Blood glucose self-monitoring in type 2 diabetes: a randomised controlled trial

AJ Farmer, AN Wade, DP French,
J Simon, P Yudkin, A Gray, A Craven,
L Goyder, RR Holman, D Mant,
A-L Kinmonth and HAW Neil, on behalf
of the DiGEM Trial Group

HTA

Blood glucose self-monitoring in type 2 diabetes: a randomised controlled trial

AJ Farmer,[1*] AN Wade,[2] DP French,[3]
J Simon,[4] P Yudkin,[1] A Gray,[4] A Craven,[1]
L Goyder,[5] RR Holman,[6] D Mant,[1]
A-L Kinmonth[7] and HAW Neil,[8] on behalf
of the DiGEM Trial Group

[1] Department of Primary Health Care, NIHR School of Primary Care Research, University of Oxford, UK
[2] Johns Hopkins Bayview Medical Center, Johns Hopkins School of Medicine, Baltimore, MD, USA
[3] Applied Research Centre in Health and Lifestyle Interventions, Coventry University, UK
[4] Health Economics Research Centre, Department of Public Health, University of Oxford, UK
[5] School of Health and Related Research, University of Sheffield, UK
[6] Diabetes Trials Unit, University of Oxford, UK
[7] General Practice and Primary Care Research Unit, University of Cambridge, UK
[8] Division of Public Health and Primary Care, University of Oxford, UK

*Corresponding author

Declared competing interests of authors: none

This report should be referenced as follows:

NIHR Health Technology Assessment Programme

The Health Technology Assessment (HTA) Programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The research findings from the HTA Programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the 'National Knowledge Service'.

The HTA Programme is needs led in that it fills gaps in the evidence needed by the NHS. There are three routes to the start of projects.

First is the commissioned route. Suggestions for research are actively sought from people working in the NHS, from the public and consumer groups and from professional bodies such as royal colleges and NHS trusts. These suggestions are carefully prioritised by panels of independent experts (including NHS service users). The HTA Programme then commissions the research by competitive tender.

Second, the HTA Programme provides grants for clinical trials for researchers who identify research questions. These are assessed for importance to patients and the NHS, and scientific rigour.

Third, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme commissions bespoke reports, principally for NICE, but also for other policy-makers. TARs bring together evidence on the value of specific technologies.

Some HTA research projects, including TARs, may take only months, others need several years. They can cost from as little as £40,000 to over £1 million, and may involve synthesising existing evidence, undertaking a trial, or other research collecting new data to answer a research problem.

The final reports from HTA projects are peer reviewed by a number of independent expert referees before publication in the widely read journal series *Health Technology Assessment*.

Criteria for inclusion in the HTA journal series

Reports are published in the HTA journal series if (1) they have resulted from work for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

Abstract

Blood glucose self-monitoring in type 2 diabetes: a randomised controlled trial

AJ Farmer,[1*] AN Wade,[2] DP French,[3] J Simon,[4] P Yudkin,[1] A Gray,[4] A Craven,[1] L Goyder,[5] RR Holman,[6] D Mant,[1] A-L Kinmonth[7] and HAW Neil,[8] on behalf of the DiGEM Trial Group

[1]Department of Primary Health Care, NIHR School of Primary Care Research, University of Oxford, UK
[2]Johns Hopkins Bayview Medical Center, Johns Hopkins School of Medicine, Baltimore, MD, USA
[3]Applied Research Centre in Health and Lifestyle Interventions, Coventry University, UK
[4]Health Economics Research Centre, Department of Public Health, University of Oxford, UK
[5]School of Health and Related Research, University of Sheffield, UK
[6]Diabetes Trials Unit, University of Oxford, UK
[7]General Practice and Primary Care Research Unit, University of Cambridge, UK
[8]Division of Public Health and Primary Care, University of Oxford, UK

*Corresponding author

Objectives: To determine whether self-monitoring of blood glucose (SMBG), either alone or with additional instruction in incorporating the results into self-care, is more effective than usual care in improving glycaemic control in non-insulin-treated diabetes.
Design: An open, parallel group randomised controlled trial.
Setting: 24 general practices in Oxfordshire and 24 in South Yorkshire, UK.
Participants: Patients with non-insulin-treated type 2 diabetes, aged ≥ 25 years and with glycosylated haemoglobin (HbA1c) ≥ 6.2%.
Interventions: A total of 453 patients were individually randomised to one of: (1) standardised usual care with 3-monthly HbA1c (control, $n = 152$); (2) blood glucose self-testing with patient training focused on clinician interpretation of results in addition to usual care (less intensive self-monitoring, $n = 150$); (3) SMBG with additional training of patients in interpretation and application of the results to enhance motivation and maintain adherence to a healthy lifestyle (more intensive self-monitoring, $n = 151$).
Main outcome measures: The primary outcome was HBA1c at 12 months, and an intention-to-treat analysis, including all patients, was undertaken. Blood pressure, lipids, episodes of hypoglycaemia and quality of life, measured with the EuroQol 5 dimensions (EQ-5D), were secondary measures. An economic analysis was also carried out, and questionnaires were used to measure well-being, beliefs about use of SMBG and self-reports of medication taking, dietary and physical activities, and health-care resource use.
Results: The differences in 12-month HbA1c between the three groups (adjusted for baseline HbA1c) were not statistically significant ($p = 0.12$). The difference in unadjusted mean change in HbA1c from baseline to 12 months between the control and less intensive self-monitoring groups was −0.14% [95% confidence interval (CI) −0.35 to 0.07] and between the control and more intensive self-monitoring groups was −0.17% (95% CI −0.37 to 0.03). There was no evidence of a significantly different impact of self-monitoring on glycaemic control when comparing subgroups of patients defined by duration of diabetes, therapy, diabetes-related complications and EQ-5D score. The economic analysis suggested that SMBG resulted in extra health-care costs and was unlikely to be cost-effective if used routinely. There appeared to be an initial negative impact of SMBG on quality of life measured on the EQ-5D, and the potential additional lifetime gains in quality-adjusted life-years, resulting from the lower levels of risk factors achieved at the end of trial follow-up, were outweighed by these initial impacts for both SMBG groups compared with control. Some patients felt that SMBG was helpful, and there was evidence that those using more intensive self-monitoring perceived diabetes as having more serious consequences. Patients using SMBG were often not clear about the relationship

between their behaviour and the test results.
Conclusions: While the data do not exclude the possibility of a clinically important benefit for specific subgroups of patients in initiating good glycaemic control, SMBG by non-insulin-treated patients, with or without instruction in incorporating findings into self-care, did not lead to a significant improvement in glycaemic control compared with usual care monitored by HbA1c levels. There was no convincing evidence to support a recommendation for routine self-monitoring of all patients and no evidence of improved glycaemic control in predefined subgroups of patients.
Trial registration: Current Controlled Trials ISRCTN47464659.

Contents

Supplementary material, the DiGEM Training Manual for Research Nurses and the DiGEM diaries used by participants, is available to download at www.hta.ac.uk/1330.

List of abbreviations

CI	confidence interval		HDL	high-density lipoprotein
CSM	Common Sense Model		ICER	incremental cost-effectiveness ratios
DiGEM	Diabetes Glycaemic Education and Monitoring (trial)		QALY	quality-adjusted life-year
EQ-5D	EuroQol 5 dimensions		SDSCA	summary of diabetes self-care activity
HbA1c	glycosylated haemoglobin		SMBG	self-monitoring of blood glucose

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

Executive summary

Introduction

Self-monitoring of blood glucose (SMBG) is a technology that is frequently incorporated into self-management interventions of diabetes, but has been separately evaluated in only a limited number of trials. Despite this lack of evidence, guidance is given to both support and discourage its use. Self-monitoring was used to guide insulin dose adjustment among individuals with type 1 diabetes in the Diabetes Control and Complications Trial (Epidemiology of Diabetes Interventions and Complications Study Research Group 2005). This trial demonstrated conclusively that tight glycaemic control reduced the risk of long-term complications. However, among non-insulin-treated patients with type 2 diabetes it is unclear whether self-monitoring is useful in providing personal feedback about the impact of changes in eating patterns and physical activity to support self-management. Self-monitoring of blood glucose is now widely accepted as part of the management of people with type 2 diabetes (European Diabetes Policy Group 1999, Blonde *et al.* 2002). The use of self-monitoring in this group of patients and the cost to health systems of the consumable test strips has become a major and increasing proportion of health-care budgets (Farmer and Neil 2004, Davidson 2005). We therefore set out to establish the benefit and cost-effectiveness of SMBG in the Diabetes Glycaemic Education and Monitoring (DiGEM) study.

Objectives

We report here the results of the DiGEM study – a trial designed to test whether self-monitoring of blood glucose, used with or without instruction in incorporating findings into self-management, can improve glycaemic control in non-insulin-treated diabetes compared with standardised usual care.

Methods

The DiGEM study was an open, parallel group randomised trial with an economic analysis, examination of impact on beliefs and self-reported behaviour, and a qualitative study to explore patient experiences. Participants were recruited from 48 general practices in Oxfordshire and South Yorkshire and were eligible if they had type 2 diabetes managed with diet or oral hypoglycaemic agents alone, were aged ≥25 years and had a glycosylated haemoglobin (HbA1c) ≥6.2%. Patients were randomised to (1) standardised usual care with 3-monthly HbA1c (control); (2) SMBG with patient training focused on clinician interpretation of results in addition to usual care (less intensive self-monitoring); and (3) SMBG with additional training of patients in interpretation and application of the results, to enhance motivation and maintain adherence to a healthy lifestyle (more intensive self-monitoring).

An intention-to-treat analysis was performed with the primary outcome of HbA1c at 12 months. Blood pressure, lipids, episodes of hypoglycaemia and quality of life measured with the EuroQol 5 dimensions (EQ-5D) were secondary measures. Further questionnaires were used to measure well-being, beliefs about use of SMBG and self-reports of medication taking, dietary and physical activities, and health-care resource use.

Results

Four hundred and fifty-three patients were randomised, with mean (standard deviation) HbA1c 7.5% (1.1). The differences in 12-month HbA1c between the three groups (adjusted for baseline HbA1c) were not statistically significant ($p = 0.12$). The difference in unadjusted mean change in HbA1c from baseline to 12 months between the control and less intensive self-monitoring groups was −0.14% [95% confidence interval (CI) −0.35 to 0.07] and between the control and more intensive self-monitoring groups was −0.17% (95% CI −0.37 to 0.03). No evidence was found of a significantly different impact of self-monitoring on glycaemic control when comparing subgroups of patients defined by duration of diabetes, therapy, diabetes-related complications and EQ-5D score.

Self-monitoring of blood glucose was found to be significantly more expensive than standardised usual care, by £92 and £84 for the less intensive SMBG and the more intensive SMBG groups respectively. There appears to be an initial negative impact of SMBG on quality of life measured on the EQ-5D. The potential additional lifetime gains in quality-adjusted life-years, resulting from the lower levels of risk factors achieved at the end of trial follow-up, were outweighed by the initial negative impacts for both SMBG groups compared with standardised usual care. Results of the extrapolation also suggest that the incremental lifetime savings in diabetes complications did not offset the additional intervention costs. The cost–utility analysis showed that it is unlikely that either investigated form of SMBG is cost-effective compared with standardised usual care.

In-depth interviews identified groups of patients who used SMBG to monitor impact of different lifestyle choices and motivate adherence to these choices. However, there were also patients who were not clear about the relationship between behaviour and test results or who experienced no improvement in test results after changing behaviour. Questionnaires about health-related beliefs did not identify an increase in perceived control over diabetes, but did find an increase in perceived seriousness of diabetes in the group carrying out more intensive self-monitoring.

Conclusions

We have found no convincing evidence to recommend routine use of SMBG by reasonably well-controlled, non-insulin-treated patients with type 2 diabetes. The specific advantages of monitoring identified by patients need to be placed in the context of a decline in compliance in the more intensive monitoring group and, at best, a small reduction in HbA1c. Neither the within-trial economic analysis nor the long-term modelling supports SMBG as a cost-effective intervention for all non-insulin-treated patients with type 2 diabetes. However, a clinically important benefit for specific subgroups of patients in initiating good glycaemic control cannot be excluded without further research.

Implications for practice

1. This trial does not provide convincing evidence to support the routine use of SMBG for non-insulin-treated patients with type 2 diabetes. However, our trial does not negate the established benefits of SMBG in insulin-treated patients, although further work is required to optimise its use.
2. Our in-depth interviews suggest that some individuals may benefit from SMBG use. However, with our present knowledge, we cannot clearly identify these patients, and clinical judgement is required to make this assessment in discussion with patients.
3. Our trial cannot exclude the possibility that SMBG may be helpful in non-insulin-treated type 2 diabetes patients with symptoms of hypoglycaemia; in those motivated to make alterations to behaviour that lead to consistent changes in blood glucose; and where there is strong patient preference.
4. If support for self-management training is available within usual care, then 3-monthly HbA1c management may be the optimum strategy. However, if HbA1c remains above 8%, then self-monitoring may provide motivation for medication adherence and lifestyle measures, as insulin therapy may be required in this group.

Research priorities

We have identified the following research priorities:

1. The qualitative element of the trial identifies a group of patients who consider that use of SMBG provides them with motivation to adopt and maintain behaviours that lead to better diabetes control. Further work is required to characterise those who gain most benefit in terms of glycaemic control and to determine whether this is related to use of the procedure.
2. Our results suggest that routine use of SMBG may not be appropriate for reasonably well-controlled patients; however, its role in the management of patients with less well-controlled diabetes is not clear. A pragmatic strategy of self-management education with HbA1c monitoring and intensifying drug therapy may be appropriate in the first instance. If glycaemic control is not then achieved, SMBG may be appropriate, first to explore any potential motivating effect, and second because insulin treatment is likely to be required. Exploration of the utility of this strategy may be useful.
3. There is an increased rate of hypoglycaemia reported among self-monitoring individuals.

Further exploration of the data is needed to establish whether these differences are likely to result from biochemical differences or greater awareness of hypoglycaemia as a cause of symptoms.

Trial registration

This trial is registered as ISRTCN47464659.

Chapter 1
Introduction

Background

The clinical problem

Diabetes is now a major public health problem. It is estimated that the number of people with diabetes will reach 330 million by 2030.[1] The disease brings with it a considerable burden: people with diabetes have a two- to fourfold increased risk of stroke and heart disease compared with the general population, along with an appreciable risk of retinopathy, peripheral nerve damage and renal problems. There is now strong evidence for the effectiveness of tight glycaemic control in reducing complications among people with diabetes.[2] However, support for self-management of diabetes to improve blood glucose levels has shown limited and transient success in improving glycosylated haemoglobin (HbA1c) levels.[3,4]

The technology

Self-monitoring of blood glucose (SMBG) is a procedure used as the basis for insulin dose adjustment in the Diabetes Control and Complications Trial among people with type 1 diabetes, which clearly demonstrated the efficacy of tight glycaemic control in reducing diabetic complications.[5,6] Self-monitoring for insulin-treated patients with type 2 diabetes is also generally accepted practice, although in both cases the frequency of testing and the algorithms for insulin adjustment need further evaluation. However, neither the rationale for SMBG nor its efficacy or effectiveness among non-insulin-treated patients with type 2 diabetes is clear. Yet SMBG is now widely accepted as a part of the management of patients with non-insulin-treated type 2 diabetes.[7,8] The use of self-monitoring in this group of patients and the cost to health systems of the consumable test strips has become a major and increasing proportion of health-care budgets.[9,10]

The majority of previous trials have used reflectance meters rather than biosensor technology. The older meters required larger quantities of blood and took longer to produce a reading than do current systems. Although, when used correctly, the older meters provided reliable results, in practice their accuracy and usability and thus potential impact were limited and may have formed a barrier to their effectiveness without high levels of motivation.

Target population

The majority of patients with diabetes treated in primary care who are not treated with insulin are within 5–10 years of diagnosis, have an average age of around 65 years, and are managed on a range of medications and lifestyle advice. Most have type 2 diabetes and are at risk from a range of macrovascular and microvascular diabetic complications. Large trials have confirmed the effectiveness of intensive glycaemic control in reducing these complications.[2,5,6] Tight glycaemic control can be achieved by means of lifestyle changes and medications.

Comparators

It is now increasingly possible to monitor glycaemia by measurement of HbA1c using standardised assays with appropriate quality assurance. HbA1c measurements provide clinical standards for glycaemic control. For patients with non-insulin-requiring type 2 diabetes, initiation and titration of medication can be managed using HbA1c measurement. Recent consensus guidelines have therefore based recommendations for SMBG on its theoretical potential benefits for improving motivation for self-care activities through greater understanding of diabetes.[11,12]

Limitations of previous research

Observational studies have been carried out in an attempt to explore the relationship between use of SMBG and diabetes outcomes,[13,14] but results were inconsistent and, despite attempts to control for differences between groups, the possibility of confounding between attitudes to self-care and use of SMBG cannot be excluded.[15]

Three systematic reviews have provided no evidence that self-monitoring is more effective in improving glycaemic control for people with type 2 diabetes than urine testing or measurement of HbA1c.[16–18] The majority of trials identified in

these reviews have been carried out in small groups of patients. Participants were not recruited from representative populations in the community and the strategies for use of the results from SMBG were not clearly defined. Two more recent trials, set both in hospitals and in a family practice setting, have adopted a more structured approach to relating blood glucose measurements to subsequent management decisions, but in one of these trials over 30% of those randomised were lost to follow-up, and in a second trial standardised counselling supporting lifestyle modification was provided only to the self-monitoring group[19] adhering to use of SMBG.[19,20]

Research on mediators of effect not investigated in trials

There are a small number of studies that offer some insight into how SMBG might improve blood glucose control in type 2 diabetes. Such monitoring may be helpful in titrating therapy by patients, practitioners or both. Evidence from qualitative studies suggests that awareness of fluctuations in blood glucose levels may promote adherence to self-care behaviours, medication taking, dietary advice and recommendations for physical activity in selected patients.[21,22]

There is accumulating research on diabetes self-management that uses psychological theory to guide intervention and measurement of the processes of behaviour change. One approach, the Common Sense Model (CSM),[23] proposes that how people understand threats to their health is central in determining efforts to minimise these health threats. For instance, if people with type 2 diabetes do not believe that physical activity affects their blood glucose levels, they have little incentive to be more actively involved in managing their condition. Beliefs about illness can be categorised in terms of whether they relate to symptoms/identity, cause, consequences, time lines, and control and cure.[23] In support of the CSM, previous research has shown that beliefs about the consequences and controllability of diabetes, and the perceived effectiveness of treatment,[24–26] predict

patient adherence to lifestyle advice. Furthermore, an intervention with myocardial infarction patients based on the CSM successfully managed to alter unhelpful beliefs, and led to a faster return to work and fewer symptoms in the intervention group.[27] Further research using this approach to guide intervention and measures with people with type 2 diabetes may inform understanding of the potential mechanisms through which SMBG may improve health. However, it remains unclear whether regular monitoring is more effective than periodic measurement of HbA1c.

Our trial to establish the effectiveness of blood glucose monitoring offered the opportunity to incorporate measures of process based on the areas identified by the CSM as potential mediators of effect. The trial intervention was delivered so that beliefs about diabetes were elicited using a standard approach to help patients understand how diabetes might present a threat to their health.[23] The roles of diet, physical activity and medication were discussed within the framework of the CSM of illness representation,[23] in which we set out to optimise the use of glycaemic feedback to facilitate behaviour change by influencing beliefs. Selection of the behaviour change techniques was based on evidence for effectiveness, and included goal setting and review of physical activity and eating patterns to help patients with lifestyle change.[28,29]

In addition, a health economic analysis was included to ensure that cost-effectiveness could be evaluated. Finally, a qualitative study was included to allow identification of the range of responses to the interventions and to provide further information about the potential mechanisms through which the intervention might work.

Objectives

We report here the results of a trial designed to test whether SMBG, used with or without instruction in incorporating findings into self-care, can improve glycaemic control in non-insulin-treated diabetes compared with standardised usual care.

Chapter 2
Methods

Study design and patients

The Diabetes Glycaemic Education and Monitoring (DiGEM) study was a 4-year open, randomised, three-arm, parallel group trial with sequential recruitment from general practices in Oxfordshire and South Yorkshire. The trial was managed from the co-ordinating centre at the Department of Primary Health Care, University of Oxford following NHS R&D Health Technology Assessment Programme guidelines. The protocol was approved by the Oxfordshire B Research Ethics Committee,[30] and registered with the International Standard Randomised Controlled Trial Number Register (ISRCTN47464659).

Our primary objective was to determine whether HbA1c at 12 months was significantly different between patients with non-insulin-treated type 2 diabetes receiving one of three allocated interventions: (1) standardised usual care with 3-monthly measurement of HbA1c by health professionals (control group); (2) use of a meter with training focused on clinician interpretation of results (less intensive self-monitoring); and (3) use of a meter with training in self-interpretation and application of the results to diet, physical activity and medication adherence (more intensive self-monitoring).

