Early Diagnosis and Treatment of COPD: The Costs and Benefits of Case-Finding

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Undiagnosed COPD: A Global Problem

In 2020, the prevalence of clinician-diagnosed chronic obstructive pulmonary disease (COPD) amongst US adults aged ≥ 18 years was 5.6% (95% CI 5.2–6.2) (1). This proportion is likely to be just 'the tip of an iceberg', as studies from across the world suggest that as many as 70-90% of individuals with COPD remain undiagnosed (2). The 2007-2012 US National Health and Nutritional Examination Survey found obstructive lung disease in 13.4% of randomly selected American adults, however 71% were undiagnosed (3).

A collaborative study assessed the prevalence of undiagnosed COPD in 27 countries. Among 30,874 participants the prevalence of COPD ($FEV_1/FVC < LLN$), was 9.7%, and 81.4% of COPD cases were undiagnosed (4). The problem of COPD underdiagnosis was worse in low and middle-income countries (LMIC). Centers in Turkey, India, Nigeria, Philippines, Colombia, Nepal, Peru, and Uganda reported that more than 90%-95% of COPD cases were undiagnosed (4, 5) .

The Clinical and Societal Burden of Undiagnosed COPD

Individuals with undiagnosed COPD are afflicted by poor quality of life, suffer from exacerbations like those seen in patients with diagnosed COPD, and are at increased risk of death (6, 7). In addition, their respiratory symptoms lead to work absenteeism, productivity loss and consumption of health care resources (8). This perspective will review the burden of disease in people with COPD who have not been diagnosed, consider why a diagnosis is not made or delayed, and summarize how patients could be identified and diagnosed earlier.

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Symptoms, and Health-Related Quality of Life (HRQOL)

A Canadian study of individuals with symptomatic undiagnosed COPD identified via case-finding, compared to age-matched controls, showed that adjusted mean between-group differences in COPD Assessment Test (CAT), St. George Respiratory Questionnaire (SGRQ), and Short Form Survey 36 total scores were 13, 33, and -20 points respectively (6). These values exceed the established minimal clinically important differences for these questionnaires. The study concluded that undiagnosed COPD was associated with greater symptom burden, poorer disease-specific HRQOL, and poorer overall general health status compared to age-matched control subjects (6). Similar findings have been reported by Miravitlles who also showed poorer HRQOL and reduced activities of daily living in Spanish individuals with undiagnosed COPD (9).

Exacerbation events and healthcare utilization

Individuals with previously undiagnosed COPD, discovered via population-based screening with spirometry, were followed for a median of 6.1 years. Their age and sex adjusted hazard ratios for exacerbations and pneumonia were 15.5 (95% CI: 11.0–21.8) and 2.8 (95% CI: 2.4–3.3) respectively, compared with individuals without COPD (7). Other authors reported more physician visits for breathing difficulties in the previous year in individuals with undiagnosed

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COPD compared to healthy controls (26% vs 9%, P <0.001), without differences in emergency department visits or hospitalizations for respiratory illness (6).

The CanCOLD study found that the exacerbation rate in undiagnosed, untreated individuals was about half that of individuals diagnosed with COPD (0.30 exacerbation events/patient-year vs. 0.63/patient-year), however undiagnosed individuals used health services to treat exacerbation events in an equivalent manner as individuals who had received a previous COPD diagnosis (10). The authors concluded that people with undiagnosed COPD contribute greatly to the health care burden of COPD.

Work Absenteeism and Productivity

Gerstein reported that individuals with undiagnosed COPD discovered via case-finding had significantly higher work absenteeism (missing work due to a respiratory illness during the previous week) compared to healthy controls (14% vs. 2%, respectively), as well as greater losses in both work productivity and regular daily activities. Interestingly, work absenteeism or productivity was similar between undiagnosed and previously diagnosed COPD patients (6).

De Sousa Sena reported that work absenteeism was higher in subjects with physician-diagnosed COPD compared to those with undiagnosed COPD (14.6% vs 5.7%). However, presenteeism (the act of attending work while sick, resulting in decreased work quality or quantity) and overall work productivity losses were similar among the groups. Individuals with undiagnosed COPD who had a high symptom burden (CAT ≥ 10) were more likely to have experienced work productivity loss (8).

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Mortality

In Denmark, subjects with undiagnosed, symptomatic COPD had an age and sex adjusted hazard ratio for death from respiratory causes of 4.3 (95% CI: 2.8–6.7), and 2.0 (95% CI: 1.8–2.3) for death from any cause, compared with individuals without COPD (7). An analysis of U.S. data demonstrated that among people with undiagnosed COPD, the risk for mortality over 20 years of follow-up was increased (hazard ratio 1.23; 95% CI 1.08–1.40) relative to those without COPD (3).

