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Effectiveness of a novel, automated telephone intervention on time to hospitalisation in patients with COPD: A randomised controlled trial

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Abstract

Introduction: Owing to its capacity to perform remote assessments, telemedicine is rising as a new force in chronic obstructive pulmonary disease (COPD) management. We conducted an eight month randomised-controlled-trial to study the effect of an automated telemedicine intervention on patients' time-to-hospitalisation.

Methods: A total of 168 patients with a diagnosis of COPD in the past 24 months were enrolled to receive the intervention at a primary care clinic. The treatment group received daily phone messages from an automated system asking them to report if they were breathing better than, worse than, or the same as the day prior. Patients reported their breathing status by responding to the text message or call. If a patient reported breathing worse, an alert was sent directly to that patient's provider within the clinic. The control group received the same daily phone messages as the treatment group. However, no proactive breathing alerts were ever generated to the provider for these subjects. The primary outcome was the subjects' time-to-first-COPD-related hospitalisation following the start of messages.

Results: The treatment group's time-to-hospitalisation was significantly different than the control group's with a hazard ratio of 2.36 (95% confidence interval 1.02–5.45, $p = 0.0443$). The number needed-to-treat ratio was 8.62. Subject engagement consistently ranged between 60% and 75%. The treatment group received both proactive monitoring and follow-up care from the providers.

Discussion: Active monitoring with provider feedback enables the detection of exacerbation events early enough for subjects to avoid admissions. The use of non-smartphone interventions reduces barriers to care presented by more complicated and expensive technologies. This intervention represents a simple, innovative, and inexpensive tool for improved COPD management.

Keywords

Telemedicine, telehealth, home telecare, self care

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Introduction

Chronic obstructive pulmonary disease (COPD) is a common condition worldwide that impacts nearly every aspect of patients' health related quality of life.[1,2] COPD is the third leading cause of death and the fifth leading cause of disability in the United States (US).[3] Patients suffer from frequent shortness of breath, exercise intolerance and respiratory infections.[4] Owing to its capacity to perform remote assessments, telemedicine is rising as a new force in COPD management.

Despite the preventable and treatable nature of COPD, it is an extremely costly disease that places a heavy burden on the US healthcare system. In 2006 alone, there were more than 1.25 million hospital admissions classified as acute exacerbation episodes resulting in a total in-patient cost of US$11.9 billion.[5]

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Around 50–75% of the total cost of COPD care is associated with acute exacerbation events.[4] Exacerbations place unnecessary physical and mental strain on the patient, and they are associated with a higher risk of short-term and long-term mortality.[6]

The hypothesis surrounding the application of telemedicine to COPD is that more frequent monitoring of patients' symptoms will allow for early detection and intervention of exacerbation events before they lead to the utilisation of clinical resources.[7,8] A well-designed COPD intervention could improve patient quality of life, lower hospitalisations, and reduce associated healthcare costs.[9] The intervention should make the patient's respiratory condition more visible to the provider, allow providers to monitor long-term trends, effectively triage patients based on their respiratory condition and, most importantly, detect exacerbation events before they result in hospitalisation.[10]

However, the results of past studies have not demonstrated a definitive clinical or economic benefit to these interventions. Several systematic reviews have concluded that while many past trials have shown positive trends, there is not sufficient evidence at this time to say that COPD telemedicine interventions have a significant effect on the standard of care.[11,12]

The Epharmix COPD system, hereafter referred to as EpxCOPD, is an intervention designed to remotely monitor the self-reported breathing status of patients with COPD through the use of automated phone calls and SMS text messages. EpxCOPD was originally developed by researchers at Washington University in Saint Louis. The product has now been commercialised in the form of Epharmix Inc. (Epharmix Inc. Saint Louis, MO, USA). The system was intentionally structured to meet the needs of patients with low technology literacy. The major goals of the system are to improve patients' quality of life, increase their connection to their care team, and reduce their rate of COPD exacerbations. We set out to demonstrate the effective implementation and clinical benefits of EpxCOPD by running an eight month randomised-controlled-trial (RCT) in a primary care medicine clinic.

