

Problem solving to improve adherence and asthma outcomes in urban adults with moderate or severe asthma: A randomized controlled trial

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Background: Improving inhaled corticosteroid (ICS) adherence should improve asthma outcomes.

Objective: In a randomized controlled trial we tested whether an individualized problem-solving (PS) intervention improves ICS adherence and asthma outcomes.

Methods: Adults with moderate or severe asthma from clinics serving urban neighborhoods were randomized to PS (ie, defining specific barriers to adherence, proposing/weighting solutions, trying the best, assessing, and revising) or standard asthma education (AE) for 3 months and then observed for 3 months. Adherence was monitored electronically. Outcomes included the following: asthma control, FEV₁, asthma-related quality of life, emergency department (ED) visits, and hospitalizations. In an intention-to-treat-analysis longitudinal models using random effects and regression were used.

Results: Three hundred thirty-three adults were randomized: 49 ± 14 years of age, 72% female, 68% African American, 7% Latino, mean FEV₁ of 66% ± 19%, and 103 (31%) with hospitalizations and 172 (52%) with ED visits for asthma in the prior year. There was no difference between groups in overall change in any outcome ($P > .20$). Mean adherence (61% ± 27%) decreased significantly ($P = .0004$) over time by 14% and 10% in the AE and PS groups, respectively. Asthma control improved overall by 15% ($P = .002$). In both groups FEV₁ and quality of

life improved by 6% ($P = .01$) and 18% ($P < .0001$), respectively. However, the improvement in FEV₁ only occurred during monitoring but not subsequently after randomization. Rates of ED visits and hospitalizations did not significantly decrease over the study period.

Conclusion: PS was not better than AE in improving adherence or asthma outcomes. However, monitoring ICS use with provision of medications and attention, which was imposed on both groups, was associated with improvement in FEV₁ and asthma control. (J Allergy Clin Immunol 2011;■■■:■■■-■■■.)

Key words: Asthma, adherence, adults, inner-city asthma, problem solving, health disparities, inhaled corticosteroids

Asthma, a chronic treatable disease affecting 15 million US adults, is characterized by a high degree of health disparity.¹ Blacks have 3 times the hospitalizations and deaths compared with whites; the rate is also disturbingly high in Latinos. Improving asthma outcomes is particularly important in these groups.

Inhaled corticosteroids (ICSs) are essential medicines for all but the mildest asthma, yet patients commonly take far less than prescribed.²⁻⁵ It is thought that improving adherence will improve asthma outcomes, but there are few interventions that show this is the case.^{6,7} Adherence has complicated determinants, including patients' perceptions of benefits compared with adverse effects, medication costs, personal priorities, and the waxing and waning of the disease.^{2,8} It might be a sign of the adequacy of patient-physician communication.^{6,7,9}

Measuring adherence to ICSs is difficult,¹⁰ serum levels cannot be measured, and canister weighing and patients' and physicians' reports are unreliable.^{4,11-16} Electronic monitoring giving the time and date of use is the best means of directly assessing medicine taking.^{10,17} Other methods are more limited in addressing how adherence affects asthma outcomes. For example, counting prescribed or filled prescriptions does not ensure medications are taken.^{3,5} Nevertheless, electronic monitoring is not without its problems. Monitors can fail to record or download data, and the act of monitoring (ie, observing behavior) can change behavior (Hawthorne effect). Additionally, monitors might be able to detect when an inhaler is actuated but not whether the medication is actually inhaled. Nevertheless, measuring adherence is absolutely essential to determine whether an intervention actually improves adherence and whether adherence improves outcomes.

In this study we investigated the use of a problem-solving (PS) approach to improve medication adherence in patients with moderate or severe asthma. The rationale for this approach is

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Abbreviations used

AE:	Asthma education
AQOL:	Asthma-related quality of life
CES-D:	Center for Epidemiologic Studies Depression Scale
DAL:	Diskus Adherence Logger
ED:	Emergency department
FVC:	Forced vital capacity
ICS:	Inhaled corticosteroid
ITT:	Intention to treat
PS:	Problem solving

that interventions that involve frequent interaction with patients, take account of patients' circumstances, and boost communication have been recommended in the past,^{6,7} and PS is an individualized intervention successful in other settings for promoting behavior change. PS considers the unique context and special barriers of patients' lives. It has been used to reduce psychological distress, increase self-efficacy, enhance overall coping skills,¹⁸⁻²¹ promote weight loss,^{22,23} and decrease destructive behaviors, such as suicide attempts,²⁴ substance abuse,²⁵ and unprotected sex.²⁶ A version of this PS model has been used to improve glucose control in patients with diabetes, a chronic disease that, like asthma, requires significant self-management skills.²⁷⁻²⁹ We adapted a version by D'Zurilla and Nezu³⁰ that consists of 4 iterative steps: (1) defining specific barriers to adherence and orientation (developing a coping perspective), (2) proposing and weighing solutions, (3) choosing the best solution, and (4) trying out the solution and revising.

We tested whether PS compared with standard asthma education (AE) improves ICS adherence and asthma-related health outcomes. The subjects were adults with moderate or severe asthma recruited from medical practices serving low-income urban neighborhoods. Participants also were asked to problem solve a problem of their own choosing to improve the relevance of PS. This was to demonstrate the applicability of PS to many problems; suggest that if one's asthma is controlled, one can better address life's other problems; and acknowledge to patients that their unique context must be considered in achieving health.

METHODS

A more detailed description of the [Methods](#) is available in this article's Online Repository at www.jacionline.org.

Study design

We conducted a randomized controlled trial (ClinicalTrials.gov no. NCT00115323) assigning asthmatic adults to either PS or AE. The study was approved by the Institutional Review Boards of the University of Pennsylvania and the Philadelphia Veterans Affairs Medical Center. Potential subjects were told that the purpose of the study "is to examine better ways to treat asthma using currently recommended medications and procedures."

Subjects

Participants were English- or Spanish-speaking adults with moderate or severe persistent asthma according to the National Heart, Lung, and Blood Institute's Expert Panel Report 3 guidelines.³¹ Inclusion criteria were designed to identify patients with sufficiently severe and reversible asthma who were likely to benefit from ICS therapy. Specific criteria were as follows: (1) age of 18 years or greater; (2) physician's diagnosis of asthma; (3)

prescription for an ICS-containing medication for asthma; and (4) evidence of reversible airflow obstruction (ie, either an increase of 15% or greater and 200 mL in FEV₁ with asthma treatment over the previous 3 years or an increase in FEV₁ or forced vital capacity [FVC] of 12% or greater and 200 mL in FEV₁ within 30 minutes of inhaled albuterol). Smokers were included. Excluded were patients with severe psychiatric problems, such as obvious mania or schizophrenia, that would make it impossible for them to understand or carry out PS.

