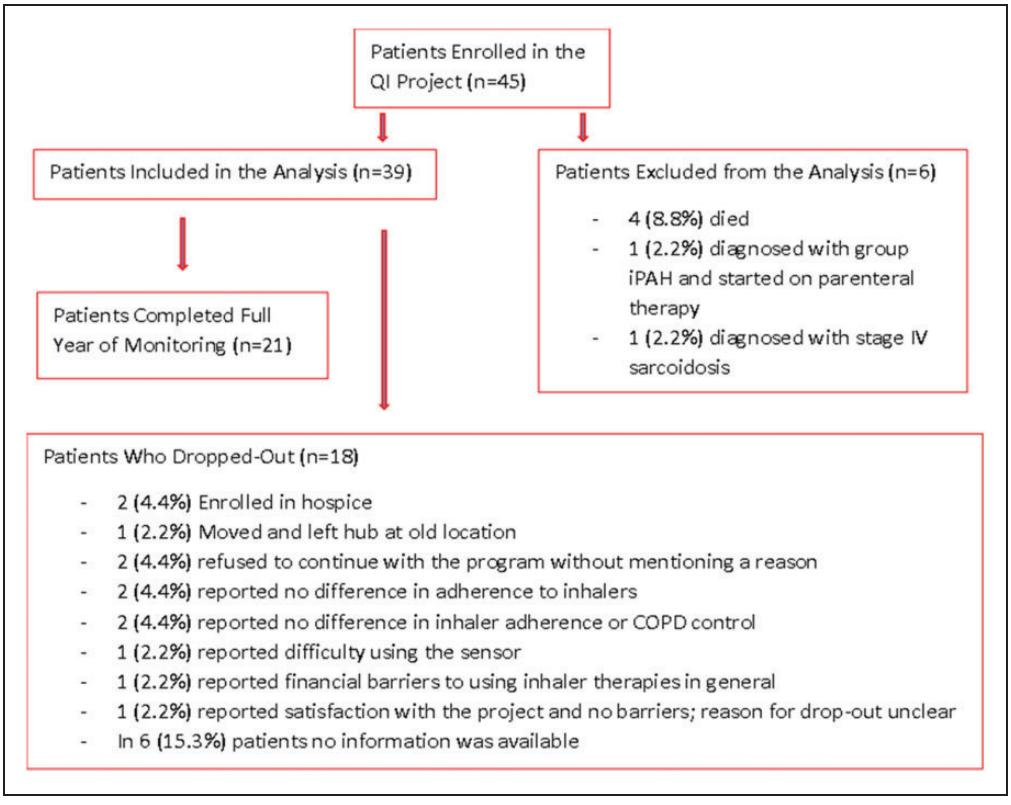

Figure 1. Study flow.
COPD: chronic obstructive pulmonary disease; iPAH: idiopathic pulmonary arterial hypertension.

Table 1. Baseline characteristics of the 39 subjects.

Parameter	Value
Age, year, mean (SD)	68.6 (9.9)
Sex, male : female	20:19
Ethnicity, Caucasian : African-American	27:12
Body mass index, kg/m^2, mean (SD)	28.2 (8.0)
Pulmonary function and gas exchange	
Post-bronchodilator FEV1, % of predicted, mean (SD)	47.2 (16.7)
Post-bronchodilator FVC, % of predicted, mean (SD)	76.2 (17.2)
DLCO, % of predicted, mean (SD)	46.4 (19.1)
Supplemental oxygen use, *n* (%)	28 (71.8%)
Initial mMRC score, mean (SD)†	2.7 (1.1), $n = 36$
Initial CAT, mean (SD)‡	19.3 (7.8), $n = 35$
Active smoking, *n* (%)	5 (12.8%)
Smoking history, pack-year, mean (SD)	33.2 (25.9)
Charlson Comorbidity Index, mean (SD)¶	5.6 (2.7)
Depression, *n* (%)	15 (38.5%)
All-cause healthcare utilization for the year prior to enrolment, mean (SD)	4.7 (4.1)
COPD-related healthcare utilization for the year prior to enrolment, mean (SD)	3.4 (3.2)

