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Differences in interpretation of haemoglobin A1c values among diabetes care professionals

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ABSTRACT

Background: To assess the expected precision of HbA_{1c} measurements and the magnitude of HbA_{1c} changes eliciting the advice to change treatment among diabetes care professionals.

Methods: A seven-item questionnaire was sent to participants through a website. The survey focused on physicians and nurses involved in diabetes care.

Results: In total, 104 physicians, 177 diabetes specialist nurses, and 248 primary care nurses responded to the survey. A large number of the nurses (44%) and only a small number of the physicians (4%) were not aware of the inherent uncertainty of HbA_{1c} results. Nurses considered adjusting therapy based on very small changes in HbA_{1c} whereas physicians in general adhere to 0.5% (5.5 mmol/mol) as a clinically meaningful cut-off point. After therapy adjustment, a very small (0.1%) or no increase in HbA_{1c} was considered to be significant enough to conclude that glucose regulation has worsened by 49% of the nurses and only 13% of the physicians.

Conclusion: Significant differences exist in the interpretation of changes in HbA_{1c} results between physicians and nurses. Nurses consider therapy changes based on very small changes in HbA_{1c}, whereas physicians preferably agree to the clinically relevant change of 0.5% (5.5 mmol/mol). Changing therapy based on relatively small changes in HbA_{1c} might lead to undue adjustments in the treatment of patients with diabetes. There is a clear need for more training for all diabetes care professionals about both the clinical significance and accuracy of HbA_{1c} measurements.

KEYWORDS

Glycated haemoglobin, interpretation, healthcare professionals, nurses, physicians

INTRODUCTION

Both in subjects with type 1 and type 2 diabetes mellitus, adequate glucose control is considered of major importance.[1] The degree of glucose control can be assessed by frequent home blood glucose measurements, but the most widely acknowledged and reliable assessment is the measurement of the concentration of glycated haemoglobin (HbA_{1c}).[2] As such, HbA_{1c} is one of the main parameters with regards to glucose control in most outcome studies.[3,4] Therefore, most diabetes care professionals rely (at least in part) on HbA_{1c} levels to decide whether or not to recommend treatment changes to patients.

Still, HbA_{1c} measurement, and thus the interpretation of results, has its pitfalls. The analytical performance of the HbA_{1c} assay is an important factor in the overall performance of the HbA_{1c} assay.[5,6] Not all laboratories may be able to measure HbA_{1c} precisely enough to allow an outcome within 0.5% (5.5 mmol/mol) of the actual value.[6] For example, in the Netherlands, initiation of insulin therapy would be considered in a person with type 2 diabetes mellitus with an HbA_{1c} > 7.0% (53 mmol/mol) on maximal oral therapy, at least based on the advice in the 2006 primary care guideline which was the prevailing document at the time of this survey.[7]

Currently, limited data are available on how healthcare professionals perceive the accuracy of the HbA_{1c} assay and how they adjust therapy based on consecutive changes in HbA_{1c}. One study demonstrated that the majority of general practitioners presumed a high (analytical) performance of the assay without considering the biological variation, and acted on even small differences in subsequent HbA_{1c} measurements.[8] Studies assessing the difference between various healthcare professionals, including physicians and nurses, with respects to interpretation of (changes in) HbA_{1c}, are lacking.

The aim of this study was to assess the daily practice regarding the interpretation of HbA_{1c} results, i.e. the expected precision of HbA_{1c}, and the magnitude of HbA_{1c} changes possibly eliciting the advice to change treatment. Therefore, we surveyed a group of diabetes care professionals regarding these aspects.

MATERIALS AND METHODS

Design

In this cross-sectional descriptive study, an internet survey was used to collect data. The study was part of a larger survey regarding the frequency of self-monitoring of blood glucose recommended by professionals and was carried out from March to June 2010.[9] Respondents were asked to indicate their profession (physician, diabetes specialist nurse or primary care practice nurse, P, DSN and PCPN, respectively). The remainder of the questionnaire included six questions regarding the use and interpretation of HbA_{1c}. The first question assessed the expected reliability of HbA_{1c} at a level of 7.0% (53 mmol/mol). In the other five questions, patient cases were presented assessing at what HbA_{1c} level or HbA_{1c} changes the healthcare professional would initiate or change therapy (*table 1*). In total, 6965 primary care assistants, diabetes specialised nurses and doctors from the database of the Langerhans Medical Research Group were invited by email to participate in this survey. The Langerhans Medical Research Group is the research division of the Langerhans Foundation, a national diabetes organisation that organises educational activities for diabetes care professionals. The database contains information and email addresses of diabetes care professionals who are interested in the activities that are organised by the Foundation. All professionals registered in the database were invited to take part in the survey. In addition, a message containing a link to the survey was placed on the website of the Dutch Association of Diabetes Care.

