Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin (Review)

Malanda UL, Welschen LMC, Riphagen II, Dekker JM, Nijpels G, Bot SDM

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TABLE OF CONTENTS

[Intervention Review]

Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin

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ABSTRACT

Background

Self-monitoring of blood glucose (SMBG) has been found to be effective for patients with type 1 diabetes and for patients with type 2 diabetes using insulin. There is much debate on the effectiveness of SMBG as a tool in the self-management for patients with type 2 diabetes who are not using insulin.

Objectives

To assess the effects of SMBG in patients with type 2 diabetes mellitus who are not using insulin.

Search methods

Multiple electronic bibliographic and ongoing trial databases were searched supplemented with handsearches of references of retrieved articles (date of last search: 07 July 2011).

Selection criteria

Randomised controlled trials investigating the effects of SMBG compared with usual care, self-monitoring of urine glucose (SMUG) or both in patients with type 2 diabetes who where not using insulin. Studies that used glycosylated haemoglobin A_{1c} (HbA_{1c}) as primary outcome were eligible for inclusion.

Data collection and analysis

Two authors independently extracted data from included studies and evaluated the studies' risk of bias. Data from the studies were compared to decide whether they were sufficiently homogeneous to pool in a meta-analysis. Primary outcomes were HbA_{1c}, health-related quality of life, well-being and patient satisfaction. Secondary outcomes were fasting plasma glucose level, hypoglycaemic episodes, morbidity, adverse effects and costs.

Main results

Twelve randomised controlled trials were included and evaluated outcomes in 3259 randomised patients. Intervention duration ranged from 6 months (26 weeks) to 12 months (52 weeks). Nine trials compared SMBG with usual care without monitoring, one study compared SMBG with SMUG, one study was a three-armed trial comparing SMBG and SMUG with usual care and one study was a three-armed trial comparing less intensive SMBG and more intensive SMBG with a control group. Seven out of 11 studies had a low risk of bias for most indicators. Meta-analysis of studies including patients with a diabetes duration of one year or more showed a statistically significant SMBG induced decrease in HbA_{1c} at up to six months follow-up (-0.3; 95% confidence interval (CI) -0.4 to -0.1; 2324 participants, nine trials), yet an overall statistically non-significant SMBG induced decrease was seen at 12 month follow-up (-0.1; 95% CI -0.3 to 0.04; 493 participants, two trials). Qualitative analysis of the effect of SMBG on well-being and quality of life showed no effect on patient satisfaction, general well-being or general health-related quality of life. Two trials reported costs of self-monitoring: One trial compared the costs of self-monitoring of blood glucose with self-monitoring of urine glucose based on nine measurements per week and with the prices in US dollars for self-monitoring in 1990. Authors concluded that total costs in the first year of self-monitoring of blood glucose, with the purchase of a reflectance meter were 12 times more expensive than self-monitoring of urine glucose ($481 or 361 EURO [11/2011 conversion] versus $40 or 30 EURO [11/2011 conversion]). Another trial reported a full economical evaluation of the costs and effects of self-monitoring. At the end of the trial, costs for the intervention were £89 (104 EURO [11/2011 conversion]) for standardized usual care (control group), £181 (212 EURO [11/2011 conversion]) for the less intensive self-monitoring group and £173 (203 EURO [11/2011 conversion]) for the more intensive self-monitoring group. Higher losses to follow-up in the more intensive self-monitoring group were responsible for the difference in costs, compared to the less intensive self-monitoring group.

There were few data on the effects on other outcomes and these effects were not statistically significant. None of the studies reported data on morbidity.

Authors' conclusions

From this review, we conclude that when diabetes duration is over one year, the overall effect of self-monitoring of blood glucose on glycaemic control in patients with type 2 diabetes who are not using insulin is small up to six months after initiation and subsides after 12 months. Furthermore, based on a best-evidence synthesis, there is no evidence that SMBG affects patient satisfaction, general well-being or general health-related quality of life. More research is needed to explore the psychological impact of SMBG and its impact on diabetes specific quality of life and well-being, as well as the impact of SMBG on hypoglycaemia and diabetic complications.

PLAIN LANGUAGE SUMMARY

Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin

Self-monitoring of blood glucose has been found to be effective as a tool in the self-management of patients' glucose levels in people with type 1 diabetes and people with type 2 diabetes using insulin therapy. Patients can use the glucose values to adjust their insulin doses. It is hypothesized that patients with type 2 diabetes who are not using insulin might use the glucose values to adjust their diet and 'lifestyle'. However, there is no consensus on the effect of self-monitoring of blood glucose for type 2 diabetes patients not using insulin. In this systematic review update six new randomised controlled trials were added to the six trials that had been included in the original review. For the comparison of the effect of self-monitoring versus no self-monitoring in patients with a diabetes duration of one year or more 2324 patients with a six months follow-up and 493 patients with a 12 months follow-up were available. Pooled results of studies including patients diagnosed with type 2 diabetes for at least one year show that self-monitoring of blood glucose has a minimal effect in improving glucose control at six months, which disappears after 12 months follow-up. The clinical benefit resulting from this effect is limited.

Two studies reported costs of self-monitoring: One study compared the costs of self-monitoring of blood glucose with self-monitoring of urine glucose based on nine measurements per week and with the prices in US dollars for self-monitoring in 1990. They concluded that total costs in the first year of self-monitoring of blood glucose, with the purchase of a reflectance meter were 12 times more expensive than self-monitoring of urine glucose ($481 or 361 EURO [11/2011 conversion] versus $40 or 30 EURO [11/2011 conversion]). Another study reported a full economical evaluation of the costs and effects of self-monitoring. At the end of the trial, costs for the intervention were £89 (104 EURO [11/2011 conversion]) for standardized usual care (control group), £181 (212 EURO [11/2011 conversion]) for the less intensive self-monitoring group and £173 (203 EURO [11/2011 conversion]) for the more intensive self-monitoring group.

We did not find good evidence for an effect on general health-related quality of life, general well-being, patient satisfaction, or on the decrease of the number of hypoglycaemic episodes. However, hypoglycaemic episodes were more often reported in the self-monitoring blood glucose groups than in the control groups (four studies). Because patients in the self-monitoring blood glucose groups can use their device to confirm both periods of asymptomatic and symptomatic hypoglycaemic episodes, this is according to expectations.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Self-monitoring of blood glucose compared to control or self-monitoring of urine glucose for type 2 diabetes mellitus

Patient or population: Patients with type 2 diabetes mellitus
Intervention: Self-monitoring of blood glucose (SMBG)
Comparison: Control, self-monitoring of urine glucose (SMUG)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Control / SMUG	Corresponding risk SMBG				
Morbidity	See comment	See comment	Not estimable	See comment	See comment	Not investigated
Health-related quality of life Follow-up: 6 to 12 months	See comment	See comment	Not estimable	523 (3 studies)	⊕⊕⊕◯ **moderate**[1]	Probably no clinically relevant differences
Well-being Follow-up: 6 to 12 months	See comment	See comment	Not estimable	928 (4 studies)	⊕⊕⊕◯ **moderate**[1]	Probably no clinically relevant differences
Patient satisfaction Follow-up: 6 to 12 months	See comment	See comment	Not estimable	928 (4 studies)	⊕⊕⊕◯ **moderate**[1]	Probably no clinically relevant differences
Hypoglycaemic episodes Follow-up: 6 to 12 months	See comment	See comment	Not estimable	2492 (6 studies)	⊕⊕⊕◯ **moderate**[2]	Probably no clinically relevant differences
Costs Follow-up: 6 to 12 months	See comment	See comment	Not estimable	514 (2 studies)	⊕⊕⊕◯ **moderate**[3]	

HbA1c [%] Follow-up: 6 to 12 months	-0.3 (-0.4 to -0.1) at 6 months -0.1 (-0.3 to 0.04) at 12 months -0.5 (-0.9 to -0.1) at 12 months* -0.2 (-1 to 0.6) at 6 months**		2324 (9 studies) 493 (2 studies)	⊕⊕⊕◯ **moderate**[4]	Results refer to subgroup-analyses * newly diagnosed diabetes ** SMBG vs SMUG

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Because few included trials reported outcomes on health-related quality of life, well-being and patient satisfaction and self-reported measures varied substantially, presenting a general effect estimate was not possible and interpretation of best-evidence synthesis is difficult. Similar effects on similar sub-scales or dimensions in similar directions suggested a clinical non-relevant effect of SMBG on general (health-related) quality of life and well-being. Since all trials that measured patient-satisfaction did not report an SMBG related effect, this is considered clinical relevant as well.

[2] Data for adverse events could not be extracted separately for intervention and control groups. Studies reported occurrence of hypoglycaemia by recording asymptomatic or symptomatic hypoglycaemic episodes and/or by using detailed graded definitions. Due to substantial variation in definitions of hypoglycaemia, high risk of bias regarding occurrence and severity of hypoglycaemia between studies exists. Experiencing hypoglycaemic events can be confirmed with SMBG. Therefore, it is in the line of expectation that more frequent hypoglycaemic events seem to have been reported when using SMBG.

[3] Only two trial, Allen 1990 and the DiGEM trial 2007 reported outcomes on approximate costs of self-monitoring. Allen 1990 compared the costs of SMBG with SMUG based on nine measurements per week and with the prices in US dollars for self-monitoring in 1990. They concluded that total costs in the first year of SMBG, with the purchase of a reflectance meter were 12 times more expensive than SMUG (SMBG = $481 or 361 EURO [11/2011 conversion]; SMUG = $40 or 30 EURO [11/2011 conversion]). In the DiGEM trial 2007 a full economical analysis was performed. At the end of the trial, costs for the intervention were £89 (104 EURO [11/2011 conversion]) for standardized usual care (control group), £181 (212 EURO [11/2011 conversion]) for the less intensive self-monitoring group and £173 (203 EURO [11/2011 conversion]) for the more intensive self-monitoring group. Higher losses to follow-up in the more intensive self-monitoring group were responsible for the difference in costs, compared to the less intensive self-monitoring group.

[4] Different levels of probability and estimates of outcome variables of included studies might account for differences in presented subgroups. In addition, differences in requested monitoring frequency, glycosylated haemoglobin A1c (HbA_{1c}) level at baseline and SMBG and diabetes education may have contributed to the differences as well.

BACKGROUND

This is an update of a previous Cochrane review (Welschen 2005a) investigating the effects of self-monitoring of blood glucose (SMBG) in patients with type 2 diabetes who are not using insulin.

Description of the condition

"Diabetes mellitus is a metabolic disorder resulting from a defect in insulin secretion, insulin action, or both. A consequence of this is chronic hyperglycaemia (that is elevated levels of plasma glucose) with disturbances of carbohydrate, fat and protein metabolism. Long-term complications of diabetes mellitus include retinopathy, nephropathy and neuropathy. The risk of cardiovascular disease and cancer is increased. For a detailed overview of diabetes mellitus, please *see* under 'Additional information' in the information on the Metabolic and Endocrine Disorders Group in *The Cochrane Library* (*see* 'About', 'Cochrane Review Groups (CRGs)'). For an explanation of methodological terms, *see* the main Glossary in *The Cochrane Library*."

Description of the intervention

Diabetes care is complex and requires patients to take an active role in the management of their disease. Currently, adequate and continuing medical care aiming at preventing acute complications, diminishing risk of long-term complications as well as patient self-management education are considered standard in the care for type 2 diabetes patients (ADA 2010). Patients who improve their skills and confidence to manage their diabetes and who take a central role in the management of their disease improve their outcomes (Olivarius 2001; Piatt 2006; Rothman 2005; Wagner 2001).
Hence, self-management skills have an important role in optimal diabetes control. They enable patients to control their glucose level by recognizing, understanding and act on symptoms related to type 2 diabetes. Self-monitoring of blood glucose levels (SMBG) is presented as such a self-management skill and is therefore recommended as an element in self-management education (ADA 2010). The hypothesis that self-monitoring of glucose empowers the patient by its feedback, is based on the principles of the self-regulation theory (Leventhal 1980; Leventhal 1997). This model proposes that individuals construct schematic perceptions of illness and health-threatening conditions according to their available sources of information. These illness perceptions determine how patients respond to their illness or related threats and are mediators in the willingness and ability to take action. Feedback on the illness condition allows adaptation of illness perceptions, which eventually may lead to changes in 'lifestyle', quality of life and subsequently glycaemic control. Furthermore, it is assumed that SMBG may improve adherence to pharmacological treatment and motivate patients to make appropriate lifestyle changes (Fontbonne 1989; Karter 2001). Collecting data of glucose levels on different time points and its feedback allows the timely identification of high and low blood glucose levels and might help patients to a better understanding of day to day variation in glucose levels. Provided that the patient is informed how to interpret the results and what actions to take, self-monitoring information can help in making adjustments in direct interacting medication (insulin dosages) and 'lifestyle'. SMBG has been found to be effective for patients with type 1 diabetes (Bode 1999; DCCT 1993) and patients with type 2 diabetes who are using insulin (Karter 2001; Nathan 1996). However, consensus on the effectiveness of SMBG for the self-management of patients with non-insulin treated type 2 diabetes still remains inconclusive (Davidson 2010; Kempf 2008; Klonoff 2008; Kolb 2010; O'Kane 2009). This can be attributed to a lack of comparability between published trials. Moreover, methodological limitations and poor quality of several performed trials investigating SMBG might have had an impact on the observed effectiveness of SMBG (Welschen 2005a).

Why it is important to do this review

Previous reviews and meta-analyses

The present review is an update of the Cochrane review performed by Welschen et al in 2005 (Welschen 2005a). In this review, substantial clinical heterogeneity between included trials was noted. Consequently, qualitative analyses were performed and it was concluded that self-monitoring of blood glucose might be effective in improving glycaemic control in patients with type 2 diabetes who are not using insulin. The same systematic review has been published in *Diabetes Care* with the addition of a meta-analysis, on request of the editor (Davidson 2005a; Kleefstra 2005; Welschen 2005b). In the meta-analysis, the overall effect of SMBG was a statistically significant and clinically relevant decrease of 0.39% in HbA_{1c} in favour of SMBG compared with control groups. Since then, 11 other reviews on the effect of SMBG in patients with type 2 diabetes not using insulin have been published. Nine reviews included RCT's only (Allemann 2009; Clar 2010; Jansen 2006; Kleefstra 2009; McIntosh 2010; Poolsup 2008; Poolsup 2009; Sarol 2005; Towfigh 2008), one included cross-sectional, longitudinal and (non)randomised trials (McAndrew 2007) and two combined observational studies and RCT's (McGeoch 2007; St John 2010). In all reviews, change in HbA_{1c} was the primary outcome measure. Seven reviews performed a meta-analysis (Allemann 2009; Clar 2010; Jansen 2006; McIntosh 2010; Poolsup 2008; Poolsup 2009; Sarol 2005; St John 2010; Towfigh 2008) with HbA_{1c} varying from -0.42% to -0.16% in favour of SMBG versus no-SMBG. Three reviews performed qualitative analyses only and concluded similar to Welschen et al (Welschen 2005a) that SMBG might be effective in glycaemic control but

that the heterogeneity in design and quality between trials complicated drawing an overall conclusion on the effectiveness of SMBG (Kleefstra 2009; McAndrew 2007; McGeoch 2007).
Since the publication of our first review new studies have been published, possibly with good or improved methodological quality and design. We performed this update in order to explore if these new trials provide new evidence of the effect of SMBG on glycaemic control in patients not requiring insulin. In addition, if possible, an estimation of the effect of SMBG on glycaemic control in patients with type 2 diabetes not requiring insulin will be obtained. Furthermore, assessment of risk of bias of included trials illustrate limitations or enhance strengths of the studies.

OBJECTIVES

To assess the effects of self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin.

METHODS

Criteria for considering studies for this review

Types of studies

Published and unpublished randomised controlled clinical trials (RCTs).

Types of participants

Patients diagnosed with type 2 diabetes and who are not using insulin therapy. To be consistent with changes in classification and diagnostic criteria of diabetes mellitus through the years, the diagnosis should be established using the standard criteria valid at the time of the beginning of the trial (for example ADA 1999; ADA 2008; WHO 1998). Ideally, diagnostic criteria should have been described. If necessary, we used authors' definition of (type 2) diabetes.

Types of interventions

Studies describing self-monitoring of blood glucose (SMBG) as primary intervention compared to control are investigated. Studies concerning the comparison between SMBG and self-monitoring of urine glucose (SMUG) were included as well (SMUG as control group).

Types of outcome measures

Primary outcomes

- glycaemic control measured by glycated haemoglobin concentration A1c (HbA_{1c}-level);
- health-related quality of life, well-being (e.g. by using the SF 36 (Ware 1992) or the well-being questionnaire (Bradley 1994a));
- patient satisfaction (e.g. by using the Diabetes Treatment Satisfaction Questionnaire (DTSQ) (Bradley 1994b)).

Secondary outcomes

- fasting plasma glucose level;
- hypoglycaemic episodes;
- morbidity;
- adverse effects;
- costs.

Co-variates thought to be effect modifiers

- baseline glycaemic control;
- change in hypoglycaemic medications;
- duration of diabetes at baseline;
- age;
- compliance to the intervention.

Timing of outcome assessment

- short-term: up to six months of follow-up;
- medium-term: between six and twelve months of follow-up;
- long-term: twelve months or more after start of follow-up.

Search methods for identification of studies

Electronic searches

Electronic search strategies were used to identify relevant RCT's and reviews or meta-analyses (for identification of additional eligible trials).
We used the following sources for the identification of trials:

- *The Cochrane Library (i*ssue 3, 2011);
- MEDLINE (until July 2011);
- EMBASE (until July 2011);
- PsycINFO (until July 2011).

We also searched databases of ongoing trials: 'Current Controlled Trials' (www.controlled-trials.com - with links to other databases of ongoing trials).
For detailed search strategies please see under Appendix 1.
Additional key words of relevance could have been detected during any of the electronic or other searches. If this was the case, we

would have modified the electronic search strategies to incorporate these terms. Studies published in any language were included.

Searching other resources

We tried to identify additional studies by searching the reference lists of included trials and (systematic) reviews, meta-analyses and health technology assessment reports noticed.

Data collection and analysis

Selection of studies

The search for publications were performed by one of the review authors (IR) supported by the Cochrane Metabolic and Endocrine Disorders' trials search coordinator. The MeSH terms and search strategy used were agreed upon and tested by two review authors (IR, UM).
Studies were selected for full text reading in three steps:

Step 1

Two review authors (UM, LW) independently made a selection of the titles of the identified references that corresponded with the criteria for inclusion in this review stated above. If the title did not provide enough information to decide whether or not to include the trial in the selection, or no consensus could be made based on the title alone it was selected as well.

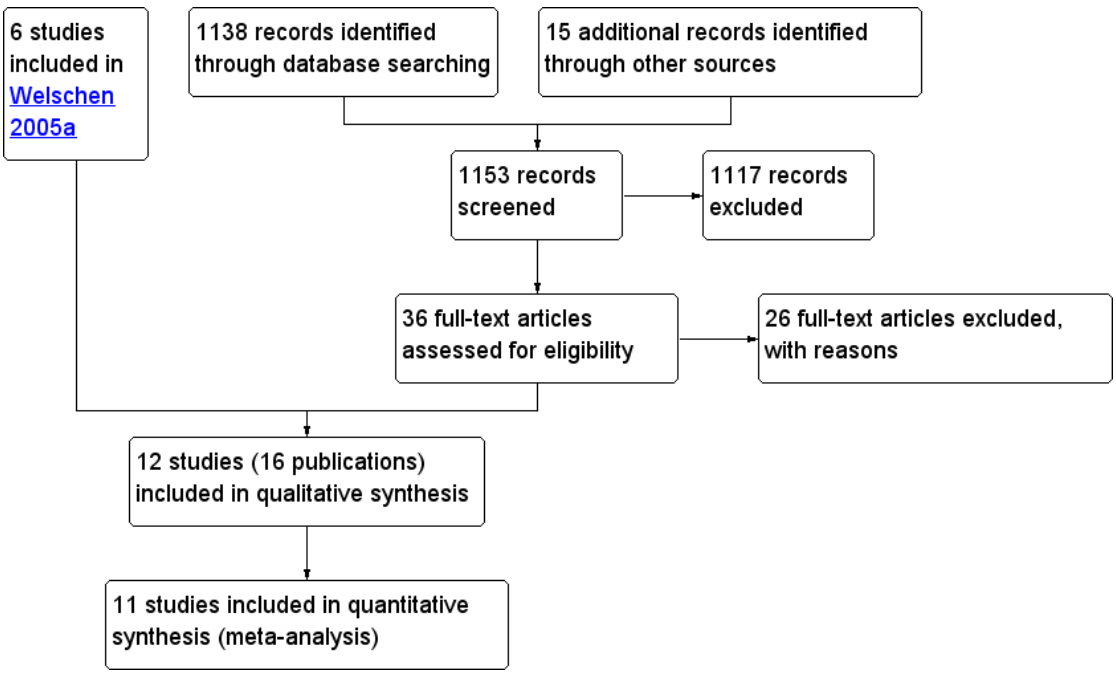
Step 2

All abstracts of selected titles were independently read (UM, LW). Full-text articles were retrieved from all abstracts potentially eligible for inclusion. In addition, if there was no abstract available the full article was retrieved.