SD: standard deviation; FEV1: forced expiratory volume in 1 s; DLCO: diffusing capacity of the lungs for carbon monoxide; mMRC: modified Medical Research Council; CAT: COPD assessment test; COPD: chronic obstructive pulmonary disease.
†The Modified Medical Research Council (MMRC) dyspnoea score is a single-item scale that is completed by the patient; the score ranges from 0 to 4, with higher score indicating greater breathlessness.
‡The COPD assessment test is an eight-item questionnaire that is used to assess the impact of COPD on health status. Each item is scored from 0 to 5. Higher scores indicate more impact of COPD on a patient's life.
¶The Charlson Comorbidity Index predicts the 10-year mortality for a patient who may have a range of comorbid conditions. A total of 22 conditions are included and each one is assigned a score of 1, 2, 3, or 6, depending on the risk of dying associated with it.

Table 2. Post- and pre-EIM all-cause and COPD-related healthcare utilization.

Parameter	Post-monitoring	Pre-monitoring	*p*-value
All-cause healthcare utilization			0.06
Mean (SD)	3.4 (2.6)	4.7 (4.1)	
Median (Q1, Q3)	3 (2, 5)	4 (2, 8)	
Range	0–10	0–15	
COPD-related healthcare utilization			0.01
Mean (SD)	2.2 (2.3)	3.4 (3.2)	
Median (Q1, Q3)	2 (0, 4)	3 (1, 5)	
Range	0–10	0–14	

EIM: electronic inhaler monitoring; SD: standard deviation; Q1 and Q3: first and third quartiles, respectively; COPD: chronic obstructive pulmonary disease.

Adherence

Cohort adherence was 44.4% (28.4%). Adjusted adherence (excluding hospitalizations or ER visits) was 46.2% (29.7%). In linear mixed-effect regression analysis, there was a decline in mean adjusted adherence by 0.46% per week ($p < 0.0001$) (Figure 2). There were a total 287 controller inhaler alerts (mean (SD), 7.4 (9.1)). The individual adjusted adherence of participants is presented in Figure 3.

A univariate linear regression analysis was performed to determine predictors of adherence. The analysis was performed for age, sex, race, post-bronchodilator FEV1 (percentage of predicted), initial COPD assessment test score, Charlson comorbidity index, need for supplemental oxygen, and depression. None of these variables reached statistical significance for determining adherence.

There was no correlation between adjusted adherence and all-cause healthcare utilization ($r = 0.13$, $p = 0.45$) or COPD-related healthcare utilization ($r = –0.004$, $p = 0.99$).

Rescue inhaler use and healthcare utilization

Daily rescue inhaler use was 0.8 (0.7) puffs. There were a total of 138 rescue alerts (mean (SD), 3.5 (7.8)).

Table 3. Pre- and post-EIM all-cause and COPD-related components of healthcare utilization, number of antibiotic and/or steroid courses, and number of pulmonary and primary care clinic visits.

Parameter	Post-monitoring	Pre-monitoring	*p*-value
All-cause hospitalization	2.3 (2.1)	2.9 (2.4)	0.14
All-cause ER visits	1.1 (1.3)	1.8 (2.4)	0.08
COPD-related hospitalization	1.6 (2.0)	2.3 (2.1)	0.04
COPD-related ER visits	0.5 (0.8)	1.1 (1.5)	0.02
Steroid and/or antibiotic courses	1.8 (2.4)	1.9 (1.9)	0.34
Pulmonary clinic visits	3.2 (1.7)	2.8 (2.4)	0.46
Primary care clinic visits	3.4 (3.2)	4.5 (3.8)	0.06

EIM: electronic inhaler monitoring; COPD: chronic obstructive pulmonary disease; ER: emergency room.