Why does COPD go Undiagnosed until Disease is Far Advanced?

Clinical diagnosis of COPD is often delayed in many patients until disease is far advanced. Indeed, a study using British Columbia's administrative data records showed that 44% of incident cases of COPD detected from 2001 to 2010 were only first diagnosed with COPD when they had a COPD-related hospitalization (11). An overview of potential patient, healthcare-provider, and healthcare-system factors that may be associated with underdiagnosis of COPD is shown in Figure 1.

Patient related factors

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Some patients with COPD may go undetected because of under-recognition and/or under-reporting of symptoms. COPD patients may adapt their activities to minimize their respiratory symptoms, deciding that their symptoms do not merit a discussion with their physician (12, 13). Chronic breathlessness may be attributed to a normal, inevitable part of aging (14). Furthermore, some patients may be reluctant to discuss their respiratory symptoms due to shame associated with smoking (15). In one sample of Dutch adults, only 34% of participants with undiagnosed obstructive lung disease had previously discussed their symptoms with a physician (16).

Failure to report respiratory symptoms is not the only factor accounting for under-diagnosis. A study evaluating undiagnosed symptomatic obstructive lung disease (detected through active case-finding) showed that 69% of undiagnosed participants reported that they had previously discussed their respiratory symptoms with a physician, and 18% had been given an alternative diagnosis, other than obstructive lung disease, to explain their respiratory symptoms (17).

Some underdiagnosed COPD may be attributable to milder disease or milder impairment, especially if undiagnosed COPD is found via population-based screening rather than active case-finding of symptomatic individuals. Colak and colleagues showed that among subjects with undiagnosed COPD found via population-based screening 71% were symptomatic, however, the majority (73%) had minimal symptoms (mMRC <2) (7). Similarly, a Spanish population-based study found that individuals with diagnosed COPD had more severe airflow obstruction, higher cumulative tobacco consumption, and more severely impaired HRQOL compared with undiagnosed subjects (9).

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Health care provider factors

Underdiagnosed COPD may also be associated with systematic health system deficiencies at the healthcare provider level (18). Primary care practitioners have limited time, lack of financial incentives, and multiple competing priorities (18). The effectiveness of COPD therapies in mild disease may be underestimated, and consequently therapeutic nihilism in primary care may play a role in underdiagnosis (18). Diagnosis may also be limited by physicians' sometimes poor understanding of COPD diagnostic criteria, inadequate training in the use and interpretation of spirometry, poor reimbursement for the test, and by poor access to diagnostic spirometry in many communities (19, 20).

Healthcare system factors

Studies from high-income countries indicate that spirometry is under-utilized. In Sweden, only a third of patients with physician-diagnosed COPD had their diagnosis confirmed with spirometry (21). A population study of all individuals newly diagnosed with COPD in Ontario, Canada, showed that only 36% had received spirometry (19). Another Canadian study showed that those with undiagnosed symptomatic COPD were less likely to have undergone spirometry or to have been referred to a specialist compared to subjects with diagnosed COPD, suggesting that underdiagnosis is associated with inadequate investigations and specialist referral for respiratory symptoms (17). Deficiencies in provision of respiratory health care may be more acute in LMIC (22). In Latin America, data from the PLATINO study revealed that only 16% of subjects with undiagnosed COPD reported ever undergoing spirometry (23).

COPD diagnosis is based on post-bronchodilator (post-BD) spirometry however measurement of post-BD airflow adds extra time and complexity to the test, and this may

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potentially discourage the use of diagnostic spirometry. An analysis of 10,192 tobacco-exposed subjects from the COPDGene study showed that both pre- and post-BD spirometry were associated with dyspnea, radiographic emphysema, gas trapping and impaired exercise capacity (24). The predictive value of pre- and post-bronchodilator spirometry for exacerbations, change in FEV_1, dyspnea, and exercise capacity were relatively similar, but post-BD measures better predicted mortality. Based on this evidence, the latest GOLD document states that if pre-bronchodilator spirometry does not show airflow obstruction, then a post-BD measurement is not necessary (25). This may help mitigate a perceived barrier to spirometry. However, if airflow obstruction is found on pre-bronchodilator spirometry, then diagnosis of COPD should be confirmed with post-BD measurements.

Many health care settings, especially in LMICs, do not have guidelines for the management of COPD (26), and even where guidelines exist there are significant challenge to their effective implementation (27). In Latin America, patients who did not visit a physician or who only attended a general practitioner, had greater risk of undiagnosed COPD compared to those who saw a specialist (28) The utility of diagnosis may be de-prioritised where there are problems with access to affordable interventions, leaving much unmet need (29).