Step 3

All selected full-text articles were read and selected if they met the criteria for including studies in the review.
Studies were excluded (step 2 and 3) if both review authors (UM, LW) agreed that the study did not meet the criteria for including studies in the review. A third party resolved possible differences in opinion (SB). An adapted PRISMA (preferred reporting items for systematic reviews and meta-analyses) flow-chart of study selection (Figure 1) is attached (Liberati 2009). Interrater agreement for selection of potentially relevant studies was measured using the kappa statistic (Cohen 1960). In the case of duplicate publications and subsequent papers of a primary study, we tried to maximise yield of information by simultaneous evaluation of all available data. In cases of doubt, the original publication (usually the oldest version) obtained priority.

Figure 1. Study flow diagram.



Data extraction and management

We used data concerning details of study design, intervention and outcomes employing a standardized extraction form and included the following items.

- **General information** (authors, title, details of journal, year of publication).
- **Trial characteristics** (study duration, design, methods, geographical region, temporal setting, sequence generation, allocation concealment, randomisation).
- **Participants** (total number per group, baseline characteristics).
- **Interventions** (specific details of intervention/control group).
- **Outcomes** (primary and secondary outcomes, timing of the outcome assessment).
- **Results** (number of participants analysed per group, dropouts/missing participants, summary data for each group, all available results on outcomes).
- **Notes** (any information reported that can be important; e.g. conflicts of interests).

A pilot test, using two trials excluded from the review preceded the data extraction of the selected RCT's. This test was likely to identify data that were not needed or missing to optimise the data extraction sheet.
Data extraction and data entry was performed independently by two review authors (UM, LW). Any discrepancies between authors were resolved by discussion. If necessary a third review author (SB) was consulted for the final decision. We sought any relevant missing information on the trial from the original author(s) of the article, if required.

Assessment of risk of bias in included studies

Two review authors (UM, LW) assessed each trial independently. Possible disagreement were resolved by consensus, or with consultation of a third party in case of disagreement. Interrater agreement for key bias indicators (e.g. allocation concealment, incomplete outcome data) was calculated using the kappa statistic (Cohen 1960). In cases of disagreement, the rest of the group was consulted and a judgement was made based on consensus. A pilot, using two trials excluded from the review, preceded the assessment of risk of bias of the RCTs.
The results and the rationale for the decision are presented in a methodological quality graph, summary and table. No trials were excluded based on the assessment of risk of bias.

The risk of bias in included studies and the internal validity of included studies was assessed with the Cochrane Collaboration's recommended 'Risk of bias' tool (Higgins 2009). With this tool, a study's risk on selection-, performance-, attrition-, detection-, and reporting bias can be critically evaluated and judged.
We used the following criteria:

- sequence generation (was the allocation sequence adequately generated?);
- allocation concealment (was the allocation adequately concealed?);
- blinding of participants, personnel and outcome assessors (was knowledge of the allocated intervention adequately prevented during the study?);
- incomplete outcome data (were incomplete outcome data adequately addressed?);
- selective outcome reporting (were reports of the study free of suggestion of selective outcome reporting?);
- other sources of bias (was the study apparently free of other problems that could put it at a high risk of bias?

Measures of treatment effect

Dichotomous data were expressed as odds ratio (OR) or risk ratio (RR) with 95% confidence intervals (CI). Continuous were expressed as differences in means (MD) with 95% CI.

Unit of analysis issues

We took into account the level at which randomisation occurred, such as cross-over trials, cluster-randomised trials and multiple observations for the same outcome.

Dealing with missing data

We obtained relevant missing data from authors, if feasible and carefully performed evaluation of important numerical data such as screened, eligible and randomised patients as well as intention-to-treat (ITT) and per-protocol (PP) population. We investigated attrition rates such as drop-outs, losses to follow-up and withdrawn study participants.

Assessment of heterogeneity

In the event of substantial clinical-, methodological-, or statistical heterogeneity, study results were not reported as meta-analytically pooled effect estimates. We identified heterogeneity by visual inspection of the forest plots, by using a standard Chi^2 test and a significance level of $\alpha = 0.1$, in view of the low power of this test.

We specifically examined heterogeneity with the I^2 statistic quantifying inconsistency across studies to assess the impact of heterogeneity on the meta-analysis (Higgins 2002; Higgins 2003), where an I^2 statistic of 75% and more indicates a considerable level of inconsistency (Higgins 2009).
When heterogeneity was found, we attempted to determine potential reasons for it by examining individual study and subgroup characteristics.

Assessment of reporting biases

We planned to use funnel plots to assess for the potential existence of small study bias. There are a number of explanations for the asymmetry of a funnel plot (Sterne 2001). Therefore, we carefully interpreted results (Lau 2006). Due to small number of included studies we did not employ funnel plots.

Data synthesis

Quantitative analyses
We summarised data statistically if they were available, sufficiently similar and of sufficient quality. We performed statistical analyses according to the statistical guidelines referenced in the newest version of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2009).
Meta-analyses were conducted using a random-effects model . The results of each RCT were plotted as point estimates with corresponding 95% confidence intervals. Statistical heterogeneity was tested using the Z score and the Chi^2 statistic with significance being set at $P < 0.10$. Quantification of the effect of heterogeneity was assessed by means of I^2, ranging from 0% to 100% including its 95% confidence interval (Higgins 2009). The I^2 statistic demonstrates the percentage of total variation across studies due to heterogeneity and was used to judge the consistency of evidence. If the evidence of statistical heterogeneity would be substantial (I^2 greater than 50%), the potential sources of variation between the RCTs would be investigated using subgroup analyses.
Qualitative analyses (best-evidence synthesis)
When severe clinical or statistical heterogeneity was found, a qualitative analysis (best-evidence synthesis) was performed to summarize the results of the included studies in terms of strength of the scientific evidence. Findings were considered consistent if more than one of the studies reported the same direction of the effect on the outcome measure.

Subgroup analysis and investigation of heterogeneity

If the data permitted, we planned to perform subgroup analyses to determine whether there were any systematic differences between groups of patients. We mainly carried out subgroup analyses if one of the primary outcome parameters demonstrated statistically significant differences between intervention groups. In any other case subgroup analyses were planned to be clearly marked as a hypothesis generating exercise.
A priori defined subgroup analyses were:

- HbA_{1c} level at baseline (subdividing into three groups of low (less than 7.0%), medium (between 7.0% and 11.0%) and high level (11.0% or higher) - based on data);
- diabetes duration (up to one year past diagnosis vs duration over one year);
- duration of intervention (short-term (up to six months follow-up), medium-term (between 6 and 12 months follow-up), long term (12 months follow-up or more)).
- age groups (below 60 years, over 60 years);
- gender;
- presence of complications (e.g. diabetic complications);
- different comparison interventions;
- type of treatment: oral hypoglycaemic agents, diet, exercise, no treatment;
- weight (normal (body mass index - BMI: women less than 25, men less than 27), overweight (BMI: women 25 to 30, men 27 to 30) obese (BMI more than 30)).

Sensitivity analysis

We planned to perform sensitivity analyses in order to explore the influence of the following factors on effect size:

- repeating the analysis excluding unpublished studies;
- repeating the analysis taking account of risk of bias:
- repeating the analysis excluding very long or large studies to establish how much they dominate the results;
- repeating the analysis excluding studies using the following filters: diagnostic criteria, language of publication, source of funding (industry versus other), country.

We also planned to test the robustness of the results by repeating the analysis using different measures of effect size (relative risk, odds ratio etc.) and different statistical models (fixed-effect model and random-effects model).

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

Results of the search

The electronic database search identified a total of 1138 citations (Figure 1). After excluding titles and abstracts clearly not related to the objective of our review, 36 full text publications were retrieved for further examination. Screening of references resulted in

another 15 citations. One trial (DiGEM trial 2007) had multiple publications which displayed the design of the trial (Farmer 2005), set out different outcome measures (Farmer 2007; French 2008; Simon 2008) and one overall publication (Farmer 2009). One retrieved publication of Siebolds et al (Siebolds 2006) described additional results of the trial of Schwedes et al (Schwedes 2002), a trial that was included in the original review. Results from that publication were used to supplement the trial of Schwedes et al, now referred to as SMBG study group 2002. The search identified one letter to the editor and four abstracts submitted to international conferences all describing a randomised controlled trial. Three of the abstracts had already been published and identified as an eligible trial (Davidson 2004; Drouin 2002; O'Kane 2006). Detailed trial information on the letter to the editor (Shiraiwa 2010) and the fourth abstract (Atsumi 1997) could not be retrieved and were therefore excluded (Atsumi 1997). One trial stopped following the control group after three months (Chidum 2011). We unsuccessfully requested additional data on the control group from the corresponding author. Therefore, we excluded this study as well (Chidum 2011).

Searching the database of ongoing trials identified five registered trials related to our objective. Two trials were completed and had already been published and identified as an eligible trial (DiGEM trial 2007; O'Kane 2008) and three trials were still ongoing (Bergenstal 2005; Malanda 2009; Kleefstra 2010). The authors of these trials were contacted and asked to provide (published or unpublished) data for the review. Only one author provided the requested data (Kleefstra 2010).

Finally, six eligible RCTs met all inclusion criteria and were added to the six trials included in our previous review. In total, 12 trials were included in this review.

We asked the corresponding authors of the DiGEM trial 2007, Durán 2010, Kleefstra 2010 and O'Kane 2008 to provide short-term follow-up data if available. They were asked if they could calculate changes in HbA_{1c} for short-term follow-up and to provide this in terms of means (SD). All authors responded and provided the additional data as requested.

Included studies

See: Characteristics of included studies and Table 1 for an overview of study populations and Appendix 2 for baseline characteristics of included studies.

Nine trials compared self monitoring of blood glucose (SMBG) with usual care without monitoring (Barnett 2008; Davidson 2005; Durán 2010; Franciosi 2011; Guerci 2003; Kleefstra 2010; Muchmore 1994; O'Kane 2008; SMBG study group 2002), one study compared SMBG with self-monitoring of urine glucose (SMUG) (Allen 1990), one study was a three-armed trial comparing SMBG and SMUG with usual care (Fontbonne 1989) and one study was a three-armed trial comparing less intensive SMBG, and more intensive SMBG with a control group (DiGEM trial 2007). Three of these 12 trials had a multi-centred design with centres in two (SMBG study group 2002), three (Franciosi 2011), and seven (Barnett 2008) countries, respectively. Trial duration ranged from 26 weeks to 12 months. The majority of the trials (seven trials) included over 100 patients in the studies (range 195 to 689). All trials investigated effects of SMBG in patients with a diabetes duration of at least one year, except for O'Kane 2008 and Durán 2010. These two trials studied SMBG effects in newly diagnosed patients exclusively. Specifications on type, doses or combinations of prescribed oral treatments were provided by Barnett 2008, DiGEM trial 2007, Durán 2010, Franciosi 2011, Davidson 2005, Kleefstra 2010 and O'Kane 2008, however details differed per trial. Furthermore, investigated SMBG interventions differed in accompanying education programmes (Appendix 3).

Excluded studies

Studies were excluded from the review because they had a control group with access to SMBG (i.e. Polonsky 2011), they had included patients using insulin (i.e. Lim 2011), they did not explored one of our primary outcome measures (i.e. Scherbaum 2008), were secondary reports of studies all ready included (i.e. Pignone 2009) or because patients were not randomised (i.e. Bajkowska-Fiedziukiewicz 2008).

Risk of bias in included studies

See Figure 2 and Figure 3 for a graphical summary of the 'Risk of bias' assessments for included studies, based on the six 'Risk of bias' domains.

Figure 2. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

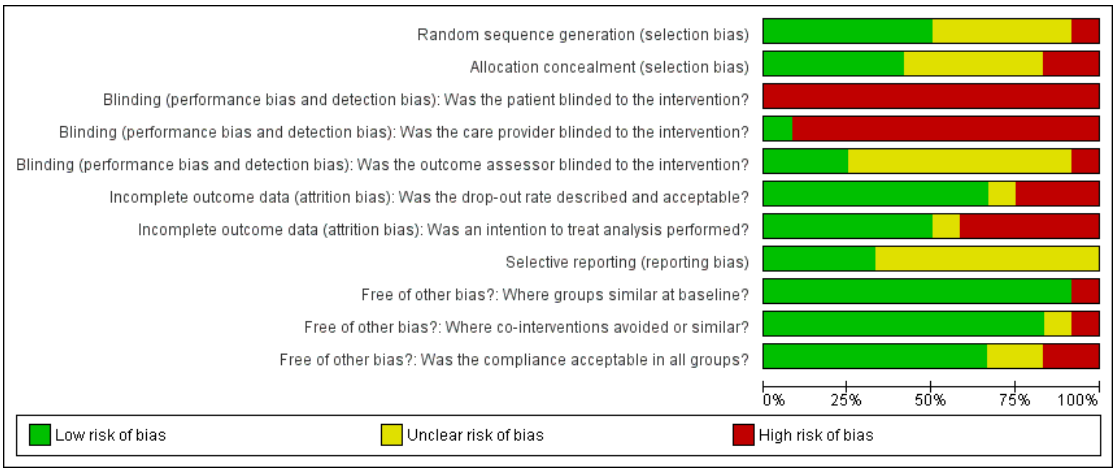


Figure 3. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

Overall risk of bias

Initial agreement between both review authors on the 'Risk of bias' domain allocation concealment was 0.56 (kappa). Disagreement was mainly based on reading errors and differences in interpretation of the standard description described in the *Cochrane Handbook for Systematic Reviews of Intervention.* After the consensus meeting, no disagreement persisted. The third review author was not called to make a final decision.

Allocation

Five trials had adequate concealment of allocation (Barnett 2008; DiGEM trial 2007; Franciosi 2011; Kleefstra 2010; O'Kane 2008) and five trials were unclear about allocation concealment (Allen 1990; Davidson 2005; Durán 2010; Fontbonne 1989; **;** SMBG study group 2002;). In the trial of Guerci et al (Guerci 2003) patients were randomised by their general practitioners who were also responsible for intervention and follow-up, and Muchmore et al (Muchmore 1994) recruited patients were divided over four groups, of which one group was not randomised. Therefore, Muchmore 1994 and Guerci 2003 had a high risk of bias for concealment of allocation.

Adequate sequence generation showed a low risk of bias in six trials (Allen 1990; Barnett 2008; DiGEM trial 2007; Franciosi 2011; Kleefstra 2010; O'Kane 2008), an unclear risk of bias in five trials (Davidson 2005; Durán 2010; Fontbonne 1989; Guerci 2003; SMBG study group 2002) and was not described in one (Muchmore 1994). The DiGEM trial 2007 used a computerised partial minimisation procedure for sequence generation; in the Allen 1990 et al trial sequence was computer generated. Barnett 2008 used a non-defined random sequence, O'Kane 2008 used randomly generated codes for consecutively numbered sealed envelopes, Kleefstra 2010 had consecutively numbered non-transparent envelopes (range 1 to 60) and Franciosi 2011 used computer-generated randomisation tables (random permuted blocks).

Blinding

In none of the studies patients were blinded to the intervention. The care provider was only blinded in the trial of Davidson et al (Davidson 2005). In that trial the care provider was a study nurse who was kept blinded for the allocated intervention and followed detailed algorithms to make therapeutic decisions, regardless of randomisation group.

The primary outcome (HbA_{1c}) was assessed independently of staff responsible for performing analyses in three trials (DiGEM trial 2007; Kleefstra 2010; O'Kane 2008). Additionaly, treatment allocation was concealed for laboratory staff. Blinding of the outcome assessor was not done in Franciosi 2011 and unclear or not described in the other trials.

Incomplete outcome data

Eight trials described drop-out rates and provided reasons for it (Allen 1990; Barnett 2008; Davidson 2005; DiGEM trial 2007; Durán 2010; Franciosi 2011; Kleefstra 2010; O'Kane 2008). Therefore, in these eight trials we assessed risk of bias concerning drop-out rate as low. Drop-out was not clearly described in the SMBG study group 2002 trial.

Intention-to-treat analysis was performed in five trials (Davidson 2005; DiGEM trial 2007; Durán 2010; Kleefstra 2010; O'Kane 2008), which we defined as having a low risk of bias. Five trials performed per-protocol analyses only and were considered having a high risk of bias (Allen 1990; Barnett 2008; Fontbonne 1989; Guerci 2003; SMBG study group 2002) and one trial did not describe performing either intention-to-treat or per-protocol analyses (Muchmore 1994).

Selective reporting

Three trials (DiGEM trial 2007; Kleefstra 2010; O'Kane 2008) had a low risk of selective reporting bias by either publishing their design (DiGEM trial 2007), by registering their protocol in a trial register (DiGEM trial 2007; Kleefstra 2010; O'Kane 2008) or both. We rated Durán 2010 and Franciosi 2011 as unclear because they both registered their protocol to a trial register three years after the start of the trial. In addition, Durán 2010 used a hard to interpret primary outcome measure. The rest of the included studies were rated as unclear as no information on pre-designated endpoints or a-priori defined subgroup analysis was identified.

Other potential sources of bias

All trials had similar groups at baseline for the most important prognostic indicators, except for Kleefstra 2010. In that study, diabetes duration differed between the intervention and control group. With the exception of SMBG study group 2002, co-interventions were similar or avoided in all studies. We evaluated that the SMBG group in SMBG study group 2002 received a co-intervention by means of a structured counselling program every four weeks during the intervention period while the control group only received non-standardised counselling.

See: Appendix 3 for an overview of education programmes for included studies.

Effects of interventions

See: **Summary of findings for the main comparison** Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin

See Appendix 4 for the effects of SMBG on glycosylated haemoglobin A1c (HbA_{1c}) and fasting plasma glucose (FPG), Appendix

5 for the effects of SMBG on health-related quality of life, well-being and patient satisfaction and Appendix 6 for adverse events (e.g. hypoglycaemic episodes).

Heterogeneity

Included studies differed in baseline characteristics and in delivered SMBG education. Due to clinical heterogeneity we decided not to conduct a pooled analysis of all trials. We performed random-effects subgroup meta-analyses on the basis of diabetes duration and follow-up.

Primary outcomes

Glycaemic control measured by HbA_{1c}

Glycaemic control as measured by change in HbA_{1c} between baseline and endpoint improved in the SMBG groups (Davidson 2005; DiGEM trial 2007; Kleefstra 2010; Muchmore 1994; O'Kane 2008), however this was not statistically significantly different from the improvement seen in the control groups. In their study Fontbonne 1989 compared control with SMBG and SMUG and found no statistically significant differences in HbA_{1c} between groups at the end of the trial. Allen 1990 compared SMBG with SMUG and found no statistically significant differences in HbA_{1c} between groups at the end of the study. Five studies detected a statistically significant difference between the outcomes of the intervention and control groups: The SMBG study group 2002 found an improvement in glycaemic control in the SMBG group compared to the control group, as measured by a statistically significant difference of 0.5% HbA_{1c} between baseline and endpoint; Guerci 2003 found a statistically significant difference of 0.4% in HbA_{1c} between SMBG and control group at the end of the study; Barnett 2008 reported an improvement in glycaemic control as measured with a statistically significant between group difference of 0.2% HbA_{1c} in favour of the SMBG group; Durán 2010 reported a statistically significant difference of 0.5% in HbA_{1c} between SMBG and control group at the end of the study; Franciosi 2011 found a statistically significant improvement of 0.5% in HbA_{1c} in the SMBG group compared to the control group between baseline and endpoint.

Subgroup analyses

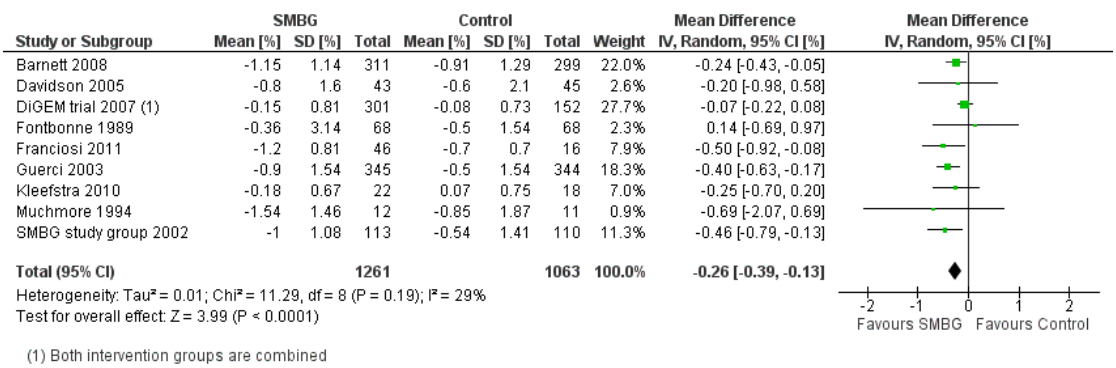
We performed subgroup analyses for diabetes duration and duration of the intervention for the comparison of SMBG versus control and SMBG versus SMUG. Data available on age groups, gender, presence of complications, different comparison interventions, type of treatment and weight could not be extracted sufficiently or could not be delivered by the original authors to investigate subgroup. In addition, we decided not to investigate baseline glycaemic control because 10 out of 12 studies (Allen 1990; Barnett 2008; Davidson 2005; DiGEM trial 2007; Fontbonne 1989; Franciosi 2011; Guerci 2003; Kleefstra 2010; O'Kane 2008; SMBG study group 2002) were in the a-priori specified medium range (between 7.0% and 11.0% HbA_{1c}). The remaining two studies (Durán 2010; Muchmore 1994) had a baseline HbA_{1c} in the low and the high category, respectively.

