Self-monitoring of glucose in type 2 diabetes mellitus: a Bayesian meta-analysis of direct and indirect comparisons

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CRD summary
This review assessed the relative effectiveness of different approaches to monitoring glycaemic control in type 2 diabetes. The review methods were rigorous and a Bayesian meta-analysis was used. The author's conclusion, that self-monitoring of blood glucose is effective and is likely to be more effective than self-monitoring of urine glucose, appears appropriate. The importance of regular feedback was noted.

Authors' objectives
To evaluate the relative effectiveness of self-monitoring of blood and urine glucose, compared with no self-monitoring, for reducing haemoglobin A1c (HbA1c) in type 2 diabetes mellitus.

Searching
Two reviewers searched MEDLINE (inception to November 2005), EMBASE (inception to 2004) and the Cochrane Library (Issue 4, 2004); the keywords were reported. Previous systematic reviews were used to identify further studies. Full reports published in English, French, German or Dutch were included.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) comparing the effectiveness of different monitoring strategies were eligible for inclusion. Validation studies, which determined the reliability of methods and instruments for SMBG, were excluded.

Specific interventions included in the review
Studies comparing self-monitoring blood glucose (SMBG) with interventions without SMBG, or with interventions including self-monitoring urine glucose (SMUG), were eligible for inclusion. Studies that used SMBG in both the intervention and control groups were eligible for inclusion if the intervention group, but not the control, also received regular medical feedback.

Reference standard test against which the new test was compared
The review did not include any diagnostic accuracy studies that compared the performance of the index test with a reference standard of diagnosis. The review included trials of the effectiveness of tests used in a monitoring application.

Participants included in the review
Studies of patients with type 2 diabetes were eligible for inclusion, regardless of treatment (with or without insulin or oral treatment). Mean baseline HbA1c levels ranged from 6.1 to 12.4%. In the majority of studies (11 out of 13) the participants were not using insulin.

Outcomes assessed in the review
Studies assessing glycated haemoglobin (GHb, HbA1c, HbA1) levels were eligible for inclusion. The length of follow-up reported by the included studies ranged from 3 to 12 months.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed studies for inclusion.

Assessment of study quality
Two reviewers independently assessed the methodological quality of the included studies using a 13 item checklist for randomised and non-randomised studies. Any discrepancies were resolved at a consensus meeting. The checklist
included items relating to blinding, randomisation, baseline equivalence, validity of analysis methods, accounting for loss to follow-up and compliance. An overall quality score (0 to 13) was calculated, where a positive item was assigned a value of one and a negative or unable-to-determine item was assigned zero.

Data extraction
Two reviewers independently extracted the data using a standard data extraction form. Where sufficient information was available, changes from baseline values and their standard deviations were calculated for glycated haemoglobin. For crossover studies, changes from baseline values were calculated as the difference between the baseline and the last follow-up measurement before crossover.

Methods of synthesis
How were the studies combined?
The studies were pooled using a Bayesian random-effects meta-analysis. The analysis comprised two parts, the first of which pooled the change from baseline in HbA1c for each of the interventions separately. The second part used a mixed treatment comparison (MTC) model to estimate the relative effectiveness of SMUG, SMBG and SMBG with feedback compared with interventions without self-monitoring. Non-informative normal prior distributions were used for the treatment effects. Estimates and 95% credible intervals (CrIs) of the mean difference between treatments were presented.

How were differences between studies investigated?
The included studies were assessed for heterogeneity in population, baseline characteristics and interventions to inform decisions on pooling. Separate meta-analyses were performed of non-insulin requiring participants and all type 2 diabetic patients (including those treated with insulin). Additional analyses were performed, adjusting for baseline glycaemic level and also weighting each study by its quality score.

Results of the review
Thirteen studies (n=2,160) were included in the review; 12 studies (n=2,011) were included in the meta-analysis. Three studies compared SMBG with SMUG, nine compared SMUG with an intervention without self-monitoring, and two compared SMBG with SMBG and feedback programmes.

The median internal validity score was 9 (range: 4 to 10) out of a possible 13. No studies reported adequate allocation concealment or patient blinding, and only one reported blinding of the outcome assessors.

Pooled estimates of change from baseline in HbA1c.
The pooled changes from baseline in HbA1c were -0.47% (95% CrI: -0.66, -0.28) for interventions without self-monitoring, -0.61% (95% CrI: -1.20, -0.05) for interventions with SMUG, -0.87% (95% CrI: -1.14, -0.58) for interventions with SMBG, and -1.48% (95% CrI: -2.06, -0.89) for interventions with SMBG and feedback.

Relative effects based on MTC meta-analysis.
It was estimated that there was a 69% probability that an intervention with SMUG results in a larger reduction in HbA1c than an intervention without self-monitoring, and a 99% probability that an intervention with SMBG results in a larger reduction in HbA1c than an intervention without self-monitoring. The probability that interventions with SMBG are more effective than interventions with SMUG was estimated as 84%.

Adjustment for baseline glycaemic control and weighting by quality score.
When estimated relative effects were adjusted for the baseline HbA1c, the differences between interventions increased, except for the difference between SMBG and SMUG which was reduced. When studies were additionally weighted by quality score, the probability that SMUG was more effective than interventions without self-monitoring reduced to 54%, and the probability that interventions with SMBG are more effective than SMUG increased to 88%. The results were similar when analyses were restricted to studies of non-insulin requiring patients.
Authors' conclusions
Evidence from currently available RCTs supported the effectiveness of SMBG for reducing HbA1c in type 2 diabetes; regular feedback on HbA1c levels is important. SMBG is likely to be more effective than SMUG.

CRD commentary
The review addressed a clearly stated question on the relative effectiveness of different approaches to monitoring glycaemic control in type 2 diabetes; appropriate inclusion criteria were defined. The search strategy was reasonable and reported clearly, though the use of some language restrictions and the limitation to published studies might have resulted in the loss of some relevant data. The review methods were clearly reported and included measures to minimise the introduction of error and bias. The methodological quality of the included studies was assessed using an appropriate tool, and the results were reported in full and incorporated in the meta-analysis as a weighting factor.

Some of the meta-analysis methods were clearly described, although further discussion of the methods used in the MTC analysis and the adjusted analyses would have aided interpretation. It is also worth noting that the use of quality scores to weight studies in a meta-analysis has its limitations as a method of assessing the impact of study quality; information on the impact of individual quality characteristics is lost and quality scores (and hence study weightings) can vary widely depending upon the tool used to generate them. The author's conclusions reflect the data presented. The author also noted that HbA1c is a surrogate end point and the effects of self-monitoring interventions on longer term clinical end points remain unknown.

Implications of the review for practice and research
Practice: The author stated that the results were positive for the effectiveness of SMBG in reducing HbA1c and that regular feedback is important.

Research: Additional, high-quality studies that include final clinical end points are required. Studies with patient-reported outcomes, such as quality of life, are also of interest.

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