Subjects were recruited from primary care and asthma specialty practices serving low-income inner-city neighborhoods with a high prevalence of asthma morbidity. Charts or electronic medical records were prescreened for patients with a diagnosis of asthma who were prescribed an ICS. Potential subjects were then approached by telephone or at the time of a clinic visit and asked to sign consent forms for further screening. Those satisfying all enrollment criteria were then asked to sign a second informed consent form to participate in the 26-week study.

Procedures

Questionnaires on sociodemographics, present and past asthma status, and comorbidities were completed. Spirometric results were obtained.³² Participants estimated their adherence over the last 3 months with the Inhaler Adherence Scale.^{33,34} An electronic monitor was attached to participants' ICS-containing inhaler. Participants were informed that the monitor recorded the time and date of inhaler actuation and that data would be downloaded at each of 8 study visits. Two weeks later (visit 2), subjects were randomized according to a computer-generated algorithm in a 1:1 ratio to either PS or AE. Subjects met with research coordinators monthly for 4 sessions (visits 2-5) of either PS or AE, spirometry, and downloading monitor data. The need for urgent medical care since the last visit was queried. Subjects then continued to meet monthly with research coordinators for 3 additional months (visits 6-8) to download monitor data, but no PS or AE occurred at visits 6 to 8.

Subjects received \$20 for the first visit, \$15 for visits 2 to 5, \$10 for short visits 6 to 7, and \$50 for completing visit 8. The ICS was supplied for subjects without any insurance coverage for an ICS. For subjects with a copayment, this sum was reimbursed if all visits were completed and medication receipts were submitted.

Interventions

PS comprised four 30-minute sessions. The individualized intervention involved 4 interactive steps, usually 1 per research session. For the 158 participants who reported missing doses of ICSs, the goal was to improve adherence. For the 7 participants who declared adherence to the prescribed regimen, the goal was to maintain adherence. The first PS step consisted of defining the problem: improving or preserving adherence to ICS use within the patient's unique context and orientation. Problem orientation facilitated the adoption of a rational, positive, and constructive appraisal of how to achieve adherence, with nonadherence being presented as a problem to be solved. PS was presented as a means of coping with problems more generally and modifying attitudes or beliefs that inhibit or interfere with attempts to solve problems. It was a motivational technique to help the participant view the occurrence of problems as inevitable, normal, and solvable. This first step involved breaking problems into small achievable pieces. The second step was brainstorming for alternative solutions. The third step was choosing the best solution by weighing the consequences, both desirable and undesirable, of each candidate solution. Between the third and fourth meetings, the solution was tried. For the fourth step, the chosen solution was evaluated and revised. As part of this intervention, downloaded data from monitored ICSs were shared with the participant in a nonjudgmental fashion at each visit. At these sessions, subjects followed the same PS steps for addressing an additional problem of their own choosing, such as increasing physical activity. The problems were sometimes interrelated; for example, a father wants to play sports with his child, and improving asthma management makes this easier.

AE, like PS, comprised four 30-minute sessions, each about an AE topic unrelated to self-management, adherence, or ICS therapy. The topics covered, 1 at each session, were the following: (1) the proper technique for using an

albuterol rescue metered-dose inhaler and a dry powder inhaler or spacer, depending on the patient's medications; (2) the use of peak flow meters; (3) common asthma triggers; and (4) the pathophysiology of asthma. These sessions did not involve discussion of PS or adherence, only didactic presentation of health information.

Research coordinators

Subjects worked with the same research coordinator for all visits, who delivered either PS or AE by script. Research coordinators were college graduates interested in health-related or education careers or further schooling who were committed to working with patients and a research experience. They were diverse in race/ethnicity similarly to patients.

Outcomes

Adherence to the ICS regimen prescribed by the participant's physician. We electronically monitored the date and time of ICS actuation. The electronic monitor can record multiple actuations over a short time period and thus can detect medication "dumping," multiple actuations of an ICS unaccompanied by inhalation.^{13,35,36}

Only 2 electronic monitors that measure the time and date of ICS use were available at the time of the study. Although no commercial monitor was available for fluticasone-salmeterol, the most frequent ICS prescribed to subjects during the study period, we were able to use the Diskus Adherence Logger (DAL), a research monitor developed by a team member (D. K. B.).¹⁷ Fluticasone and beclomethasone administered by means of metered-dose inhalers were the next most frequently prescribed; for these, we used a commercial monitor, MDILog (Life Link Monitoring, Inc, Kingston, NY). Approximately 90% of study participants were prescribed an ICS that could be monitored with the DAL or MDILog. Fourteen patients were initially prescribed inhaled mometasone, but they were switched to a medication that could be monitored, fluticasone, during the study period with their physician's permission.

Daily ICS adherence was calculated as follows:

$$(\text{Number of actuations downloaded} / \text{Number prescribed}) \times 100.^{2,37}$$

We truncated adherence at 100% for each monitoring period to control for multiple actuations over a very short period of time and to provide a better measure of adherence.^{2,17,36-38}

Asthma outcomes. Asthma-related quality of life (AQOL) was measured at visits 1, 5, and 8 with the Mini-Asthma Quality of Life Questionnaire.³⁹⁻⁴¹ This 15-item questionnaire, reflecting well-being over the past 2 weeks, has a 7-point response scale that provides a mean summary score. A 0.5-unit change is considered clinically meaningful.⁴¹ The Asthma Quality of Life Questionnaire has been shown to be a useful indicator of AQOL in low-income adults.⁴² Asthma control was measured at each visit by using the 7-item version of the Asthma Control Questionnaire,⁴³⁻⁴⁵ which asks about symptoms over the past week. The score is the mean of all responses (0, total control; 6, extremely uncontrolled). The minimal important clinical difference is 0.5. A score of greater than 1.5 is considered inadequate control.⁴⁶ Spirometry was obtained by using American Thoracic Society procedures for FEV₁ and FVC.³² At each research visit, participants reported hospitalizations and emergency department (ED) visits for asthma or any cause that had occurred since the previous meeting. Participants were queried about satisfaction with and benefits of the study at its end.

Independent variables (baseline data)

Demographic characteristics (ie, age, race, ethnicity, educational attainment, and household income) were participant reported. Household income was ascertained in categories to make responses by participants more acceptable and feasible: less than \$30,000/y, \$30,000 to \$49,999/y, \$50,000 to \$99,999/y, and \$100,000/y or more. Baseline depressive symptoms were measured with the Center for Epidemiologic Studies Depression Scale (CES-D).⁴⁷ Self-efficacy was obtained at baseline with a 14-item questionnaire reported previously.^{37,48,49} Literacy was measured by using the Short Test of Functional Health Literacy in Adults⁵⁰ and the Asthma Numeracy Questionnaire.⁵¹

Exposure to community violence was queried: "In the past 6 months, did you witness any violence in your neighborhood (yes/no)?"⁵² Social support was assessed at baseline by using the MOS Social Support Survey.⁵³ The Inhaler Adherence Scale asked for the participant's report of nonadherence at baseline.^{33,34} It is a 6-item scale, with each item scored 1 (nonadherence) or 0 (adherence). The range is 0 to 6, with 0 being optimal adherence.

