# Efficacy of self-monitoring of blood glucose in patients with type 2 diabetes mellitus managed without insulin: a systematic review and meta-analysis

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# Abstract

# Background: Self-monitoring of blood glucose (SMBG) is commonly performed by patients with diabetes mellitus. There is debate surrounding the clinical utility and cost-effectiveness of SMBG in patients with type 2 diabetes who do not use insulin. We conducted a systematic review and meta-analysis to determine: 1) the effect of SMBG versus no self-monitoring; 2) the effect of patient education regarding self-interpretation and application of SMBG results; and 3) the optimal frequency of self-monitoring.

# Methods: Electronic databases, conference proceedings, and grey literature sources were searched up to March 2009 to identify randomized controlled trials (RCTs) and observational studies investigating the use of SMBG in patients not using insulin. Where appropriate, data related to clinical, surrogate, and patient-reported outcomes were pooled using random-effects meta-analysis.

# Results: SMBG was associated with a statistically significant improvement in hemoglobin A1c (weighted mean difference -0.25%, 95% CI -0.36%, -0.15%). There was no significant difference between studies that employed education for self-interpretation and application of results and those that did not. Based on limited evidence, SMBG failed to demonstrate consistent benefits in terms of quality-of-life, patient satisfaction, hypoglycemia, long-term complications of diabetes, or mortality. There was insufficient evidence pertaining to the optimal frequency of SMBG.

# Interpretation: SMBG was associated with a clinically modest, statistically significant reduction in hemoglobin A1c, regardless of whether subjects were provided with education on interpreting and using results. Further studies are required to determine whether self-monitoring reduces the risk of long-term complications of diabetes, and to identify patients most likely to benefit from SMBG.

Introduction

Diabetes mellitus is associated with serious long-term complications and premature death.1,2 In 2004/05, diabetes was diagnosed in about 5.5% (1.8 million) of Canadians aged 20 years and older.3 Type 2 diabetes accounts for approximately 90% of all diabetes cases.4 Maintaining a hemoglobin A1c (HbA1C) concentration of 7.0% or less is recommended for all patients with diabetes to reduce the risk of long-term complications.2

Self-monitoring of blood glucose (SMBG) may contribute to glycemic control by allowing for adjustments in diet, physical activity, and pharmacotherapy in response to meter readings. While the need for SMBG for patients treated with insulin is well-established,2 the utility of the practice for patients with type 2 diabetes managed without insulin is controversial.5-8 Nevertheless, SMBG use is highly prevalent in this population. In a recent study, blood glucose test strip claimants covered by the Ontario Public Drug Program who did not use insulin claimed, on average, more than 1 test strip per day.9 Apart from the economic costs, SMBG may be associated with patient discomfort and inconvenience. Hence, there is a need for evidence-based information to guide optimal use of this technology in patients with type 2 diabetes who do not use insulin.

Existing systematic reviews in this area have reported marginal advantages of SMBG in terms of HbA1C, but have not usually assessed other outcomes of interest such as hypoglycemia, long-term complications of diabetes, or quality of life.10-16 Furthermore, previous reviewers have not accounted for differences across trials in the degree to which subjects were educated on how to interpret and act upon SMBG results. This is a key limitation since users must be able to act appropriately in response to abnormal readings if SMBG is to be effective. In this article, we report the results of a systematic review and meta-analysis of a number of patient-relevant outcomes associated with the use of SMBG in patients with type 2 diabetes not treated with insulin. Detailed methods and complete results are reported elsewhere.17

Methods

***Literature Search***

Medline, Medline In-Process & Other Non-Indexed Citations, EMBASE, Biosis Previews, CINAHL and PsycINFO were searched for studies published in English from 1990 to March 2009. The search was restricted to studies published after 1990 to increase the likelihood that study conditions were reflective of current practices for managing diabetes. Parallel searches were also run in the Cochrane Library and the Centre for Reviews and Dissemination databases. The search strategy was comprised of both controlled vocabulary, such as Medical Subject Headings, and keywords. The main search concepts were ‘blood glucose test strips’ and ‘type 2 diabetes mellitus’. Additional citations were obtained through internet searching, conference proceedings, and from stakeholder feedback.

***Outcomes of interest***

This report presents results for HbA1C, hypoglycemia, health-related quality-of-life, patient satisfaction, and long-term complications of diabetes. Results for other clinical outcomes are presented elsewhere.17

***Selection Criteria***

Full-text articles and conference abstracts reporting controlled clinical trials and observational studies (i.e., cohort, case-control, time series) were selected for inclusion if they compared either SMBG versus no self-monitoring, or different frequencies of SMBG, in patients with type 2 diabetes. We excluded studies that did not report outcomes by type of diabetes or type of therapy, were of less than four weeks duration, or demonstrated substantial differences between treatment groups in terms of management practices other than SMBG.

