Received: 23 June 2017 | Accepted: 30 January 2018
DOI: 10.1002/ppul.23978

ORIGINAL ARTICLE: CYSTIC FIBROSIS

WILEY PEDIATRIC PULMONOLOGY

Outcome evaluation of a pharmacy-based therapy management program for patients with cystic fibrosis

Heather S. Kirkham PhD[1] | Francis Staskon PhD[1] | Nishita Hira PharmD[2] | Darren McLane PharmD[2] | Karl M. Kilgore PhD[3] | Alexis Parente PhD[3] | Seung Kim PhD[3] | Gregory S. Sawicki MD, MPH[4]

[1] Walgreen Co., Deerfield, Illinois

[2] AllianceRx Walgreens Prime, Pittsburgh, Pennsylvania

[3] Avalere Health-an Inovalon Company, Bowie, Maryland

[4] Boston Children's Hospital, Boston, Massachusetts

Correspondence
Heather S. Kirkham, PhD, Walgreen Co., 102 Wilmot Road, MS 125D, Deerfield 60015, IL.
Email: heather.kirkham@walgreens.com

Funding information
Walgreen Co.

Abstract

Objective: To compare medication adherence, pulmonary exacerbations, healthcare utilization, and costs for patients with cystic fibrosis (CF) who utilized a pharmacy-based therapy management program to a matched control group. We hypothesized that patient management services would be associated with better medication adherence, and thus require fewer visits to the emergency room or hospitalizations.

Methods: This retrospective, observational cohort study used claims data from the MORE^2 claims Registry®. The sample consisted of CF patients, aged 6+, who had ≥1 pharmacy claim for inhaled tobramycin, inhaled aztreonam, ivacaftor, or dornase alfa from 6/2/2014-5/31/2015. Adherence was measured as proportion of days covered (PDC). Propensity score matching and multivariable regression techniques were used to compare outcomes in program participants to matched controls.

Results: Of the 236 intervention and 724 control patients meeting selection criteria, 202 were propensity-matched from each cohort. Relative to the control cohort, program patients had 23% higher mean PDC for tobramycin (*IRR* = 1.23, *P* = 0.01) and were twice as likely to be adherent to tobramycin (PDC ≥ 80%) than matched controls (*OR* = 2.14, *P* = 0.04). Program patients had fewer ER visits (*IRR* = 0.52, *P* < 0.01) and slightly lower ER costs (*IRR* = 0.66, *P* = 0.06) than the control patients.

Conclusion: A pharmacy-based therapy management program for CF patients was associated with higher adherence to inhaled tobramycin and lower ER rates. Pharmacies that provide therapy management can support effective CF care management.

KEYWORDS
costs and cost analysis, cystic fibrosis, medication adherence, pharmacy, program evaluation

1 | INTRODUCTION

Medication nonadherence among patients with cystic fibrosis has been found to be a predictor of both lung function decline and pulmonary exacerbations requiring IV antibiotics.[1,2] A 2014 study noted that patients with low or moderate adherence to pulmonary medications were more likely to have CF-related or all-cause hospitalizations compared to patients with high adherence.[3] Not

surprisingly, poor adherence also was associated with higher healthcare costs, ranging from $8000 to $14 000 more annually, compared to patients with high adherence.[3] However, at least one study found that adherence was associated with length of hospital stay but not exacerbations or costs.[4]

Given the high treatment burden for cystic fibrosis, it is not surprising that medication adherence among patients with CF is generally low.[2,4–10] A recent study reported an average claims-based composite medication possession ratio (CMPR) to several long-term pulmonary medications to be 48%, and only 20% of CF patients had a CMPR of at least 80%.[3] Published adherence rates vary greatly by measurement methodology, drug class, and patient characteristics.[11] Self-reported rates were generally higher compared to claims-based or electronic monitoring rates.[12]

Although barriers to adherence change over a patient's lifetime,[5,11] lack of time is often a primary reason cited for non-adherence.[6,11,13] Medication adherence was found to be higher for medications that are perceived to have more immediate health benefits (eg, digestive and respiratory drugs) than for more distal benefits (eg, physiotherapy and nutritional supplements).[5,14] Other factors associated with non-adherence were age and seasonality.[4,10,11] Although some studies did not find financial barriers to adherence,[15] new, more expensive treatment options, such as ivacaftor, may increase issues of financial barriers.[16,17] In a study assessing pediatric patients' utilization of their high-frequency chest wall oscillation device, adherence was significantly impacted by patients' socioeconomic status.[18]

