NETSCC, HTA

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1. Title: Self monitoring of blood glucose in type 2 diabetes

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3. Plain English summary

Type 2 diabetes (T2DM) is usually seen in people who are overweight or obese, and the prevalence is increasing. In most patients, it is a progressive disease, in the sense that treatment starts with diet and other lifestyle measures such as physical activity, but that tablet therapy is soon required, and progression to needing insulin is common as time passes. This is not invariable, in that some people manage to lose weight and be physically active, and may not progress.

The problems underlying progression are two-fold. Firstly, overweight and obesity make the body less sensitive to insulin ("insulin resistance"), so that the pancreas needs to produce more to keep blood glucose levels normal. Secondly, the beta cells in the pancreas, which produce insulin, can become exhausted so that insulin production cannot be maintained. By the time someone is diagnosed with T2DM, they have usually lost about half their beta cell capacity.
Progression may mean that patients go through the following treatment stages;

- Diet and physical activity, aiming to achieve weight loss and reduce insulin needs and resistance
- Treatment with a single oral drug, usually metformin
- Treatment with two oral drugs, usually by adding a sulphonylurea to the metformin
- Treatment with three oral drugs
- The addition of insulin, usually with a once daily long-acting ("basal") insulin, taken along with metformin and a perhaps reduced dose of sulphonylurea
- When that fails, moving to more complex insulin regimens, such as adding short-acting insulin at meal-times, or twice daily mixed insulins, with the sulphonylurea being discontinued

Each step in the treatment pathway is triggered by rising blood glucose levels. The NICE guideline recommends that the target should usually be an HbA1c of 6.5% or less. HbA1c is a blood test, taken by a doctor or nurse and measured in a laboratory, which gives an average blood glucose over the past 2 to 3 months. The HbA1c (or glycated haemoglobin) test measures the amount of glucose being carried by the red blood cells.

If not well-controlled, diabetes will increase the risk of heart disease, blindness, renal failure, amputation and other complications. So patients need to keep their blood glucose under as good control as possible. To do so, they need to know what it is. They will usually have HbA1c measured at intervals which will let them know if control is poor. However, HbA1c, being an average, will not explain why control is poor. Blood glucose can fluctuate from hour to hour, and blood glucose testing with meters and strips can identify the times when blood

glucose is too high. It can also be used to check on when the level might be going too low – hypoglycaemia or "hypos".

Nowadays, patients can measure their blood glucose level by putting a drop of blood on to a test strip, and using a meter to read colour changes in that. This is painful as patients are required to prick their finger with a lancet to obtain a blood sample. The strips are expensive. Knowledge of high blood glucose levels may cause anxiety, and fear of the long-term complications. However, it can also give patients information which they can use to improve control of their blood glucose. They can also measure the amount of glucose in their urine, which is a guide to blood glucose level.

4. Decision problem.

The use of blood glucose monitoring in England has risen steadily and in 2006 cost the NHS ~ £136M (up from ~£ 107M in 2002). There have been several recent trials and systematic reviews to evaluate its clinical and cost-effectiveness, but self monitoring of blood glucose (SMBG) still remains a controversial area. So the first question may be – why is there still a question?

There are (at least) five answers to that.

Firstly, the evidence is to some extent conflicting, with different types of study design giving different results. There is also the issue of what harm it may do. Studies have shown that SMBG can increase anxiety.

Secondly, as with other diagnostic interventions, there is a hierarchy of questions;

- The technical level – does it accurately measure what it is supposed to?
- The treatment level – does SMBG lead to changes in treatment?
- The outcomes level – does SMBG reduce the risk of heart disease, visual loss, etc

Thirdly, SMBG is not an end in itself, but only an aid to management, and another question is who uses the results? Do the patients record the results and bring them to the clinic or surgery to discuss the implications, so that the doctor or nurse can adjust treatment accordingly? Or do the patients use the information themselves and self-adjust diet, or doses of oral drugs or insulin?

