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This is the podcast from *Clinical Chemistry*. I am Bob Barrett. Diabetes is one of the most challenging health problems of the 21st century. The International Diabetes Federation estimates that today more than 250 million people around the world have diabetes.

Diagnosis and follow-up is often performed in special diabetes care centers. Patients have their blood drawn a week before they visit the physician to ensure that laboratory results were available for appropriate clinical action.

By providing results rapidly, following blood collection, point-of-care instruments could minimize patient inconvenience and possibly avoid an extra visit to the clinic. Studies have confirmed that immediate feedback of hemoglobin A_{1c} results improves glycemic control in type 1 and insulin-treated type 2 diabetic patients.

Drs. Erna Lenters and Robbert Slingerland recently investigated the acceptability of eight different hemoglobin A_{1c} point-of-care instruments using generally accepted performance criteria. Their findings published in an article in the January issue of *Clinical Chemistry* show that many of these devices fall short of clinical needs.

Dr. Lenters has been involved in hemoglobin A_{1c} standardization since 1993 and has performed numerous evaluations of different hemoglobin A_{1c} methods.

Dr. Slingerland is a Clinical Chemist and Laboratory Director at the Isala Clinic in Zwolle, in the Netherlands. He is responsible for diabetes testing and point-of-care testing and is Chair of the European Reference Laboratory for glycohemoglobin.

They are our guests in this podcast. So, tell us, what prompted you to do this study?

Dr. Erna Lenters:

Well, I was at the NGSP Steering Committee Meeting in San Diego in July 2007, and at this meeting, somebody asked, I believe it was David Sacks, if anybody knew what the performance was of the HbA_{1c} point-of-care instruments in the field. Nobody gave an answer, only a rough estimation was given. However, at that moment, we were already preparing this study and that meeting encouraged us to continue with the study.

- Host: Now, how was the study performed, and what differentiates it from similar studies?
- Dr. Erna Lenters: We used the well-defined CL SI, EP-10, EP-5, and EP-9 protocols to investigate imprecision, accuracy, and bias. Moreover, we used three different certified IFCC and NGSP secondary reference measurement procedures in combination with IFCC secondary HbA_{1c} reference material. This is the best reference material currently available and is also provided through the manufacturers to assign values to their calibrators. A better method comparison can't be performed, according to my opinion.
- Dr. Robbert Slingerland: So, in other words, we used the best methods available, the best calibrators in the market with the best protocols known.
- Dr. Erna Lenters: The power of this study also lies in the fact that we use two different lot numbers of reagents or cartridges, and we looked whether or not the NGSP criteria were met with each lot number with sometimes surprising results for the uses of point-of-care instruments.
- Dr. Robbert Slingerland: And I think it was sometimes perhaps also surprising for the manufacturers whose instruments were investigated.
- Host: So, tell us, what are the results of your research?
- Dr. Erna Lenters: Only two instruments, the Afinion and the DCA Vantage had a CV less than 3%. This CV was acceptable in the clinical relevant range. The CV of the other instruments was too high for optimal clinical use and was higher than 3%.
- Dr. Robbert Slingerland: One instrument had even a CV of 5.3%, which is way too much for clinical use.
- Dr. Erna Lenters: There is also too much variability in the results produced the different reagent lot numbers. One lot number passed the NGSP criterion and another lot number failed.
- Dr. Robbert Slingerland: Yes, and let us keep in mind that you are asking manufacturers prior to the study to provide us with normal lot numbers for use in the market. So, the variability reflects the daily use.

Dr. Erna Lenters: As a result of this, we conclude that the manufacturer NGSP certification doesn't always guarantee analytical performance of a result produced in the field. I think a reason for this might be that a manufacturer NGSP certification is done at the manufacturer's site, in ideal circumstances using experienced technologies. Apart from the InnovaStar, all methods were NGSP certified at the time the study started.

Dr. Robbert Slingerland: I must say that NGSP states that manufacturer's certification is performed only once a year with one lot number of reagent, and it's up to the manufacturer to ensure consistency among different lots during a year.

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The Steering Committee of the NGSP may need to reconsider their point of view based on the fact that apparently manufacturers can't guarantee consistency among different lots. That's what's shown in our article. However, that's not up to us and needs to be decided by the NGSP Steering Committee.

Host: So, in your opinion, what are the consequences of this study for the application of hemoglobin A_{1c} point-of-care instruments, and what should be done in your opinion?

Dr. Erna Lenters: Well, in general, the performance of all the devices we tested cannot be used for diagnosis of diabetes. The total error observed in either one or the other lot number tested was simply too large. Moreover, these devices cannot be used for monitoring of glycemic control until the variability between different lot numbers of reagents is resolved and assured.