For all comparisons, six months follow-up data (published or retrieved by contacting the authors) or 12 months follow-up data were used only:

SMBG vs control (diabetes duration greater than one year, six months follow-up)

In the meta-analysis, the overall effect for short-term follow-up (up to six months of follow-up) showed a statistically significant decrease of 0.3% in HbA_{1c} (95% CI -0.4 to -0.1; 2324 participants, 9 trials, Analysis 1.1) in favour of SMBG compared with the control group. For this analysis mild statistical heterogeneity was noticed (I^2 = 29%) (Figure 4).

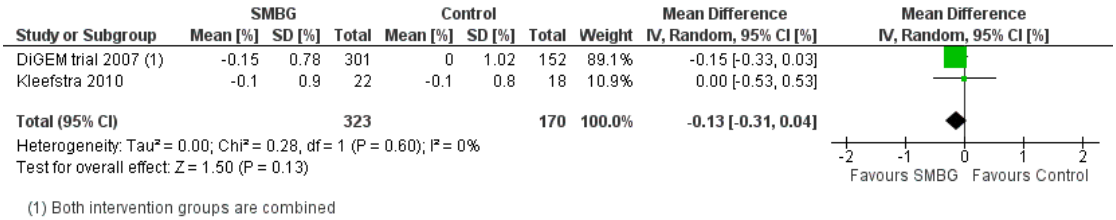
Figure 4. Forest plot of comparison: 1 SMBG (self-monitoring of blood glucose) vs control (6 months follow-up), outcome: 1.1 HbA1c [%].



SMBG vs control (diabetes duration greater than one year, 12 months follow-up)

For medium term follow-up (between 6 and 12 months of follow-up) analysis revealed a statistically non-significant decrease in HbA_{1c} of 0.1% (95% CI -0.3 to 0.04; 493 participants, 2 trials, Analysis 2.1) and no statistical heterogeneity (I^2 = 0%) (Figure 5).

Figure 5. Forest plot of comparison: 2 SMBG (self-monitoring of blood glucose) vs control (12 months follow-up), outcome: 2.1 HbA1c [%].



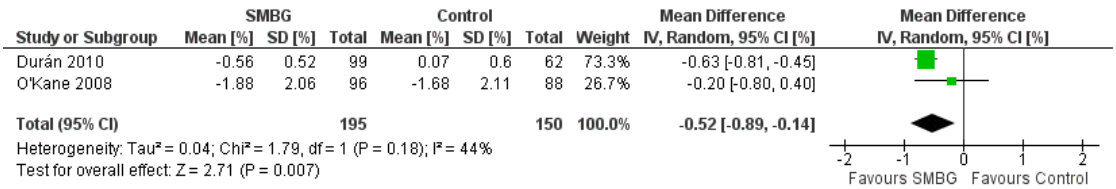
SMBG vs control (newly diagnosed diabetes, six months follow-up)

The pooled analysis for short-term follow-up (up to six months of follow-up) in newly diagnosed patients (345 participants, 2 trials) showed notable statistical heterogeneity (I^2 = 68%), indicating a substantial inconsistency in the direction of effect. Therefore, we do not present an effect estimate for HbA_{1c} for this analysis.

SMBG vs control (newly diagnosed diabetes, 12 months follow-up)

The meta-analysis for medium-term follow-up (between 6 and 12 months of follow-up) in newly diagnosed patients revealed a statistically significant decrease in HbA_{1c} of 0.5% (95% CI -0.9 to -0.1; 345 participants, 2 trials, Analysis 4.1) accompanied by moderate statistical heterogeneity (I^2 = 44%) (Figure 6).

Figure 6. Forest plot of comparison: 4 SMBG (self-monitoring of blood glucose) vs control (newly diagnosed patients, 12 months follow-up), outcome: 4.1 HbA1c [%].



SMBG vs SMUG (diabetes duration greater than one year, six months follow-up)

The pooled comparison between SMBG and SMUG for a short-term follow-up (up to six months of follow-up) showed a statistical non-significant decrease in HbA_{1c} of 0.2% (95% CI -1.0 to 0.6; 194 participants, 2 trials, Analysis 5.1) in HbA_{1c}. Statistical heterogeneity was not observed (I^2 = 0%).

Sensitivity analyses

Not enough adequate data to perform meaningful sensitivity analyses.

Quality of life, well-being and patient satisfaction

A total of five trials reported outcomes on either patient satisfaction (DiGEM trial 2007; Kleefstra 2010; O'Kane 2008; SMBG study group 2002), well-being (DiGEM trial 2007; Kleefstra 2010; O'Kane 2008; SMBG study group 2002) and/or health-related quality of life (DiGEM trial 2007; Kleefstra 2010; Muchmore 1994).

Because of the fragmentation in used (validated) instruments and underlying sub-dimensions for measuring patient satisfaction, well-being and quality of life, risk of bias regarding differences between studies should be taken into account. A detailed specification of used measures can be found in Appendix 5.

None of the trials reporting outcomes on treatment satisfaction (DTSQ) found significant between group changes (DiGEM trial 2007; Kleefstra 2010; O'Kane 2008; SMBG study group 2002;). Well-being was assessed with the Well-being Questionnaire in SMBG study group 2002**,** O'Kane 2008 and DiGEM trial 2007, and with the Wellbeing Index in Kleefstra 2010**.** SMBG study group 2002 reported a statistically significant decrease of the 22-item Well Being Questionnaire (WBQ-22) sub scale depression in favour of the SMBG group (-0.83 vs -0.26; range 0 to 18). O'Kane 2008 reported a 6% increase (1.08 points) in the depression sub scale of the WBQ-22 (range 0 to 18) in the SMBG group compared to the control group at 12 months (P = 0.01). Information on baseline differences was not presented. Both studies did not find statistically significant differences on general well-being or the other three well-being sub-scales (anxiety, energy, positive well-being). The DiGEM trial 2007 found no between group differences in well-being scores (12-item Well Being Questionnaire (WBQ-12)). Kleefstra 2010 found no significant changes between groups in psychological well-being measured with the 5-item Wellbeing Index (WHO-5). Outcomes on health-related quality of life were reported by Muchmore 1994, DiGEM trial 2007 and Kleefstra 2010. Muchmore 1994 found no significant differences between the SMBG group and the control group in the four sub-scales (satisfaction, impact, diabetes related worry, and the social/vocational worry) of the Diabetes Quality-of-Life Inventory. The DiGEM trial 2007 found that health-related quality of life as measured with the EuroQol 5 dimensions (EQ5D) questionnaire showed a statistically significant difference of -0.1, (95% CI -0.127 to -0.017; range 1 to 3) at the end of the trial when comparing the more intensive monitoring group with the control group. Kleefstra 2010found no significant changes between groups in health related quality of life (36-item Short Form Health Survey (SF-36)). Separate analyses of the SF-36 sub scales identified a statistical significant between groups difference in the sub scale health change at the end of the study in favour of the control group (a 4.2 points decrease in the SMBG group and a 9.7 points increase in the control group; range 0 to 100).

Secondary outcomes

Glycaemic control measured by fasting plasma glucose

Allen 1990**,** Guerci 2003 and Barnett 2008 measured fasting plasma glucose levels. All three studies found that fasting plasma glucose levels decreased as a result of SMBG, however there were no statistically significant differences between SMBG and SMUG and SMBG and no monitoring.

Adverse effects, hypoglycaemic episodes

Guerci 2003, DiGEM trial 2007, Barnett 2008, O'Kane 2008, Durán 2010 and Franciosi 2011 investigated SMBG related hypoglycaemia. Studies reported occurrence of hypoglycaemia by recording asymptomatic or symptomatic hypoglycaemic episodes and/or by using detailed graded definitions. Because of the fragmentation in definitions of hypoglycaemia, risk of bias regarding occurrence and severity of hypoglycaemia between studies should be taken into account. A specification of definitions and cut-off points can be found in Appendix 6. In Guerci 2003 10.4% SMBG group and 5.2% control group patients reported at least one episode of symptomatic or asymptomatic hypoglycaemia during the study (P = 0.003). This significant difference was caused by a between-group difference in patients reporting asymptomatic hypoglycaemia only (P = 0.001). No patients reported serious episodes of hypoglycaemia. In the DiGEM trial 2007 episodes of hypoglycaemia with mild symptoms were reported by 9.2%, 22% and 28.5% of the patients in the control group, less intensive group and more intensive group, respectively (P < 0.001). Episodes of severe hypoglycaemia were reported in one patient in the control group (DiGEM trial 2007). In the Barnett 2008 study a hypoglycaemic event (symptomatic, asymptomatic or SMBG confirmed) was reported in 8.7% and 7% of the patients in the SMBG group and control group, respectively. All reported events were considered mild (grade 1), moderate (grade 2) or were non-graded. No significant between-group differences were found in reported hypoglycaemia at any time point in the O'Kane 2008 trial. In the Durán 2010 trial no severe hypoglycaemic episodes requiring third-party or medical assistance were reported in either

group. In the Franciosi 2011 trial no adverse events including hypoglycaemic events occurred.
Barnett 2008 and Guerci 2003 reported adverse effects, but did not specify them. For details on adverse effects see Appendix 6.

Costs

Allen 1990 and the DiGEM trial 2007 reported outcomes on approximate costs of self-monitoring. Allen 1990 compared the costs of SMBG with SMUG based on nine measurements per week and with the prices in US dollars for self-monitoring in 1990. They concluded that total costs in the first year of SMBG, with the purchase of a reflectance meter were 12 times more expensive than SMUG (SMBG = $481 or 361 EURO [11/2011 conversion]; SMUG = $40 or 30 EURO [11/2011 conversion]).
As part of the DiGEM trial 2007 a full economical evaluation of the costs and effects of self-monitoring in the DiGEM trial population was performed and presented in UK Pounds Sterling. At the end of the trial, costs for the intervention were £89 (104 EURO [11/2011 conversion]) for standardized usual care (control group), £181 (212 EURO [11/2011 conversion]) for the less intensive self-monitoring group and £173 (203 EURO [11/2011 conversion]) for the more intensive self-monitoring group.Higher losses to follow-up in the more intensive self-monitoring group were responsible for the difference in costs, compared to the less intensive self-monitoring group.

Morbidity, mortality

The DiGEM trial 2007 and Guerci 2003 reported mortality (death of patients during the trial). None of the studies reported data on morbidity. We have summarised the data in Appendix 6.

DISCUSSION

Summary of main results

The aim of this systematic review was to assess the effects of SMBG in patients with type 2 diabetes who are not using insulin. Six randomised controlled trials were added to the six trials included in the original review (Welschen 2005a). In non-insulin treated type 2 diabetes patients with a diabetes duration of at least one year the overall effect of SMBG compared to control groups and a follow-up of six months showed a statistically significant 0.3% HbA_{1c} decrease. In contrast, we saw a non-significant decrease of 0.1% in HbA_{1c} in patients in SMBG groups compared to control groups over a 12 months follow-up period.
Secondly, the overall effect of SMBG compared to SMUG over a follow-up of six months showed a statistically non-significant decrease of 0.2% HbA_{1c}. Thirdly, it was not possible to estimate an overall effect of SMBG over a follow-up of six months for newly diagnosed non-insulin treated type 2 diabetes patients, due to substantial inconsistency in the direction of the effect. However, the overall effect of SMBG with a follow-up of 12 months demonstrated a statistically significant decrease of 0.5% in HbA_{1c} compared to control groups (two trials).
Concerning health-related quality of life, well-being and patient satisfaction outcomes, based on a best-evidence synthesis we conclude that there was no significant evidence available that SMBG had an effect on patient satisfaction (4 out of 4 trials), general well-being (4 out of 4 trials) or general health-related quality of life (3 out of 3 trials). Regarding levels of depression (WBQ-22, sub scale), inconsistent findings were observed (2 out of 2 trials).
Lastly, regarding the secondary outcomes we conclude that based on a best-evidence synthesis periods of both asymptomatic and symptomatic hypoglycaemia are more frequent in patients performing SMBG (3 out of 4 trials); and secondly, there is no statistically significant difference in fasting plasma glucose levels between SMBG and control intervention groups (3 out of 3 trials).

Clinical relevance of findings

The main results suggest that long-term SMBG in new-onset patients is beneficial in lowering HbA_{1c}. However, when diabetes duration is over one year, the overall glycaemic effect of SMBG is small and more likely to be present at short-term. Because subgroup meta-analyses could not fully take the presence of clinical heterogeneity into account, clinical interpretation and translation into practice of these results is difficult and should be done with caution. Different levels of probability and estimates of outcome variables of included studies might account for differences in presented subgroups. In addition, differences in requested monitoring frequency, HbA_{1c} level at baseline and SMBG and diabetes education may have contributed to the differences as well. Besides HbA_{1c} we paid attention to important outcome measures such as health-related quality of life, well-being, patient-satisfaction and hypoglycaemic episodes as well. Because few included trials reported outcomes on health-related quality of life and well-being and used self-report measures varied, presenting a general effect estimate is not possible and interpretation of best-evidence synthesis is difficult. However, similar effects on similar sub-scales or dimensions in similar directions suggested a clinical non-relevant effect of SMBG on general (health-related) quality of life and well-being. In addition, since all trials that measured patient-satisfaction did not report an SMBG related effect, this is considered clinical relevant as well. Experiencing hypoglycaemic events can be confirmed with SMBG. Therefore, it is in the line of expectation that more frequent hypoglycaemic events are reported when using SMBG.

Overall completeness and applicability of

evidence

Risk of bias

Most included trials and specifically earlier trials were exposed to selection and attrition bias . With the advent of new studies (Barnett 2008; DiGEM trial 2007; Durán 2010; Franciosi 2011; Kleefstra 2010; O'Kane 2008) performed after our first review (Welschen 2005a) the risk of bias was reduced.

Primary outcome

SMBG was embedded differently in usual care across included trials and instructions for self-monitoring frequency, 'lifestyle' adjustment and SMBG integration in diabetes management varied between trials. However, we considered clinical heterogeneity induced by trial design not significant and decided to combine the data in subgroup meta-analyses.

We made an a-priori decision to separate pooled estimates of the effect of SMBG on HbA_{1c} for newly diagnosed patients and patients with a diabetes diagnosis of at least one year. Initiating diabetes management in newly diagnosed and never treated patients results in larger and differential effects in glycaemic control compared to patients with a longer diabetes duration (Schwedes 2002). In addition, being confronted with having a major chronic disease as type 2 diabetes can be accompanied with newly gained worries, which directly reflects in glycaemic control (Schwedes 2002).

Secondary outcomes

In none of the trials, psychological measures were the primary outcome measures. Some trials mentioned contradictory or no psychological effects as secondary outcome measures. Finally, hypoglycaemic episodes were more reported in SMBG groups than in the control groups (Barnett 2008; DiGEM trial 2007; Guerci 2003; O'Kane 2008). Because patients in the SMBG groups can use their SMBG device to confirm both periods of asymptomatic and symptomatic hypoglycaemic, this is according to expectations.

Quality of the evidence

This update identified six new studies. Inclusion of these new studies made it possible to perform subgroup meta-analyses on duration of diabetes and duration of intervention. Initially, subgroup analyses of studies with a short intervention duration (9 studies, 2324 participants) showed a larger positive effect of self-monitoring compared to studies with a medium duration (2 studies, 493 participants). Effects of short- and medium-term duration in patients with newly diagnosed type 2 diabetes (2 studies, 345 participants) were subject to notable (I^2 = 68%) and moderate (I^2 = 44%) statistical heterogeneity, respectively. Therefore, no summary estimate can be presented for short-term follow-up and long-term follow-up should be interpreted with caution. Concerning the studies evaluating the effect of SMBG compared with SMUG the results of the current review are insufficient to draw final conclusions. Only two studies with 194 participants were identified and included in the analysis. Pooling the data from these two studies showed a non-significant positive effect of SMBG on HbA_{1c} compared to SMUG. However, one of the trials (Fontbonne 1989) had serious limitations in design and implementation, which may have resulted in selection, attrition and reporting bias.

Potential biases in the review process

With an extensive search without language restriction in four electronic databases, the meta-register of current controlled trials and by scanning references of identified reviews and included studies we attempted to minimise publication bias. Nevertheless, we cannot rule out the possibility that we have missed relevant studies that were not published or are still ongoing. Not all data needed to perform a full effect-modifier investigation could be extracted from the data available or revealed from the original authors. Therefore, differences in baseline glycaemic control, changes in hypoglycaemic medication, age and compliance to the protocol might modify or confound the presented results. In addition, the proposed sensitivity analyses could not be performed.

Agreements and disagreements with other studies or reviews

The efficacy of SMBG in type 2 diabetes patients not using insulin has been subject of a considerable number of systematic reviews and meta-analyses over time. Most included randomised controlled trials only (Allemann 2009; Clar 2010; Jansen 2006; Kleefstra 2009; McIntosh 2010; Poolsup 2008; Poolsup 2009; Sarol 2005; Towfigh 2008), but some included other designs as well (McAndrew 2007; McGeoch 2007; St John 2010). The aim of our review was to assess the effects of SMBG in type 2 diabetes patients not using insulin. Therefore, studies in which the results of non-insulin users could not be separated from patients using insulin were excluded. Although this stringent exclusion criterion contributes to a decrease in included patients we believe that this has lead to a more clinically homogeneous data set and more valid conclusions about the effect of SMBG in this particular patient group. Furthermore, in contrast to other reviews, clinical and methodological heterogeneity between included studies have been taken into account. We believe that this distinguishes our systematic review and its associated conclusions from previous ones and emphasises the importance of comparability and internal validity of RCTs.

AUTHORS' CONCLUSIONS

Implications for practice

In this update, the addition of six new trials to the original review made it possible to create subgroups to counter the initial lack of clinical and methodological homogeneity between studies. With the present findings it can be concluded that self-monitoring of blood glucose (SMBG) in newly diagnosed type 2 diabetes patients who are not using insulin is beneficial in lowering HbA_{1c}. However, when diabetes duration is over one year, the overall glycaemic effects of SMBG are small at short-term and subside after one year. Despite possible glycaemic benefits we conclude that SMBG has no relevant effect on general well-being and health-related quality of life. In addition, patients performing SMBG are equally satisfied with their treatment as those not using SMBG. Furthermore, SMBG increases reported hypoglycaemic episodes. However, different definitions of hypoglycaemic episodes make it difficult to distinguish between reported severities.

Implications for research

Qualitative research (Farmer 2009; Peel 2007) suggests that SMBG and its feedback can be important factors for individual patients to improve medication adherence, empower the patient to gain control over their disease or to motivate 'lifestyle' changes. Future studies should investigate whether SMBG attributes to other parts of self-management. In addition, SMBG postulated positive changes in diabetic complications should be investigated as well. Furthermore, more research is needed to explore the psychological impact of SMBG and its accompanying demands on diabetes specific quality of life and well-being.

