The Impact of Case Finding on the Recruitment Yield for COPD Research in Primary Care: An Observational Study

Stefan Markun Thomas Rosemann Kaba Dalla-Lana Claudia Steurer-Stey

Institute of Primary Care, University Hospital of Zurich, University of Zurich, Zurich, Switzerland

Key Words

Chronic obstructive pulmonary disease · Trial recruitment · Case finding · Underdiagnosis · Primary care

Abstract

Background: Recruiting patients for research in primary care is difficult with diseases that tend to remain underdiagnosed, such as chronic obstructive pulmonary disease (COPD). Researchers may consider introducing case finding into patient recruitment, but the impact on recruitment yield is largely unknown. **Objectives:** To assess the impact of case finding on recruitment yield and population characteristics in primary care-based COPD research. **Methods:** For a cluster randomized controlled trial of COPD in primary care, an opportunistic case finding strategy was introduced into patient recruitment, in addition to recruiting patients with previously diagnosed COPD. The recruitment process and performance of the primary care physicians (PCPs) were analysed. The numbers and characteristics of patients identified by case finding were compared with those of patients with previously diagnosed COPD. **Results:** Thirty-five PCPs approached 398 patients and successfully recruited 216 patients during 1 year. The mean number of patients recruited was 6.3 (range 0–16) per PCP. Case finding contributed 71

patients (32.9%) with significantly milder disease, with FEV₁ % predicted +16.7 (95% CI: +11.3 to +22.0), a COPD Assessment Test difference of –4 points (95% CI: –2 to –6; $p < 0.001$), and fewer exacerbations resulting in a higher rate of GOLD class A (85.9 vs. 45.5%; $p < 0.001$). The smoking rate was significantly higher among patients with newly diagnosed COPD (70.4 vs. 48.6%; $p = 0.002$). **Conclusion:** Case finding increased the number of patients recruited by 50%. The COPD patients identified by case finding differed importantly from those with previously diagnosed COPD. Researchers should be aware of COPD underdiagnosis and the potential impact of case finding during patient recruitment.

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Introduction

Research in primary care is complicated by a number of well-recognized factors. For example, the prevalence rates for individual diseases are low, and even the most common chronic conditions account for only a minority of reasons for their encounter [1]. Consecutively, compared to specialized settings, only a small proportion of patients are eligible for studies on specific diseases. Therefore, researchers need to allow for comparably long re-

recruitment periods or need to include large numbers of primary care physicians (PCPs) volunteering to participate in a study in order to achieve sufficient patient recruitment. Unfortunately, trials in primary care most often fail to achieve the intended recruitment goals or need to be prolonged substantially [2]. Moreover, PCPs themselves are difficult to motivate for study participation. Time constraints, a low interest in research in general, and increasing regulatory and administrative requirements are often mentioned as important barriers in this context [3–11].

Strategies supporting the recruitment of patients and/or physicians to research projects in primary care have been developed and assembled [12]. Still, data on the effectiveness of these strategies are limited, and recruitment remains an unpredictable but critical stage in primary care-based research [13, 14]. To facilitate patient recruitment, electronic medical records can be used, and such strategies will become increasingly feasible with their ongoing implementation also in primary care. It is only logical, however, that such records can only identify patients with previously diagnosed diseases. Therefore, such a sampling method may be unreliable with diseases that tend to be underdiagnosed in the healthcare setting of the research project.

Chronic obstructive pulmonary disease (COPD) is of indisputable epidemiologic importance given its high and increasing prevalence and socioeconomic burden and the loss of quality of life in affected patients [15, 16]. Despite the fact that the majority of patients with COPD are treated in primary care, clinical research on COPD concentrates on secondary or tertiary care, leaving the majority of the affected population underrepresented in trials [17–19]. Moreover, the selection criteria for COPD commonly used in trials admit only a minority of the affected population, and their representativeness of ‘real-life’ COPD patients has been questioned as well [20].

Research in primary care is needed to answer the question of the external validity of trials conducted on COPD in specialized settings. However, COPD is known to be widely underdiagnosed in primary care, which creates a further obstacle to COPD research in this important healthcare setting [21, 22]. To address the issue of COPD underdiagnosis, several case finding strategies have been proposed and opportunistic strategies (focusing on the at-risk population during a routine practice visit) are thought to be efficient [23].