***Quality assessment***

Two reviewers independently assessed the methodological quality of included studies using modified Scottish Intercollegiate Guideline Network-50 instruments for RCTs and cohort studies.18 Disagreements were resolved by consensus or a third reviewer.

***Data extraction***

Two reviewers independently extracted data from each included article using a form designed *a priori*.17 Disagreements were resolved by consensus or a third reviewer. Study authors were contacted in case data were missing.

***Data analysis***

Data were pooled across RCTs using random effects meta-analysis.19,20 Sensitivity analyses tested the effect of removing studies of poor quality, and those that presented pooled results for patients using oral antidiabetes agents or no pharmacotherapy. Subgroup analyses were conducted based on: provision of education regarding interpretation and application of SMBG results; medication class; SMBG frequency; SMBG duration; and patient characteristics. Heterogeneity was assessed using the I2 statistic.21 Data from observational studies were not pooled due to a high degree of methodological heterogeneity.

**Results**

***Study selection***

The literature search identified 1624 citations, of which 324 were reviewed as full text articles, and 9 RCTs and 16 observational studies were selected for inclusion (Figure 1).8,22-47

***Study characteristics and methodological quality***

Sample sizes ranged from 2834 to 68923 in the included RCTs, and from 11537 to 1278626 in the observational studies. Study duration ranged from 6 to 12 months for RCTs, and from 3 months44 to 6.5 years33 for observational studies. The frequency of SMBG in RCTs varied from one strip per week29,45 to 6 strips per day on 6 days per week8.

Four RCTs,31,36,45,47 were rated as being of good methodological quality, and four8,23,24,34 as poor quality (Appendix A). (One RCT29 was reported as an abstract and could not be assessed for quality.) Reasons for assigning ratings of poor quality were: inadequate descriptions of randomization and allocation concealment procedures; high dropout rates; and failure to conduct an intention-to-treat analysis. All included observational studies were rated as being of poor quality except for three time series studies,25,35,42 which could not be assessed for quality (Appendix B).

***Meta-analysis Results***

**Patients using oral antidiabetes drugs**

***Effect of self-monitoring on HbA1C***

Seven RCTs (N = 2,270) reported the effect of SMBG versus no self-monitoring on change in HbA1C from baseline.8,23,24,31,34,36,47 Meta-analysis yielded a statistically significant difference in HbA1C in favour of SMBG (weighted mean difference -0.25%, 95% CI -0.36% to -0.15%) (Figure 2a, Table 1). Results were similar when the analysis was restricted to good quality studies,31,36,47 or to studies in which all subjects used oral antidiabetes agents (Table 1).23,31,47

We conducted a subgroup analysis based on whether study participants were instructed on interpretation and application of results from SMBG (figure 2b). The pooled differences in HbA1C were similar regardless of whether trials implemented such an educational component (Table 1). In the Diabetes Glycaemic Education and Monitoring (DiGEM) trial, the only RCT31 that directly compared the effect of SMBG with either less intensive or more intensive education, there was no statistically significant difference in HbA1C [mean difference 0.03%, 95% CI -0.15% to 0.21%)].

Additional subgroup analyses were conducted to determine whether the HbA1C estimate was affected by differences across studies in frequency or duration of SMBG, baseline HbA1C, time of diabetes diagnosis, and type of oral antidiabetes agent used (Table 1). Results were generally similar to the overall analysis across all subgroups, although the pooled estimate across the two trials employing a SMBG frequency of more than twice daily was somewhat higher than trials testing lower frequencies. Also noteworthy is the finding that there was no statistically significant effect of SMBG on HbA1C in the only RCT that enrolled newly-diagnosed patients [mean difference -0.40%, 95% CI -0.96% to 0.16%].36

The only RCT directly comparing one SMBG frequency with another reported no significant difference in HbA1C at six months between a frequency of one per week versus four per week.45

Results from observational studies were mixed with respect to the effect of SMBG on HbA1C levels (Table 2).26,32,37,39,43,44,48 In general, mean HbA1C levels were lower in patients performing SMBG, and higher daily SMBG frequencies were associated with incremental reductions in HbA1C. However, effect sizes varied considerably across studies.