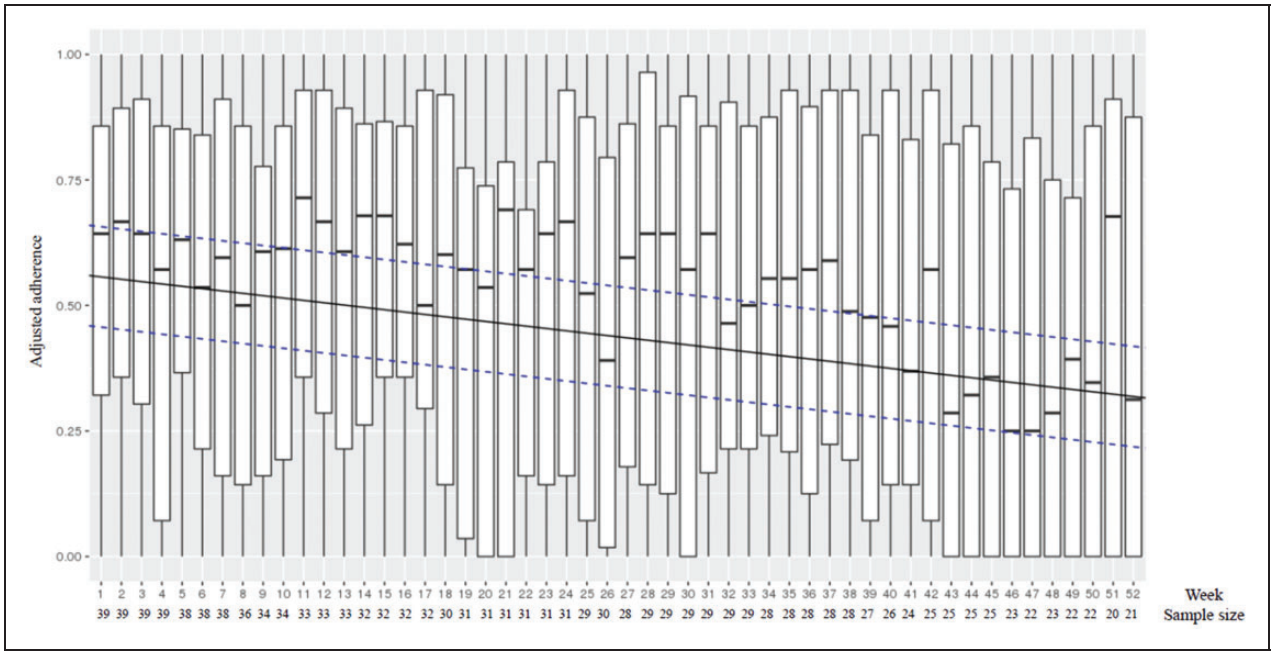

Figure 2. Box-and-whisker plot showing weekly adjusted adherence of the 39 subjects over the study period. Mean adjusted adherence of the entire cohort is represented by the black horizontal line, with the blue dotted lines showing the 95% confidence interval.

Thirty (21.7%) of the rescue alerts predicted a moderate exacerbation within a week. Ten (7.2%) predicted a severe exacerbation within a week. Thirty-eight (27.5%) predicted a moderate-to-severe exacerbation within a week.

Fifty-five moderate and 66 severe exacerbations occurred during active EIM. Fifteen moderate exacerbations were preceded by a rescue alert (five moderate exacerbations preceded by two alerts each, and five exacerbations preceded by three alerts each). Eight severe exacerbations (12.1%) were preceded by a rescue alert (two exacerbations preceded by two alerts each). The sensitivity, specificity, and positive and negative likelihood ratios of the rescue alerts for predicting a moderate-to-severe exacerbation within a week were 27.9%, 99%, 29, and 0.7, respectively (Table 4).

Nineteen patients (48.7%) completed the survey. The results are presented in Table 5.

Discussion

To our knowledge, this is the first report on the impact of an EIM-coupled disease management program on healthcare utilization in COPD patients. The program was feasible and, overall, well received in this cohort, with moderate-to-severe COPD, high healthcare utilization, and multiple comorbidities. We found that EIM was associated with a significant reduction in COPD-related healthcare utilization. All-cause healthcare utilization was reduced without statistical significance, although the trend in our data suggests that a larger sample size may have demonstrated statistical

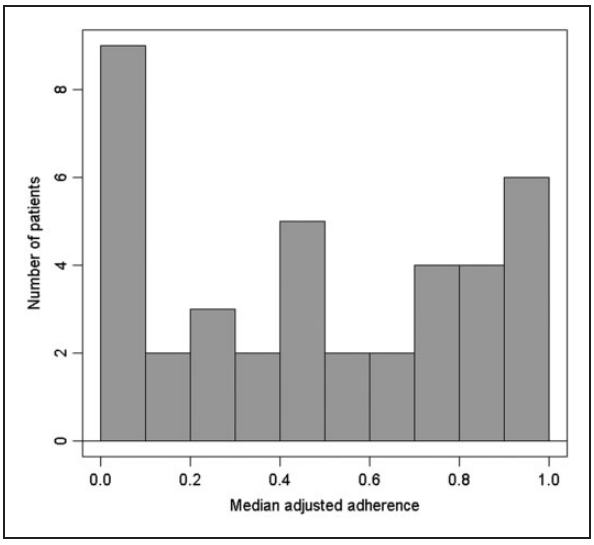

Figure 3. The median adjusted adherence of the individual subjects who were included in the analysis.