In this study we describe the recruitment process of a cluster randomized trial of COPD in primary care where a case finding strategy has been implemented. The aim of

the study was to assess recruiting performance and the contribution of case finding to the total number of patients recruited as well as to compare the characteristics of the subpopulation with COPD identified by case finding with those of the subpopulation previously diagnosed with COPD.

Methods

Study Design, Setting, Registration, and Ethics Statement

This observational study was conducted with data collected during the recruitment process and with baseline data from the Improving Care in Chronic Obstructive Lung Disease (CAROL) study. It is a cluster randomized multicentre trial conducted in primary care practices located in the 2 largest cities of the Canton of Zurich, Switzerland. The trial has been registered at ClinicalTrials.gov (NCT01921556) and the trial’s study protocol has been published [24]. In brief, the trial’s intervention aimed at improving chronic care for COPD patients in primary care. The intervention was based on the Chronic Care Model and consists of a multifaceted training for PCPs and their practice assistants in COPD care [25].

The local ethics committee approved the study (Ethics Committee of the Canton of Zurich, reference No. KEK-ZH 2013-0189), informed consent was obtained from all participating subjects, and the study was conducted according to tenets of the Declaration of Helsinki and good clinical practice guidelines.

Recruitment of PCPs

According to the trial’s power calculation, our goal was to recruit at least 30 PCPs (each recruiting 8–10 patients). About 1,300 PCPs practicing in the trial’s locations were sent a formal letter from our institute and the Cantonal Department of Health in July 2013. Additionally, the study was presented at peer group meetings of regional PCP networks. All PCPs were given a brief description of the study including the study aim and eligibility criteria as well as a prominent description of the requirements and benefits of study participation (incentives were CHF 50 per recruited patient and CHF 200 compensation for those randomized to the intervention group involving participation in the teaching sessions). Interested PCPs and their practice assistants were invited to kick-off meetings where the complete background information and study aims were presented. After the kick-off meetings, we enrolled 35 PCPs and their practice assistants, who all completed training in how to conduct and interpret spirometry results according to international standards [26].

Case Finding Strategy and Implementation of Patient Recruitment

We chose our case finding strategy to be to opportunistically approach consecutive patients in routine practice visits who were aged at least 45 years and who were smokers or ex-smokers with at least 10 pack-years. With this feasible strategy we expected to newly detect COPD in at least 20% of the individuals approached [27]. In addition to the criteria derived from case finding, the inclusion criteria for participating in the CAROL study were available informed consent and diagnosis or confirmation of airflow obstruction.

tion ($FEV_1/FVC < 0.7$) in spirometry. The exclusion criteria were visiting the practice for emergency purposes only, insufficient German language skills, asthma or hay fever, or a co-occurring disease with an estimated life expectancy of less than 6 months. The case finding strategy and the following recruitment process were instructed and exemplified in a teaching session after spirometry training. The PCPs entered the patient recruitment period after completion of their training.

The patient recruitment period started in December 2013 (after the PCPs had completed spirometry training) and ended in January 2014. To support recruitment in practices, we followed recommended principles of minimal administrative complexity and disruption, giving feedback (monthly e-mails to PCPs with benchmarking recruitment performance and 3-weekly outreach calls to practice assistants) and placing reminders on desks in practices [12]. Furthermore, we supported the PCPs in their interpretation of specific spirometry results if needed.

Measures and Data Collection

The PCPs completed a questionnaire about themselves at their own enrolment in the study. The questionnaire comprised sociodemographic questions, questions about medical specialization, full- or part-time working, practice organization, and the estimated number of patient contacts each day.

For each recruited patient, the following set of data was collected by the PCP: time of COPD diagnosis (identified by case finding or previously), spirometry results, dyspnoea according to the modified British Medical Research Council (mMRC) Dyspnoea Scale [28], comorbidities, smoking status, COPD medication, and health service utilization because of COPD.

The patient questionnaire was self-administered and piloted with 6 COPD patients in order to improve comprehensibility. The following set of data was collected: sociodemographic information; smoking habits and attitudes; COPD management recommendations and therapies received from the PCP during the previous year (i.e. process indicators, primary endpoint of the CAROL trial); current COPD symptoms; exacerbations during the previous year; and actions taken if exacerbations occurred, including health service utilization and the COPD Assessment Test (CAT) [29]. The PCPs and patients received prepaid envelopes for sending the completed questionnaires directly to the study centre. The PCPs and patients had no access to each other's answers.