***Effect of self-monitoring on other outcomes***

The pooled relative risk of overall hypoglycemia across three RCTs23,31,47 (N=1752) reporting this outcome was significantly higher with SMBG compared with no SMBG [RR (95% CI) = 1.99 (1.37, 2.89)] (Table 3), although the rate of overall hypoglycemia was significantly lower [rate ratio (95% CI) = 0.73 (0.55, 0.98)].36,47 There were no statistically significant differences in severe or nocturnal hypoglycemia (Table 3). However, Barnett *et al* reported a statistically significant reduction in the number of symptomatic hypoglycemic events reported by patients using a sulfonylurea who were performing SMBG versus no SMBG [rate ratio (95% CI) = 0.57 (0.38, 0.85)].47

Five RCTs reported the effect of SMBG on health-related quality of life and patient satisfaction22,23,36,40,41 (Table 4). There were no statistically significant differences between SMBG and no SMBG in terms of patient scores on the Well-being Questionnaire,22,40 the Diabetes Treatment Satisfaction Questionnaire,22,24 or the overall EuroQol-5D utility score. Interestingly, quality of life measured using the EuroQol-5D was significantly lower in the arm of the DiGEM trial in which patients who were using SMBG were provided with intensive education (mean difference -0.072, 95% CI -0.127 to -0.017), due primarily to increased levels of anxiety and depression.41 However, results from two studies reporting subscale scores from the Well-being Questionnaire were conflicting with respect to the effect of SMBG on depression.36,40

Two observational studies30,33 that compared the effect of SMBG versus no self-monitoring reported mixed results for mortality. A retrospective cohort study of newly-diagnosed patients reported that SMBG was associated with significantly decreased risks for all-cause mortality and non-fatal diabetes-related events at 6.5 years.33 Conversely, a prospective cohort study of previously-diagnosed patients reported no change in all-cause mortality with SMBG at 10 years.30

**Patients not using diabetes pharmacotherapy**

One RCT31 and two observational studies26,32 compared SMBG with no SMBG in patients managed without diabetes pharmacotherapy. In the subgroup of subjects in the DiGEM trial not treated with antidiabetes agents, there were no significant differences in HbA1C between users and non-users of SMBG, regardless of whether or not users were educated to interpret SMBG results.31 In contrast, a large retrospective cohort study reported statistically significant differences in HbA1C favouring SMBG versus no testing.26 A second retrospective cohort study reported a 0.35% reduction (*p* < 0.0001) in HbA1C for every additional test strip dispensed per day in new users of SMBG, but not in patients who had used SMBG for at least 3.5 years.32

**Interpretation**

Our systematic review identified seven RCTs that compared SMBG with no self-monitoring in patients with type 2 diabetes managed without insulin. Meta-analysis of study results indicated that SMBG is associated with a statistically significant improvement in HbA1C of 0.25%, a result that is consistent with findings of previous systematic reviews.10-14,16 The clinical relevance of this effect is questionable in light of published minimal clinically important differences in HbA1C.49,50 For patients who were not using diabetes pharmacotherapy, the improvement in HbA1C was even smaller and statistically non-significant.

Data from observational studies were not pooled due to the presence of substantial methodological variation. Compared with evidence from RCTs, the greater likelihood of selection bias in observational studies and the inability to adjust fully for the effect of confounders rendered it difficult to isolate the effects of SMBG on glycemic control.

This review also examined whether SMBG is more effective when used in conjunction with patient education regarding the interpretation of results and appropriate responses.11,15,51 We found that results from studies that provided such education were similar to those that did not. Our findings are consistent with the results of the DiGEM trial, which also reported no significant difference in glycemic control between patients instructed in self-interpretation and those who were directed to have a health professional interpret SMBG results.31 These results appear to indicate that SMBG offers little benefit regardless of whether education is also provided. However, the failure to observe an added benefit of patient education could also be related to study factors such as poor compliance with the study protocol, or the lack of a specific algorithm for patients and clinicians to use SMBG results to make therapeutic decisions.

According to the *Diabetes in Canada Evaluation* study, the average HbA1C of patients with type 2 diabetes in Canada is 7.5%, and only 20% of patients have a HbA1C in excess of 8.5%.52 Six of the seven RCTs included in our meta-analysis enrolled patients with mean baseline HbA1C ranging from 8.1% to 10.5%. Therefore, our results may be more applicable to patients with poorly controlled diabetes. The DiGEM study, the only RCT that included subjects with a baseline HbA1C less than 8.0%, reported a statistically non-significant benefit of SMBG.31

Improvements in quality of life due to SMBG are typically attributed to a greater level of self-efficacy and control,53,54 while pain, discomfort, and inconvenience associated with SMBG may reduce quality of life.53-58 In our analysis, there were no significant differences between SMBG and no SMBG in terms of overall health-related quality of life, patient satisfaction, or patient well-being, although evidence for these outcomes was sparse and analysis was complicated by the use of different scales. Analysis of sub-scales related to psychological well-being demonstrated discrepant findings across studies with respect to the effect of SMBG on anxiety and depression, The available data on the effects of SMBG on quality of life and patient satisfaction are thus inconclusive. Further studies employing standardized instruments are required to determine the benefits, if any, of SMBG on these outcomes.