Early diagnosis of COPD- Screening vs Case-Finding:

Although no consensus definition exists for ‘early diagnosis of COPD’ it is generally accepted that early diagnosis happens when an individual undergoes targeted assessment for COPD, and the disease is identified prior to a conventional diagnosis being made by the

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individual's healthcare professionals (30, 31). Early diagnosis can be potentially achieved by either screening or case-finding, and differentiating between these two methodologies is important. The goal of screening is to detect unrecognized COPD in apparently healthy individuals. As such, screening is performed in the general population, and involves testing mostly asymptomatic individuals, potentially based on demographic factors (such as age or smoking history). This approach has been shown to be relatively low yield and cost inefficient for detecting unrecognized COPD. For these reasons, the US Preventive Services Task Force (USPSTF) recommends against screening for COPD in asymptomatic individuals (32). In contrast, case-finding involves an assessment of an individual's respiratory symptoms and disease risk factors to determine the need for further testing. Case-finding is a potential strategy for identifying undiagnosed individuals at high risk of COPD to allow earlier identification of disease and to direct resources to these individuals.

Active vs. Opportunistic Case-Finding:

The objective of targeted case-finding is to detect the largest possible number of cases in the community through assessment of at-risk individuals who present with symptoms (33). Case-finding approaches include active or opportunistic case-finding, and the two differ based on the approach and the target population. Active case finding involves proactively searching for individuals at higher risk of the condition, often based on presence of symptoms. In active case-finding, respiratory symptoms and risks for COPD are elicited from the individual via questionnaire, and based on their responses if the individual exceeds a pre-set threshold, they are

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targeted to receive spirometry. In contrast opportunistic case-finding involves a passive approach to case identification, and screening of individuals occurs when they present themselves for healthcare services for reasons unrelated to the condition being screened for. Opportunistic case finding doesn't focus on a specific group or population. Instead, it captures cases as they arise in the general patient population during routine healthcare encounters.

An active case-finding strategy targeting symptomatic individuals with risk factors for COPD was more effective at detecting new COPD cases than opportunistic case-finding conducted in the general patient population during routine healthcare encounters (adjusted OR 2.34), and was more cost-effective (£333 vs £376 per case detected, respectively (34). However, opportunistic case finding conducted in specific target populations (such as smokers being screened for lung cancer), has been shown to be effective and relatively inexpensive (35, 36).

Case-Finding Tools:

The optimal strategy for identifying undiagnosed COPD remains an area of controversy. Different tools have been assessed for COPD case-finding (questionnaires, hand-held devices, or combination of tools) with wide heterogeneity among them.

Questionnaires

Several COPD risk questionnaires have been developed and validated in different populations. Among them the COPD diagnostic questionnaire (CDQ), COPD-Population Screener (COPD-PS), Lung Function Questionnaire (LFQ) questionnaire, COPD assessment in primary care to identify undiagnosed respiratory disease and exacerbation risk (CAPTURE) and PUMA study questionnaire (PUMA) are the most widely used (37-53). All include the following

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elements: age, smoking history, and respiratory symptoms. In addition, some include other items such as body mass index (BMI), allergic history, sex, previous use of spirometry, and history of acute respiratory diseases. Table 1 shows the performance results (area under the curve; AUC) reported for some questionnaires. The UCAP questionnaire detects both undiagnosed COPD and asthma (53). The PUMA and COLA questionnaires were developed in LMICs setting and had similar performance to other questionnaires when they were used in LMICs settings (5). The evidence indicates that all diagnostic case-finding questionnaires are valuable tools to discriminate between subjects with or without COPD (37-53).

A meta-analysis aimed to assess the best practice in COPD case-finding in a primary care setting found that the LFQ was a slightly stronger tool to identify high-risk individuals who require diagnostic evaluation for COPD than the CDQ and the COPD-PS questionnaires (54). A study from China showed that the LFQ and the COPD-PS were those that showed the highest diagnostic accuracy and the CAPTURE the lowest. Except for CAPTURE, the other five questionnaires demonstrated moderate diagnostic accuracy (55). Another Chinese study in primary care settings showed that PUMA as a screening tool performed better than CDQ and COPD-PS (AUC: 0.75 vs 0.66 and 0.61 respectively) (42).

Hand-held Airflow Measurement Devices

Devices such as the maximum expiratory flow (PEF) and micro-spirometers (COPD-6 and the Piko-6) have been widely tested. In general, studies have reported that micro-spirometers have high accuracy in the diagnosis of COPD, therefore, they could be of great diagnostic help in primary care settings with limited resources. Table 1 shows the AUC reported for COPD-6 and Piko-6 using the FEV_1/FEV_6 ratio.

