ORIGINAL ARTICLE

Early Diagnosis and Treatment of COPD and Asthma — A Randomized, Controlled Trial

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ABSTRACT

BACKGROUND

Many persons with chronic obstructive pulmonary disease (COPD) or asthma have not received a diagnosis, so their respiratory symptoms remain largely untreated.

METHODS

We used a case-finding method to identify adults in the community with respiratory symptoms without diagnosed lung disease. Participants who were found to have undiagnosed COPD or asthma on spirometry were enrolled in a multicenter, randomized, controlled trial to determine whether early diagnosis and treatment reduces health care utilization for respiratory illness and improves health outcomes. Participants were assigned to receive the intervention (evaluation by a pulmonologist and an asthma–COPD educator who were instructed to initiate guideline-based care) or usual care by their primary care practitioner. The primary outcome was the annualized rate of participant-initiated health care utilization for respiratory illness. Secondary outcomes included changes from baseline to 1 year in disease-specific quality of life, as assessed with the St. George Respiratory Questionnaire (SGRQ; scores range from 0 to 100, with lower scores indicating better health status); symptom burden, as assessed with the COPD Assessment Test (CAT; scores range from 0 to 40, with lower scores indicating better health status); and forced expiratory volume in 1 second (FEV_1).

RESULTS

Of 38,353 persons interviewed, 595 were found to have undiagnosed COPD or asthma and 508 underwent randomization: 253 were assigned to the intervention group and 255 to the usual-care group. The annualized rate of a primary-outcome event was lower in the intervention group than in the usual-care group (0.53 vs. 1.12 events per person-year; incidence rate ratio, 0.48; 95% confidence interval [CI], 0.36 to 0.63; P<0.001). At 12 months, the SGRQ score was lower than the baseline score by 10.2 points in the intervention group and by 6.8 points in the usual-care group (difference, −3.5 points; 95% CI, −6.0 to −0.9), and the CAT score was lower than the baseline score by 3.8 points and 2.6 points, respectively (difference, −1.3 points; 95% CI, −2.4 to −0.1). The FEV_1 increased by 119 ml in the intervention group and by 22 ml in the usual-care group (difference, 94 ml; 95% CI, 50 to 138). The incidence of adverse events was similar in the trial groups.

CONCLUSIONS

In this trial in which a strategy was used to identify adults in the community with undiagnosed asthma or COPD, those who received pulmonologist-directed treatment had less subsequent health care utilization for respiratory illness than those who received usual care. (Funded by Canadian Institutes of Health Research; UCAP ClinicalTrials.gov number, NCT03148210.)

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*The UCAP investigators are listed in the Supplementary Appendix, available at NEJM.org.

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CME

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As many as 70% of persons with chronic obstructive pulmonary disease (COPD) or asthma do not receive a diagnosis of the condition,[1-6] especially in low- and middle-income countries.[4,7] Such persons have worse disease-specific and overall quality of life, greater health care utilization, and poorer work productivity than healthy age-matched controls.[8] The global health burden of COPD and asthma is thus likely to be underestimated, since a substantial number of cases remain undetected.[5,9-11]

Early detection of undiagnosed COPD or asthma can be achieved through targeted case finding among at-risk persons who have unexplained respiratory symptoms.[12-14] Case finding is a strategy in which subgroups of people at increased risk for having a disease (such as those with unexplained symptoms) are evaluated to make a diagnosis earlier than would otherwise occur. This approach is different from screening, which involves testing large numbers of apparently healthy people to detect unrecognized disease.

Both asthma and COPD manifest with similar respiratory symptoms (dyspnea, cough, wheeze, chest tightness, or combinations thereof), share expiratory airflow obstruction as a common physiological impairment, and can be detected by the same diagnostic test (i.e., spirometry). Accordingly, because both chronic lung diseases are highly prevalent among adults, it is reasonable to conduct case finding for COPD and asthma simultaneously to identify participants with either undiagnosed disease.[15,16]

Identification of patients with undiagnosed COPD or asthma could potentially allow for preventive environmental and lifestyle interventions to mitigate disease progression, offer opportunities for earlier treatment to alleviate symptoms, and reduce the need for future acute care for exacerbations.[16-19] The objective of this trial was to identify symptomatic adults in the community who have undiagnosed COPD or asthma by means of a case-finding approach and to couple early diagnosis of disease with a pulmonologist-directed treatment strategy to determine whether early diagnosis and treatment of undiagnosed COPD or asthma reduces health care utilization for respiratory illness and improves health outcomes.