The relative risks for severe and nocturnal hypoglycemia were not significantly affected by SMBG, but the risk of overall hypoglycemia was significantly higher with SMBG. This may have been due to greater detection of asymptomatic hypoglycemia10,14,23,47. Interestingly, the number of events of overall hypoglycemia was significantly lower with SMBG. The reason for this apparently counter-intuitive result is unclear, although it may be that increased detection of hypoglycemia with SMBG soon after initiation of self-monitoring (which results in a higher relative risk) ultimately produces behavioural changes that reduce future hypoglycemic events (resulting in a lower rate ratio). The finding by Barnett *et al* that rates of symptomatic hypoglycemia are lower in patients treated with a sulfonylurea using SMBG may indicate that self-monitoring prevents asymptomatic hypoglycemia from progressing. However, it should be noted that this is a highly subjective outcome that is significantly prone to ascertainment bias. Further studies employing more rigorous methods are therefore required to confirm this possible benefit of SMBG.

Data regarding long-term clinical endpoints were infrequently reported in observational studies; no such data were reported in RCTs. Given the many possible confounders and likelihood of selection bias in observational studies, further RCTs of adequate size and duration are required to determine whether SMBG reduces long-term complications of diabetes in patients with type 2 diabetes not using insulin.

***Strengths and Limitations***

Our review is the first to systematically evaluate the available RCT and observational evidence related to SMBG in patients with type 2 diabetes not using insulin across a wide range of outcomes, and over numerous clinically relevant subgroups. However, certain limitations of our analysis warrant mention. In terms of the literature search strategy, potentially relevant studies may have been overlooked by excluding non-English language articles. However, a number of methodological reviews have suggested that this practice has minimal impact on the results of systematic reviews and meta-analyses.59-62 Furthermore, previous systematic reviews in this area did not identify additional RCTs published in a language other than English,10-14,16 hence the likelihood of bias arising from the imposed language restriction is minimal. Another limitation is the relatively low statistical power to detect differences within some subgroups, although it is reassuring that the HbA1C point estimates across subgroups were generally similar.

Possible limitations in the internal validity and generalizability of the RCTs included in this review should also be noted. The lack of blinding may have resulted in overestimation of SMBG-related benefits because subjects randomized to SMBG may have been more motivated to perform other behaviours that resulted in better glycemic control. However, it could be argued that any effects of SMBG in terms of increased patient motivation are important ancillary benefits that may also be realized in clinical practice, hence they do not necessarily limit the internal validity of studies. Perhaps more importantly, only one RCT47 described a treatment algorithm in which SMBG results were used to adjust antidiabetes treatments. The remaining studies either based therapeutic decisions upon HbA1C levels8,23,31,36 or did not specify how treatments were modified in response to SMBG results.24,34 Furthermore, the degree to which subjects acted appropriately in response to SMBG results was not documented in studies, even when education regarding interpretation and application was provided. It is therefore possible that the benefits of SMBG, particularly in combination with patient education, were underestimated. However, results of qualitative research indicate that SMBG results are not often reviewed by physicians,63 hence the manner in which SMBG was employed in RCTs may be reflective of clinical practice.

The remaining limitations stem from the paucity of studies addressing key issues pertaining to self-monitoring in patients with type 2 diabetes not using insulin. Much of the evidence of SMBG efficacy relates to HbA1C levels rather than prevention of complications related to diabetes. Whether HbA1C is an adequate surrogate endpoint for clinically relevant outcomes in patients with type 2 diabetes is controversial, especially in terms of the risk for cardiovascular events.64,65 There was also insufficient evidence regarding optimal frequency or timing of self-monitoring. Although some studies implemented patient education regarding interpretation of results from self-monitoring, there was considerable heterogeneity in both the format and intensity of education and co-interventions provided. Therefore, specific educational components that are of value in conjunction with SMBG could not be identified. Finally, patients with type 2 diabetes not using insulin represent a heterogeneous clinical population. It is therefore possible that certain subgroups are more likely to benefit from self-monitoring, for example, patients undergoing significant changes in medication regimen. Further studies are needed to adequately define the place of SMBG in these subgroups.

***Conclusion***

Our findings suggest that SMBG is associated with modest improvements in glycemic control among patients with non-insulin treated type 2 diabetes. The provision of education to help patients translate results from SMBG into appropriate responses appeared to result in no greater benefit than self-monitoring without education, although studies may have been limited in their ability to adequately assess the effects of education. There was little evidence to suggest that SMBG confers benefits in terms of health-related quality-of-life, patient satisfaction, long-term complications, or mortality. Additional high-quality RCTs of sufficient size and duration are required to determine whether self-monitoring reduces the burden of diabetes complications, and to identify the patient subgroups and clinical scenarios in which SMBG is most likely to provide benefit.