Materials and methods

Trial design

Participants were recruited between January and April 2016 at a resident-run primary care medicine clinic at an academic institution in St. Louis, Missouri for an eight month, double-blinded RCT (Figure 1). The trial registration number is NCT03002311 (see https://clinicaltrials.gov/show/NCT03002311). Residents participating in the trial included 1st, 2nd, and 3rd year residents. In the case of one resident being temporarily unable to participate due to other residency commitments, co-residents filled in to cover each other's patients.

A list of 633 potential trial participants was queried from the clinic's EMR based on an ICD-9 or ICD-10 diagnostic code for COPD in the 24 months preceding the trial. Inclusion criteria included those with a diagnosis of COPD made in the preceding 24 months, age greater than 18 years, and a willingness to provide a telephone number at which they can receive text messages or voice phone messages. Exclusion criteria included people with intention to transfer care away from the clinic during the trial period. Mental status was not specifically assessed prior to enrolment. Ability to complete the enrolment process was accepted as appropriate capacity to participate in the trial and understand English voice calls. Subjects elected themselves to choose the text message or voice phone option.

Research staff independent from the trial investigators performed the trial recruitment and informed consent over the phone between January and April 2016. Consenting subjects were randomised by simple randomisation and allocated into two cohorts in a 1:1 ratio using the Excel Random Number generator function. Once subjects were consented and randomised, they were enrolled in the EpxCOPD system. All subjects were given the option of receiving messages via either SMS text message or voice phone and selected the time of day that they preferred to receive messages. Usual care was continued for both groups.

EpxCOPD is part of broader telemedicine platform, Epharmix, that has recently been developed and applied to many different disease states. EpxCOPD differs from many previously attempted interventions since all it requires of patients is the capability to receive phone calls or simple SMS (short message service) text messages. Patients send and receive automated messages from the Epharmix central server in order to communicate disease-specific biometric data (Figure 2). The message algorithms, built in association with physicians, nurses, patients, and medical students from our affiliated programs, use Bayesian branching logic to generate meaningful provider alerts and reports to keep providers up-to-date on their patients' conditions.

Intervention

The treatment group received a daily message from the EpxCOPD system via automated phone call or text message asking them 'Are you breathing better than, worse than, or the same as yesterday'? (Figure 3). After considering his or her current breathing status, the subject then responded to the question by typing a response into their telephone. If a subject responded 'better' or 'the same', then no action was taken by