METHODS

TRIAL DESIGN

The Undiagnosed COPD and Asthma Population (UCAP) trial was a combined case-finding study and randomized, controlled trial that was conducted from June 2017 through January 2024 at 17 sites in Canada. The protocol, available with the full text of this article at NEJM.org, was designed by the authors. The trial was approved by the ethics board at each participating site. All the participants provided written informed consent. Trial data were collected by the investigators and analyzed at the coordinating center. The manuscript was drafted by the first author, and all the authors participated in the interpretation of the data and provided input into the preparation and submission of the manuscript for publication. The authors vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol. No agreements regarding data confidentiality were in place between the authors and the sponsor (Canadian Institutes of Health Research).

PARTICIPANTS

Adults 18 years of age or older were recruited in a two-step process. A commercial survey company was employed to generate lists of landline telephone and cell-phone numbers registered within a 90-minute driving distance from the trial sites. The company randomly dialed numbers from these lists, and a recorded, scripted message questioned whether anyone in the household was 18 years or older and had had respiratory symptoms including shortness of breath, wheezing, increased mucus or sputum production, or prolonged cough in the previous 6 months. Households that responded affirmatively were contacted by the local trial coordinator, and the consenting household member with the respiratory symptom or symptoms was assessed with the use of case-finding questionnaires to determine trial eligibility.[15]

All the participants completed the Asthma Screening Questionnaire over the telephone.[20] Participants 60 years of age or older, as well as those younger than 60 years of age with a score lower than 6 on the Asthma Screening Questionnaire (scores range from 0 to 20, with higher scores indicating worse respiratory symptoms),

also completed the COPD Diagnostic Questionnaire (scores range from 0 to 38, with higher scores indicating greater risk of COPD).[21,22] Participants with a score of 6 or higher on the Asthma Screening Questionnaire or a score of 20 or higher on the COPD Diagnostic Questionnaire were invited to the trial site to undergo spirometry.

Exclusion criteria were a previous physician-documented diagnosis of lung disease; use of respiratory inhalers, except for as-needed short-acting beta-agonists; contraindications to spirometry, such as a history of myocardial infarction, stroke, aortic or cerebral aneurysm, eye surgery, or detached retina within the previous 3 months; inability or unwillingness to provide informed consent; or third-trimester pregnancy status.

CLASSIFICATION OF UNDIAGNOSED CASES

Participants underwent prebronchodilator and postbronchodilator spirometry, which was conducted by certified personnel according to standards of the American Thoracic Society. The smoking status of each participant was made available to the interpreting pulmonologist. Participants who had minimum increases of 12% and 200 ml in the forced expiratory volume in 1 second (FEV_1) after the administration of 400 μg of salbutamol were classified as having "spirometry consistent with asthma."[23] Participants whose postbronchodilator ratio of FEV_1 to forced vital capacity (FVC) was below the fifth percentile (defined as the lower limit of the normal range) were classified as having "spirometry consistent with COPD." Participants who had minimum increases of 12% and 200 ml in the FEV_1 after bronchodilator use but who still had a postbronchodilator ratio of FEV_1 to FVC that was below the lower limit of the normal range (i.e., those who met the criteria for both conditions) were classified as having COPD.[24]

RANDOMIZATION AND TRIAL PROCEDURES

Randomization was performed with the use of a computer-generated random listing of the two treatment assignments in variable blocks of two or four and was stratified according to site and diagnosis (asthma or COPD). Participants were randomly assigned in a 1:1 ratio to receive treatment provided by a trial pulmonologist and an asthma–COPD educator who were instructed to initiate guideline-based care[23,24] (the intervention group) or by their primary care practitioner (the usual-care group). Centralized assignment of the Web-based randomization was coordinated by the Ottawa Hospital Research Institute.

A copy of the participant's interpreted spirometry report with a diagnosis was provided to each participant and sent to the participant's primary care practitioner, regardless of trial-group assignment. The participants in either group who were current smokers received smoking-cessation counseling and were offered referral to a smoking-cessation program. In both groups, the participants were advised to see their primary care practitioners or, alternatively, to visit an urgent care center or emergency department if they had respiratory symptoms warranting medical attention during the 12-month follow-up period.