Figure 1: Study selection process

Citations identified

in literature search

***n = 1624***

**1300 citations excluded:**

reviews, letters, comments, recommendations/guidelines, RCTs unrelated to diabetes or not containing relevant comparisons, and duplicate citations

Full-text articles and abstracts retrieved for review ***n = 324***

|  |  |
| --- | --- |
| **295 articles excluded:** | |
| * duplicates (22) * study design not of interest (27) * reviews (52) * intervention not of interest (4) * letters (3) * outcomes not reported by diabetes type (8) * comparators not of interest (66) * recommendations/ guidelines (2) * abstract prior to 2004 (1) | * non-English (32) * outcomes not of interest (21) * comments (20) * population not of interest (5) * study protocol (6) * research question not of interest (19) * outcomes not reported by type of therapy (6) * data not extractable (1) |

Articles and abstracts included in systematic review ***n = 29***

Heterogeneity: Tau² = 0.00; Chi² = 3.44, df = 7 (P = 0.84); I² = 0%

Test for overall effect: Z = 4.70 (P = 0.00001)

**Study**

**(N)**

**Weight**

**SMBG**

**No SMBG**

**Mean Difference [95% CI]**

**(N)**

Barnett *et al* 2008

**Total**

311

**1221**

299

**1049**

29.5%

**100.0%**

-0.24 [-0.43, -0.05]

**-0.25 [-0.36, -0.15]**

Davidson *et al* 2005

Farmer *et al* 2007

*Self-interpretation*

Guerci *et al* 2003

Muchmore *et al* 1994

O'Kane *et al* 2008

Schwedes *et al* 2002

43

151

150

345

12

96

113

45

76

76

344

11

88

110

1.8%

16.7%

15.8%

20.9%

0.6%

4.5%

10.1%

-0.20 [-0.98, 0.58]

-0.14 [-0.40, 0.12]

-0.70 [-2.08, 0.68]

-0.40 [-0.90, 0.10]

-0.46 [-0.79, -0.13]

*No self-interpretation*

-0.17 [-0.43, 0.09]

-0.28 [-0.51, -0.05]

-2

-1

0

1

2

**Favours SMBG**

**Favours No SMBG**

**a**

**b**

**Subgroups**

**(N)**

**Weight**

**SMBG**

**No SMBG**

**Mean Difference [95% CI]**

**(N)**

**Education**

Schwedes *et al* 2002

Test for overall effect: Z = 3.70 (P = 0.0002)

113

110

33.3%

-0.46 [-0.79, -0.13]

**Figure 2:** Forest plots showing meta-analytic results for randomized controlled trials that compared the effect of SMBG versus no self-monitoring on HbA1C (change from baseline) in adults with type 2 diabetes treated with oral antidiabetes drugs or no pharmacotherapy: **(a)** Overall pooled estimate of effect for 7 randomized controlled trials; **(b)** Results of subgroup analysis based on whether patients were provided with education regarding self-interpretation and application of results from SMBG.

**-0.24 [-0.36, -0.11]**

-0.24 [-0.43, -0.05]

-0.20 [-0.98, 0.58]

-0.17 [-0.43, 0.09]

-0.28 [-0.51, -0.05]

-0.70 [-2.08, 0.68]

**-0.29 [-0.51, -0.08]**

-0.14 [-0.40, 0.12]

-0.40 [-0.90, 0.10]

**Favours No SMBG**

**Favours SMBG**

2

1

0

-1

**100.0%**

-2

Barnett *et al* 2008

43

151

345

12

**359**

150

96

Heterogeneity: Tau² = 0.00; Chi² = 0.84, df = 4 (P = 0.93); I² = 0%

**Total**

311

Davidson *et al* 2005

Farmer *et al* 2007

Guerci *et al* 2003

Muchmore *et al* 1994

**No education**

Test for overall effect: Z = 2.67 (P = 0.008)

Heterogeneity: Tau² = 0.01; Chi² = 2.44, df = 2 (P = 0.29); I² = 18%

**Total**

Farmer *et al* 2007

299

42.5%

2.6%

24.0%

30.0%

0.8%

**100.0%**

52.0%

14.7%

**775**

O'Kane *et al* 2008

45

76

344

11

**274**

76

88

**862**

Table 1: Summary of meta-analytic results for HbA1C from randomized controlled trials comparing SMBG with no self-monitoring, or various frequencies of SMBG, in adults with type 2 diabetes treated with oral antidiabetes drugs or no antidiabetes therapy.