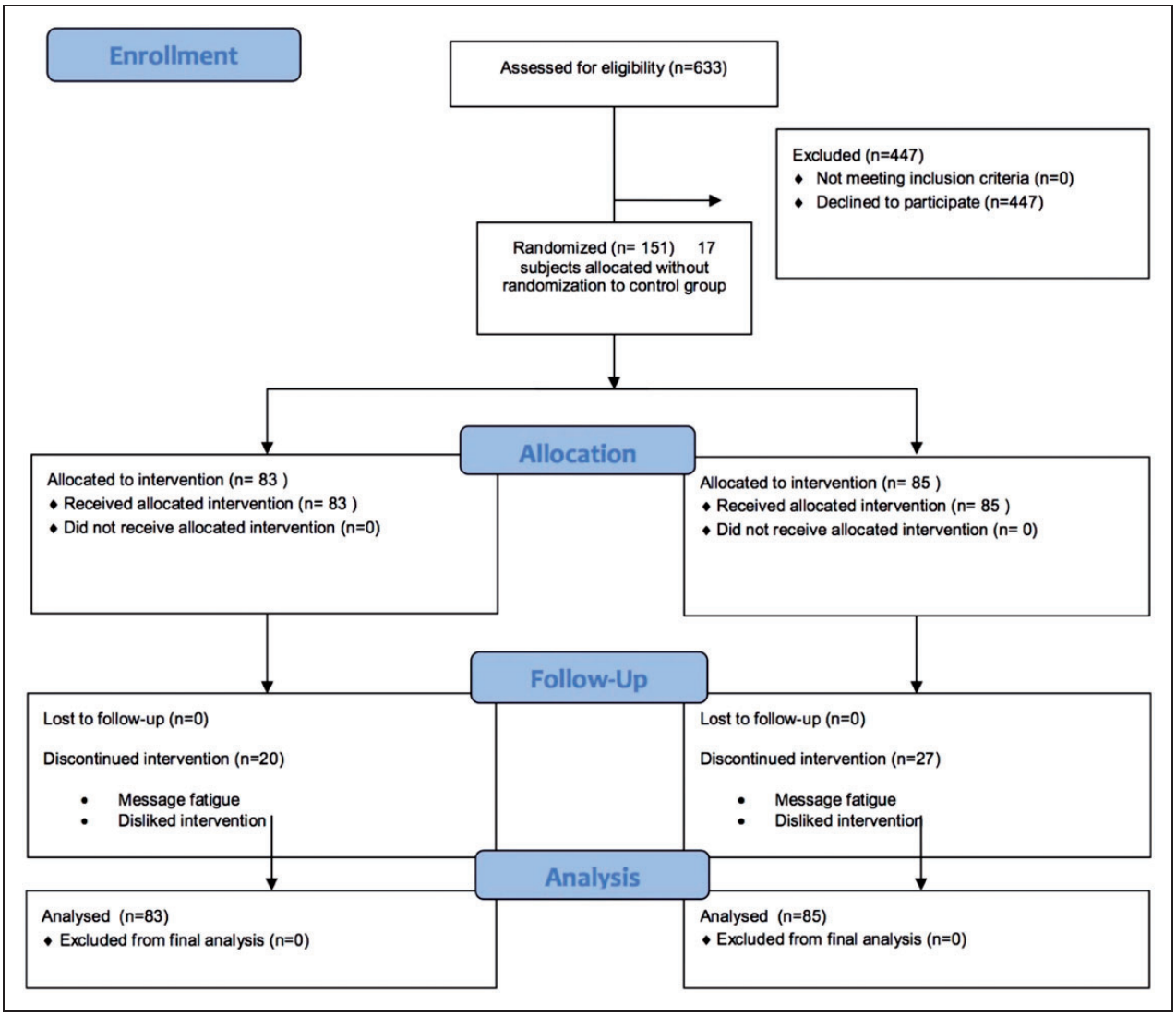

Figure 1. In the EpxCOPD trial, all subjects received the same breathing messages but only the treatment group had reports of worse breathing relayed to providers.

the EpxCOPD system. If a subject responded 'worse', then the EpxCOPD system immediately triggered an alert to the subject's assigned provider in the resident clinic. To minimise any potential liability, all EpxCOPD message sequences ended by instructing the subject that if they were experiencing a medical emergency, to present to the emergency department to seek care.

The medical residents assigned to the subjects received alerts in the form of a text message and in messages placed in their task folders in the clinic EMR. The alert message included a notice that the subject had reported breathing worse and provided a phone number and subject-specific alert code to use to contact the subject for follow-up. When residents dialled this subject-specific alert code, they were routed through the Epharmix server directly to the subject who had set off the alert. The provider then had the opportunity to counsel the subject on how to return to a stable breathing state or to order the appropriate clinical intervention.

The control group received the same daily message from the EpxCOPD system via automated phone call or text message asking them 'Are you breathing better than, worse than, or the same as yesterday'? However, the control group did not have their alerts proactively transmitted to their providers. When a subject in the control group reported breathing worse, no alert was generated to inform their provider to provide follow-up care. However, these subjects still had the capability to call into the system on their own accord and be connected to their provider.

