

Self-monitoring in Type 2 diabetes mellitus: a meta-analysis

S. Coster*, M. C. Gulliford*, P. T. Seed*, J. K. Powrie† and R. Swaminathan‡

*Department of Public Health Sciences,
†Department of Endocrinology, Diabetes and
Metabolic Medicine, ‡Department of Chemical
Pathology, Guy's, King's and St Thomas' School of
Medicine, King's College London, London, UK

Accepted 6 September 2000

Abstract

Aims Self-monitoring of blood or urine glucose is widely used by subjects with Type 2 diabetes mellitus. This study evaluated the effectiveness of the technique at improving blood glucose control through a systematic review and meta-analysis.

Methods Randomized controlled trials were identified that compared the effects of blood or urine glucose monitoring with no self-monitoring, or blood glucose self-monitoring with urine glucose self-monitoring, on glycated haemoglobin as primary outcome in Type 2 diabetes.

Results Eight reports were identified. These were rated for quality and data were abstracted. The mean (SD) quality score was 15.0 (1.69) on a scale ranging from 0 to 28. No study had sufficient power to detect differences in glycated haemoglobin (GHb) of less than 0.5%. One study was excluded because it was a cluster randomized trial of a complex intervention and one because fructosamine was used as the outcome measure. A meta-analysis was performed using data from four studies that compared blood or urine monitoring with no regular monitoring. The estimated reduction in GHb from monitoring was -0.25% (95% confidence interval -0.61 to 0.10%). Three studies that compared blood glucose monitoring with urine glucose monitoring were also combined. The estimated reduction in GHb from monitoring blood glucose rather than urine glucose was -0.03% (-0.52 to 0.47%).

Conclusions The results do not provide evidence for clinical effectiveness of an item of care with appreciable costs. Further work is needed to evaluate self-monitoring so that resources for diabetes care can be used more efficiently.

Diabet. Med. 17, 755–761 (2000)

Keywords blood glucose self-monitoring, meta-analysis, systematic review, Type 2 diabetes mellitus

Abbreviations GHb, glycated haemoglobin; FPG, fasting plasma glucose; UKPDS, UK Prospective Diabetes Study

Correspondence to: Dr M. C. Gulliford, Department of Public Health Sciences, Guy's, King's and St Thomas' School of Medicine, King's College London, Capital House, 42 Weston St, London SE1 3QD, UK.
Email: martin.gulliford@kcl.ac.uk

Introduction

In the UK Prospective Diabetes Study (UKPDS) in Type 2 diabetes mellitus, a long-term mean difference in glycated haemoglobin (HbA_{1c}) between groups of 7.0 compared with 7.9%, was associated with a relative risk reduction of 25% (95% confidence interval 7–40%) for the aggregate

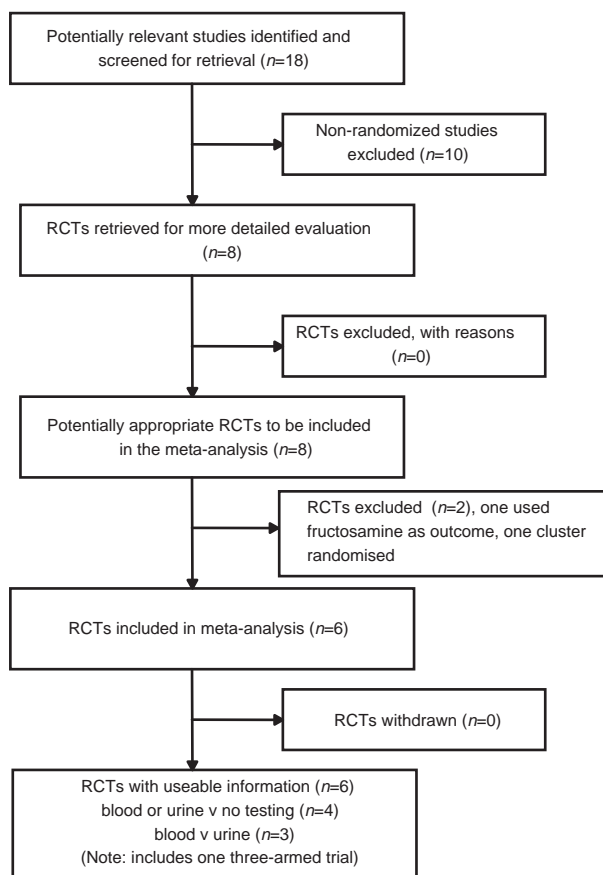


Figure 1 Flowchart showing selection of studies. (Adapted from QUOROM statement [27].)