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A meta-analysis showed an overall AUC of micro-spirometers (including COPD-6 and Piko-6) of 0.84 (95% CI: 0.80–0.89). Additionally, it showed that micro-spirometers were the most accurate tools for COPD diagnosis compared with diagnostic questionnaires (19). Another meta-analysis reported that the pooled AUC of portable spirometers was 0.91 (0.89–0.94). The accuracy of PIKO-6 was higher (0.95) than that of COPD-6 (0.91) and PEF (0.82) (43).

Combining Questionnaires with Hand-held Airflow Measurement Devices

The use of combined tools has shown better diagnostic accuracy than either tool alone. Table 1 shows results of studies that have assessed the accuracy of combining tools for COPD diagnosis (44, 50, 52, 56).

Soriano et. al. showed that the combination of COPD-PS and PEF (AUC 0.76) presented greater diagnostic accuracy than COPD-PS alone (AUC 0.71) or PEF alone (AUC 0.66). Case-finding for COPD using COPD-PS + PEF led to a 90% reduction in the number of spirometry tests performed (56). Another study showed that the use of the combination of the CAPTURE questionnaire with a PEF device yielded a higher AUC (0.95) in comparison with the CAPTURE questionnaire alone (0.93) (50).

Taken together, these findings suggest that the combined use of a questionnaire and a hand-held device is a more effective strategy for identifying individuals at increased risk for COPD, although questionnaires used alone are still valuable tools to predict COPD.

Other potentially sensitive tools for COPD case finding, such as DLCO, oscillometry, and nitrogen washout, need further research. To date, no prospective study has compared the diagnostic

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accuracy of these tools with screening questionnaires or hand-held flow devices and the practicality of using such approaches in community settings needs to be assessed.

Potential target populations for COPD case-finding

Since both COPD and lung cancer share similar risk factors, using a single test to simultaneously target early diagnosis of both diseases may be cost-effective. Mets et al. reported that low dose CT (LDCT) scans for lung cancer screening could identify participants with COPD. The diagnostic model showed an AUC of 0.87 for participants with symptoms and 0.78 for those without symptoms (35). In some LDCT lung cancer screening studies the prevalence of COPD within the study cohorts was between 19% and 57%, and between 49 to 86% of these individuals were undiagnosed (36, 57, 58). Emphysema prevalence established by CT scan in those with known and undiagnosed COPD was 73% and 68%, respectively, suggesting that imaging-confirmed emphysema can help find undiagnosed COPD cases in current or former smokers who are at risk for lung cancer (36, 57).

Tang et al. evaluated a residual network-based software pipeline for identifying people with COPD using LDCT scans performed for lung cancer screening on smokers (59). The results showed that using artificial intelligence in case-finding approaches was feasible; the best performing networks achieved an AUC of 0.88 and 0.89 in three-way cross-validation experiments in two independent cohorts (59).

Multimorbidity is the norm rather than the exception in patients with COPD. The coexistence of COPD with cardiac diseases, including ischemic heart disease or heart failure, is common, and these diseases share similar risk factors, including cigarette smoking, ageing, low

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socio-economic status, and sedentary behavior (60). The co-occurrence of COPD and cardiovascular diseases has led investigators to recommend a proactive search for these conditions using diagnostic tests that help to differentiate COPD symptoms from those of cardiac diseases (61). Efforts to enhance detection of COPD in patients with cardiovascular disease present an opportunity to explore broader medical collaborations amongst primary care physicians, pulmonologists, and cardiologists, and potentially allow an assessment of the general wellness of their patients.

Taken together, these findings suggest that incorporating COPD case-finding tools and targeting at-risk populations, such as those with cardiac disease, or those being screened for lung cancer, is feasible and could identify a significant number of individuals with undiagnosed COPD. Figure 2 shows a possible proposal for COPD case-finding.

Cost-Effectiveness of Case-Finding:

Lambe et al compared the cost-effectiveness of a systematic case-finding program administered every three years to ever smokers aged ≥50 years, against routine diagnostic process in UK primary care (62). The results indicated an incremental cost-effectiveness ratio (ICER) of systematic case-finding versus current care of £16596 per additional quality-adjusted life-year (QALY) gained. The active case-finding strategy was more expensive but more effective, with a greater number of QALYs gained over a lifetime time horizon (62). This ICER of £16,596/QALY is below NICE's common threshold to consider an intervention cost-effective (ie, £30,000/ QALY). It is important to highlight that the treatment effect in this model only captured the

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benefits associated with inhaled medications, so the effect of other interventions that can slow progression of COPD and improve HRQoL, such as smoking cessation, pulmonary rehabilitation, and self-management, were not considered. Therefore, it is very likely that the inclusion of non-pharmacologic interventions for COPD could have made systematic case-finding even more cost-effective.