Statistical analysis

Pre-enrollment power calculations based on an intention-to-treat (ITT) framework estimated that enrollment of 390 with a final sample size of 330 would detect a 10% effect size with a power of 0.80. STATA 11.0 (StataCorp, College Station, Tex) and SAS version 9.2 (SAS Institute, Inc, Cary, NC) software were used. A descriptive analysis was performed for all variables. We compared the PS and AE groups for the adequacy of randomization, examining whether covariates or baseline variables, including potential moderators of the intervention, were equally distributed among patient groups. The statistical tests were as follows: *t* tests or Wilcoxon rank sum tests for continuous variables, depending on the symmetry of the distributions; logistic regression for binary or ordinal variables; and Poisson log-linear regression for count data.

The analysis of PS versus AE differences with respect to each longitudinal continuous outcome was based on the ITT principle, involving mixed-effects linear regression with random intercepts and slopes to account for clustering by patient. These models also included separate fixed main effects for the intervention factor and each of the follow-up visits (treated as categorical), as well as separate interaction terms between the randomized intervention and each visit. The ITT test comparing PS and AE across all visits was based on a model-based F test of all interaction-visit interaction terms. Additionally, tests of change across all visits within each group or overall were based on F-tests of corresponding combinations of model parameters. For count data across the entire follow-up period (eg, emergency visits), we used a log-linear model with SEs adjusted for overdispersion and ITT tests of the intervention effect on the outcome based on the log risk ratio parameter corresponding to the intervention in the log-linear model.

Exploratory moderation and subgroup analysis. For each of the subgroup factors, we tested whether the PS versus AE contrast in longitudinal outcomes differed between subgroup levels (moderation) based on an interaction among the intervention, time, and subgroups in the longitudinal models. We conducted exploratory subgroup analyses to determine whether certain baseline characteristics, sociodemographic or asthma severity variables, distinguished participants who were more likely to have improved outcomes (adherence, FEV₁, and AQOL) as a result of PS. The groups tested were age, sex, baseline FEV₁, hospitalizations or ED visits for asthma in the year before entry, baseline AQOL, household income, minority status, baseline depressive thoughts, literacy, baseline self-efficacy concerning adherence to taking ICSs, social support, and exposure to community violence. We dichotomized these subgroups according to the median. For each of these subgroups, we tested whether asthma outcomes differed by intervention assignment.

RESULTS

Recruitment

We prescreened more than 49,000 patient charts. These patients were either scheduled to have a physician's appointment in participating general or specialty clinics within the following 2 weeks or were admitted to the ED for asthma (see Fig E1 in this article's Online Repository at www.jacionline.org). Charts were reviewed more than once if the patient had more than 1 appointment. This prescreening process identified approximately 7000 appointments for patients 18 years or older with a doctor's diagnosis of asthma who were prescribed an ICS. Some patients had multiple appointments. After counting patients only once and screening for the other enrollment criteria, we identified 585 eligible patients. Of these, 397 completed the surveys for this study (visit 1). Of the 188 who declined, 70 stated they were too busy, 57

TABLE I. Baseline characteristics of 333 randomized patients according to study group

Characteristic	Total (n = 333)	PS (n = 165)	AE (n = 168)	P value†
Sociodemographics				
Age (y)*	49 ± 14	49 ± 13	49 ± 14	.85
Female sex	241 (72%)	122 (74%)	119 (71%)	.53
Race				.32
Black/African American	228 (68%)	118 (72%)	110 (65%)	
White	67 (20%)	30 (18%)	37 (22%)	
Other‡	9 (3%)	5 (3%)	4 (2%)	
No response or declined to answer	29 (9%)	12 (7%)	17 (10%)	
Ethnicity: Hispanic/Latino	23 (7%)	10 (6%)	13 (8%)	.56
Household income (/y)				.34
<\$30,000	176 (53%)	84 (51%)	92 (55%)	
\$30,000-\$49,999	83 (25%)	49 (30%)	34 (20%)	
\$50,000-\$99,999	46 (14%)	22 (13%)	24 (14%)	
≥\$100,000	18 (5%)	7 (4%)	11 (7%)	
No response or declined to answer	10 (3%)	3 (2%)	7 (4%)	
High school graduate	275 (83%)	144 (87%)	131 (78%)	.19
Asthma numeracy questionnaire score*¶	2.3 ± 1.2	2.3 ± 1.2	2.2 ± 1.2	.69
Reading comprehension score*#	31.2 ± 7.3	31.1 ± 7.6	31.4 ± 7.0	.68
Depression*§	17.5 ± 11.5	17.4 ± 11.3	17.3 ± 12.2	.66
Social support*	73 ± 22	72 ± 22	73 ± 22	.75
Self-efficacy*,**	53 ± 7	52 ± 7	54 ± 7	.09
Never smoked	141 (42%)	68 (41%)	73 (43%)	.49
No. of years smoked	11 ± 15	11 ± 15	11 ± 14	.51
Total witnessing violence in the last 6 mo	67 (20%)	33 (20%)	34 (20%)	.98
Asthma severity at baseline				
FEV ₁ (% predicted)*	66 ± 19	66 ± 19	64 ± 19	.40
No. with ≥1 ED visit for asthma in past year	172 (52%)	86 (52%)	86 (51%)	.93
No. with ≥1 hospitalization for asthma in past year	103 (31%)	52 (32%)	51 (30%)	.82
AQOL*.40	4.0 ± 1.4	4.0 ± 1.5	4.0 ± 1.4	.83
Asthma control*.44	1.67 ± 1.10	1.68 ± 1.09	1.65 ± 1.11	.91
No. of comorbidities				
Hypertension	172 (52%)	83 (50%)	89 (53%)	.63
Diabetes	73 (22%)	37 (22%)	36 (21%)	.83
BMI (kg/m ²)††	33.4 ± 8.8	34.2 ± 8.6	32.6 ± 8.9	.07

BMI, Body mass index.

*Mean ± SD.

†Comparing PS and AE groups.

‡“Other” is defined as American Indian/Alaskan Native, Asian, or Native Hawaiian/Pacific Islander.

