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Frameworks of Health Outcomes for Performance Specifications in Laboratory Medicine

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Guest: Dr. Patrick Bossuyt is a professor of Clinical Epidemiology at the University of Amsterdam.

Bob Barrett: This is a podcast from *Clinical Chemistry*, a production of the Association for Diagnostics & Laboratory Medicine. I'm Bob Barrett.

It has been said that the vast majority of clinical decisions depend on laboratory test results. To help ensure that these decisions are correct, clinical laboratorians must maintain test methods with sufficient accuracy and measurement certainty that the results reflect the patient's state of health. These analytical performance specifications, essentially the minimum criteria that need to be met to support correct patient management, should be defined for each analyte. But how best to do this? Ideally by studying the impact of test performance on clinical outcomes. This sounds straightforward enough, but these studies can't be performed without first identifying which clinical outcomes should be measured. General categories like physical, social, or mental well-being? Or a more granular approach where these broad categories are broken down into subparts, each given a score from a severity gradient scale?

A review article in the May 2026 issue of *Clinical Chemistry* describes seven frameworks for assessing health outcomes, highlights their differences and similarities and proposes the design of health outcome studies to define laboratory test analytical performance characteristics. Today, we welcome the article's lead author, Dr. Patrick Bossuyt. He is a professor of Clinical Epidemiology at the University of Amsterdam. He started the Amsterdam UMC Biomarker and Test Evaluation research program, which appraises medical tests and biomarkers and applies these methods in clinical studies. So Dr. Bossuyt, first off, why was this study needed?

Patrick Bossuyt: Well, this study was needed because there was a lot of discussion about what outcomes are in laboratory medicine. So, some people suggested that test results are outcomes. And others said, 'No, no, no, it's not the test result, it's communicating the test results.' And others were saying that results are not outcomes, actual outcomes, but for example, starting treatment based on outcomes are outcomes. So a lot of discussion about what outcomes. And if you want to define analytical performance based on outcomes, we

thought we needed a clear definition of an overview what outcomes are and an overview that should be aligned with the current views on outcomes in the evaluation of measures in healthcare in general.

Bob Barrett: What other methods exist for developing analytical performance specifications?

Patrick Bossuyt: Well, the Milan criteria defined three methods for defining performance specifications in laboratory medicine, analytical performance specifications. And these three models are not a hierarchy, but they can be used alternatively depending on the circumstances. And apart from a model based on outcomes, we have a model based on biological variation. So the more variable your test results are, the less precise measurements are needed, or stated otherwise, if you have less variable test results, you need more precision. And the third model, model three, is a model based on state of the art. So basically you're looking what the best available assays can achieve in terms of analytical performance specifications and you try to match that.

Bob Barrett: So what did your group do?

Patrick Bossuyt: Well, in order to provide an overview of different frameworks of outcomes, we did a systematic review of the literature. There had been a previous systematic review developed by colleagues, and we updated that systematic review and used web searches based on AI to identify existing frameworks. And then based on similarities and some other specifications, we selected seven frameworks. So we did not include specific frameworks for specific diseases, for example, or specific treatments, but tried to identify general frameworks. And in the end, we included seven of those in the systematic review that appeared in the journal.

Bob Barrett: So doctor, what were your conclusions?

Patrick Bossuyt: Well, we identified these seven frameworks and we concluded that there were a lot of similarities between these seven frameworks. So many of these were based on the WHO definition of health, which is quite old. It was already specified in 1948 and it specified two things that health is not just the absence of disease, which is running through all the frameworks, and the second element is that the WHO definition distinguishes between physical, mental, and social well-being. And you see these three components of health return in most of the frameworks that we identified.

So in essence, they don't look at disease specifically, but how an individual is able to function in daily life, in society, in terms of its physical health, his mental health or her mental health, and the social health, how that individual can interact

with other people in the family, in the neighborhood, in society in general.

Bob Barrett: Doctor, this study started from the perspective of developing analytical performance specifications. Is your study also relevant for lab professionals who are not involved in setting analytical performance specifications?

Patrick Bossuyt: We believe it is, Bob, and that's why we offered this overview, this systematic review of frameworks to the journal. We believe it's especially relevant in this day and age where there are a lot of discussions about the contribution of laboratory medicine to healthcare. And there are discussions that focus on cost and added value, and in many of these discussions, the concept of outcomes and improved outcomes appears. And we believe it's helpful to have a shared set of frameworks when discussing health outcomes. So in essence, this is not just about producing test results or guiding clinical management, but the actual effect that these outcomes have, these tests, these assays have on the way people actually function in their daily life and function in society. So functional health is a very central element in all of these frameworks of health.

Bob Barrett: Have outcomes-based methods for developing analytical performance specifications been successfully applied so far?

Patrick Bossuyt: Well, less so, so far. And in part this has to do with the confusion about what outcomes are or outcomes should be, but also because of another fact. So most tests that clinicians order do not have a direct effect on these outcomes that we identified in the frameworks. So test results affect outcomes through the way in which they can guide clinical management, for example starting or stopping or modifying treatment.

So it's not just the result itself, the test result, but the downstream consequences of communicating and acting on the test results. And because of that indirect link, it's not very easy to define analytical performance specifications based on outcomes. And what we have seen are mostly models and studies that look at outcomes through proxies. For example, a diagnosis is a proxy for an outcome because many diagnoses are linked to specific actions to handle based on the test result in order to improve outcomes. So most studies so far have looked at proxies for health outcomes and not at the actual outcomes.

Bob Barrett: Well, finally Dr. Bossuyt, let's look ahead. Where do we go from here? What do you expect to see in the future?

Patrick Bossuyt: We expect to see more studies that try to define analytical performance specifications based on outcomes. And that's

because of the relevance of improving health outcomes is increasing in lab medicine in general. And I think through our increased experience in developing model studies and other studies, we will see more and more studies that actually try to define specifications based on outcomes. And the way test results can act to guide clinical management and improve health outcomes.

Now, that will not happen for all analytes because I believe it will happen for analytes that have a specific role in clinical management. Many of the analytes in lab medicine are quite general and they can be used for many different testing purposes and for many different clinical actions. And for these analytes with wide applicability, it will be more difficult to set performance specifications. But we will see more and more analytical performance specifications based on outcomes. And we hope that our overview of existing frameworks can help in that process.

Bob Barrett: That was Dr. Patrick Bossuyt from the University of Amsterdam in the Netherlands. He wrote a review in the May 2026 issue of *Clinical Chemistry* discussing health outcome studies to define lab test analytical performance characteristics, and he's been our guest in this podcast on that topic. I'm Bob Barrett. Thanks for listening.