Statistical analysis

Differences in the distribution of answers between the groups (P, DSN and PCPN, respectively) were tested using Fisher's exact test. P-values < 0.05 were considered statistically significant. Comparisons between pairs of groups were adjusted for multiple testing using the Bonferroni correction. SPSS version 20 (IBM Corporation, Armonk, NY) was used for the analysis.

Table 1. *Questions / patient cases*

A. At an HbA_{1c} value of 7.0% (53 mmol/mol) I expect an uncertainty of ...
B. When someone with T2DM and < 70 years is on maximal oral therapy and you consider starting insulin, at which HbA_{1c} level do you decide to start insulin?
C. Consider someone with T1DM (< 70 years) without signs or symptoms of hypoglycaemia or hyperglycaemia. HbA_{1c} was 6.9% (52 mmol/mol) at the previous visit. After three months you get a new result. At which HbA_{1c} value would you consider and propose a treatment adjustment?
D. Consider someone with T2DM (< 70 years) without signs or symptoms of hypoglycaemia or hyperglycaemia and treated with a combination of insulin and metformin. Three months previously, the HbA_{1c} was 7.3% (56 mmol/mol). The insulin dose was increased. At which HbA_{1c} level would you consider further treatment changes?
E. Consider someone with T2DM and an HbA_{1c} value of 9.0% (75 mmol/mol). Treatment adjustments are made. How much decrease in HbA_{1c} value would you consider sufficient to allow the conclusion that glucose regulation has improved?
F. Again consider someone with T2DM and an HbA_{1c} value of 9.0% (75 mmol/mol). Treatment adjustments are made. How much increase in HbA_{1c} value would you consider sufficient to allow the conclusion that glucose regulation has worsened?

T1DM = diabetes mellitus type 1 ; T2DM = diabetes mellitus type 2.