§CES-D range is 0 to 60 points, with scores of 16 or greater suggestive of depressive symptoms or general distress.

||The MOS Social Support Survey⁵³ has 19 items on a 5-point Likert scale. The overall score of the survey is given by the mean of all 19 items rescaled to a range of 0 to 100; a higher score represents more support. These scores were in the range of a multiethnic urban sample of postpartum women attending a community health center⁵⁴ and lower than in a group of ovarian cancer survivors.⁵⁵¶Asthma Numeracy Questionnaire (score range, 0-4).⁵¹#Short Test of Functional Health Literacy in Adults⁵⁰ (score range, 0-36, with a score of 23 or greater adequate).**Self-efficacy is a 14-item questionnaire. Items are measured on a 5-point Likert scale, with the score the sum of item scores.^{37,48,49} The range is 14 to 70, with a higher score indicating higher self-efficacy.

††Body mass index of 30 or greater is classified as obese, and scores of 25 to 29 are considered overweight.

did not come for appointments scheduled with researchers, 39 thought the travel time for appointments too burdensome, and 18 did not consider the research likely to be beneficial to themselves or others. In addition, another 4 eligible patients declined, 1 for each of the following reasons: “concerns about research,” “concerns about data privacy/protection of personal medical information,” the patient’s doctors believed the study was not likely to be beneficial, and the patient was unable to switch to an inhaled steroid for which we had a monitor. Three hundred thirty-three returned for visit 2 and were randomized.

Patients’ characteristics

The 333 subjects were mostly female, African American, and from households earning less than \$30,000/y (Table I).^{37,48-51,53-55} Baseline mean CES-D scores were high,

suggesting a prevalence of depressive symptoms frequently seen in poor urban populations.⁵⁶ Likewise, quality-of-life scores were low.^{39,40}

The study population had significant asthma morbidity, with the cohort having a low mean FEV₁ (66% ± 19%). More than half had had an asthma-related ED visit in the year before enrollment, and about one third had been hospitalized for asthma in that time interval. Comorbidities were common. For example, half had hypertension, and almost a quarter had diabetes. In addition, mean body mass index was high (Table I); 107 (67%) in the PS group and 90 (56%) in the AE group had body mass indexes of at least 30 kg/m².

Baseline participant report of nonadherence, as measured by using the Inhaler Adherence Scale, had a mean score of 4.2 ± 1.4 and did not differ by PS/AE assignment (*P* = .59, Table II).

TABLE II. Nonadherence at baseline by patient report with the Inhaler Adherence Scale* did not differ between groups

During the last 3 mo, have you...	No. of participants reporting nonadherence (n = 333)	PS (n = 165)	AE (n = 168)	P value
at times been careless about using your ICS?	168	83	85	.96
ever forgotten to use your ICS?	115	52	63	.25
ever stopped using your ICS because you felt better?	275	136	139	.94
ever used less than the doctor prescribed because you felt better?	245	118	127	.35
ever stopped using your ICS because you felt worse?	321	159	162	.98
ever used your ICS more than prescribed because you felt you were having breathing problems?	286	143	143	.69

Shown is the number of participants who endorsed an item of nonadherence of the scale over the last 3 months.

*Morisky et al³⁴ and Dolce et al.³³

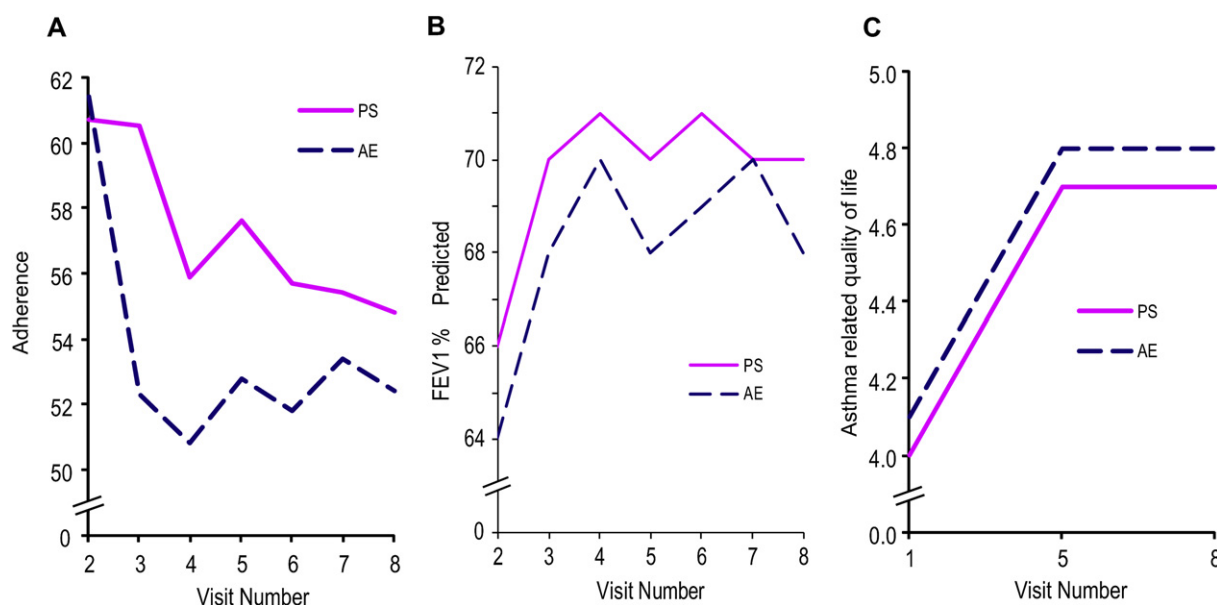


FIG 1. A, Adherence over the study period by PS versus AE. Data collected at a visit represent adherence data collected between that and the previous visit; for example, the adherence point at visit 4 represents adherence between visits 3 and 4. The approximately 61% adherence point at visit 2 represents adherence between visits 1 and 2 and thus baseline adherence (ie, adherence before the interventions). B and C, FEV₁ percent predicted (Fig 1, B) and asthma-related quality of life (Fig 1, C) over the study period.

Fifty participants received at least 1 container of ICS; 25 were assigned to PS and 25 to AE. Of the 14 patients switched from mometasone to fluticasone, 7 were randomized to PS and 7 to AE. Ninety-nine participants received copayment reimbursement, 54 assigned to PS and 45 to AE.

Eighty-three percent of the PS and 82% of the AE group patients had fluticasone/salmeterol monitored with the DAL. The remaining participants had a pure ICS monitored with an MDILog.

The 64 who did not return after visit 1 to be randomized in visit 2 differed from those who were randomized in that they were slightly younger (mean age, 36 ± 13 years), had a slightly higher FEV₁ ($72\% \pm 19\%$ of predicted value), and were slightly more likely to be African American.