ACKNOWLEDGEMENTS

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Allen 1990

Methods	Randomised controlled trial. Randomised in groups of 10 with the use of a computer-generated table of random numbers
Participants	Country: USA Number of participants: 54 Inclusion criteria: • type 2 diabetes, not treated with insulin; • fasting plasma glucose level > 8.8 and <22 mM; • no history of ketoacidosis; • current treatment with diet alone or diet and an oral hypoglycaemic agent; • no active infection or serious illness; • no physical or mental handicap precluding participation in the treatment program (determined by the Cognitive-capacity screening examination and a physical-abilities questionnaire). Exclusion criteria: • SMBG devices used previously; • serum creatinine level > 177 mM. Mean age (years ± SD): • SMBG: 58.2 ± 9.7 • SMUG: 57.9 ± 10.7 Diabetes duration (years ± SD): • SMBG: 6.8 ± 6.5 • SMUG: 9.0 ± 10.3
Interventions	1. SMBG group (n = 27) and standardized treatment program including diet and exercise counselling. At least 36 blood glucose determinations/month, before each meal every other day. 2. SMUG group (n = 27) and standardized treatment program including diet and exercise counselling. At least 36 urine glucose determinations/month, before each meal every other day.
Outcomes	1. Fasting plasma glucose, obtained monthly by glucose oxidase method. 2. Glycosylated haemoglobin, obtained initially and at 3 and 6 months by affinity chromatography. 3. Total cholesterol and high-density lipoprotein cholesterol, measured by spectrophotometer with Beckman Dri-STAT reagents. 4. Weight, obtained monthly, patients fully clothed. 5. Respective costs of the two monitoring techniques.
Study details	Duration: 6 months
Publication details	Language of publication: English Funding: the Veterans Administration Health Services Research and Development Service and additional funds from the A.W. Mellon Foundation Publication status: Peer reviewed journal

Allen 1990 (*Continued*)

Stated aim of study	"To compare the relative efficacy and cost of self-monitoring of blood glucose with routine urine testing as part of a standardized treatment programme in the management of patients with type 2 non insulin dependent diabetes, not treated with insulin"
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomised in groups of 10..... with the use of a computer-generated table of random numbers"
Allocation concealment (selection bias)	Unclear risk	Comment: No information is available
Blinding (performance bias and detection bias) Was the patient blinded to the intervention?	High risk	Quote: " Blinding of the patients or study physician to the interventions, either urine or blood testing, was not possible"
Blinding (performance bias and detection bias) Was the care provider blinded to the intervention?	High risk	Quote: " Blinding of the patients or study physician to the interventions, either urine or blood testing, was not possible"
Blinding (performance bias and detection bias) Was the outcome assessor blinded to the intervention?	Unclear risk	Comment: No information is available
Incomplete outcome data (attrition bias) Was the drop-out rate described and acceptable?	Low risk	Quote: "Five patients were inappropriately randomised and participated for less than one week". Quote: After 2 months of participation, 2 patients dropped out for unknown reasons"
Incomplete outcome data (attrition bias) Was an intention to treat analysis performed?	High risk	Quote: "Of the 61 patients randomised to the competing interventions, 54 completed the study". Comment: Only 54 out of 61 patients were included in the analysis
Selective reporting (reporting bias)	Unclear risk	Comment: No trial registration or protocol available
Free of other bias? Where groups similar at baseline?	Low risk	Quote: "The two groups were similar in all baseline measurements"

Allen 1990 (*Continued*)

Free of other bias? Where co-interventions avoided or similar?	Low risk	Comment: All patients received the same diet instructions and were individually instructed in testing techniques Quote: "Physician-initiated treatment alterations were guided by an explicit algorithm with the patients's urine or blood test results and the monthly fasting glucose values"
Free of other bias? Was the compliance acceptable in all groups?	Low risk	Quote: "Compliane levels were similar for both groups of patients" Comment: 87% SMUG and 90% SMBG of patient records were complete and attendance exceeded 98% in both groups

Barnett 2008

Methods	Multicentre randomised parallel-group trial
Participants	Countries: Czech Republic, Hungary, Iran, Malaysia, Poland, Slovakia, Turkey Number of participants: 610 Inclusion criteria: • patients with type 2 diabetes; • 40 to 80 years of age; • treatment with diet alone ≥ 3 months, diet and biguanides or alpha-glucosidase inhibitor or diet plus any inulin secretagogue for < 12 months; • HbA_{1c} between 7 and 10%. Exclusion criteria: • current management with SMBG; • lifestyle or concurrent condition (medical or psychiatric) that could interfere with end-point evaluation (serious anaemia, haemoglobinopathy and haemolysis) or ability to comply with study procedures including SMBG and diary keeping; • abnormalities on laboratory screening including creatinine clearance < 20 ml/min and/or serum creatinine > 140 mM and alanine aminotransferase or aspirate aminotransferase more than 3 times the upper limit of normal range; • therapy with systemic glucocorticoids; • known contraindication to gliclazide; • know drug or alcohol dependence; • pregnancy, lactation or planned pregnancy. Mean age (years ± SD): • SMBG: 56.1 ± 9.1 • Control: 55.9 ± 9.3 Diabetes duration (years ± SD): • SMBG: 2.8 ± 3.7 • Control: 2.8 ± 4.5
Interventions	1. SMBG (n = 311): measurement of glucose levels 2 days a week (one working and one non-working day) at 5 times (before each meal (breakfast, lunch, dinner), 2 h after

	main meal and before bedtime). Once per month postprandial measurements after each of the three meals. Instructions in SMBG included information on how to use the glucose metre, how to check it was working, when to take measurements, how to record them in a patient diary and what to do in the event of asymptomatic hypoglycaemia (measured glucose < 3 mmol/L without symptoms suggestive of hypoglycaemia) or SMBG-confirmed glycaemia. 2. Control (n = 299): all randomised patients received diet and lifestyle advice, reinforced at each clinic visit. Oral antidiabetic agent therapy (gliclazide MR) was standard for all patients. Those on insulin secretagogue were transformed to gliclazide MR. A diary was used to record symptoms of hypoglycaemia, actions taken.
Outcomes	Primary outcome: 1. Δ HbA_{1c} between groups at week 27. Secondary outcomes: 1. Mean changes from baseline HbA_{1c} and FPG at week 27. 2. Gliclazide MR dose.
Study details	Duration of intervention: 27 weeks.
Publication details	Language of publication: English Funding: Unristricted grant from Servier Publication status:Peer reviewed journal
Stated aim of study	"First, to evaluate the contribution of SMBG in the management of patients with type 2 diabetes, with an emphasis on glycaemic control. Second, to compare the efficacy, tolerability and acceptability of an identical once daily gliclazide modified release (MR) based regimen in patients with type 2 diabetes with and without SMBG"
Notes	DYNAMIC-1 study

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Eligible patients were randomised in a sequential manner using a centrally generated random allocation sequence..."
Allocation concealment (selection bias)	Low risk	Quote: "....a centrally generated random allocation sequence" was used for randomisation
Blinding (performance bias and detection bias) Was the patient blinded to the intervention?	High risk	Comment: patient cannot be blinded to the intervention

Blinding (performance bias and detection bias) Was the care provider blinded to the intervention?	High risk	Comment: care provider cannot be blinded to the intervention
Blinding (performance bias and detection bias) Was the outcome assessor blinded to the intervention?	Unclear risk	Comment: Primary outcome was difference between groups in HbA_{1c}. Though HbA_{1c} values were measured in a central national laboratory according to DCCT standards, un sufficient information on the HbA_{1c} outcome assessor is given.
Incomplete outcome data (attrition bias) Was the drop-out rate described and acceptable?	Low risk	610 randomised. SMBG: 37 withdrawals; Control: 47 withdrawals Quote: "...271 subjects (87%) in the SMBG group and 248 (83%) in the non-SMBG group completed the study"
Incomplete outcome data (attrition bias) Was an intention to treat analysis performed?	High risk	Quote: "the primary analysis population was the full analysis set, defined a priori in the protocol as all randomised patients who took at least one dose of gliclazide MR during the study, who performed SMBG at least once (SMBG group) and with a baseline HbA_{1c} and at least one post baseline HbA_{1c} value".
Selective reporting (reporting bias)	Unclear risk	Comment: Insufficient information about the study protocol is available
Free of other bias? Where groups similar at baseline?	Low risk	Quote: "patient characteristics at study entry were similar between the randomisation groups with the exception of a higher proportion of menopausal women in the SMBG group"
Free of other bias? Where co-interventions avoided or similar?	Low risk	Comment: Care for both groups is equal. However, no information is given on a joint multicenter training on giving diet and lifestyle advice
Free of other bias? Was the compliance acceptable in all groups?	Unclear risk	Comment: insufficient information on compliance is provided

Davidson 2005

Methods	Randomised controlled trial
Participants	Country: USA Number of participants: 89 Inclusion criteria: • patients not taking insulin. Mean age (years ± SD): • SMBG: 49.8 ± 11.2 • Control: 50.9 ± 11.0 Diabetes duration (years ± SD): • SMBG: 5.5 ± 4.7 • Control: 5.8 ± 5.8
Interventions	1. SMBG (n = 43): measurement of glucose levels before and between one and two hours after eating meals six days a week. 2. Control (n = 45): patients in both groups were scheduled to meet with dietician five times; at randomisation and 2, 4, 8 and 12 weeks later. Dietician used glucose levels and meal descriptions in nutritional counselling. A nurse followed detailed algorithms to make therapeutic decisions.
Outcomes	1. HbA_{1c}, measured at entry to the study and every two months
Study details	Duration: 6 months
Publication details	Language of publication: English Funding: Publication status: Peer reviewed journal
Stated aim of study	"To answer the important question of whether self monitoring of blood glucose concentrations improves HbA_{1c} responses" through a blinded and randomised study.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Comment: No randomisation method described
Allocation concealment (selection bias)	Unclear risk	Comment: No treatment allocation described
Blinding (performance bias and detection bias) Was the patient blinded to the intervention?	High risk	Comment: The patient cannot be blinded
Blinding (performance bias and detection bias)	Low risk	Quote: "the nurse ,who acted as care provider, was unaware of whether the patient was randomised to the mon-

Davidson 2005 (*Continued*)

Was the care provider blinded to the intervention?		itoring group or not..."
Blinding (performance bias and detection bias) Was the outcome assessor blinded to the intervention?	Unclear risk	Comment: No detailed information described
Incomplete outcome data (attrition bias) Was the drop-out rate described and acceptable?	Low risk	Quote: "one patient did not return after being randomised to see the nurse or dietician and was not included in the study"
Incomplete outcome data (attrition bias) Was an intention to treat analysis performed?	Low risk	Quote: "an intention to treat analysis was used".
Selective reporting (reporting bias)	Unclear risk	Comment: No trial record or protocol publication with pre-designated endpoints is available
Free of other bias? Where groups similar at baseline?	Low risk	Quote: "There were no differences in the baseline characteristics of the patients randomised to the monitoring group and those who were randomised to the control group"
Free of other bias? Where co-interventions avoided or similar?	Low risk	Comment: All patients received the same care with the same detailed algorithm and dietician care
Free of other bias? Was the compliance acceptable in all groups?	High risk	Quote: "patients in the monitoring group averaged 4.0 vs 3.2 visits in the control group Comment: The monitoring group performed an average number of 129 tests per person instead of the maximum of 6x6x26=936

DiGEM trial 2007

Methods	Three arm, open, parallel group randomised trial
Participants	Country: United Kingdom Number of participants: 453 Inclusion criteria: • patients with type 2 diabetes; • 25 years of age or more at diagnosis; • managed with diet or oral hypoglycaemic agents alone; • HbA_{1c} level $\geq$6.2% at the assessment visit; • independent in activities of daily living. Exclusion criteria: • use of blood glucose monitor twice a week or more often over the previous three months; • current use of insulin;

DiGEM trial 2007 (*Continued*)

	• co-morbidity or limited life expectancy that would make intensive glycaemic control inappropriate; • inability to follow trial procedures. Mean age (years ± SD): • Less intensive SMBG: 65.2 ± 10.6 • More intensive SMBG: 65.6 ± 9.9 • Control: 66.3 ± 10.2 Diabetes duration (median years (q1-q3)): • Less intensive SMBG: 3 (2-7) • More intensive SMBG: 3 (2-6) • Control: 3 (2-6)
Interventions	1. Less intensive SMBG (n = 150): Self testing group performing blood glucose self testing 2 days a week, 3 tests daily (1 after fasting, 2 before meal or 2 hours after meal) with instruction to aim for 4-6mmol/Lfasting and 6-8 mmol/L after meals. Results were interpreted by the study nurse. 2. More intensive SMBG (n = 151): Self monitoring group who, in addition to self testing group, are provided with training and support in interpreting and applying the results of blood glucose readings to enhance motivation and maintain adherence to diet physical activity and medication regimens. 3. Control (n = 152): Standardised usual care and three monthly HbA_{1c} measurements. All patients received the use of goal setting and review techniques. A diary was used to record self care goals and strategies for achieving them
Outcomes	Primary outcome: 1. HbA_{1c} level at 12 months Secondary outcomes: 1. Blood pressure. 2. Weight. 3. Total cholesterol level. 4. Ratio of total cholesterol to high density lipoprotein cholesterol. 5. Body mass index. 6. Well-being (WBQ-12). 7. Self-reported smoking status, dietary intake and physical activity (DSCAQ). 8. Medication adherence (MARS). 9. Patient treatment satisfaction (DTSQ). 10. Beliefs about diabetes and its management (IPQ). 11. Beliefs about medicine (BMQ). 12. Beliefs about physical activity, eating and (using) blood glucose monitoring. 13. Quality adjusted life years (EQ5D). 14. Healthcare costs.
Study details	Duration of intervention: 12 months.
Publication details	Language of publication: English Funding: National Health Service and the National Institute for Health Research health technology assessment programme Publication status:Peer reviewed journal

DiGEM trial 2007 (*Continued*)

Stated aim of study	"To test whether elf monitoring of blood glucose with or without instruction in incorporating findings into self care, compared with standardised usual care can improve glycaemic control in patients with non-insulin treated diabetes"
Notes	Diabetes Glycaemic Education Monitoring (DiGEM) trial Data was extracted from four manuscripts: Farmer 2007, *BMJ*; French 2008, *Diabetic Medicine*; Simon 2008, *BMJ*; Farmer 2009, *Health Technology Assessment*.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: " we used computerised randomisation incorporating a partial minimisation procedure to adjust the randomisation probabilities between groups..."
Allocation concealment (selection bias)	Low risk	Quote: "the minimisation procedure to assign patients to their allocated intervention was conducted independently of the research nurses who managed recruitment and carried out assessment visits. The allocation was also concealed from laboratory staff"
Blinding (performance bias and detection bias) Was the patient blinded to the intervention?	High risk	Comment: Patient cannot be blinded to the intervention
Blinding (performance bias and detection bias) Was the care provider blinded to the intervention?	High risk	Comment: Care provider cannot be blinded to the intervention
Blinding (performance bias and detection bias) Was the outcome assessor blinded to the intervention?	Low risk	Quote: "Treatment allocation was concealed for study nurses and laboratory staff"
Incomplete outcome data (attrition bias) Was the drop-out rate described and acceptable?	Low risk	Quote; " only 57 patients where lost to follow up (12,6%) which did not differ between groups"
Incomplete outcome data (attrition bias) Was an intention to treat analysis performed?	Low risk	Quote: "we carried out a single intention to treat analysis of the main trial end points at the end of the study using ANCOVA to compare mean levels of HbA_{1c} at follow up between the three allocated groups,

DiGEM trial 2007 (*Continued*)

		with the baseline level of HbA_{1c} as covariate. If no follow-up data were available we imputed values by carrying forward the last available measurement"
Selective reporting (reporting bias)	Low risk	Comment: All outcomes are pre-specified available in the published study protocol
Free of other bias? Where groups similar at baseline?	Low risk	Quote: "Baseline, personal and clinical characteristics were well balanced between the groups"
Free of other bias? Where co-interventions avoided or similar?	Low risk	Comment: All groups received the same goal setting and review techniques
Free of other bias? Was the compliance acceptable in all groups?	Low risk	Quote: Ninety nine (67%) in the less intensive group and 52% in the more intensive group continued to use the meter at least twice a week for the 12 months of the study"

Durán 2010

Methods	a prospective randomised clinic-based interventional study with parallel groups
Participants	Country: Spain Number of participants: 195 Inclusion criteria: • newly diagnosed type 2 diabetes after two fasting glucose plasma values > 125 mg dL; • age 18 to 80 years; • < 6 months from the first fasting plasma glucose value > 126 mg dL; • absence of ketones in two first morning urine samples. Exclusion criteria: • any fasting glucose levels > 125 mg dL in previous 12 months; • HbA_{1c} levels > 8% at diagnosis; • unable to perform SMBG; • life threatening disease. Mean age (years ± SD): • SMBG: 62.5 ± 10.4 • Control: 64.7 ± 9.6 Diabetes duration (years): • SMBG: 0 • Control: 0
Interventions	1. SMBG based step-by-step treatment (n = 99): lifestyle intervention that used SMBG as an educational tool to adhere to lifestyle changes, as well as a therapeutic tool to apply step-by-step pharmacological treatment. 2. HbA_{1c} based step-by-step treatment (n = 62): standard treatment based on

Durán 2010 (*Continued*)

	HbA_{1c} values without SMBG. All patients were treated with 850 mg metformin (half a tablet at breakfast, nothing at lunch and another half tablet at dinner; ½-0-½). Lifestyle interventions were similar for all patients and were developed after a 2h session for each patient individually and were reinforced at each follow-up visit
Outcomes	Primary outcome: 1. Remission and regression rate of type 2 diabetes. Secondary outcomes: changes in 1. $HbA_{1c;}$ 2. fasting insulin; 3. homeostasis model assessment of insulin resistance (HOMA-IR); 4. total cholesterol (high-density lipoprotein (HDL) and low density lipoprotein (LDL)); 5. triglycerides; 6. apolipoprotein B; 7. body weight; 8. waist circumference; 9. blood pressure; 10. adherence to the suggested lifestyle changes.
Study details	Duration: 12 months
Publication details	Language of publication: English Funding: Ministerio de Sanidad from Spain (Fondos de Cohesion 2008) Publication status:Peer reviewed journal
Stated aim of study	To investigate the hypothesis that " in combination with simple algorithms that modify the doses of glucose-lowering medication, SMBG can prevent acute complications, such as hypoglycaemia as well as alerting the patient when specialist help and support are needed"
Notes	St. Carlos study

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Newly diagnosed T2DM patients who were eligible for inclusion in the study were randomly (2:1) assigned to one of two groups" Comment: No further information provided.
Allocation concealment (selection bias)	Unclear risk	Comment: No information provided

Blinding (performance bias and detection bias) Was the patient blinded to the intervention?	High risk	Comment: The patient cannot be blinded to the intervention
Blinding (performance bias and detection bias) Was the care provider blinded to the intervention?	High risk	Comment: The care provider cannot be blinded to the intervention
Blinding (performance bias and detection bias) Was the outcome assessor blinded to the intervention?	Unclear risk	Comment: No information stated
Incomplete outcome data (attrition bias) Was the drop-out rate described and acceptable?	Low risk	Quote: " 29 patients from the supervised exercise program subgroup of the SMBG arm were excluded and 5 patients (SMBG 2, control 3) were lost to follow-up"
Incomplete outcome data (attrition bias) Was an intention to treat analysis performed?	Low risk	Comment: Ninety-nine out of 130 randomised patients in the SMBG group were analysed and 62 in the control group were analysed Quote: "a supervised exercise program was offered to half the patients in the SMBG group (we expected a 1:1 allocation in these subgroups) but, surprisingly, only 29 patients agreed to participate. Given the small number of SMBG patients in the exercise program and the possible influence of physical activity on the three endpoints evaluated, the patients in this subgroup were excluded from subsequent analysis"
Selective reporting (reporting bias)	Unclear risk	Comment: Outcomes in the report are identical to those stated in the recorded trial register. "Clinical trial number ISRCTN81672669 available at http://www.controlled-trials.com/ISRCTN81672669". However, the trial started in January 2006 but was registered in 2009. All outcomes are expressed as median (q1-q3) which indicates skewness
Free of other bias? Where groups similar at baseline?	Low risk	Quote: "Patient characteristics at the time of study entry were similar between the two groups, with the exception of higher LDL

Durán 2010 (*Continued*)

		cholesterol levels in the SMBG compared with the HbA_{1c} group".
Free of other bias? Where co-interventions avoided or similar?	Low risk	Quote: "a supervised exercise program was offered to half the patients in the SMBG group (we expected a 1:1 allocation in these subgroups) but, surprisingly, only 29 patients agreed to participate. Given the small number of SMBG patients in the exercise program and the possible influence of physical activity on the three endpoints evaluated, the patients in this subgroup were excluded from subsequent analysis"
Free of other bias? Was the compliance acceptable in all groups?	Low risk	Quote: "In the SMBG group, 96 of 99 patients (97%) performed a median of 251 capillary measurements (range 148-300) during follow-up". Comment: This is approximally 1 six point profile per week, which was recommended

Fontbonne 1989

Methods	Randomised controlled trial. Randomisation procedure stratified by clinic.
Participants	Country: France Number of participants: 208 Inclusion criteria: • non-insulin dependent diabetes patients; • treated with diet and/or oral hypoglycaemic agents; • poorly controlled at entry to trial, FPG > 8.8 mmol/L, or postprandial blood glucose level > 11.1 mmol/L, 3 times within the preceding year; • presence of at least occasional glucosuria (renal glucose threshold < 11 mmol/L) was to be ascertained; • no rapidly progressing diabetic complications, no severe illness; • at least 3 years duration of diabetes; • first contact to the diabetes clinic at least 6 months before entry to trail; • having attended to at least 2 outpatient visits since their first contact; Mean age (years ± SD): • SMBG: 54.5 ± 10.7 • Urine glucose: 54.9 ± 10.2 • Control: 56.3 ± 9. Diabetes duration (years ± SD): • SMBG: 12.2 ± 6.6 • Urine glucose: 13.3 ± 6.8 • Control: 12.7 ± 0.8

Fontbonne 1989 (*Continued*)

Interventions	1. SMUG: self-urine glucose monitoring, twice every other day (n = 54). 2. SMBG: self blood glucose monitoring, twice every other day (n = 56). 3. Control: regular HbA_{1c} determinations every two months, no self-monitoring (n = 54).
Outcomes	1. Weight, measured every two months. 2. HbA_{1c} assayed by low-pressure liquid chromatography, measured every 2 months. 3. Number of reactive strips reported in a diary, recorded every two months.
Study details	Duration: 6 months
Publication details	Language of publication: English Funding: Ames Division, Miles Laboratories. Publication status:Peer reviewed journal
Stated aim of study	"To determine if the use of self glucose monitoring could help this rather common type of non insulin-treated diabetic patients (poorly controlled) in achieving improved metabolic control, by increasing their disease awareness and hence their compliance with treatment, as well as by giving the physician new evidence on which to adjust diet and oral treatment"
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "They then were randomly assigned to one of three monitoring groups. The randomisation procedure was stratified by clinic." Comment: No information on the sequence generation available
Allocation concealment (selection bias)	Unclear risk	Comment: No information on allocation concealment available
Blinding (performance bias and detection bias) Was the patient blinded to the intervention?	High risk	Comment: Patient cannot be blinded
Blinding (performance bias and detection bias) Was the care provider blinded to the intervention?	High risk	Comment: Care provider cannot be blinded

Fontbonne 1989 (*Continued*)

Blinding (performance bias and detection bias) Was the outcome assessor blinded to the intervention?	Unclear risk	Comment: No information presented
Incomplete outcome data (attrition bias) Was the drop-out rate described and acceptable?	High risk	Quote: "Two-hundred and eight patients entered the trial..." "Forty-four patients were lost to follow-up, i.e. did not attend the last visit...."
Incomplete outcome data (attrition bias) Was an intention to treat analysis performed?	High risk	Comment: Differences for outcome criteria between last and first visits are analysed per protocol
Selective reporting (reporting bias)	Unclear risk	Comment: No trial register or published design available
Free of other bias? Where groups similar at baseline?	Low risk	Comment: No differences between groups were observed.
Free of other bias? Where co-interventions avoided or similar?	Low risk	Comment: No specific information is mentioned. However, none of the groups received any extra or different advice or treatment
Free of other bias? Was the compliance acceptable in all groups?	High risk	Quote: "The number of urine strips used in the SMUG group was significantly lower than expected indicating low compliance.. ." The number of blood strips used was as expected"

Franciosi 2011

Methods	Randomised controlled pilot study
Participants	Country: Italy Number of participants: 62 Inclusion criteria: • patients with type 2 diabetes; • age 45 to 75 years; • HbA_{1c} between 7% and 9% ; • treated with oral hypoglycaemic agent monotherapy; • no experience in SMBG in previous 12 months; • first time in diabetes clinic. Exclusion criteria: • incapable of performing SMBG; • requiring insulin or multiple oral hypoglycaemic agent therapy; • requirement of regular use of SMBG;

Franciosi 2011 (*Continued*)

	• diabetes care not exclusive managed by diabetes clinic. Mean age (years ± SD): • SMBG: 48.9 ± 0.5 • Control: 48.7 ± 0.6 Diabetes duration (years ± SD): • SMBG: 3.4 ±3.5 • Control: 3.2 ± 4.4
Interventions	1. Standardized Specific education addressing how to perform SMBG, how to modify diet and level of physical activity according to blood glucose levels and the actions to undertake in case of abnormal values. 2. Control group receiving standard counselling with focus on diet and lifestyle.
Outcomes	Primary outcome: 1. Change in HbA_{1c}, between groups after 6 months. Secondary outcomes: 1. Percentage of patients reaching HbA_{1c} target (< 7.0%) . 2. Percentage of patients requiring therapy modifications. 3. Changes in body weight. 4. Changes in lipid profile. 5. Changes in blood pressure values.
Study details	Duration: 6 months
Publication details	Language of publication: English Funding: Unconditionally support by LifeScan Inc. Clinical Research Management and Monitoring Publication status:Peer reviewed journal
Stated aim of study	"To evaluate the feasibility and efficacy of a self-monitoring disease management strategy in patients with Type 2 diabetes on oral hypoglycaemic agent therapy"
Notes	ROSES-study

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Eligible patients were centrally randomised by telephone to intervention group vs. control group on the basis of random permuted block computer-generated randomisation tables, stratified by centre and produced by the coordinating centre."
Allocation concealment (selection bias)	Low risk	Quote: "...patients were centrally randomised by telephone..."