Between January 2003 and December 2005, 453 patients from 48 practices were randomised (see *Figure 1*) to receive standardised usual care (*n* = 152), less intensive self-monitoring (*n* = 150) or more intensive self-monitoring (*n* = 151). The mean number of patients per practice recruited in 24 Oxfordshire practices and 24 South Yorkshire practices was 10.2 and 8.3 respectively.

Patients

Patients were eligible for randomisation if they had type 2 diabetes, were aged 25 years or more at diagnosis and were managed with diet or oral hypoglycaemic agents alone, if their HbA1c at the assessment visit was ≥ 6.2% and they were independent in activities of daily living. Exclusion criteria were: the use of a blood glucose monitor twice a week or more often over the previous 3 months; serious disease or limited life expectancy that would make intensive glycaemic control inappropriate; or inability to follow trial procedures.

Measures

The primary outcome was HbA1c at the 12-month visit. Secondary outcomes were blood pressure, weight, total cholesterol, total/high-density lipoprotein (HDL) cholesterol ratio and body mass index. HbA1c was measured using a Variant II Hemoglobin Testing System (Bio-Rad Laboratories, Hercules, CA, USA) certified by the US National Glycohemoglobin Standardization Program and comparable to the Diabetes Control and Complications Trial Standard with an inter-assay co-efficient of variation (CV) across the range of the assay of < 2%. Cholesterol was assayed in local laboratories and results were aligned with the results of a sample of paired specimens analysed with an Olympus AU400 (Olympus, Tokyo, Japan) automated chemistry analyser, with an inter-assay CV across the range of < 2%. Blood pressure was measured twice in the right arm, with the subject seated, using a UA-779 electronic blood pressure monitor (A&D Instruments Ltd, Abingdon, UK), and the mean of these values was analysed.

Frequency of blood glucose testing and episodes of hypoglycaemia were transcribed from patient-held diaries. Episodes of hypoglycaemia were categorised as grade 2 (mild symptoms requiring minor intervention), grade 3 (moderate symptoms requiring immediate third-party intervention) or grade 4 (unconscious). Increases in hypoglycaemic medication collected from practice computer systems were defined as an increase in the dose or frequency prescribed, progression from use of a single oral agent to combination oral therapy, or addition of insulin to the treatment regimen.

Additional demographic and clinical data on duration of diabetes, diabetes-related complications and EuroQol 5 dimensions (EQ-5D) score[31] were collected to characterise the groups and to identify subgroups for predefined analysis.

Additional data collection for health economic, quality of life, and qualitative analyses will be detailed separately.

Randomisation

We used computerised randomisation[32] incorporating a partial minimisation procedure to adjust the randomisation probabilities between groups to balance three important covariates collected at baseline: duration of diabetes, HbA1c and current treatment (diet, oral monotherapy or oral combination therapy). The minimisation procedure to assign patients to their allocated intervention was conducted independently of recruitment and research nurses. The allocation was concealed from laboratory staff.

Procedures

Patients suitable for trial inclusion were identified from lists held on computer by their general practitioners (GPs). Those eligible were sent an invitation to participate signed by their GP, accompanied by an information sheet and a reply-paid envelope to facilitate response. One further letter was sent if no response was received within 1 month.

Eligibility for the trial and willingness to be randomised to blood glucose self-testing were confirmed with a pre-assessment telephone call and at the assessment visit. At the assessment visit, following informed consent, beliefs about diabetes were elicited using a standard approach to help patients understand how diabetes might present a threat to their health.[23] The roles of diet, physical activity and medication were discussed. Behaviour change techniques were selected on evidence for effectiveness, and included goal setting and review to help patients with lifestyle change.[28,29] The goal-setting and review approach was continued in subsequent visits. Baseline blood tests and clinical measurements were taken and questionnaires completed at the assessment visit.

Interventions

Following the assessment visit and confirmation of eligibility, patients were allocated to receive one of the three interventions. Their rationale is described in more detail in a previous paper.[30] The intervention was initiated at the first visit following

randomisation and continued at the scheduled 1-, 3-, 6-, and 9-month visits. Each of the three interventions included a series of standardised components.

Patients allocated to the *control* (standardised usual care) intervention received further information about use of goal setting and review as a means of monitoring health-related behaviours, such as eating and physical activity. They were asked not to use a blood glucose meter unless their GP considered it essential for their clinical management. They were told that information about the success of the strategies used to keep blood glucose levels under control would be provided in the form of feedback on 3-monthly HbA1c test results. A diary was used to record self-care goals and strategies for achieving them.

Patients allocated to the *less intensive* self-monitoring intervention continued to use the goal-setting and review techniques introduced at the assessment visit. In addition, they were given a blood glucose meter. They were asked to record three values a day on 2 days during the week, one of which should be fasting, and the other two pre meal or 2 hours post meal, and to aim for fasting and pre-meal glucose levels glucose of 4–6 mmol/l, and 2-hour post meal levels of 6–8 mmol/l. The nurses gave advice about the need to consider contacting their clinician if readings were consistently high (> 15 mmol/l) or low (< 4 mmol/l). They were not given information about how to interpret their blood glucose readings. Separate diaries were used to record identified goals and activity, and blood glucose results.

Patients allocated to the *more intensive* self-monitoring intervention continued to use goal setting and review and were also given a meter. In addition, they were given training and support in timing, interpreting and using the results of their blood glucose test results to enhance motivation and maintain adherence to diet, physical activity and medication regimens. They were encouraged to experiment with monitoring to explore the effect of specific activities such as exercise on their blood glucose, and to reflect on abnormal values in an attempt to identify what might have contributed to them. A single diary was used to record goals, activities and blood glucose results.

Follow-up visits differed in content according to the allocated intervention, in line with usual practice. Patients allocated to the control intervention had a blood test for HbA1c measurement 2 weeks before

their scheduled visit, which was then fed back to them as an indication of the impact of their self-care activities on their glycaemic control. HbA1c measurements were taken at the scheduled visit for those allocated to use of self-monitoring, but SMBG results were used to provide glycaemic feedback. Therefore, patients in each arm of the trial received feedback on glycaemic control, which was used to explore success of goals and set new ones. The patient's GP was notified of all HbA1c results and asked to consider changes in medication in line with the National Institute for Clinical Excellence diabetes guidelines for all patients.[33] The GP was also notified if blood glucose readings were consistently above 15 mmol/l.

Blood glucose meters were calibrated to provide plasma-equivalent results (Optium, Abbott Diabetes Care, Maidenhead, UK). Calibration of meters was checked by the research nurses using a test aliquot at baseline and 6 months.

Data on adverse reactions or complications were collected at each study visit, along with information about use of medication.

Intervention delivery

Training and support for the research nurses delivering the intervention were designed to ensure adherence to the study protocol.[34] Research nurses were taught psychological theory, and were trained in behaviour change techniques and skills in delivering the intervention (6 days case-based training spread over 5 weeks). Intervention protocols included scripts of the topics to be covered to guide the nurses when talking to patients. Additional measures to ensure adherence to the intervention protocols included self-review of taped consultations by the research nurses and external review by a sociologist. Prompts were also built into the patient diaries to help patients adhere to their allocated intervention.

Statistical analysis

Power calculations

We aimed to detect a difference of 0.5% in HbA1c. We estimated a standard deviation (SD) of HbA1c of 1.5 based on a previous trial of patients with type 2 diabetes[35] and a two-sided α of 0.05, took into account a loss to follow-up of 10% and planned a trial of 630 patients with 90% power. We revised the estimate of HbA1c SD to 1.25% after recruitment

of the first 235 patients, when it became clear that it had been overestimated. We retained a 10% dropout and 90% power and revised the recruitment target to 450 patients.

Analysis

We conducted a single analysis of main trial end points at the end of the study. An intention-to-treat analysis using analysis of covariance was carried out to compare mean levels of HbA1c at 12-month follow-up between the three allocated groups, with baseline HbA1c as a covariate. If no follow-up data were available, we imputed values by carrying forward the last available measurement. We specified that, in the event of a statistically significant overall result, comparisons of the two self-monitoring groups independently with the control group would be conducted using *t*-tests. Levels of HbA1c over the course of the trial were compared between groups using a repeated measures analysis of variance.

We also estimated whether the intervention effect differed in subgroups defined at baseline: duration of diabetes (above or below median), current management (oral hypoglycaemic drugs or dietary management only), health status (above or below median EQ-5D score) and presence or absence of diabetes-related complications. Again, we used analysis of covariance with baseline HbA1c as a covariate. In addition, subgroup was included as a main effect in the model, and effect modification was assessed by the significance of the interaction term: subgroup × treatment.

A Kaplan–Meier plot was used to explore adherence to a minimal level of self-monitoring, defined as at least 26 tests over 3 months (equivalent to two tests each week); significance was assessed with a log-rank test. The mean number of tests performed by those carrying out at least 26 tests in each quarter was also reported, with differences between the less and more intensive self-monitoring groups compared using a repeated measures analysis of variance.

Role of the funding source

The trial was funded by grants from the NHS and the National Institute for Health Research (NIHR) Health Technology Assessment Programme, which nominated an independent chair of the trial steering committee, but had no role in data collection, analysis, interpretation or decision to

publish. As principal investigator, AJ Farmer had full access to the data and takes final responsibility for the data as presented in the manuscript. The views and opinions expressed in this report are not necessarily those of the Department of Health.

Chapter 3
Clinical outcomes

Principal results

Baseline demographic and clinical characteristics were well balanced between the groups (*Table 1*). The median (interquartile range) duration of diabetes was 3.0 (1.8–6.4) years, mean (SD) age was 65.7 (10.2) years and mean (SD) HbA1c was 7.5% (1.1). Only 57 (12.6%) patients were lost to follow-up and this did not differ between groups (*Figure 1*). HDL cholesterol measurements were not obtained for 39 patients at baseline. At follow-up, HbA1c measurements were not collected for two patients, blood pressure measurements were not obtained for five patients, cholesterol measurements were not obtained for 10 patients and HDL cholesterol measurements were not obtained for 15 patients.

Primary results

The main results are shown in *Table 2*. At 12 months, there was no difference in HbA1c between the groups adjusted for baseline ($p = 0.12$). The mean difference in HbA1c from baseline to 12 months between the control and less intensive self-monitoring groups (not adjusted for baseline) was −0.14% [95% confidence interval (CI) −0.35 to 0.07], and between the control and more intensive self-monitoring groups was −0.17% (95% CI −0.37 to 0.03). *Figure 2* shows the change in HbA1c over the 12-month period of follow-up, with no evidence of differences in HbA1c between groups over the period of follow-up ($p = 0.38$).

Secondary outcomes

There was a significant difference in the change in total cholesterol between the three groups ($p = 0.010$). The mean difference in total cholesterol from baseline to 12 months between the control and less intensive self-monitoring groups (not adjusted for baseline) was −0.06. mmol/l (95% CI −0.26 to 0.14), and between the control and more intensive self-monitoring groups was −0.23 (95% CI −0.43 to −0.04). There were no differences in the other secondary outcome measures (see *Table 2*). Within the pre-specified subgroups there were no significant interactions with the allocated group (*Table 3*).

Hypoglycaemia

Over the duration of the trial, 14 patients in the control group, 33 patients in the less intensive group and 43 patients in the more intensive group experienced one or more grade 2 hypoglycaemic episodes ($\chi^2 = 18.3$, $p < 0.001$). Only one patient in the control group experienced a grade 3 hypoglycaemic episode.

Use of meter

Patients allocated to less intensive self-monitoring were significantly more likely to persist with use of the meter than those allocated to more intensive monitoring. Ninety-nine (66.0%) of those receiving the less intensive intervention and 79 (52.3%) of those receiving the more intensive intervention continued to use the meter at least twice a week for the full 12 months ($p = 0.012$) (*Figure 3*). Among those who continued to use a meter, the mean number of readings over the period of the trial was significantly higher among patients receiving the more intensive intervention than among those receiving the less intensive intervention ($p = 0.022$) (*Figure 4*). In the control group, eight patients initiated SMBG.

Increases in hypoglycaemic and lipid-lowering medication

There were no between-group differences in the proportion of patients who were prescribed increased hypoglycaemic medication between baseline and 12 months. Medication was increased in 45 (29.6%) patients in the control group, 43 (28.7%) patients in the less intensive group and 48 (31.8%) patients in the more intensive group. One patient in the control group, four patients in the less intensive monitoring group and five patients in the more intensive monitoring group were using insulin therapy by 12 months.

There were no differences between groups in the proportion of patients in whom hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase inhibitor (statin) treatment was increased or added to therapy. The number of patients not taking a statin at baseline, but who were taking one by 12 months were 17 (11.2%) in the control

TABLE I *Demographic and pre-intervention baseline characteristics by randomisation group [numbers are n (%) unless stated otherwise]*

		No meter	Use of meter	
		Control group (n = 152)	Less intensive self-monitoring (n = 150)	More intensive self-monitoring (n = 151)
Demographic characteristics				
Age (years)	Mean (SD)	66.3 (10.2)	65.2 (10.6)	65.5 (9.9)
Gender	Male	85 (55.9)	88 (58.7)	87 (57.6)
Occupational group	Professional, managerial and clerical	80 (52.6)	81 (54.0)	84 (55.6)
	Skilled manual/manual	69 (45.4)	68 (45.3)	66 (43.7)
	No occupation stated	3 (2.0)	1 (0.7)	1 (0.7)
Age on leaving full-time education (years)	<17	109 (71.7)	114 (76.0)	121 (80.1)
	17–18	20 (13.2)	14 (9.3)	13 (8.6)
	>18	23 (15.1)	22 (14.7)	17 (11.3)
Cigarette-smoking status	Never smoked	58 38.2)	54 (36.2)	54 (35.8)
	Ex-smoker	80 52.6)	74 49.7)	77 (51.0)
	Current smoker	14 (9.2)	21 (14.1)	20 (13.2)
Diabetes duration and treatment				
Duration of diabetes (months)	Median (Q₁, Q₃)	36 (24, 72)	36 (18, 84)	36 (19, 72)
Therapy	Diet only	44 (28.9)	39 (26.0)	41 (27.2)
	Monotherapy	57 (37.5)	58 (38.7)	58 (38.4)
	Combined oral therapy	51 (33.6)	53 (35.3)	52 (34.4)
Diabetes-related complications	Present	32 (21.1)	32 (21.3)	39 (25.8)
Use of blood glucose meter	Not using	104 (68.4)	110 (73.3)	102 (67.5)
	Using ≤ once per week	48 (31.6)	40 (26.7)	49 (32.5)
Physical and laboratory findings				
HbAlc (%)	Mean (SD)	7.49 (1.09)	7.41 (1.02)	7.53 (1.12)
Total cholesterol (mmol/l)	Mean (SD)	4.7 (1.1)	4.6 (1.1)	4.7 (1.1)
Blood pressure (mmHg)	Systolic, mean (SD)	140.0 (18.1)	140.7 (17.0)	137.4 (18.3)
	Diastolic, mean (SD)	79.6 (10.1)	79.9 (10.1)	77.9 (9.9)
Body mass index (kg/m)	Mean (SD)	30.9 (6.1)	31.9 (6.2)	31.0 (5.3)
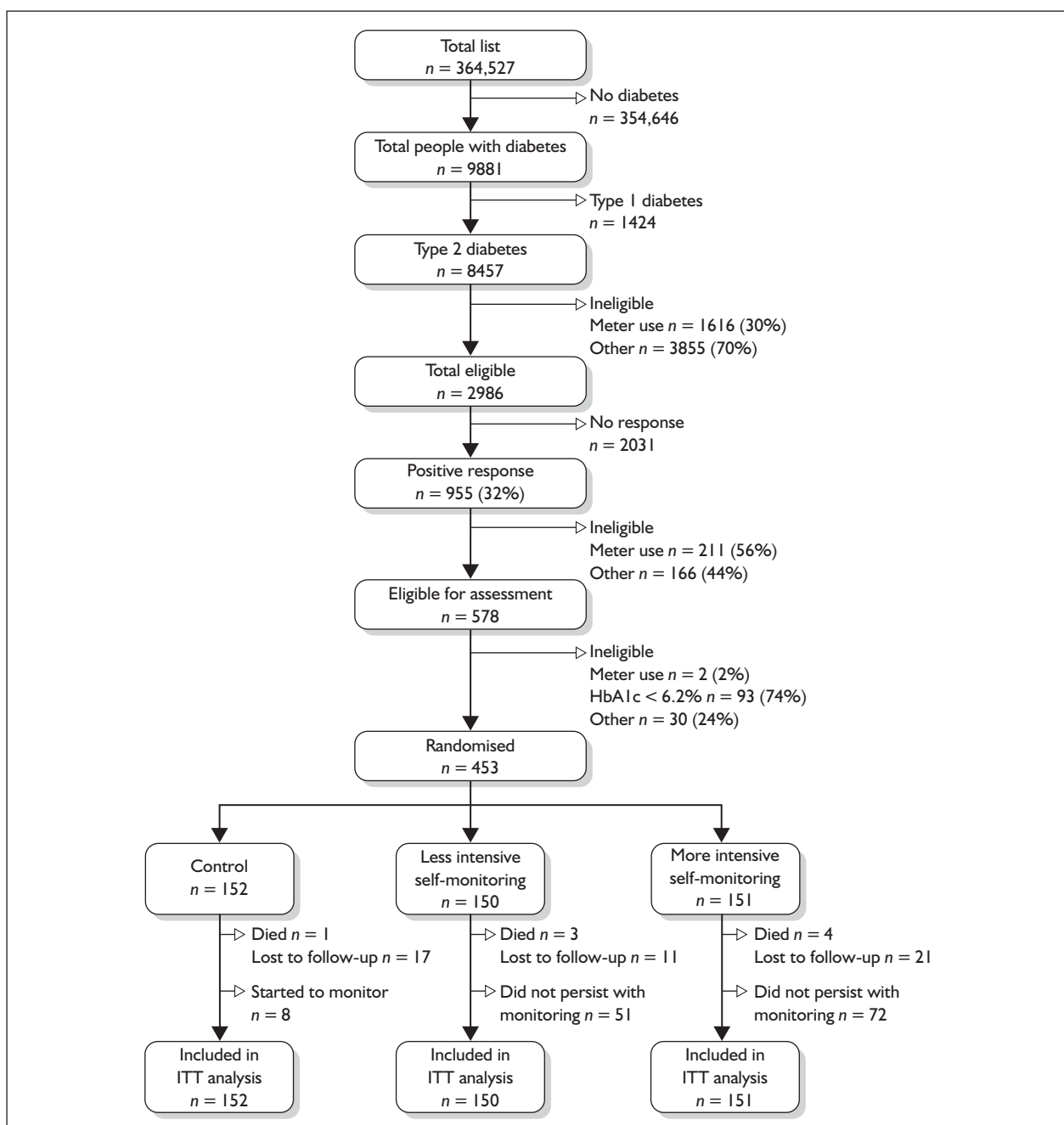
FIGURE 1 *Trial profile. ITT analysis, intention-to-treat analysis.*

group, 11 (7.3%) in the less intensive group and 19 (12.6%) in the more intensive group.

Loss to follow-up and deaths

Losses to follow-up are identified in *Figure 1*. The number of patients who withdrew consent was eight in the control group, eight in the less intensive monitoring group and 16 in the more intensive monitoring group. Reasons given were similar in each category, including 'unable to comply with protocol', 'does not like using the meter',

'withdrawn due to family commitments' and 'too busy to continue with study'. We were unable to contact eight patients in the control group, two in the less intensive group and four in the more intensive group. One patient in each group was too ill to continue participating. One patient died in the control group (B-cell lymphoma), three died in the less intensive group (chest infection, biliary duct carcinoma and acute myocardial infarction), and four died in the more intensive group (multiple organ failure, hypertensive heart disease, ischaemic heart disease and chest infection).