As a consequence, either tens of millions of people would be wrongly diagnosed with diabetes or millions will not receive diabetes treatment of proven value.

Dr. Robbert Slingerland: In other words, our study supports the accumulating evidence that at this moment, no point-of-care device for measuring HbA_{1c} can be used for diagnosis of diabetes, as was recently recommended by the International Expert Committee on the role of A_{1c} assay in the diagnose of diabetes.

Another thing I would like to bring up is that HbA_{1c} point-of-care instruments fall under the so-called

“CLIA-Waived” regime. This may need to be reconsidered, because errors in the measurement of HbA_{1c} may have serious consequences as was pointed out in the editorial from Bruns and Boyd accompanying our article.

In our opinion, it's better to place the HbA_{1c} point-of-care instruments under the CLIA rules.

Dr. Erna Lenters:

We realized that it may sound that we are against the use of point-of-care instruments, but that's not the case. In fact, it's the opposite. We noticed the advantages of HbA_{1c} point-of-care instruments in a previous study at our diabetes care center.

The patients were eager to know their HbA_{1c}. The healthcare professional informed the patients about the importance of low HbA_{1c} and measured at the same time the HbA_{1c} with a point-of-care device. Most of the patients were very motivated in getting the HbA_{1c} fairly lower when it was too high. So, we definitely see the benefits of point-of-care instruments but we think that they can only be used on certain conditions.

Our conditions, which have to be met before a point-of-care instrument will be installed in or in the neighborhood of our hospital are, first of all, the performance should be of course excellent, that means no bias and a CV less than 2%.

Secondly, there should be connectivity to the central laboratory for data management. Third, it should be guided by and under responsibility of the Central Laboratory. Fourth, education and training for users should be done by experienced point-of-care coordinators. The point-of-care coordinator is the only one who can accredit the user. Only accredited users can use the instrument, and the instrument must be blocked for users who are not accredited.

Last one, internal quality control and proficiency testing should be coordinated by the point-of-care coordinator.

Dr. Robbert Slingerland:

Let's keep it in mind, also certain HbA_{1c} laboratory methods have problems concerning analytical performance. Dr. Westgard wrote an essay about the performance of HbA_{1c} laboratory methods based on the CAP survey results and it wasn't a very positive message according to our opinion. The current quality aspects for HbA_{1c} measurement are not

adequate to meet the clinical needs. This is recognized by the NGSP and the College of American Pathologist in both criteria.

Dr. Erna Lenters:

Fortunately, there is also good news. We know from experience that new versions of cation exchange HPLC have a total CV of approximately 0.5%, which is superior in comparison with immunoassay and point-of-care devices. These instruments can easily meet the clinical needs, in other words, no bias and a CV less than 2%.

Host:

Well lastly, can you give us a glimpse of where your research in this field is going?

Dr. Erna Lenters:

When I discussed the results of this study with our Diabetologist, Professor Bilo, we both realized that there is a gap between clinical chemistry where the results are produced and the healthcare professional who interpret the results.

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We think that the biggest problem is that most of the healthcare professionals don't know what the performance is of the HbA_{1c} method, which is used to produce an HbA_{1c} result, when I am talking about lab and point-of-care instruments.

For instance, most of the nurse practitioners see an HbA_{1c} value as a true value without uncertainties and don't know there was much variability in the HbA_{1c} result measured with some HbA_{1c} methods. Therefore, we designed a survey to evaluate the knowledge among care providers about the HbA_{1c} assay and our intention is to send the survey to different diabetes healthcare professionals.

Dr. Robbert Slingerland:

And in addition to this, if I may add, it's important that the limitations of current point-of-care instruments and laboratory methods be understood by healthcare professionals as these may have important clinical implications as was pointed out in the editorial from Bruns and Boyd.

Clinical chemists can play and in my opinion must play an important role by providing healthcare professionals with the information they need, by measurement and certainty to properly interpret the laboratory and point-of-care HbA_{1c} results.

So, we like to combine the findings of this study, presented in this article with answers we get from the survey on the knowledge of HbA_{1c} results among healthcare providers.

Dr. Erna Lenters: Hopefully, we will get the answers we need, we'll be continued.

Host: Dr. Erna Lenters is a Researcher and Dr. Robbert Slingerland is a Laboratory Director at the Isala Clinic in Zwolle, in the Netherlands. They have been our guests in this podcast from *Clinical Chemistry*. I am Bob Barrett. Thanks for listening.

Total Duration: 12 Minutes