Two male subjects died while enrolled of causes unrelated to the study interventions: 1 of pneumonia and 1 of a cardiac arrest during surgery to remove a blood clot. Both were assigned to the AE group and had not been seen by the research team for several weeks.

PS

Participants assigned to the PS group were asked to identify a specific problem related to either improving or maintaining adherence. Table E1 (available in this article's Online Repository at www.jacionline.org) describes the barriers to adherence (asthma problem), solutions proposed, and the other problems the 165 participants addressed.

Outcomes

Overall mean adherence was $61\% \pm 27\%$. It decreased ($P = .0004$) over time by 14% in the AE group and 10% in the PS group (Fig 1, A). Monitor downloads failed in 380 (20%) of 2360 downloads, 18% of the PS group and 22% of the AE group. Failures were attributed to monitor failure, battery failure, and proximity to other batteries or magnets.

There were no differences between groups with respect to overall change in any outcome ($P > .20$). Table III^{2,17,36-38,46} presents outcomes at baseline, the end of the intervention (visit 5),

TABLE III. Adherence and asthma outcomes at baseline, the end of the intervention (visit 5), and the end of observation (visit 8)

Outcome	Baseline		Visit 5		Visit 8		P value of change from baseline
	PS	AE	PS	AE	PS	AE	
Adherence (%) [*]	61 ± 26	61 ± 28	58 ± 28	53 ± 27	55 ± 29	52 ± 28	.0004
Asthma control [†]	1.7 ± 1.1	1.7 ± 1.1	1.6 ± 1.3	1.5 ± 1.1	1.5 ± 1.2	1.3 ± 1.1	.002
Quality of life [‡]	4.0 ± 1.4	4.1 ± 1.4	4.7 ± 1.4	4.8 ± 1.4	4.7 ± 1.3	4.8 ± 1.4	<.0001
FEV ₁ % predicted	66 ± 19	64 ± 19	70 ± 18	68 ± 20	70 ± 19	68 ± 18	.01
ED for asthma [§]	4.27	4.76	6.21	4.23	7.30	2.96	>.20
ED for any cause [§]	9.09	8.33	9.66	9.15	13.87	7.41	>.20
Hospitalizations for asthma [§]	1.82	2.98	2.76	2.82	1.46	0.74	>.20
Hospitalizations for any cause [§]	3.03	2.98	6.90	6.34	3.65	5.93	>.20

There was no significant statistical or clinical difference between groups ($P > .20$). The P value indicates change from baseline to the end of the intervention: decrease in adherence but improvement in asthma control, quality of life, and FEV₁.

^{*}ICS adherence was calculated from the date-time record of the ICS data downloaded from the monitors as the mean of daily adherence, where daily adherence is determined as follows: (No. of actuations/No. prescribed) $\times$ 100.^{2,37} Adherence was truncated at 100% for each monitoring period to control for multiple actuations over a very short period of time and thus provides a better measure of adherence.^{2,17,36-38}

[†]Asthma Control Questionnaire: The score is the mean of all responses (0, total control; 6, extremely uncontrolled). The minimal important clinical difference is 0.5. A score of greater than 1.5 is considered inadequate control.⁴⁶

[‡]Asthma Quality of Life Questionnaire: A change of 0.5 points in an individual patient is considered clinically meaningful.

[§]Percentage of participants reporting an ED visit or hospitalization occurring since the last visit; for example, the percentage of participants reporting an event since visit 4 at visit 5.

and the end of the observation period (visit 8). Asthma control measured by using the Asthma Control Questionnaire improved significantly ($P = .002$) for both groups (20% in the AE group and 11% in the PS group), but there was no significant statistical or clinical difference between groups. In both groups FEV₁ percent predicted and quality of life improved from baseline: 6% ($P = .01$) and 18% ($P < .0001$), respectively, for the AE and PS groups (Fig 1, B and C). However, the improvement in FEV₁ occurred only between visits 1 and 2; changes in FEV₁ for subsequent visits were not significant. There was no association between adherence and asthma outcomes ($P > .50$, data not shown).

There was no difference between the PS and AE groups with respect to ED visits for asthma ($P = .51$) or any cause ($P = .30$). Likewise, there was no difference in hospitalizations for asthma ($P = .79$) or any cause ($P = .95$). There also was no statistically significant change in the rate of these events across the study period ($P > .20$, Table III).

In end-of-study questionnaires (see the Methods section in this article's Online Repository) given to the last 95 enrollees, 68 of 95 thought they had learned about asthma, and 40 of 59 thought PS was helpful. Interestingly, of the 26 of 36 in the AE group who thought the study was worthwhile, 11 of 26 specifically thought they learned about the benefits of adherence.

Within the exploratory moderation/subgroup analysis, we found those patients with low baseline social support ($P = .003$), more exposure to violence ($P = .007$), and low income ($P = .03$) had better adherence if randomized to the PS group compared with the AE group. Those with low CES-D scores were more likely to have improved AQOL ($P = .007$) if randomized to the PS group. Those with low numeracy ($P = .007$) and low AQOL ($P = .03$) were more likely to have higher FEV₁ if assigned to the PS group. There was no difference in outcomes between PS and AE in subgroups defined by age, sex, hospitalizations or ED visits in the year before enrollment, baseline FEV₁, low self-efficacy, or low educational attainment. There was no change in self-efficacy over the observation period ($P > .1$).

DISCUSSION

To study whether an individualized intervention focused on PS could improve adherence for vulnerable patients, we conducted a randomized controlled trial in adults from low-income inner-city neighborhoods with moderate or severe asthma. Even with a relatively large sample size, a long observation period, and the use of electronic monitoring rather than self-report, we could not detect any differences in outcomes between the group that received PS and the group that received standard AE. Adherence decreased over the 6-month monitoring period, but both groups demonstrated improved quality of life, FEV₁, and asthma control. These observed improvements could have been due to monitoring, attention, provision of medications, or regression to the mean. Additionally, there were no statistically detectable differences or changes over time with respect to ED visits or hospitalizations, either overall or asthma related. Future work should explore the contribution to outcomes from the common elements in both treatment groups to isolate the factors most responsible for the favorable outcomes (ie, attention, electronic monitoring, and the provision of medications), keeping in mind that adherence decreased.