Subjects in both the treatment and control groups began the trial by receiving the EpxCOPD message

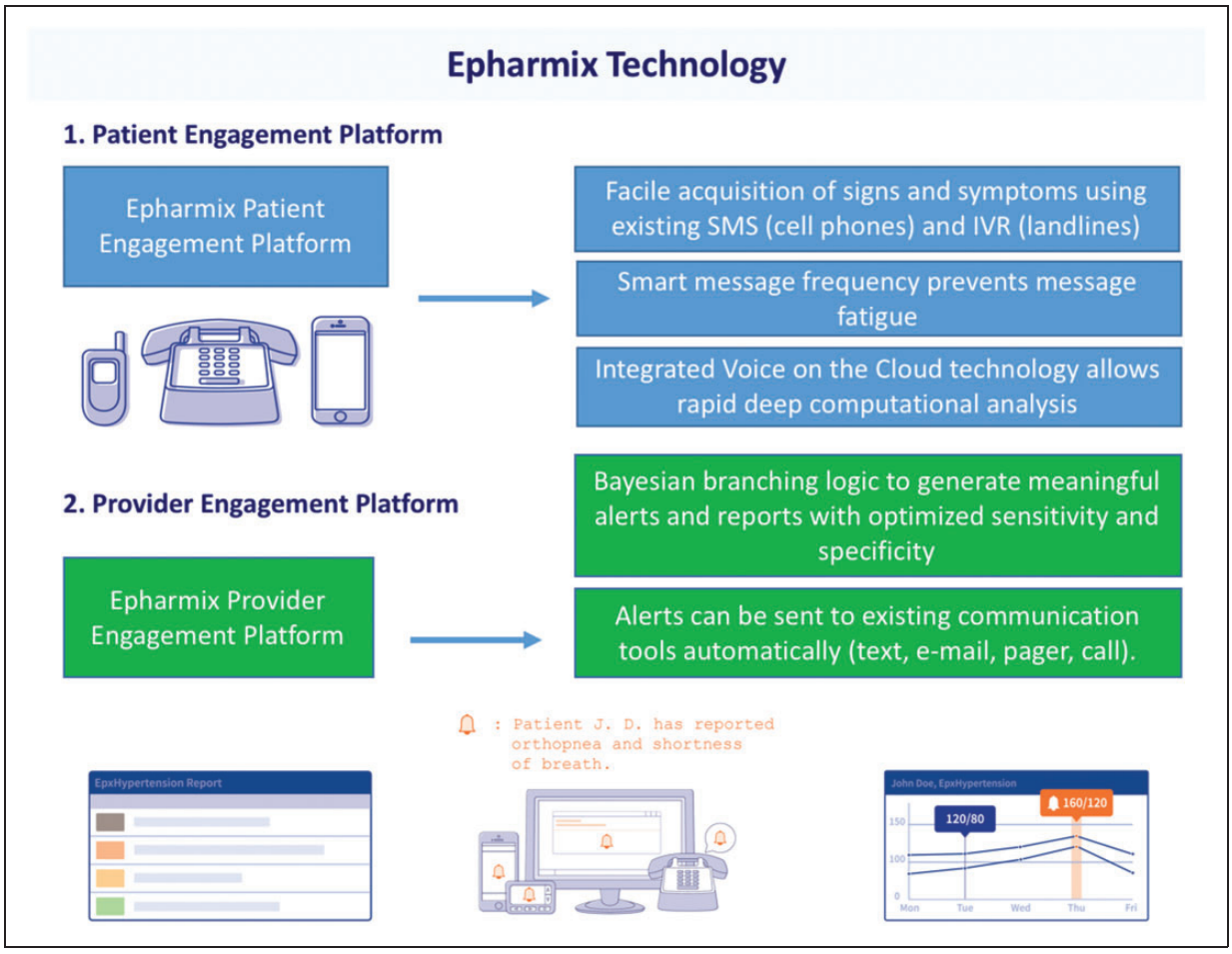

Figure 2. Epharmix is a platform that facilitates bidirectional communication between patients and providers. Messages are sent and stored on a HIPAA-secured web server.
HIPAA: Health Insurance Portability and Accountability Act.

