CHEST

POINT:

Can Screening for COPD Improve Outcomes? Yes

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PODCAST

ABBREVIATIONS: MDD = major depressive disorder; USPSTF = US Preventive Services Task Force; WHO = World Health Organization

COPD is a common but often underrecognized and underdiagnosed condition, especially in primary care settings in the United States.[1] Despite being the fourth leading cause of death in the United States, both diagnosed and undiagnosed COPD are a major cause of morbidity, mortality, disability, hospitalizations, and health-care expenditures.[2] The slow decline in lung function and compensatory activity limitation often results in failure of symptom reporting to clinicians, with patients attributing symptoms to aging, obesity, poor conditioning, or "smoker's cough." Primary care physicians also fail to query regarding chronic respiratory symptoms or note recurrent respiratory events as significant, leaving these patients to appear to be "asymptomatic."

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The US Preventive Services Task Force recommends against screening *asymptomatic* adults for COPD, pointing to the lack of data to demonstrate an impact on the outcomes of individuals so screened.[3] However, identifying or screening for individuals who have unacknowledged and unaddressed respiratory symptoms (not truly asymptomatic) is a very different approach and should not be considered to fall under the cautionary USPSTF's recommendation.[4]

Within the primary care setting, where most people with undiagnosed COPD receive care, studies demonstrate up to a fourfold increase in COPD diagnoses when using tools to identify chronic or recurrent respiratory symptoms.[5,6] These symptomatic patients are candidates for immediate initiation of treatment that may alleviate lung function decline and prevent exacerbations.[7] On the basis of these observations, COPD is a good candidate for facilitated symptom recognition, which could be termed screening.

Unfortunately, many COPD screening tools focus not on respiratory symptoms but on risk factors such as age, smoking, and environmental exposures,[8-10] resulting in modest sensitivity and specificity and failing to identify those nonsmokers who have COPD.[11] In testing the impact of these tools, the most common "outcome" is a new diagnosis of COPD—a very limited outcome that is deemed insufficient to support widespread COPD screening.[10] Case finding is sometimes confused with screening but is actually more like a two-part screening, first assessing for smoking exposure and then "screening" only those with significant smoking exposure, and has had impact similar to screening.[6]

A Need to Rethink the Definition of Screening

The classic definition of screening often muddies the view of COPD screening. Identifying asymptomatic COPD may not improve patient outcomes since therapy is directed at symptom reduction.[7,12] We need to rethink the goals and design of COPD screening tools, focusing on identifying the large group of individuals with unrecognized respiratory symptoms of COPD who are candidates for immediate therapy.

The World Health Organization (WHO) addresses this issue with its pragmatic recommendation for screening.

The WHO recommendation can be summarized as: Screening should be carried out only for conditions that are common and treatable with known natural history and accepted policies or recommendations for whom and when to treat with a diagnostic test that is available and resources exist to treat those diagnosed.[13] COPD fits this nicely. Using the WHO definition more closely fits the issues surrounding undiagnosed COPD in the United States.[10,14] Identifying asymptomatic COPD is not likely to be feasible or helpful for most individuals except to further stress the importance of exposure, for example, smoking avoidance. Rather, we need screening to identify those with unrecognized respiratory symptoms.

Screening for clinically significant COPD requires a focus on unaddressed symptoms and signs of respiratory dysfunction or disease. While it would be ideal to have all patients report those symptoms spontaneously, several primary care studies have shown this does not happen. Even if respiratory events are noted, health-care professionals are not following up with evaluations appropriate for chronic respiratory issues, for example, spirometry or pulmonary function testing.[15] "Don't ask, don't tell" strategies are not working.

COPD is not the only common chronic condition with a similar paradigm of don't ask/don't tell-based care. Depression is common and its symptoms and occurrence are grossly underrecognized or acknowledged among patients and primary care clinicians. This has led to recommendations for universal symptom-based depression screening, not screening for asymptomatic individuals at increased risk but universal symptom-based screening of all adults and adolescents.[16] Screening for depressive symptoms is now an expected part of primary care—an appropriate goal for COPD care in the United States.

To improve outcomes, we need to change the paradigm of COPD screening. Symptomatic individuals who are confirmed to have COPD are likely to be candidates for available pharmacotherapy, enhanced smoking cessation support, appropriate immunization, and pulmonary rehabilitation.[17] Few of the early studies of COPD screening or case finding have results that are based on this paradigm.[10] As such, it is not surprising that many of them fail to measure or demonstrate improved longer-term outcomes.