In 2017, Zobell et al[2] published the first study to demonstrate a positive impact of pharmacy services on medication adherence for CF patients. This study found significantly higher adherence to dornase alfa after initiation of an integrated pharmacy team model and dedicated CF clinic pharmacist compared to before the interventions. This study was limited to a small sample of pediatric patients in a single health system in one state and calculated adherence for one only medication. Certainly, more research is needed to understand the types of interventions that can decrease treatment barriers and improve adherence.[3] In fact, concerns about non-adherence led the Cystic Fibrosis Foundation to initiate the *I Change Adherence and Raise Expectations* (iCare) study to investigate the efficacy of such interventions.[19]

In May of 2014, a large pharmacy chain in the United States, Walgreens, launched the Connected Care® Cystic Fibrosis (CC-CF) clinical program to assist in the holistic management of four key aspects of CF clinical care: (a) patient medication management; (b) access to CF medications and products; (c) patient and caregiver education; and (d) barriers to access. The CC-CF program provides comprehensive clinical management of the CF patient by pharmacists, patient care coordinators, and others within the pharmacy call centers trained in program services. Staff receive comprehensive training on cystic fibrosis—the disease state, including medications, other therapies, as well as the CC-CF program. Additionally, clinical and CC-CF program updates are communicated out to staff on a continual basis. Scripting within the CC-CF program guides the conversation between patient care coordinators, pharmacists, and patients.

When a CC-CF patient starts a new CF program medication (see Appendix A), the specialty pharmacy pharmacist provides medication-specific education, including administration (and nebulizer use), storage/stability, and common and serious side effects. The patient/caregiver also receives adherence and infection control education. This counseling is provided anytime the patient switches or starts additional CF medications as well. Thereafter, monthly touchpoints consist of refill reminder calls which also screen the patient for medication related side effects, missed doses and barriers to adherence, including financial. Patients who report side effects or adherence of less than 80% are then escalated to a pharmacist for counseling and management. The patient's physician is notified via fax of patient-reported side effects and adherence of less than 80% if he/she was previously unaware. This individualized patient counseling and education is provided at the time of patient interaction or can be scheduled at a later date based on patient need. As the needs of the patient may change, the CC-CF program is intended to support the patient/caregiver at the onset as well as throughout the duration of therapy. Hence, the primary goal of the program is to help patients get and stay adherent to the CF specialty medications. Most patients refill at least one of their medications monthly, and receive medication management services through the CC-CF program with every fill, providing support between quarterly visits at their CF care center.

The objective of this study was to assess associations between the provision of program services, medication adherence, pulmonary exacerbations, healthcare utilization, and costs. We hypothesized that patient management services would be associated with better medication adherence, and thus require fewer visits to the emergency room or hospitalizations. Although increased medication adherence to CF therapies will likely result in higher pharmacy costs, we also posited that lower utilization of expensive ER and admissions could translate into lower annual medical healthcare costs. Compared to Zobell et al our study can fill a gap in the literature by assessing three additional CF medications (vs just dornase alfa) and healthcare costs (vs only utilization) in a national sample (vs one state) of adults as well as children (vs only pediatric patients) insured by a variety of payers (vs a single payer).

2 | MATERIALS AND METHODS

This study used a retrospective cohort design based on administrative pharmacy and medical claims data. The intervention cohort included CF patients who participated in the CC-CF clinical program and met all other study criteria. The control cohort included CF patients who had no indication of being a patient of the studied pharmacy (based on the pharmacy claims). This design allows us to estimate the differences in medication adherence, pulmonary exacerbations, healthcare utilization, and costs between the two cohorts.

The specialty pharmacy contracted with a technology company to obtain medical claims data for CC-CF program patients and to identify a comparison cohort. Inovalon's Medical Outcomes Research for Effectiveness and Economics Registry (MORE^2 Registry®) is a data

warehouse that contains information derived from more than nine billion medical events generated by more than 140 million unique members nationwide. In addition to claims data, the registry includes information about demographics, enrollment, diagnoses, procedures, pharmacy, and laboratory results. The registry also comprises a significant mix of commercial insurance (private insurance usually provided by employers), Affordable Care Act Marketplace (private insurance often facilitated by government funds), Medicare Advantage (insurance for seniors managed by private insurers with public funds), and managed Medicaid (insurance predominantly for lower income individuals managed by private insurers with public funds) memberships. The specialty pharmacy program patients were matched to patients in the registry using a direct matching protocol. Matched patients who were in the CC-CF clinical program were flagged as potential members of the intervention cohort. Patients in the registry who were identified as neither CC-CF clinical program nor receiving other services from the study pharmacy were flagged as potential members of the control cohort, as described more fully in the next section.