| **Analysis** | **Number of studies**  **(sample size)** | **WMD (%) (95% CI)** | **I2 (%)** |
| --- | --- | --- | --- |
| **SMBG compared with no SMBG** | | | |
| Overall | 7 RCTs8,23,24,31,34,36,47 (n = 2270) | -0.25 (-0.36, -0.15) | 0 |
| ***Sensitivity and subgroup analyses*** | | | |
| Good quality RCTs only | 3 RCTs31,36,47 (n = 1247) | -0.21 (-0.34, -0.08) | 0 |
| Studies in which all subjects used oral antidiabetes agents | 3 RCTs23,31,47 (n = 1628) | -0.24 (-0.36, -0.11) | 0 |
| Education regarding application of SMBG results | | | |
| Education | 3 RCT24,31,36 (n = 710) | -0.28 (-0.47, -0.08) | 17.8 |
| No education | 5 RCTs8,23,31,34,47 (n = 1712) | -0.22 (-0.34, -0.10) | 0 |
| Testing frequency\* | | | |
| < 1 test per day | 3 RCTs8,23,31 (n = 1230) | -0.20 (-0.35, -0.06) | 0 |
| 1-2 tests per day | 2 RCT36,47 (n = 794) | -0.26 (-0.44, -0.07) | 0 |
| > 2 tests per day | 2 RCTs24,34 (n = 246) | -0.47 (-0.79, -0.15) | 0 |
| Duration of self-monitoring | | | |
| SMBG for 6 months | 5 RCTs8,23,24,36,47 (n = 1794) | -0.28 (-0.41, -0.15) | 0 |
| SMBG for > 6 months | 3 RCTs31,34,36 (n = 660) | -0.19 (-0.36, -0.01) | 0 |
| Proximity to diagnosis | | | |
| Previously diagnosed | 6 RCTs8,23,24,31,34,47 (n = 2086) | -0.25 (-0.35, -0.14) | 0 |
| Newly diagnosed | 1 RCT36 (n = 184) | -0.40 (-0.96, 0.16) | N/A |
| Baseline glycemic control | | | |
| A1c < 8.0% | 1 RCT31 (n = 453) | -0.16 (-0.34, 0.03) | N/A |
| A1c ≥ 8.0% | 6 RCTs8,23,24,34,36,47 (n = 1817) | -0.30 (-0.43, -0.17) | 0 |
| Type of oral antidiabetes agent | | | |
| Sulfonylurea | 1 RCT47 (n = 610) | -0.24 (-0.43, -0.05) |  |
| Various | 2 RCTs23,31 (n = 1018) | -0.24 (-0.40, -0.07) | 0 |
| **Frequency comparison** | | | |
| 1 SMBG per week vs. 4 SMBG per week | 1 RCT45 (n = 178) | -0.08 (-0.41, 0.25) | N/A |

Note: CI – confidence interval, RCT - randomized controlled trial, WMD – weighted mean difference, N/A – not applicable, OADs – oral antidiabetes drugs

\* Average daily use of blood glucose test strips is based upon actual testing frequency, when reported. Otherwise, we assumed that patients in the RCT adhered to testing frequencies outlined in the study protocol.

Table 2: Mean differences in HbA1C reported in retrospective cohort studies comparing SMBG with no self-monitoring, or various frequencies of SMBG, in adults with type 2 diabetes treated with oral antidiabetes drugs or no antidiabetes therapy.

|  |  |  |  |
| --- | --- | --- | --- |
| **Comparison** | | **Number of studies (n)** | **Mean difference in A1C (%) (95% CI)** |
| **SMBG compared with no SMBG** | | | |
| ≥ 1 strip/day vs. no SMBG | | 1 R. cohort26 (n = 8735) | -0.68 (-0.77, -0.59) |
| < 1 strip/day vs. no SMBG | | 1 R. cohort26 (n = 10243) | -0.21 (-0.30, -0.12) |
| Prescription of 2-4 strips per week vs. no prescription of strips | | 1 R. cohort37 (n = 115) | -0.20 (-0.77, 0.37) |
| Prescription of 0.56 strips per day vs. no prescription of strips | | 1 R. cohort43 (n = 299) | -0.13 (-0.28, 0.02) |
| SMBG vs. no SMBG for patients with baseline A1c ≥10% | | 1 time-series42 (n = 133) | -0.63 (-1.14, -0.12) |
| **Frequency comparisons** | | | |
| SMBG once per day vs. less than once per day | | 1 R. cohort26 (n = 6594) | -0.47 (-0.57, -0.37) |
| SMBG increased by one strip per day | Patients using OADs | 1 R. cohort39 (n = 1795) | 0.09 (p = 0.5392) |
| Patients using sulfonylureas | 1 R. cohort44 (n = 216) | 0.02 (p > 0.50) |
| New users of SMBG | 1 R. cohort32 (n = 5546) | -0.42 (p < 0.0001) |
| Prevalent users of SMBG | 1 R. cohort32 (n = 7409) | -0.16 (p < 0.0001) |
| SMBG increased by 10 test strips per week | | 1 R. cohort48 (n = 5862) | -0.06 (p = 0.38) |