The participants in the intervention group attended a scheduled visit with a trial pulmonologist and an asthma–COPD educator on the day of randomization. A second brief visit, either in-person or by means of telephone, with these two health care professionals was scheduled at follow-up month 4. These participants received pulmonologist-issued prescriptions for medications to manage their asthma or COPD according to recommendations from international guidelines.[23,24] Pharmacologic and nonpharmacologic treatment recommendations from the 2017 Global Initiative for Asthma guidelines and the 2017 Global Initiative for Chronic Obstructive Lung Disease guidelines were reviewed with the trial pulmonologists at trial initiation, and the trial pulmonologists were asked to stay current with annual guideline updates and to modify their prescribing accordingly. The trial pulmonologist could provide participants with an action plan to help them manage their asthma or COPD and could refer the participants to pulmonary rehabilitation, if appropriate. The trial pulmonologist and the asthma–COPD educator provided disease education, exercise and weight counseling, and instructions on inhaler technique and allergen and smoke avoidance. Pneumococcal vaccine was provided if indicated, and influenza vaccination was encouraged during influenza season. Current smokers were offered pharmacologic therapy for smoking cessation.

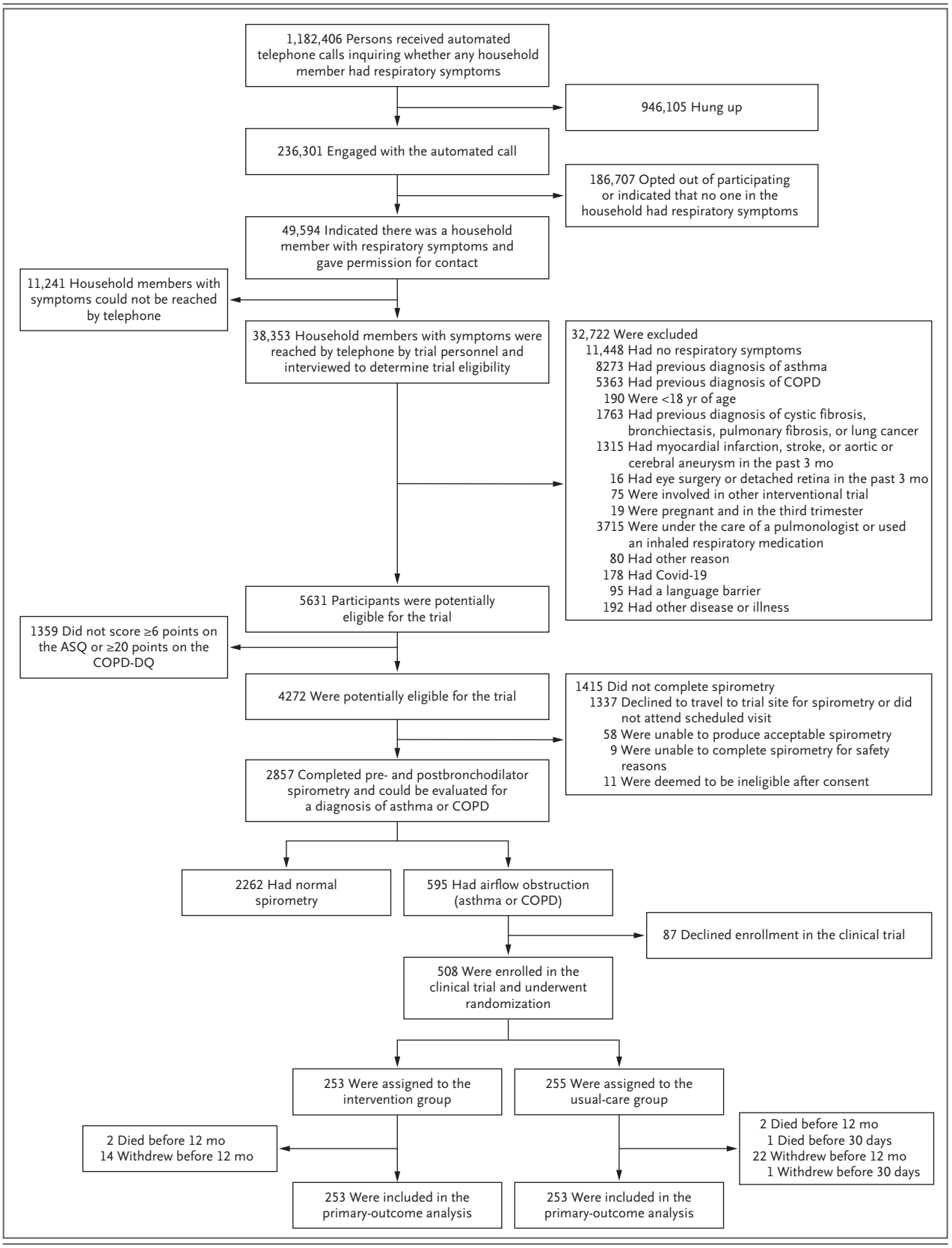

Figure 1 (facing page). Case Finding, Randomization, and Analysis.