endpoint ‘microvascular complications’ [1]. This observation has given added impetus to attempts to improve blood glucose control in people with Type 2 diabetes. Self-monitoring is used extensively in Type 2 diabetes but there is uncertainty concerning its effectiveness at improving blood glucose control [2–4]. A systematic review and meta-analysis were carried out to estimate the size of effect of self-monitoring on glycated haemoglobin in Type 2 diabetes.

Methods

The review was restricted to studies that investigated the effectiveness of blood or urine glucose self-monitoring at improving blood glucose control in subjects with Type 2 diabetes. The search included the authors’ personal reference collections; searches of Medline, Embase, IBSS (Index of Bibliography of Social Science) and the Cochrane Library; as well as hand searches of *Diabetes Care*, *Diabetic Medicine* and *Diabetologia* for the years 1990–1999. The search strategy included a series of keywords including ‘diabetes mellitus’ and ‘self-monitoring of blood glucose’ combined with a search for randomized controlled trials. Citations of retrieved references were also screened. Letters were sent to the two leading manufacturers (Bayer and Roche Diagnostics) and the British

Diabetic Association (UK Diabetes) to request information, but these enquiries did not yield any additional material. No attempt was made to review non-English language publications and authors of the studies reviewed were not contacted. Two of the authors independently rated papers for quality using a checklist designed for randomized and non-randomized studies [5]. This was used so that non-randomized studies could be appraised in the same way as randomized controlled trials. The checklist included subscales to rate the quality of reporting, external validity, and internal validity (bias and confounding). The checklist was modified by adding an item concerning whether a full range of outcome measures was reported. Assessment of external validity was found to be unreliable, but it was nevertheless thought important to appraise this aspect of the studies. The statistical power of the studies was considered separately by estimating whether the study had sufficient power to detect differences in GHb of $\leq 3\%$, $\leq 2\%$, $\leq 1\%$, $\leq 0.5\%$ or $\leq 0.25\%$. The outcome data abstracted from the papers were checked thoroughly.

Meta-analyses were performed using the ‘meta’ command [6] in the statistical package Stata [7]. In both of the meta-analyses, fixed and random effects analyses gave identical results and a test for heterogeneity was negative [6,8]. For each trial, the most reliable estimate of the treatment differences for which a standard error could be estimated based on the published data was used [9]. Thus, if data were reported for the change from baseline with standard errors then these were used, otherwise the difference between post-intervention values was used. As this approach only allowed for the analysis of differences between post-treatment values for some trials, we carried out a sensitivity analysis. Analyses were repeated using estimates for the change in GHb between the start and the end of the study. The standard error for the change was estimated by assuming a correlation between pre and post-intervention GHb values of 0.7. Meta-analysis results were plotted as a graph in which the point estimate for each study was plotted using a box whose area was inversely related to the variance of the estimate in that study [6]. Thus the area of the box was dependent, not just on the number of subjects, but also the design of the study and the data provided in the published report. Publication bias was evaluated using funnel plots and associated tests using the ‘metabias’ command in Stata [10].