To be eligible for the study, a patient had to satisfy all of the following inclusion criteria:

1. ≥1 pharmacy claim with an NDC for tobramycin, aztreonam, ivacaftor, or dornase alfa (ie, the targeted drugs; see E-table 1, supporting information) from June 2, 2014 to May 31, 2015 (ie, the "observation period"). The index date for a patient was identified as the date of the first prescription fill for any of the targeted drugs during the observation period. These drugs were selected because they qualified a patient to be eligible for the therapy management program during the observation period, so we applied this criteria to both groups to decrease bias. Patients could have been on other CF medications.
2. Aged 6+ (Age was calculated at index date).
3. ≥2 medical claims with a diagnoses for CF (ICD-9 CM Code: 277.0X) occurring ≥30 days apart between December 1, 2013 and March 31, 2016 (ie, the "study period").
4. Continuously enrolled in the same health plan with both medical and pharmacy benefits 12 months prior to (ie, "baseline period") and 12 months after (ie, "evaluation period") the index date.

Patients were excluded from the study if they received services anytime during the study period from the specialty pharmacy, but had never enrolled in the CC-CF clinical program.

The dependent variables were categorized into four types: (a) medication adherence; (b) healthcare utilization; (c) pulmonary exacerbations; and (d) healthcare costs:

a. Medication adherence rates were calculated as proportion of days covered (PDC) for four CF medications that would qualify a patient for the therapy management program during the study period (ie, tobramycin, aztreonam, ivacaftor, and dornase alfa). For cycled medication, calculations were adjusted as described in Quittner et al.[3] PDC was also converted to a dichotomous variable: low (<0.80) or high (≥0.80), as 80% is a common cut-point in the medication adherence literature and to better compare to Quittner et al.[3]
b. Healthcare utilization for hospitalizations, ER visits, and outpatient visits was calculated as rates (per 1000 members). Similar to percentages, utilization rates per 1000 are commonly used in healthcare literature to compare infrequent events between groups of different sizes. Average length of hospitalization was calculated as the average bed days per member per year.
c. Pulmonary exacerbations were measured using a proxy of hospitalizations with IV antibiotics (excluding azithromycin).
d. Healthcare costs were reported as *allowed amounts* (ie, the amount paid by the health plan plus the amount contributed by the patient). Allowed amounts were imputed based on the Centers for Medicare and Medicaid Services fee schedules to control for cost variation by region and payer (see E-text 1-A, supporting information for further description). Medical costs included inpatient, outpatient, ER, and other professional services (eg, ambulance, durable medical equipment, ambulatory surgery centers). Total costs summed pharmacy and medical costs. ER costs were a subset of medical costs.

All outcomes were based on a 12-month evaluation window; however, the evaluation window varied for each patient, based on their index date.

The primary independent (explanatory) variable was whether or not a person participated in the CC-CF program. Because the design of this study was quasi-experimental (ie, no random assignment to groups), these two groups could differ on various factors that may impact their outcomes and mask true differences in treatment effectiveness. To control for these potential confounding factors, patients in the two groups were statistically matched using propensity score matching on demographic, prior clinical history, and treatment factors hypothesized to be correlated with our outcomes. Any predictor variables which did *not* demonstrate appropriate balance between the two groups were subsequently included as covariates in post-propensity regression models. Technical details of the match process are provided in E-text 1-B, supporting information.

Multivariable regression analyses were used to (a) identify significant differences between the intervention and control groups on cost, utilization, and medication adherence and (b) estimate adjusted means (ie, means that are adjusted by the regression model for covariates). Post hoc analyses were conducted to assure that high cost outliers were not disproportionally influencing results and to understand whether differences in pharmacy costs were influenced by difference in adherence or drug costs. Full details of these statistical analyses are presented in E-text 1-C, supporting information. All analyses and the generation of output were performed using SAS software, version 9.4 (SAS Institute Inc., Cary, NC).

3 | RESULTS

Of the 236 intervention and 724 control patients meeting selection criteria, 202 were propensity score matched from each cohort.

Figure 1 provides the counts of patients in each cohort that results from the application of each inclusion and exclusion criterion sequentially.

Overall, program participants and the comparison group were similar in most characteristics. Table 1 displays the descriptive characteristics of the program participants and the comparison group after propensity score matching. After propensity score matching, only one variable—the indication of anxiety/depression—had a large standardized difference (0.13), indicating program participants experienced a higher prevalence of depression/anxiety compared to the comparison group. In order to control for this difference in prevalence of depression/anxiety, all post-propensity outcome models included this variable as a covariate in addition to the main explanatory cohort variable.