Franciosi 2011 (*Continued*)

Blinding (performance bias and detection bias) Was the patient blinded to the intervention?	High risk	Quote: "participants, providers and assessors were not blinded on group/treatment allocation."
Blinding (performance bias and detection bias) Was the care provider blinded to the intervention?	High risk	Quote: "participants, providers and assessors were not blinded on group/treatment allocation."
Blinding (performance bias and detection bias) Was the outcome assessor blinded to the intervention?	High risk	Quote: "participants, providers and assessors were not blinded on group/treatment allocation."
Incomplete outcome data (attrition bias) Was the drop-out rate described and acceptable?	Low risk	Quote: "Sixty-two patients were recruited , of whom five did not complete the follow-up"
Incomplete outcome data (attrition bias) Was an intention to treat analysis performed?	Low risk	Quote: "all the efficacy analyses were performed on the intention-to-treat population" Quote: "all randomised patients were included in the analyses"
Selective reporting (reporting bias)	Low risk	Comment: The trial is registered in the Clinical Trials register but was registered 3 years after study start date
Free of other bias? Where groups similar at baseline?	Low risk	Quote: "clinical and socio-demographic characteristics compared well between the two groups. Some variables varied slightly but not significantly"
Free of other bias? Where co-interventions avoided or similar?	Unclear risk	Quote: "The control group received standard counselling with focus on diet and lifestyle". No information is provided whether the intervention group received this also
Free of other bias? Was the compliance acceptable in all groups?	Low risk	Quote: "..mean number of SMBG measurements during the trial was 71 ±11 as compared with the 76 required by protocol. Only 7.1% of the patients performed less than 80% of the required number of measurements"

Guerci 2003

Methods	Randomised controlled trial
Participants	Country: France Number of participants: 689 Inclusion criteria: • type 2 diabetes with a known duration over 1 year; • insufficiently controlled with oral antidiabetic treatment (HbA_{1c} > 7.5 and < 11. 0%); • age between 40 and 75 years; • not previously treated with insulin; • not requiring insulin at inclusion; • not previously received SMBG; • able to carry out SMBG. Exclusion criteria: • type 1 diabetes, MODY and secondary diabetes; • recent weight loss of more than 3 kg during the last 3 months; • impending complications of diabetes; • pregnant women; • unable to read or write; • uncooperative. Mean age (years ± SD): • SMBG: 60.9 ± 9.4 • Control: 62.2 ± 9.1 Diabetes duration (years ± SD): • SMBG: 7.7 ± 6.3 • Control: 8.4 ± 6.6
Interventions	1. SMBG (n = 345) in addition to the conventional laboratory work-up. Education on weight loss and physical activity; treatment alterations by physician. Measurements at least 6 times per week, on 3 different days, including weekends. 2. Control (n = 344): conventional laboratory work-up based solely on laboratory measurement of HbA_{1c} every 12 weeks. Education on weight loss and physical activity; treatment alterations by physician.
Outcomes	1. Weight, systolic and diastolic blood pressure at baseline, 3 and 6 months. 2. HbA_{1c}, determined using the DCA analyser and blood glucose. Measured at baseline, 3 and 6 months. 3. Number of hypoglycaemic episodes.
Study details	Duration: 6 months
Publication details	Language of publication: English Funding: Publication status:Peer reviewed journal
Stated aim of study	”To compare, over a 6-month period, metabolic control in patients with poorly controlled type 2 diabetes, managed wither with usual recommendations alone (conventional assessment group) or combined with self-monitoring of blood glucose (SMBG group)“

Notes	ASIA-study	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "the patients were randomised to two groups...". Comment: No information on randomisation sequence is available
Allocation concealment (selection bias)	High risk	Comment: Patients were randomised by their GPs who also carried out the usual care, dietary advice and the follow-up
Blinding (performance bias and detection bias) Was the patient blinded to the intervention?	High risk	Comment: Patient cannot be blinded
Blinding (performance bias and detection bias) Was the care provider blinded to the intervention?	High risk	Comment: Care provider cannot be blinded
Blinding (performance bias and detection bias) Was the outcome assessor blinded to the intervention?	Unclear risk	Comment: No information about the outcome assessor available
Incomplete outcome data (attrition bias) Was the drop-out rate described and acceptable?	High risk	Comment: Nine hundred and eighty-eight patients were randomised. Of those 689 patients had at least two evaluations for the primary criterion HbA_{1c}. Quote: "Three hundred and three patients discontinued the study early (164 SMBG; 139 control)".
Incomplete outcome data (attrition bias) Was an intention to treat analysis performed?	High risk	Comment: The primary criterion was not estimable for 299 patients in the initial intention to treat analysis. A modified intention to treat analysis is performed with 689 patients
Selective reporting (reporting bias)	Unclear risk	Comment: No trial registration or protocol available
Free of other bias? Where groups similar at baseline?	Low risk	Quote: "No statistically significant difference was observed between the two groups.."
Free of other bias? Where co-interventions avoided or similar?	Low risk	Quote: "At visit 3 each GP could modify treatment of their patients according to HbA_{1c}, keeping with ANAES

Guerci 2003 (*Continued*)

		recommendations. At each consultation both groups were equally informed“
Free of other bias? Was the compliance acceptable in all groups?	Unclear risk	Quote: No statistically significant difference between the two groups was found during the study in terms of diet prescribed”. “Compliance to physical activity was similar in both groups” Comment: No information is available on performance of SMBG

Kleefstra 2010

Methods	Randomised controlled trial
Participants	Country: The Netherlands Number of participants: 41 Inclusion criteria: • type 2 diabetes patients from the ZODIAC shared care project; • 18 to 70 years of age; • HbA_{1c} between 7 and 8.5% at current annual check-up and inclusion; • use of 1 or 2 different oral blood glucose lowering agents; • oral blood glucose lowering agents were not changed during the past 3 months; • no use of insulin; • no use of devices for SMBG at the start of the study or in the previous 6 months; • sufficient knowledge of the Dutch language to understand the requirements of the study; Mean age (years ± SD): • SMBG: 59.5 ± 8.0 • Control: 58.7 ± 7.8 Diabetes duration (median years (q1-q3)): • SMBG: 5.0 (4.0 - 7.0) • Control: 8.0 (3.8 - 11.3)
Interventions	1. SMBG (n = 22): SMBG with no further education except for handling the device and knowing which glucose values were considered normal or acceptable (fasting 4-8 mmol/L and post-prandial 4-10 mmol/L) and which abnormal. 2. Control (n = 18): Usual care provided by their own health care giver. No other instructions were given, except for the explicit request not to use any form of SMBG during the study.
Outcomes	Primary outcome: 1. Δ HbA_{1c} between groups. Secondary outcomes: 1. Differences between groups in Health Related Quality of Life measures (SF-36; WHO-5). 2. Diabetes related complaints (DSC-r). 3. Treatment satisfaction (DTSQ). 4. Cumulative incidence of (necessity to start) insulin therapy. 5. Bodyweight.

	6. Body mass index.
Study details	Duration of intervention: 12 months.
Publication details	Language of publication: English Funding: Roche Diagnostics Publication status: Peer reviewed journal
Stated aim of study	"To investigate the effects of SMBG on glycaemic control, quality of life and treatment satisfaction in patients with T2DM not using insulin, who are in persistent moderate glycaemic control"
Notes	ZODIAC study

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "After inclusion.... a telephone call to a third party was made, who had numbers ranging from 1 to 60 in non-transparent envelopes, and was asked to draw an envelope"
Allocation concealment (selection bias)	Low risk	Quote: "Randomisation was done using an independent third party"
Blinding (performance bias and detection bias) Was the patient blinded to the intervention?	High risk	Comment: Patient cannot be blinded to the intervention
Blinding (performance bias and detection bias) Was the care provider blinded to the intervention?	High risk	Comment: Care provider cannot be blinded to the intervention
Blinding (performance bias and detection bias) Was the outcome assessor blinded to the intervention?	Low risk	Quote: " All laboratory tests were performed in local hospital laboratories,, where staff was unaware of treatment allocation"
Incomplete outcome data (attrition bias) Was the drop-out rate described and acceptable?	Low risk	Quote: "..one patient in the control group refused to continue the study and withdrew"
Incomplete outcome data (attrition bias) Was an intention to treat analysis performed?	Low risk	Comment: Data from all patients initially randomised were retrieved and analysed. (40 patients)

Kleefstra 2010 (*Continued*)

Selective reporting (reporting bias)	Low risk	Comment: Primary outcomes are pre-specified in trial register
Free of other bias? Where groups similar at baseline?	High risk	Quote: "BMI and diabetes duration where different between groups"
Free of other bias? Where co-interventions avoided or similar?	Low risk	Comment: No education was given to ensure there are no education differences between groups
Free of other bias? Was the compliance acceptable in all groups?	Low risk	Quote: "Of the 22 patients in the SMBG group 17 performed at least 80% of the requested glucose registrations"

Muchmore 1994

Methods	Randomised controlled trial
Participants	Country: USA Number of participants: 23 Inclusion criteria: • obese participants (BMI 27.5-44 kg/m2); • aged 40 to 75 years; • history of at least 1 year of non-insulin requiring diabetes; • treated either with diet alone or diet plus oral sulphonylurea hypoglycaemic agents; • HbA_{1c} within the range of 9.5%-13.5%; • ability to comply with the protocol; • absence of serious underlying medical or psychiatric illness, drug abuse or alcohol. Exclusion criteria: • participants who had performed SMBG within the previous 3 months; • participants who have previously been instructed in dietary carbohydrate counting. Mean age (years ± SD): • SMBG: 57.3 ± 8.0 • Control: 60.1 ± 7.3 Diabetes duration (years ± SD): • SMBG: 5.7 ± 4.8 • Control: 5.2 ± 4.6
Interventions	Four groups were formed over a period of 6 months, blocking for variables of weight, HbA_{1c}, diet vs. oral agent use, and sex. Weeks -8 to 0: identical run-in for all 4 groups: weekly behavioural weight control program + counselling by diabetes nurse educator + session with dietician. Follow-up session educator at weeks 1, 3 and 24 and dietician at weeks 1 and 3 Week 0: randomly assignment to control or SMBG interventions 1. Intervention (n = 12): individual and group teaching on CarboHydrate counting and SMBG, measured 6 times daily for 4 weeks. Reduced to pre- and postprandial testing of a single meal per day for weeks 4-20. Beyond week 20, individual's election

	and expense. 2. Control (n = 11): identical amount of attention, focus on general principles of diabetes nutrition.Groups continued to meet weekly for weeks 0-4 and then every 4 weeks for weeks 4-20.
Outcomes	1. HbA_{1c}, measured at weeks -8, 0, 16, 28 and 44. 2. Body weight measured at every patient encounter. 3. Diabetes Quality of Life Inventory at weeks 0, 24 and 44.
Study details	Duration: 28 weeks (-8, 0-20 intervention) and follow-up till 44 weeks
Publication details	Language of publication: English Funding: Department of Academic Affairs, Scripps Clinic and Research Foundation Publication status: Peer reviewed journal
Stated aim of study	"To test the hypothesis that measuring and linking carbohydrate intake to incremental postprandial SMBG results would allow to modify specific, proximate behaviours in the management of type 2 diabetic patients"
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Quote: "At week 0, groups I-III were randomly assigned to control or SMBG interventions, group IV being assigned to control status in order to equalize the number of groups in each intervention" Comment: No information presented on randomisation sequence.
Allocation concealment (selection bias)	High risk	Quote: "At week 0, groups I-III were randomly assigned to control or SMBG interventions, group IV being assigned to control status in order to equalize the number of groups in each intervention"
Blinding (performance bias and detection bias) Was the patient blinded to the intervention?	High risk	Comment: Patient cannot be blinded
Blinding (performance bias and detection bias) Was the care provider blinded to the intervention?	High risk	Comment: Care provider cannot be blinded

Muchmore 1994 (*Continued*)

Blinding (performance bias and detection bias) Was the outcome assessor blinded to the intervention?	Unclear risk	Comment: It is not clear who assessed the primary outcome, HbA_{1c}
Incomplete outcome data (attrition bias) Was the drop-out rate described and acceptable?	High risk	Quote: "Of the 29 individuals recruited to the study, 6 dropped out prior to or at the time of randomisation..."
Incomplete outcome data (attrition bias) Was an intention to treat analysis performed?	Unclear risk	Comment: Even though endpoint data was available for 23 patients, no information is available on the number of patients included in the analyses
Selective reporting (reporting bias)	Unclear risk	Comment: No trial registration or protocol publication available
Free of other bias? Where groups similar at baseline?	Low risk	Quote: "...treatment groups were well matched for all pre randomisation variables except initial treatment modality...."
Free of other bias? Where co-interventions avoided or similar?	Low risk	Quote: " Throughout the study, individuals remained under medical care of their primary GP and decisions on medical adjustments were coordinated through these providers"
Free of other bias? Was the compliance acceptable in all groups?	Low risk	Quote: "Subject compliance with protocol requirements was good"

O'Kane 2008

Methods	Prospective randomised controlled trial
Participants	Country: Norhtern Ireland Number of participants: 195 Inclusion criteria: • Patients with newly diagnosed type 2 diabetes; • < 70 years of age. Exclusion criteria: • secondary diabetes; • use of insulin; • previous use of SMBG; • major illness within the previous six months; • chronic kidney disease; • chronic liver disease; • alcohol misuse. Mean age (years ± SD): • SMBG: 57.7 ± 11.04

	• Control: 60.9 ± 11.5 Diabetes duration (years ± SD): • SMBG: 0 • Control: 0
Interventions	1. SMBG (n = 96): SMBG and ongoing advice and support in interpretation of and response to high or low readings. 2. Control (n = 88): no SMBG. All patients received a structured education programme with nurse practitioners, dieticians, podiatrist and medical staff at 3-monthly intervals and a treatment algorithm for dietary and pharmacological management of glycaemia based on HbA_{1c} targets. At each visit aspects of diabetes care including glycaemic control (HbA_{1c}) were reviewed.
Outcomes	Primary outcome: 1. Δ HbA_{1c} between groups. 2. Psychological indices (DTSQ, modified diabetes attitude scale, WBQ). 3. incidence of hypoglycaemia. Secondary outcomes: 1. Δ body mass index between groups. 2. Use of oral hypoglycaemic drugs.
Study details	Duration of intervention: 12 months.
Publication details	Language of publication: English Funding: Northern Ireland research and development office Publication status: Peer reviewed journal
Stated aim of study	"To investigate the effect of self monitoring on glycaemic control and attitudes and satisfaction with treatment in patients with newly diagnosed type 2 diabetes"
Notes	ESMON study

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: ".. with a randomly generated allocation code in consecutively numbered sealed envelopes"
Allocation concealment (selection bias)	Low risk	Quote: "The study diabetes nurse at each hospital site performed the treatment allocation" Comment: Information is not presented if these diabetes nurses are involved in the three monthly patient reviews
Blinding (performance bias and detection bias) Was the patient blinded to the interven-	High risk	Comment: Patient cannot be blinded to the intervention

tion?		
Blinding (performance bias and detection bias) Was the care provider blinded to the intervention?	High risk	Comment: Care provider cannot be blinded to the intervention
Blinding (performance bias and detection bias) Was the outcome assessor blinded to the intervention?	Low risk	Quote: "Measurement of HbA_{1c} was performed in the local hospital laboratory with a DCCT aligned HbA_{1c} assay". "All laboratory tests were also performed in the local hospital laboratory, where staff were blinded to treatment allocation"
Incomplete outcome data (attrition bias) Was the drop-out rate described and acceptable?	Low risk	Comment: No patients were lost to follow up. Quote: "4 patients failed to complete the study (2 in each group)"
Incomplete outcome data (attrition bias) Was an intention to treat analysis performed?	Low risk	Quote: "The analysis was performed on an intention to treat basis, with missing data imputed through the use of full information likelihood"
Selective reporting (reporting bias)	Low risk	Comment: All described pre-designated primary endpoints were reported in trial register
Free of other bias? Where groups similar at baseline?	Low risk	Quote: "There was no significant difference in baseline HbA_{1c}, age, or sex between groups, although participants in the self monitoring group had a higher baseline body mass index"
Free of other bias? Where co-interventions avoided or similar?	Low risk	Quote: "Patients in both groups underwent an identical structured education programme. .."
Free of other bias? Was the compliance acceptable in all groups?	Low risk	Quote: "...63 patients in the intervention group carried out at least 80% of the requested blood glucose monitoring" Comment: Compliance was defined as a monitoring frequency of > 80% of that requested

SMBG study group 2002

Methods	Multicenter, randomised controlled design Randomised in blocks of eight.
Participants	Country: Germany and Austria Number of participants: 250 patients. Inclusion criteria: • type 2 diabetes patients; • body mass index > 25 kg/m2; • HbA_{1c} values between 7.5 and 10%; • treated either with diet alone or diet in combination with sulphonylureas or metformin; • age between 45 and 70 years; • diabetes known for at least 3 months; • participation in a diabetes educational program within the previous 2 years. Exclusion criteria: • incapable of maintaining an eating diary and of documenting their state of well-being; • sensomotor disturbances; • used regular SMBG during the 6 months before the start of the study; • participated in another clinical trial within 30 days before the start of the study-pregnant or lactating females or without a safe contraception method; • treatment with other antidiabetic agents such as insulin or with nonselective ß-blockers, glucocorticoids, amphetamines, or anabolic agents; • diet reduction during course of the study (< 1,000 kcal/day); • serum creatinine > 3 mg/dl-serum transaminases > 50 units/L; • serious underlying medical or psychiatric disorders or drug or alcohol abuse; • use of acarbose. Mean age (years ± SD): • SMBG: 58.7 ± 7.6 • Control: 60.5 ± 6.6 Diabetes duration (years ± SD): • SMBG: 5.5 ± 4.8 • Control: 5.2 ± 3.9
Interventions	1. SMBG (n = 113): Measurements of blood glucose 6 times on 2 days per week and recordings of values obtained in a diary for blood glucose data and documentation of eating habits and state of well-being. Continuing of using the glucometer during the follow-up period. 2. Control (n = 110): non standardized counselling with a focus on their diet and lifestyle.
Outcomes	1. HbA_{1c}, determined using the DCA 2000 analyser. 2. Body weight. 3. Lipids and micro albumin. 4. Well-being and treatment satisfaction, measured by the Patient Well-being Questionnaire and the Diabetes Treatment Satisfaction Questionnaire. Laboratory parameters and body weight were assessed at randomisation and at 8, 16 and 24 weeks. Questionnaires were completed at randomisation, 24 weeks and follow-up. HbA_{1c}, body weight, SMBG acceptance, treatment satisfaction, and well-being were

SMBG study group 2002 (*Continued*)

	also assessed during two visits in the 6-month follow-up period
Study details	Duration: 6 months and 6 months follow-up
Publication details	Language of publication: English Funding: Unrestricted grant from Bayer AG & Bayer Vital GmbH Publication status:Peer reviewed journal
Stated aim of study	"To investigate the effect of meal-related SMBG on diabetes control in non-insulin-treated type 2 diabetic patients on a biometrical basis"
Notes	SMBG study group Data was extracted from 2 manuscripts: Schwedes 2002, *Diabetes Care*; Siebolds 2006, *Patient Education and Counseling*.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: " a total of 250 patients were enrolled and randomised within blocks of eight to receive one of the two treatments" Comment: Information on randomisation method is not presented
Allocation concealment (selection bias)	Unclear risk	Comment: Method of allocation concealment is not described
Blinding (performance bias and detection bias) Was the patient blinded to the intervention?	High risk	Comment: Patient cannot be blinded to the intervention
Blinding (performance bias and detection bias) Was the care provider blinded to the intervention?	High risk	Comment: Care provider cannot be blinded to the intervention
Blinding (performance bias and detection bias) Was the outcome assessor blinded to the intervention?	Unclear risk	Quote: "Assistants and nursing staff received structured instructions on the correct use of the monitoring device, DCA 2000, and HemoCue and learned how to supervise and document the correct use and documentation by the patients"
Incomplete outcome data (attrition bias) Was the drop-out rate described and acceptable?	Unclear risk	Comment: Twenty-seven patients were not included in the analysis, but reasons for exclusion are not described

SMBG study group 2002 (*Continued*)

Incomplete outcome data (attrition bias) Was an intention to treat analysis performed?	High risk	Quote: "Of the 250 randomised patients, 223 per-protocol analysis" Quote: "Per-protocol analysis was performed as the main efficacy analysis'
Selective reporting (reporting bias)	Unclear risk	Comment: Although planned no information on the follow-up data is reported
Free of other bias? Where groups similar at baseline?	Low risk	Quote: "The baseline demographic characteristics compared well for both groups". "There were no statistically significant differences regarding baseline efficacy parameters"
Free of other bias? Where co-interventions avoided or similar?	High risk	Quote: "SMBG patients received a defined counselling algorithm..." "The control group received non standardized counselling with a focus on their diet an lifestyle..." Comment: The intervention group received counselling focused on psychological aspects and the control group counselling was non standardized. Both interventions could therefore cause bias. Furthermore, no details are given whether both groups had different nurses delivering the counselling
Free of other bias? Was the compliance acceptable in all groups?	Low risk	Quote: "Patients were included in the analysis if they met protocol criteria, completed the entire study, showed valid efficacy parameter measurements and were over 70% compliant" Comment: Twenty-seven out of 250 were excluded.