Fourthly, if patients are going to self-adjust management, are they given sufficient education with which to do that?

Fifthly, knowledge alone does not always lead to action. Education might have two strands – knowledge of how to adjust treatment, but also "motivational knowledge" which makes people understand the importance of good control.

The NICE Clinical Guideline 66, which was written before the two recent trials (DIGEM and ESMON) had reported, supported SMBG in certain circumstances, but stated that past research had failed *"to address the complicated issue of its integration into patient education and self-management behaviours"*.

4.1 Questions

Primary question
Is SMBG worthwhile in patients, or selected patients, with type 2 diabetes,

- on diet alone

- on metformin monotherapy
- on combination oral therapy
- on combinations of oral therapy and basal insulin?

For the purposes of this review, we will assume, in line with NICE guidance 66, that SMBG is worthwhile in those on more complicated insulin regimens such as basal + mealtimes, or twice daily mixed insulins, and the evidence on that will not be examined.

Additional questions include;

- which sub-groups of patients benefit most from SMBG?
- which are harmed?
- what education is required to enable the patients, and their health care professionals, to use the SMBG results to improve their diabetes control?

Additional questions, if time permitted, would be;

- how do we motivate those groups of patients that could benefit from SMBG to use it to improve their diabetes control?
- For those patients in whom SMBG is shown to be worthwhile, a subsidiary question might be how to best deliver SMBG (in terms of frequency and quality of testing, education, use of results, costs)?

- *Intervention*

The intervention will be self testing of blood glucose with a meter and test strips.

- *Place of SMBG*

According to NICE CG66, the intervention is recommended for all T2DM patients, including newly diagnosed. Evidence from existing reviews suggests that not all groups of patients benefit.

Patients could be grouped by

- type of treatment (diet alone, metformin monotherapy, dual therapy (met + su), triple oral therapy, the combination of once daily basal insulin + orals
- baseline HbA1c
- duration of diabetes
- age
- patient preference
- previous use of SMBG
- levels of education
- motivation for self-care.

If possible, the review would try to stratify the sub-groups of patients with respect to effectiveness of SMBG.

- *Relevant comparators*

The comparators will be;

- self monitoring of urine glucose (SMUG)
- monitoring with HbA1c
- a combination of the above
- no monitoring

- *Population and relevant sub-groups*

The population will be people with type 2 diabetes, of all ages. Subgroups: treatment groups; elderly.

Exclusions: Pregnant women. People on insulin regimens more complex than once daily basal, such as MDI or twice daily pre-mixes.

- *Key factors to be addressed*

Clinical effectiveness (main outcome HbA1c), costs, barriers to SMBG, (eg. education, patient preference, anxiety/depression, visual impairment), harms (due to devices or counterfeit strips).

5. Methods

Report methods for synthesis of evidence of clinical effectiveness

A review of the evidence for clinical effectiveness will be undertaken systematically following the general principles recommended in the QUOROM statement[1].

- **Population**
  - Inclusion criteria:
    - Studies including adults patient with type 2 diabetes on any treatment or combination of regimens, including lifestyle, oral agents or insulin.
    - Minimum duration of study = 12 weeks. (As it may take longer for people using SMBG to assess the effects of changes and fine tune their treatment, a trial giving a positive result at 12 weeks would be give useful information.. However, a negative result at 12 weeks would not be regarded as proof that SMBG was ineffective).
  - Exclusion criteria:
    - Pregnant women with diabetes.
    - Studies where some patients had type 1 diabetes and results were not given separately

- **Interventions**

SMBG

- **Comparators**

SMUG (self-monitoring of urine glucose)
Monitoring with HbA1c
No monitoring

- **Outcomes**

HbA1c
Hypos
QoL, anxiety,depression
Costs
Treatment satisfaction
Complications such as retinopathy (but very few studies long enough)
Weight
Treatment change in response to measurement (insulin dose, oral drug use, diet, exercise)
Lipids (Patients who adjust their diet in order to control hyperglycaemia may improve cholesterol levels as a by-product)
Blood pressure