Table 2 reports the PDC means and percent adherence (ie, a PDC of 80% or higher) by CF medication. All means are regression adjusted, as described in the methods section. Mean adjusted adherence to tobramycin was 23% higher among program patients relative to the control group (65% vs 52%, Incidence Rate Ratio, *IRR* = 1.23; 95%CI [1.05, 1.43], *P* = 0.01). In addition, program patients were twice as likely have a PDC of 80% or higher for tobramycin than matched controls (Odds Ratio, *OR* = 2.14 [1.02, 4.49]; *P* = 0.04). The means and adherence levels for the other three medications did not differ significantly in the models, but trended at a higher level in the program group compared to the control group for both ivacaftor and dornase alfa.

Among the four utilization outcomes (see Table 3), the difference in the ER visits rate between two groups was statistically significant (*IRR* = 0.52 [0.34, 0.78], *P* < 0.01). In fact, program patients had around half the rate of ER visit rate than the control group: 755 per 1000 ([557-1024]) versus 1462 per 1000 ([1103-1939]) or a difference of

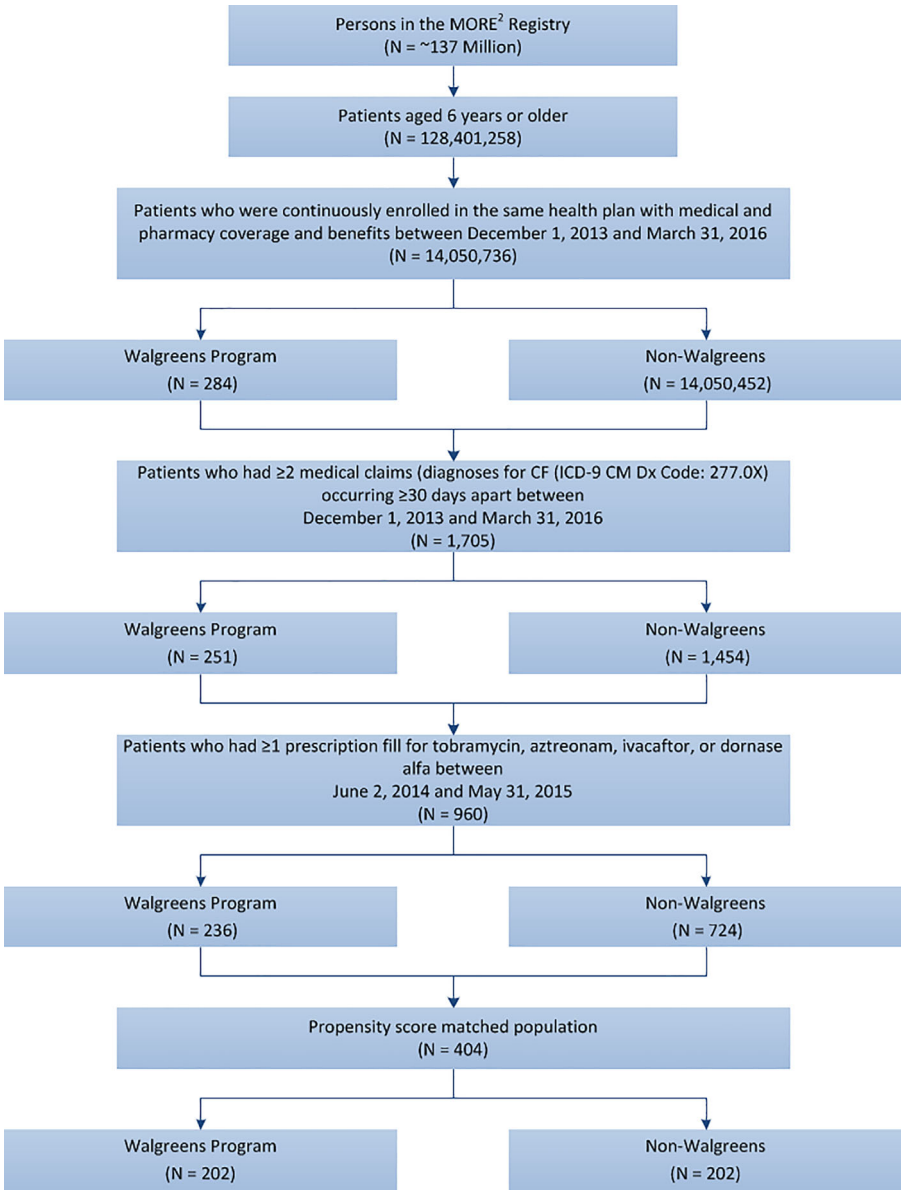

FIGURE 1 Patient selection process

TABLE 1 Descriptive characteristics for the CF-CC program participants and non-CF-CC comparison group (*N* = 202 per group)