Implementing Screening in Primary Care to Achieve Better Outcomes

Few COPD screening studies include the full scope of screening. Simply introducing a screening tool without supporting implementation and follow-up is inadequate as demonstrated in screening for other chronic conditions, for example, depression.[18] Consider the implications of ordering a mammogram or blood glucose but not acting on the abnormal results. It is difficult to imagine 75% of physicians ignoring these results, yet that is what happened in a large US primary care COPD screening study. In the $>$ 9,700 patients screened, new COPD diagnoses increased twofold compared with those screened. However, medical record review could not identify any response to over 75% of abnormal screening results.[15] It is therefore not surprising that many COPD screening studies fail to demonstrate longer term impact.

COPD screening must develop better, more symptom-based tools and appropriate follow-up support. Following the above example, depression screening in primary care has been shown to improve outcomes but only in a setting in which appropriate follow-up processes are present, supported, or developed. This is highlighted in the clinical considerations section of the USPSTF depression screening recommendations (https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/depression-in-adults-screening1#Pod5). We must do the same for COPD screening. If we are to assess the impact of COPD screening it must be in the context of a screening implementation package that supports clinical action based on screening results.

Recognizing these imperatives has been embedded in the development and assessment of the CAPTURE (COPD Assessment in Primary Care to Identify Undiagnosed Respiratory Disease and Exacerbation Risk) tool—a five-item screening tool supported by assessing peak expiratory flow.[19] Introduction of the tool is coupled with clear pragmatic education on how to address abnormal screening assessments, including availability of adequate spirometry testing and possibly point-of-care tools and a decision support system embedded in electronic health records. These have been helpful in other chronic diseases.[20]

Before deciding whether or not screening impacts outcomes, we must develop, validate, and determine how to implement the screening tools and the follow-up process for addressing abnormal screening results within

the primary care setting—the place where COPD and other chronic condition screening will need to occur. Such a comprehensive approach is now being tested within a broad range of practice-based research networks.[21]

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COUNTERPOINT:

Can Screening for COPD Improve Outcomes? No

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In 2016, the US Preventive Services Task Force (USPSTF) "did not find evidence that screening for COPD in asymptomatic persons improves health-related quality of life, morbidity, or mortality."[1] The Task Force also concluded that early detection of COPD does not alter the course of disease or improve patient outcomes.[1] The thought process underlying this decision could be summarized as follows: the only known intervention shown to change the natural history of COPD is smoking cessation; there is no evidence that knowledge of a COPD diagnosis increases the likelihood of smoking cessation; every smoker should stop smoking; thus there is no rationale to screen for COPD (particularly in a person who has no symptoms). The way this recommendation is written, neither spirometry nor other screening tools, such as

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TABLE 1] Components Applied in the Screening, Diagnosis, and Treatment of COPD

Wilson and Jungner[5] Classic Screening Criteria	Application in COPD
1. The condition sought should be an important health problem	+ + + +
2. There should be an accepted treatment for patients with recognized disease	+ + +
3. Facilities for diagnosis and treatment should be available	+ + +
4. There should be a recognizable latent or early symptomatic stage	+
5. There should be a suitable test or examination	+ +
6. The test should be acceptable to the population	+ +
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood	+
8. There should be an agreed policy on whom to treat as patients	+
9. The cost of case-finding (including diagnosis and treatment of patients with COPD) should be economically balanced in relation to possible expenditure on medical care as a whole	+ +
10. Case-finding should be a continuing process and not a "once and for all" project	+ +

questionnaires, provide a net benefit in asymptomatic persons.

The recommendations against screening for COPD are not limited to those of the USPSTF. In the 2011 consensus statement of the American College of Physicians, the American College of Chest Physicians, the American Thoracic Society, and the European Respiratory Society the first recommendation is that spirometry results be obtained to diagnose airflow obstruction in patients with respiratory symptoms, but that spirometry should *not* be used to screen for airflow obstruction in individuals without respiratory symptoms (grade: strong recommendation, moderate-quality evidence).[2] Likewise, the American Academy of Family Physicians stresses that screening for COPD in asymptomatic patients who are at increased risk is not recommended.[3] The Global Initiative for Chronic Obstructive Lung Disease (GOLD) strategy document notes that "there are no data to indicate that screening spirometry is effective in directing management decisions or in improving COPD outcomes in patients who are identified before the development of significant symptoms."[4]

The answer to the question addressed by this editorial, "Can Screening for COPD Improve Outcomes?" is, at the present time, "No," in agreement with the recommendation from the USPSTF and others. We address here the several different components to this issue, including the rationale for screening for disease, defining COPD, and how one ascertains outcomes in COPD and their improvement.

