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Report of the ADA/EASD/IDF Working Group of the HbA_1c Assay

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Robert Rizza (ADA)
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Staff: Richard Kahn,
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Guests: Kor Miedema (IFCC)
David Sacks (NGSP)

Meeting objective

The charge to the Workgroup was to review the opportunities arising from the development of a new IFCC reference method for the measurement of HbA_1c, and to make recommendations on its implementation.

Meeting synopsis

The meeting began with a presentation on the current technology regarding the measurement of HbA_1c and in particular, the history of the new IFCC reference method. This was followed by a presentation demonstrating the convergent effect of standardisation within the global network of NGSP. Also, the status of NGSP certification was reviewed.

After some discussion the Workgroup agreed that the IFCC reference method should become the global reference standard ("anchor"), and that all manufacturers should now calibrate their instruments to the new method.

The workgroup acknowledged that such a change tentatively implies that the reported HbA_1c numbers would be 1-2% less than those currently reported. Thus, the cut-off points for what is normal, or good/poor control would shift downward.

The Workgroup then discussed how the HbA_1c results should be reported: should they be reported using the IFCC numbers, which would mean an abrupt lowering of individual test results? Or should the linear relationship with the DCCT method be used to convert the new numbers back to the current range of values, which would mean little or no perceptible change in reported numbers? Some of the pros and cons discussed were:

Method	**Report new IFCC range**	**Maintain current values**
Advantages	– the reported values reflect the actual values – opportunity to re-educate professionals and people with diabetes about meaning and value of the HbA_1c test – opportunity to redefine HbA_1c (see below)	– familiar to patients and clinicians – relates HbA_1c values to existing evidence base e.g. UKPDS, DCCT
Dis-advantages	– high cost, and prolonged timeline for education necessary to prevent confusion – partial or piecemeal implementation will worsen existing differences between laboratories – risk of deterioration in glucose control as experienced in a Swedish study[1] – lower numbers make it even more difficult to convince patients that small changes in percent A1C have a big impact on health	– not the 'pure' result – frequently confused with glucose levels in countries where mmol/l used – missed opportunity to reinforce the importance of the test.

The above points were discussed at great length and each Workgroup member articulated his or her concerns and recommendations. Discussion then centered on how we might use the opportunity / challenges pre-

sented by the introduction of the new IFCC method to re-define the HbA_1c and its importance in diabetes care. Of paramount importance was the agreement that the entire world should be using / reporting the same reference values.

All Workgroup members agreed that the very name of the test "A1C" or "hemoglobin A1C" was confusing, especially to patients who do not understand its connection to glucose / diabetes (since the name suggests a blood disorder). Also, everyone agreed that the small numbers (e.g. 7%, 9%) do not readily convey to patients that even a 0.5-1% change has a major effect on health. Consumers believe that since it takes a 10-40 unit change in most measurements for there to be a meaningful difference (e.g. outdoor temperature), so when their diabetologist reports a 1% change their response is "that's trivial".

The Workgroup decided that with the above concerns, we now have the opportunity to redefine the entire assay. A suggestion was made by both the European and American representatives, enthusiastically supported by all other members, that the name of the assay be changed to something that reflects the "MBG" (mean blood glucose) and that we should avail ourselves of the close relationship between HbA_1c and mean blood glucose. This relationship, which is one of direct proportionality, was observed on a retrospective examination of 7-point glucose assays during the DCCT study. The relationship is:

MBG (mmol/l) = 1.84 x IFCC HbA_1c

(Of course a different factor will arrive at MBG if expressed in mg/dl.) If this relationship can be confirmed in a prospective study, then we will have the opportunity to report the new IFCC figures as to mean blood glucose. Hence the HbA_1c test will have a new name (e.g. MBG), a new range (in familiar glucose units), and a more direct and recognizable link to glucose levels for people with diabetes and their health care professionals.

Advantages of this approach are: a clear revision of the test along with a new range, with no real opportunity for confusion (although substantial preparation and re-education will still be needed); a simplification of the range allowing every person with diabetes to understand their own target level, particularly if already using home glucose-monitoring; and more likely potential for future use as a diagnostic tool.

Disadvantages include the possibility that the simple proportionality, or even a straight linear relationship, may not apply to all populations or to extremes of MBG/HbA_1c, in which case we might be forced to adopt more complex conversions or reconsider the idea altogether. Also, to obtain the full benefit of a link with home tests, the MBG will be reported in two different units (mmol/l vs mg/dl) with the usual minor but frustrating conversion problems. Overall, the group favoured proceeding with this innovative approach to implementation of the new standard.

The Workgroup then voted unanimously to endorse this plan, and outlined the following steps:

Action	Timing	Lead Responsibility
1. Adoption of IFCC reference method as the new global standard for calibration	Immediate	IFCC/NGSP
2. Use the new IFCC methodology to anchor an "international certification process" within the existing international laboratory networks.	Immediate	NGSP/IFCC
3. The IFCC and NGSP will direct manufacturers NOT to change the HbA_1c report out values until further work, outlined below, has been completed i.e. DCCT/UKPDS range and numbers will continue to be used	Immediate	IFCC/NGSP
4. Determine if there are other retrospective data (in addition to references 2-4 below) that can be used to link HbA_1c to MBG. In particular, data for non-white Type 2 patients would be valuable	4–6 months	IFCC
5. Design and conduct prospective studies on various populations world-wide to confirm/establish the HbA_1c-MBG relationship	2004–2007	ADA/ EASD/IDF
6. Plan public and professional information programme about the new reporting system	2005–2007	Current Workgroup

The Workgroup now submits this final report to its respective sponsors for review and approval. If satisfactory, the above plan will be announced at the upcoming ADA and EASD meetings and a research consortium should be established as soon as possible to address item 5 above.

References

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