Despite an intervention aimed at adherence, there was no difference between PS and AE in asthma outcomes, nor was there a difference in the decrease in adherence. It is noteworthy that adherence was already relatively good at baseline and remained so throughout the observation period at a mean of 61%.⁷ This is especially remarkable considering a recent study by Williams et al⁵⁷ that measured ICS adherence of less than 30% by using prescription-fill data for asthmatic patients in southeastern Michigan. Actual total adherence was likely lower than their estimates because not all filled medications are taken.⁵⁷

In our study we monitored both groups from the beginning, informing participants that monitor use was recorded, which could have resulted in higher adherence than would have occurred had medicine-taking behavior not been monitored (the Hawthorne effect). Additionally, the relatively high adherence found in both groups might help explain the improvements in quality of life and asthma control observed for both the PS and AE groups. However, hospitalizations and ED visits did not decrease. It is

possible that within the context of our particular sample, although attention and monitoring and providing medications can improve asthma status to some degree, they are not sufficient to mitigate the use of other medical resources, such as hospitalization, over the 6-month period. This might be a result of the vulnerability of our sample of adults, who, in addition to their unusually severe asthma (mean baseline FEV₁, 66%), are high baseline users of hospitalization and the ED, have many comorbidities, have significant tobacco exposure, and have limited financial and social resources.

It is noteworthy that our interventions, both PS and AE, are focused solely on the patient. Medical services and the patient's larger context were not addressed. Patients' concerns, detailed in their choice of the other problem (see Table E1), indicate that additional significant health and social problems are common. These other problems suggest that it is important for practices to take into account these "external" factors, which might be extremely difficult.

Some support for this argument comes from Table II. Patients readily admitted that there were times when they did not take medications. Self-efficacy was relatively good and did not change over the course of the study, suggesting that patients were not motivated to achieve better adherence. Thus this intervention is too far "downstream"; instead, motivation needs to be addressed and addressed better, considering patients' other priorities and problems.

The limitations of our study are informative. As noted, electronic monitoring of adherence cannot be achieved divorced from the Hawthorne effect. Because of monitoring, many members of the AE group (66%) thought researchers were teaching about adherence. Thus the interventions might have been perceived similarly by participants. Although the intervention was complicated and labor intensive, it focused only on the patient's behavior and did not consider the environment of the practice site or that of the patient's larger social context. The study design had important elements of pragmatic research, although its complexity limits it as a "real-world" pragmatic intervention.⁵⁸ The pragmatic elements that can inform subsequent studies are as follows: inclusion of patients with comorbidities and those with significant tobacco exposure, use of a flexible individualized intervention, and delivery of PS and AE by research staff who were not trained medical personnel. The latter factor demonstrates that interventions such as attention and provision of medications could be delivered by a variety of health care workers.

In summary, our study indicates that PS does not improve adherence or decrease asthma morbidity in this population. Provision of medications, monitoring, and attention are associated with improvement in some asthma outcomes, but research is needed to identify interventions to alleviate the need for ED visits and hospitalizations for asthma and to improve the health of high-morbidity patients living in low-income inner-city neighborhoods. Such interventions likely should be incorporated into practice procedures⁵⁹ and include consideration of the larger social context.

We dedicate this manuscript to the memory of Thomas R. Ten Have, PhD, brilliant biostatistician, collaborator, and friend, who passed away unexpectedly after the completion of this report.

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Key messages

- PS was not better than AE in improving adherence or asthma outcomes in low-income inner-city adults with moderate or severe asthma.
- Monitoring inhaled steroid use with provision of medication was associated with improvement in FEV₁, AQOL, and asthma control but did not reduce asthma-related hospitalizations or ED visits for these patients.

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METHODS

Study design

We conducted a randomized controlled trial, assigning asthmatic adults to either PS or AE. The study was approved by the Institutional Review Boards of the University of Pennsylvania and the Philadelphia Veterans Affairs Medical Center. Potential subjects were told that the purpose of the study “is to examine better ways to treat asthma using currently recommended medications and procedures.”

Subjects

Participants were English- or Spanish-speaking adults with moderate or severe persistent asthma according to the National Heart Lung and Blood Institute's Expert Panel Report 3 guidelines.^{E1} Inclusion criteria were designed to identify patients with sufficiently severe and reversible asthma who were likely to benefit from ICS therapy. Specific criteria were as follows: (1) age of 18 years or greater; (2) physician's diagnosis of asthma; (3) prescription for an ICS-containing medication for asthma; and (4) evidence of reversible air-flow obstruction (ie, an increase of 15% or greater and 200 mL in FEV₁ with asthma treatment noted in the previous 3 years or an increase in FEV₁ or FVC of 12% or greater and 200 mL in FEV₁ within 30 minutes of 2 to 4 puffs of albuterol administered by means of metered-dose inhaler or 2.5 mg administered by means of nebulizer). Smokers were included. Excluded were patients with severe psychiatric problems, such as obvious mania or schizophrenia, that would make it impossible for them to understand or carry out PS.

Subjects were recruited from practices serving low-income inner-city neighborhoods with a high prevalence of asthma morbidity. These included outpatient primary care and asthma specialty practices of the University of Pennsylvania Health System; Woodland Avenue Health Center, a federally qualified health center; the Comprehensive Health Center at Episcopal Hospital; and the Philadelphia Veterans Affairs Medical Center. Charts or electronic medical records of participating practices were prescreened for patients with a diagnosis of asthma who were prescribed an ICS. Potential subjects were then approached by telephone or at the time of a clinic visit and asked to sign consent forms for further screening, which included spirometry with standard procedures.^{E2} Those satisfying all enrollment criteria were then asked to sign a second informed consent form to participate in the 26-week study.

Procedures

On enrollment, participants completed questionnaires on sociodemographics, present and past asthma status, and comorbidities. Spirometric results were obtained.^{E2} Participants estimated their adherence over the last 3 months with the Inhaler Adherence Scale.^{E3,E4} An electronic monitor was attached to participants' ICS-containing inhalers. Participants were informed that the monitor recorded the time and date of inhaler actuation and that data would be downloaded at each of 8 study visits. Two weeks later (visit 2), subjects were randomized according to a computer-generated algorithm in a 1:1 ratio to either the PS or AE groups. Subjects met with research coordinators monthly for 4 sessions (visits 2-5) of either PS or AE, spirometry, and downloading of monitor data. At each visit, asthma control was assessed, and subjects were queried about the need for urgent medical care, including ED visits and hospitalizations. Subjects then continued to meet monthly with research coordinators for 3 additional months (visits 6-8) to download monitor data, obtain spirometric results, and collect information on medication use, ED visits, and hospitalizations. No PS or AE occurred at visits 6 to 8.

Questionnaires were administered by reading the items to the participant while the participant looked at the written questionnaire. For patients whose primary language was Spanish, bilingual research coordinators administered the questionnaires and PS or AE in Spanish. All validated questionnaires were available in English and Spanish; clinic scripts were translated into Spanish by native speakers, translated back into English, and compared with the original English version. Additionally, both English and Spanish versions were reviewed independently by other bilingual speakers to be sure the Spanish scripts were equivalent to the English versions.