COPD denotes chronic obstructive pulmonary disease, and Covid-19 coronavirus disease 2019. Scores on the Asthma Screening Questionnaire (ASQ) range from 0 to 20, with higher scores indicating worse respiratory symptoms. Scores on the COPD Diagnostic Questionnaire (COPD-DQ) range from 0 to 38, with higher scores indicating greater risk of COPD.

OUTCOMES

The primary outcome was the annualized rate of participant-initiated health care utilization for respiratory illness over the 1-year prospective follow-up period. Visits (either in-person or virtual during the coronavirus disease 2019 [Covid-19] pandemic) to a nurse practitioner, a primary care physician, a specialist, or an emergency department and hospitalizations for respiratory-related illness were included as outcome events. Participants received monthly telephone calls from a central trial assessor during the 12 months after randomization to ascertain whether these outcome events had occurred. The assessor was unaware of the trial-group assignments. Although the participants in both groups were told to see their primary care practitioners for care, if a participant in the intervention group contacted the trial pulmonologist or the asthma–COPD educator for immediate care of their respiratory symptoms, the contact was included as an outcome event.

Trial participants in both trial groups underwent repeat spirometry and assessment of the secondary trial outcomes, which were performed at 6 months and 12 months after randomization. Secondary outcomes included changes from baseline to 1 year in disease-specific quality of life, as assessed with the St. George Respiratory Questionnaire (SGRQ[25]; total scores range from 0 to 100, with lower scores indicating better health status and negative changes indicating improvements in disease-specific quality of life [minimal clinically important within-person change, −4 points[26]]); respiratory symptom burden and its effects on daily activities and health status, as assessed with the COPD Assessment Test[27] (CAT; total scores range from 0 to 40, with lower scores indicating better health status and negative changes indicating reductions in symptom burden and its effect on daily activities and health status [minimal clinically important within-person change, −2 points[28]]); prebronchodilator FEV_1 and percentage of the predicted normal FEV_1; and overall quality of life, as assessed with the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36[29]; scores ranges from 0 to 100, with higher scores indicating better health status [no minimal clinically important change has been established for this questionnaire]).

Participant-reported smoking cessation, an additional secondary outcome, was assessed at 1 year and was verified by urinary cotinine measurements when feasible. During the Covid-19 pandemic, data on secondary outcomes were obtained at 6 months and 12 months by means of telephone or virtual encounters rather than in-person visits.

STATISTICAL ANALYSIS

After accounting for premature withdrawal by participants who would not contribute data to the primary analysis, we calculated that a sample of 500 participants would provide the trial with 94% power to detect a clinically important annual incidence rate ratio of 0.50 for participant-initiated health care utilization events at a two-sided type I error of 5%. The incidence rate ratio was estimated with the use of a negative binomial regression model to account for potential overdispersion. The annual incidence was prorated if follow-up ended before 12 months owing to death or premature withdrawal. The absolute change in the FEV_1 over 1 year was analyzed with the use of an analysis of covariance regression model with the baseline FEV_1 included as a covariate.

Analyses were performed according to the intention-to-treat principle. Many participants who had undergone randomization within 1 year before the onset of the Covid-19 pandemic were unable to return to the trial sites to undergo 12-month spirometry; therefore, multiple imputation was performed to estimate missing 12-month spirometry values for these participants with the use of their baseline and 6-month spirometry values.

Because the statistical analysis plan did not include a provision for correcting for multiplicity when tests were conducted for secondary outcomes, the results are reported as point estimates with 95% confidence intervals. The widths of the confidence intervals have not been adjusted for multiplicity and should not be used to infer definitive treatment effects.