significance. There was no increase in the number of clinic visits to suggest a role in reducing healthcare utilization (ER visits and hospitalizations).

EIM provides point-of-care data for clinicians that can assist with the management of COPD patients. EIM is resource consuming, so it is important to determine whether it improves clinical outcomes. The finding of reduced COPD-related healthcare utilization is encouraging in this regard.

The cohort mean adjusted adherence was 46.2%; this is higher than what is reported in the literature.[30] For example, in a large retrospective study of 55,076 COPD patients, adherence averaged 23–43.3%.[22] We speculate that the higher adherence in our study may have been responsible for the reduction in healthcare utilization. Higher adherence could have resulted from study team feedback to patients on their inhaler use as well as the AV reminders that most devices had. AV reminders and provider feedback have been shown to improve adherence to inhaler therapy.[4–6,9–14] AV reminders' role in improving adherence is supported by the significant reduction in all-cause healthcare utilization we observed in the subgroup that had AV reminders. One should be mindful that adherence might improve because of awareness of being studied due to the observer effect (also known as the Hawthorne effect).

The majority of patients had adherence <50% despite EIM and frequent contacts by the study team (Figure 3). Only 10 participants (25%) had a median-adjusted adherence >80%. This is similar to other published reports. In an analysis of pharmacy data, only 18–30% of veterans had an adherence >80%.[24] This is a serious problem, as poor adherence is associated with

Table 4. The 2 × 2 table used to calculate the sensitivity, specificity, and likelihood ratios of the rescue alert for predicting moderate-to-severe exacerbations within a week.

		Moderate-to-severe exacerbation	
		Yes	No
Rescue alerts	Yes	38	100
	No	98	10264*

*"D" value: total number of monitoring days (10940) – days spent in the emergency room/hospital (498) – days of non-alerted moderate exacerbations (40) – alert days (138) = 10264.

morbidity and mortality in COPD patients.[21,31–33] In our end-of-study survey, many patients identified multiple barriers to adherence including forgetfulness (unwitting nonadherence), financial barriers, and others (Table 5). Future programs should also focus on identifying barriers to adherence and solutions to their root causes. The World Health Organization has identified five factors that determine adherence: patient-related factors (e.g. forgetfulness and health literacy), socioeconomic status (e.g. costs), healthcare system (e.g. access to providers), disease-related (e.g. duration and severity), and treatment-related (e.g. frequency and complexity) factors, which all interact and contribute to the complexity of this problem.[34] Addressing these factors holistically is key to improving adherence in any chronic disease. Depression, sense of lack of efficacy or necessity of medications, presence of multiple comorbidities, cognitive impairment, and lack of trust in the healthcare provider have all been reported as determinants of low adherence among COPD patients.[23,30,35] Multidisciplinary team-based interventions that combine feedback (automated and/or provider-initiated) with other approaches (e.g. coaching, motivational interviews, and shared decision-making) are, therefore, more likely to result in better improvement in adherence.[2,30]

Lack of correlation between adjusted adherence and healthcare utilization in our study may be related to small sample size. EIM could have improved the adherence for the entire group and intra-subject difference may have been too small to correlate with healthcare utilization. Furthermore, only a minority of patients had an adjusted adherence >80%, the typical threshold that was used to show this correlation in larger studies.[21,33]

Adherence tends to decline with time.[12,13] Average adherence declined by 13.5% toward the end of our study. Similar findings were reported by Simmons et al. in a randomized control study using EIM-coupled provider feedback to improve adherence. They showed that mean adherence in the intervention group declined by 9.3% over two years.[26] We

Table 5. End-of-study survey.