Outcomes

The outcomes assessed in this study were: (1) PCP recruiting performance; (2) the contribution of case finding to the total number of patients recruited; and (3) the characteristics of the recruited patients and differences between the COPD patients identified by case finding and those with previously diagnosed COPD.

Statistical Analysis

We report counts and proportions for categorical data as well as means and standard deviations (SD) or medians and interquartile ranges (IQR), as appropriate. We compared groups by applying bivariate statistics – using the t test or Wilcoxon rank-sum test for continuous data and the χ^2 test or Fisher's exact test for nominal data – and report p values or 95% confidence intervals (95% CI) when appropriate. The minimum clinically important difference in the CAT was defined as 2 points [30]. Missing values were enquired from the respondents, and completed accordingly if available.

Results

Characteristics and Recruiting Performance of the PCPs

Thirty-five PCPs from 21 different practices entered the patient recruiting period. Recruitment of these PCPs took 9 months. The PCPs' median age was 49.7 years (IQR 42.8–58.3), and 26 (74.3%) were male. Thirty-one PCPs (88.6%) worked in group practices together with 1–5 colleagues (not necessarily participating in the study). Twenty-three (65.7%) were specialized in general medicine, and 13 (37.1%) in internal medicine. Twenty-three (65.7%) of the PCPs reported working full time; 60% was the lowest part-time assignment. On average, the PCPs estimated to see 24.6 patients (SD 5.9) on a typical working day.

During the 1-year patient recruitment period, on average each PCP approached 11.4 patients (SD 8.6), with considerable variability between the individual PCPs ranging from 0 to 31 patients. Of a total of 398 eligible patients, 51 (12.8%) declined study participation or spirometry testing. Of the 147 consenting patients with previously diagnosed COPD, 2 were excluded because obstruction was not confirmed on spirometry. Of the 200 consenting patients who were identified via the case finding criteria, 71 (35.5%) had obstruction on spirometry. Therefore, from the total of 398 patients approached, the PCPs recruited 216 (54.3%). The flow chart of the recruitment process is shown in figure 1.

Each PCP recruited 6.3 patients (SD 4.5, range 0–16) on average. The maximum of recruited patients per month was reached in the 4th month after the beginning of the study, followed by a rapid decline with stabilization after 9 months. The recruiting performance over time is shown in figure 2.

Contribution of Case Finding to the Total Number of Patients Recruited

Among the 216 recruited patients, 145 (67.1%) had a previously diagnosed COPD and the median duration of illness was 5 years (IQR 2–8). Of the 200 patients who underwent spirometry without having a previous COPD diagnosis (case finding population), 71 had COPD. This corresponded to a 35.6% specificity of case finding among individuals without previously diagnosed COPD. These 71 individuals identified by case finding composed 32.9% of the study population; case finding therefore increased the overall recruitment yield by 49.0%.

Fig. 1. Flow chart of the recruitment process.

Fig. 2. Overall number of COPD patients (n = 216) recruited per month by the 35 PCPs.

Patient Characteristics and Differences between Subpopulations

Overall, the included patients were 68.1 (SD 9.7) years old on average, and 59.5% were male. The clinically most important differences between the subpopulation identified by case finding and that with a previous COPD diag-

nosis appeared in the severity of airflow limitation as reflected in FEV₁, which was +16.7 (95% CI: +11.3 to +22.0) percentage points higher in the subpopulation identified by case finding. Also the between-group difference in the CAT summary score was clinically significant, indicating milder symptoms and impairment in the subpopulation identified by case finding – i.e. a between-group difference in medians of –4 points (95% CI: –2 to –6). Moreover, a lower proportion of patients having 2 or more exacerbations or at least 1 exacerbation with hospitalization in the previous 12 months was noted among this subpopulation (5.6 vs. 23.4%; p = 0.001). In terms of the updated GOLD guidelines [26] this translated into a significantly higher rate of GOLD classification A (85.9 vs. 45.5%; p < 0.001) in the subpopulation with a COPD diagnosis via case finding. Furthermore, the proportion of active smokers was higher in the subpopulation with case finding-identified COPD (70.4 vs. 48.6%; p = 0.002). Chronic comorbidities were more common in the subpopulation with a previous COPD diagnosis (mean number of chronic comorbidities: 1.2 vs. 0.8; p = 0.01). A more detailed comparison of the patient characteristics is given in table 1.