Results

The initial search identified 18 studies, of which 10 were excluded because they were non-randomized (Fig. 1). The main design features of the eight controlled trials [11–18] are shown in Table 1. The study by Rutten *et al.* [17] used cluster randomization. The study by Miles *et al.* [15] changed patient allocation on a weekly basis and was not truly randomized. The study by Allen *et al.* [11] reported that ‘patients were randomized in groups of 10 to a urine testing group or a self-monitoring blood glucose group with the use of a computer-generated table of random numbers’. Thus the mode of allocation was not entirely clear. The remaining five studies used individual randomization. The criteria used to select subjects for the studies

Table 1 Randomized controlled trials of self-monitoring in Type 2 diabetes

Study	Design	Number of subjects recruited	Mean age (range) (years)	Inclusion criteria	Interventions	Drop-outs	Duration of study
Allen [11]	Randomization by patient groups, method of allocation to groups not clear	61	58	FPG \geq 8.8 and $<$ 22 mmol/l. No history of ketoacidosis No prior experience of monitoring	Blood glucose self-monitoring Urine glucose self-monitoring	7	6 months
Estey [12]	Individual randomization	60	Control: 54 Intervention: 56	Referred for diabetes education. On diet or oral hypoglycaemic drugs Access to telephone for follow up	Education (including monitoring) Education + blood glucose monitoring reinforcement by phone and home visit	7	3 months
Fontbonne [13]	Individual randomization, stratified by clinic	208	Control: 56 Blood: 55 Urine: 55	Poor control – \geq 8.8 mmol/l FPG or postprandial \geq 11 mmol/l three times in year. Diabetes for $>$ 3 years On diet or oral hypoglycaemic drugs	Blood glucose self-monitoring Urine glucose self-monitoring No monitoring	44	6 months
Gallichan [14]	Individual randomization	27	64 (47–80)	All taking oral hypoglycaemic drugs	Blood glucose self-monitoring Urine glucose self-monitoring	7	6 months
Miles [15]	Allocation alternated weekly, crossover trial	150	65 (31–91)	Newly diagnosed diabetes Diet or oral hypoglycaemic agents	Blood glucose self-monitoring Urine glucose self-monitoring Instruction was included in a patient education programme	36	3 month
Muchmore [16]	Individual randomization	29	Control: 60 Intervention: 57 (40–75)	Obese, diabetes for 1 year No use of self-monitoring for 3 months No calorie control diet program in last 3 months HbA _{1c} 9.5 to 13.5%	Blood glucose self-monitoring No monitoring Both groups received advice on a calorie restricted diet.	6	44 weeks
Rutten [17]	Cluster randomization by general practice, pair matched	149	Control: 63 Intervention: 64 (40–75)	Diabetes for at least 6/12 Not taking insulin Not under treatment for other conditions	Patients of intervention practices given a protocol for diabetes management including blood glucose self-monitoring Patients in control practices were given conventional GP care	10	12 months
Wing [18]	Individual randomization to patient groups	50	54 (35–65)	120% or more ideal body weight On oral hypoglycaemic drugs or insulin Development of diabetes $>$ 30 years	Blood glucose monitoring and weight reduction programme. No monitoring and weight reduction programme	5	12 months

GHb, glycated haemoglobin; FPG, fasting plasma glucose.

varied with respect to age distribution, duration of diabetes, quality of blood glucose control, and previous experience of monitoring. One study included subjects taking insulin [18] but the remaining studies included subjects treated with diet or oral hypoglycaemic drugs. A range of different methods were used to estimate glycated haemoglobin as outcome. Studies also varied with respect to the recommended frequency of self-monitoring, the advice given on modification of therapy, the methods used to assess reliability and adherence with monitoring, and the duration of study. Loss to follow-up was substantial in some trials (Table 1). Quality ratings were generally low (Table 2). It was estimated that three studies had sufficient statistical power to detect differences in glycated haemoglobin (GHb) of between 0.5 and 1% but four studies only had sufficient power to detect differences of more than 1%. Further details of the literature searches, excluded studies, critical appraisals, quality ratings (including assessments of reliability) and power calculations may be obtained from our full project report [19].