Note: CI – confidence interval, R. cohort – retrospective cohort, OADs – oral antidiabetes drugs

Table 3: Summary of meta-analytic results for overall, severe, and nocturnal hypoglycemia from RCTs comparing SMBG with no self-monitoring, or various frequencies of SMBG, in adults with type 2 diabetes treated with oral antidiabetes drugs or no antidiabetes therapy.

| **Analysis** | **Number of studies**  **(sample size)** | **Effect Estimate**  **(95% CI)** | **I2 (%)** |
| --- | --- | --- | --- |
| **SMBG vs. no SMBG** | | | |
| Overall hypoglycemia | 3 RCTs23,31,47 (n = 1752) | RR: 1.99 (1.37, 2.89) | 33.8 |
| 2 RCTs36,47 (n = 794) | Rate ratio:  0.73 (0.55, 0.98) | 0 |
| Severe hypoglycemia | 3 RCTs24,31,47 (n = 1752) | RR: 0.17 (0.01, 4.12) | N/A |
| Nocturnal hypoglycemia | 1 RCT47 (n = 610) | RR: 0.41 (0.11, 1.58) | N/A |
| **Frequency comparison (1 SMBG per week vs. 4 SMBG week)** | | | |
| Overall hypoglycemia | 1 RCT45 (n = 202) | RR: 0.28 (0.11, 0.73) | N/A |
| Severe hypoglycemia | 1 RCT45 (n = 202) | No events | N/A |

95% CI - 95% confidence intervals; SMBG - self-monitoring of blood glucose; RR - relative risk; RCT - randomized controlled trial; N/A - not applicable

Table 4: Mean differences in patient satisfaction with diabetes treatment, well-being, and quality of life reported in randomized controlled trials comparing SMBG with no self-monitoring in adults with type 2 diabetes treated with oral antidiabetes drugs or no antidiabetes therapy.

|  |  |  |
| --- | --- | --- |
| **Analysis** | **Number of studies (n)** | **WMD (95% CI)** |
| DTSQ | 2 RCTs22,23 (n = 562) | -0.26 (-1.38, 0.86) |
| WBQ-12 | 1 RCT22 (n = 339) | -0.85 (-2.27, 0.56) |
| WBQ-22 | 1 RCT40 (n = 223) | 1.83 (-0.05, 3.71) |
| EQ-5D |  |  |
| SMBG overall | 1 RCT41 (n = 453) | -0.06 (-0.13, 0.02) |
| SMBG + education | 1 RCT41 (n = 302) | -0.029 (-0.084, 0.025) |
| SMBG w/o education | 1 RCT41 (n = 301) | -0.072 (-0.127,-0.017) |

Note: CI – confidence interval, DTSQ – diabetes treatment satisfaction questionnaire, EQ-5D – EuroQoL-5D, RCT - randomized controlled trial, WBQ – well being questionnaire, WMD – weighted mean difference

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APPENDIX A: Results of Quality Assessment of RCTs

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **SIGN-50 elements (RCT checklist)** | | | | | | | | | | **Overall quality rating** |
| Appropriate and clearly focused question | Randomized assignment | Adequate concealment | Blinding of subjects and investigators | Groups are similar at baseline | The only difference between groups is treatment under investigation | Standard, valid, and reliable measurement of outcome(s) | The drop- out rate is acceptable and is comparable between the groups | ITT analysis  performed | Comparable results for multiple study sites |
| Barnett, et al., 200850 | AA | AA | NAd | NAd | AA | AA | AA | 13% SMBG | AA | NAd | good |
| 17% no SMBG |
| Davidson, et al., 20054 | AA | NR | NAd | AA | AA | PA | PA | 1 | AA | NAp | poor |
| Farmer, et al., 200734 | AA | WC | WC | NAd | AA | AA | AA | 7.3 SMBG | AA | AA | good |
| 11.2 control |
| Guerci, et al., 200328 | AA | NR | NAd | NAd | AA | AA | AA | 32.2 SMBG | PA | AA | poor |
| 29.1 control |
| Muchmore, et al., 199437 | AA | PA | NAd | NAd | PA | PA | NR | ~ 10% | NAd | NAp | poor |
| O’Kane, et al., 200839 | WC | WC | PA | PA | PA | AA | PA | 2.0 SMBG | WC | NAp | good |
| 2.2 control |
| Scherbaum, et al., 200848 | WC | AA | AA | NAd | AA | WC | NAd | 12% 1/week | PA | NAd | good |
| 11% 4/week |
| Schwedes, et al., 200229 | AA | PA | NAd | PA | AA | PA | WC | 10.8 | PA | PA | poor |
| Siebolds, et al., 200643 | AA | PA | NAd | NAd | AA | PA | AA | 10.8 | PA | PA | poor |