Variables	Program	Control	Standardized differences
Age *N* (%)			
6-10	38 (18.8)	38 (18.8)	
11-17	61 (30.2)	64 (31.7)	
18-25	47 (23.3)	44 (21.8)	
26-35	34 (16.8)	31 (15.4)	
36-45	12 (6.0)	15 (7.4)	
46+	10 (4.9)	10 (4.9)	
Age, mean[a]	20.51 (11.7)	20.36 (11.9)	0.01
Gender *N* (%)			
Female	103 (51.0)	98 (48.5)	0.05
Payer *N* (%)			
Commercial	65 (32.2)	59 (29.2)	−0.06
Managed medicaid	130 (64.3)	136 (67.3)	−0.06
Medicare advantage	7 (3.5)	7 (3.5)	0.00
Region *N* (%)			
Midwest	35 (17.3)	36 (17.8)	0.01
Northeast	103 (51.0)	99 (49.0)	0.04
South	45 (22.3)	47 (23.3)	−0.02
West	19 (9.4)	20 (9.9)	−0.02
Quarter *N* (%)			
Jun 2014-Aug 2014	175 (86.6)	177 (87.6)	
Sep 2014-Nov 2014	17 (8.4)	17 (8.4)	
Dec 2014-Feb 2015	7 (3.5)	7 (3.5)	
Mar 2015-May 2015	3 (1.5)	1 (0.5)	
Quarter, mean[a]	1.20 (0.6)	1.17 (0.5)	0.06
Baseline 6-month pre-utilization and comorbidities			
Hospitalization	53 (26.2)	48 (23.8)	0.06
Diabetes	30 (14.9)	31 (15.4)	−0.01
Depression/anxiety	20 (9.9)	13 (6.4)	0.13
Charlson comorbidity index[a]	0.6 (0.7)	0.6 (0.9)	0.04
Drug utilization (6-month post)			
Ivacaftor	17 (8.4)	15 (7.4)	0.04
Inhaled aztreonam	79 (39.1)	80 (39.6)	−0.01

[a]Mean (standard deviation)

707 visits per 1000 members. The other three utilization measures of hospitalizations, average length of hospitalization (bed days), and outpatient visits were similar between groups.

Pulmonary exacerbations as measured by the proxy of the proportion of patients with hospitalizations with IV antibiotics was lower among the intervention group than controls, though not statistically significant (17% vs 21%, $P = 0.19$; see Table 3).

Adjusted mean costs did not differ significantly for overall medical, pharmacy, or total costs between the program participants. Annual adjusted ER costs trended 34% lower for program patients compared to controls, trending toward a significant difference (*IRR* = 0.66 [0.43, 1.02], $P = 0.06$). Interestingly, the program participants spent on average $1670 less on medical costs while spending $3098 more on pharmacy cost compared to matched controls, and although these differences were not statistically significant, they led us to explore the post-hoc analysis described below.

To investigate the impact of medication adherence on pharmacy costs, pharmacy costs were modeled with (a) the primary independent variable; (b) an additional variable to indicate when the patient had PDC ≥ 0.80 for any of the four targeted drugs (ie, adherent patient indicator); and (c) an interaction variable. As expected, higher medication adherence was significantly associated with higher drug

TABLE 2 Adjusted PDC means and adherence rates (12-month, *N* = 202 per group)

	Program		Control		*p*-value	
Drug	***n* Mean (SD)**	**≥80% (SD)**	***n* Mean (SD)**	**≥80% (SD)**	**Mean**	**≥80%**
Tobramycin	83 63% (26%)	33% (47%)	76 52% (25%)	18% (39%)	0.01	0.04
Aztreonam	87 59% (23%)	25% (44%)	69 63% (26%)	36% (48%)	>0.3	>0.14
Ivacaftor	17 68% (28%)	41% (51%)	16 56% (28%)	19% (40%)	>0.3	>0.2
Dornase alfa	167 58% (28%)	28% (45%)	151 57% (26%)	27% (45%)	>0.8	>0.9

costs ($P < 0.0001$). The adjusted mean pharmacy costs of this model were $51 336 for program participants versus $50 364 in the control group, or a difference of about $1000, compared to a larger difference of about $3100 for the model without the adherent patient indicator. Hence, the majority of the pharmacy cost difference can be attributed to the difference in medication adherence.