SMBG = Self-Monitoring of Blood Glucose; SMUG = Self-Monitoring of Urine Glucose
DCCT= Diabetes Control and Complications Trial
BMQ: Beliefs about Medicine Questionnaire; DSC-r: Diabetes Symptom Checklist; DSCAQ: Diabetes Self-care Activities Questionnaire; DTSQ: Diabetes Treatment Satisfaction Questionnaire; DQOL: Diabetes Quality Of Life Inventory; EQ5D: EuroQol-5D; MARS: Medication Adherence Reporting Scale; SF-36: Short-Form 36; WBQ-12/22: Well Being Questionnaire-12/22; WHO-5: World Health Organization-5.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abdelgadir 2006	not randomised, also included patients with type 1 diabetes
Atsumi 1997	abstract, no detailed information could be retrieved
Bajkowska-Fiedziukiewicz 2008	not randomised
Chidum 2011	after 3 months follow-up, no data on control group
Cho 2006	intervention group received an Internet based SMBG system. SMBG not the main intervention
Davidson 2004	abstract that has been identified as an already included study
Drouin 2002	abstract that has been identified as an already included study
Franciosi 2005	not randomised
Gallego 2007	not randomised
Hoffmann 2011	not randomised
Johnson 2006	control group is using SMBG
Kelly 2007	non-relevant study design (letter to the editor)
Kwon 2004	both groups received SMBG; the intervention group received an Internet-based SMBG system and the control group just the SMBG. SMBG was not the main intervention
Laffel 2007	insulin treated patients
Lecomte 2008	not randomised, also included patients with type 1 diabetes
Lim 2011	included insulin treated patients
Mohan 2010	both intervention and control used SMBG
Moreland 2006	also included patients with type 1 diabetes and insulin users
O'Kane 2006	abstract that has been identified as an already included study
Pignone 2009	reprint of already included trial
Polonsky 2011	control group uses SMBG also
Scherbaum 2008	control group uses SMBG also

(*Continued*)

Shiraiwa 2010	detailed information on trial could not be retrieved (letter to the editor)
Tengblad 2007	not randomised
Wen 2004	not randomised, no control group, SMBG not the prime intervention
Wysocki 1989	not randomised

Characteristics of ongoing studies *[ordered by study ID]*

Bergenstal 2005

Trial name or title	Impact of Self-Monitoring Blood Glucose Frequency on Glycemic Control in Patients With Type 2 Diabetes
Methods	Allocation: Randomised, Control: Uncontrolled, Endpoint Classification: Safety/Efficacy Study, Intervention Model: Parallel Assignment, Masking: Open Label, Primary Purpose: Treatment
Participants	Type 2 diabetes patients with the following criteria: • Treatment with diet and exercise alone or with the addition of 1 or 2 oral agent • Enrolled in Type 2 BASICS program • A1c between 7.0 and 11%, inclusive • Able to understand spoken English Exclusion Criteria: • Insulin therapy • Unable/unwilling to perform SMBG • Participating in another research study • Currently performing SMBG > 3 times/week
Interventions	Behavioral: frequency of self monitoring blood glucose
Outcomes	Primary: HbA_{1c} 2 years Secondary: blood glucose testing frequency 2 years
Starting date	September 2004
Contact information	Richard M Bergenstal, MD, Principal Investigator, Park Nicollet Institute/International Diabetes Center International Diabetes Center Minneapolis Minnesota 55416
Notes	

Malanda 2009

Trial name or title	Effect of self-monitoring of glucose in non-insulin treated patients with type two diabetes: The In Control Trial
Methods	Three-armed randomised controlled active parallel group trial
Participants	Type 2 diabetes patients with the following criteria: • known disease duration of over 1 year • recent HbA_{1c} 7.0% or higher • treated with diet and/or oral hypoglycaemic agents • do not require insulin at inclusion • aged between 45 and 75 years • used SMBG or SMUG less than 3 times in the previous year
Interventions	• intervention group A, performing SMBG with specific SMBG education, in addition to usual diabetes care provided by the regional diabetes care system. • intervention group B, performing SMUG with specific SMUG education, in addition to usual diabetes care provided by the regional diabetes care system. • control group receiving usual diabetes care provided by the regional diabetes care system
Outcomes	Primary outcome measures: • changes in diabetes specific emotional distress • changes in self-efficacy. Secondary outcomes • changes in glycaemic control, • changes in patient treatment satisfaction, • changes in physical activity, • changes in health status, • status of depression, • occurrence of hypoglycaemia, • cost-effectiveness and cost-utility. • process evaluation
Starting date	01-07-2007
Contact information	VU Medical Centre Amsterdam EMGO-Instituut Afdeling Huisartsgeneeskunde g.nijpels@vumc.nl
Notes	IN CONTROL study

DATA AND ANALYSES

Comparison 1. SMBG vs control (6 months follow-up)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 HbA1c	9	2324	Mean Difference (IV, Random, 95% CI)	-0.26 [-0.39, -0.13]

Comparison 2. SMBG vs control (12 months follow-up)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 HbA1c	2	493	Mean Difference (IV, Random, 95% CI)	-0.13 [-0.31, 0.04]

Comparison 3. SMBG vs control (newly diagnosed patients, 6 month follow-up)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 HbA1c	2	345	Mean Difference (IV, Random, 95% CI)	-0.53 [-1.06, -0.01]

Comparison 4. SMBG vs control (newly diagnosed patients, 12 months follow-up)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 HbA1c	2	345	Mean Difference (IV, Random, 95% CI)	-0.52 [-0.89, -0.14]

Comparison 5. SMBG vs SMUG (6 months follow-up)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 HbA1c	2	194	Mean Difference (IV, Random, 95% CI)	-0.17 [-0.96, 0.61]

Analysis 1.1. Comparison 1 SMBG vs control (6 months follow-up), Outcome 1 HbA1c.

Review: Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin

Comparison: 1 SMBG vs control (6 months follow-up)

Outcome: 1 HbA1c

Study or subgroup	SMBG N	Mean(SD)[%]	Control N	Mean(SD)[%]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Barnett 2008	311	-1.15 (1.14)	299	-0.91 (1.29)		22.0 %	-0.24 [-0.43, -0.05]
Davidson 2005	43	-0.8 (1.6)	45	-0.6 (2.1)		2.6 %	-0.20 [-0.98, 0.58]
DiGEM trial 2007 (1)	301	-0.15 (0.81)	152	-0.08 (0.73)		27.7 %	-0.07 [-0.22, 0.08]
Fontbonne 1989	68	-0.36 (3.14)	68	-0.5 (1.54)		2.3 %	0.14 [-0.69, 0.97]
Franciosi 2011	46	-1.2 (0.81)	16	-0.7 (0.7)		7.9 %	-0.50 [-0.92, -0.08]
Guerci 2003	345	-0.9 (1.54)	344	-0.5 (1.54)		18.3 %	-0.40 [-0.63, -0.17]
Kleefstra 2010	22	-0.18 (0.67)	18	0.07 (0.75)		7.0 %	-0.25 [-0.70, 0.20]
Muchmore 1994	12	-1.54 (1.46)	11	-0.85 (1.87)		0.9 %	-0.69 [-2.07, 0.69]
SMBG study group 2002	113	-1 (1.08)	110	-0.54 (1.41)		11.3 %	-0.46 [-0.79, -0.13]
Total (95% CI)	**1261**		**1063**			**100.0 %**	**-0.26 [-0.39, -0.13]**

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 11.29$, df = 8 (P = 0.19); $I^2 = 29\%$

Test for overall effect: Z = 3.99 (P = 0.000067)

Test for subgroup differences: Not applicable

(1) Both intervention groups are combined

Analysis 2.1. Comparison 2 SMBG vs control (12 months follow-up), Outcome 1 HbA1c.

Review: Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin

Comparison: 2 SMBG vs control (12 months follow-up)

Outcome: 1 HbA1c

Study or subgroup	SMBG N	Mean(SD)[%]	Control N	Mean(SD)[%]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
DiGEM trial 2007 (1)	301	-0.15 (0.78)	152	0 (1.02)		89.1 %	-0.15 [-0.33, 0.03]
Kleefstra 2010	22	-0.1 (0.9)	18	-0.1 (0.8)		10.9 %	0.0 [-0.53, 0.53]
Total (95% CI)	**323**		**170**			**100.0 %**	**-0.13 [-0.31, 0.04]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.28$, df = 1 (P = 0.60); $I^2 = 0.0\%$

Test for overall effect: Z = 1.50 (P = 0.13)

Test for subgroup differences: Not applicable

(1) Both intervention groups are combined

Analysis 3.1. Comparison 3 SMBG vs control (newly diagnosed patients, 6 month follow-up), Outcome 1 HbA1c.

Review: Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin

Comparison: 3 SMBG vs control (newly diagnosed patients, 6 month follow-up)

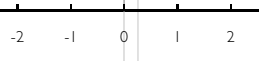
Outcome: 1 HbA1c

Study or subgroup	SMBG N	Mean(SD)[%]	Control N	Mean(SD)[%]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Dur n 2010	99	-0.68 (0.45)	62	0.05 (0.37)		64.5 %	-0.73 [-0.86, -0.60]
O'Kane 2008	96	-1.81 (2.1)	88	-1.64 (2.08)		35.5 %	-0.17 [-0.77, 0.43]
Total (95% CI)	**195**		**150**			**100.0 %**	**-0.53 [-1.06, -0.01]**

Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 3.16$, df = 1 (P = 0.08); $I^2 = 68\%$

Test for overall effect: Z = 1.98 (P = 0.047)

Test for subgroup differences: Not applicable



Analysis 4.1. Comparison 4 SMBG vs control (newly diagnosed patients, 12 months follow-up), Outcome 1 HbA1c.

Review: Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin

Comparison: 4 SMBG vs control (newly diagnosed patients, 12 months follow-up)

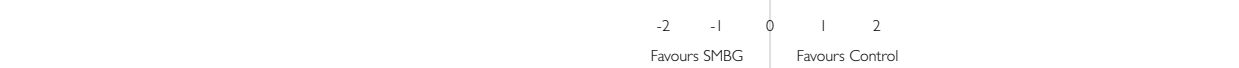
Outcome: 1 HbA1c

Study or subgroup	SMBG N	Mean(SD)[%]	Control N	Mean(SD)[%]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Dur n 2010	99	-0.56 (0.52)	62	0.07 (0.6)		73.3 %	-0.63 [-0.81, -0.45]
O'Kane 2008	96	-1.88 (2.06)	88	-1.68 (2.11)		26.7 %	-0.20 [-0.80, 0.40]
Total (95% CI)	**195**		**150**			**100.0 %**	**-0.52 [-0.89, -0.14]**

Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 1.79$, df = 1 (P = 0.18); $I^2 = 44\%$

Test for overall effect: Z = 2.71 (P = 0.0067)

Test for subgroup differences: Not applicable

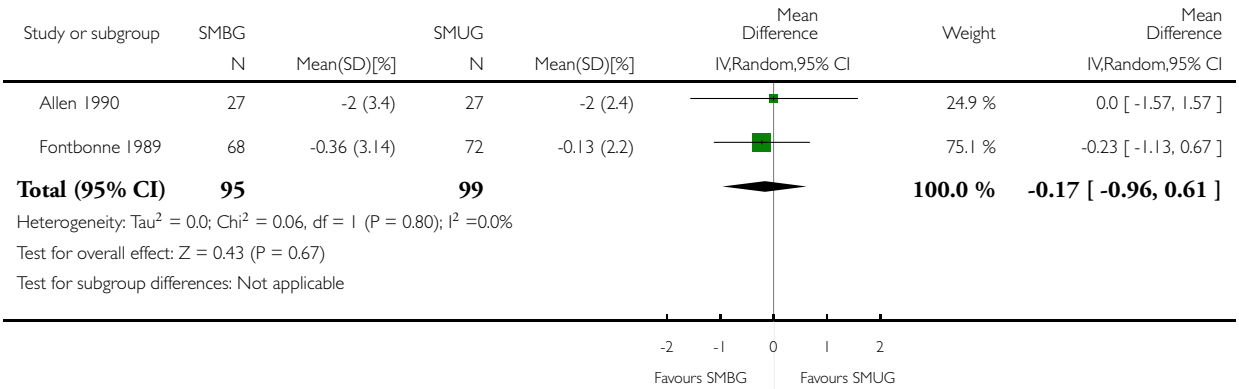


Analysis 5.1. Comparison 5 SMBG vs SMUG (6 months follow-up), Outcome 1 HbA1c.

Review: Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin

Comparison: 5 SMBG vs SMUG (6 months follow-up)

Outcome: 1 HbA1c



ADDITIONAL TABLES

Table 1. Overview of study populations

Characteristic ▸ Study ID ▾	Intervention (s) & control (s)	Screened (n)	Randomised (n)	ITT (n)	Randomised patients finishing study (%)	Finishing study (n)	Comments
Allen 1990	SMBG	-	-	-	-	27	
	SMUG	-	-	-	-	27	
	(total)	-	61	-	89	54	Seven patients dropped out (5 were inappropriately randomised, 2 gave no reasons for drop-out)
Barnett 2008	SMBG	-	311	311	87	271	
	Control	-	299	299	83	248	
	(total)	-	610	610	85	519	

Table 1. Overview of study populations (*Continued*)

Davidson 2005	SMBG	-	-	43	-	43	
	Control	-	-	45	-	45	
	(total)	89	89	88	99	88	Initially 89 patients were randomised. One patient did not return after randomisation. It is not stated in which group this patient was randomised
DiGEM trial 2007	SMBG more intensive	-	151	151	89	134	
	SMBG less intensive	-	150	150	91	136	
	Control	-	152	152	83	126	
	(total)	364,527	453	453	87	396	
Durán 2010	SMBG	-	130	99	76	99	Twenty-nine patients participated in an exercise supervised program and were excluded. Two were lost to follow-up
	Control	-	65	62	95	62	Three patients were lost to follow-up
	(total)	250	195	161	83	161	
Fontbonne 1989	SMBG	-	68	-	82	56	Twelve patients were lost to follow-up
	SMUG	-	72	-	75	54	Eighteen patients were lost to follow-up

Table 1. Overview of study populations (*Continued*)

	Control	-	68	-	79	54	Fourteen patients were lost to follow-up
	(total)	-	208	-	79	164	
Franciosi 2011	SMBG	-	46	46	91	42	
	Control	-	16	16	94	15	
	(total)	-	62	62	92	57	
Guerci 2003	SMBG	-	510	345	68	346	
	Control	-	478	344	71	339	
	(total)	-	988	689	69	685	Two-hundred and forty patients had a reason for discontinuation
Kleefstra 2010	SMBG	-	22	22	100	22	
	Control	-	19	19	95	18	One patient withdrew consent
	(total)	-	41	41	98	40	
Muchmore 1994	SMBG	-	15	-	80	12	Three patients dropped out
	Control	-	14	-	79	11	Three patients dropped out
	(total)	40	29	-	79	23	
O'Kane 2008	SMBG	-	96	96	98	94	Two patients withdrew from intervention
	Control	-	88	88	98	86	Two patients withdrew from intervention
	(total)	212	184	184	98	180	

Table 1. Overview of study populations (*Continued*)

SMBG study group 2002	SMBG	-	-	-	-	113	
	Control	-	-	-	-	110	
	(total)	250	250	-	89	223	Per protocol analysis performed
total			3259		80	*2590*	

"-" denotes not reported
ITT = intention-to-treat analysis; SMBG = self-monitoring of blood glucose; SMUG = self-monitoring of urine glucose

APPENDICES

Appendix 1. Search strategies

Search terms
Unless otherwise stated, search terms are free text terms; MeSH = Medical subject heading (Medline medical index term); exp = exploded MeSH; the dollar sign ($) stands for any character(s); the question mark (?) substitutes one or no characters; tw = text word; pt = publication type; sh = MeSH; adj = adjacent **MEDLINE** 1. exp Blood glucose self-monitoring/ 2. self monitor$.ti,ab. 3. exp Blood Glucose/ or (blood adj glucos$).ti,ab. or (blood adj sugar$).ti,ab. 4. 1 or (2 and 3) 5. exp Diabetes mellitus, non insulin dependent/ or exp Insulin resistance/ 6. (impaired glucose toleran$ or glucose intoleran$ or insulin resistan$).ti,ab. 7. (obes$ adj2 diabet$).ti,ab. 8. (mody or niddm).ti,ab. 9. (diabet$ and (non insulin$ depend$ or noninsulin$ depend$ or noninsulindepend$ or non insulindepend$ or noninsulinsdepend$ or non insulinsdepend$)).ti,ab. 10. ((typ$ 2 or typ$ II) adj diabet$).ti,ab. 11. ((ketoresist$ or keto$ resist$ or nonketo$ or non keto$) adj diabet$).ti,ab. 12. ((adult$ or matur$ or late or slow or stabl$) adj diabet$).ti,ab. 13. ((plurimetabolic$ or metabolic) adj syndrom$).ti,ab. 14. (insulin$ defic$ adj relativ$).ti,ab.

