mechanisms. Although we basically agree, we argue that the underlying mechanism(s) motivating the use of vasopressor(s) must be kept in mind. Increasing BP by a pressor combination increasing the vascular tone via different mechanisms might be correct. This approach will work well if hypotension results mainly from the loss of vascular tone. In this case, the proposed approach fits well with the physiological acute cardiovascular response. Sympathetic stimulation, vasopressin release, and angiotensin level increase interact synergistically to increase the vascular tone. However, the decrease in BP in critically ill patients results from more complex interactive mechanisms (eg, heart failure, hypovolemia, abnormal ventriculo-arterial coupling), for which the pure vascular tone control might be insufficient or dangerous. We do not share the "no sense of a norepinephrine association with epinephrine." Epinephrine is the emergency hormone, which links vascular tone, heart function, and metabolic effects to "escape" the life-threatening situation. Its combination with norepinephrine can be then logical for some patients.

The second concept ("catecholamine vasopressor support-sparing strategies") proposes the use of "adjunctive" therapies to reduce pressor support. Although theoretically appealing, such adjunctive therapies are not easy to use in practice.

The last concept ("microcirculatory protection") is the oldest but the most recently investigated in critical care. Until now, it seemed obvious that the microcirculation changes might be corrected by therapeutic actions focused on macrocirculation, suggesting that microcirculation is passively impaired. This is very different when microcirculation is impaired by a combination of abnormal systemic circulation associated with pure inflammatory mechanisms at the microcirculation level (activated adhering white cells with microthrombosis). This situation frequently occurs in critically ill patients and could be improved by a combination of cardiovascular hemodynamic supports with modulation of the inflammation-induced interaction between endothelial cells and circulating immune cells.

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COPD

Should Diagnosis Match Physiology?

To the Editor:

We are very grateful to Dr Vanfleteren and colleagues[1] for commenting on our data regarding overdiagnosed COPD[2] and for putting this evidence into the framework of current understanding of the disease. Based on the data presented on overdiagnosis, and on prior Burden of Obstructive Lung Disease (BOLD) observations on underdiagnosis,[3] we truly believe that our worldwide community of pulmonary specialists could do much better in caring for this extremely prevalent and devastating disease.

Overall, our data indicate that for one patient with a "matched" COPD diagnosis (ie, the presence of post-bronchodilator airways obstruction and a positive recall of such a diagnosis), there is always another "mismatched," false-positive patient with COPD. This patient possibly experiences all the untoward consequences, such as receiving expensive and possibly harmful medication, and missing chances for treatment of cardiac disease or asthma. On the contrary, for each "known" patient with COPD who has poorly reversible airways obstruction, there are four to five other patients out there with yet undetected airways obstruction. Again, we are missing opportunities in these patients for

smoking intervention, symptom relief, and prolongation of their lives.

Dr Vanfleteren and colleagues[1] argue that the epidemiological picture might not reflect clinical reality, or might not be relevant for clinical practice. Is this the case? Epidemiology is always about having a "population-based" perspective, thus putting observations into perspective clinicians might miss. Only epidemiologists would, for example, systematically measure spirometry, regardless of the presence of symptoms, hypothesizing that signs of early airways obstruction might be missed by some patients.[4]

It has only been two decades since the Global Initiative for Chronic Obstructive Lung Disease (GOLD) initiative defined COPD diagnosis based on post-bronchodilator spirometry. Are we moving away from that? We think, yes. The later GOLD editions have put much more emphasis on measuring symptoms and exacerbations, moving away from the measurement of spirometry. This move was most likely driven by results from COPD mega trials that lung function decline cannot be changed with COPD medication,[5] and consequently all later major COPD trials were then based on exacerbation as the primary outcome, which was then consequently followed by the GOLD initiative.

Fortunately, population-based evidence is moving us back toward physiology. According to available data, we strongly advise not only to measure spirometry but to repeat this measurement over time.[6] This approach will be the only way to "diagnose" the presence of progressive lung function decline and differentiate it from airways obstruction resulting from early life injury.

Why is this so difficult? BOLD[7] has proven that measurement of spirometry is simple, easy, and can be done anywhere at any time. However, the future may move us toward tele-spirometry anyway. In the meantime, we make use of spirometry, and not only measure it once, but—if in the gray zone of normality or if in doubt about progressive disease—we repeat measurements. Although spirometry appears simple, it is a measure of precision medicine. Not using precise instruments will leave us with nonprecise diagnoses and treatments.

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Response

To the Editor:

We thank Dr Studnicka and colleagues for taking the time to comment on our editorial,[1] and overall we agree on everything they have written. More specifically, we underline the importance of high-quality spirometry in establishing a correct diagnosis of COPD in symptomatic patients at risk. Indeed, spirometry must be measured to make the initial diagnosis and assessment of severity, the latter being useful for prognostication, as always recommended by the Global Initiative for Chronic Obstructive Lung Disease document (including the last version).[2]

We also agree with Dr Studnicka and colleagues that we must be careful in interpreting a self-reported heterogeneously defined clinical physician's diagnosis of COPD in the context of a general population epidemiological study. Their study clearly confirmed that spirometry is essential for diagnosis and to avoid overdiagnosis. However, we still believe that epidemiological studies have purposes different from clinical studies, with a much larger degree of freedom in selecting the subjects to study without the responsibility of then identifying whom to treat. Dr Studnicka and colleagues state that basing the diagnosis of COPD on spirometry results in the detection of many more subjects with COPD. However, spirometry simply identifies subjects with airflow limitation, not patients with COPD. For a COPD diagnosis, symptoms and exposure to smoking or pollutants are required together with persistent airflow limitation. In this respect, we stated that epidemiologic studies are not necessarily relevant for clinical practice. Indeed, if airflow limitation is identified and the patient is asymptomatic or has no risk of exacerbations, we should not treat the individual. Similarly, if airflow limitation is present in a nonsmoker together or not with chronic respiratory symptoms, we should not prescribe any treatment, because no randomized controlled trials have ever been conducted in these subjects.

Having said that, spirometry is mandatory for confirmation of the diagnosis of COPD in symptomatic individuals with a significant history of smoking and/or exposure to pollutants. It also has a critical role in excluding the diagnosis in symptomatic individuals with a significant history of smoking and/or exposure to pollutants but normal or restricted spirometry; this was nicely shown and discussed in the article of Sator et al.[3] In addition, we agree with Dr Studnicka and colleagues that it is wise to repeat spirometry over time, not only because results may vary over time, making the diagnosis problematic,[4] but also to identify fast decliners, particularly if they have a history of frequent exacerbations.[5]

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