AA=adequately addressed; DM=diabetes mellitus; ITT=intention to treat; NAd=not addressed; NAp=not applicable; PA=poorly addressed; QA=quality assessment; WC=well-covered

# APPENDIX B: Results of Quality Assessment of observational studies

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Study** | **SIGN-50 elements (Cohort study checklist)** | | | | | |
| Appropriate and clearly focused question | Groups are comparable other than the factor under investigation | Recruitment rate reported | Likelihood that subjects have the outcome at the time of enrollment is assessed | The dropout rate is acceptable and is comparable between the groups | Comparison is made between full participants and those lost to follow-up, by exposure status |
| Aydin et al., 200531 | AA | AA | NAd | AA | NR | NAp |
| Bajkowska-Fiedziukiewicz et al., 200849 | AA | PA | PA | NAd | NR | NAd |
| Davis et al., 200733 | AA | AA | NAd | AA | 1.08 | NAd |
| Evans et al., 199925 | AA | AA | NAd | NAd | 63 | NAd |
| Karter et al., 200124 | WC | AA | AA | NAd | NR | NAd |
| Karter et al., 200635 | AA | AA | NAd | PA | NR | NAd |
| Martin et al., 200636 | WC | AA | NR | PA | 0.2 | NAd |
| Murata et al., 200954 | AA | AA | NAp | NAd | NR | NAp |
| Rindone et al., 199740 | AA | AA | NAd | NAd | 0 | NAp |
| Schneider et al., 200741 | WC | AA | NR | AA | 0.52 | NAd |
| Secnik et al., 200742 | AA | AA | NAd | NAd | 29 insulin | PA |
| 26 OAD |
| Wen et al., 200446 | AA | AA | NAp | AA | NAp | NAp |
| Wieland et al., 199747 | AA | AA | NAp | NAd | NR | NAp |

AA=adequately addressed; DM=diabetes mellitus; ITT=intention to treat; NAd=not addressed; NAp=not applicable; PA=poorly addressed; QA=quality assessment; WC=well-covered

APPENDIX B (cont’d)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **SIGN-50 elements (Cohort study checklist cont’d)** | | | | | | |  |
| Outcomes are clearly defined | Assessment of  outcome  is made blind to exposure status | Recognition that knowledge of exposure status could have influenced the assessment | The measure of assessment of exposure is reliable | Evidence used to show the method of outcome assessment is valid and reliable | Exposure level or prognostic factor is assessed more than once | Main confounders are taken into account | **Overall quality rating** |
| Aydin et al., 200531 | AA | NAd | NAd | PA | NAd | NAd | PA | poor |
| Bajkowska-Fiedziukiewicz, et al., 200849 | AA | NAd | NAd | PA | AA | NAd | NAd | poor |
| Davis et al., 200733 | AA | NAd | NAp | NAd | NAd | NAd | AA | poor |
| Evans et al., 199925 | PA | NAd | NAp | PA | PA | NAd | AA | poor |
| Karter et al., 200124 | PA | WC | NAp | PA | PA | AA | AA | poor |
| Karter et al., 200635 | AA | NAd | NAp | AA | NAd | PA | AA | poor |
| Martin et al., 200636 | AA | NAp | NAp | PA | AA | NAd | AA | poor |
| Murata et al., 200954 | AA | NAd | NAp | PA | NAd | NAd | PA | poor |
| Rindone et al., 199740 | AA | NAd | NAp | AA | NAd | PA | PA | poor |
| Schneider et al., 200741 | AA | NAp | NAp | PA | AA | NAd | AA | poor |
| Secnik et al., 200742 | AA | NAd | NAp | AA | AA | PA | AA | poor |
| Wen et al., 200446 | AA | NAd | NAp | PA | NAd | PA | AA | poor |
| Wieland et al., 199747 | AA | NAd | NAp | PA | AA | NAd | NR | poor |

AA=adequately addressed; DM=diabetes mellitus; ITT=intention to treat; NAd=not addressed; NAp=not applicable; PA=poorly addressed; QA=quality assessment; WC=well-covered