Table 1. Characteristics of the total study population (n = 216) and comparison of the characteristics of the subpopulations with previously identified COPD and COPD identified by case finding

Variable	Total population		COPD previously diagnosed		COPD identified by case finding		p value previous vs. case finding-identified COPD
Total number of patients	216	100%	145	100%	71	100%	
Age, years	68.1	(9.7)	69.96	(9.2)	64.32	(9.7)	<0.001 ¹
Sex – male	128	59.5%	84	58.3%	44	62.0%	0.609 ²
BMI	25.76	(5.34)	25.74	(5.6)	25.81	(4.9)	0.924 ¹
GOLD Class							<0.001 ³
A	127	58.8%	66	45.5%	61	85.9%	
B	22	10.2%	20	13.8%	2	2.8%	
C	41	19.0%	35	24.1%	6	8.5%	
D	26	12.0%	24	16.6%	2	2.8%	
Severity of airflow limitation by FEV ₁ % predicted							<0.001 ³
Mild (≥80%)	56	26.0%	25	17.4%	31	43.7%	
Moderate (≥50 and <80%)	115	53.5%	78	54.2%	37	52.1%	
Severe (≥30 and <50%)	37	17.2%	34	23.6%	3	4.2%	
Very severe (<30%)	7	3.3%	7	4.9%	0	0.0%	
FEV ₁ % predicted	66.06	(20.15)	60.55	(18.5)	77.23	(18.8)	<0.001 ¹
CAT impact of disease							0.005 ³
Low (<10 points)	80	42.6%	44	34.4%	36	60.0%	
Medium (10–20 points)	89	47.3%	67	52.3%	22	36.7%	
High (21–30 points)	17	9.0%	15	11.7%	2	3.3%	
Very high (>30 points)	2	1.1%	2	1.6%	0	0.0%	
CAT summary score	11	7–16	12	8–18	8	5–12	<0.001 ⁴
mMRC Dyspnoea Scale score							<0.001 ³
0	51	24.1%	21	14.7%	30	43.5%	
1	91	42.9%	61	42.7%	30	43.5%	
2	50	23.6%	41	28.7%	9	13.0%	
3	16	7.5%	16	11.2%	0	0.0%	
4	4	1.9%	4	2.8%	0	0.0%	
Current smoking	120	55.6%	70	48.6%	50	70.4%	0.002 ²
Exacerbation at inclusion	33	17.3%	30	22.4%	3	5.3%	0.004 ³
Comorbidities							
Diabetes	29	13.8%	23	16.3%	6	8.7%	0.133 ²
Hypertension	112	53.1%	76	53.9%	36	51.4%	0.735 ²
Coronary heart disease	37	17.7%	31	21.8%	6	9.0%	0.023 ²
Congestive heart failure	20	9.5%	17	11.8%	3	4.5%	0.091 ³
Depression	41	19.8%	28	19.9%	13	19.7%	0.978 ²

Values are presented as n and %, means (SD), or medians with IQR. ¹ Welch's two-sample t test. ² Pearson's χ^2 test. ³ Fisher's exact test for count data. ⁴ Wilcoxon's rank-sum test.

Discussion

Main Findings

Case finding substantially supported recruitment by contributing 1 out of 3 patients to the total study population. The population identified by case finding differed significantly from the population with previously diag-

nosed COPD and notably influenced important characteristics of the total population recruited.

Interpretation of the Findings in Relation to Previously Published Work

In population-based studies, patients with undiagnosed COPD have been found to outnumber patients with

diagnosed COPD, and also to have higher current smoking rates and have less severe limitations of airflow. Furthermore, considerable variation was found between international healthcare systems, with the proportion of undiagnosed versus diagnosed individuals ranging from 50 to 98% [21]. In primary care, proportions of undiagnosed COPD patients are similarly variable, and undiagnosed individuals have consistently been shown to be less symptomatic [22, 27, 31–34]. The results from our study are in line with previous epidemiological research, as we identified a relevant proportion of patients with undiagnosed COPD in primary care in significantly earlier stages of the disease. Concerning case finding, we identified an undiagnosed case of COPD in every 3rd patient fulfilling the predefined case finding criteria. This detection rate was above our expectations; however, our case finding criteria might have had a higher specificity – since older age and a minimum number of pack-years were included – than the criteria for opportunistic case finding recently described, which showed a detection rate around 20% [23].