What is the rationale for screening for disease? Wilson and Jungner[5] described the necessary components of a screening program in a classic World Health Organization report in 1968. Table 1 lists these components, along with our assessment of how these criteria may be applied in the screening, diagnosis, and treatment of COPD.

Some of the questions and challenges represented in Table 1 revolve around the question of defining COPD. While COPD is characterized and diagnosed by the physiologic parameter of airflow obstruction,[6] the causes of this physiologic abnormality can arise from a number of different processes, including those involving large airways, small airways, alveoli, and the pulmonary vasculature.[7] In addition, by the time physiologic impairment is present (Fig 1), disease is well established and often advanced, with limited opportunity for disease modification.[8]

Returning to Table 1, some of the gaps and uncertainties are apparent. The progression of COPD from early or latent disease to established disease is not well defined. Many patients with mild impairment do not progress to more severe impairment,[9] and there is a growing body of evidence that other abnormalities, such as radiographic or physiologic ones, might occur early in the course of disease development.[10] Even if early disease were defined and established, there is no known treatment that has been shown to be effective or capable of modifying disease progression among those with early disease.

The use of spirometry as the primary way of defining disease is a particular problem. The spirometer was invented by Dr John Hutchinson in the 1840s, and its basic structure is still used today.[11] The spirometer, however, is a flawed screening and diagnostic tool, especially if one is looking for latent or early disease. Campaigns for primary care physicians to use spirometry in their offices have generally failed.[12] Most

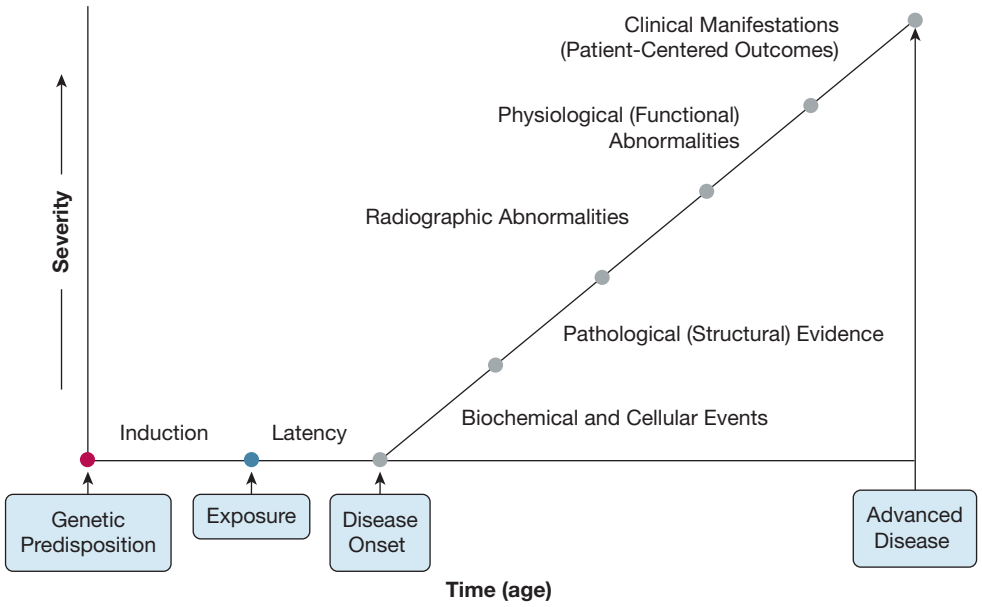

Figure 1 – *Conceptual diagram of disease progression in COPD. Reprinted with permission from Decramer and Cooper.*[8]

primary care physicians do not have a spirometer; those who do rarely use them, and many of the spirometric procedures performed in primary care do not meet American Thoracic Society quality guidelines.[13,14] Furthermore, postbronchodilator spirometry is almost never performed in primary care, and considering the millions at potential risk for COPD, the cost of just prebronchodilator spirometry would be extreme.