4 | DISCUSSION

This study implemented the same selection and exclusion criteria for CF patient identification as Quittner et al[3] and had similar outcome measures, but utilized a different claims source, applied a different research design, and included ivacaftor therapy. Given the genetic influence to this rare disease condition, one would expect some similar results with respect to Quittner et al,[3] but differences were also present.

Higher adherence levels were obtained in this study than the medications common to Quittner et al.[3] Mean PDC levels for tobramycin and dornase alfa in our study cohort (63%) were more similar to values reported for the 13-21 years old cohort in Shakkottai et al[11] (66.7%, tobramycin; 64.7%, dornase alfa). Both variation of adherence by age and variation of age distribution by study may be contributing toward variation of adherence rate by study.[3,11] In this research, the highest adherence level was for the new medication ivacaftor ($n = 17$), and the 12% difference to the control cohort ($n = 15$) was not significant likely due to the small matched count. High adherence to ivacaftor and low adherence to other CF treatments is consistent with findings from the recent literature review by Narayanan et al.[10]

Hospitalizations and outpatient visit rates were rather similar across cohorts in this study, but were about half the rates noted in Quittner el al.[3] Recently, an analysis of the Cystic Fibrosis Foundation Patient Registry found significant regional variability in hospitalization length and subsequent hospitalization risks in the United States.[20] However, Kopp et al[20] did not look at geographic variations for emergency department events. Hence, the difference across studies may be due, in part, to unknown regional differences in patient selection. Similar to our results, Zobell et al[2] noted trends toward reduced hospitalizations after the pharmacy team intervention (though not significant given the sample size). Emergency room claims indicated a much lower rate among our program patients, as well as reduced level of ER costs, compared to the control group. However, the rates discovered in this study were much higher than those previously reported in Quittner et al[3] This difference could be because Quittner only included commercially insured patients,[3] while both our program and control groups had a high proportion of managed Medicaid patients, who tend to have high ER utilization.[21]

TABLE 3 Adjusted means in healthcare utilization, pulmonary exacerbations, and cost by cohort (12-month, *N* = 202 per group)

Outcomes	**Program**		**Control**		
Utilization	**Mean**	**CL**	**Mean**	**CL**	***P*-value**
Hospitalization (events per 1000 members)	530	415-677	676	538-848	0.15
ER visits (events per 1000 members)	755	557-1024	1462	1103-1939	0.00
Outpatient visits (events per 1000 members)	11 186	9988-12 528	12 419	11 097-13 898	0.20
Average length of stay (per member)	2.28	2.01-4.03	2.43	2.18-4.35	0.76
Pulmonary exacerbations					
Hospitalization with IV antibiotics (%)	17.3%	37.9%[a]	21.3%	41.0%[a]	0.19
Costs					
Medical cost ($)	$8513	$6991-$10 366	$10 183	$8362-$12 399	0.21
ER costs ($)	$346	$255-$471	$522	$384-$710	0.06
Pharmacy cost ($)	$58 154	$51 260-$65 976	$55 056	$48 468-$62 541	0.55
Total cost ($)	$67 138	$59 375-$75 917	$64 951	$57 441-$73 443	0.71

[a]The pulmonary exacerbation outcome (binary variable) is presented with standard deviation, while the other outcomes (continuous variables) are presented with 95% confidence limits.

Pulmonary exacerbations are rather common in CF and treated with IV antibiotics.[22–24] In this study, the intervention cohort had a relatively low proportion of patients with such exacerbations compared to the control cohort. The recent VanDevanter et al[22] study on a sample of registry patients determined this event was most associated with a similar event in the prior year compared to 65 other covariates, suggesting a phenotypic expression for some patients. Hence, unmatched patient mix influences across cohorts may have produced the noted trend.

Finally, while our patient characteristics were similar in age, gender, and CCI level to Quittner et al,[3] our annual healthcare costs were lower ($8.5-$10.4 K vs $34.4-$54.1 K). This differential is likely due to various factors, including insurance mix and our cost imputation method being based on Medicare payment schedules (which would be lower than typical private payer costs found in Quittner et al, but was used to reduce bias for between-group comparisons in our study).[25]

