Guest: Dr. Patrick Bossuyt is Professor of Clinical Epidemiology at the University of Amsterdam, and has spearheaded the STARD Initiative for the improved reporting of diagnostic test accuracy studies.

Bob Barrett: This is a podcast from C*linical Chemistry* sponsored by the Department of Laboratory Medicine at Boston Children's Hospital. I am Bob Barrett.

Where are all the new omics-based tests? That's the question that Patrick Bossuyt asks in his paper appearing in the October 2014 issue of *Clinical Chemistry*. After billions of dollars worldwide have been spent upon omics-based research and announcements of many biomarker discoveries, clinical medicine has not gone through a radical change, despite all of the investment of time, money, and the collaboration of thousands of study participants.

Dr. Bossuyt joins us in this podcast to review the omics landscape. He is a Professor of Clinical Epidemiology at the University of Amsterdam, The Netherlands, and has spearheaded the STARD Initiative for the improved reporting of diagnostic test accuracy studies and leads the biomarker in test evaluation research program in Amsterdam.

Doctor, your article is a commentary on so-called omics-based tests. What are these?

Dr. Patrick Bossuyt: Well, omics is a term that refers to a number of disciplines that try to characterize sets of molecules and sets of biological molecules, such as DNAs, RNAs, proteins. One example is genomics which investigates DNA sequences, but we also have transcriptomics looking at gene transcripts, and proteomics, a discipline that looks at proteins, and metabolomics, discipline that looks at metabolites.

So these disciplines are relatively new. They gathered force in the mid-90s, and the typical elements of these omics-based disciplines is that they generates high dimensional data. In most cases, there are more variables, more data points than study participants or study samples.

Bob Barrett: In your article, you mentioned a report from the Institute of Medicine on omics-based predictors and clinical trials. Why was that report written?

Dr. Patrick Bossuyt: Well, the omics-based disciplines gathered force because people were looking forward to personalized medicine, where these large sets of data could be used to develop predictors that could identify patients who benefit from therapy and separating them from those who do not benefit from therapy or are even harmed by therapy, so the essence of stratified medicine or personalized medicine.

But as it turned out, actually there were a number of failures where omics-based predictors did not perform as well as expected. This report from the Institute of Medicine was set up by committee to learn from these failures in the past and to identify criteria and other initiatives that could move to field forward. It was, in particular, written after a series of rather dramatic events at Duke University.

Bob Barrett: Well, could you tell us what happened at Duke University?

Dr. Patrick Bossuyt: Well, researchers at Duke University were involved with the discovery of omics-based predictors and they also want to take the next step, which means that they were planning on using omics-based predictors in clinical trials.

So between October 2007 and April 2008, there were three cancer clinical trials launched at Duke University and in these trials, patients with lung cancer and patients with breast cancer were assigned to a chemotherapy regimen on the basis of the results of omics-based predictors.

Now, a number of researchers voiced concerns about these omics-based predictors, because they failed to reproduce a result in their own institution. And later, 30 researchers go to MCI, again voicing concerns which were later confirmed, because it turned out that these omics-based predictors were not entirely fit for purpose, that several things had gone wrong in the developments of these predictors, and that patients had been prematurely included in these clinical trials. So, in short, these three cancer clinical trials should never had gone forward based on the evidence that was available at the time of their initiation.

Bob Barrett: Doctor, could you summarize for us the key elements of that report from the Institute of Medicine?

Dr. Patrick Bossuyt: I think the report looks back at what went wrong, but it also looks forward and it presents a number of criteria that can be used to verify whether omics-based predictors are fit for purpose or maybe not yet fit for purpose, but when they can be used in clinical trials with actual patients, and a short version of that checklist appeared in *Nature* last year, which initiated my Perspective in *Clinical Chemistry*.

	That checklist, something about 30 criteria, that people can use to see whether omics-based predictors are ready to take the next step, whether they are ready to be used in clinical trials. So these 30 criteria look at different elements in the discovery phase and the validation phase of these omics-based predictors. They look at the technical features but also look, for example, at statistical features.
Bob Barrett:	Are the elements in this report new?
Dr. Patrick Bossuyt:	I don't think they are new in itself, but what is new and original is that these 30 elements are now combined into a single concise checklist. Although I must say that the checklist is still quite long, it contains no less than 30 criteria, an explanatory document covers over 20 dense pages. So they're not new, but I think putting them together in a single document will be of benefit to many people who are interested in omics and people that are looking at omics-based predictors to be used in clinical trials.
Bob Barrett:	Finally Dr. Bossuyt, will this report bring us closer to personalized medicine?
Dr. Patrick Bossuyt:	I think the report is a very good step in the right direction. It clearly shows that there are pitfalls and potential failures in the discovery phase and the validation phase of these omics-based predictors. These are, as I said in response to your question, these are high dimensional data and many things can go wrong. So, the use of the report and use of the checklist in that report will help researchers to avoid some of these pitfalls. Whether it actually will bring us closer to personalized medicine is an open question, because in general development of these omics-based predictors and especially introduction of predictors that improve patient health have been much slower than everyone expected, and probably there are other reasons in addition to these pitfalls that can help explain why it is so difficult to build on the technological innovation that we have seen in the development of all these omics-based discipline.

So, as a future patient, I hope that the promises by this omics-based discipline to bring us closer to personalized medicine will materialize in the years to come, but I think it will take much more time than anyone anticipated. |
| Bob Barrett: | Dr. Patrick Bossuyt is Professor of Clinical Epidemiology at the University of Amsterdam, and has spearheaded the STARD Initiative for the improved reporting of diagnostic test accuracy studies, and leads the biomarker in test evaluation research program in Amsterdam. He has been our guest in this podcast from *Clinical Chemistry*. I am Bob Barrett. Thanks for listening. |