(*Continued)*

15. 6 or 11 or 7 or 9 or 12 or 14 or 8 or 10 or 13 or 5
16. exp Diabetes insipidus/
17. (exp Child/ or exp Infant/) not (exp adult/ or exp adolescent/)
18. (4 and 15) not (16 or 17)
19. (randomised controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.
20. clinical trial.mp. or clinical trial.pt. or random$.mp. or tu.xs.
21. Cross-over Studies/ or exp Double-blind method/ or exp Single-blind method/ or exp Control groups/ or exp Random Allocation/ or exp Evaluation studies/ or exp Comparative study/
22. 18 and (19 or 20 or 21)
23. limit 22 to yr="2004 -Current"

EMBASE

1. ((ketoresist$ or keto$ resist$ or nonketo$ or non keto$) adj diabet$).ti,ab.
2. ((adult$ or matur$ or late or slow or stabl$) adj diabet$).ti,ab.
3. (insulin$ defic$ adj relativ$).ti,ab.
4. ((plurimetabolic$ or metabolic) adj syndrom$).ti,ab.
5. ((typ$ 2 or typ$ II) adj diabet$).ti,ab.
6. (diabet$ and (non insulin$ depend$ or noninsulin$ depend$ or noninsulindepend$ or non insulindepend$ or noninsulin?depend$ or non insulin?depend$)).ti,ab.
7. (mody or niddm).ti,ab.
8. (obes$ adj2 diabet$).ti,ab.
9. (impaired glucose toleran$ or glucose intoleran$ or insulin resistan$).ti,ab.
10. exp Non insulin dependent diabetes mellitus/ or exp Insulin resistance/ or exp Diabetic obesity/
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12. exp Blood glucose monitoring/
13. self monitor$.ti,ab.
14. exp Glucose blood level/ or (blood adj glucos$).ti,ab. or (blood adj sugar$).ti,ab.
15. 13 and 14
16. 12 or 15
17. 11 and 16
18. 17 not exp Diabetes insipidus/
19. exp Randomized controlled trial/ or exp Controlled clinical trial/ or exp Crossover-procedure/ or exp Double-blind procedure/ or exp Single-blind procedure/ or exp Control group/ or exp Randomization/ or exp Evaluation/ or exp Comparative study/
20. (random$ or factorial$ or crossover$ or cross over$ or placebo$ or (doubl$ adj blind$) or (singl$ adj blind$) or assign$ or allocat$ or volunteer$).ti,ab.
21. limit 18 to (human and yr="2004 - 2010")
22. 21 not (exp Child/ not exp adult/)
23. limit 22 to "treatment (1 term high sensitivity)"
24. 23 or (22 and (19 or 20))

The Cochrane Library

(CENTRAL)

1. (impaired NEXT glucose NEXT toleran* OR glucose NEXT intoleran* OR insulin* NEXT resistan* OR obes* NEAR diabet* OR MODY OR NIDDM) in Clinical Trials
2. (diabet* AND (non NEXT insulin* NEXT depend* OR noninsulin* NEXT depend* OR noninsulindepend* OR non NEXT insulindepend* OR noninsulinsdepend* OR non NEXT insulinsdepend*)) in Clinical Trials
3. (typ* NEXT 2 OR typ* NEXT II) NEAR/2 diabet* in Clinical Trials
4. ((keto* NEXT resist*) OR nonketo*) NEAR/2 diabet* in Clinical Trials
5. (adult* OR matur* OR late OR slow or stabl*) NEAR/2 diabet* in Clinical Trials
6. (insulin* NEXT defic* NEAR relativ*) in Clinical Trials

(*Continued*)

7. (plurimetabolic NEXT syndrom*) in Clinical Trials
8. (blood NEAR/2 glucos* OR blood NEAR/2 sugar*) AND (self NEXT monitor* OR selfmonitor*) in Clinical Trials
9. ((#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7) AND #8), from 2004 to 2010

(NHSEED, CDSR, DARE, HTA)

1. (glucos* OR sugar* OR insulin* OR diabet*) and (selfmonitor* OR self-monitor*), from 2004 to 2010

PsycINFO

1 (glucose or sugar).mp. or Blood sugar/ (7319)
2 Self monitor*.mp. or Self monitoring/ (3801)
3 1 and 2 (98)
4 limit 3 to yr="2004 -Current" (54)

Current Controlled Trials

1. (monitoring) AND (glucose OR sugar) AND (diabetes OR diabetic)
2. (self) AND (monitoring) AND (glucose OR sugar) AND (diabetes OR diabetic)
3. (self-monitoring) AND (glucose OR sugar) AND (diabetes OR diabetic)
4. (self monitoring) AND (glucose OR sugar) AND (diabetes OR diabetic)

Appendix 2. Baseline characteristics of included studies

Characteristic ▸ Study ID ▾	Participating population	Male (%)	Female (%)	Age (years)	HbA1c (%)	Body mass index (kg/m^2)	Diabetes duration (years)	Duration of intervention (weeks)	Duration of follow-up (weeks)
Allen 1990	SMUG	100	0	57.9 ± 10.7	11.7 ± 3.0	-	9.0 ± 10.3	26	26
	SMBG	100	0	58.2 ± 9.7	12.4 ± 3.3	-	6.8 ± 6.5	26	26
Barnett 2008	Control	51.8	47.8	55.9 ± 9.3	8.1 ± 0.84	30.3 ± 5.0	2.8 ± 4.5	27	27
	SMBG	48.2	50.5	56.1 ± 9.1	8.1 ± 0.89	30.5 ± 5.3	2.8 ± 3.7	27	27
Davidson 2005	Control	31.1	68.9	50.9 ± 11.0	8.5 ± 2.2	33.4 ± 7.0	5.8 ± 5.8	26	26
	SMBG	20.9	79.1	49.8 ± 11.2	8.4 ± 2.12	31.7 ± 6.7	5.5 ± 4.7	26	26
DiGEM trial 2007	Control	55.9	44.1	66.3 ± 10.2	7.5 ± 1.09	30.9 ± 6.1	3 (2 to 6)	52	52
	SMBG less intensive	58.7	41.3	65.2 ± 10.6	7.4 ± 1.02	31.9 ± 6.2	3 (2 to 7)	52	52

(*Continued*)

	SMBG more intensive	57.6	42.4	65.6 ± 9.9	7.5 ± 1.12	31.0 ± 5.3	3 (2 to 6)	52	52
Durán 2010	Control	46.8	53.2	64.7 ± 9.6	6.7 ± 0.54	29.8 ± 5.1	0	52	52
	SMBG	45.5	54.5	62.5 ± 10.4	6.7 ± 0.17	30.1 ± 5.2	0	52	52
Franciosi 2011	Control	87.5	12.5	48.7± 0.6	7.9 ± 0.6	30.2 ± 3.9	3.2 ± 4.4	26	26
	SMBG	69.6	30.4	48.9 ± 0.5	7.9 ± 0.6	31.8 ±4.8	3.4 ± 3.5	26	26
Fontbonne 1989	Control	58.8	41.2	56.3 ± 9.1	8.2 ± 2.5	27.0 ± 4.1	12.7 ± 0.8	26	26
	SMUG	72.2	27.8	54.9 ± 10.2	8.6 ± 2.5	26.0 ± 3.4	13.3 ± 6.8	26	26
	SMBG	52.9	47.1	54.5 ± 10.7	8.2 ± 2.5	27.1 ± 4.1	12.2 ± 6.6	26	26
Guerci 2003	Control	56.6	43.4	62.2 ± 9.1	8.9 ± 1.3	29.7 ± 4.8	8.4 ± 6.6	24	26
	SMBG	53.7	46.3	60.9 ± 9.4	9.0 ± 1.3	30.4 ± 6.1	7.7 ± 6.3	24	26
Kleefstra 2010	Control	72.2	27.8	58.7 ± 7.8	7.7 ± 0.4	32.7 ± 5.8	8.0 (3.8 to 11.3)	52	52
	SMBG	54.5	45.5	59.5 ± 8.0	7.6 ± 0.5	29.0 ± 4.6	5.0 (4.0 to 7.0)	52	52
Much-more 1994	Control	45.5	54.5	60.1 ± 7.3	10.5 ± 1.5	33.3 ± 4.3	5.2 ± 4.6	28	44
	SMBG	33.3	66.7	57.3 ± 8.0	10.3 ± 1.1	35.1 ± 4.8	5.7 ± 4.8	28	44
O'Kane 2008	Control	63.6	36.4	60.9 ± 11.5	8.6 ± 2.3	32.0 ± 6.2	0	52	52
	SMBG	57.3	42.7	57.7 ± 11.0	8.8 ± 2.1	34.0 ± 7.0	0	52	52
SMBG study group	Control	51.8	48.2	60.5 ± 6.6	8.4 ± 0.75	31.9 ± 5.5	5.2 ± 3.9	26	52

(*Continued*)

2002									
	SMBG	52.2	47.8	58.7 ± 7.6	8.5 ± 0.86	31.0 ± 4.6	5.5 ± 4.8	26	52

Footnotes
values are displayed as mean (SD), median (q1 to q3) or proportion of patients
"-" denotes not reported
SMBG = self-monitoring of blood glucose; SMUG = self-monitoring of urine glucose

Appendix 3. Overview of trial SMBG education programmes

Characteristic ▸ Study ID ▾	Intervention	(SMBG) instructions	SMBG frequency	Feedback on SMBG	Education	Diaries
Allen 1990	SMUG	Patients were individually instructed in the prescribed testing technique, which they practised for 7 to 10 days	A measurement before each meal every other day	Ongoing feedback by physician	Dietary instructions based on weight and activity level and focused on increasing fiber intake by a dietician; Instruction booklet including ADA's exchange list for food fiber classification	Food and exercise diaries
	SMBG					
Barnett 2008	Control	No self-monitoring			All randomised patients received diet and lifestyle advice, reinforced at each clinic visit;	None
	SMBG	Instructions included information on how to use, check the glucose metre, when to take measurements and what to do in the event of hypoglycaemia	5 measurements a day (before every meal, 2h after the main meal and before bedtime) on 2 days a week (one working day, one non-working day). Once a month 3 postprandial	No information available	All randomised patients received diet and lifestyle advice, reinforced at each clinic visit; Written Information on the management of hypoglycaemia; blood	Hypoglycaemia and food diary

(*Continued*)

			measurements are asked		glucose	
Davidson 2005	Control	No self-monitoring			5 dietician visits and nutritional counselling using glucose values and meal descriptions on the effects of meal components and portion sizes on rise in postprandial glucose levels	Food diary
	SMBG	No information available	6 measurements a day around meals (pre- and 2h post prandial) for 6 days a week	The nurse used SMBG values to make therapeutic decisions following detailed algorithms		
DiGEM trial 2007	Control	No self-monitoring			Behaviour change techniques based applied using a goal setting and review approach and discussed within the framework of the commonsense model of illness representation. Continued at follow-up visits	Self-care goals and strategies; activity;
	Less intensive SMBG		2 days a week, 3 tests daily (1 after fasting, 2 before meal or 2 hours after meal)	Instruction to aim for 4-6mmol/l fasting and 6-8 mmol/l after meals. Results were interpreted by the study nurse at follow-up		Self-care goals and strategies; activity; blood glucose results;
	More intensive SMBG		2 days a week, 3 tests daily (1 after fasting, 2 before meal or 2 hours after meal)	Training and ongoing support in interpreting and applying the results of blood glucose readings to enhance motivation and maintain adherence to diet physical activity and medication regimens		
Durán 2010	Control	No self-monitoring			Lifestyle interventions based on a 2h individual session, reinforced at each follow-up visit	None

(*Continued*)

	SMBG	1h session with information how to perform measurements and how to collect data	6 measurements a day around meals (pre- and 2h post prandial) and after change in medication, every 3 days	Reviewing of know-how and evaluation of possible confounding factors on recorded glucose values		
Franciosi 2011	Control	No self-monitoring			Standard counselling with focus on diet and lifestyle, every 3 months	
	SMBG	Specific education how to perform SMBG	2 weekly, pre-and 2h post prandial measurements around one main meal (1st day breakfast, 3rd day lunch, 5th day dinner)	Structured telephone interviews every month discussing relations for elevated glucose values and quality/ quantity of foods and exercise	Standardized specific education addressing how to perform SMBG, ho to modify diet an level of physical activity according to blood glucose levels and the actions to undertake in case of abnormal values. Povided by diabetes nurses	Food, blood glucose and physical activity diary
Fontbonne 1989	Control				No education, except for (renewal of) personalized dietary recommendations	
	SMUG	Instructions how to perform SMUG	Twice every other day, fasting and 2 hours after the evening meal, with an extra test 2 hours after lunch on Sundays	Ongoing feedback by physician		Glucose diaries
	SMBG	Instructions how to perform SMBG	Twice every other day, on the first urine voided in the morning and the first urine voided after the evening			

(*Continued*)

			meal, with an extra test after lunch on Sundays			
Guerci 2003	Control				Education on weight loss and physical activity	
	SMBG	Patients received specific initial training in SMBG given by their general practitioner	At least 6 measurements a week on 3 different days of the week, including weekends	Ongoing feedback at each consultation		
Kleefstra 2010	Control	Explicit request not to self-monitor during the study			No education	
	SMBG	Information on how to handle the device and target glucose values were provided	4 measurements a day (1 fasting, 3postprandial), twice a week on a weekday and a weekend day	No information available		Glucose diaries;
Muchmore 1994	Control	No self-monitoring			8-weeks behavioral weight control program before onset of the intervention; individual counselling by diabetes nurse educator and individual sessions with a dietician at baseline and at follow-up. From baseline, sessions on general principles of diabetes nutrition according to ADA guidelines	
	SMBG	SMBG training by diabetes nurse	6 measurements a day (pre- and	No information available	8-weeks behavioral weight	Food, carbohydrate and blood

(*Continued*)

		educator given in individual and group sessions	2h postprandially) for 4 weeks. Subsequently, 2 measurements a day (pre- and 2h postprandially) for 16 weeks		control program before onset of the intervention; individual counselling by diabetes nurse educator and individual sessions with a dietician at baseline and at follow-up. From baseline individual and group teaching on carbohydrate counting	glucose diary
O'Kane 2008	Control	No self-monitoring			Structured education programme involving diabetes nurse practitioners, dieticians, podiatrists and medical staff	None
	SMBG	Instructions in the use of a glucose monitor	Four fasting and 4 postprandial measurements per week	Ongoing advice and support in interpretation of and response to glucose measurements		
SMBG study group 2002	Control	No self-monitoring			Non-standardized counselling focused on diet and lifestyle	
	SMBG	Instructions in self-monitoring and a request to continue of using the glucose meter during the follow-up period	6 measurements a day around meals (pre- and 2h post prandial) for 2 days a week (one weekday and a Sunday)	No information available	SMBG education and predefined counselling algorithm on self-perception, self-reflection and self regulation	Combined food, well-being and glucose diary

Footnotes
SMBG = self-monitoring of blood glucose; SMUG = self-monitoring of urine glucose

Appendix 4. Effects of SMBG in patients with type 2 diabetes who are not using insulin (biochemical outcomes)

Characteristic ▸ Study ID ▾	Intervention	Included patients (n)	Baseline HbA1c (%)	6 months HbA1c (%)	12 months HbA1c (%)	6 months change in HbA1c (%)	12 months change in HbA1c (%)	Baseline FPG (mmol/L)	6 months FPG (mmol/L)	6 months change in FPG (mmol/L)	Patients reporting hypoglycaemic events (%)
Allen 1990	SMUG	27	11.7 ± 3.0	9.7 ± 2.6		-2.0 ± 2.4		12.0 ± 2.6	10.5 ± 3.0	-1.5 ± 2.8	
	SMBG	27	12.4 ± 3.3	10.4 ± 2.9		-2.0 ± 3.4		12.0 ± 2.4	10.6 ± 3.6	-1.4 ± 3.2	
Barnett 2008	Control	299	8.1 ± 0.84	7.2 ± 1.22		-0.9 ± 1.29		9.0 ± 2.5	8.0	-1.0 ± 2.5	7
	SMBG	311	8.1 ± 0.89	7.0 ± 0.97		-1.2 ± 1.14 *		8.9 ± 2.3	7.6	-1.3 ± 2.5	8.7
Davidson 2005	Control	45	8.5 ± 2.2	7.9 ± 1.5		-0.6 ± 2.1					
	SMBG	43	8.4 ± 2.12	7.5 ± 1.55		-0.8 ± 1.6					
DiGEM trial 2007	Control	152	7.5 ± 1.09	7.4 ± 1.00	7.5 ± 1.20	-0.1 ± 0.73	0.0 ± 1.02				9.2
	less intensive SMBG	150	7.4 ± 1.02	7.3 ± 1.02	7.3 ± 0.88	-0.1 ± 0.84	-0.1 ± 0.82				22
	more intensive SMBG	151	7.5 ± 1.12	7.3 ± 1.0	7.4 ± 1.05	-0.2 ± 0.79	-0.2 ± 0.73				28.5
Durán 2010	Control	62	6.7 ± 0.54	6.8 ± 0.84	6.8 ± 0.52	0.1 ± 0.37	-0.1 ± 0.60				-
	SMBG	99	6.7 ± 0.17	6.1 ± 0.43	6.1 ± 0.52	-0.7 ± 0.45 *	-0.6 ± 0.52 *				-
Franciosi 2011	Control	16	7.9 ± 0.6	7.2 ± 0.8		0.7 ± 0.2					0

(*Continued*)

	SMBG	46	7.9 ± 0.6	6.7 ± 0.7		1.2 ± 0.1 *				0
Font-bonne 1989	Control	68	8.2 ± 2.5	7.7		-0.5 ± 1.5				
	SMUG	72	8.6 ± 2.5	8.5		-0.1 ± 2.2				
	SMBG	68	8.2 ± 2.5	7.8		-0.4 ± 3.1				
Guerci 2003	Control	344	8.9 ± 1.3	8.4 ± 1.4		-0.5 ± 1.5		7.5 ± 4.8	6.9 ± 4.6	-0.6	5.2
	SMBG	345	9.0 ± 1.3	8.1 ± 1.6		-0.9 ± 1.5 *		7.2 ± 5.1	6.7 ± 4.8	-0.5	10.4
Kleefstra 2010	Control	18	7.7 ± 0.4	7.7 ± 0.6	7.5 ± 0.5	0.07 ± 0.75	-0.1 ± 0.8				
	SMBG	22	7.6 ± 0.5	7.4 ± 0.7	7.5 ± 0.8	-0.2 ± 0.67	-0.1 ± 0.9				
Much-more 1994	Control	11	10.5 ± 1.5	9.6 ± 2.09		-0.9 ± 1.87					
	SMBG	12	10.3 ± 1.1	8.8 ± 1.7		-1.5 ± 1.46					
O'Kane 2008	Control	88	8.6 ± 2.3	7.0 ± 1.1	6.9 ± 1.2	-1.6 ± 2.08	-1.7 ± 2.11				-
	SMBG	96	8.8 ± 2.1	7.0 ± 0.9	6.9 ± 0.8	-1.8 ± 2.1	-1.9 ± 2.06				-
SMBG study group 2002	Control	110	8.4 ± 0.75	7.8 ± 1.52		-0.5 ± 1.4					
	SMBG	113	8.5 ± 0.86	7.5 ± 1.27		-1.0 ± 1.1*					

Footnotes
* statistically significant difference between groups (P < 0.05)
"-" denotes not reported
FPG: fasting plasma glucose; HbA1c: glycosylated haemoglobin A1c; SMBG: self-monitoring of blood glucose; SMUG: self-moni-

(*Continued*)

toring of urine glucose

Appendix 5. Effects of SMBG in patients with type 2 diabetes who are not using insulin (other outcomes)

									Within group differences		Between group differences[3]	
Outcome	**Study ID**	**Intervention**	**N**	**Measure**	**Subscales**	**Range**	**Baseline[1]**	**End of study[1]**	**Difference[2]**	**P value**	**Intervention vs control**	**P value between groups[4]**
Quality of life	Di-GEM trial 2007	Control	152	EQ5D		0 to 1	0.799 ± 0.023	0.798 ± 0.034	-0.001 (-0.060 to 0.059)			
		Less intensive SMBG	150			0 to 1	0.781 ± 0.022	0.755 ± 0.024	-0.027 (-0.069 to 0.015)		-0.029 (-0.084 to 0.025)	
		More intensive SMBG	151			0 to 1	0.807 ± 0.024	0.733 ± 0.024	-0.075 (-0.119 to -0.031)		-0.072 (-0.127 to 0.017)	
	Kleefstra 2010	Control	18	SF-36	Physical component	0 to 100	48.5 ± 10.6	47.9 ± 7.9				
					Mental component	0 to 100	50.6 ± 10.6	51.6 ± 7.7				
					Health change	0 to 100	46.9 ± 18.0	56.3 ± 11.2			-12.0 (-20.9 to -3.1)	> 0.01
		SMBG	22		Physical component	0 to 100	42.2 ± 10.4	44.3 ± 9.8			-0.0 (-5.2 to 5.1)	

(*Continued*)

					Mental component	0 to 100	55.5 ± 7.4	53.1 ± 9.5			-1.4 (-6.6 to 3.7)	
					Health change	0 to 100	48.6 ± 10.4	44.4 ± 13.7				
	Muchmore 1994	Control	11	DQOL	Satisfaction		3.0	2.7		< 0.05		
					Impact		3.9	3.9				
					Worry-social/ vocational		4.3	4.6				
					Worry diabetes related		4.1	4.5				
		SMBG	12		Satisfaction		3.1	2.7		< 0.05		
					Impact		4.0	4.1				
					Worry-social/ vocational		4.6	4.6				
					Worry diabetes related		4.0	4.6				
Well-being	DiGEM trial 2007	Control	113	WBQ-12	Total well-being	0 to 36	25.1 ± 6.3	25.9 ± 5.8				
					Negative well-being	0 to 12	1.5 ± 2.1	1.3 ± 2.0				
					Energy	0 to 12	6.5 ± 2.9	6.8 ± 2.6				

(*Continued*)

					Positive well-being	0 to 12	7.6 ± 3.2	8.3 ± 2.8				
		Less intensive SMBG	121		Total well-being	0 to 36	24.3 ± 6.8	24.5 ± 7.0				0.38
					Negative well-being	0 to 12	1.6 ± 2.3	1.4 ± 2.2				0.92
					Energy	0 to 12	6.3 ± 2.9	6.4 ± 2.9				0.73
					Positive well-being	0 to 12	7.6 ± 3.2	7.6 ± 3.4				0.20
		More intensive SMBG	105		Total well-being	0 to 36	25.2 ± 6.3	24.9 ± 6.4				0.38
					Negative well-being	0 to 12	1.4 ± 2.2	1.4 ± 2.2				0.92
					Energy	0 to 12	6.6 ± 2.8	6.7 ± 2.7				0.73
					Positive well-being	0 to 12	7.9 ± 3.0	7.6 ± 3.0				0.20
	Kleefstra 2010	Control	18	WHO-5	Total score	0 to 100	71.0 ± 17.9	76.3 ± 11.4				
		SMBG	22		Total score	0 to 100	68.0 ± 20.7	74.4 ± 14.5			-0.6 (-8.2 to 7.0)	
	O'Kane 2008	Control	88	WBQ-22	Depression	0 to 100	-	-				
					Anxiety	0 to 100	-	-				

(*Continued*)