One study was not included in the meta-analysis because fructosamine was used as the outcome measure [14]. One study was excluded because it was a cluster randomized study of a complex intervention [17]. One of the studies included in the meta-analysis was a three-armed trial which compared groups using either blood testing, urine testing or no testing [13]. The data abstracted from the studies for the meta-analysis are shown in Table 2. A meta-analysis was performed using data from four studies which compared patients who monitored blood or urine glucose with patients who did not monitor regularly. This analysis included data for 285 subjects. The estimated reduction in GHb from monitoring was -0.25% (95% confidence interval -0.61 to 0.10%) (Fig. 2). This result indicated a small reduction in GHb from monitoring which was not significantly different from zero. Three studies which compared GHb in patients who monitored blood glucose with those monitoring urine glucose were also combined. For the cross-over study by Miles *et al.* [15], a comparison of subjects who used blood monitoring initially was made with those who used urine monitoring first. The analysis included 278 subjects. The estimated reduction in GHb from monitoring blood glucose rather than urine glucose was -0.03% (-0.52 to 0.47%). This difference was not statistically significant. Tests for heterogeneity were not significant for either meta-analysis. There was no evidence for publication bias in either of the analyses presented.

The results of the sensitivity analyses gave estimated intervention effects of -0.138% (-0.597 to 0.318%) for blood or urine monitoring compared with no monitoring, and -0.024% (-0.505 to 0.458%) for blood monitoring compared with urine monitoring.

Analyses were also repeated after excluding the trial by Estey *et al.* [12] because the intervention in this trial was

complex. This analysis gave an estimated difference in GHb between groups performing any monitoring and no monitoring of 0.010% (-0.578 to 0.598%). The analysis was also repeated after excluding the study by Miles *et al.* [15] because it was not fully randomized. This gave a difference in GHb between blood and urine monitoring groups of -0.182% (-0.915 to 0.552%). These sensitivity analyses provided evidence that the results presented were not particularly sensitive to the approach used for meta-analysis.

Discussion

Self-monitoring of blood or urine glucose is often advocated as a means to improve blood glucose control, and the technique was an integral part of the management strategy for the Diabetes Control and Complications Trial in Type 1 diabetes [20]. In the UKPDS [1], advice on monitoring varied according to the quality of blood glucose control and the trial results did not help to clarify whether self-monitoring was of benefit (R Turner, personal communication).

This meta-analysis did not provide evidence of benefit from self-monitoring. The results were imprecise and neither an appreciable beneficial effect nor a small adverse effect could be excluded. The confidence intervals associated with the estimate of GHb reduction were wide and it is possible that self-monitoring of blood or urine glucose might be associated with a reduction in GHb of up to 0.6% . In the UKPDS, a difference between groups of 7.0% compared with 7.9% was of clinical benefit over 10 years [1]. Over the study cohort, a 1% reduction in average HbA_{1c} was associated with a 21% (17 – 24%) lower risk of any diabetes-related endpoint [21]. Analyses of data from the Diabetes Control and Complications Trial in Type 1 diabetes also suggested that small differences in HbA_{1c} would be clinically important [22]. There was no evidence from this review to show that blood glucose monitoring was superior to urine glucose monitoring in terms of improved blood glucose control. The individual studies did not provide clear evidence of other benefits such as the avoidance of hypoglycaemia or improvements in health-related quality of life.

The meta-analysis inevitably reflected the limitations of the studies which it included. The studies included were generally poorly reported and lacking in statistical power. Several of the trials were of short duration and this may not have permitted a full assessment of the effects of self-monitoring. It might also be argued that it is undesirable to combine results obtained using different methods for glycated haemoglobin estimation. It is well known that systematic reviews of the same topic may give differing results [23], it was therefore reassuring that a number of sensitivity analyses confirmed the essential findings of the main analyses. Two other recent reviews of self-monitoring

Table 2 Randomized controlled trials of self-monitoring in Type 2 diabetes. Quality ratings, statistical power and main results