9

TABLE 2 Changes in HbA1c, blood pressure, weight, cholesterol and body mass index between baseline and 1 year [numbers are mean (SD)]

		No meter	Use of meter		p-value for difference between groups[a]
		Control group (n = 152)	Less intensive self-monitoring (n = 150)	More intensive self-monitoring (n = 151)	
HbA1c (%)	Baseline	7.49 (1.09)	7.41 (1.02)	7.53 (1.12)	0.12
	Follow-up	7.49 (1.20)	7.28 (0.88)	7.36 (1.05)	
	Change	–0.00 (1.02)	–0.14 (0.82)	–0.17 (0.73)	
Systolic blood pressure (mmHg)	Baseline	140.0 (18.1)	140.7 (17.0)	137.4 (18.3)	0.77
	Follow-up	136.2 (17.8)	137.3 (16.8)	134.1 (17.2)	
	Change	–3.8 (14.0)	–3.4 (15.6)	–3.3 (13.6)	
Diastolic blood pressure (mmHg)	Baseline	79.6 (10.1)	79.9 (10.1)	77.9 (9.9)	0.67
	Follow-up	77.1 (9.7)	77.8 (9.6)	75.8 (9.5)	
	Change	–2.5 (8.5)	–2.1 (8.8)	–2.1 (7.5)	
Weight (kg)	Baseline	86.7 (18.9)	90.4 (18.9)	86.9 (16.4)	0.37
	Follow-up	86.4 (19.4)	89.9 (19.0)	86.1 (15.7)	
	Change	–0.3 (2.7)	–0.5 (2.6)	–0.8 (3.3)	
Total cholesterol (mmol/l)	Baseline	4.73 (1.02)	4.64 (1.11)	4.67 (1.07)	0.010
	Follow-up	4.56 (1.03)	4.42 (0.95)	4.28 (0.84)	
	Change	–0.16 (0.84)	–0.22 (0.93)	–0.40 (0.90)	
Total/HDL cholesterol ratio[b]	Baseline	4.33 (1.12)	4.40 (1.33)	4.48 (1.35)	0.013
	Follow-up	4.18 (1.12)	4.11 (1.17)	4.02 (1.17)	
	Change	–0.15 (0.72)	–0.29 (0.86)	–0.46 (0.91)	
Body mass index (kg/m²)	Baseline	30.9 (6.1)	31.9 (6.2)	31.0 (5.3)	0.41
	Follow-up	30.8 (6.3)	31.8 (6.3)	30.7 (5.0)	
	Change	–0.1 (1.0)	–0.2 (0.9)	–0.3 (1.2)	

HDL, high-density lipoprotein.
a p-value for difference after adjustment for baseline.
b Based on 414 participants with paired values (137/152, 136/150, 141/151).
Change is measured as 1-year follow-up minus baseline.
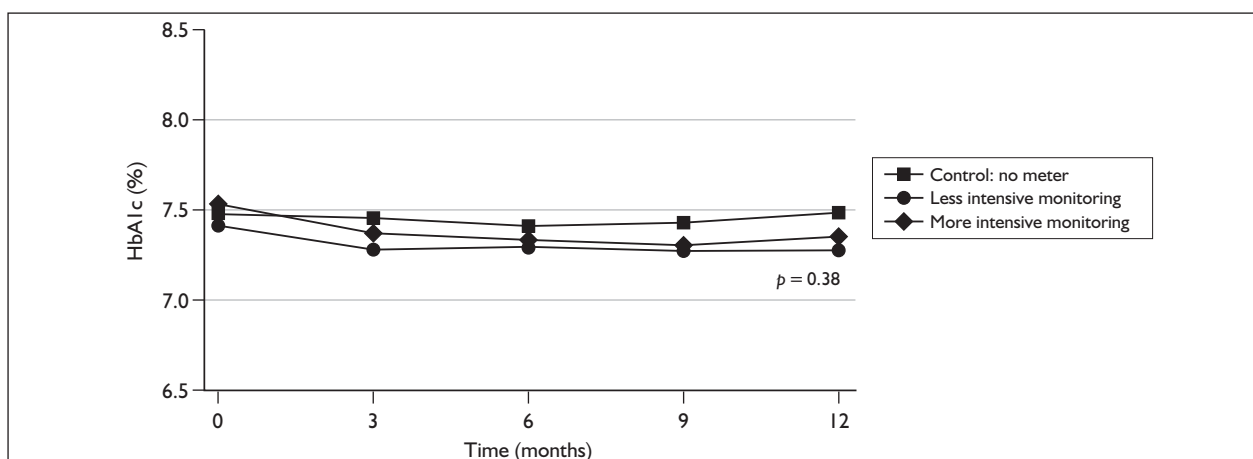
FIGURE 2 *Change in HbA1c over the duration of the trial.*
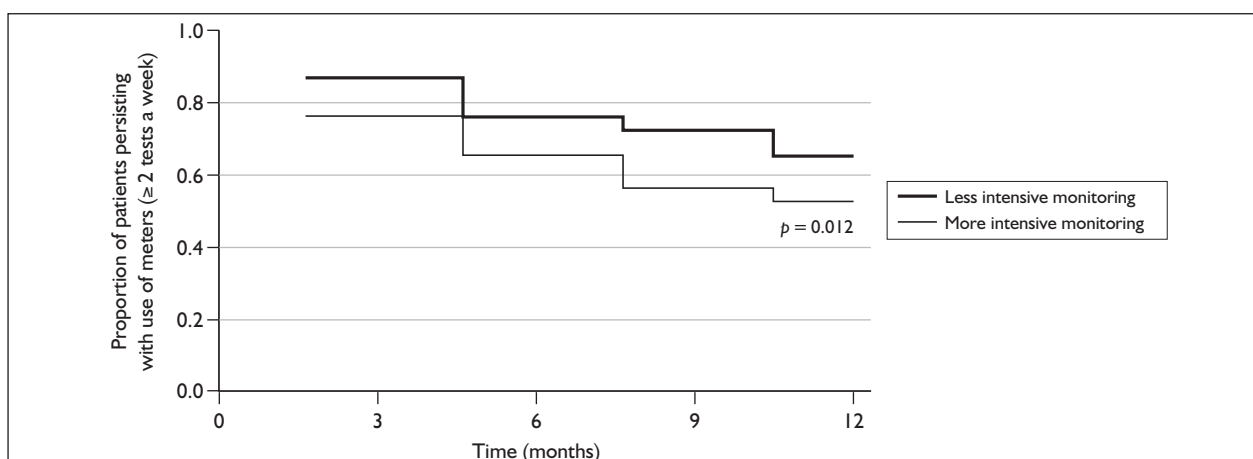
FIGURE 3 *Adherence to a minimal level of self-monitoring.*
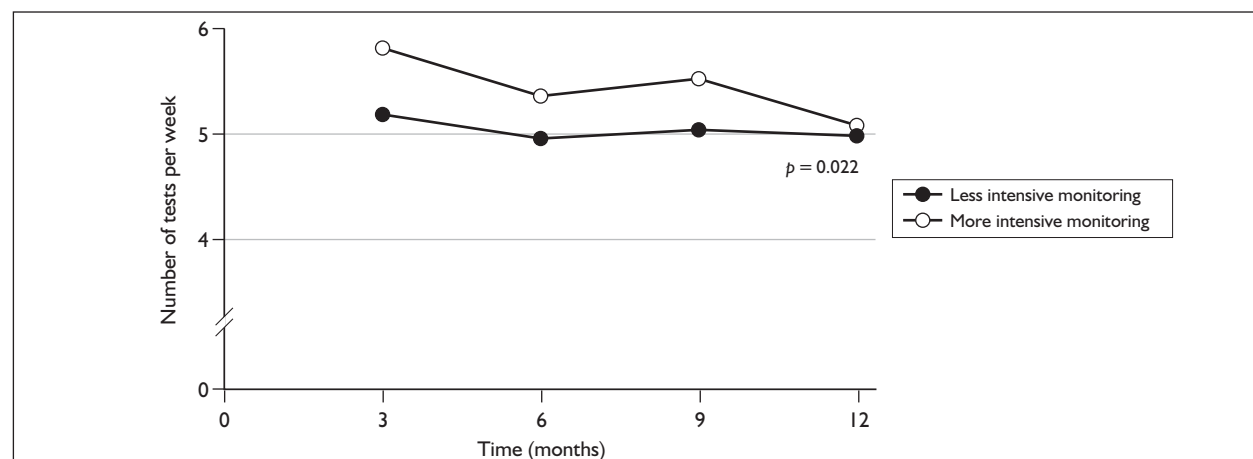
FIGURE 4 *Frequency of self-monitoring by randomisation group.*

TABLE 3 *Changes in HbA1c (%) between baseline and 1 year by subgroup [numbers are mean (SD)]*

		No meter	**Use of meter**		
		Control group	**Less intensive self-monitoring**	**More intensive self-monitoring**	**p-value for interaction[a]**
Number at baseline		**152**	**150**	**151**	
Duration of diabetes					
≤ Median[b]	Baseline	7.29 (1.02)	7.35 (1.02)	7.41 (1.03)	0.82
	Follow-up	7.30 (1.24)	7.23 (0.93)	7.25 (1.01)	
	Change	0.01 (1.03)	−0.12 (0.85)	−0.16 (0.73)	
> Median	Baseline	7.70 (1.13)	7.48 (1.02)	7.67 (1.20)	
	Follow-up	7.70 (1.11)	7.33 (0.84)	7.49 (1.08)	
	Change	−0.01 (1.01)	−0.15 (0.80)	−0.18 (0.73)	
Baseline therapy					
Diet only	Baseline	7.18 (0.98)	6.85 (0.66)	7.18 (1.11)	0.90
	Follow-up	7.21 (1.05)	6.90 (0.70)	7.09 (0.94)	
	Change	0.03 (0.80)	0.04 (0.64)	−0.09 (0.72)	
Oral drug therapy	Baseline	7.61 (1.11)	7.61 (1.05)	7.66 (1.10)	
	Follow-up	7.61 (1.24)	7.41 (0.91)	7.46 (1.07)	
	Change	−0.01 (1.10)	−0.20 (0.87)	−0.20 (0.73)	
Health status (EQ-5D)[c]					
> Median	Baseline	7.38 (1.02)	7.30 (0.96)	7.57 (1.21)	0.63
	Follow-up	7.46 (1.16)	7.22 (0.76)	7.43 (1.16)	
	Change	0.07 (0.99)	−0.08 (0.84)	−0.13 (0.77)	
≤ Median	Baseline	7.54 (1.16)	7.50 (1.09)	7.34 (0.80)	
	Follow-up	7.43 (1.22)	7.37 (1.04)	7.14 (0.78)	
	Change	−0.11 (1.14)	−0.13 (0.80)	−0.20 (0.67)	
Diabetes-related complications					
No	Baseline	7.53 (1.11)	7.51 (1.09)	7.71 (1.19)	0.86
	Follow-up	7.48 (1.16)	7.32 (0.92)	7.43 (1.13)	
	Change	−0.05 (1.02)	−0.19 (0.88)	−0.28 (0.74)	
Yes	Baseline	7.32 (1.02)	7.07 (0.63)	7.00 (0.64)	
	Follow-up	7.52 (1.34)	7.12 (0.73)	7.16 (0.73)	
	Change	0.20 (1.02)	0.05 (0.56)	0.16 (0.56)	

EQ-5D, EuroQol 5 dimensions.
a *p*-value for interaction after adjustment for baseline.
b Median value duration of diabetes 36 months.
c Median EQ-5D score 0.814. Paired data for EQ-5D score available for 384 patients; this section based only on these patients.

Chapter 4
Economic analysis

Methods

A cost–utility analysis was undertaken from a health-care perspective. The within-trial analysis estimated the total health-care costs and quality-adjusted life-years (QALYs) per patient for the 12-month trial period in each of the three groups: (1) standardised usual care, (2) less intensive SMBG and (3) more intensive SMBG; and then calculated the incremental total health-care costs and QALYs gained per patient of (1) less intensive SMBG compared with standardised usual care and (2) more intensive SMBG compared with standardised usual care. The effects of the changes in the main risk factors observed in the 12-month trial period on life expectancy, quality-adjusted life expectancy and diabetes complication costs were extrapolated to a lifetime horizon using the UK Prospective Diabetes Study (UKPDS) Outcomes Model.[36]

Resource use

Data were collected on relevant health-care resource use during the 12-month period prior to study baseline at the recruitment visit (C2). The intervention was delivered at a visit 2 weeks later (C3) and reviewed at a visit 1 month later (C4). Further resource data were collected at subsequent follow-up visits at 3 months (C5), 6 months (C6), 9 months (C7) and 12 months (C8) during the trial period. Information was obtained on SMBG, nurse visits, medications and other health-care resource use including primary care, hospital care, and auxiliary (such as podiatry, optician and dietician services) and private health care, by means of a specific health service use questionnaire, patients' blood glucose monitoring diaries and nurse notes. The recorded lengths of nurse visits were adjusted to exclude resource use elements that were strictly trial related, such as trial administration and blood taking. Questionnaire information was supplemented by data from the patients' medical records where available. Measurement of the length of nurse contacts was carried out on a subset of patients which varied between 64% and 68% of all attended visits and was balanced between the groups. For missing information on SMBG and medication use, the last known value was carried forward. Randomly missing data in other resource

use categories were computed in STATA 9[37] by multiple imputation conditional on randomisation group, age, gender, duration of diabetes and comorbidity. Imputation of unavailable data on the length of nurse contacts was based on the adjusted values and was conditional on the type of contact and the randomisation group.

Costs

Costs were calculated by multiplying the product of each resource use category by its associated UK national level unit cost in 2005–6 prices (*Table 4*). Average costs were estimated in each arm of the study for the 12-month period prior to study baseline and the 12-month follow-up period of the trial. Each resource use item was then categorised as contributor to the cost of intervention (including nurse intervention and SMBG), the cost of medication or the cost of 'other health-care resource use' (including primary care, hospital care or auxiliary health care) (see *Table 4*). Mean intervention and medication costs were calculated across all patients in each arm of the study. Mean costs of 'other health-care use' were censored for patients who were lost to follow-up.

Changes in mean costs between baseline and 12-month follow-up were calculated for each treatment group. For the incremental analysis between the treatment groups, follow-up costs were adjusted for baseline variations by regression analysis. For censored cost items, the difference in changes between the pre-baseline and follow-up periods was used for this purpose.

Outcomes

The impact of SMBG on quality of life was estimated using the EQ-5D at baseline and at 12 months.[38] The distribution of EQ-5D responses across the different levels of each dimension was calculated for complete cases, and differences between treatment groups were analysed using a categorical chi-squared test. Mean utility values were derived using the UK 'tariff'[38] both for complete cases and for a full data set, where missing values were replaced by conditional multiple imputation in STATA 9.[37] Changes in

TABLE 4 *Resource use categories measured and their unit costs (2005–6 prices)*

Unit	Cost	Source
Intervention		
Nurse per hour of client contact	26	Curtis and Netten 2006[39]
Meter	17.50	British Medical Association 2006[40]
Lancets (100)	3.40	British Medical Association 2006[40]
Test strips (50)	17.50	British Medical Association 2006[40]
Medication		
Oral medication per prescription	See source	Department of Health 2007[41]
Insulin per unit	See source	British Medical Association 2006[40]
Dispensing fee	1.54[a]	Department of Health 2007[41]
Other health care		
Primary care		
GP per visit: surgery	21	Curtis and Netten 2006[39]
GP per visit: home	60	Curtis and Netten 2006[39]
Nurse per visit: surgery	8	Curtis and Netten 2006[39]
Nurse per visit: home	11	Curtis and Netten 2006[39]
Hospital care		
A&E care per episode	85[a]	National Health Service 2007[42]
Outpatient care per episode	96[a]	Netten and Curtis 2002[43]
Day hospital care per episode	100[a]	Netten and Curtis 2002[43]
Inpatient care per day: medical	269[a]	National Health Service 2007[42]
Inpatient care per day: surgical	496[a]	National Health Service 2007[42]
Inpatient care per day: other	288[a]	National Health Service 2007[42]
Auxiliary health care		
Dietician per session	35	Department of Health 2007[44]
Optician per session	18.39	Department of Health 2004[50]
Podiatrist per session: NHS	31	Department of Health 2007[44]
Podiatrist per session: private	50	Department of Health 2007[44]
Private/allied health-care professional per session	49[b]	Obtained from relevant agencies

A&E, accident and emergency.
a Inflated to year 2005–6 from the published cost using the Department of Health's Pay and Price Inflation Indices[39]
b Average of unit costs.

mean utility values between baseline and 12-month follow-up and baseline-adjusted 12-month utility differences between treatment groups were calculated and analysed using standard parametric techniques.

For the economic analysis, within-trial survival times were weighted by the average change in quality of life between baseline and end-of-trial utility values to estimate QALYs gained for each patient during the study period.[45]

Lifetime extrapolation

Lifetime extrapolation of the clinical results was carried out using the UKPDS Outcomes Model.[36] The Outcomes Model is a computer simulation model for forecasting quality-adjusted life

expectancy and other outcomes of people with type 2 diabetes. It involves probabilistic discrete-time computer simulation and is based on an integrated system of parametric proportional hazards risk equations developed using patient-level data from the large UKPDS trial.[36] The equations estimate the probability of occurrence of different complications given risk factors such as patient's age, sex, duration of diabetes, systolic blood pressure, HbA1c, lipid levels and smoking status. Costs and utility decrements associated with these complications are also summed within the model.

The model was used to assess the long-term impact of the disease on morbidity and mortality, and to estimate health-care costs associated with the disease with or without the interventions for patients in each treatment group of the DiGEM trial. For this, both costs and outcomes were discounted at a 3.5% annual rate.[46]

Cost-effectiveness

The long-term cost and QALY projections were added to the within-trial results to estimate the overall lifetime effects of the interventions. The differences in mean costs were then divided by the differences in mean QALYs between the two SMBG groups and the standardised usual care group to calculate the incremental cost-effectiveness ratios (ICERs).

Uncertainty

Within-trial results are reported as means, together with their SDs or standard errors, and as changes/differences, together with their 95% CIs to address uncertainty. These summary statistics were calculated and analysed using standard parametric techniques, except for censored cost items where non-parametric bootstrapping was used.[47] For the extrapolation, Monte Carlo uncertainty was eliminated by performing 10,000 repeated simulations in the model.[36]

Non-parametric bootstrapping was used to demonstrate the uncertainty around the point estimate of the ICERs.[47] The probability that SMBG is cost-effective compared with standardised usual care is illustrated by cost-effectiveness acceptability curves.[48]

Results

Resource use and costs

The mean length of nurse visits differed significantly between the three interventions to which patients were allocated (*Table 5*). Visits C3 and C4 were shorter for the standardised usual care group than for the SMBG groups, and C2 and C5 were longer for the more intensive SMBG group than for the other two groups.

Costs
Intervention and medication costs

The intervention and medication cost results are summarised in *Table 6*. The 12-month cost of SMBG is similar (£96 versus £89) in both self-monitoring groups. Nurse time spent on standardised patient care is significantly greater in both SMBG groups than in the control group. The additional cost per patient over 1 year (including 10% opportunity cost for non-attended visits), however, is minor: £6 (95% CI 1–11) in the less intensive SMBG group and £5 (95% CI 0–10) in the more intensive SMBG group. The differences in overall intervention costs were statistically significant: £92 (95% CI 80–103) between less intensive SMBG and standard usual care and £84 (95% CI 73–96) between more intensive SMBG and standard usual care.

A substantial increase in overall medication costs (£70–98) compared with baseline is evident in all three groups. Although there is some indication that more patients started on insulin in the more and less intensive SMBG groups than in the control group (5, 4 and 1 patients respectively), no significant differences were found in the overall cost of diabetes medications between patients using SMBG and those receiving standardised usual care.

Other health-care costs
Table 7 summarises details of 'other health-care costs' by resource use items based on the available data. Nine patients (2%) had at least one 'other health-care resource use' item missing for the pre-baseline period and 76 patients (17%) had incomplete data over the 12-month follow-up. *Table 8* presents the results of the 'other health-care costs' analysis after imputing randomly missing data and censoring for patients who were lost to follow-up, together with the total health-care cost estimates, which include the intervention and medication costs.

TABLE 5 *Mean length of attended nurse visits (SD) per patient*

		Available data					Imputed full data set	
		Unadjusted for trial related-factors			Adjusted for trial-related factors		Adjusted for trial-related factors	
	Visit	Minutes	*n*		Minutes	*n*	Minutes	*n*
Control group	C2	53 (13)	104		29 (7)	104	28 (6)	152
	C3	42 (14)	96		39 (13)	96	41 (11)	145
	C4	32 (14)	92		33 (15)	92	35 (13)	138
	C5	35 (11)	96		30 (10)	96	30 (8)	133
	C6	37 (12)	85		32 (10)	84	33 (8)	129
	C7	39 (13)	80		34 (11)	79	33 (9)	124
Less intensive self-monitoring	C2	51 (12)	104		27 (6)	104	26 (5)	150
	C3	52 (13)	105		48 (12)	101	50 (11)	140
	C4	42 (14)	91		39 (13)	90	38 (10)	138
	C5	46 (14)	90		32 (10)	90	32 (8)	139
	C6	49 (13)	88		32 (9)	88	32 (7)	131
	C7	46 (13)	86		32 (9)	86	33 (8)	122
More intensive self-monitoring	C2	54 (13)	94		30 (7)	94	29 (6)	151
	C3	56 (17)	98		52 (16)	94	51 (13)	140
	C4	43 (17)	82		40 (16)	82	40 (13)	125
	C5	49 (14)	86		35 (10)	86	35 (8)	128
	C6	53 (14)	70		36 (9)	70	34 (8)	118
	C7	49 (13)	74		35 (9)	74	33 (8)	113

C2, assessment visit; C3, initial intervention delivery; C4, 1-month follow-up; C5, 3-month follow-up; C6, 6-month follow-up; C7, 9-month follow-up.
Trial-related factors include trial administration and blood taking unrelated to patient care and the 12-month follow-up visit (C8) which is not reported here.