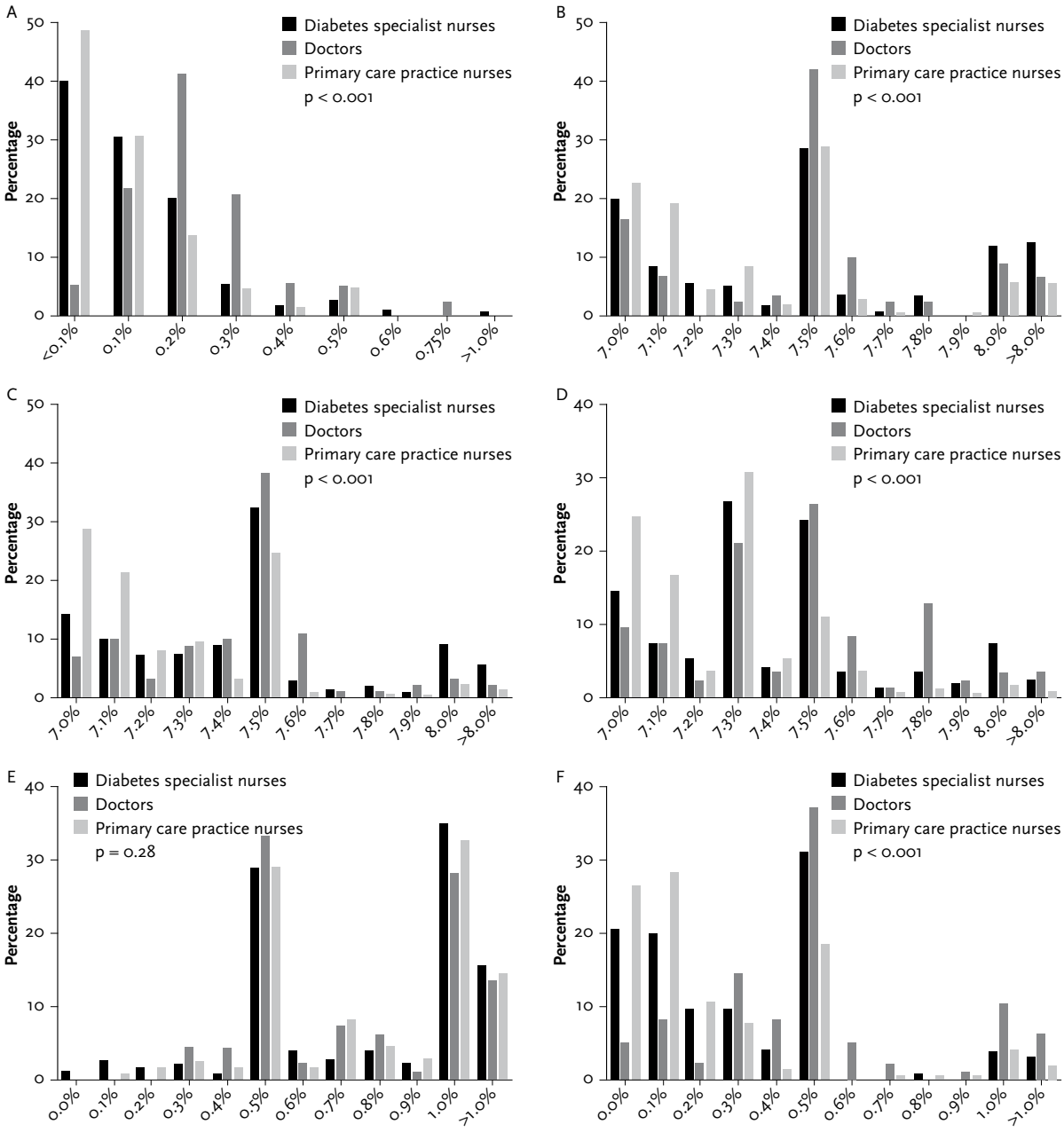
RESULTS

For this analysis, 529 healthcare professionals were included: 48 internists, 28 general practitioners, 28 paediatricians (total physicians = 104), 177 diabetes specialist nurses and 248 primary care practice nurses (total nurses = 425). The questionnaire only contained cases and questions in connection to HbA_{1c}. No questions were included detailing the demographics of the responders, except for the specific role as caregiver.

The responses to Question A (*table 1A, figure 1A*) show that a large number of the nurses (44%) and only a small number of the physicians (4%) were not aware of the inherent uncertainty of the HbA_{1c} result. When comparing the responses of the two groups of nurses, they were not significantly different from each other ($p = 0.714$, Bonferroni corrected), but each group of nurses significantly differed from the physicians ($p < 0.01$, Bonferroni corrected).

The responses to Case B (*table 1B, figure 1B*) show that a cut-off point of 7.0% (53 mmol/mol) is regarded as a signal for treatment changes by 19.8% of the healthcare

Figure 1. *Responses of the healthcare providers to the presented cases*



professionals, and a level of 7.5% (58 mmol/mol) is regarded by 32.2% of the healthcare professionals as a sufficiently powerful signal to consider starting insulin. Overall there was a significant difference in the responses between the three groups ($p < 0.001$); however, the difference between the diabetes specialised nurses and physicians was not significant ($p = 0.051$, Bonferroni corrected). Case C (*table 1C, figure 1C*) shows that a sustained HbA_{1c} level between 7.0% (53 mmol/mol) and 7.5% will prompt the vast majority (87%) of the healthcare providers to consider changing therapy in order to reach the predefined target value. Of them, 29.9% chose a level of 7.5%, in accordance with a difference of 0.6% (6 mmol/mol). Almost all other respondents (57%) chose a value between 7% and 7.4%. Overall the responses differed significantly between the groups ($p < 0.001$). PCPN were mainly responsible for this difference since they were more inclined to choose a level below 7.2%. Physicians

and DSN did not differ significantly from each other (p = 0.084, Bonferroni corrected). Case D (*table 1D, figure 1D*) provides a somewhat mixed response, with healthcare professionals tending to either start treatment changes with an HbA_{1c} which stays at a consistently higher level of 7.3% (56 mmol/mol) or, again, at the cut-off point of 7.5% (58 mmol/mol) and 7.0% (53 mmol/mol). PCPN seem more focused on trying to reach lower HbA_{1c} values than doctors (p < 0.001), specifically to reach the treatment goal of 7.0% (53 mmol/mol), whereas the responses of physicians and diabetes specialised nurses were not significantly different (p = 0.201, Bonferroni corrected). Case E addresses which change in HbA_{1c} is considered sufficient to allow the conclusion that glucose regulation has improved after treatment adjustment. A change of 1.0% (11 mmol/mol) was considered to be clinically relevant by 32.6% of the healthcare professionals, whereas 29.8% thought 0.5% (5.5 mmol/mol) was clinically relevant. There was no significant difference (p = 0.28) in responses between the different healthcare professionals (P, DSN and PCPN). Case F (*table 1F, figure 1F*) shows that especially DSN (40.0%) and PCPN (54.8%) seem to conclude that glucose regulation has worsened even when the HbA_{1c} value was the same or only slightly (0.1% (1 mmol/mol)) increased. The difference in responses between these two groups was not significant (p = 0.186, Bonferroni corrected). A major portion of the doctors (37.1%) follow the clinically relevant change of 0.5% (5.5 mmol/mol).