Study	Quality rating				Detectable difference in GHb (%)	Main findings	Data abstracted for GHb (Mean (SD) except where indicated)
	Reporting [12]	External validity [3]	Internal validity – bias [7]	Internal validity – confounding [6]			
Allen [11]	9	0	3	3	> 2.0–3.0	No difference in FPG, GHb or body weight	Blood: pre 12.4 (3.3), post 10.4 (2.9), diff – 2.0 (3.4) Urine: pre 11.7 (3.0), post 9.7 (2.6), diff –2.0 (2.4)
Estey [12]	8	0	4	4	> 0.5–1.0	No difference in HbA _{1c} or body weight	Blood: pre 6.3 (1.1), post 5.6 (0.7), diff –0.7 (0.9) Control: pre 6.1 (1.4), post 5.8 (1.5), diff – 0.3 (0.7)
Fontbonne [13]	10	0	4	4	> 1.0–2.0	No difference in HbA _{1c} or body weight	Blood: pre 8.2 (SE 0.3), diff –0.36 (SE 0.29) Urine: pre 8.6 (SE 0.30), diff –0.13 (SE 0.30) None: pre 8.2 (SE 0.3), diff –0.50 (SE 0.21)
Gallichan [14]	4	3	3	3	–	No difference in fructosamine concentration	–
Miles [15]	5	2	3	3	> 0.5–1.0	No difference in GHb or well-being between groups	Blood: pre 10.3 (2.6), post 8.8 (1.9), diff –1.5 Urine: pre 10.3 (2.3), post 8.7 (1.7), diff –1.6
Muchmore [16]	8	0	5	5	> 1.0–2.0	No difference in HbA _{1c} , body weight or quality of life between groups	Blood: pre 10.29 (SE 0.33), post 8.75 (SE 0.48) None: pre 10.45 (SE 0.44), post 9.60 (SE 0.63)
Rutten [17]	8	2	4	4	> 0.5–1.0	A small reduction in HbA _{1c} was achieved in the intervention group	Blood: pre 9.7 (2.1), post 9.2 (1.49) Control: pre 8.9 (1.9), post 9.4 (1.14)
Wing [18]	9	0	4	4	> 1.0–2.0	No difference between groups in GHb, FPG or body weight	Blood: pre 10.19 (2.51), post 10.19 (2.29) Control: pre 10.86 (2.00), post 10.44 (2.16)

'pre', before intervention; 'post', after intervention; 'diff', difference between before and after. GHb, glycosylated haemoglobin.

Urine or blood monitoring compared with no monitoring

Trial	Number of subjects	Intervention effect GHb (%)
Wing [13]	23/22	-0.25 (-1.56 to 1.08)
Estey [7]	28/25	-0.40 (-0.85 to 0.05)
Fontbonne [8]	110/54	0.25 (-0.46 to 0.97)
Muchmore [11]	12/11	-0.85 (-2.47 to 0.78)
Pooled effect		-0.25 (-0.61 to 0.10)

Blood monitoring compared with urine monitoring

Allen [6]	27/27	0.00 (-1.60 to 1.60)
Fontbonne [8]	56/54	-0.23 (-1.05 to 0.59)
Miles [10]	58/56	0.10 (-0.57 to 0.77)
Pooled effect		-0.03 (-0.52 to 0.47)

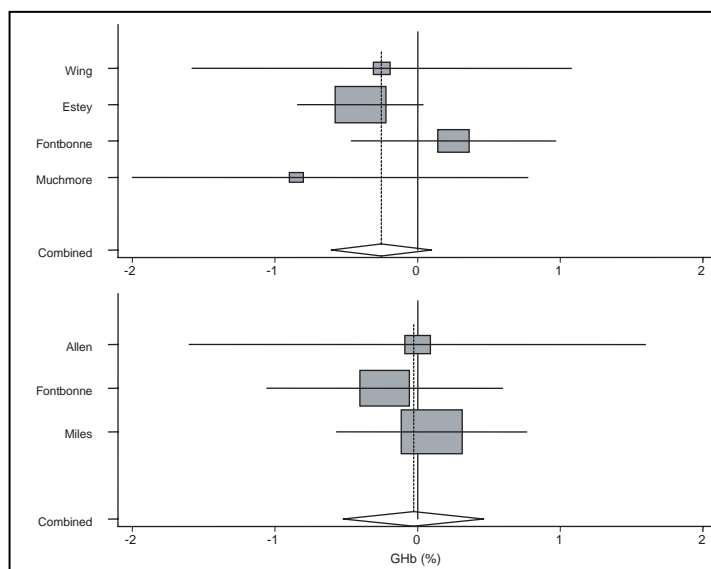


Figure 2 Results of meta-analysis.

in Type 2 diabetes also reached similar conclusions to the present review [3,4], although neither included a meta-analysis.