While other means of determining early COPD are potentially available, such as CT imaging or measurement of diffusion capacity,[10] these are neither practical nor of low enough cost for use in primary care or as a screening tool.

The final component of the question to be addressed is whether screening (and resulting interventions coming from that screening) would improve outcomes. Ideally, an intervention would keep a disease from becoming established, or if the disease was established, keep it in its milder stages. A number of different outcomes have been used in COPD clinical trials and population studies, with the most common ones being lung function decline, exacerbations of disease, symptoms, quality of life measures, and mortality. Of these, the metric thought to best represent disease modification is lung function decline, which is plagued by the same issues noted previously in discussing spirometry. Decreasing mortality is also a type of disease modification, but to date only smoking cessation,[15] domiciliary oxygen[16] (for hypoxemic patients), and lung volume reduction surgery (in selected patients)[17] have been shown to demonstrate this benefit. Of these interventions, only smoking cessation would apply across the entire continuum of patients with COPD.

Returning to the question concerning whether COPD screening would improve outcomes: while the answer is currently "No," our hope is that with advances in knowledge we can change this narrative. We have a roadmap for this from the world of cardiovascular medicine, where great advances have been made in the early detection of precursors of cardiovascular disease, which respond to treatment. People with risk factors for cardiovascular disease, and who have evidence of elevated low-density lipoprotein (LDL) cholesterol, can be treated with statins to decrease their risk of developing disease before they have had their first myocardial infarction.[18] What the respiratory health world needs is a similar biomarker of very early disease that would be responsive to early and acceptable intervention. This biomarker, or set of biomarkers, should be easy to detect and interpret, and usable in the primary care setting. In addition, new therapies and interventions that would interrupt disease in its earliest phases, before lung function is lost and symptoms become established, are critically needed.

Another critical need, returning to the rationale as to why screening for COPD is not currently recommended (other than to urge every smoker to stop smoking), is for better treatment of tobacco and nicotine addiction. Despite the advancement in knowledge gained from the initial Surgeon General's Report in 1964,[19] a large proportion of the population in the United States and the world continues to smoke cigarettes and other

tobacco products.[20] In addition, a new generation of products is being marketed to the next generation of users, with no demonstration that these products are less harmful than cigarettes. While therapies, both pharmacologic and nonpharmacologic, exist for tobacco addiction their success is limited.

To conclude, screening for COPD, which as currently defined represents disease that is well advanced and not amenable to disease-modifying interventions, does not appear to be the best use of resources. Identifying and targeting changes in the lungs before they become established seems to be the best potential way of actually modifying the natural history of COPD.

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Rebuttal From Drs Yawn and Martinez

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We read with great interest Drs Mannino and Thomashow's discussion of COPD screening for asymptomatic individuals[1] and agree it provides limited ability to identify, prevent, or treat COPD before

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TABLE 1] Components Applied in the Screening, Diagnosis, and Treatment of COPD: Streamlined Version

Abbreviated Wilson and Jungner Classic Screening Criteria[4]	Application in COPD
1. The condition sought should be an important health problem	+ + + +
2. There should be an accepted treatment for patients with recognized (symptomatic) disease[5]	+ + + +
3. Facilities for diagnosis and treatment should be available	+ + +
4. There should be a suitable test or examination to identify COPD and its symptoms[5]	+ + +
5. The test should be acceptable to the population	+ +
6. There should be an agreed policy on whom to treat as patients when symptoms are present[5]	+ + + +
7. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole	+ +

symptoms appear. Indeed, smoking cessation and prevention remain key to disease prevention and progression.

However, we do have many individuals with symptomatic COPD who remain undiagnosed and untreated.[2] It is these individuals for whom we suggest that screening is appropriate. It is these individuals who are candidates for the available symptomatic COPD therapies currently licensed, of course in addition to smoking intervention, which we agree requires expansion and improvement.

To ignore all those who are currently unrecognized but in the later and symptomatic stages of COPD is problematic. To believe that we will change the primary care recognition of these symptomatic individuals is unreasonable in view of current successes in practice changes. Drs Mannino and Thomashow selected cardiovascular disease for comparison, a condition with nonspecific biomarkers for early disease that results in treating millions of individuals for elevated lipids—a biomarker with high sensitivity and modest specificity.[3] We highlighted similar concerns for fasting glucose as a biomarker for "prediabetes." It seems unlikely that such a biomarker for COPD is going to gain the same type of acceptance as lipid or hypertension screening for cardiovascular disease or fasting blood sugar for "prediabetes" in the near future, although it is a laudable goal for investigation.