The clinical importance of case finding and early detection of COPD consists in creating opportunities for early preventive interventions, especially if modifiable risk factors can be targeted. In this context, smoking cessation is the intervention with the highest beneficial impact on disease progression, and specific recommendations on increasing smoking cessation rates in COPD patients exist [26, 35]. In primary care, where most COPD patients are in early disease stages, the potential of preventive measures is highest. Here, in addition to clinical aspects, we describe important methodological implications for case finding in COPD research. Knowing about the difficulties of implementing patient recruitment in primary care, researchers are naturally tempted to make use of electronic medical record searches in order to identify eligible cases. Such approaches are already followed and thought to generate representative patient samples [36, 37]. Without knowledge about COPD underdiagnosis in the studied population, however, such strategies risk producing biased samples, since they might miss large proportions of the population they intend to represent. In our setting, an approach only relying on previously identified cases would most likely have led to recruitment of a different population. Of particular concern is the fact that differences appeared in the most important prognostic variables – namely, airflow limitation and smoking status. Underdiagnosis of COPD can therefore be an important source of sampling bias by systematically occurring in individuals in milder disease stages. Since the diagnostic performance for COPD is known to be setting specific,

recruitment methods drawing only on previously identified cases of COPD are likely to produce heterogeneous patient samples in different healthcare settings. Consecutively, populations are difficult to compare across studies; moreover, they still not represent the majority of the diseased population even if performed in primary care.

Strengths and Limitations of the Study

To our knowledge, this is the first report emphasizing the implications of case finding for recruitment of COPD patients in primary care-based research. This paper described the advantages of case finding for research purposes and contributes to the study of research methodologies in primary care and COPD. Furthermore, this is the first comprehensive report giving detailed insights into the recruitment strategy and recruitment outcomes of a primary care-based cluster randomized study on COPD, thus supporting researchers embarking on similar research projects.

The main limitation of this study is its observational design. We can only assume that patients with undiagnosed COPD truly would not have gained access to our total study population without the introduction of case finding. We are, however, confident that no similarly relevant proportion of patients with undiagnosed COPD would have been identified. Furthermore, the recruitment of PCPs themselves proved to be difficult and progressed slowly. We have to assume that the participating PCPs represent a comparably highly motivated sample with a higher interest in COPD, research per se, or both. Therefore, the implementation of case finding – and also its yield – may function differently in non-research environments; however, in both clinical and research settings, volunteer bias occurs.

Implications for Future Research, Policy, and Practice

For future research on COPD in primary care, we recommend that diagnostic performance should at least be measured by implementing a case finding protocol before relying on electronic medical record searches only. This is how the risk of bias from underdiagnosis and selective recruiting can at least be assessed if researchers are still to rely on electronic medical record-based recruitment. There is little consensus, however, on which of the specific case finding strategies is best. In this study, the efforts of implementing an opportunistic case finding strategy were moderate and consisted of raising the awareness of the disease among PCPs as well as strengthening their diagnostic skills in spirometry testing. Opportunistic case finding is already considered to be needed in everyday clinical practice, and we believe that COPD research in

primary care would benefit from it as well – not only by facilitating notoriously difficult recruitment processes, but also by increasing the representativeness and comparability of the patient samples selected.

Conclusions

Opportunistic case finding increased the number of recruited patients by almost 50%. The COPD patients identified by case finding differed importantly from those with previously diagnosed COPD. Researchers should be aware of the impact of case finding during recruitment, especially in healthcare settings with high rates of COPD underdiagnosis.

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Authors' Contributions

C.S.-S., T.R., and K.D.-L. conceived and designed the study; S.M., C.S.-S., and K.D.-L. acquired the data; S.M. and C.S.-S. analysed and interpreted the data and drafted the manuscript to be revised critically by T.R. and K.D.-L.; all authors approved the final version for publication and agreed to be accountable for all aspects of the study.

Financial Disclosure and Conflicts of Interest

S.M., T.R., and K.D.-L. declare that no competing interests exist. C.S.-S. received fees for participation in advisory boards organized by Boehringer Ingelheim, AstraZeneca, and Novartis. C.S.-S. provided consultancy to or gave talks about the topic at Boehringer Ingelheim, AstraZeneca, and GlaxoSmithKline.

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