Subjects received \$150 for completion of all visits in the 26-week study: \$20 for the first visit; \$15 for visits 2 to 5; \$10 for visits 6 to 7, which were short; and \$50 for completing visit 8. They received tokens for public

transportation to research visits. ICSs were supplied for subjects without any insurance coverage for ICSs. For subjects with a copayment, this sum was reimbursed if all visits were completed and medication receipts were submitted.

Interventions

PS comprised four 30-minute sessions. The individualized intervention involved 4 interactive steps, usually 1 per research session, taken by the participant in discussion with a research coordinator. For the 158 participants who reported missing doses of ICS, the goal was to improve adherence. For the 7 participants who declared that they were adherent to the prescribed regimen, the goal was to maintain adherence. The first step in PS consisted of defining the problem: improving or preserving adherence to ICS use within the patient's unique context and orientation. Problem orientation facilitated the adoption of a rational, positive, and constructive appraisal of how to achieve adherence, with nonadherence being presented as a problem to be solved. It involved introducing PS as a means of coping with problems more generally and modifying attitudes or beliefs that inhibit or interfere with attempts to engage in PS tasks. It was a motivational technique to help the participant view the occurrence of problems as inevitable, normal, and solvable. This first step also involved breaking problems into small achievable pieces. The second step was brainstorming for alternative solutions. The third step was choosing the best solution by weighing the consequences, both desirable and undesirable, of each candidate solution. Between the third and fourth meeting, the solution was tried. For the fourth step, the chosen solution was evaluated and revised. Worksheets accompany each step to guide participants and standardize procedures. As part of this intervention, downloaded data from monitored ICSs was shared with the participant in a nonjudgmental fashion at each visit, incorporating improving adherence into the PS step. If downloaded adherence was optimal, PS focused on maintenance of adherence.

At these sessions, subjects followed the same PS steps for addressing an additional problem of their own choosing, such as increasing physical activity. The problems were sometimes interrelated; for example, a father wants to play sports with his child, and improving asthma management makes this easier.

AE, like PS, comprised four 30-minute sessions, each about a patient education topic unrelated to self-management, adherence, or ICS therapy. The topics covered, 1 at each session, were as follows: (1) the proper technique for using an albuterol rescue metered-dose inhaler and a dry powder inhaler or spacer, depending on the patient's medications; (2) the use of peak flowmeters; (3) common asthma triggers; and (4) the pathophysiology of asthma. These sessions did not involve discussion of PS or adherence but only didactic presentation of health information.

Research coordinators

Subjects worked with the same research coordinator for all visits, who delivered either PS or AE by script. Research coordinators were college graduates interested in health-related or education careers or further schooling who were committed to working with patients and a research experience. They were diverse in race/ethnicity similar to the patients. Two of 4 were native Spanish speakers.

Research coordinators trained for 3 weeks initially, using training manuals detailing recruitment, protocol, and data collection procedures. Other topics included asthma pathophysiology and education; spirometry; human subjects research; cultural competence; interpersonal skills; relating to practice personnel; administrative tasks required of patients; and procedures for reviewing medical records, screening, enrolling, obtaining consent, recognition of adverse and serious adverse events, data collection, and institutional review board procedures. Researchers were trained to deliver PS or AE strictly by script, with researchers practicing the scripts during role-playing training sessions. Fidelity to the protocol was then monitored, first by having the researcher-patient interactions observed by project managers in the early stage of the project and second by periodic unannounced observations of visits with participants in the later stages. Procedures and problems were discussed at weekly team meetings with the primary investigator. In this way 100% fidelity to the protocol was achieved.

Outcomes

Adherence to the ICS regimen prescribed by the participant's physician. We electronically monitored the date and time of ICS actuation. The electronic monitor can record multiple actuations over a short time period and thus can detect medication "dumping." This is in contrast to inhalers with built-in counters, which display doses remaining; such counters cannot capture deliberate multiple actuations of an ICS unaccompanied by inhalation.^{E5-E7}

Only 2 electronic monitors that measure the time and date of ICS use were available at the time of the study. Although no commercial monitor was available for fluticasone-salmeterol, the most frequently prescribed ICS to subjects during the study period, we were able to use the Diskus Adherence Logger or DAL, a research monitor developed by a team member (D. K. B.).^{E8} Fluticasone and beclomethasone administered through metered-dose inhalers were the next most frequently prescribed; for these, we used a commercial monitor, MDILog (Life Link Monitoring, Inc). Approximately 90% of study participants were prescribed an ICS that could be monitored with the DAL or MDILog. Fourteen patients were initially prescribed inhaled mometasone by using the Veterans Affairs formulary, but they were switched to a medication that could be monitored, fluticasone, during the study period with their physicians' permission.

ICS adherence was calculated from the date-time record of the ICS data downloaded from the monitors. Daily adherence was defined as follows:

$$(\text{No. of actuations}/\text{No. prescribed}) \times 100.^{E9,E10}$$

We truncated adherence at 100% for each monitoring period to control for multiple actuations over a very short period of time and to provide a better measure of adherence.^{E7-E11}

Asthma outcomes. AQOL was measured at visits 1, 5, and 8 with the Asthma Quality of Life Questionnaire.^{E12-E14} This 15-item questionnaire, reflecting well-being over the past 2 weeks, has a 7-point response scale that provides a mean summary score. A 0.5-unit change is considered clinically meaningful.^{E14} The Asthma Quality of Life Questionnaire has been shown to be a useful indicator of AQOL in low-income adults.^{E15} Asthma control was measured at each visit by using the 7-item version of the Asthma Control Questionnaire,^{E16-E18} which asks about symptoms over the past week. The score is the mean of all responses (0, total control; 6, extremely uncontrolled). The minimal important clinical difference is 0.5. A score of greater than 1.5 is considered inadequate control.^{E19} Spirometric results were obtained by using American Thoracic Society procedures for FEV₁ and FVC.^{E2} At each research visit, participants reported hospitalizations and ED visits for asthma or any cause that had occurred since the previous meeting. Participants were queried about satisfaction with and benefits of the study at the end of the study.