Diabetes care is a complex intervention made up of a number of different components of treatment, care and education. Mulrow and Pugh [24] observed that for complex interventions 'although treatments aimed at certain facets may be more efficacious than others, we cannot expect interventions aimed at single parts of a complicated treatment to be highly efficacious' [24]. In the present context, the use of self-monitoring may be highly dependent on the type and quality of diabetes education which patients receive. In the trials included in this review, there was an obvious lack of standardization of training and advice on use of self-monitoring. In a study in Type 1 diabetes, Worth *et al.* [25] showed that patients taking part in an intensive, 6-month education programme with urine glucose monitoring, showed an improvement in blood glucose control. During a subsequent 9 month evaluation of blood glucose monitoring, there was no further improvement in control. The authors suggested that the main benefit of self-monitoring was as an educational modality, leading to increased contact time with diabetes care staff and greater motivation. Any effects were, they suggested, short-lived and they suggested that future research should focus on long-term results.

Several studies noted that blood glucose self-monitoring was more costly than urine glucose self-monitoring, which in turn was more costly than no self-monitoring. In the absence of evidence for clinical effectiveness of blood glucose self-monitoring, there seems little justification for encouraging Type 2 diabetic patients to purchase costly testing equipment. This is particularly relevant in countries with fewer resources. Healthcare costs include not just the costs of equipment and supplies, but also the staff time used

in busy clinics to teach patients to test, and to review their results. In terms of opportunity cost, more time spent teaching self-monitoring may result in less attention being given to other aspects of self-management such as foot care. Further work to clarify the use of self-monitoring in Type 2 diabetes appears to be needed so that resources for diabetes care can be used more efficiently. In agreement with the recommendation by Faas *et al.* [3], a large randomized trial of the effect of blood glucose self-monitoring in Type 2 diabetes is desirable. It would also be feasible to conduct trials of discontinuation of self-monitoring in subjects with stable Type 2 diabetes. Finally, where good quality clinical data are available it may be possible to carry out observational analyses to attempt to identify groups of patients in whom self-monitoring may be unnecessary [26].

Acknowledgements

This work was supported by the NHS Research and Development Health Technology Assessment Programme. The views expressed are those of the authors and not the NHS Executive.

References

- 1 United Kingdom Prospective Diabetes Study Group. Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998; **352**: 837–853.
- 2 Gallichan M. Self monitoring of glucose by people with diabetes: evidence based practice. *Br Med J* 1997; **314**: 964–7.
- 3 Faas A, Schellevis FG, van Eijk JTM. The efficacy of self-monitoring of blood glucose in NIDDM subjects. *Diabetes Care* 1997; **20**: 1482–1486.

