subgroup of patients with solid tumors who are at high risk of VTE and at low risk of bleeding.

The panel referred to the eligibility criteria of the nine trials to identify the group of patients at a higher risk and who are likely to benefit. We welcome and strongly support the suggestion of the authors for clinicians to use structured and validated tools to risk stratify patients. An ideal tool would predict not only VTE but also major bleeding and mortality, the latter being the most important outcome for this specific intervention in this specific population.

The authors state, “It is quite possible that institutional review boards may identify these suggestions as a standard of care.” Such misinterpretation would reflect a grave misunderstanding of guideline methodology as laid out clearly in relevant publications.1,2,3

Finally, we hope that the transparency with which the panel made and reported its judgments will allow clinicians to interpret the recommendation in the individual patients’ specific context and help them make the decisions that are appropriate for them.

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REFERENCES


Responsiveness of the COPD Assessment Test

The Minimal Clinically Important Difference Does Matter

To the Editor:

With the inclusion of symptoms/health status in the most recent GOLD (Global Initiative for Chronic Obstructive Lung Disease) guidelines,1 a large step has been made to involve the patient’s view of the burden of disease in decision making. We welcome this development but wonder why the GOLD committee chose the COPD Assessment Test (CAT) by GlassSmithKline.

Clinicians and researchers need information on how to interpret scores, and the study by Jones et al2 in this issue of CHEST (see page 134) provides important information about this topic. However, we would like to raise two issues. First, how much change in scores would one expect after exacerbations and pulmonary rehabilitation? Second, what would be the minimal clinically important difference (MCID) of the CAT based on this study?3

Jones et al2 describe the CAT score changes during an exacerbation and after rehabilitation. Exacerbation recovery resulted in a mean CAT score improvement of −1.4 points in all 67 patients

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and −2.6 points in clinician-defined responders. Are these clinically relevant changes in scores? We would suppose so considering the clinicians’ judgment. However, to enable good interpretation of the −2.6-point change, the CAT MCID should be known.

Jones et al.2 would allow proper calculations of the MCID by both distribution and anchor-based methods. Based on their study, the CAT MCID can be estimated using one of the distribution-based methods: the SEM.3 The MCID would be 1.96 × 7.7 ×√1 − 0.5 = 6.75 points in this study. In a study of 90 Greek patients, the 1.96 SEM was 4.94, 5.76, and 0.41 for the St. George Respiratory Questionnaire (SGRQ), CAT, and Clinical COPD Questionnaire (CCQ), respectively,4 which is similar to previously published MCIDs for the St. George Respiratory Questionnaire and CCQ.3,5 The reported changes in responders (−2.6 points) will not reach this MCID by far, suggesting limited responsiveness of the CAT to exacerbation recovery.

In the second study described by Jones et al.,2 the effects of pulmonary rehabilitation (one of the most effective treatments for patients with COPD) is −2.2 points, which is also disappointingly low when considering the MCID calculated from the exacerbations study. The disappointing sensitivity for change is also confirmed by a study by Dodd et al.6 who showed that the effect size of the Chronic Respiratory Questionnaire is −0.8, whereas the effect sizes of the CCQ and CAT are 0.6 and 0.4, respectively. We, therefore, challenge the conclusion that the CAT is sensitive to change and would ask the authors to calculate the MCID on the data from the presented study and reconsider their conclusion.

I appreciate the questions posed by Dr Kocks and colleagues following our article in CHEST1 concerning the responsiveness of the minimal clinically important difference (MCID) for the COPD Assessment Test (CAT). They discuss two methods for estimating the MCID: one that is clinical (anchor based) and the other statistical (distribution based).

The definition of the MCID is key to this debate. One of the most comprehensive is “the smallest difference in score which patients perceive as beneficial and would mandate, in the absence of troublesome side effects and excessive cost, a change in the patient’s management.”2 If a patient’s perception of benefit is accepted as a core principle, it is difficult to justify use of distribution-based estimates of the MCID for patient-reported outcomes.

Anchor-based estimates are often made by comparing the patient-reported outcome score with a global change score. Investigators sometimes apply this approach retrospectively, using a global scale that was applied in the study for another purpose (as used by Dr Kocks and colleagues on our data). That is a mistake. Global scales are designed for a specific purpose, in our case to test whether the CAT could measure recovery after a specific period (14 days). Our scales were not worded to identify minimum beneficial change; furthermore, a change judged worthwhile at 14 days may be different from one at 28 days.

No single MCID estimate is sufficient. For the St. George Respiratory Questionnaire (SGRQ), multiple approaches were used.3 Clinically-based methods produced consistent estimates (≈4 units), but distribution-based estimates were quite different and dependent on methodology.

Mapping techniques are also used for MCID estimation and are applicable to the CAT because the relationship between the CAT and the SGRQ is constant across the scaling range.4 The mathematical relationship is CAT = 0.4 × SGRQ, so, the estimate for the CAT MCID is 1.6.

Dr Kocks and colleagues suggest using the effect size to estimate treatment effect. This is another statistical approach that compares change within individuals to the distribution of scores between individuals. They did not mention that the effect size for the SGRQ with rehabilitation in the study they quoted4 was very small at 0.2, whereas the measured SGRQ change was 3.9 (ie, very close to the MCID). Distribution-based estimates of change and clinical estimates of benefit clearly measure different things, which takes us back to the reason for using MCIDs: to identify the size of the benefit to the patient.

Using our mapped estimate of the CAT MCID, the mean improvement in CAT score reported by Dodd et al.5 was 1.8 times the MCID. This shows that the CAT was very responsive, not unresponsive as suggested by Dr Kocks and colleagues.

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### References


### Response
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