There was a non-significant increase in the 'other health-care costs' between the pre-baseline and the follow-up periods, averaging approximately £100–150 per patient in each group, which was attributable mainly to additional hospitalisation.

Total mean health-care costs per patient (see *Table 8*), including medications, intervention costs and other health-care costs, averaged £1042 for standardised usual care, £1048 for less intensive SMBG and £1145 for more intensive SMBG over the 12-month period prior to baseline. They increased by about £300–400 over the trial period to £1371, £1434 and £1482 respectively. There were no statistically significant differences between the groups.

In summary, only the intervention costs differed significantly between the control group and the two SMBG groups. All other cost changes during the trial follow-up compared with the 12-month period prior to baseline were similar between the groups.

Outcomes
Within-trial outcomes

Table 9 summarises the results of both the complete case-based and the imputed full data set-based EQ-5D utility analyses. Three hundred and thirteen patients (69%) completed the whole EQ-5D questionnaire both at baseline and at 12-month follow-up. There was no significant change during the trial in the mean utility per patient for the standardised usual care group. In contrast, both SMBG groups showed a reduction in their quality of life, and this reached statistical significance for the more intensive monitoring group. As there was some imbalance between the groups at baseline, follow-up results were adjusted for this variation using standard parametric techniques for

TABLE 6 *Mean intervention and medication costs (SD) and cost differences [95% CI] per patient (£, 2005–6 prices)*

| | 1 | | | 2 | | | 3 | | | Difference | |
| | Control group (n = 152) | | | Less intensive self-monitoring (n = 150) | | | More intensive self-monitoring (n = 151) | | | | |
	12 months pre-baseline	12-month follow-up	Change	12 months pre-baseline	12-month follow-up	Change	12 months pre-baseline	12-month follow-up	Change	2 vs 1	3 vs 1
Intervention	–	89 (27)	89 [85–93]	–	181 (49)	181 [173–189]	–	173 (68)	173 [162–184]	92ᵃ [80–103]	84ᵃ [73–96]
SMBG	–	10 (16)	10 [8–13]	–	96 (37)	96 [90–102]	–	89 (48)	89 [82–97]	86ᵃ [78–94]	79ᵃ [71–87]
Nurse visits	–	79 (21)	79 [75–82]	–	85 (20)	85 [81–88]	–	84 (26)	84 [80–88]	6ᵃ [1–11]	5ᵃ [0–10]
Medication	444 (278)	534 (309)	90ᵃ [66–114]	480 (311)	578 (342)	98ᵃ [73–123]	452 (302)	522 (317)	70ᵃ [47–93]	9.4 [–24 to 43]	–20 [–53 to 14]
Diabetes medication	98 (151)	124 (163)	26ᵃ [12–39]	120 (178)	144 (191)	25ᵃ [10–39]	113 (173)	123 (170)	10 [–3 to 23]	1 [–18 to 20]	–14 [–33 to 5]
Insulin	0 (0)	0.3 (4.0)	0.3 [–0.3 to 1.0]	0 (0)	2.5 (20.7)	2.5 [–0.8 to 5.9]	0 (0)	4.8 (33.7)	4.8 [–0.6 to 10.2]	2.2 [–3.0 to 7.4]	4.5 [–0.7 to 9.7]
Other medication	346 (222)	410 (240)	64ᵃ [46–83]	360 (241)	431 (279)	71ᵃ [49–93]	339 (253)	394 (264)	55ᵃ [35–75]	7 [–21 to 35]	–9 [–37 to 19]

a $p < 0.05$.

TABLE 7 Mean 'other health-care' costs (SD) per patient (£, 2005–6 prices): available cases

	1 Control group (n = 152)				2 Less intensive self-monitoring (n = 150)				3 More intensive self-monitoring (n = 151)			
	12 months pre-baseline		12-month follow-up		12 months pre-baseline		12-month follow-up		12 months pre-baseline		12-month follow-up	
	n	Cost	n	Cost	n	Cost	n	Cost	n	Cost	n	Cost
Other health care	148	581 (817)	129	774 (1612)	148	549 (933)	131	670 (964)	148	690 (1480)	117	786 (1424)
Primary care												
GP surgery	152	111 (87)	134	98 (84)	150	110 (93)	139	89 (74)	151	89 (61)	129	92 (68)
GP home	152	8 (34)	135	9 (39)	150	8 (25)	139	8 (30)	150	5 (20)	128	5 (21)
Nurse surgery	152	33 (33)	134	35 (26)	150	36 (41)	139	30 (26)	151	28 (23)	127	29 (24)
Nurse home	152	0.4 (3.8)	134	2.0 (13.9)	150	0.8 (5.4)	139	0.5 (2.9)	150	3.2 (23.4)	126	1.1 (8.3)
Hospital care												
A&E	152	10 (31)	133	12 (36)	150	11 (31)	138	9 (28)	150	16 (41)	128	14 (35)
Outpatient	152	133 (243)	134	142 (218)	150	125 (196)	138	165 (358)	151	132 (229)	128	161 (302)
Day hospital	152	9 (31)	134	8 (39)	150	11 (35)	137	14 (46)	151	5 (22)	129	9 (32)
Inpatient	152	172 (674)	132	342 (1490)	149	141 (821)	137	253 (807)	151	309 (1362)	129	389 (1577)
Auxiliary health care												
Dietician	151	5 (18)	134	4 (15)	150	5 (15)	137	3 (16)	151	9 (37)	127	3 (16)
Optician	151	17 (10)	134	19 (14)	150	18 (9)	137	18 (15)	151	17 (7)	127	18 (13)
Podiatrist: NHS	149	34 (55)	134	35 (63)	149	44 (68)	135	42 (52)	150	43 (90)	128	36 (53)
Podiatrist: private	152	43 (132)	132	27 (81)	150	29 (102)	137	20 (67)	151	26 (97)	128	16 (62)
Private health care	152	19 (71)	134	26 (126)	150	27 (86)	138	14 (58)	151	10 (43)	129	13 (62)

A&E, accident and emergency.

TABLE 8 *Mean 'other health-care' costs (SE) and cost differences [95% CI] per patient (£, 2005–6 prices)*

	1 Control group (n = 152)			2 Less intensive self-monitoring (n = 150)			3 More intensive self-monitoring (n = 151)			Difference	
	12 months pre-baseline	12-month follow-up	Change	12 months pre-baseline	12-month follow-up	Change	12 months pre-baseline	12-month follow-up	Change	2 vs 1	3 vs 1
Other health care	596 (66)	747 (130)	151 [–77 to 431]	567 (74)	676 (77)	109 [–93 to 297]	693 (120)	786 (145)	93 [–173 to 347]	–41 [–396 to 257]	–57 [–447 to 288]
Primary care											
GP surgery	111 (7)	100 (7)	–11 [–25 to 3]	110 (7)	90 (6)	–20[a] [–36 to –5]	89 (5)	93 (6)	3 [–9 to 16]	–9 [–32 to 11]	14 [–5 to 34]
GP home	8 (3)	9 (3)	2 [–5 to 9]	8 (2)	8 (3)	0 [–5 to 6]	5 (2)	5 (2)	0 [–4 to 5]	–1 [–11 to 8]	–2 [–10 to 7]
Nurse surgery	33 (3)	35 (2)	1 [–5 to 6]	36 (3)	30 (2)	–6 [–15 to 0]	28 (2)	32 (3)	3 [–3 to 11]	–7 [–17 to 2]	2 [–6 to 12]
Nurse home	0.4 (0.3)	1.9 (1.2)	1.5 [–0.4 to 4.4]	0.8 (0.4)	0.5 (0.3)	–0.3 [–1.3 to 0.5]	3.2 (1.9)	1.1 (0.7)	–2.1 [–6 to 1]	–1.8 [–4.8 to 0.2]	–3.6 [–8.3 to 0.7]
Hospital care											
A&E	10 (3)	12 (3)	2 [–5 to 9]	11 (2)	9 (2)	–3 [–9 to 4]	16 (3)	14 (3)	–3 [–11 to 6]	–5 [–14 to 4]	–5 [–17 to 7]
Outpatient	133 (19)	140 (18)	7 [–35 to 54]	125 (16)	163 (29)	37 [–12 to 102]	132 (18)	161 (25)	29 [–24 to 87]	30 [–35 to 102]	23 [–47 to 93]
Day hospital	9 (2)	9 (3)	–1 [–8 to 7]	11 (3)	13 (4)	3 [–6 to 12]	5 (2)	9 (3)	4 [–3 to 10]	4 [–9 to 16]	5 [–6 to 14]
Inpatient	172 (54)	327 (121)	155 [–55 to 410]	143 (66)	267 (67)	124 [–61 to 304]	309 (111)	383 (137)	74 [–172 to 314]	–30 [–385 to 245]	–81 [–449 to 237]

TABLE 8 Mean 'other health-care' costs (SE) and cost differences [95% CI] per patient (£, 2005–6 prices) (continued)

| | 1 | | | 2 | | | 3 | | | Difference | |
| | Control group (n = 152) | | | Less intensive self-monitoring (n = 150) | | | More intensive self-monitoring (n = 151) | | | | |
	12 months pre-baseline	12-month follow-up	Change	12 months pre-baseline	12-month follow-up	Change	12 months pre-baseline	12-month follow-up	Change	2 vs 1	3 vs 1
Auxiliary health care											
Dietician	5 (1)	4 (1)	–1 [–4 to 2]	5 (1)	3 (1)	–2 [–5 to 2]	9 (3)	4 (1)	–5ᵃ [–11 to 0]	–1 [–6 to 3]	–4 [–11 to 2]
Optician	17 (1)	19 (1)	2 [–1 to 4]	18 (1)	18 (1)	0 [–2 to 2]	17 (1)	18 (1)	1 [–1 to 4]	–2 [–5 to 2]	–1 [–4 to 3]
Podiatrist: NHS	34 (4)	36 (5)	2 [–8 to 13]	44 (5)	42 (4)	–2 [–12 to 6]	44 (7)	36 (5)	–8 [–18 to 0]	–5 [–19 to 8]	–10 [–25 to 4]
Podiatrist: private	43 (11)	28 (7)	–16ᵃ [–34 to –1]	29 (8)	21 (6)	–8 [–22 to 5]	26 (8)	16 (5)	–10ᵃ [–20 to –2]	7 [–14 to 30]	6 [–12 to 25]
Private health care	19 (6)	25 (10)	7 [–8 to 22]	27 (7)	14 (5)	–13 [–27 to 1]	10 (3)	15 (6)	5 [–3 to 16]	–20 [–40 to 1]	–1 [–19 to 16]
Total health careᵇ	1042 (70)	1371 (136)	329ᵃ [103–625]	1048 (82)	1434 (84)	387ᵃ [188–573]	1145 (127)	1482 (150)	337ᵃ [77–588]	58 [–305 to 349]	8 [–381 to 354]

A&E, accident and emergency.
a   p < 0.05.
b   Includes intervention and medication costs.

TABLE 9 *Mean utility values (SE) and utility differences [95% CI] per patient*

		Utility			Difference	
	n	Baseline	12-month follow-up	Change	2 vs 1	3 vs 1
Complete cases						
Control group (1)	105	0.802 (0.021)	0.804 (0.024)	0.002 [−0.034 to 0.038]		
Less intensive self-monitoring (2)	111	0.798 (0.025)	0.761 (0.029)	−0.037 [−0.080 to 0.005]	−0.040 [−0.094 to 0.015]	−0.053 [−0.109 to 0.004]
More intensive self-monitoring (3)	97	0.828 (0.020)	0.772 (0.028)	−0.056 [−0.099 to −0.013][a]		
Imputed full data set						
Control group (1)	152	0.799 (0.023)	0.798 (0.034)	−0.001 [−0.060 to 0.059]		
Less intensive self-monitoring (2)	150	0.781 (0.022)	0.755 (0.024)	−0.027 [−0.069 to 0.015]	−0.029 [−0.084 to 0.025]	−0.072 [−0.127 to −0.017][a]
More intensive self-monitoring (3)	151	0.807 (0.024)	0.733 (0.024)	−0.075 [−0.119 to −0.031][a]		

a　$p < 0.05$.

the incremental comparison. The full case-based analysis suggests that the negative impact of the more intensive SMBG results in significantly lower quality of life (−0.072 (95% CI −0.127 to −0.017)] compared with the control group. Sensitivity analysis based only on patients alive at the end of the trial showed very similar results [−0.062 (95% CI −0.112 to −0.012)].

Table 10 shows the distribution of responses to the EQ-5D across the different levels of each dimension. This table indicates that decrease in the quality of life among patients in the SMBG groups was due primarily to greater levels of anxiety and depression at 12-month follow-up than at baseline.

Life-time extrapolation

The extrapolated effects of the interventions compared with usual care, and the total QALYs gained and total costs incurred by the different treatment groups are given in *Table 11*. The mean gain in QALYs beyond the trial period was estimated to be 0.045 per patient for standardised usual care, 0.049 per patient for less intensive SMBG and 0.060 per patient for more intensive SMBG. Complication costs were reduced in the beyond-trial period, by £69, £102 and £97 respectively in the three groups, with no significant difference between groups.

Cost-effectiveness

Table 11 presents the overall differences in costs and outcomes between the SMBG groups and the control group. The mean estimates suggest that both forms of SMBG are more costly (£59 and £56) and less effective (−0.004 and −0.020 QALYs) than standardised usual care, with relatively wide CIs around the point estimates.

A formal ICER is not reported, as its calculation is meaningful only when the intervention is more costly and more effective than the comparator. Uncertainty intervals surrounding the ICER point estimates were assessed by recalculating the differences in costs and effects 1000 times using non-parametric bootstrapping with replacement.[47] *Figure 5* illustrates the distribution of the incremental cost and effect pairs between the control group and the less and more intensive SMBG groups plotted on the cost-effectiveness plane.[45] This shows that the 95% CIs of the ICERs cannot be meaningfully defined, as they range from the interventions dominating standardised usual care to the SMBG groups being dominated by the control group (points falling into all four quadrants of the plane).

The cumulative probability that SMBG is cost-effective compared with standardised usual care

TABLE 10 *Proportion (%) of EQ-5D answers across the dimensions: complete case analysis*

	Mobility			Self-care			Usual activities			Pain			Anxiety		
	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
Baseline															
Control group	62	38	0	92	8	0	82	17	1	51	44	5	71	29	0
Less intensive self-monitoring	66	34	0	92	8	0	78	22	0	52	41	7	77	21	2
More intensive self-monitoring	67	33	0	95	5	0	85	14	1	55	42	3	77	23	0
12-month follow-up															
Control group	66	34	0	90	10	0	77	23	0	53	43	4	82	16	2
Less intensive self-monitoring	61	39	0	90	10	0	78	19	3	55	38	7	72	24	4
More intensive self-monitoring	67	33	0	91	9	0	78	22	0	52	43	5	69	29	2

TABLE 11 *QALYs gained and costs[a] [95% CI] per patient over a lifetime*

	1	2	3	Difference	
	Control group (*n* = 152)	Less intensive self-monitoring (*n* = 150)	More intensive self-monitoring (*n* = 151)	2 vs 1	3 vs 1
Trial period					
QALYs gained	0.000 [−0.013 to 0.014]	−0.008 [−0.023 to 0.007]	−0.035 [−0.050 to −0.020][a]	−0.008 [−0.029 to 0.012]	−0.036 [−0.056 to −0.015][b]
Costs	89 [85–93]	181 [173–189]	173 [162–184]	92 [80–103][b]	84 [73–96][b]
Beyond trial extrapolation[c]					
QALYs gained	0.045 [0.021–0.069]	0.049 [0.027–0.071]	0.060 [0.040–0.080]	0.004 [−0.027 to 0.035]	0.015 [−0.016 to 0.046]
Costs	−69 [−147 to 9]	−102 [−176 to −28]	−97 [−158 to −37]	−33 [−133 to 67]	−28 [−128 to 72]
Lifetime total					
QALYs gained	0.045 [0.016–0.074]	0.041 [0.013–0.069]	0.025 [−0.002 to 0.051]	−0.004 [−0.043 to 0.035]	−0.020 [−0.059 to 0.019]
Costs	20 [−58 to 98]	79 [5–152]	76 [15–137]	59 [−41 to 159]	56 [−44 to 156]

QALY, quality-adjusted life-year.
a   Costs for year, 2005–6 prices.
b   *p* < 0.05.
c   Compared with no intervention.

as a function of decision makers' maximum willingness-to-pay for an additional QALY can be illustrated by cost-effectiveness acceptability curves[48] (*Figure 6*). In the UK, the current cost-effectiveness ceiling ratio is £20,000–30,000 per QALY gained.[49] The probability of the more intensive SMBG having a cost-effectiveness ratio lower than this does not reach 15%, and the
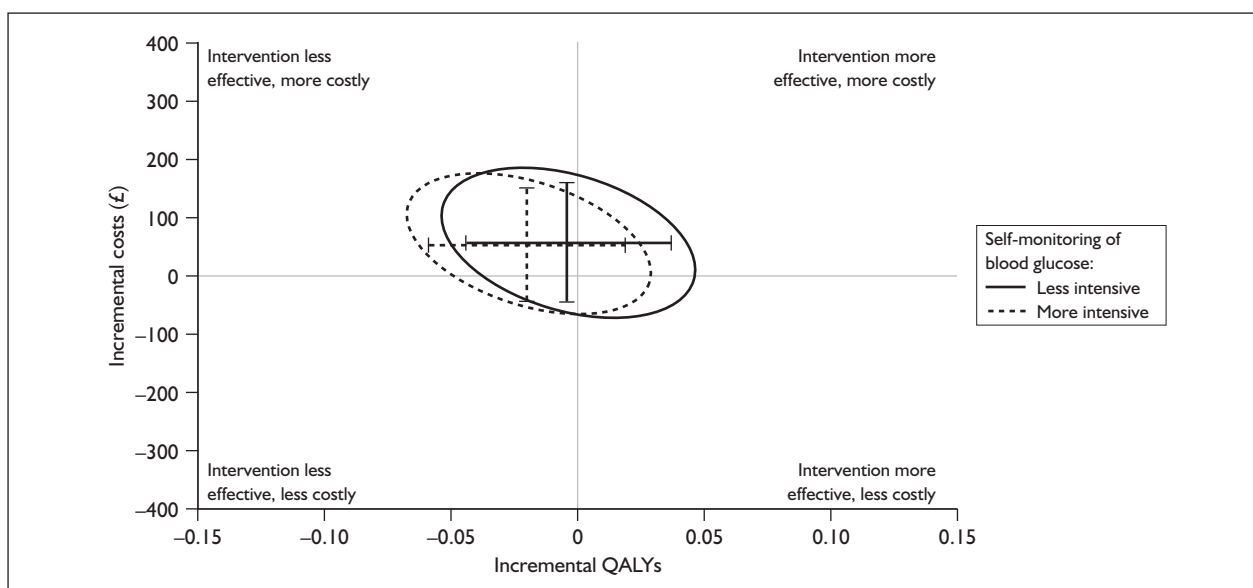
FIGURE 5 *Cost–utility analysis of self-monitoring of blood glucose compared with standardised usual care on the cost-effectiveness plane.*

probability of the less intensive SMBG being cost-effective remains below 40% at this threshold. Overall, the cost–utility analysis suggests that the investigated forms of SMBG are not cost-effective in comparison with standardised usual care.