- 4 Halimi S. Apports de l'auto-surveillance glycémique dans le prise en charge des diabétiques insulino (DID) et non-insulino-dépendants (DNID). *Diabète Métabolisme* 1998; **24**: 35–41.
- 5 Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health* 1998; **52**: 377–84.
- 6 Sharp S, Sterne JAC. Meta-analysis for an outcome of two exposures or two treatment regimens. In *Stata Technical Bulletin Reprints* Volume 7. College Station, TX: Stata Corporation, 1998; 100–108.
- 7 Stata Corporation. *Stata*. Release 6. College Station, TX: Stata Corporation, 1999.
- 8 Der Simonian R, Laird N. Meta-analysis in clinical trials. *Controlled Clin Trials* 1986; **7**: 177–188.
- 9 Frison L, Pocock SJ. Repeated measures in clinical trials: analysis using mean summary statistics and its implications for design. *Statist Med* 1992; **11**: 1685–1704.
- 10 Steichen TJ. Tests for publication bias in meta-analysis. In *Stata Technical Bulletin Reprints* Volume 7. College Station, TX: Stata Corporation, 1998; 125–133.
- 11 Allen BT, DeLong ER, Feussner JR. Impact of glucose self-monitoring on non-insulin-treated patients with type 2 diabetes mellitus. Randomized controlled trial comparing blood and urine testing. *Diabetes Care* 1990; **13**: 1044–1050.
- 12 Estey A, Mengh T, Mann K. Follow up intervention: its effect on compliance behaviour to a diabetes regimen. *Diabetes Educator* 1989; **16**: 291–295.
- 13 Fontbonne A, Billault B, Acosta M, Percheron C, Varenne P, Besse A *et al.* Is glucose self-monitoring beneficial in non-insulin-treated diabetic patients? Results of a randomized comparative trial. *Diabète Métabolisme* 1989; **15**: 255–260.
- 14 Gallichan MJ. Self-monitoring by patients receiving oral hypoglycaemic agents: a survey and a comparative trial. *Pract Diabetes* 1994; **11**: 28–30.
- 15 Miles P, Everett J, Murphy J, Kerr D. Comparison of blood or urine testing by patients with newly diagnosed non-insulin dependent diabetes: patient survey after randomised crossover trial. *Br Med J* 1997; **315**: 348–349.
- 16 Muchmore DB, Springer J, Miller M. Self-monitoring of blood glucose in overweight type 2 diabetic patients. *Acta Diabetol* 1994; **31**: 215–219.
- 17 Rutten G, van Eijk J, de Nobel E, Beek M, van der Velden H. Feasibility and effects of a diabetes type II protocol with blood glucose self-monitoring in general practice. *Family Prac* 1990; **7**: 273–278.
- 18 Wing RR, Epstein LH, Nowalk MP, Scott N, Koeske R, Hagg S. Does self-monitoring of blood glucose levels improve dietary compliance for obese patients with type II diabetes? *Am J Med* 1986; **81**: 830–836.
- 19 Coster S, Gulliford MC, Seed PT, Powrie JK, Swaminathan R. Monitoring blood glucose control in diabetes mellitus: a systematic review. *Health Technol Assessment* 2000; **4**: 1–93.
- 20 Diabetes Control and Complications Trial (DCCT) Research Group. Implementation of treatment protocols in the Diabetes Control and Complications trial. *Diabetes Care* 1995; **18**: 361–376.
- 21 Stratton IM, Adler AI, Neil HAW, Matthews DR, Manley SE, Cull CA *et al.* Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *Br Med J* 2000; **321**: 405–412.
- 22 Diabetes Control and Complications Trial (DCCT) Research Group. The relationship of glycaemic exposure (HbA_{1c}) to the risk of development and progression of retinopathy in the Diabetes Control and Complications trial. *Diabetes* 1995; **44**: 968–983.
- 23 Katerndahl DA, Lawler WR. Variability in meta-analytic results concerning the value of cholesterol reduction in coronary heart disease: a meta-meta-analysis. *Am J Epidemiol* 1999; **149**: 429–441.
- 24 Mulrow CD, Pugh J. Making sense of complex interventions. *J Gen Int Med* 1995; **10**: 111–2.
- 25 Worth R, Home PD, Johnston DG, Anderson J, Ashworth L, Burrin JM *et al.* Intensive attention improves glycaemic control in insulin-dependent diabetes without further advantage from home blood glucose monitoring: results of a controlled trial. *Br Med J* 1982; **285**: 1233–1240.
- 26 Evans JMM, Newton RW, Ruta DA, MacDonald TM, Stevenson RJ, Morris AD. Frequency of blood glucose monitoring in relation to blood glucose control: observational study with diabetes database. *Br Med J* 1999; **319**: 83–86.
- 27 Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF, for the QUOROM group. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. *Lancet* 1999; **354**: 1896–1900.