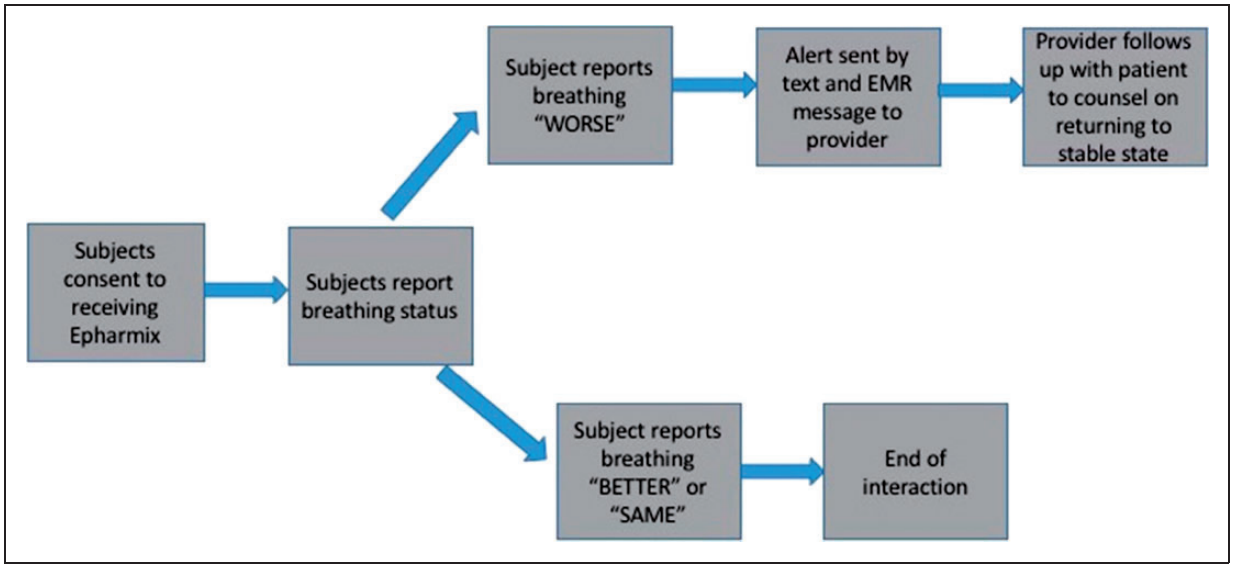

Figure 3. After consenting to receive Epharmix messages, subjects began receiving a daily message inquiring them of their breathing status.

sequence once per day. EpxCOPD included a smart schedule feature that scaled back the number of messages if there was evidence that a subject was doing relatively well. If a subject reported breathing 'better' or 'the same' for 30 consecutive days, they were shifted to a twice-weekly message schedule. If a subject on the twice-weekly schedule ever reported breathing 'worse', the subject would be temporarily placed back onto the daily schedule plan for a period of time until their breathing stabilised.

Data analysis

The primary outcome was subjects' time-to-hospitalisation, defined as the number of days between a subject's enrolment in the EpxCOPD system and their day of admittance to the hospital. For the purposes of this study, we defined the onset of an 'exacerbation' as a subject's day of admittance to the hospital. The secondary outcome was subjects' cumulative weekly engagement with the Epharmix telemedicine system.

Time-to-hospitalisation data was collected by analysis of subjects' medical records in the EMR. Using Kaplan–Meier survival analysis, powered at 80%, with an a priori alpha set at 0.05 and expecting an absolute delta of 10%, from an estimated pre-trial 20% hospitalisation rate, we expected to require 296 patients. The hypothesis was that subjects in the treatment group receiving proactive communication with alerts transmitted to their primary care providers would be detected sooner when an exacerbation occurred.