					Positive well-being	0 to 100	-	-				
					Energy	0 to 100	-	-				
		SMBG	96		Depression	0 to 100	-	-			6.05 (2.37)	0.01
					Anxiety	0 to 100	-	-			5.86 (3.19)	0.07
					Positive well-being	0 to 100	-	-			4.16 (2.88)	0.15
					Energy	0 to 100	-	-			-0.84 (2.83)	0.77
	SMBG study group 2002	Control	110	WBQ-22	Total well-being	0 to 66	50.66 ± 9.46	52.55 ± 10.47	1.75 ± 7.33			
					Depression	0 to 18	3.33 ± 2.73	3.01 ± 2.61	-0.26 ± 2.23			
					Anxiety	0 to 18	4.88 ± 3.37	4.34 ± 3.66	-0.51 ± 3.26			
					Energy	0 to 12	8.17 ± 2.42	9.0 ± 2.45	0.81 ± 2.61			
					Positive well-being	0 to 12	14.6 ± 3.14	14.91 ± 3.38	0.27 ± 2.85			
		SMBG	113		Total well-being	0 to 66	50.52 ± 8.47	54.03 ± 8.24	3.58 ± 7.01			0.05
					Depression	0 to 18	3.18 ± 2.69	2.38 ± 2.26	-0.83 ± 2.66			0.03
					Anxiety	0 to 18	5.24 ± 3.24	3.91 ± 3.0	-1.35 ± 3.34			> 0.05
					Energy	0 to 12	7.91 ± 2.5	9.04 ± 2.19	1.13 ± 2.29			> 0.05

(*Continued*)

					Positive well-being	0 to 12	1481 ± 2.83	15.27 ± 2.8	0.49 ± 2.37			> 0.05
Patient satisfaction	Di-GEM trial 2007	Control	113	DTSQ	Total satisfaction	0 to 36	29.3 ± 6.8	30.0 ± 5.3				
					Perceived hyperglycaemia frequency	0 to 6	1.7 ± 1.7	1.9 ± 1.9				
					Perceived hypoglycaemia frequency	0 to 6	0.6 ± 1.2	0.7 ± 1.3				
		Less intensive SMBG	121		Total satisfaction	0 to 36	29.4 ± 6.5	29.7 ± 5.6				0.93
					Perceived hyperglycaemia frequency	0 to 6	1.5 ± 1.6	2.3 ± 1.5				0.05
					Perceived hypoglycaemia frequency	0 to 6	0.7 ± 1.3	0.7 ± 1.2				0.97
		More intensive SMBG	105		Total satisfaction	0 to 36	29.7 ± 5.4	30.1 ± 5.5				0.93

(*Continued*)

					Perceived hyperglycaemia frequency	0 to 6	2.0 ± 1.7	2.4 ± 1.7				0.05
					Perceived hypoglycaemia frequency	0 to 6	0.8 ± 1.3	0.8 ± 1.3				0.97
	Kleefstra 2010	Control	18	DTSQ	Total satisfaction	0 to 36	30.7 ± 4.2	30.7 ± 4.0				
					Perceived hyperglycaemia frequency	0 to 6	2.6 ± 1.7	1.9 ± 1.9				
					Perceived hypoglycaemia frequency	0 to 6	0.0 (0.0, 1.0)	0.0 (0.0, 2.0)				
		SMBG	22		Total satisfaction	0 to 36	29.3 ± 4.8	32.1 ± 3.8			1.2 (-1.6 to 4.1)	
					Perceived hyperglycaemia frequency	0 to 6	2.2 ± 1.6	2.3 ± 1.9			0.5 (-0.8 to 1.8)	

(*Continued*)

					Perceived hypoglycaemia frequency	0 to 6	1.0 (0.0, 2.5)	1.0 (0.0, 2.0)			0.3 (-0.5 to 1.1)	
	O'Kane 2008	Control	88	DTSQ	Total satisfaction	0 to 36	-	-				
		SMBG	96		Total satisfaction	0 to 36	-	-				> 0.05
	SMBG study group 2002	Control	110	DTSQ	Total satisfaction	0 to 36	26.95 ± 6.61	30.57 ± 5.54	3.6 ± 7.63			
		SMBG	113		Total satisfaction	0 to 36	27.58 ± 7.13	31.1 ± 4.78	3.52 ± 7.19			0.9

Footnotes
[1] numbers are mean difference ± SD or median (Q25, Q75)
[2] numbers are mean difference (95% CI) or mean difference (SD)
[3] numbers are mean difference (95% CI) or b coefficient (SE)
[4] P value represents a three-group comparison for DiGEM trial
"-" denotes not reported
DTSQ: diabetes treatment satisfaction questionnaire; EQ5D: EuroQol-5D; DQOL: diabetes quality of life inventory; SMBG = self-monitoring of blood glucose; SMUG = self-monitoring of urine glucose; SF-36: Short-Form 36; WBQ-12/22: well-being questionnaire-12/22; WHO-5: World Health Organization-5

Appendix 6. Adverse events

Study ID ▸ Characteristic[1] ▾	Allen 1990	Barnett 2008	Davidson 2005	DiGEM trial 2007	Durán 2010	Franciosi 2011	Fontbonne 1989	Guerci 2003	Kleefstra 2010	Muchmore 1994	O'Kane 2008	SMBG study group 2002
Intervention (n)	27	311	43	301	99	46	140	345	22	12	96	113

(*Continued*)

Control (n)	27	299	45	152	62	16	68	344	18	11	88	110
Deaths (n)	-	0	0	8	0	0	-	4	0	-	0	-
Adverse events (n)	-	86	-	-	-	0	-	167	-	-	-	-
Adverse events (n / %)	-	14	-	-	-	0	-	24	-	-	-	-
Drop-outs due to adverse events (n)	-	2	-	-	-	0	-	6	-	-	-	-
Definitions of recorded hypoglycaemic episodes		• Grade 1: suspected mild hypo • Grade 2: suspected moderate hypo • Grade 3: suspected severe hypo with need of third party assistance • Grade		• Grade 1: self-reported hypo with no accompanying symptoms • Grade 2: mild symptoms requiring minor intervention • Grade 3: moderate	• Severe hypoglycaemia: requiring assistance from a third person	• (any) Hypoglycaemic episode		• Asymptor hypo: no definition available • Symptom hypo: no definition available			-	

(*Continued*)

		4: suspected severe hypo with need of medical assistance		symptoms requiring immediate third party intervention • Grade 4: unconscious								
Cut-off point for hypoglycaemic episode		Capillary blood glucose < 3mM/L		Capillary blood glucose < 4mM/L	-	Capillary blood glucose < 3.3 mM/L		Capillary blood glucose < 3mM/L			-	
Hypoglycaemic episodes (n)	-	117	-	90	-	0	-	78	-	-	67	-
Hypoglycaemic episodes (%)	-	19	-	20	-	0	-	11	-	-	37	-
Severe hypoglycaemic episodes (n)	-	0	-	1	0	0	-	0	-	-	-	-
Severe hypoglycaemic episodes (%)	-	0	-	0	0	0	-	0	-	-	-	-

(*Continued*)

Nocturnal hypoglycaemic episodes (n)	-	10	-	-	-	-	-	-	-	-	-	-
Nocturnal hypoglycaemic episodes (%)	-	2	-	-	-	-	-	-	-	-	-	-

Footnotes
"-" denotes not reported
[1] Data for adverse events could not be extracted separately for intervention and control groups

FEEDBACK

Comment to the review by Welschen

Summary

Welschen reports some conclusions and implications for the practice that do not seem to be closely and accurately based in the results of the review.
The conclusions of Welschen are: …self-monitoring of blood glucose (SMBG) might be effective in improving glycaemic control in patients with type 2 diabetes who are not using insulin.……by using SMBG, patients can achieve a more individual management of their disease and thereby a better quality of life and this might result in a decrease in consultations with the general practitioner.
In my opinion, it is unclear on what results is Welschen based to write these conclusions. In fact, after reading the results I believe the conclusions should have been neutral or even the opposite ones. In Results Welschen wrote:
- The studies of Allen 1990 and Davidson 2005 [no efficacy of SMBG] were considered of high quality… The studies of Fontbonne 1989, Muchmore 1994 ……and Schwedes 2002 and Guerci 2003 [the only two trials reporting efficacy of the SMBG] …were considered to be of low quality.
- Heterogeneity... Because of differences in baseline data of the patients and type of interventions between the studies, it was not possible to perform either a meta-analysis and/or subgroup or sensitivity analyses.
- Glycaemic control measured by HbA1c… Fontbonne 1989, Muchmore 1994 and Davidson 2005 [the only one blinded and with a high quality score] found no statistically significant differences in the decrease of HbA1c between the SMBG and the control groups…

Schwedes 2002 [low quality] found a statistically significant difference of 0.5% in HbA1c in favour of SMBG…Guerci 2003 [low quality] also found a statistically significant difference of 0.4% in HbA1c at the end of the study between the SMBG and control group.
- We considered that the SMBG group in Schwedes 2002 did receive a co-intervention by means of a structured counseling program every four weeks during the intervention period. The control group only received a non-standardised counseling [see results]……. However, because this was considered as a co-intervention, the effect of SMBG only is not clear [see Discussion].
- Guerci 2003 reported a dropout rate of more than 40% [48% in the intervention group], which was considered non-acceptable.
- In addition, there is no evidence that SMBG has a beneficial effect on fasting plasma glucose, quality of life, well-being, patient satisfaction and number of hypoglycaemic episodes.
In medical statistics the presumption of efficacy does not exist, but it is the opposite. It starts with the null hypothesis (there are not significant differences between an intervention [SMBG] versus other [blood glycated haemoglobin every 2-4 months]) and clinical trials are performed to try to pull the null hypothesis down.
Welschen has failed to achieve it in her review. Her conclusions on the efficiency of the self-monitoring are based on two studies that herself has almost rejected before for deficient quality: one because a co-intervention in favour of the group of self-monitoring (risk of attrition bias), and the second because a clinical trial where the drop-outs and withdrawals rise up to 48 % of the participants loses the benefit of the randomisation, of the sample size, set doubts about the internal validity and more obvious doubts about the external validity (the applicability to the general population) of the results.
None of these inconveniences have been reported in the conclusions.
1. Coster S. Monitoring blood glucose control in diabetes mellitus: a systematic review. NHS R&D HTA Programme. Health Technology Assessment. 2000;4(12).

Reply

In our review, we tried to assess the effects of self-monitoring of blood glucose (SMBG) in patients with type 2 diabetes who are not using insulin in order to eliminate the debate on the effectiveness of SMBG as a tool in the self-management of these patients.
Sáenz comment was that our conclusions were not based on accurate results. We respectfully disagree with Sáenz and we will argue below that we still stick to the conclusion from our review that SMBG might improve glycaemic control.
The review of Coster 2000 (1) cannot be used as an adequate summary of the evidence for the effect of SMBG by health care professionals, as was suggested by Sáenz, because it is out-dated and because of the inclusion of a trial with patients using insulin (Wing 1986).
Our review included all randomised controlled trials until September 2004 (2).
The direction of the effect of the combined studies is clearly in favour of SMBG and definitely not the opposite as Sáenz stated. The absence of a statistical significant effect should not be interpret as evidence of no effect (3). Moreover, since the largest studies included in our review found statistically significant differences suggests that the other smaller studies possibly did not include enough patients.
In our review we reported clearly that the evidence for an effect of SMBG on HbA1c was moderate, based on the overall methodological quality of the trials. In addition, in our methods section it was described that we did not intend to exclude trials on the basis of methodological quality criteria as suggested by Sáenz. In our discussion section, we explicitly described all methodological issues that should be taken into account before reading definitive conclusions.
We concluded that SMBG might be effective which in our opinion implies that the conclusions should be interpreted with caution. Because of the remaining uncertainty we also recommend a high quality randomised controlled trial to provide more solid evidence of the effect of SMBG on a large range of outcomes. We believe that, apart from glycaemic control, quality of life, well-being and patient satisfaction are all very important outcome measures. Unfortunately, these outcome measures where not measured in most of the studies and therefore we could not draw conclusions on these important outcomes.
With respect to our review, we conclude that we paid sufficient attention to all the limitations in the available evidence in our review. In our view it is too early to reject a potentially helpful tool for patients with diabetes who need to incorporate their chronic disease into their daily lives.
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Comments to the review by Malanda et al, 6 March 2012

Summary

In the review, the authors conclude that "the overall effect of self-monitoring of blood glucose on glycaemic control in patients with type 2 diabetes who are not using insulin is small up to six months after initiation and subsides after 12 months" [1]. For the meta-analysis on the effects of SMBG vs. control in patients with a diabetes duration greater than one year, nine studies with a six months follow-up (2324 patients) were included. For the corresponding 12 months follow-up, two of the 9 studies (493 patients) were included. The HbA1c reduction of -0.3% (-0.4 to -0.1) at six months [1] was statistically significant and in view of UKPDS, in which a 1% reduction in HbA1c was associated with a 37% decrease in risk for microvascular complications and a 21% decrease in the risk of any end point or death related to diabetes [2], a statistically significant reduction of HbA1c 0.3% at six months should be recognized and valued for the treatment of type 2 diabetes. We feel it is a limitation of the analysis that only two studies, DiGEM trial and ZODIAC-17 [3,4], were included in the 12 month follow-up meta-analysis. In the analysis a non-significant decrease in HbA1c (-0.13% (-0.13 to -0.04)) was reported. Both studies, furthermore, are characterized by several limitations, which need to be considered: In the DiGEM trial, HbA1c values of the patients in the three different groups ranged from 7.41% to 7.53%. Inclusion of patients with a stable and relatively good metabolic control at entry into the study may have attenuated the need for a modification or intensification of treatment within any of the three groups. In the study, therefore, the usage of oral antidiabetic agents (OADs) was increased only in less than one-third of the patients. In both the less intensive and the more intensive intervention groups, OADs were not increased more frequently as compared with the control group (29% and 32% vs 30%). No specific algorithm for modification of treatment plans was mentioned. It is also noteworthy, that the enrolled patients were a highly selected population (453 patients out of 2986 total eligible ones) [5]. ZODIAC-17 is a small Dutch study, in which only 22 patients were included in the SMBG group, of whom 17 performed at least 80% of the requested glucose measurements. The authors of the study mention in the discussion the sample size as an important limitation of the study. In the study, structured testing of blood glucose was not applied and any information on modification of treatment is missing [3]. We, therefore, would like to point out that due to the limitations of the two studies the conclusions given in the Cochrane analysis for the 12 months follow-up are not warranted. The fact that recent prospective and randomized studies which demonstrated benefits of structured self-monitoring of blood glucose approaches in non-insulin treated type 2 diabetes mellitus, e.g. STeP-study, St. Carlos study and ROSES [6-8], report significant outcome results opposite to your meta-analysis, further limits your conclusions.

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Reply

In our review[1], we explored whether newer trials with possible good or improved methodological quality and design, published after Welschen et al.[2] would provide new evidence of the effects of self-monitoring of blood glucose on glycaemic control in patients with type 2 diabetes mellitus who are not using insulin.

We thank Schnell et al. for their comments regarding the clinical relevance of a 0.3% reduction in HbA1c after six months of self blood glucose monitoring and the limited amount of available evidence for longer-term effects in patients with longer duration of diabetes.

In our discussion we have acknowledged that the reduction in HbA1c of 0.3% observed in the subgroup of patients with diabetes duration of at least one-year and a six month follow-up is statistically significant. Indeed, in the UKPDS the observed difference of 7.9% and 7.0 % between the control and the intervention groups was associated with considerably reduced morbidity and mortality. Since then, a reduction of 0.5% had generally been accepted to be of clinical relevance[3] and most included and more recent trials have based their power on this[4–7]. These expected effects were not achieved, and compared to the expectations, a reduction of 0.3% is relatively small.

We agree that from a public health perspective, small reductions might have an important role - however, under the condition that these are achieved at a large scale and at low cost. For SMBG so far, this is not the case[3;8].

With respect to the limited number of longer-term studies, we like to stress that our review was performed under the stringent conditions of the Cochrane Collaboration. Therefore, an extensive assessment of risk of bias was performed following previously determined guidelines. Both the DiGEM trial and ZODIAC-17[4;9] were assessed with low risk of bias on most domains, indicating proper internal validity.

Both trials assessed and compared SMBG effects with patients not using SMBG in an existing usual diabetes care structure and with oral glycaemic titration schedules in line with the national diabetes guidelines at the time the study was performed[9;10].

The subgroup under critique was a-priori defined, was designed to limit clinical heterogeneity and met the widely acknowledged GRADE working group criteria[11]. The results from the 12-months analysis show an estimate of the effect comparable to the estimate found in the 12 months analysis ([-0.4 to -0.1] vs. [-0.3 to 0.04]) indicating a similar precision in effect. Further, a best-evidence synthesis would have shown a similar non-significant direction in effect.

Summarized, we stress that the 12-months analysis is correctly performed, that included studies met the highest criteria for inclusion and thus results are valid.

We agree that patients in the specific subgroup were moderately controlled (range 7.4% to 7.7%) and therefore potentially less susceptive to benefit from SMBG. However, this was according to the predefined cut points. Furthermore, in a recent published individual patient data meta-analysis[12] the effects of SMBG did not differ between groups with different levels of baseline entry HbA1c.

All studies that were mentioned to demonstrate benefits of structured SMBG were indeed included in our review and taken up in the appropriate subgroup analyses, except for the STeP study[5]. This study did not comply with our inclusion criteria having a control-group with access to self-monitoring. The ROSES-study[7] is included in the subgroup of patients with a diabetes duration of one year and a follow-up of six months; the St. Carlos study[13] is taken up in the subgroup of newly diagnosed patients with a follow-up of six and 12 months. Conclusions resulting from these subgroup analyses are not comparable with the conclusion of the subgroup under critique and therefore do not limit our analysis.

Thus, though we acknowledge the amount of available evidence for longer-term effect in patients with diabetes duration of over one year is limited, predefined protocols were followed leading to the inclusion of good quality studies.

At the present state of evidence, we feel our conclusions are justified. Of course, in future studies, with more innovative interventions, extended behavioural strategies or in additional subgroups, SMBG may be proven beneficial on the long-term. Still, these future studies have to prove cost-effectiveness. As we stated in our discussion: translation into practice of the presented results is difficult, and should be done with caution.

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Submitter agrees with default conflict of interest statement: I certify that I have no affiliations with or involvement in any organization or entity with a financial interest in the subject matter of my feedback.

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Uriëll Malanda on behalf of the authors.

WHAT'S NEW

Last assessed as up-to-date: 7 July 2011.

Date	Event	Description
5 April 2012	Feedback has been incorporated	New feedback received on 6 March 2012, authors replied on 12 March 2012

HISTORY

Protocol first published: Issue 4, 2004

Review first published: Issue 2, 2005

Date	Event	Description
8 December 2011	New search has been performed	Updated with six new trials (Barnett 2008; DiGEM trial 2007; Durán 2010; Franciosi 2011; Kleefstra 2010; O'Kane 2008)
8 December 2011	New citation required and conclusions have changed	Conclusions were changed.
20 October 2010	New search has been performed	Review has been updated with 5 new trials. Conclusions have been changed. Four authors have left the team and three others have joined
1 January 2009	Amended	Uriëll Malanda, Sandra Bot and Ingrid Riphagen has joined the review team Evelien Bloemendal, Robert Jan Heine, Wim Stalman and Lex Bouter have left the team Uriëll Malanda is the new contact person: u.malanda@vumc.nl

CONTRIBUTIONS OF AUTHORS

URILL MALANDA: wrote the draft of this review that was commented on and discussed by LAURA WELSCHEN, INGRID RIPHAGEN, GIEL NIJPELS, JACQUELINE DEKKER and SANDRA BOT.

INGRID RIPHAGEN: performed the searches.

URILL MALANDA and LAURA WELSCHEN: independently inspected the titles and abstracts of the references identified to evaluate their potential eligibility.

URILL MALANDA and LAURA WELSCHEN: independently assessed the risk of bias of the relevant trials and performed data extraction and data entry.

URILL MALANDA, LAURA WELSCHEN, INGRID RIPHAGEN, JACQUELINE DEKKER, GIEL NIJPELS and SANDRA BOT: interpreted the findings and helped writing the final manuscript.

DECLARATIONS OF INTEREST

URILL MALANDA, JACQUELINE DEKKER, GIEL NIJPELS and SANDRA BOT all take part in an ongoing study on the topic of interest of this review.

SOURCES OF SUPPORT

Internal sources

- EMGO Institute for Health and Care Research, Netherlands.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

This section relates to the differences between the first review (Welschen 2005a) and the present review-update (Malanda 2011).

1. Four authors have left the team and three others have joined.

2. Because HbA_{1c} reflects a more constant view of glycaemic control over time, we believe that changes in fasting plasma glucose are of less value for assessing the effect of self-monitoring of blood glucose (SMBG). We therefore assessed effects on fasting plasma glucose level as a secondary outcome whereas this was a primary outcome in the first review.

3. We have added PsycInfo to our search strategy because studies investigating the effect of SMBG on quality of life or well-being might not be published in regular medical databases.

4. The mandatory Cochrane 'Risk of Bias' tool has replaced the Amsterdam-Maastricht list.

5. Review has been updated with six new trials (Barnett 2008; DiGEM trial 2007; Durán 2010; Franciosi 2011; Kleefstra 2010; O'Kane 2008).

6. Addition of six new studies made it possible to perform pooled random-effects subgroup analyses on the basis of diabetes duration and follow-up.

7. Conclusions could be drawn on the effect of SMBG on glycaemic control for subgroups and for patient satisfaction, general well-being or general health-related quality of life.

8. Conclusions have been changed

INDEX TERMS

Medical Subject Headings (MeSH)

*Blood Glucose Self-Monitoring [methods]; Diabetes Mellitus, Type 2 [*blood; urine]; Hyperglycemia [prevention & control]; Hypoglycemic Agents [administration & dosage]; Insulin [administration & dosage]; Quality of Life; Randomized Controlled Trials as Topic

MeSH check words

Humans