DISCUSSION

The results of this study indicate that nurses seem to be well aware of the importance of HbA_{1c} for the management of diabetes, but are now overly reacting to too small changes in the value of HbA_{1c} observed in their patients. This observation could partly be explained by the fact that most of the nurses consider an HbA_{1c} value to be an absolute value and are less aware of the fact that every HbA_{1c} result has uncertainty based on the analytical performance of the HbA_{1c} method used. As a consequence, nurses tend to consider treatment changes based on very small or even no differences in subsequent HbA_{1c} results. Indeed, physicians and nurses interpret HbA_{1c} differently in concluding that there is a decline or improvement of glycaemic control. A decrease of at least 0.5% (5.5 mmol/mol) or 1.0% (11 mmol/mol) at an HbA_{1c} value of 9.0% (75 mmol/mol) after adjustment of therapy is considered sufficient by all healthcare professionals to allow the conclusion that glucose regulation has improved. In contrast, a very small or no increase of HbA_{1c} is considered by most of the nurses as sufficient to come to the conclusion that glucose regulation has worsened.

In general, guidelines consider a difference of 0.5% (5.5 mmol/mol) to be clinically significant.[1,7] However, a recent study showed that the analytical performance of some HbA_{1c} assays may not be accurate enough to sufficiently support treatment decisions in the management of patients with diabetes when differences in serial HbA_{1c} measurements amount to 0.5% (5.5 mmol/mol) or less.[6] Combining this with the outcome of this survey, we can conclude that many of the nurses may react to HbA_{1c} outcome variations based on the variability of the HbA_{1c} method used instead of the true changes in the degree of glucose control. As a consequence, this could lead to undue treatment changes with accompanying costs and/or inconvenience for the patient. Furthermore, several studies have confirmed that, especially for older patients, the benefit of lowering the HbA_{1c} value at all costs (including patient inconvenience) is limited and may even lead to a higher mortality rate.[10,11]

Average HbA_{1c} of patients with diabetes in primary healthcare in the Netherlands is amongst the lowest in the world,[12] and studies such as the Diabetes Control and Complications Trial and the UK Prospective Diabetes Study showed very clearly that strictly controlled patients have a lower risk of developing microvascular and macrovascular complications.[3,4] We believe that every healthcare professional should be supplied with the information they need to interpret HbA_{1c} values properly. The reference change value which is defined as the critical difference between two consecutive HbA_{1c} measurements representing a significant change in health status might be a valuable tool.[13,14] The analytical performance of different HbA_{1c} methods ranges from poor (most of the point of care instruments and some immunoassays) to state of the art (newer version cation-exchange HPLC methods).[15,2] It is not realistic to assume that every healthcare professional is aware of the analytical performance of every HbA_{1c} method, not even if the method used by the main laboratory is state-of-the-art. Laboratory directors or other decision makers are responsible for the choice of the HbA_{1c} method. This choice is based on many factors such as analytical performance (which is hopefully the most important factor), sample throughput (commercial laboratories), costs per test, support of and contact with the manufacturer etc. The reference change value provides insight into the impact of poorly performing methods.

One of the limitations of this study is that only healthcare providers in the Netherlands were invited to participate in this survey. Since healthcare systems may be organised differently in different countries, the results presented here may preclude generalisation. An international survey among different healthcare providers should be performed to confirm our findings. Furthermore, a limitation of the present study is the low response to the internet survey.

This limited response may have led to a non-response bias. Unfortunately, data on the characteristics of the non-respondents could not be compared with the characteristics of responders, since demographic data were lacking for both groups, thus preventing proper assessment of the magnitude of this potential bias.

In conclusion, significant differences in interpretation of (changes in) HbA_{1c} results between physicians and nurses exist. Nurses consider therapy changes based on very small changes in HbA_{1c}, whereas physicians preferably agree to the clinically relevant change of 0.5% (5.5 mmol/mol). Changing therapy based on relatively small changes in HbA_{1c} might lead to undue adjustments in the treatment of patients with diabetes. There is a clear need for more training for all diabetes care professionals about both the clinical significance and accuracy of HbA_{1c} results. The authors are planning a follow-up study to further explore the observed differences between the diabetes healthcare professionals with respect to interpretation of HbA_{1c}.

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DISCLOSURES

No funding was received. The authors declare no conflicts of interest.

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