Independent variables (baseline data)

Demographic characteristics (ie, age, race, ethnicity, educational attainment, and household income) were participant reported. Household income was ascertained in categories to make responses by participants more acceptable and feasible: less than \$30,000/y, \$30,000/y to \$49,999/y, \$50,000/y to \$99,999/y, and \$100,000/y or more. Baseline depressive symptoms were measured with the CES-D.^{E20} Self-efficacy was measured at baseline with a 14-item questionnaire reported previously.^{E10,E21,E22} This questionnaire specifically evaluates self-efficacy for self-administration of ICS. The range is 14 to 70, with a higher score indicating higher self-efficacy. Literacy was measured by using the Short Test of Functional Health Literacy in Adults^{E23} and the Asthma Numeracy Questionnaire.^{E24} Exposure to community violence was queried: "In the past 6 months, did you witness any violence in your neighborhood (yes/no)?"^{E25} Social support was assessed at baseline by using the MOS Social Support Survey.^{E26} The survey has 19 items, each on a 5-point Likert scale. The overall score is the mean of all 19 items rescaled to a range of 0 to 100. A higher score represents more support. The Inhaler Adherence Scale assessed participant report of nonadherence at baseline.^{E3,E4} It is a 6-item scale, with each item scored 1 (nonadherence) or 0 (adherence). The range is 0 to 6, with 0 being optimal adherence.

Statistical analysis

Pre-enrollment power calculations based on an ITT framework estimated that an enrollment of 390 with a final sample size of 330 would detect a 10% effect size with a power of 0.80. STATA 11.0 (StataCorp) and SAS version 9.2 (SAS Institute, Inc) software were used. A descriptive analysis was performed for all variables. We compared the PS and AE groups for the adequacy of randomization, examining whether covariates or baseline variables, including potential moderators of the intervention, were equally distributed among patient groups. The statistical tests were as follows: *t* tests or Wilcoxon rank sum tests for continuous variables, depending on the symmetry of the distributions; logistic regression for binary or ordinal variables; and Poisson log-linear regression for count data.

The analysis of PS versus AE differences with respect to each longitudinal continuous outcome was based on the ITT principle, involving mixed-effects linear regression with random intercepts and slopes to account for clustering by patient. These models also included separate fixed main effects for the intervention factor and each of the follow-up visits (treated as categorical), as well as separate interaction terms between the randomized intervention and each visit. The ITT test comparing the PS and AE groups across all visits was based on a model-based F test of all interaction-visit interaction terms. Additionally, tests of change across all visits within each group or overall were based on F-tests of corresponding combinations of model parameters. For count data across the entire follow-up period (eg, emergency visits), we used a log-linear model with SEs adjusted for overdispersion and ITT tests of the intervention effect on the outcome based on the log risk ratio parameter corresponding to the intervention in the log-linear model.

Exploratory moderation and subgroup analysis. For each of the subgroup factors, we tested whether the PS versus AE contrast in longitudinal outcomes differed between subgroup levels (moderation) based on an interaction among the intervention, time, and subgroups in the longitudinal models. We conducted exploratory subgroup analyses to determine whether certain baseline characteristics, sociodemographic or asthma severity variables, distinguished participants who were more likely to have improved outcomes (adherence, FEV₁, and AQOL) as a result of PS. The groups tested were age, sex, baseline FEV₁, hospitalizations or ED visits for asthma in the year before entry, baseline AQOL, household income, minority status, baseline depressive thoughts, literacy, baseline self-efficacy concerning adherence to taking ICSs, social support, and exposure to community violence. We dichotomized these subgroups according to the median. For each of these subgroups, we tested whether asthma outcomes differed by intervention assignment.

We categorized the adherence problems reported by the 165 participants randomized to PS, along with proposed solutions and the nonadherence problems selected by participants for PS. Five investigators reviewed the data collection sheets (R. G., C. P., B. A., S. G., and A. A.), first independently, categorizing adherence problems, solutions, and the other nonadherence problems. After these 5 independent classifications were completed, the investigators, referring back to the original data sheets, agreed on a consensus classification (Table E1).

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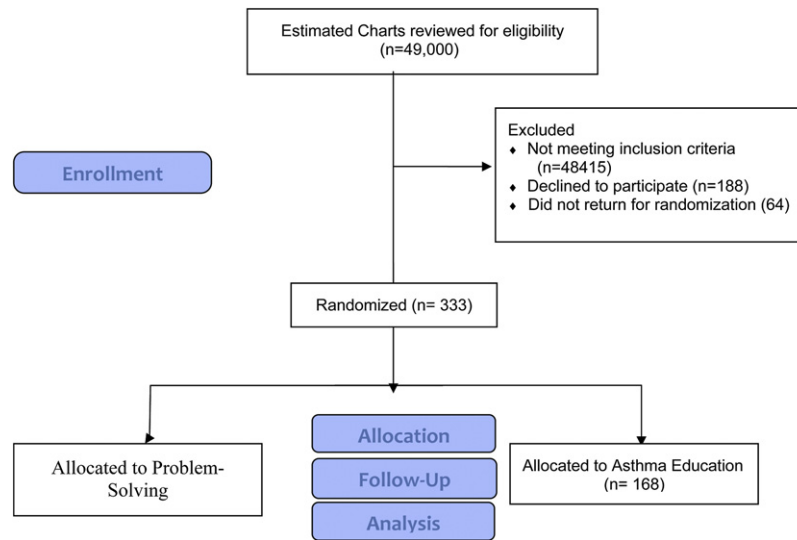


FIG E1. Flow diagram according to CONSORT 2010 guidelines.^{E27}

TABLE E1. PS selected by the 165 participants randomized to PS

Inhaled steroid adherence problem*	Asthma solution*
Too busy or hurried (41%)	Keeping inhaler in a visible location (33%)
"Just forgot" (25%)	Using an alarm (cell phone, watch) (19%)
Too tired (17%)	Incorporating medicine taking into daily routine (18%)‡
Feels good and/or does not believe ICS is needed (15%)	Carrying ICS wherever they went (10%)
Leaves medication at home or misplaces it (13%)	Keeping a calendar or checklist (7%)
Changes in routine (9%)	Use notes or a reminder (3%)
Concerns about adverse effects or harm (8%)†	Did not try a solution (2%)
Problems with pharmacy/copayment/cost (5%)	Adherent and therefore no solution (4%)
Stated always takes medication and improving and adherence is not a problem (4%)	Lost to follow-up (12%)
Too much stress (1%)	
Personal problem*	
Weight/nutrition management (36%)	
Stress (12%)	
Finding or changing jobs, starting a business, getting more education (8%)	
Too little exercise (9%)	
Other health problems (8%)	
Time management (8%)	
Balancing a busy life (5%)	
Financial problems (4%)§	
Smoking (4%)	
Difficulty sleeping (4%)	
Caring for family member (3%)	
Fix house or move (2%)	
Transportation problems (2%)	
Writing a book/novel (0.01%)	

The top left section shows the precipitants reported for forgetting to take the ICS doses. The top right section describes the proposed solutions used in PS for reducing lapses in medication taking. The bottom section lists the personal problems chosen for PS.

*Some participants listed more than 1 problem option.

†Fear of gaining weight, taking too many medications or having adverse effects from interacting with other medications, raising blood pressure, and steroids in general.

‡For example, tooth brushing.

§One participant was homeless.