Table 1. Characteristics of the Participants at Baseline.*

Characteristic	Intervention (N=253)	Usual Care (N=255)
Age — yr	63.4±13.4	62.8±13.6
Male sex — no. (%)	162 (64)	148 (58)
Body-mass index†	29.6±7.7	30.0±6.5
Diagnosis — no. (%)		
Asthma	123 (49)	127 (50)
COPD	130 (51)	128 (50)
Income in Canadian $ — no. (%)		
<$30,000	28 (11)	33 (13)
$30,000 to $75,000	89 (35)	78 (31)
>$75,000 to $100,000	41 (16)	38 (15)
>$100,000 to $200,000	41 (16)	63 (25)
>$200,000	13 (5)	13 (5)
Data unavailable	41 (16)	30 (12)
Highest level of education — no. (%)		
Less than grade 8	0	3 (1)
Less than grade 12	29 (11)	23 (9)
Graduated from high school	44 (17)	53 (21)
Some college or university	39 (15)	46 (18)
Graduated from college	58 (23)	56 (22)
Graduated from university	73 (29)	69 (27)
Data unavailable	10 (4)	5 (2)
Prebronchodilator spirometry		
FEV_1 — liter	2.25±0.76	2.29±0.81
FEV_1 — % of predicted normal value	76.1±17.5	78.5±18.6
Ratio of FEV_1 to FVC	0.62±0.10	0.63±0.10
Postbronchodilator spirometry		
FEV_1 — liter	2.46±0.80	2.48±0.86
FEV_1 — % of predicted normal value	83.0±17.5	85.2±19.0
Ratio of FEV_1 to FVC	0.65±0.11	0.66±0.10
Change in FEV_1 from prebronchodilator value — %	9.7±7.9	9.1±7.9
Smoking status — no. (%)		
Lifetime nonsmoker	64 (25)	69 (27)
Former smoker	125 (49)	117 (46)
Current smoker	64 (25)	69 (27)
Smoking history		
Mean total pack-years	24.0±25.5	23.2±26.1
Median pack-years (IQR)	20 (0–40)	18 (0–40)
Symptom or quality-of-life questionnaire score‡		
CAT	17.6±7.3	17.6±7.2
SGRQ	39.2±18.7	38.4±17.3
SF-36	61.6±17.3	64.0±17.3

Table 1. (Continued.)

Characteristic	Intervention (N=253)	Usual Care (N=255)
Respiratory medication use — no. (%)		
No medication	205 (81)	224 (88)
SABA as needed	45 (18)	28 (11)
LAMA, LABA, or ICS§	3 (1.2)	3 (1.2)
Severity of baseline airflow obstruction — no. (%)¶		
Mild	90 (36)	99 (39)
Moderate	131 (52)	110 (43)
Severe	15 (6)	18 (7)
Prebronchodilator FEV_1 of ≥100% of the predicted normal value but with ≥12% and ≥200-ml increases in post-bronchodilator FEV_1	17 (7)	28 (11)
Case-finding questionnaire score‖		
Asthma Screening Questionnaire	7.7±3.7	7.6±3.8
COPD Diagnostic Questionnaire	22.6±5.3	22.8±5.6

* Plus–minus values are means ±SD. COPD denotes chronic obstructive pulmonary disease, ICS inhaled glucocorticoid, IQR interquartile range, LABA long-acting beta-agonist, LAMA long-acting muscarinic antagonist, and SABA short-acting beta-agonist.
† The body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ Total scores on the COPD Assessment Test (CAT) range from 0 to 40, with lower scores indicating better health status. Total scores on the St. George Respiratory Questionnaire (SGRQ) range from 0 to 100, with lower scores indicating better health status. Total scores on the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) range from 0 to 100, with higher scores indicating better health status.
§ Participants receiving LAMA, LABA, or ICS were enrolled in error.
¶ Mild airflow obstruction was defined as a prebronchodilator forced expiratory volume in 1 second (FEV_1) of 80 to less than 100% of the predicted normal value; moderate airflow obstruction as a prebronchodilator FEV_1 of 50 to less than 80% of the predicted normal value; and severe airflow obstruction as a prebronchodilator FEV_1 of less than 50% of the predicted normal value.
‖ Scores on the Asthma Screening Questionnaire range from 0 to 20, with higher scores indicating worse respiratory symptoms. Scores on the COPD Diagnostic Questionnaire range from 0 to 38, with higher scores indicating greater risk of COPD.

A data and safety monitoring board conducted two interim analyses for safety events but not for efficacy. A prespecified subgroup analysis was performed to determine outcomes in participants with asthma and COPD separately. Statistical analyses were conducted with the use of Stata software, version 16 (StataCorp).

RESULTS

PARTICIPANTS

The results of the case-finding study are shown in Figure 1.[8] From June 2017 through January 2023, a total of 508 of 595 eligible participants (85%) with undiagnosed COPD or asthma underwent randomization; 253 were assigned to the intervention group and 255 to the usual-care group. The baseline demographic and clinical characteristics of the participants were similar in the two groups (Table 1 and Tables S1 and S2 in the Supplementary Appendix, available at NEJM.org). The representativeness of the trial population is shown in Table S3.