The subject engagement rate was calculated from data stored on the Epharmix HIPAA-secure web server as the fraction of total subjects responding to at least one message during a 1-week period. Subject demographic information was collected by pre-trial enrolment survey. Pre-trial disease severity was assessed by retrieving subject's most recent pulmonary function test (PFT) from the EMR, if available. Not all of the subjects had a PFT available for inclusion.

Because some subjects revoked their consent to receive Epharmix messages during the trial, it was necessary to consider in some cases if a subject revoked their consent before or after the date of any COPD-related hospitalisation found in the medical record. No efforts were made to prevent subjects from revoking their consent or to recruit subjects back onto the system after they withdrew their consent to receive messages. To test the effectiveness of EpxCOPD in preventing hospitalisations, those subjects who stopped messages in the intervention group were censored from the Kaplan–Meier analysis the day they stopped messages. For the control group, subjects were censored from the analysis on the last day data was collected, whether or not the subjects stopped the placebo messages themselves.

Results

At the end of the enrolment period, 168 subjects were successfully consented and enrolled into the EpxCOPD telemedicine system, of which 83 subjects were randomised into the treatment group. Only the clinic residents served as 'providers' receiving alerts for the purpose of the trial. However, 17 subjects receiving care from the clinic site were included in the trial even though they were not assigned to one of the residents at the time of enrolment. This occurred because these patients had been seen in previous years by resident physicians who had graduated at the time of the start of the study. These patients not been yet assigned to a new resident as a PCP, but still appeared on the initial list of 633 patients queried from the medical record. Because these subjects could not functionally be placed into the intervention group, they were included in the control group without randomisation. Therefore, 68 subjects were randomised into the control group; 17 subjects were placed by default into the control group without randomisation. Demographic information collected during the enrolment suggests that the cohorts were mostly non-white individuals of low socioeconomic status. There were no statistically significant differences in the distribution of age, gender, race, smoking status, smoking history or annual income between the two cohorts (Table 1).

Table 1. Trial demographics.

	Study group		
	Treatment	Control	*P*
Characteristic	$n = 83$	$n = 85$	
Age	59.89 ± 1.09	61.94 ± 1.07	0.18
Gender			
Male	29	32	0.72
Female	54	53	
Race			
White	24	24	0.41
African American	55	55	
Native American	1	0	
Asian	1	0	
Declined to answer	2	6	
Smoking status			
Current smoker	41	32	0.50
Previously but quit	34	43	
Never smoker	3	4	
Declined to answer	5	6	
Smoking history			
Pack Years	33.66 ± 2.29	32.42 ± 2.61	0.72
Annual income	US$11,402 $\pm$ 626	US$12,774 $\pm$ 1,029	0.26

Table 2. Degree of COPD severity between cohorts.

	Study group		
	Treatment	Control	*P*
PFTs available	$n = 63$	$n = 72$	
FEV1 Post/FVC Post	0.64 ± 0.02	0.61 ± 0.02	0.17
FEV1 Post (% of predicted value)	0.65 ± 0.03	0.63 ± 0.02	0.69
Gold criteria			
Mild (FEV1 post > 0.8)	14	16	
Moderate (0.5 > FEV1post > 0.8)	38	35	
Severe (0.3 > FEV1 post > 0.5)	7	16	
Very severe (FEV1post < 0.3)	4	5	

Analysis of the subjects' most recent PFTs revealed that the treatment and control groups were very similar in their pre-trial lung function. No significant difference in the FEV_1/FVC or FEV_1% predicted existed between groups. The subjects were grouped according to their classification in the GOLD criteria (Table 2). Subjects for whom we were unable to locate PFTs were excluded from this analysis. Additionally, we compared the lung function of the 68 randomised and 17 non-randomised members of the control group. The FEV_1% predicted refers to the forced expiratory volume of air that a subject is able to expel in 1 s compared with predicted values for a reference population with similar age and body weight. The FEV_1/FVC ratio compares the forced expiratory volume in 1 s relative to the subject's total forced vital capacity. The FEV_1/FVC is used clinically to measure the severity of lung damage in patients with COPD. Although there was no significant difference in FEV_1% predicted, there was a significant difference in the FEV_1/FVC ratio between the randomised and non-randomised members (Table 3).