Summary

Within the trial, SMBG was found to be significantly more expensive than standardised usual care, by £92 and £84 for the less and more intensive SMBG groups respectively. There appears to be an initial negative impact of SMBG on quality of life measured using the EQ-5D. Potential additional lifetime gains in QALYs resulting from the lower levels of risk factors achieved at the end of trial follow-up were outweighed by the initial negative impacts for both SMBG groups compared with standardised usual care. Results of the extrapolation also suggest that the incremental lifetime savings in diabetes complications did not offset the additional intervention costs. The cost–utility analysis showed that it is unlikely that either investigated form of SMBG is cost-effective compared with standardised usual care.
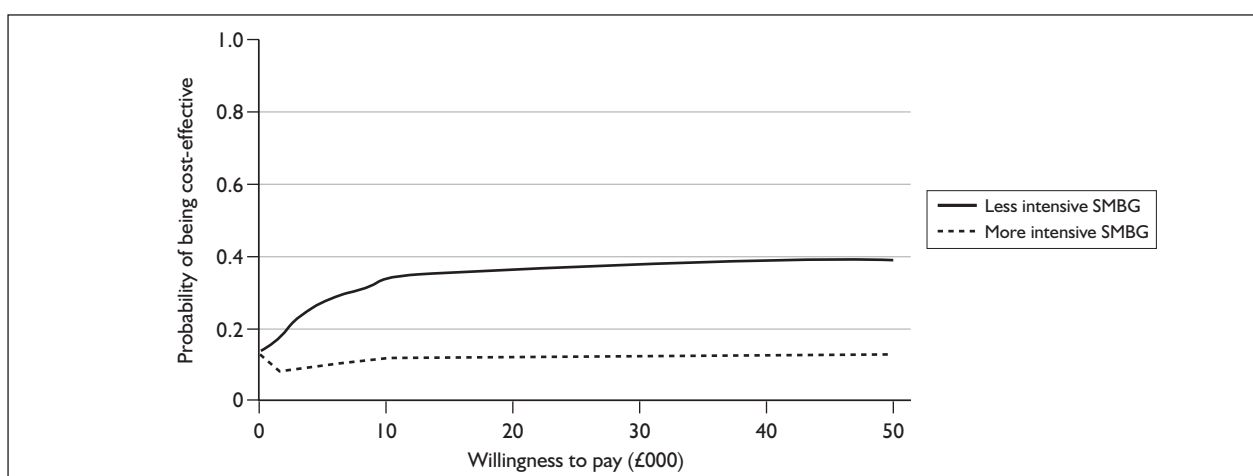

FIGURE 6 *Cost-effectiveness acceptability curves: probability that self-monitoring of blood glucose (SMBG) is cost-effective compared with standardised usual care as a function of decision makers' maximum willingness to pay for an additional QALY.*

Chapter 5
Well-being, beliefs and self-reported behaviour

Methods

Questionnaires were included at baseline and 12 months to measure dietary intake and physical activity (the diabetes self-care activities questionnaire with five subscales),[51] medication adherence (the medication adherence rating scale),[52] and the scores in the diabetes treatment satisfaction questionnaire[53] and the well-being questionnaire (12 items).[54]

Beliefs about diabetes and its management were assessed using the revised illness perceptions questionnaire (IPQ-R)[55] which has eight subscales. The beliefs about medicines questionnaire (BMQ)[56] with two-subscales was used to assess beliefs about medication benefits and harms; the medication adherence report schedule (MARS,[57] one subscale) was used to report medication adherence, and a self-reported questionnaire (summary of diabetes self-care activity, SDSCA,[58] five subscales) assessed eating and physical activity. Treatment satisfaction was assessed with the Diabetes Treatment Satisfaction Questionnaire (DTSQ,[58] three sub-scales) and overall well-being with the well-being questionnaire (W-BQ12).[59] Attitudes to SMBG were assessed with the self-monitoring blood glucose beliefs questionnaire (4 subscales).[60]

The response set used for the analysis presented here comprises those patients responding to questionnaires at both baseline and 12 months. All analyses are conducted using analysis of covariance (ANCOVA), adjusting for baseline values.

Mediation analysis

We set out to establish whether differences between groups in the extent to which any change over time in outcome measures (behavioural, emotional or clinical) was due to differences in beliefs about SMBG or illness perceptions by means of formal mediation analyses, conducted using the approach recommended by Baron and Kenny.[61] This approach involves the calculation of four separate regression equations and satisfaction of the following criteria: (1) the outcome measure was significantly predicted by group; (2) the belief measure was significantly predicted by group; (3) the outcome measure was significantly predicted by the belief measure; (d) the outcome measure was significantly predicted by the belief measure and group in the same regression equation, with the belief variable remaining statistically significant. If the relationship between group and outcome measure is reduced in the fourth regression analysis, then we have at least partial mediation. If the effect of group is reduced by a significant amount to a level of non-significance (i.e. $p > 0.05$), then there is complete mediation: the differences on the outcome measure between groups is due entirely to its effect on the belief measure. To ensure the mediation analyses reflect change in outcome measures, the outcome measure scores used in these analyses were the unstandardised residuals saved after the baseline scores were used to predict the follow-up scores.

Results

Of the 453 patients randomised in the trial, 339 (74.8%) completed questionnaires at baseline and 12 months and were included in the final analysis.

Differences between groups in belief changes over time

Group differences in mean scores on belief measures at follow-up, adjusted for baseline scores, are shown in *Table 12*. Changes in illness beliefs did not significantly differ between groups, with the exception of beliefs about consequences ($p = 0.004$). The mean difference in change in consequence scores from baseline to 12 months between the control group and the less intensive intervention group (not adjusted for baseline) was 0.92 (95% CI −0.07 to 1.91; Cohen's $d = 0.19$), and between the control group and the more intensive intervention group was 1.59 (95% CI 0.66–2.51; $d = 0.36$).

A significant difference was also found in the change in mean belief scores between the three groups for beliefs concerning feeling negative about self-testing ($p < 0.001$) and the importance of self-testing ($p < 0.001$). The mean difference in change in feeling negative about self-testing scale scores from baseline to 12 months between the

TABLE 12 Comparison of changes in mean scores (SD) between groups on measures assessing beliefs about illness, self-monitoring of blood glucose and medication from baseline to 1 year

	Cronbach's α	Usual care: no meter (n = 113)		Self-testing (n = 121)		Self-monitoring (n = 105)		p-value for difference between groups
		Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up	
Illness perceptions (IPQ-R)								
Identity[1]	NA	2.2 (2.8)	1.7 (2.2)	1.7 (2.2)	2.0 (2.4)	1.8 (2.1)	1.8 (2.0)	0.054
Timeline: acute/chronic[2]	α = 0.81	24.5 (4.1)	25.0 (3.6)	24.4 (4.0)	24.6 (4.3)	25.3 (3.5)	25.4 (4.0)	0.61
Timeline: cyclical[3]	α = 0.87	10.4 (3.3)	10.0 (3.1)	10.4 (3.0)	10.4 (3.1)	10.6 (2.9)	10.7 (3.1)	0.33
Consequences[4]	α = 0.68	17.3 (3.9)	16.8 (4.3)	16.9 (3.7)	17.4 (4.2)	17.2 (3.4)	18.3 (3.8)	0.004
Personal control[5]	α = 0.76	24.1 (3.1)	24.3 (2.8)	24.2 (2.7)	24.1 (3.5)	24.7 (3.1)	25.0 (3.6)	0.30
Treatment control[6]	α = 0.40	18.2 (1.9)	17.8 (2.0)	18.3 (2.0)	18.3 (1.9)	18.6 (2.0)	18.1 (2.5)	0.29
Illness coherence[7]	α = 0.88	16.9 (4.1)	17.4 (4.4)	16.6 (4.5)	17.8 (4.1)	17.1 (4.1)	18.2 (4.1)	0.36
Emotional representations[8]	α = 0.87	15.3 (4.3)	15.0 (4.0)	15.1 (4.7)	15.3 (4.6)	15.6 (4.7)	15.4 (4.8)	0.58
Self-monitoring of blood glucose beliefs								
Feel negative about self-testing[9]	α = 0.65	5.5 (1.8)	5.9 (1.9)	5.5 (1.7)	4.6 (1.4)	5.3 (1.7)	4.3 (1.6)	< 0.001
Symptoms make test unnecessary[10]	α = 0.69	5.1 (1.4)	5.2 (1.7)	5.0 (1.6)	5.3 (1.7)	5.1 (1.8)	5.2 (1.7)	0.96
Important to self-test[11]	α = 0.36	6.4 (1.4)	6.1 (1.3)	6.4 (1.4)	6.9 (1.5)	6.5 (1.6)	7.3 (1.6)	< 0.001
Checking is painful[12]	NA	2.1 (0.8)	2.2 (0.9)	2.3 (0.8)	2.1 (0.9)	2.2 (0.8)	2.0 (0.9)	0.21
Beliefs about medication (BMQ)								
Necessity[13]	α = 0.82	19.1 (2.3)	18.9 (2.4)	18.5 (3.2)	18.6 (2.9)	18.7 (2.9)	19.4 (2.8)	0.28
Concerns[14]	α = 0.77	13.7 (2.9)	13.3 (3.2)	13.6 (3.9)	13.1 (3.5)	13.3 (3.8)	13.4 (3.9)	0.75

IPQ-R, revised illness perceptions questionnaire; NA, not applicable.
Missing data for scales: [1]0; [2]25; [3]23; [4]25; [5]19; [6]26; [7]29; [8]18; [9]31; [10]40; [11]37; [12]35; [13]104; [14]106.
BMQ scales completed only by patients taking medication at baseline.

control group and the less intensive intervention group (not adjusted for baseline) was −1.37 (−1.83 to −0.91; $d = 0.57$), and between the control group and the more intensive intervention group was −1.52 (−2.01 to −1.02; $d = 0.63$). The mean difference in change in the importance of self-testing scale scores from baseline to 12 months between the control group and the less intensive intervention group (not adjusted for baseline) was 0.72 (0.24–1.19; $d = 0.31$) and between the control group and the more intensive intervention group was 1.08 (0.55–1.61; $d = 0.45$). No differences in change between groups were found in either of the other two measures concerning beliefs about SMBG, nor were differences found in changes in beliefs about medication between groups.

Differences between groups in outcome changes over time

Group differences between the mean scores on behavioural and emotional measures at follow-up, adjusted for baseline scores, are shown in *Table 13*. There were significant differences in scale score changes on the general diet scale of the SDSCA between groups ($p = 0.014$), as well as the specific diet items concerning fruit and vegetables ($p = 0.006$) and high-fat foods ($p = 0.022$). The mean difference in change in SDSCA general diet scores from baseline to 12 months between the control group and the less intensive intervention group (not adjusted for baseline) was 0.12 (−0.33 to 0.57; $d = 0.06$) and between the control group and the more intensive intervention group was −0.50 (−1.00 to 0.01; $d = 0.23$). The mean difference in change in the SDSCA fruit and vegetables item from baseline to 12 months between the control group and the less intensive intervention group (not adjusted for baseline) was −0.26 (−0.72 to 0.19; $d = 0.12$) and between the control group and the more intensive intervention group was −0.79 (−1.30 to −0.28; $d = 0.34$). The mean difference in change in the SDSCA high-fat foods item from baseline to 12 months between the control group and the less intensive intervention group (not adjusted for baseline) was −0.03 (−0.48 to 0.40; $d = 0.02$), and between the control group and the more intensive intervention group was 0.51 (0.01–1.00; $d = 0.23$).

No differences were found in changes in either self-reports of exercise or medication adherence between groups, nor did groups differ in terms of their changes in treatment satisfaction or well-being scores.

Mediation analysis

Formal mediation analyses were used to investigate the effects of the intervention groups on all outcomes that had statistically significant differences in mean change score between groups. There were such differences on four outcome measures: cholesterol ($p = 0.010$), general diet ($p = 0.014$), specific diet (fruit and vegetables, $p = 0.006$) and specific diet (high fat, $p = 0.022$). Only three belief measures were significantly different between groups: beliefs about consequences ($p = 0.004$), feeling negative about self-testing ($p < 0.001$) and the belief that it is important to self-test ($p < 0.001$). Of the four outcome measures, only two were significantly related to any of the three belief measures: change in cholesterol was predicted by feeling negative about self-testing ($β = 0.130$, $p = 0.016$) and change in self-reported fruit and vegetable consumption was predicted by consequence beliefs ($β = −0.125$, $p = 0.031$). In a regression analysis with group and feeling negative about self-testing used to predict change in cholesterol, group remained a significant predictor ($β = −0.114$, $p = 0.046$), while feeling negative about testing became non-significant ($β = −0.090$, $p = 0.113$). Similarly, in a regression analysis with group and beliefs about consequences used to predict change in self-reported fruit and vegetable consumption, group remained a significant predictor ($β = −0.168$, $p = 0.004$), while beliefs about consequences were non-significant ($β = −0.099$, $p = 0.086$). There was no evidence of even partial mediation of the effects of the intervention on any outcome measure by the belief measures.

Summary of findings

Among patients allocated to use of more intensive SMBG compared with those allocated to usual care over 1 year, there was a small, but significant increase in level of beliefs about the severity of the consequences of diabetes. However, there were no differences between groups in mean changes in beliefs about personal control over diabetes and the perceived effectiveness of treatment. In addition, there was no observed effect on the mean change in well-being between groups. There was a small but significant effect on self-reported dietary behaviour, with patients allocated to usual care reporting changes towards healthier eating patterns than those allocated to more intensive monitoring. Change in beliefs about the consequences of diabetes did not mediate the self-reported changes in dietary behaviour observed between groups.

TABLE 13 *Comparison of changes in mean scores (SD) between groups on behavioural and emotional outcome measures from baseline to 1 year*

	Cronbach's α	Usual care: no meter (n = 113)		Self-testing (n = 121)		Self-monitoring (n = 105)		p-values for differences between groups
		Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up	
Self-care behaviours (SDSCA)								
General diet[1]	0.93	5.2 (1.8)	5.6 (1.5)	5.0 (1.8)	5.5 (1.3)	5.2 (1.8)	5.1 (1.9)	0.014
Specific diet[2]	0.08	5.4 (1.2)	5.9 (1.1)	5.3 (1.2)	5.7 (1.0)	5.5 (1.4)	5.4 (1.3)	< 0.001
Specific diet: fruit and vegetables[3]		5.2 (1.8)	5.7 (1.6)	5.1 (2.0)	5.4 (1.7)	5.4 (1.9)	5.2 (2.0)	0.006
Specific diet: high fat foods[4]		2.4 (1.7)	1.9 (1.5)	2.5 (1.6)	2.0 (1.4)	2.3 (1.8)	2.4 (1.5)	0.022
Exercise[5]	0.75	3.3 (2.1)	4.0 (2.2)	3.2 (2.2)	3.6 (2.2)	3.4 (2.2)	3.9 (2.4)	0.45
MARS[6]	0.62	24.0 (1.6)	24.1 (2.0)	23.9 (1.6)	24.0 (1.4)	24.0 (1.3)	24.1 (1.2)	0.91
DTSQ	0.84	29.3 (6.8)	30.0 (5.3)	29.4 (6.5)	29.7 (5.6)	29.7 (5.4)	30.1 (5.5)	0.93
How often felt blood sugar unacceptably high[7]		1.7 (1.7)	1.9 (1.9)	1.5 (1.6)	2.3 (1.5)	2.0 (1.7)	2.4 (1.7)	0.053
How often felt blood sugar unacceptably low[8]		0.6 (1.2)	0.7 (1.3)	0.7 (1.3)	0.7 (1.2)	0.8 (1.3)	0.8 (1.3)	0.97
W-BQ12[9]	0.87	25.1 (6.3)	25.9 (5.8)	24.3 (6.8)	24.5 (7.0)	25.2 (6.3)	24.9 (6.4)	0.38

DTSQ, diabetes treatment satisfaction questionnaire; MARS, medication adherence rating scale; SDSCA, summary of diabetes self-care activity; W-BQ12, well-being questionnaire.
Missing data for scales: [1]40; [2]32; [3]28; [4]30; [5]37; [6]96; [7]92; [8]93, [9]32.
MARS completed only by those taking medication at baseline. DTSQ scales completed only if some experience of SMBG.

Chapter 6
Qualitative interviews: methods and results

Methods

Semi-structured interviews with patients taking part in the DiGEM trial were used to explore the experiences and perspectives of SMBG. A sample of 40 patients was recruited from participants in the clinical trial. Trial participants were contacted by post and asked if they would like to take part in a related substudy, involving a single, semi-structured interview, to discuss their experience of having diabetes and taking part in the trial. Invitations were sent to those who had been in the trial for a minimum of 3 months to ensure that patients had at least undergone their 3-month follow-up visit with the study nurse, and so would be able to discuss their views on the feedback they had received about their glycaemic control, enabling a comparison across the three intervention groups.

Interviews were conducted with the first 20 participants who replied positively to the invitation. After the first group of interviews had been conducted and the characteristics of these participants determined, we adopted a purposive sampling technique to recruit the remaining participants. Further letters of invitation were sent only to those whose characteristics had not been represented in the initial interviews with patients selected to span a range of age groups, socioeconomic classifications, both genders and the three intervention groups. Selection was also balanced to obtain an equal number of participants attending clinics with each study facilitator, as well as a range of baseline medication adherence scores (as assessed by the self-reported MARS questionnaire) and dietary and exercise behaviours (assessed by the self-reported SDSCA questionnaire). All respondents were given the option of being interviewed on a weekday or at the weekend and in a place of their choosing so that employed people and those who were not mobile would not be excluded.

Interviews were semi-structured in design to allow both open-ended questioning, which would allow respondents to speak in an undirected fashion, and inquiry about specific topics. The interview began with questions about demographics, followed by an illness narrative, in which patients were encouraged to talk at length about their experiences since being diagnosed with diabetes. In the second part of the interview, inquiry was made about specific topics, which are summarised in *Box 1*. The interviews lasted between 25 and 90 minutes.

BOX I *Topics for specific inquiry in qualitative interviews*

Self-care behaviours affecting control of diabetes

Understanding of the randomised controlled trial (RCT) process

Usefulness of taking part in the RCT

Comparison of SMBG and clinic monitoring

Usefulness of knowledge of glycaemic control

Use of SMBG – ease, prompts, timing, relationship to behaviour

Analysis of the interviews was conducted concurrently with data collection to facilitate exploration of emergent themes in ongoing interviews. The grounded theory approach was used, in which the analytical themes are derived from or 'emerge' from the data.[16] The transcripts from the semi-structured interviews were imported into the NU*DIST computer program (QSR International, 2002).

Interview transcripts were read and reread in order to identify general themes. Any text relating to SMBG was highlighted and assigned a unique code under one of these general themes. These themes were determined as the transcripts were read and added to the coding structure as necessary. Items in general themes were compared with each other and coding was refined to produce subthemes based on the similarities and differences between items. Broader categories were then identified and text units reviewed to ensure all categories emerging from the data had been identified. Results were gathered into broad categories to facilitate discussion.

Results of in-depth interviews on trial participants

Participant characteristics

Forty patients were interviewed. Their characteristics are summarised in *Table 14*. Characteristics of patients sampled represented the range of participants included in the trial, including age, socioeconomic status and participation in each of the trial's three allocated interventions.

Perspectives of SMBG

Interviewees' perspectives of SMBG focused around three main themes: awareness, influence on health behaviour and empowerment. Both benefits and disadvantages associated with these themes were expressed and these are presented together to illustrate the range of patient views.

Awareness
Increased awareness of diabetes

Several patients raised an increased awareness of having diabetes as a consequence of SMBG. The presence of an elevated blood sugar on monitoring was viewed by respondents as tangible evidence of an abnormality. One interviewee, who earlier in her interview had commented that she had thought her diabetes was curable and only temporary when diagnosed, noted that SMBG had helped to demonstrate that there was a persistent abnormality:

Well, it makes it real that you've got it. That there, there is sugar there.

(D21, 57-year-old woman, group 3)

Although the increased awareness of diabetes was typically viewed as beneficial, two respondents considered it a disadvantage. In one instance, this was a perceived disadvantage as the respondent had never self-monitored. She controlled her illness with lifestyle changes and felt quite strongly that monitoring her blood sugar would distress her:

I would feel like an ill person. I would walk about feeling 'I am a sick person' and I'd hate that because I know that I'm not, I'm a healthy animal.

(D22, 71-year-old woman, group 1)

This respondent clearly placed significant emphasis on her self-image as a 'healthy' person which she felt would be threatened by constant reminders of illness. SMBG may have been particularly significant for her because she did not have the daily reminder of taking medication which might reinforce the presence of disease in other patients. This illustrates a potential barrier to initiating SMBG in non-pharmacologically treated patients who may not consider themselves ill, and find close monitoring unnecessary and distressing. This did not seem to be a concern once SMBG had been started; however, none of the non-pharmacologically treated patients who self-monitored during the trial expressed distress that their awareness of their diabetes had increased.

TABLE 14 *Characteristics of interview participants*

	Patients interviewed (*n* = 40)
Age, years [mean (SD)]	68.5 (9.0)
Socioeconomic classification [n (%)]	
Managerial and professional occupations	26 (65)
Intermediate occupations	3 (7.5)
Small employers and own account workers	1 (2.5)
Lower supervisory and technical occupations	6 (15)
Semi-routine and routine occupations	3 (7.5)
Group allocation (%)	
Standard care (group 1)	12 (30)
Less intensive self-monitoring (group 2)	12 (30)
More intensive self-monitoring (group 3)	16 (40)

A second respondent, who felt increased awareness of diabetes, acknowledged that she had never made a concerted effort to control her illness. She reported that SMBG was:

> … a sort of reminder of the fact that you know that I've got something wrong with me…I don't like to be reminded particularly.
>
> (D15, 67-year-old woman, group 2)

It is difficult to distinguish whether she preferred not to be reminded of her diabetes because she was not actively controlling it or whether she did not actively control it because she tended not to be conscious of it.

Increased understanding of the relationship between physical symptoms and blood sugar

Some participants noted that SMBG helped them to establish the relationship between their physical symptoms and their blood sugar. Most of the interviewees who reported this benefit checked their blood sugar to confirm suspected hypoglycaemia, rather than suspected hyperglycaemia. One participant who had a medical condition whose symptoms were similar to hypoglycaemia commented:

> And as I said, whenever I have one of these bad bouts I always, now I've got the equipment, I always go and check my blood to make sure that, which one or what, which one it is that's doing the problem.
>
> (D3, 65-year-old man, group 3)

Only those respondents who had been exposed to monitoring, either as part of the trial or previous occasional users, considered SMBG as a tool to detect hypoglycaemia. Those who had never used the technology perceived it solely as a tool for detecting hyperglycaemia, analogous to the blood tests that they had at their GP surgery. As such, several felt that SMBG was a redundant further check on glycaemic control and could lead to unnecessary worry:

> I feel I get it done often enough so that quite suits me. I think very often [um] you could get worried if you keep doing it …I'd rather just have it done there at the doctor's surgery.
>
> (D18, 78-year-old woman, group 1).