We believe that a comparison with major depressive disorders (MDDs) is more appropriate for the current state of COPD knowledge regarding pathophysiology and disease progression. In MDDs, we have no biomarkers of early disease and have chosen to address the MDD epidemic with symptomatic screening. We believe the same symptom-based approach is appropriate to COPD screening and is consistent with the World Health Organization screening recommendations.[4] Noting the World Health Organization categories Drs Mannino and Thomashow listed, we suggest a streamlined version of this table (Table 1[4,5]). COPD currently addresses the streamlined criteria and perhaps with greater strength in symptomatic COPD than suggested in the original table.[1]

COPD screening is not feasible or likely cost effective if based on screening asymptomatic individuals with spirometry or CT scans—we agree. We have no treatments other than avoidance of smoking and other environmental exposures to clearly address COPD prevention or possible progression from the latent stages to symptomatic stages. However, to therefore abandon case finding or screening for individuals with unreported chronic respiratory symptoms is also problematic. We have symptomatic treatments, and initial assessment of at least one tool to identify symptomatic individuals that can lead to diagnostic evaluation and provision of symptom-based therapy. The concept of screening for COPD needs to move away from a singular focus on identifying early latent disease but also address the large group of unrecognized but symptomatic COPD sufferers who are candidates not just for diagnosis but immediate therapy. At the same time, it is important to continue efforts to move beyond current antiquated spirometry and expensive CT scans as the "biomarkers" for earlier COPD.

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In their argument supporting the idea that screening for COPD can improve outcomes, Drs Yawn and Martinez[1] argue that "COPD screening must develop better, more symptom-based tools and appropriate follow-up support." We certainly agree with that conclusion and hope that CAPTURE (COPD Assessment in Primary Care to Identify Undiagnosed Respiratory Disease and Exacerbation Risk) will lead to earlier diagnosis and earlier therapy.[2] However, even if the ongoing study attempting to validate the utility of this tool in primary care confirms earlier results without disrupting practice patterns,[3] the patients identified will be symptomatic but will not have received a diagnosis. It remains unclear whether treating that group with current COPD therapies, such as bronchodilators and inhaled steroids, and improving their symptoms will ultimately affect the natural history of disease.

Some of the challenges with a symptom-based approach to COPD screening are as follows: symptoms of COPD (dyspnea, cough, wheeze, sputum production) are fairly common in the population and can be related to other diseases (both acute and chronic); individuals may over- or underestimate their symptoms; patients have a difficult time discerning between what are important symptoms and what may be related to deconditioning or aging.

To expand our previous comparison with what has happened in cardiology, better tools to detect the symptoms of cardiovascular disease is not what has led to improvement in outcomes—it was the identification of biomarkers that are the targets of intervention prior to the appearance of clinical disease.

Interventions prior to the appearance of chronic symptoms fits into the concept of preserving lung health.[4] There is mounting evidence that a large proportion of COPD has its origins in childhood, with early exposures or other factors leading to inadequate lung development.[5] Identifying and intervening in these individuals is an important strategy to address respiratory disease in the entire population.

Another important concept worth stressing is that COPD is not a monolithic disease, but rather a heterogeneous collection of diseases with different risk factors, pathophysiologies, manifestations, and treatments.[6] As a results, screening and case-finding strategies that work in some subtypes may be ineffective in other subtypes.

Even if CAPTURE is successful in finding cases of undiagnosed but symptomatic COPD, it is unlikely to provide information on all subtypes of COPD, which may have varying degrees of symptomatology, and may require and respond to different therapeutic approaches.

A final gap that needs to be considered is that obstructed airways are increasingly being seen among people with risk factors other than smoking. An analysis of data from the 2007-2010 NHANES (National Health and Nutrition Examination Surveys) found that nearly 30% of people with spirometric evidence of obstruction had never smoked.[7] As the prevalence of smoking decreases in the population, this group of patients may become increasingly important, even though they are rarely studied and typically excluded from most COPD clinical trials.

We conclude with our previous assessment that better tools that are used to find moderately advanced disease, while important, are unlikely to improve COPD outcomes. We need biomarkers to identify patients before their lung disease become impactful, and we also

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need affordable interventions that can alter the natural history of disease.

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