Throughout the trial, the cumulative subject engagement rate consistently ranged between 65% and 87% (Figure 4); 13 members of the intervention group and 15 members of the control group revoked their consent to receive message prior to the stop date of the trial. The reasons cited for revoking consent included message fatigue, not enough contact with their provider, or loss of interest in participating in the study. There was a significant change in time to hospitalisation between the treatment group and control groups, with a hazard ratio of 2.36 (95% confidence interval 1.02–5.45, $p = 0.0443$ (Figure 5). The number of subjects at risk at the start of each month of the trial is shown in Table 4. There were significantly fewer COPD-related hospitalisations in the treatment group than the control group, with six and 16 respectively. The absolute risk reduction was 11.6% and the relative risk reduction was 61.7%. The number needed to treat (NNT) was 8.62.

Table 3. COPD severity between randomised and non-randomised members of control group.

	Study group		
	Randomised control	Non-randomised control	*P*
PFTs available	$n = 56$	$n = 16$	
FEV1 Post/FVC Post	0.62 ± 0.02	0.54 ± 0.03	0.03
FEV1 Post (% of predicted value)	0.64 ± 0.02	0.60 ± 0.06	0.45
Gold Criteria			
Mild (FEV1 post > 0.8)	13	3	
Moderate (0.5 > FEV1post > 0.8)	27	8	
Severe (0.3 > FEV1 post > 0.5)	13	3	
Very severe (FEV1post < 0.3)	3	2	

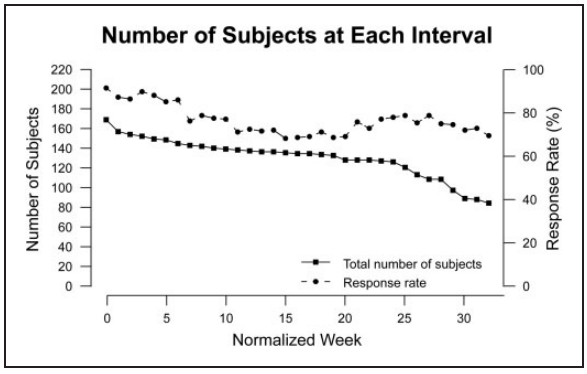

Figure 4. The engagement rate was calculated as the fraction of total subjects responding to at least one Epharmix message during a 1-week period.

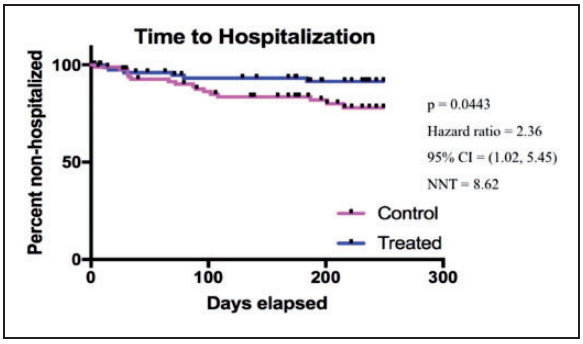

Figure 5. The Kaplan–Meier survival analysis indicates that the primary outcome – time to COPD hospitalisation after the start of EpxCOPD messages – was significant after eight months of messages.

Table 4. Number of subjects at risk.

	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	Month 8
Treatment	83	82	81	80	78	78	78	77
Control	85	83	80	79	74	74	73	71

Discussion

The management of patients with COPD remains an extremely complex, multifactorial process. The ambiguity of the disease's primary symptom, dyspnoea, has made designing a COPD telemedicine intervention a particular challenge. The intervention must be easy-to-use for patients, easy for providers to manage, and provide measurable clinical benefits.