Reassurance about health status

Awareness of blood sugar levels provided reassurance for several respondents. Some interviewees used SMBG to ensure that previously detected high readings had returned to normal, while others felt that readings within normal parameters indicated their diabetes had not worsened. This could be comforting, particularly given the time frame between visits to their health professional. For example:

> So if I woke up one morning and took it on a fasting reading and it was, I don't know, 22 or 24, for example, then the alarm bells really would start to ring. But because it's, they've been contained within a, a band which doesn't seem to ever increase as dramatically as what I've indicated, then there is a crumb of comfort there, if you see what I mean.
>
> (D8, 62-year-old man, group 2)

Reassurance was clearly associated with normal readings. Readings outside the specified parameters were associated with feelings of failure. These participants described making efforts to adhere to dietary and physical activity recommendations as part of their diabetes control strategies, and abnormally high readings may have been considered a failure of these efforts:

> I think I'm disappointed because I feel, I suppose, in a way that I've failed, even though you know, I sit there afterwards and think, well no, I didn't actually, I haven't done anything I shouldn't have done, so why do I feel it, but I still do. I feel guilty and, and a bit of a failure and I don't know why.
>
> (D33, 45-year-old woman, group 3)

Some respondents in both the comparison and the less intensive monitoring groups felt that other patients might become obsessed with checking blood sugar if they had access to a monitor. This was not a concern in the more intensive monitoring group, perhaps because the readings were being used to support behaviour change and were therefore thought necessary.

Understanding of diabetes

Two participants volunteered that SMBG helped them to understand their diabetes by illustrating the fluctuations in blood sugar. One commented:

> I would have thought that was a good idea, just to give every, anybody, when they first get it a meter, and to do it for 3 months, even just for 2, 2 or 3 months, even if you take it back off them then, at least they can see what, you know, what's happening to the body and [um],

and they'd understand it more.

(D25, 69-year-old man, group 2)

Respondents in both monitoring groups reported frustration when they were unable to understand why they got the SMBG values they did:

> … it seems to me that the figures, other than the fasting reading, are very high some days, reasonable the next, I cannot see why this should be, because when I think I, I think 'Ooh I've over-indulged a little bit my figures will be really high', they're not necessarily high. And other times when I've had a very lean day in terms of what I've eaten, the figures can be high. And I can't, I cannot see a, a, a balance of why this should be as I've said, and that's the only thing about taking these readings that tends to confuse me a little, because I just cannot make sense of it.

(D8, 62-year-old man, group 2)

This suggests that the benefits derived from illustrating fluctuations are related to the ability to understand the relationship between fluctuations and behaviour, rather than simply observing them.

Health behaviour
Assessing the effect of self-management behaviour

Some participants felt they had the ability to use SMBG to assess the effects of behaviour. Facilitators encouraged participants in the more intensive monitoring group to experiment with the timing of their monitoring to see, for example, how certain food affected their blood sugar. Interviewees confirmed that this was a useful strategy for SMBG:

> I think you can certainly tell whether you've eaten the wrong things. Or whether you've overdone it and then you obviously need to go and correct that by doing exercise or being extremely good, you know.

(D33, 45-year-old woman, group 3)

Although participants in the less intensive monitoring group were not encouraged to use SMBG as a check on their behaviour, some reported having done so. One participant noted:

> But, the thing that has, has also been extremely helpful with the exercise is that because you're monitoring your blood sugar levels, you actually see what pushes it up and what, what doesn't. Not only in connection with what you eat, but what you're doing, so that you can stray

from straight and, and narrow in terms of diet provided you are active enough. Whereas you can eat the same things and if you're not active you know it shows – immediately.

(D15, 67-year-old woman, group 2)

Promoting adherence to self-management behaviour

A related theme, promotion of adherence to self-management, also emerged as a benefit of SMBG. As noted previously, adherence to these behaviours is often less than optimal in people with diabetes. Interviewees in both the less and more intensive monitoring groups felt that SMBG was a useful tool in providing discipline and helping them to adhere, because it demonstrated what happened when they failed to do so:

> I think it has, yes, that it is really important that I do take the medication. Because I've seen exactly what happens if I forget to take those night time pills from monitoring the blood sugar, I can see what happens and, so yes it has had an effect, yeah.

(D15, 67-year-old woman, group 2)

The previous subtheme relates to behaviour change which was prompted when specific instances of non-adherence, such as not taking medication, demonstrated elevated blood glucose. Elevated readings also prompted behaviour change even when they were not attributable to a particular behaviour.

> So if I'm very, if I'm high which, by that I mean by over ten which I know that's probably much too high by everyone else's standards but by my standards I think ten isn't too bad, but if I go over ten then I will take great care with my diet for two or three days till I bring it right down to about five or six.

(D4, 67-year-old man, group 3)

Respondents in both monitoring groups with a range of characteristics reported using SMBG to provide information about the general state of their diabetes, suggesting that this was a widely derived perceived benefit of SMBG. The trial intervention was based on the hypothesis that SMBG could provide two types of feedback to patients: feedback on their general diabetes control and feedback on specific behaviour which might influence glycaemic control. The data from the qualitative study suggest that both these methods of feedback were employed by some respondents in both monitoring groups.

Failure to see improvement after modifying behaviour was discouraging. Several interviewees, all of whom were in the more intensive monitoring group, commented on how little their behaviour seemed to impact on their blood sugar. For example:

> But, but, even if I, even if I do everything they say, for a couple of days, I still don't get good readings, so you know there's nothing there to encourage me, saying oh, you know 'I didn't have a drink for two days, I didn't eat a pork pie, I didn't have a packet of crisps, I didn't have any bacon, I didn't fry any food and look at that, my reading is six, that is wonderful'. Oh no, it's still seven, it's still eight, you know, and so you don't think to yourself that's the way forward, because nothing's happening, I'm just the same, it doesn't seem to matter whether I have ten pints, I mean I don't have ten pints, but you know, it doesn't seem to matter if I have a lot to drink or a little to drink, my readings very, very rarely alter, they're all between 7 and 10, depending which time of day I take them.
>
> (D1, 60-year-old man, group 3)

Participants in the more intensive self-monitoring group were encouraged to make lifestyle changes and to keep track of them by SMBG. Although changes such as those discussed by this interviewee, if maintained, might result in longer-term improvements in glycaemic control by contributing to weight loss, the impact would not be apparent in the shorter term. The lack of immediate feedback from the monitoring may have contributed to this perspective. Other incentives might be needed to encourage maintenance of behaviour change in these patients.

Comments regarding the role of SMBG in assessing and promoting behaviour were generally made by those who had been exposed to the technology either before or during the trial. Only one SMBG-naïve respondent in the comparison group commented on this use of SMBG. Not surprisingly, she placed less emphasis on its role than those who had used the technology:

> And you see you can't, whether you, you check it at home or not it doesn't make any difference, you have to, still have to do the right thing you see.
>
> (D20, 73-year-old woman, group 1)

Two participants volunteered that they timed their SMBG to ensure they only got satisfactory readings. One respondent did this by testing only on days on which he felt he had adhered to his regimen, while the other strayed from her regimen only when not testing:

> I have to say this now, that I be – be completely honest here, on the days I check me blood I behave meself, whereas I can come – I come in this morning lunch time, I say when I have me breakfast about, quarter past eight this morning, then I went into town, I come back, well I might have a, I might have occasionally have a treat, a cup of tea, about half ten I'll read the paper and have a cake, but I won't when I'm about to have the blood check, so that makes me stick to something, now I don't know what the difference to me to have the cake because, I guess there'll be some sugar in it so that would probably send it the wrong way really, you know.
>
> (D11, 64-year-old man, group 2)

Empowerment
The third major theme emerging from the data was empowerment. This related to respondents' access to a convenient method of assessing glycaemic control that allowed them more control over their health care and their ability to contribute to their physician's evaluation of their status.

Convenience
Several participants raised the convenience of SMBG as a benefit. It allowed them to check on their glycaemic control whenever they wanted, without having to visit their surgery:

> You've only got to press a button and it will show you your averages for the period, so it's no problem, no difference but then you haven't got the inconvenience of making appointments and sitting in doctor's surgery, etc. and then going back for the results.
>
> (D30, 53-year-old man, group 2)

These participants might be using SMBG to support their self-care activities, and therefore desire frequent feedback on their glycaemic control, which would be inconvenient to arrange at a GP surgery.

The convenience of SMBG was tempered by the physical discomfort reported by some respondents. Several previous studies identify physical

discomfort as a barrier to or disadvantage of SMBG.[4,5,8,18] While interviewees in both monitoring groups reported some physical discomfort associated with use of SMBG, this was noted to be trivial:

> It, it's not particularly pleasant, but it's not that bad.
>
> (D12, 68-year-old man, group 3)

Fear of the discomfort associated with SMBG was not a significant deterrent to the respondents in either of the monitoring groups or the comparison group, where only one respondent raised a fear of needles as a potential barrier to the use of SMBG. The interruption of routine caused by SMBG and the expense to the NHS were also raised by respondents.

Initiation of physician visits

Respondents also noted that SMBG allowed them to initiate physician visits if they thought it was warranted, allowing them to take more responsibility for their care. One reported:

> … any trend that comes up with, I don't have to wait for a doctor to tell me the answer. I mean if I have any problems, if I find my blood sugar low, low, low, I can go straight into the doctor and say 'Look what's happening.' If I have to wait for somebody else then I could be done by then.
>
> (D3, 65-year-old man, group 3)

Initiation of physician visits was reported by patients in both monitoring groups as well as in one patient in the comparison group who had been previously exposed to monitoring, suggesting that this was a widely experienced benefit.

Informing health-care decisions

Although respondents appeared to use their SMBG results primarily to inform their own behaviour, some did report that they considered these values an important source of information and, as such, showed their values to their health-care professionals outside the setting of the trial. As described previously, trial participants received two different levels of advice and feedback from study facilitators, depending on group allocation, but adjustments to medication were done by the participant's GP. Some participants, all of whom were in the more intensive monitoring group, felt that SMBG values were important in informing treatment. This may reflect their trial group allocation, as the potential of SMBG to evaluate

and inform treatment decisions was emphasised in this group. The emphasis may also account for the confusion described by these participants when discussing the value placed by health-care professionals on their SMBG. Participants felt more emphasis was placed on HbA1c than on SMBG, especially if these elicited contrasting information. One participant who was monitoring intensively felt her physician was ignoring important information, rendering monitoring a waste of time.

> Well, I think what a waste of, what a waste of effort, you know, there's a lot of information here that that would give them more feedback than they can obviously do from one reading, once in six months.
>
> (D40, 71-year-old woman, group 3)

Comparison of SMBG and HbA1c

Although use of SMBG may have enabled some participants to feel more in control of their diabetes, only two respondents expressed an absolute preference for SMBG over periodic clinic visits and HbA1c. One was concerned that the feedback from her health-care professional was deficient and felt her only source of feedback was SMBG. The other participant, in the less intensive monitoring group, felt that clinic assessment was unable to give an accurate measurement as it was a one-off reading:

> I can keep a more up-to-date tab on it. I mean, for example, if it were every 3 months, on the occasion of that third month, I might go along when it, it could be as low as anything on here. Now, another day before or after it might be high, but I wouldn't know that, so this is by far the better thing, in my view.
>
> (D8, 62-year-old man, group 2)

This respondent thought that the blood tests carried out at his surgery provided the same information (i.e. his blood sugar at that point in time) as those taken at home and therefore could not detect variations. Consequently, he felt more regular monitoring to detect such variations was necessary. This reflects a misunderstanding of the nature of HbA1c tests, which was not noted in other interviews.

Some respondents, all of whom were in the comparison group, expressed a preference for clinic testing. While willing to test if their health-care professionals thought it necessary, they were somewhat reluctant to do so, commenting on the appropriateness of that level of health-care involvement and their ability to carry it out:

I don't think it's a good thing for people to mess about like that, unless the doctor suggests that I get something of that nature, then I would. But I would only do it, under his instruction or if he told me or showed me how to do it, or the nurse. I don't mess about with those sort of things on my own.

(D10, 80-year-old man, group 1)

I think I might prefer possibly to, to do, stick to the 3 months, really. I mean I would do the other way if, if, if they thought it was of benefit to, to them and to me. But I think I, as I say, my, my, my memory is not the best. I, I'd forget it now and again and then that would, you know, probably upset the whole system.

(D27, 74-year-old woman, group 1)

Most of the respondents in this study reported using their SMBG values to guide their behaviour, rather than depending on interpretation by their health-care professional or study nurse. Participants who require continued significant input from health-care professionals may therefore not benefit as much from use of the technology. Anxieties about misuse of SMBG might be allayed by reassurance that SMBG was an adjunct rather than a replacement for standard care. The absence of these concerns in those actually monitoring suggests that they might be overcome with exposure to SMBG and appropriate education.

Most respondents, however, described benefits of utilising both HbA1c and SMBG. The value of HbA1c in giving a longer-term assessment of glycaemic control than SMBG gave was widely praised, as were the other services provided at clinic visits:

The nurse does checks on me feet and she does me urine, urine test and things like that, and weighs me and all that.

(D25, 69-year-old man, group 2)

The wide range of participants who reported this benefit suggests that most people recognise a role for dual monitoring strategies, with distinct objectives for each strategy.

Comparison of SMBG and urine monitoring

Perceptions about accuracy were relevant to perceptions of empowerment, with participants who felt that SMBG was inaccurate being less likely to use it or to feel that their results were relevant to their management. Concerns about the accuracy of SMBG, in comparison with urine testing, were also reported.

Three participants compared SMBG to their experience with urine monitoring. While urine monitoring was simple, all felt it was not as accurate and did not provide adequate information, supporting previously published findings:[21]

Well I had some little strips which you put in your urine and I think it's, is it red is it? And they go blue, or they go a different colour anyway, and I noticed once when I'd just checked it a- and I had had some chocolate or something and it, went the wrong colour completely, and I thought 'Well, I know that was wrong for me.' But no, there wasn't, it wasn't the same as with this because it's not very good method that really. It's like – if it goes the wrong colour, you don't know how bad it is really, do you?

(D11, 64-year-old man, group 2)

Although SMBG was thought to be more accurate than urine monitoring, participants expressed reservations about its accuracy when compared with HbA1c. Three participants across both monitoring groups expressed reservations about the accuracy of SMBG. Doubts about accuracy were related to the volume of blood, with one patient feeling that the blood tests done at the surgery should have been more accurate by virtue of the larger quantity of blood. Another patient obtained a lower reading after washing his hands and felt this was a reflection of the accuracy of the technique:

I have my doubts sometimes, have my doubts. Like I washed my hands. I came down, where did I come from, I went somewhere. Anyway I came in, took my blood sugar and it was 11 something. And I said to my wife, I said that's got to be wrong. She said wash your hands. So I did and it went down to 10.0. That makes a difference.

(D29, 75-year-old man, group 3)

In this instance, the patient attributed the difference in readings to deficiencies in the meter, rather than in his technique. Appropriate technique and informing patients about potential sources of error might reduce this and increase confidence in the accuracy of the meter.

Chapter 7
Discussion

Interpretation of results

Clinical outcomes

Our results showed no convincing evidence of improvement in glycaemic control after 12 months in patients with non-insulin-treated type 2 diabetes using SMBG, compared with those not using SMBG. There was no evidence of improved glycaemic control in predefined subgroups of patients although the data do not exclude the possibility of a clinically important benefit for specific subgroups of patients in initiating good glycaemic control. There was no evidence that monitoring plus additional training in interpretation compared with monitoring alone was effective in improving glycaemic control. Despite the lack of clinical benefit, more patients receiving the SMBG interventions recorded harm in terms of grade 2 hypoglycaemia, but this may be due to an increased awareness of the possibility of low blood glucose from using a meter.

Health economic outcomes

The economic analysis showed that SMBG was significantly more expensive than standardised usual care, by £92 and £84 for the less and the more intensive SMBG groups respectively. There appears to be an initial negative impact of SMBG on quality of life measured using the EQ-5D. The potential additional lifetime gains in QALYs resulting from the lower levels of risk factors achieved at the end of trial follow-up were outweighed by the initial negative impacts for both SMBG groups compared with standardised usual care. Results of the extrapolation also suggest that the incremental lifetime savings in diabetes complications did not offset the additional intervention costs. The cost–utility analysis showed that it is unlikely that either investigated form of SMBG is cost-effective compared with standardised usual care.

Generalisability

This was a large, rigorously designed and conducted randomised controlled trial. We successfully conducted independent randomisation, concealed allocation for measurement of the main outcome and had a low loss to follow-up. Participants were drawn from a well-defined sampling frame with reasons for exclusion recorded. The majority were taking oral hypoglycaemic medication and were not using a meter, with a minority testing no more than once a week. The demographic and clinical characteristics of the trial population at entry were similar to those seen in other trials, although with slightly lower HbA1c. These non-insulin-treated patients under good control represent the target group for current recommendations of up to twice-daily self-monitoring and testing after meals.[62,63] However, it could be argued that the trial does not include sufficient patients with very poor glycaemic control to exclude a benefit of self-monitoring in this subgroup to initiate better control.

Design of trials to evaluate SMBG is difficult because of the need to include education about the use and interpretation of testing,[64] while maintaining an appropriate comparison group which is also given the opportunity to improve self-care activities.[65] We achieved this by providing a common structure for interventions incorporating standardised best practice in all three arms of the trial, within which nurses discussed issues of glycaemic control, assessed by either HbA1c or SMBG, and its role in setting and monitoring self-care goals.[30] The stepwise approach to the interventions across the three arms of the trial allowed examination of what aspects of the intervention, if any, were responsible for improved outcomes. Recent consensus guidelines have based recommendations for SMBG on a theoretical potential to better self-manage glycaemic control.[11,12] We incorporated SMBG into a framework that, based on psychological theory, should have optimised its utility. Careful specification, training and monitoring of consultations ensured that the allocated interventions were delivered as planned.[66]

Although our trial included only 15% of those potentially eligible, it is unlikely that the patients enrolled in our trial were less able to make best use of the procedure than those who were not enrolled. In addition, patients enrolled in our trial were able

to have 3-monthly HbA1c testing. Our results may not be generalisable to groups where this is not possible, although again this seems unlikely. The main limitation to generalisability is, therefore, that the relatively good control of the motivated patients who enrolled for the trial left less room for improvement of HbA1c than in those with initially poorer control who were not motivated to join the study. It remains possible that a subgroup of patients with high initial HbA1c levels, who would gain significant clinical benefit from self-monitoring in initiating better control, might be identifiable.

Comparisons with other studies

Comparisons with early trials of blood glucose monitoring are of limited relevance owing to their small size, the large quantity of blood required by older meters and the skill required for their use. However, more recent trials have been conducted with meters utilising technologies that require smaller amounts of blood and simplified procedures for testing. Our findings support those of a recent small trial using standardised counselling for both intervention and control groups. The trial reported a non-significant HbA1c reduction of 0.17% in the intervention group compared with the control group.[67] However, our findings are less encouraging than the findings of two of the largest trials of SMBG to date, although CIs of differences encompass the estimated effect from recent meta-analyses.[65] One of these trials reported a significant decrease in HbA1c of 0.3% in the intervention group compared with the control group.[20] However, more than 30% of those randomised were lost to follow-up. Initial specific training in use of a blood glucose meter was not matched by additional training for the control group, although all patients received dietary advice regardless of randomisation. A second trial reported a reduction in HbA1c of 0.46% in the intervention group compared with the control group. However, standardised counselling supporting lifestyle modification was provided only to the self-monitoring group.[19] This type of educational support for self-management in itself has been estimated as improving HbA1c by 0.26%.[4]

Fewer people allocated to more intensive monitoring than to less intensive monitoring continue testing. Previous studies have found that trying to understand blood glucose measurements may lead to frustration when results do not fall into a pattern, or may cease to be of interest when they are entirely predictable.[21] The increased recording of hypoglycaemia in the self-monitoring arms may be due to an increased awareness of low blood glucose from using the meter rather than a true biochemical difference between groups. Although no improvement in glycaemic control was observed, there was a small but significant improvement in total cholesterol with the monitoring intervention. Although it is possible that an increased intensity of self-management might lead to this change, it is counter-intuitive that an intervention targeted at glycaemic control should not also have led to improved glycaemic outcomes. These findings may represent a statistical anomaly.

Interpretation of in-depth interviews and questionnaires about well-being, beliefs and behaviour

Changes in beliefs and self-reported behaviour

Questionnaires administered as part of the trial identified that, after 12 months, patients given the more intensive self-monitoring intervention were more likely to consider diabetes a serious condition than those not using a meter. However, there were no differences in the extent to which they felt they had greater control over their condition. The more intensive meter-using group felt less negative about self-testing and considered it more important to self-test than those not using a meter.