In a high-risk population for COPD in China, Qu et al used a modeling approach and found that portable spirometer screening was cost-saving compared with questionnaire screening and no screening (i.e. usual care), with an incremental ICER of 5026 and 1766 renminbi per QALY, respectively (63).

Johnson et al. assessed the cost effectiveness of primary care-based case detection strategies for COPD in Canada using economic models relying on case-simulations (64). The eligible patients (based on age, smoking history, or symptoms) received the CDQ or screening spirometry, at 3- or 5-year intervals, during routine visits to a primary care physician. Newly diagnosed patients received treatment for smoking cessation and guideline-based inhaler pharmacotherapy. The most efficient scenario (all patients aged ≥ 40 years received the CDQ at 3-year intervals) was associated with an incremental cost of $287 and incremental effectiveness of 0.015 QALYs per eligible patient over the 20-year time horizon, resulting in an ICER of $19,632/QALY compared to no case detection (64).

Taken together, the results of these 3 modeling studies are consistent, and suggest that both questionnaire-based methods and screening spirometry, implemented in routine primary care visits, are cost-effective methods for early COPD detection in those at risk by virtue of exposure history and/or symptoms.

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Potential benefits of case-finding and early diagnosis of COPD:

A retrospective study of UK primary care centers found that only 33% of patients identified with COPD were diagnosed within five years after first presentation and were considered early diagnoses. Those defined as early diagnosis had slightly poorer lung function, however they had a longer time to first exacerbation, decreased exacerbation rates (57 vs 109 exacerbations/100 person-years), and decreased rate of hospitalizations over 3 years (65). Although this observational study could not establish causality, the study showed an association between early diagnosis of COPD and outcome benefits to both the patients and the healthcare system.

Similar findings were reported in a Swedish study which showed that receiving a COPD diagnosis soon after having visited a doctor due to respiratory symptoms was associated with lower risk of exacerbations, fewer comorbidities, and lower costs compared with delayed diagnosis (66). It is important to note that both the UK and Swedish studies evaluated patients who were diagnosed conventionally by their physicians, and early diagnosis was not achieved through case-finding.

Seven randomized controlled trials in adult smokers evaluated the effect of providing spirometry results (FEV_1 and/or lung age) in addition to counselling on smoking cessation rates compared to counselling alone (67). Although participants did not necessarily report respiratory symptoms, these can be considered COPD case-finding studies conducted in an at-risk population. Only two studies showed improved results when smokers were informed of spirometry results (67). Although there is currently only limited evidence to suggest that the use of feedback from spirometry improves smoking quit rates when added to smoking cessation

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counselling, it needs to be noted that many of the individuals enrolled in these studies did not have COPD on spirometry.

Case-finding and Early Diagnosis of COPD Coupled to Interventions

Two comparative studies have combined active COPD case finding coupled with non-pharmacologic interventions to potentially improve patient health outcomes. One trial conducted in Australia, assessed the effectiveness of early intervention by a practice nurse-GP team on HRQOL and process of care in patients with newly diagnosed COPD discovered via case-finding, compared with usual care. Among patients invited to a case-finding appointment, 16% attended and 18% were diagnosed with COPD. Only 15% of patients in the intervention group saw the nurse for COPD care following case finding. There was no between-group difference in SGRQ score at follow-up. The investigators concluded that intervention uptake was low and had no additional beneficial effect, over usual care, on participants' HRQOL (68).

The second clinical trial was conducted in three LMICs. Individuals with COPD (GOLD B-D) were identified through case-finding and randomized to a community health worker-supported one-year self-management intervention, or to standard of care. The trial did not find differences in SGRQ scores between the two groups at one year (69).

The USPSTF recommends against screening for COPD in asymptomatic adults, mainly because they concluded that there was no evidence to support pharmacological therapy in patients identified by screening (32). In contrast, the USPSTF recommends annual lung cancer screening with low-dose CT in adults aged 50 to 80 years who have a 20 pack-year smoking history and

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currently smoke or have quit within the past 15 years. It is interesting that this same approach is not recommended for COPD, which kills more people each year in the United States than lung cancer and shares the same risk factors. Importantly, the evidence indicates that, once diagnosed, COPD has therapies that not only improve lung function, health status, and lung function decline, but also decrease exacerbations rates, hospitalizations, and risk of death.