Limitations in this study include its observational design, a relatively small matched sample size, reliance on administrative claims, and a high variance for economic outcomes. Given the reliance on medical and pharmacy claims, we could not account for various clinical factors, such as genotype or disease severity. However, patients were matched on several characteristics to account for differences in severity of illness (eg, previous history of diabetes and depression/anxiety, Charlson comorbidity index, baseline evidence of hospitalization) and the propensity score matched results indicated comparable propensity score distributions across cohorts. Hence, several potential threats to validity were addressed in using this type of propensity score matching to compare cohorts. The rate of hospitalization, while not statistically significant, was higher in the control group, so adherence for hospitalized patients may be underreported due to medications given as an inpatient. However, both average length of stay and the proportion of patients with a hospitalization with IV antibiotics were similar between groups (both $P > 0.10$). Given the observation period of our study, we were able to assess adherence to ivacaftor but not the lumacaftor/ivacaftor combination therapy.[10]

A pharmacy-based therapy management program for CF patients was associated with higher adherence to inhaled tobramycin and lower ER rates. Relative to the control cohort, program patients had 21% higher mean PDC for tobramycin and were twice as likely to be adherent to tobramycin (PDC ≥ 80). In addition, program patients had fewer ER visits and lower ER insurance costs than matched control patients, and annual ER insurance costs were 34% lower for the CC-CF patients compared to controls. Future studies should examine what components of such programs are most effective to improve adherence and related outcomes.

4.1 | Practical implications

Patient-focused, pharmacy-based clinical management programs may increase adherence to CF medication therapy when implemented as part of a comprehensive pharmacy service for specialty medications. Monthly refill reminders as well as screening for and counseling/management of patient-reported adherence barriers may contribute toward higher medication adherence. This increased patient adherence should result in less utilization of the healthcare system for ER visits or hospitalizations.

5 | INFORMED CONSENT AND PATIENT DETAILS

The authors confirm all patient/personal identifiers have been removed or disguised so the patient/person(s) described are not identifiable and cannot be identified through the details of the story. This research was reviewed and approved by Quorum Review IRB (#30931/1) with a waiver of HIPAA authorization and a waiver of informed consent.

ACKNOWLEDGMENTS

The authors would like to acknowledge Heidi Hilker, Chet Robson, and Harry Leider for their contributions to this research. This study was funded by Walgreen Co. Results from this research were presented as a poster at the 2016 North American Cystic Fibrosis Conference.

CONFLICTS OF INTEREST

All Walgreens authors are full time employees of the study sponsor. All authors have contributed to, read, and approved the final article.

ORCID

Heather S. Kirkham http://orcid.org/0000-0003-1247-1005

REFERENCES

1. Eakin MN, Bilderback A, Boyle MP, Mogayzel PJ, Riekert KA. Longitudinal association between medication adherence and lung health in people with cystic fibrosis. *J Cyst Fibros*. 2011;10:258–264.
2. Zobell JT, Schwab E, Collingridge DS, Ball C, Nohavec R, Asfour F. Impact of pharmacy services on cystic fibrosis medication adherence. *Pediatr Pulmonol*. 2017;52:1006–1012.
3. Quittner AL, Zhang J, Marynchenko M, et al. Pulmonary medication adherence and health-care use in cystic fibrosis. *Chest*. 2014;146:142–151.
4. Nasr SZ, Chou W, Villa KF, Chang E, Broder MS. Adherence to dornase alfa treatment among commercially insured patients with cystic fibrosis. *J Med Econ*. 2013;16:801–808.
5. Arias Llorente RP, Bousono Garcia C, Diaz Martin JJ. Treatment compliance in children and adults with cystic fibrosis. *J Cyst Fibros*. 2008 72008:359–367.
6. Geller DE, Madge S. Technological and behavioral strategies to reduce treatment burden and improve adherence to inhaled antibiotics in cystic fibrosis. *Respir Med*. 2011;105:S24–S31.
7. Latchford G, Duff A, Quinn J, Conway S, Conner M. Adherence to nebulised antibiotics in cystic fibrosis. *Patient Educ Couns*. 2009;75:141–144.
8. McNamara PS, McCormack P, McDonald AJ, Heaf L, Southern KW. Open adherence monitoring using routine data download from an adaptive aerosol delivery nebuliser in children with cystic fibrosis. *J Cyst Fibros*. 2009;8:258–263.