The trial was designed around the framework of the CSM of illness representations. The results concerning the beliefs and behaviour measures are in line with the clinical results in suggesting that the intervention failed to modify beliefs and behaviour to the extent necessary to lead to clinical changes. Our prior hypothesis, that SMBG increases patients' perceptions of self-control over their disease, is not supported by these findings. It appears instead that SMBG may increase concerns about the consequences of diabetes.

Views of participants

Patients who perceive themselves as independently interpreting results of SMBG in the light of their self-management behaviour and using them to support improved adherence to self-management had a positive attitude towards the use of SMBG. However, there were also people who expressed a

favourable view[21] of the idea of adherence to health behaviours who seemed to be demotivated if SMBG results did not reflect their efforts. Conversely, negative perspectives were expressed by those who found difficulty in understanding the relationship between their SMBG values and their behaviour, or who experienced no improvement after behaviour modification. Exposure to SMBG appeared to affect these perspectives. Anticipated disadvantages such as physical discomfort, distress from increased awareness of diabetes and undue responsibility for care, which were raised by respondents in the comparison group, were not concerns for those actually monitoring.

Interviews and questionnaires reveal important differences between patients allocated to the three trial interventions in changes in beliefs and attitudes towards diabetes and blood glucose over 12 months. However, the mediation analysis indicated that observed differences between groups of patients allocated to the different interventions in behaviour and outcomes were not explained by the observed changes in beliefs. Despite the perceived conceptual advantages of SMBG revealed though both the interviews and questionnaires, these results need to be placed in the context of the decline in compliance with the more intensive self-monitoring group and the reduction of, at best, 0.2% in HbA1c.

Health economic study – meaning and implications

This is the first detailed economic evaluation of SMBG to be performed prospectively alongside a randomised trial. The economic analysis was closely related to the trial design and was designed to be conservative: the length of the interventions was 1 year and no long-term treatment effects were assumed beyond the first year for any of the groups. As the evaluation was carried out on an intention-to-treat basis, one should be careful when drawing conclusions for specific subgroups of patients (e.g. compliant patients only) from the current cost–utility estimates.

A validated simulation model was used to extrapolate the effects of the interventions beyond the trial period. The uncertainty investigated in this analysis incorporated the first-order uncertainties inherent in the trial design and the simulation model. We also examined the effects

of parameter uncertainty by repeatedly running the model with different sets of bootstrapped parameters, which had the effect of increasing the width of the CIs around the base-case results without any substantial influence on the final cost-effectiveness results.

If the utility analysis had been restricted only to those patients with complete data, it would have greatly reduced the sample size and would also have resulted in biased estimates, as those included are likely to be a non-representative subset of the overall sample by being healthier and more compliant to the allocated intervention. The use of conditional multiple imputation for missing values allowed the whole data set to be analysed.

The increased costs of the enhanced support offered to all groups within the trial may overestimate the costs of implementation in practice, but the additional costs of blood glucose measurement test supplies are of a similar order to this enhanced care. The trial does not provide evidence that the use of SMBG is cost-effective, but if the technology were to be offered to patients, the fall in EQ-5D score observed over 1 year suggests that they should be reviewed regularly and that any concerns about the use of meters should be closely monitored.

Implications for health care

Although the trial did not provide evidence that routine use of SMBG is beneficial, the qualitative study suggests that some individuals may benefit. Our trial suggests that if support for self-management training is available along with 3-monthly HbA1c management, then titration of medication without self-monitoring may be the optimum strategy. However, if HbA1c remains above 8% and progressively deteriorates, then self-monitoring may be necessary in this group and insulin therapy may eventually be required.

Hypoglycaemia remains an issue for some patients using sulfonylurea drugs. However, the majority of such events are associated with changes in food intake or exercise, and therefore are not predictable by SMBG. Nevertheless, use of a monitor may be helpful for people reporting frequent hypoglycaemia, in order to establish whether therapy is too intensive if HbA1c levels are equivocal.

39

Recommendations for research

The qualitative element of the trial identifies a group of patients who consider that use of SMBG provides them with motivation to adopt and maintain behaviours that lead to better diabetes control. Further work is required to characterise those who gain most benefit in terms of glycaemic control and whether this is related to use of the procedure.

Our results suggest that routine use of meters may not be appropriate for reasonably well-controlled patients, although their role in the management of patients with less well-controlled diabetes is not clear. However, a pragmatic strategy of self-management education with HbA1c monitoring may be appropriate in the first instance. If glycaemic control is not then achieved, SMBG may be appropriate, first to explore any potential motivating effect, and second because insulin treatment is likely to be required. Exploring the utility of this strategy may be appropriate, although the potential adverse effect on mood would need to be actively addressed.

There is an increased rate of hypoglycaemia reported among individuals using self-monitoring. Further exploration of hypoglycaemia rates during the trial, questionnaire, HbA1c measures and medication adjustment measures are needed to establish whether these differences are likely to result from biochemical differences or greater awareness of hypoglycaemia as a cause of symptoms.

Conclusions

Routine SMBG for non-insulin-treated patients with type 2 diabetes is not well accepted and appears to offer, at best, small advantages; the cost, effort and time involved in the procedures may be better directed to supporting other health-related behaviours. SMBG may be associated with a negative impact on health status, and is not associated with anticipated improvements in perceived personal control over self-management. Current guidelines for the use of SMBG require review. This trial does not provide convincing evidence to support the routine use of SMBG for non-insulin-treated patients with reasonably well-controlled type 2 diabetes.

Acknowledgements

Contribution of authors

The DiGEM trial group

Publications

Farmer A, Neil A. Variations in glucose self-monitoring during oral hypoglycaemic therapy in primary care. *Diabet Med* 2005;**22**:511–12.

Farmer A, Neil A. In response to 'Variations in glucose self-monitoring during oral hypoglycaemic therapy in primary care' [letter]. *Diabet Med* 2005;**24**:511–12.

Farmer A, Wade A, Frence DP, Goyder E, Kinmouth AL, Neil A. The DiGEM tial protocol – a randomised controlled trial to determine the effect on glycaemic control of different strategies of SMBG in people with type 2 diabetes [ISRCTN47464659]. *BMC Family Practice* 2005;**6**(25):6–25.

Farmer A, Wade A, Goyder E, Yudkin P, French D, Craven A, *et al*. Impact of self monitoring of blood gluscose in the management of patients with non-insulin treated diabetes: open parallell group randomised trial. *BMJ* 2007;**335**(7611):132.

Farmer A, Wade A, Yudkin P, Kinmonth AL, Neil A. Impact of self monitoring of blood glucose on patients with non-insulin dependent diabetes – sub group analysis. EASD Annual Meeting Amsterdam, Amsterdam, 2007.

French DP, Wade A, Yudkin P, Neil HAW, Kinmonth AL, Farmer A. Self-monitoring of blood glucose changed non-insulin treated type 2 diabetes patients' beliefs about diabetes and self-monitoring in a randomised trial. *Diabet Med* 2008;**25**:1218–28.

Simon J, Gray A, Clarke P, Wade A, Neil A, Farmer A. Cost effectiveness of self monitoring of blood glucose in patients with non-insulin treated type 2 diabetes: economic evaluation of data from the DiGEM trial. *BMJ* 2008;**336**:1177–80.

References

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care* 2004;**27**(5):1047–53.

2. UK Prospective Diabetes Study (UKPDS) 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**:837–53.

3. Garfield SA, Malozowski S, Chin MH, Venkat Narayan KM, Glasgow RE, Green LW, *et al*. Considerations for diabetes translational research in real-world settings. *Diabetes Care* 2003;**26**(9):2670–4.

4. Norris SL, Lau J, Smith SJ, Schmid CH, Engelgau MM. Self-management education for adults with type 2 diabetes: a meta-analysis of the effect on glycemic control. *Diabetes Care* 2002;**25**(7):1159–71.

5. The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *New Engl J Med* 2005;**353**(25):2643–53.

6. DAFNE Study Group. Training in flexible, intensive insulin management to enable dietary freedom in people with type 1 diabetes: dose adjustment for normal eating (DAFNE) randomised controlled trial. *BMJ* 2002;**325**(7367):746.

7. Blonde L, Ginsberg BH, Horn S. Frequency of blood glucose monitoring in relation to glycaemic control in patients with type 2 diabetes. *Diabetes Care* 2002;**25**(1):245–6.

8. European Diabetes Policy Group. A desktop guide to type 2 diabetes mellitus. *Diabet Med* 1999;**16**:716–30.

9. Farmer AJ, Neil A. Variations in glucose self-monitoring during oral hypoglycaemic therapy in primary care (letter). *Diabet Med* 2004;**22**(4):511.

10. Davidson MB. Counterpoint: self-monitoring of blood glucose in type 2 diabetic patients not receiving insulin: a waste of money. *Diabetes Care* 2005;**28**(6):1531–3.

11. Owens DR, Barnett AH, Pickup J, Kerr D, Bushby P, Hicks D, *et al*. Blood glucose self-monitoring in type 1 and type 2 diabetes: reaching a multi-disciplinary consensus. *Diabetes Prim Care* 2004;**6**(1):398–402.

12. American Diabetes Association. Standards of medical care in diabetes – 2006. *Diabetes Care* 2006;**29**(Suppl 1):4–42.

13. Martin S, Schneider B, Heinemann L, Lodwig V, Kurth J, Kolb H, *et al*. Self-monitoring of blood glucose in type 2 diabetes and long-term outcome: an epidemiological cohort study. *Diabetologia* 2006;**49**(2):271–8.

14. Davis WA, Bruce DG, Davis ME. Does self-monitoring of blood glucose improve outcome in type 2 diabetes? The Fremantle Diabetes Study. *Diabetologia* 2007;**50**(3):510–15.

15. Karter AJ, Ackerson LM, Darbinian JA, D'Agostino RB, Ferrara A, Liu J, *et al*. Self-monitoring of blood glucose levels and glycaemic control: the Northern Kaiser Permanente Registry. *Am J Med* 2001;**111**:1–9.

16. Coster S, Gulliford MC, Seed PT, Powrie JK, Swaminatham R. Self-monitoring in type 2 diabetes mellitus: a meta-analysis. *Diabet Med* 2000;**17**:755–61.

17. Halimi S. Apports de 'auto surveillance glycemique dans la prise en charge des diabetique insulino (DID) et non insulino dependents (DNID). *Diabetes Metab* (Paris) 1998;**24**(Suppl 3):35–41.

18. Faas A, Schellevis FG, van Eijk JT. The efficacy of self-monitoring of blood glucose in NIDDM subjects: a criteria-based literature review. *Diabetes Care* 1997;**20**:1482–6.

19. Schwedes U, Siebolds M, Mertes G. Meal-related structured self-monitoring of blood glucose: effect on diabetes control in non-insulin-treated type 2 diabetic patients. *Diabetes Care* 2002;**25**(11):1928–32.

20. Guerci B, Drouin P, Grange V, Bougneres P, Fontaine P, Kerlan V, *et al*. Self-monitoring of blood glucose significantly improves metabolic control in patients with type 2 diabetes mellitus: the Auto-Surveillance Intervention Active (ASIA) study. *Diabetes Metab* 2003;**29**(6):587–94.

21. Peel E, Parry O, Douglas M, Lawton J. Blood glucose self-monitoring in non-insulin-treated type 2 diabetes: a qualitative study of patients' perspectives. *Br J Gen Pract* 2004;**54**(500):183–8.

22. Fox MA, Cassmeyer V, Eaks GA, Hamera E, O'Connell K, Knapp T. Blood glucose self-monitoring usage and its influence on patients' perceptions of diabetes. *Diabetes Educ* 1984;**10**(3):27–31.

23. Leventhal H, Nerenz DR, Steele DJ. Illness representations and coping with health threats. In Baum A, Taylor SE, Singer JE, editors. *Handbook of psychology and health*. Hillsdale, NJ: Erlbaum; 1984. pp. 219–52.

24. Hampson SE, Glasgow RE, Toobert DJ. Personal models of diabetes and their relations to self-care activities. *Health Psychol* 1990;**9**(5):632–46.

25. Hampson SE, Glasgow RE, Foster LS. Personal models of diabetes among older adults: relationship to self-management and other variables. *Diabetes Educ* 1995;**21**(4):300–7.

26. Hampson SE, Glasgow RE, Strycker LA. Beliefs versus feelings: a comparison of personal models and depression for predicting multiple outcomes in diabetes. *Br J Health Psychol* 2000;**5**(1):27–40.

27. Petrie KJ, Cameron S, Ellis CJ, Buick D, Weinman J. Changing illness perceptions following myocardial infarction: an early intervention randomized controlled trial. *Psychosom Med* 2002;**64**:580–6.

28. Hardeman W, Griffin S, Johnston M, Kinmonth AL, Wareham NJ. Interventions to prevent weight gain: a systematic review of psychological models and behaviour change methods. *Int J Obes Relat Metab Disord* 2000;**24**(2):131–43.

29. Strecher VJ, Seijts GH, Kok GJ, Latham GP, Glasgow R, DeVellis B *et al*. Goal setting as a strategy for health behavior change. *Health Educ Q* 1995;**22**(2):190–200.

30. Farmer A, Wade A, French DP, Goyder E, Kinmonth AL, Neil A. The DiGEM trial protocol – a randomised controlled trial to determine the effect on glycaemic control of different strategies of SMBG in people with type 2 diabetes [ISRCTN47464659]. *BMC Fam Pract* 2005;**6**:25.

31. EuroQol Group. EuroQol: a new facility for the measurement of health related quality of life. *Health Pol* 2001;**16**:199–208.

32. Evans S, Royston P, Day S. Minim: allocation by minimisation in clinical trials. 2004. URL: www-users.york.ac.uk/~mb55/guide/minim.htm. Accessed 9 December 2008.

33. National Institute for Clinical Excellence. *Management of type 2 diabetes: management of blood glucose*. London: National Institute for Clinical Excellence; 2002.

34. Hardeman W, Sutton S, Griffin S, Johnston M, White AJ, Wareham NJ, *et al*. A causal modelling approach to the development of theory-based behaviour change programmes for trial evaluation. *Health Educ Res* 2005;**20**(6):676–87.

35. Turner RC, Cull CA, Frighi V, Holman RR. Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49). UK Prospective Diabetes Study (UKPDS) Group. *JAMA* 1999;**281**(21):2005–12.

36. Clarke PM, Gray AM, Briggs A, Farmer A, Fenn P, Stevens R *et al*. A model to estimate the lifetime health outcomes of patients with type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model. *Diabetologia* 2004;**47**:1747–59.

37. Royston P. Multiple imputation of missing values: update of ice. *Stata J* 2005;**5**:527–36.

38. Dolan P, Gudex C, Kind P, Williams A. *A social tariff for EuroQol: results from a UK population survey*. York: CHE University of York; 1995.

39. Curtis L, Netten A. *Costs of health and social care 2006*. Kent: PSSRU; 2006.

40. British Medical Association and Royal Pharmaceutical Society of Great Britain. *British National Formulary (BNF) 52*. London: BMA/RPSGB; 2006.

41. Department of Health. *Prescription cost analysis, 2005*. 2007. URL: www.ic.nhs.uk/pubs/prescostanalysis2005. Accessed 3 April 2007.

42. National Health Service. *Annual financial returns of NHS trusts 2003–2004*. Leeds: National Health Service; 2007.

43. Netten A, Curtis L. *Costs of health and social care 2002*. Kent: PSSRU; 2002.

44. Department of Health. *NHS reference costs 2005/06*. 2007.

45. Drummond MF, O'Brien B, Stoddart GL, Torrance GW. *Methods for the economic evaluation of health care programmes*. Oxford: Oxford University Press; 1997.

46. Great Britain HM Treasury. *Green book, appraisal and evaluation in central government*. London: Stationery Office; 2003.

47. Briggs AH, Wonderling DE, Mooney CZ. Pulling cost-effectiveness analysis up by its bootstraps: a non-parametric approach to confidence interval estimation. *Health Econ* 1997;**6**:327–40.

48. Briggs AH, Gray AM. Handling uncertainty when performing economic evaluations of healthcare interventions. *Health Technol Assess* 1999;**3**:47–59.

49. National Institute for Health and Clinical Excellence. *Social value judgements: principles for the development of NICE guidance*. London: NICE; 2005.

50. Department of Health. *Review body of doctors' and dentists' remuneration: review for 2004*. 2004.

51. Toobert DJ, Hampson SE, Glasgow RE. The summary of diabetes self-care activities measure: results from 7 studies and a revised scale. *Diabetes Care* 2000;**23**(7):943–50.

52. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res* 2001;**47**:555–67.

53. Lewis KS, Jennings AM, Ward JD, Bradley C. Health belief scales developed specifically for people with tablet-treated type 2 diabetes. *Diabet Med* 1990;**7**:148–55.

54. Riazi A, Bradley C, Barendse S, Ishii H. Development of the well-being questionnaire short-form in Japanese: the WBQ-12. *Health Qual Life Outcomes* 2006;**4**(1):40.

55. Moss-Morris R, Weinman J, Petrie KJ, Horne R, Cameron LD, Buick D. The revised illness perception questionnaire (IPQ-R). *Psychol Health* 2002;**17**:1–6.

56. Horne R. Nonadherence to medication: causes and implications for care. In Gard P, editor. *A behavioural approach to pharmacy practice*. Oxford: Blackwell; 2001. pp. 111–30.

57. Toobert DJ, Hampson SE, Glasgow RE. The summary of diabetes self-care activities measure: results from seven studies and a revised scale. *Diabetes Care* 2000;**23**:943–50.

58. Bradley C. Diabetes treatment satisfaction questionnaire (DTSQ). In Bradley C, editor. *Handbook of psychology and diabetes*. Switzerland: Harwood Academic Publishers; 1994, pp. 111–32.

59. Riazi A, Bradley C, Barendse S, Ishii H. Development of the well-being questionaire short-form in Japanese: the W-BQ12. *Health Qual Life Outcomes* 2006;**4**:40.

60. Wade A. *Impact of self-monitoring of blood glucose in non-insulin dependant diabetes*. PhD thesis. Oxford; University of Oxford;2006.

61. Baron RM, Kenny DA. The moderator–mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol* 1986;**51**(6):1173–82.

62. Bergenstal RM, Gavin III JR. The role of self-monitoring of blood glucose in the care of people with diabetes: report of a global consensus conference. *Am J Med* 2005;**118**(9, Suppl 1):1–6.

63. Gerich JE. Clinicians can help their patients control postprandial hyperglycemia as a means of reducing cardiovascular risk. *Diabetes Educ* 2006;**32**(4):513–22.

64. Franciosi M, Pellegrini F, De Berardis G, Belfiglio M, Di Nardo B, Greenfield S *et al*. Self-monitoring of blood glucose in non-insulin-treated diabetic patients: a longitudinal evaluation of its impact on metabolic control. *Diabet Med* 2005;**22**:900–6.

65. Welschen LMC, Bloemendal E, Nijpels G, Dekker JM, Heine RJ, Stalman WAB, *et al*. Self-monitoring of blood glucose in patients with type 2 diabetes who are not using insulin: a systematic review. *Diabetes Care* 2005;**28**(6):1510–17.

66. Bellg AJ, Borrelli B, Resnick B, Hecht J, Minicucci DS, Ory M, *et al*. Enhancing treatment fidelity in health behavior change studies: best practices and recommendations from the NIH Behavior Change Consortium. *Health Psychol* 2004;**23**(5):443–51.

67. Davidson MB, Castellanos M, Kain D, Duran P. The effect of self-monitoring of blood glucose concentrations on glycated hemoglobin levels in diabetic patients not taking insulin: a blinded, randomized trial. *Am J Med* 2005;**118**(4):422–5.