Although no trials have coupled case-finding and early pharmacologic treatment of COPD, evidence from randomized clinical trials suggests that treatment of mild and/or moderate COPD can lead to improved clinical outcomes. Two trials (SUMMIT and UPLIFT) found that LABA, LAMA, ICS, or LABA/ICS reduced exacerbations in persons with symptomatic moderate COPD (70, 71). One trial (UPLIFT) found that tiotropium also reduced exacerbations in a subgroup analysis of persons with minimal symptoms (i.e., GOLD A) (71). However, these trials enrolled individuals with physician-diagnosed COPD and subjects were not discovered through case-finding.

Two ongoing randomized, controlled trials couple active case-finding with interventions designed to improve health outcomes. The CAPTURE clinical trial is a pragmatic, cluster-randomized trial that explores the impact of using the CAPTURE COPD case-finding tool to identify clinically significant COPD in primary care. The study has randomized 68 practices to either usual care or clinician receipt of patient-level CAPTURE results. One-year follow-up chart reviews and participant surveys will assess the impact of sharing versus not sharing CAPTURE results with clinicians on clinical outcomes including clinicians' initiation of recommendation-concordant COPD care and changes in CAT respiratory symptom scores in those diagnosed with COPD (72).

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The **U**ndiagnosed **C**OPD and **A**sthma in the **P**opulation (UCAP) study is an ongoing Canadian clinical trial being conducted to explore the potential benefits of case-finding to discover previously undiagnosed asthma or COPD in symptomatic individuals coupled with an intervention strategy. Participants with previously undiagnosed asthma or COPD identified in the community via case-finding have been randomly assigned to one of two trial arms: early treatment with guideline-based therapy provided by a pulmonologist and nurse educator, or standard care (6). This trial aims to determine if early intensive treatment for undiagnosed obstructive lung disease reduces health-care utilization and improves QOL. A pre-defined subgroup analysis will explore outcomes in the COPD subgroup, exclusive of those with asthma. The trial has completed enrollment and will conclude in January 2024.

Conclusion and Future Research:

Undiagnosed COPD is a major global health problem. Most patients diagnosed with COPD in clinical practice are only recognized when their disease is already relatively advanced, and therapy is less effective. As has been shown for lung cancer detection in at-risk subjects, COPD case-finding is a potential strategy for identifying individuals with COPD who are still undiagnosed, to allow earlier identification of disease, and to direct non-pharmacologic and pharmacologic treatments to these individuals.

Newer evidence suggests that active case-finding of symptomatic people in the community, and opportunistic case-finding in people at risk for lung cancer or other co-morbidities, is effective. Three cost-effectiveness modeling studies from the UK, China, and Canada suggest that case-finding for COPD is cost-effective with incremental cost effectiveness ratios below $50,000/per

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QALY gained (62-64). However, these economic models rely on case-simulations rather than data derived from actual clinical studies. Although there are theoretical clinical and economic benefits of case-finding, the causal benefits of case-finding have not been conclusively established, since there are to date, no randomized, controlled trials that have demonstrated that patient outcomes are improved when COPD case-finding strategies are coupled to pharmacological or non-pharmacological interventions.

It is hoped that upcoming results from two ongoing randomized, controlled trials will provide hard evidence demonstrating that early diagnosis of COPD achieved via case-finding, coupled with pharmacologic and non-pharmacologic treatments for previously undiagnosed COPD, improves patient outcomes (6, 72). Subsequent health economic studies linked to these clinical trials can determine if the strategies are cost-effective.

A nihilistic approach to the growing health problem of COPD across the world has resulted in poor outcomes for patients with COPD. Case-finding will provide opportunities for healthcare providers to intervene early and be proactive.

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Table 1. Performance of COPD Case-Finding strategies

Case-Finding Tools	Study	AUC
Questionnaires		
COPD-PS	Ronaldson (2018)	0.66
	Spyratos (2017)	0.79
	Sogbetun (2016)	0.62
	Llordes (2017)	0.65
	Miravitlles (2012)	0.79
	Au-Doung (2022)	0.61
	Zhou (2022)	0.74
CDQ	Fujita (2020)	0.73
	Ronaldson (2018)	0.67
	Spyratos (2017)	0.80
	Stanley (2014)	0.71
	Frith (2011)	0.72
	Kotz (2008)	0.65
	Price (2006)	0.82
	Au-Doung (2022)	0.66
	Zhou (2022)	0.73
LFQ	Spyratos (2017)	0.81
	Sogbetun (2016)	0.66
	Zhou (2022)	0.78
Simple PUMA	Lopez Varela (2016)	0.70
	Lopez Varela (2019)	0.70-0.76
	Au-Doung (2022)	0.75
Weighted PUMA	Lopez Varela (2016)	0.79
CAPTURE	Quezada (2017)	0.93
	Martinez (2017)	0.79
	Zhou (2022)	0.67
UCAP-Q	Huynh C (2022)	0.81-0.82
Hand devices		
PEF	Ronaldson (2018)	0.77
COPD-6 score	Fujita (2020)	0.82
COPD-6	Labor (2016)	0.83
	Kim (2016)	0.76
	Llordes (2017)	0.87
	Represas-Represas (2016)	0.80
	Thorn (2012)	0.84
	Miravitlles (2012)	0.85
Piko-6	Van den Bemt (2014)	0.94
	Frith (2011)	0.85
	Hidalgo Sierra (2018)	0.86
Spirobank Smart	Lin (2021)	0.90
	Chen (2021)	0.87
Combination tools		
Changed CDQ + COPD-6 score	Fujita (2020)	0.87
COPD-PS+PEF	Soriano (2018)	0.76
CAPTURE +PEF	Quezada (2017)	0.95
	Martinez (2017)	0.90
	Martinez (2023)	0.81