EpxCOPD was designed to address the economic and social barriers that may limit a COPD patient's access to high quality telemedicine monitoring. The system is inexpensive to operate, and all messages are free to patients. The cost of operating the messaging system is approximately US$10 per patient per month. Message sequences were designed to be understood by anyone with at least a fourth-grade reading level. The messages are accessible with any type of phone, mobile or landline, smartphone or burner phone.

The study population consisted primarily of elderly subjects with low annual income. Elderly populations are sometimes considered to have too low technology literacy to use telemedicine tools. However, the rate at which subjects complied with EpxCOPD seems to discredit this theory (Figure 4). Well-designed, simple to use telemedicine interventions can be accessible to patients drawn from any age group or socioeconomic class.

Survival analysis of the treatment and control groups indicated a statistically significant difference in subjects' time-to-hospitalisation. We are highly encouraged by this result as confirmation that this intervention is having a meaningful effect not only on patient engagement, but also on clinical outcomes. The number of patients needed to treat to prevent one COPD hospitalisation was 8.62; this is an extremely economically efficient alternative to both alternative COPD telemedicine interventions and certainly less expensive that the cost of a COPD hospitalisation. This study is one of the first, if not the first, RCTs of a COPD telemedicine system to demonstrate a statistically significant clinical outcome among a large patient population with many participating providers. No other trial has used simple text messages or phone calls to reach a more underserved population with many different participating providers.

There are several limitations to this study which we wish to address. First, the analysis of the primary outcome was limited to specifically examining COPD-related hospitalisations as opposed to all-cause hospitalisations. We wished to limit the scope of the analysis in order to expressly show the effect of EpxCOPD on hospital admissions related to changes in respiratory status. In addition, the data collection for the primary outcome was performed only within the host clinic's EMR. The hospitalisations recorded in the clinic EMR are limited to admissions that occurred within the affiliated hospital system. It is possible that some hospitalisations occurred outside the scope of record of the EMR and thus were omitted from the analysis of the primary outcome.

Analysis of the subjects' pulmonary function tests revealed that the 17 non-randomised members of the control group may have had slightly worse lung function at the start of the trial than the randomised members of the control group. However, during the trial period, the fraction of subjects in the group of 17 subjects not assigned to a resident who experienced a COPD hospitalisation during the trial (17.6%) was less than the fraction of patients hospitalised in the rest of the control group (19.1%). Therefore, we do not believe the 17 patients affected the analysis of the primary outcome.

There was some variability in the rate at which the residents responded to subjects' alerts. Some providers were very good at responding to alerts in a timely manner; other providers took longer to respond or failed to respond at all. If some alerts went without follow-up, subjects in the intervention group who may have benefited from receiving attention from their provider did not receive it. Despite this variability, enough residents complied with the intervention to demonstrate a significant change in the primary outcome.

We intend to expand the EpxCOPD algorithm to include additional questions beyond the current question, 'Are you breathing better than, worse than, or the same as yesterday'? When EpxCOPD was created, it was intentionally limited to just one question in order to keep the algorithm as simple as possible. Adding additional questions to the algorithm will hopefully increase the specificity of alerts, so providers only receive alerts that critically require follow-up.

Conclusion

This eight month RCT demonstrated the successful implementation of the EpxCOPD telemedicine system among a large cohort of subjects and a large number of providers. EpxCOPD facilitated a statistically significant change in subjects' time to hospitalisation, and subjects remained highly compliant with messages throughout the trial. EpxCOPD is a cost-effective, easy-to-use clinical tool for improved COPD management accessible by nearly all potential patients, including those in underserved urban communities.

Supporting Information

S1 Checklist. CONSORT Checklist.
S2 Protocol. Trial Protocol as Approved by Ethics Committee.

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Declaration of Conflicting Interests

The author(s) declare the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: JG and AS have a financial interest in Epharmix, Inc. These authors assisted in the design of the intervention and trial but did not contribute to the data analysis or writing of the manuscript.

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