All the participants who were assigned to see a trial pulmonologist and an asthma–COPD educator received the intervention on the day of randomization (Fig. 1). A total of 16 participants in the intervention group and 24 participants in the usual-care group withdrew or died before completing the 12-month trial period. Two participants in the usual-care group did not contribute data toward the primary outcome (one withdrew and one died within 30 days after randomization). Multiple imputation was performed to estimate missing 12-month spirometry values for 78 participants who had undergone randomiza-

tion within 1 year before the onset of the Covid-19 pandemic and were unable to return to the trial sites to undergo 12-month spirometry.

TRIAL CONDUCT

During the 12-month trial period, 232 participants (92%) in the intervention group and 153 participants (60%) in the usual-care group began a new treatment for asthma or COPD. The specific treatments are summarized in Table 2.

Among the 253 participants in the intervention group, action plans were provided to 88 (35%), exercise advice was provided to 155 (61%), weight loss advice was provided to 56 (22%), and 20 (8%) received a referral to a pulmonary rehabilitation program. Of the 64 current smokers in the intervention group, 34 (53%) received pharmacologic treatment for smoking cessation. These outcomes were unknown for the participants in the usual-care group.

OUTCOMES

The annualized rate of participant-initiated health care utilization for respiratory illness (primary outcome) was lower in the intervention group than in the usual-care group (0.53 vs. 1.12 events per person-year; incidence rate ratio, 0.48; 95% confidence interval [CI], 0.36 to 0.63; P<0.001) (Fig. 2). The rate of hospitalization was 0.021 per person-year in the intervention group and 0.030 per person-year in the usual-care group (incidence rate ratio, 0.71; 95% CI, 0.17 to 2.99). There were two hospitalizations for pneumonia and none for COPD exacerbation in the intervention group and one hospitalization for pneumonia and two for COPD exacerbation in the usual-care group. The rate of emergency department visits was 0.069 per person-year in the intervention group and 0.075 per person-year in the usual-care group (incidence rate ratio, 0.92; 95% CI, 0.46 to 1.87). The rate of primary care visits for respiratory illness was 0.36 per person-year in the intervention group and 0.91 per person-year in the usual-care group (incidence rate ratio, 0.39; 95% CI, 0.29 to 0.53). The rate of specialist visits was 0.085 per person-year in the intervention group and 0.096 per person-year in the usual-care group (incidence rate ratio, 0.89; 95% CI, 0.45 to 1.76). The results of a subgroup analysis of the primary outcome with respect to diagnosis (asthma vs. COPD) are shown in Figure 2 and Table S4.

Secondary outcomes are presented in Table 3. At 12 months, the total score on the SGRQ was lower (indicating better health) than the baseline score by 10.2 points in the intervention group and by 6.8 points in the usual-care group (difference, −3.5 points; 95% CI, −6.0 to −0.9). In a post hoc analysis, a reduction of at least 4 points in the SGRQ total score occurred in 64% of the participants in the intervention group and in 56% of those in the usual-care group (odds ratio, 1.38; 95% CI, 0.95 to 2.00). The total score on the CAT at 12 months was lower (indicating better health) than the baseline score by 3.8 points in the intervention group and by 2.6 points in the usual-care group (difference, −1.3 points; 95% CI, −2.4 to −0.1). In a post hoc analysis, a reduction of at least 2 points was observed in 65% of the participants in the intervention and in 54% of those in the usual-care group (odds ratio, 1.57; 95% CI, 1.08 to 2.27). The prebronchodilator FEV_1 increased from baseline to 12 months by 119 ml in the intervention group and by 22 ml in the usual-care group; the intervention effect, as assessed by analysis of covariance, was an increase of 94 ml (95% CI, 50 to 138) as compared with usual care. Changes in the percentage of the predicted normal FEV_1 and in the SF-36 total score are shown in Table 3.

Of the 64 active smokers in the intervention group and the 69 active smokers in the usual-care group, 9 (14%) and 5 (7%), respectively, quit smoking at 12 months. A case of Covid-19 during the 12-month follow-up period was reported by 27 participants (11%) in the intervention group and by 15 participants (6%) in the usual-care group.