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Abbreviations: Area under the curve (AUC); COPD diagnostic questionnaire (CDQ); COPD-Population Screener (COPD-PS); Lung Function Questionnaire (LFQ); COPD assessment in primary care to identify undiagnosed respiratory disease and exacerbation risk (CAPTURE); PUMA study questionnaire (PUMA); Undiagnosed COPD and Asthma Population Questionnaire (UCAP-Q); Peak expiratory flow (PEF).

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Figure Legends

Figure 1: Patient, healthcare-provider, and healthcare-system factors that may be associated with underdiagnosis of COPD.

Figure 2: An algorithm for COPD case-finding.

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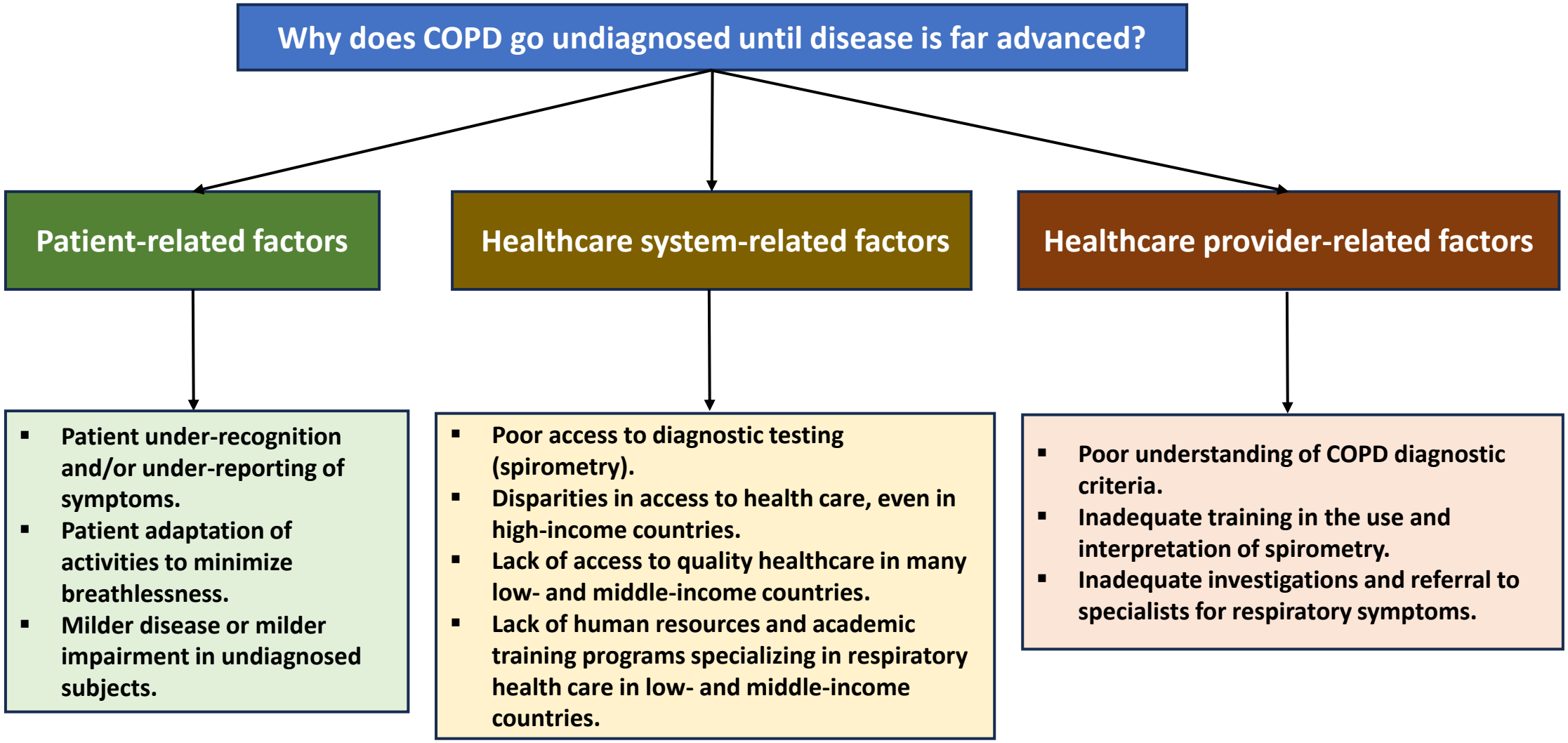