Question	Choices	Number (%) of participants Total $n = 19$
Reasons for enrolling in the study	To contribute to science	14 (73.6%)
	To help people with similar condition	16 (84.2%)
	To improve medical condition	16 (84.2%)
	To gain insight into medical condition	16 (84.2%)
	To benefit from additional care	15 (78.9%)
Ease of using EIM sensor	Very easy to use	9 (47.3%)
	Easy to use	5 (26.3%)
	Neutral	3 (15.7%)
	Difficult to use	2 (10.5%)
	Very difficult to use	0 (0%)
Adherence to controller inhaler	Significantly improved	3 (15.7%)
	Improved	11 (57.8%)
	No change	5 (26.3%)
	Worse	0 (0%)
	Significantly worse	0 (0%)
COPD control	Significantly improved	4 (21%)
	Improved	10 (52.6%)
	No change	4 (21%)
	Worse	1 (5.2%)
	Significantly worse	0 (0%)
Barriers to adherence	Financial	6 (31.5%)
	Forgetfulness	8 (42.1%)
	Exhausted supply of medicines	9 (47.3%)
	Lack of effectiveness	4 (21%)
Overall satisfaction	Highly satisfied	9 (47.3%)
	Satisfied	7 (36.8%)
	Neutral	3 (15.7%)
	Unsatisfied	0 (0%)
	Highly unsatisfied	0 (0%)

EIM: electronic inhaler monitoring; COPD: chronic obstructive pulmonary disease.

anticipate an initial surge in the adherence and a decline with time as the enthusiasm to use EIM decreases. Therefore, it is important to develop comprehensive long-term strategies to maintain adherence.

Monitoring of rescue inhaler use may have a role in predicting AECOPD.[27] We found that rescue alerts have a low sensitivity and high specificity in detecting exacerbations. There are several explanations for the low sensitivity in detecting exacerbations. First, the association between rescue inhaler use increase and AECOPD is not very strong. For instance, Calverley et al. showed that only 51% of patients with moderate-to-severe exacerbations had an increase by one rescue inhalation for three consecutive days in the week prior.[36] Second, the threshold (increase use by 1.64 SD) to trigger an alert may have been too high. A pilot study involving 35 COPD patients by Sumino et al. showed a 14.1% increase in median albuterol use (interquartile range: 2.7–56%) in moderate-to-severe exacerbation days.[27] Testing different thresholds to maximize the sensitivity of rescue alerts is an area for future study.

One concern medical providers might have is using newer technology with COPD patients, who tend to be older than asthma patients. Our end-of-study survey showed that patients in general felt that devices were easy to use. The study performed by Sumino et al. also supports this finding.[27] In our study, two patients reported difficulty transferring the sensor from one inhaler to another and needed help from our team. It is important for providers utilizing this technology to understand the technical aspects of the device and how to troubleshoot when issues arise.

This is the first study assessing the effect of EIM on healthcare utilization in COPD patients. Both adherence to controller inhalers and use of rescue inhalers were assessed and integrated to a disease management program. The study duration was 12 months, to account for seasonal variation and assess long-term outcomes.

There are several limitations to this study. This was a pre-post study without a control group and the outcomes could be subject to regression to the mean, which is when the mean observed from a non-random sample with an extreme value (high healthcare utilization in our study) is selected for analysis. The extreme variable can spontaneously regress to the mean and this can be falsely interpreted as a result of an intervention.[37] Second, this was a single-centre pilot study, and a larger sample size/multi-centre study is needed to confirm the results. Lastly, the dropout rate was high. Nonetheless, the average time of monitoring was equivalent to nine months and outcomes were ascertained based on healthcare utilization for the entire year.

Conclusion

EIM allows clinicians to assess adherence at the point-of-care and can assist decision-making regarding therapy based on adherence status. For optimal cost-effectiveness, EIM may be more appropriate for patients who have uncontrolled disease and high healthcare utilization. In this pilot study, patients with severe COPD, multiple comorbidities, and history of frequent hospital visits adopted EIM with relative ease. This confirms the feasibility of EIM in this challenging population. Measured adherence to inhalers was higher than what has been reported in the literature and healthcare utilization was reduced. These findings reflect favourably on the utility of EIM in the management of patients with severe COPD and high healthcare utilization, but are subject to further validation in the context of a rigorous experimental design.

Declaration of Conflicting Interests

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