SAFETY

Two deaths occurred in each of the trial groups over the 12-month follow-up period. One participant in each trial group died from sudden cardiac arrest, and there was one death from lung cancer in the intervention group and one death from liver failure in the usual-care group. A total of 5 serious adverse events resulting in hospitalization were reported in the intervention group, and 7 such events were reported in the usual-care group (Table S5). A total of 24 adverse events were reported in 21 participants in the intervention group, and 16 adverse events were reported in 14 participants in the usual-care group (Table S6). Adverse events were often related to dizziness

Table 2. Respiratory Treatments Received during the 12-Month Trial Period.*

Treatment†	Intervention (N=253)	Usual Care (N=255)
	number (percent) of participants	
No respiratory treatments during the entire trial period	19 (7.5)	92 (36.1)
SABA only	15 (5.9)	35 (13.7)
LAMA	32 (12.6)	27 (10.6)
LABA	0	11 (4.3)
ICS	56 (22.1)	32 (12.5)
LTRA	1 (0.4)	2 (0.8)
LAMA + LABA	34 (13.4)	6 (2.4)
LABA + ICS	101 (39.9)	53 (20.8)
LAMA + LABA + ICS	29 (11.5)	9 (3.5)
Supplemental oxygen at home	3 (1.2)	1 (0.4)
Short-course systemic glucocorticoid	13 (5.1)	7 (2.7)

* Totals can exceed 100% because some participants had their medications changed during the 12-month trial period. ICS denotes inhaled glucocorticoid, LABA long-acting beta-agonist, LAMA long-acting muscarinic antagonist, LTRA leukotriene-receptor antagonist, and SABA short-acting beta-agonist.
† Most participants who received a LAMA, a LABA, an ICS, or an LTRA also received an as-needed prescription for a SABA.

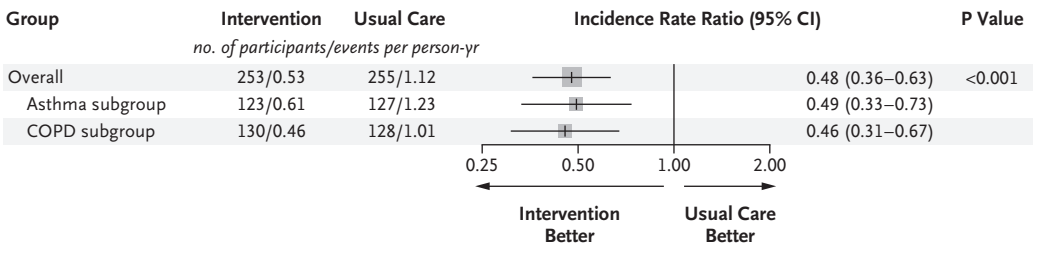

Figure 2. Primary and Subgroup Analyses of the Primary Outcome.
The incidence rate ratio of patient-initiated health care utilization events for respiratory illness over 1 year is shown for the overall cohort (primary-outcome analysis) and for the two subgroups defined according to diagnosis.

or syncope (provoked by spirometry) or muscle cramping (possibly provoked by prescribed respiratory medications).

DISCUSSION

Our trial used targeted case finding to identify symptomatic adults in the community who have undiagnosed COPD or asthma. The results showed that symptomatic persons with previously undiagnosed COPD or asthma who received treatment from a pulmonologist and asthma–COPD educator had less participant-initiated health care utilization for respiratory illness over a 1-year period than those who received usual care from their primary care practitioner. Both trial groups showed clinically important reductions in symptoms and improvements in disease-specific quality of life at 1 year. The results suggest that clinical care of persons with undiagnosed asthma or COPD was associated with health benefit, whether care was provided by a specialist or a primary care practitioner.

In a trial such as ours, the most scientifically rigorous trial design would have kept the usual-care group unaware of their diagnosis for 12

Table 3. Secondary Outcomes.

Outcome	Intervention	Usual Care	Mean Difference (95% CI)*
SGRQ total score†			
At baseline	39.0	38.3	
At 12 mo	28.8	31.5	
Change over 12 mo — points	–10.2	–6.8	–3.5 (–6.0 to –0.9)
CAT total score‡			
At baseline	17.5	17.5	
At 12 mo	13.7	14.9	
Change over 12 mo — points	–3.8	–2.6	–1.3 (–2.4 to –0.1)
Prebronchodilator FEV_1§			
At baseline — % of predicted normal value	76.1	78.9	
At 12 mo — % of predicted normal value	80.8	80.4	
Change over 12 mo — percentage points	4.7	1.5	3.2 (1.5 to 4.9)
SF-36 total score¶			
At baseline	61.9	64.2	
At 12 mo	66.3	66.7	
Change over 12 mo — points	4.4	2.5	1.9 (–0.4 to 4.2)

* The mean between-group difference is the value in the intervention group minus the value in the usual-care group. The widths of the confidence intervals have not been adjusted for multiplicity and should not be used to infer definitive treatment effects.