Figure 1

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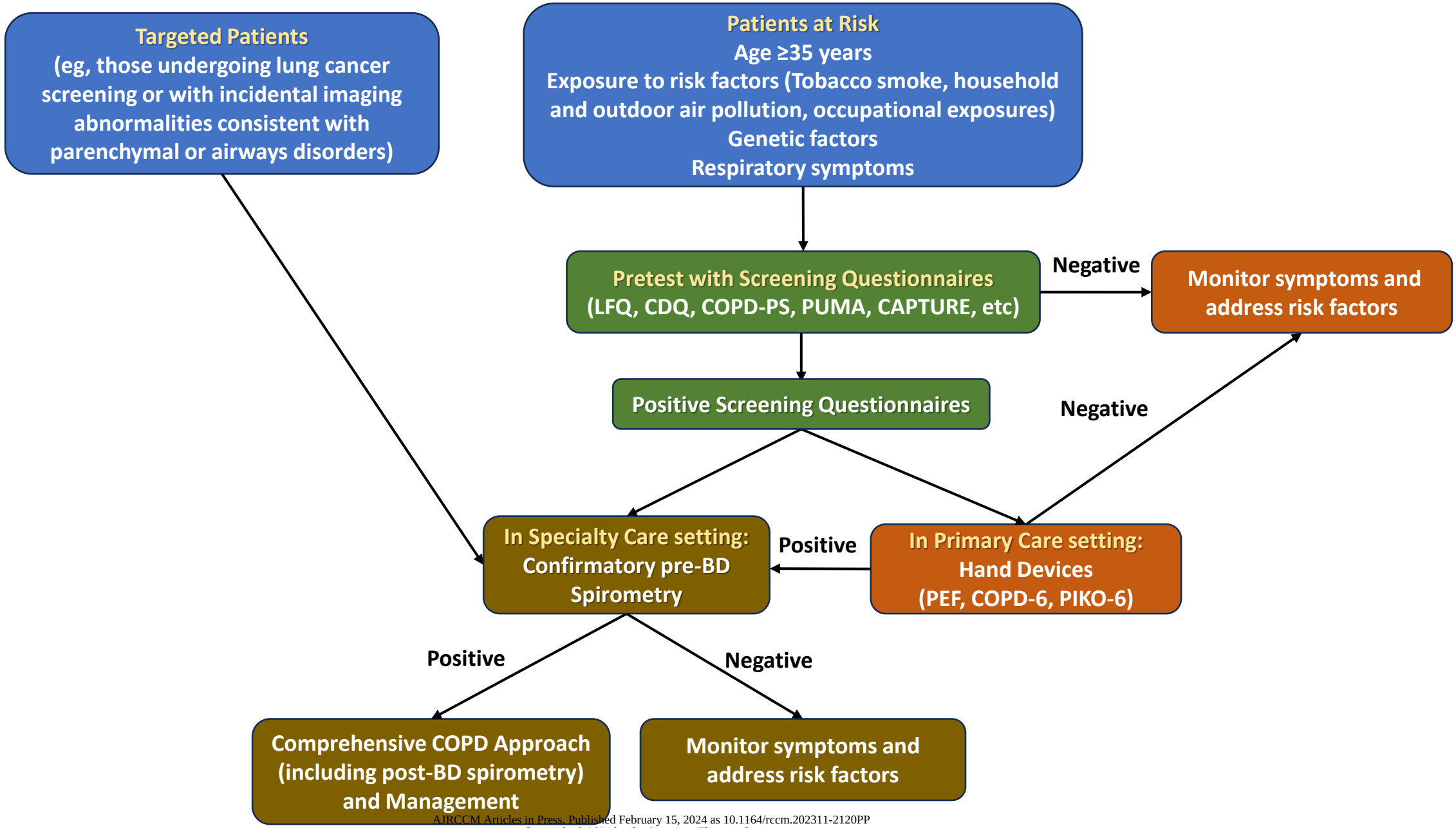

Figure 2

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