9. Moore BM, Laguna TA, Liu M, McNamara JJ. Increased adherence to CFF practice guidelines for pulmonary medications correlates with improved FEV1. *Pediatr Pulmonol*. 2013;48:747–753.
10. Narayanan S, Mainz JG, Gala S, Tabori H, Grossoehme D. Adherence to therapies in cystic fibrosis: a targeted literature review. *Expert Rev Respir Med*. 2017;11:129–145.
11. Shakkottai A, Kidwell KM, Townsend M, Nasr SZ. A five-year retrospective analysis of adherence in cystic fibrosis. *Pediatr Pulmonol*. 2015;50:1224–1229.
12. Daniels T, Goodacre L, Sutton C, Pollard K, Conway S, Peckham D. Accurate assessment of adherence: self-report and clinician report vs electronic monitoring of nebulizers. *Chest*. 2011;140:425–432.
13. Bregnballe V, Schiotz PO, Boisen KA, Pressler T, Thastum M. Barriers to adherence in adolescents and young adults with cystic fibrosis: a questionnaire study in young patients and their parents. *Patient Prefer Adherence*. 2011;5:507–515.
14. Bucks RS, Hawkins K, Skinner TC, Horn S, Seddon P, Horne R. Adherence to treatment in adolescents with cystic fibrosis: the role of illness perceptions and treatment beliefs. *J Pediatr Psychol*. 2009;34:893–902.
15. Dziuban EJ, Saab-Abazeed L, Chaudhry SR, Streetman DS, Nasr SZ. Identifying barriers to treatment adherence and related attitudinal patterns in adolescents with cystic fibrosis. *Pediatr Pulmonol*. 2010;45:450–458.
16. Deeks ED. Ivacaftor: a review of its use in patients with cystic fibrosis. *Drugs* 2013;73:1595–1604.
17. Hadjiliadis D. 2011 – Ivacaftor improved lung function in cystic fibrosis with G551D mutation. *ACP J Club*. 2012;156:9–10.
18. Oates GR, Stepanikova I, Gamble S, Gutierrez HH, Harris WT. Adherence to airway clearance therapy in pediatric cystic fibrosis: socioeconomic factors and respiratory outcomes. *Pediatr Pulmonol*. 2015;50:1244–1252.
19. Cystic Fibrosis Foundation. Additional Clinical Initiatives. 2013.
20. Kopp BT, Nicholson L, Paul G, Tobias J, Ramanathan C, Hayes D, Jr. The geographic impact on hospitalization in patients with cystic fibrosis. *J Pediatr*. 2016;170:246–252. e241-244.
21. Kim H, McConnell KJ, Sun BC. Comparing emergency department use among medicaid and commercial patients using all-payer all-claims data. *Popul Health Manag*. 2017;20:271–277.
22. VanDevanter DR, Pasta DJ, Konstan MW. Treatment and demographic factors affecting time to next pulmonary exacerbation in cystic fibrosis. *J Cyst Fibros*. 2015;14:763–769.
23. Waters VJ, Stanojevic S, Sonneveld N, et al. Factors associated with response to treatment of pulmonary exacerbations in cystic fibrosis patients. *J Cyst Fibros*. 2015;14:755–762.
24. Cystic Fibrosis Foundation. PATIENT REGISTRY ANNUAL DATA REPORT 2015. Bethesda, Maryland Cystic Fibrosis Foundation; 2015.
25. Ouyang L, Grosse SD, Amendah DD, Schechter MS. Healthcare expenditures for privately insured people with cystic fibrosis. *Pediatr Pulmonol*. 2009;44:989–996.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

How to cite this article: Kirkham HS, Staskon F, Hira N, et al. Outcome evaluation of a pharmacy-based therapy management program for patients with cystic fibrosis. *Pediatr Pulmonol*. 2018;1–8. https://doi.org/10.1002/ppul.23978

APPENDIX A

TABLE A1 CC-CF clinical program medications

Medication/product DESC	NDC	Class
Kalydeco/ivacaftor 150 mg (14 Tab/Card)	51167020001	CFTR potentiator
Kalydeco/ivacaftor 150 mg Tab	51167020002	CFTR potentiator
Cayston/aztreonam 75 mg inhaled solution	61958090101	Antibiotic
Pulmozyme/dornase alfa sol 1 mg/mL Ampul	50242010039	Mucolytic enzyme
Pulmozyme/dornase alfa 2.5 mg/2.5 mL Neb 90 = 30	50242010040	Mucolytic enzyme
Tobi/tobramycin 300 mg/5 mL Neb (20 mL = 4 Neb)	00078049471	Antibiotic
Tobi podhaler/tobramycin 28 mg Cap 224 = 4PK	00078063035	Antibiotic
Tobi podhaler/tobramycin 28 mg inhaled cap	00078063056	Antibiotic
Tobramycin 300 mg/5 mL 20 mL = 4 Neb	00093408563	Antibiotic
Bethkis/tobramycin 300 mg/4 mL Amp 224 = 1 Box	10122082056	Antibiotic
Kitabis pak/tobramycin 300/5 mL Neb 20 mL = 4	24492085056	Antibiotic
Tobi neb/tobramycin 300 mg/5 mL (280 = 1 Box)	53905006501	Antibiotic