† Total scores on the SGRQ range from 0 to 100. Negative changes indicate improvements in disease-specific quality of life; the minimal clinically important change within individuals over time is –4 points. Baseline and 12-month data on the SGRQ total score were available for 238 participants in the intervention group and for 228 participants in the usual-care group.

‡ Total scores on the CAT range from 0 to 40. Negative changes indicate reductions in symptom burden and its effect on daily activities and health status; the minimal clinically important change within individuals over time is –2 points. Baseline and 12-month data on the CAT total score were available for 241 participants in the intervention group and for 228 participants in the usual-care group.

§ Baseline and 12-month data on the percentage of the predicted normal prebronchodilator FEV_1 were available for 223 participants in the intervention group and for 198 participants in the usual-care group.

¶ Total scores on the SF-36 range from 0 to 100. Positive changes in the SF-36 indicate improvements in general quality of life. There is no minimal clinically important change established for this questionnaire. Baseline and 12-month data on the SF-36 total score were available for 241 participants in the intervention group and for 228 participants in the usual-care group.

months. This would have allowed a comparison of outcomes between an intervention group of participants who received a diagnosis and treatment and a control group of participants in whom the conditions remained undiagnosed and largely untreated. However, because all the participants were symptomatic, this trial design would have been unethical. We therefore provided all the participants who had undergone randomization, as well as their primary care practitioners, with a printout of the interpreted spirometry report and the diagnosis at the time of randomization. After receiving a diagnosis of COPD or asthma in the trial, many participants in the usual-care group sought treatment for their condition, which probably contributed to improved outcomes in this group. In addition, knowledge of the diagnosis may have changed participant behavior and may have spurred more visits to health care practitioners than would have occurred if the participants had remained unaware of their diagnoses.[30]

Our trial has several strengths. Data on whether early diagnosis and treatment of undiagnosed COPD or asthma are associated with clinical benefits have been lacking. We recruited a randomly sampled cohort of undiagnosed adults with respiratory symptoms through active case finding in the community. The trial evalu-

ated the effect of early diagnosis and treatment on participants' overall health status by assessing symptoms, quality of life, and health care utilization. Although the trial intervention by its nature could not be concealed, the outcome assessors were unaware of the trial-group assignments.

Our trial also has limitations. The trial did not have sufficient power to detect differences in secondary outcomes or within subgroups. Although we conducted random population-based sampling, participation required a registered landline telephone or cell-phone number. Older adults were more likely to volunteer to participate, and this may explain why the mean age of participants was 63 years. Our trial was restricted to the Canadian health care system, so the results may not be generalizable to other systems. The participants in the intervention group received care from a trial pulmonologist and an asthma–COPD educator, and this intervention may not be feasible in health care environments where access to specialists and educators is constrained. Finally, the pulmonologists who delivered the intervention were instructed to follow international guidelines; however, they were not provided with treatment algorithms, and we did not monitor how often the provision of care adhered to guidelines.

Our case-finding approach was designed to randomly sample the communities and was relatively inefficient. The process involved having trial coordinators conduct almost 27,000 telephone interviews with symptomatic persons to ultimately identify 595 adults with undiagnosed COPD or asthma. Future studies could use a less resource-intensive case-finding strategy, perhaps one that is initiated by patients. Persons with unexplained respiratory symptoms could complete a Web-based case-finding questionnaire online, and if their responses yielded a risk score exceeding a specified threshold, they could be referred through a Web-based program for diagnostic spirometry. This approach would empower patients to take an active role in their health management and would make diagnostic spirometry available to those who need it most.

Worldwide, up to 5% of adults may be living with undiagnosed asthma or COPD; many of these adults are symptomatic, and most remain untreated.[31-33] The case-finding symptom questionnaires and spirometry tools that we used in our trial are safe and relatively inexpensive. The clinical care delivered to participants in either trial group is achievable within many health care systems. Although the results favored a pulmonologist-based intervention, the findings in the usual-care group suggest that management of previously undiagnosed asthma or COPD by a primary care practitioner may also be associated with positive changes in a patient's health status 1 year after diagnosis.

In this trial in which a strategy was used to identify adults in the community with undiagnosed asthma or COPD, those who received pulmonologist-directed treatment had less subsequent health care utilization for respiratory illness than those who received usual care.

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APPENDIX

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