- **Search strategy**

[1] http://www.consort-statement.org/QUOROM.pdf

The search strategy will comprise the following main elements:

- Searching of electronic databases: including The Cochrane Library (all sections), MEDLINE, Embase, Web of Science (SCI and Conference Proceedings), meeting abstracts of EASD, ADA and Diabetes UK.
- websites of FDA, MHRA, SMBG International Working Group, Current Controlled Trials, ClinicalTrials.gov,
- Contact with experts in the field
- Scrutiny of bibliographies of retrieved papers

The MEDLINE search strategy (see Appendix 10.1) will be adapted as appropriate for other databases

The search will be limited to English language and to articles published since 1996 (due to the number of recent good quality systematic reviews) and in order to reflect current meter technologies.

The search strategy will not include limits for study design, as all types of studies will be screened for potential inclusion (see Methods below)

- **Inclusion criteria**
    - For the review of clinical effectiveness, only systematic reviews and RCTs will be included.
    - Large observational studies of adequate duration will be included for information on adverse events, longer term outcomes (eg.cardiovascular events, retinopathy) and qualitative issues (motivation, adherence and quality of life, patient preferences). We will define large as 500 or more patients.
    - Editorials, letters in journals, and small observational studies will be discussed if they throw light on the reasons for controversy.
    - Titles and abstracts will be examined for inclusion by two reviewers independently. Disagreement will be resolved by consensus.

- **Exclusion criteria**
    - Non-English language papers
    - Papers published pre-1996
    - Reports published as meeting abstracts only, where insufficient methodological details are reported to allow critical appraisal of study quality.

- **Quality assessment strategy**

Consideration of study quality for systematic reviews and trials will include the following factors:

Systematic review characteristics

1. Were inclusion/exclusion criteria reported that addressed the review question?
2. Was the search adequate?
3. Was the validity of the included studies assessed?
4. Are sufficient details about the individual included studies presented?

Trial characteristics:

1. Timing, duration and location of the study
2. Method of randomisation
3. Allocation concealment
4. Numbers of participants randomized, excluded and lost to follow up.
5. Whether intent to treat analysis is performed
6. Methods for handling missing data

7. Appropriateness of statistical analysis
8. Funding of study

- **Methods of analysis/synthesis**

Initially existing systematic reviews of SMBG will be summarised and results compared. Reasons for differences between the reviews will be investigated and possible reasons for conflicting results will be investigated in a narrative review. Any RCTs not included in the existing systematic reviews will be data extracted and included.

Evidence synthesis of all RCTs which meet our inclusion criteria will be done using a narrative review. Meta-analysis is unlikely to be feasible due to heterogeneity of trials.

6. Report methods for synthesising evidence of cost-effectiveness

We will review the literature on cost-effectiveness but will not undertake any de novo modelling

7. Expertise in this TAR team

We have sufficient expertise in literature searching and systematic reviews. We would not have health economic or other support for de novo modelling, but that is not intended.

The working group set up by the Department of Health's Diabetes Support team would act as our expert advisory group, and has representatives of all the groups required.

8 Competing interests of authors

None

9. Timetable/milestones

Timing would depend on when the project was commissioned, but we would aim to deliver the report by August 2009.

Appendix 10.1. *Draft search strategy*

1. (self monitor* adj3 blood glucose).tw.
2. (home monitor* adj3 blood glucose).tw.
3. (HMBG or HBGM or SMBG or BGSM).tw.
4. exp Blood Glucose Self-Monitoring/
5. (glucose adj2 monitor* adj3 (self or home)).tw.
6. exp Diabetes Mellitus, Type 2/
7. type 2 diabetes.tw.
8. 6 or 7
9. 4 or 1 or 3 or 2 or 5
10. 8 and 9
11. limit 10 to english language