Appendix 1

Patients lost to follow-up

Practice number	Patient number	Randomised to: 1 = usual care; 2 = less intensive monitoring; 3 = more intensive monitoring	Comments	Reasons for loss to follow-up: 1 = withdrawn; 2 = uncontactable; 3 = too ill to continue; 4 = died	Gender: 1 = male 2 = female	Age at baseline
10	9	2	Carcinoma of breast diagnosed; mastectomy	3	2	71
10	10	2	Refused further contact	1	1	87
9	18	3	Unable to comply with protocol; consent to follow-up later declined	1	2	76
8	24	3	Died; cause of death multiple organ failure	4	1	82
12	48	1	Unable to comply with protocol; consent to follow-up later declined	1	2	71
5	68	2	Refused further contact	1	1	80
19	86	1	Unable to comply with protocol; consent to follow-up later declined	1	2	61
12	91	2	Uncontactable	2	1	77
11	93	3	Withdrew; consent to follow-up later declined	1	1	63
4	100	1	Uncontactable	2	2	70
22	109	1	Moved out of area	2	1	58
4	121	3	Uncontactable	2	1	58
10	145	1	No response to letters	2	2	65
14	162	3	Unable to comply with protocol; consent to follow-up later declined	1	1	73
14	165	3	Unable to comply with protocol; consent to follow-up later declined	1	2	66
18	172	2	'Difficulties at present'	1	2	40
14	195	3	No reply to follow-up letters	2	1	48
4	239	2	Died; cause of death respiratory distress	4	1	64
1	266	1	Died; cause of death lymphoma	4	1	70
11	296	2	Withdrew; consent to follow-up later declined	1	1	83
20	313	3	No reply to follow-up letters	2	2	54
11	322	3	Died; cause of death hypertensive heart disease	4	1	68
11	324	2	Died; cause of death biliary duct carcinoma	4	2	72

Practice number	Patient number	Randomised to: 1 = usual care; 2 = less intensive monitoring; 3 = more intensive monitoring	Comments	Reasons for loss to follow-up: 1 = withdrawn; 2 = uncontactable; 3 = too ill to continue; 4 = died	Gender: 1 = male 2 = female	Age at baseline
11	336	2	Withdrew owing to work commitments	1	2	41
14	337	3	Meter issued but did not use; declined follow-up	1	1	77
18	343	1	Gone to West Indies until August	2	1	72
12	355	1	Unable to comply with protocol	1	2	78
26	400	3	Finding meter use stressful; declined follow-up	1	1	62
25	401	1	Patient left surgery last November; notes removed – unable to contact	2	2	58
26	404	1	Patient does not wish to continue in study	1	1	44
25	410	3	Died; cause of death ischaemic heart disease	4	1	59
25	423	1	Unable to contact	2	1	72
40	430	1	Cancelled final visit owing to illness	3	1	61
36	443	3	Does not wish to use meter; declined follow-up	1	1	53
30	453	3	Patient refuses further contact	1	1	74
35	464	1	Too busy but agreed to follow-up; patient declined 12-month visit	1	1	77
36	467	1	Withdrawn owing to family commitments	1	1	64
26	468	2	Died; cause of death coronary artery disease	4	2	60
26	479	1	Patient refused final visit; too busy to continue with study	1	1	66
46	480	2	Uncontrolled diabetes and finds it stressful using meter; did not attend final visit	1	2	60
35	489	3	Patient decided that study is too big a commitment	1	1	73
30	497	3	Patient felt unable to take part in study after randomisation	1	1	70
42	500	3	Died; cause of death chest infection. Underlying malignancy	4	1	73
36	523	3	Declined final follow-up visit	1	1	73
27	535	1	Patient does not wish to continue with study	1	1	53

Practice number	Patient number	Randomised to: 1 = usual care; 2 = less intensive monitoring; 3 = more intensive monitoring	Comments	Reasons for loss to follow-up: 1 = withdrawn; 2 = uncontactable; 3 = too ill to continue; 4 = died	Gender: 1 = male 2 = female	Age at baseline
37	545	3	Husband terminally ill; declined follow-up	1	2	68
34	547	1	Patient has gone abroad for several weeks	2	2	45
34	555	2	Patient has left surgery and unable to contact	2	1	48
41	561	3	Patient became ill with chronic renal failure	3	1	66
43	563	3	Patient declined further contact	1	2	47
37	565	2	Withdrawn; does not like using meter	1	1	69
35	566	1	Uncontactable	2	2	77
35	568	3	Uncontactable	2	1	79
44	596	2	Unable to cope with being in the trial	1	2	69
49	615	3	Patient works long hours and could not keep regular appointments	1	1	50
35	623	3	Patient feels she can't cope with study requirements	1	2	67
50	628	3	Patient has reconsidered the study and has decided against meter use; meter not issued	1	1	61

Health Technology Assessment reports published to date

Volume 1, 1997

No. 1
Home parenteral nutrition: a systematic review.
By Richards DM, Deeks JJ, Sheldon TA, Shaffer JL.

No. 2
Diagnosis, management and screening of early localised prostate cancer.
A review by Selley S, Donovan J, Faulkner A, Coast J, Gillatt D.

No. 3
The diagnosis, management, treatment and costs of prostate cancer in England and Wales.
A review by Chamberlain J, Melia J, Moss S, Brown J.

No. 4
Screening for fragile X syndrome.
A review by Murray J, Cuckle H, Taylor G, Hewison J.

No. 5
A review of near patient testing in primary care.
By Hobbs FDR, Delaney BC, Fitzmaurice DA, Wilson S, Hyde CJ, Thorpe GH, *et al*.

No. 6
Systematic review of outpatient services for chronic pain control.
By McQuay HJ, Moore RA, Eccleston C, Morley S, de C Williams AC.

No. 7
Neonatal screening for inborn errors of metabolism: cost, yield and outcome.
A review by Pollitt RJ, Green A, McCabe CJ, Booth A, Cooper NJ, Leonard JV, *et al*.

No. 8
Preschool vision screening.
A review by Snowdon SK, Stewart-Brown SL.

No. 9
Implications of socio-cultural contexts for the ethics of clinical trials.
A review by Ashcroft RE, Chadwick DW, Clark SRL, Edwards RHT, Frith L, Hutton JL.

No. 10
A critical review of the role of neonatal hearing screening in the detection of congenital hearing impairment.
By Davis A, Bamford J, Wilson I, Ramkalawan T, Forshaw M, Wright S.

No. 11
Newborn screening for inborn errors of metabolism: a systematic review.
By Seymour CA, Thomason MJ, Chalmers RA, Addison GM, Bain MD, Cockburn F, *et al*.

No. 12
Routine preoperative testing: a systematic review of the evidence.
By Munro J, Booth A, Nicholl J.

No. 13
Systematic review of the effectiveness of laxatives in the elderly.
By Petticrew M, Watt I, Sheldon T.

No. 14
When and how to assess fast-changing technologies: a comparative study of medical applications of four generic technologies.
A review by Mowatt G, Bower DJ, Brebner JA, Cairns JA, Grant AM, McKee L.

Volume 2, 1998

No. 1
Antenatal screening for Down's syndrome.
A review by Wald NJ, Kennard A, Hackshaw A, McGuire A.

No. 2
Screening for ovarian cancer: a systematic review.
By Bell R, Petticrew M, Luengo S, Sheldon TA.

No. 3
Consensus development methods, and their use in clinical guideline development.
A review by Murphy MK, Black NA, Lamping DL, McKee CM, Sanderson CFB, Askham J, *et al*.

No. 4
A cost–utility analysis of interferon beta for multiple sclerosis.
By Parkin D, McNamee P, Jacoby A, Miller P, Thomas S, Bates D.

No. 5
Effectiveness and efficiency of methods of dialysis therapy for end-stage renal disease: systematic reviews.
By MacLeod A, Grant A, Donaldson C, Khan I, Campbell M, Daly C, *et al*.

No. 6
Effectiveness of hip prostheses in primary total hip replacement: a critical review of evidence and an economic model.
By Faulkner A, Kennedy LG, Baxter K, Donovan J, Wilkinson M, Bevan G.

No. 7
Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomised controlled trials.
By Song F, Glenny AM.

No. 8
Bone marrow and peripheral blood stem cell transplantation for malignancy.
A review by Johnson PWM, Simnett SJ, Sweetenham JW, Morgan GJ, Stewart LA.

No. 9
Screening for speech and language delay: a systematic review of the literature.
By Law J, Boyle J, Harris F, Harkness A, Nye C.

No. 10
Resource allocation for chronic stable angina: a systematic review of effectiveness, costs and cost-effectiveness of alternative interventions.
By Sculpher MJ, Petticrew M, Kelland JL, Elliott RA, Holdright DR, Buxton MJ.

No. 11
Detection, adherence and control of hypertension for the prevention of stroke: a systematic review.
By Ebrahim S.

No. 12
Postoperative analgesia and vomiting, with special reference to day-case surgery: a systematic review.
By McQuay HJ, Moore RA.

No. 13
Choosing between randomised and nonrandomised studies: a systematic review.
By Britton A, McKee M, Black N, McPherson K, Sanderson C, Bain C.

No. 14
Evaluating patient-based outcome measures for use in clinical trials.
A review by Fitzpatrick R, Davey C, Buxton MJ, Jones DR.

No. 15

Ethical issues in the design and conduct
of randomised controlled trials.

A review by Edwards SJL, Lilford RJ,
Braunholtz DA, Jackson JC, Hewison J,
Thornton J.

No. 16

Qualitative research methods in health
technology assessment: a review of the
literature.

By Murphy E, Dingwall R,
Greatbatch D, Parker S, Watson P.

No. 17

The costs and benefits of paramedic
skills in pre-hospital trauma care.

By Nicholl J, Hughes S, Dixon S,
Turner J, Yates D.

No. 18

Systematic review of endoscopic
ultrasound in gastro-oesophageal
cancer.

By Harris KM, Kelly S, Berry E,
Hutton J, Roderick P, Cullingworth J,
et al.

No. 19

Systematic reviews of trials and other
studies.

By Sutton AJ, Abrams KR, Jones DR,
Sheldon TA, Song F.

No. 20

Primary total hip replacement surgery:
a systematic review of outcomes
and modelling of cost-effectiveness
associated with different prostheses.

A review by Fitzpatrick R, Shortall
E, Sculpher M, Murray D, Morris R,
Lodge M, *et al*.

Volume 3, 1999

No. 1

Informed decision making: an
annotated bibliography and systematic
review.

By Bekker H, Thornton JG,
Airey CM, Connelly JB, Hewison J,
Robinson MB, *et al*.

No. 2

Handling uncertainty when performing
economic evaluation of healthcare
interventions.

A review by Briggs AH, Gray AM.

No. 3

The role of expectancies in the placebo
effect and their use in the delivery of
health care: a systematic review.

By Crow R, Gage H, Hampson S,
Hart J, Kimber A, Thomas H.

No. 4

A randomised controlled trial of
different approaches to universal
antenatal HIV testing: uptake and
acceptability. Annex: Antenatal HIV
testing – assessment of a routine
voluntary approach.

By Simpson WM, Johnstone FD,
Boyd FM, Goldberg DJ, Hart GJ,
Gormley SM, *et al*.

No. 5

Methods for evaluating area-wide and
organisation-based interventions in
health and health care: a systematic
review.

By Ukoumunne OC, Gulliford MC,
Chinn S, Sterne JAC, Burney PGJ.

No. 6

Assessing the costs of healthcare
technologies in clinical trials.

A review by Johnston K, Buxton MJ,
Jones DR, Fitzpatrick R.

No. 7

Cooperatives and their primary care
emergency centres: organisation and
impact.

By Hallam L, Henthorne K.

No. 8

Screening for cystic fibrosis.

A review by Murray J, Cuckle H,
Taylor G, Littlewood J, Hewison J.

No. 9

A review of the use of health status
measures in economic evaluation.

By Brazier J, Deverill M, Green C,
Harper R, Booth A.

No. 10

Methods for the analysis of quality-
of-life and survival data in health
technology assessment.

A review by Billingham LJ,
Abrams KR, Jones DR.

No. 11

Antenatal and neonatal
haemoglobinopathy screening in the
UK: review and economic analysis.

By Zeuner D, Ades AE, Karnon J,
Brown J, Dezateux C, Anionwu EN.

No. 12

Assessing the quality of reports of
randomised trials: implications for the
conduct of meta-analyses.

A review by Moher D, Cook DJ,
Jadad AR, Tugwell P, Moher M,
Jones A, *et al*.

No. 13

'Early warning systems' for identifying
new healthcare technologies.

By Robert G, Stevens A, Gabbay J.

No. 14

A systematic review of the role of
human papillomavirus testing within a
cervical screening programme.

By Cuzick J, Sasieni P, Davies P,
Adams J, Normand C, Frater A, *et al*.

No. 15

Near patient testing in diabetes clinics:
appraising the costs and outcomes.

By Grieve R, Beech R, Vincent J,
Mazurkiewicz J.

No. 16

Positron emission tomography:
establishing priorities for health
technology assessment.

A review by Robert G, Milne R.

No. 17 (Pt 1)

The debridement of chronic wounds: a
systematic review.

By Bradley M, Cullum N, Sheldon T.

No. 17 (Pt 2)

Systematic reviews of wound care
management: (2) Dressings and topical
agents used in the healing of chronic
wounds.

By Bradley M, Cullum N, Nelson EA,
Petticrew M, Sheldon T, Torgerson D.

No. 18

A systematic literature review of
spiral and electron beam computed
tomography: with particular reference
to clinical applications in hepatic
lesions, pulmonary embolus and
coronary artery disease.

By Berry E, Kelly S, Hutton J,
Harris KM, Roderick P, Boyce JC, *et al*.

No. 19

What role for statins? A review and
economic model.

By Ebrahim S, Davey Smith
G, McCabe C, Payne N, Pickin M,
Sheldon TA, *et al*.

No. 20

Factors that limit the quality, number
and progress of randomised controlled
trials.

A review by Prescott RJ, Counsell CE,
Gillespie WJ, Grant AM, Russell IT,
Kiauka S, *et al*.

No. 21

Antimicrobial prophylaxis in total hip
replacement: a systematic review.

By Glenny AM, Song F.

No. 22

Health promoting schools and health
promotion in schools: two systematic
reviews.

By Lister-Sharp D, Chapman S,
Stewart-Brown S, Sowden A.

No. 23

Economic evaluation of a primary
care-based education programme for
patients with osteoarthritis of the knee.

A review by Lord J, Victor C,
Littlejohns P, Ross FM, Axford JS.

Volume 4, 2000

No. 1
The estimation of marginal time preference in a UK-wide sample (TEMPUS) project.
A review by Cairns JA, van der Pol MM.

No. 2
Geriatric rehabilitation following fractures in older people: a systematic review.
By Cameron I, Crotty M, Currie C, Finnegan T, Gillespie L, Gillespie W, *et al*.

No. 3
Screening for sickle cell disease and thalassaemia: a systematic review with supplementary research.
By Davies SC, Cronin E, Gill M, Greengross P, Hickman M, Normand C.

No. 4
Community provision of hearing aids and related audiology services.
A review by Reeves DJ, Alborz A, Hickson FS, Bamford JM.

No. 5
False-negative results in screening programmes: systematic review of impact and implications.
By Petticrew MP, Sowden AJ, Lister-Sharp D, Wright K.

No. 6
Costs and benefits of community postnatal support workers: a randomised controlled trial.
By Morrell CJ, Spiby H, Stewart P, Walters S, Morgan A.

No. 7
Implantable contraceptives (subdermal implants and hormonally impregnated intrauterine systems) versus other forms of reversible contraceptives: two systematic reviews to assess relative effectiveness, acceptability, tolerability and cost-effectiveness.
By French RS, Cowan FM, Mansour DJA, Morris S, Procter T, Hughes D, *et al*.

No. 8
An introduction to statistical methods for health technology assessment.
A review by White SJ, Ashby D, Brown PJ.

No. 9
Disease-modifying drugs for multiple sclerosis: a rapid and systematic review.
By Clegg A, Bryant J, Milne R.

No. 10
Publication and related biases.
A review by Song F, Eastwood AJ, Gilbody S, Duley L, Sutton AJ.

No. 11
Cost and outcome implications of the organisation of vascular services.
By Michaels J, Brazier J, Palfreyman S, Shackley P, Slack R.

No. 12
Monitoring blood glucose control in diabetes mellitus: a systematic review.
By Coster S, Gulliford MC, Seed PT, Powrie JK, Swaminathan R.

No. 13
The effectiveness of domiciliary health visiting: a systematic review of international studies and a selective review of the British literature.
By Elkan R, Kendrick D, Hewitt M, Robinson JJA, Tolley K, Blair M, *et al*.

No. 14
The determinants of screening uptake and interventions for increasing uptake: a systematic review.
By Jepson R, Clegg A, Forbes C, Lewis R, Sowden A, Kleijnen J.

No. 15
The effectiveness and cost-effectiveness of prophylactic removal of wisdom teeth.
A rapid review by Song F, O'Meara S, Wilson P, Golder S, Kleijnen J.

No. 16
Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views.
By Bricker L, Garcia J, Henderson J, Mugford M, Neilson J, Roberts T, *et al*.

No. 17
A rapid and systematic review of the effectiveness and cost-effectiveness of the taxanes used in the treatment of advanced breast and ovarian cancer.
By Lister-Sharp D, McDonagh MS, Khan KS, Kleijnen J.

No. 18
Liquid-based cytology in cervical screening: a rapid and systematic review.
By Payne N, Chilcott J, McGoogan E.

No. 19
Randomised controlled trial of non-directive counselling, cognitive–behaviour therapy and usual general practitioner care in the management of depression as well as mixed anxiety and depression in primary care.
By King M, Sibbald B, Ward E, Bower P, Lloyd M, Gabbay M, *et al*.

No. 20
Routine referral for radiography of patients presenting with low back pain: is patients' outcome influenced by GPs' referral for plain radiography?
By Kerry S, Hilton S, Patel S, Dundas D, Rink E, Lord J.

No. 21
Systematic reviews of wound care management: (3) antimicrobial agents for chronic wounds; (4) diabetic foot ulceration.
By O'Meara S, Cullum N, Majid M, Sheldon T.

No. 22
Using routine data to complement and enhance the results of randomised controlled trials.
By Lewsey JD, Leyland AH, Murray GD, Boddy FA.

No. 23
Coronary artery stents in the treatment of ischaemic heart disease: a rapid and systematic review.
By Meads C, Cummins C, Jolly K, Stevens A, Burls A, Hyde C.

No. 24
Outcome measures for adult critical care: a systematic review.
By Hayes JA, Black NA, Jenkinson C, Young JD, Rowan KM, Daly K, *et al*.

No. 25
A systematic review to evaluate the effectiveness of interventions to promote the initiation of breastfeeding.
By Fairbank L, O'Meara S, Renfrew MJ, Woolridge M, Sowden AJ, Lister-Sharp D.

No. 26
Implantable cardioverter defibrillators: arrhythmias. A rapid and systematic review.
By Parkes J, Bryant J, Milne R.

No. 27
Treatments for fatigue in multiple sclerosis: a rapid and systematic review.
By Brañas P, Jordan R, Fry-Smith A, Burls A, Hyde C.

No. 28
Early asthma prophylaxis, natural history, skeletal development and economy (EASE): a pilot randomised controlled trial.
By Baxter-Jones ADG, Helms PJ, Russell G, Grant A, Ross S, Cairns JA, *et al*.

No. 29
Screening for hypercholesterolaemia versus case finding for familial hypercholesterolaemia: a systematic review and cost-effectiveness analysis.
By Marks D, Wonderling D, Thorogood M, Lambert H, Humphries SE, Neil HAW.

No. 30
A rapid and systematic review of the clinical effectiveness and cost-effectiveness of glycoprotein IIb/IIIa antagonists in the medical management of unstable angina.
By McDonagh MS, Bachmann LM, Golder S, Kleijnen J, ter Riet G.

53

No. 31
A randomised controlled trial
of prehospital intravenous fluid
replacement therapy in serious trauma.
By Turner J, Nicholl J, Webber L,
Cox H, Dixon S, Yates D.

No. 32
Intrathecal pumps for giving opioids in
chronic pain: a systematic review.
By Williams JE, Louw G,
Towlerton G.

No. 33
Combination therapy (interferon
alfa and ribavirin) in the treatment
of chronic hepatitis C: a rapid and
systematic review.
By Shepherd J, Waugh N,
Hewitson P.

No. 34
A systematic review of comparisons of
effect sizes derived from randomised
and non-randomised studies.
By MacLehose RR, Reeves BC,
Harvey IM, Sheldon TA, Russell IT,
Black AMS.

No. 35
Intravascular ultrasound-guided
interventions in coronary artery
disease: a systematic literature review,
with decision-analytic modelling, of
outcomes and cost-effectiveness.
By Berry E, Kelly S, Hutton J,
Lindsay HSJ, Blaxill JM, Evans JA, *et al*.

No. 36
A randomised controlled trial to
evaluate the effectiveness and cost-
effectiveness of counselling patients
with chronic depression.
By Simpson S, Corney R,
Fitzgerald P, Beecham J.

No. 37
Systematic review of treatments for
atopic eczema.
By Hoare C, Li Wan Po A,
Williams H.

No. 38
Bayesian methods in health technology
assessment: a review.
By Spiegelhalter DJ, Myles JP,
Jones DR, Abrams KR.

No. 39
The management of dyspepsia: a
systematic review.
By Delaney B, Moayyedi P, Deeks J,
Innes M, Soo S, Barton P, *et al*.

No. 40
A systematic review of treatments for
severe psoriasis.
By Griffiths CEM, Clark CM,
Chalmers RJG, Li Wan Po A,
Williams HC.

Volume 5, 2001

No. 1
Clinical and cost-effectiveness
of donepezil, rivastigmine and
galantamine for Alzheimer's disease: a
rapid and systematic review.
By Clegg A, Bryant J, Nicholson T,
McIntyre L, De Broe S, Gerard K, *et al*.

No. 2
The clinical effectiveness and cost-
effectiveness of riluzole for motor
neurone disease: a rapid and systematic
review.
By Stewart A, Sandercock J, Bryan S,
Hyde C, Barton PM, Fry-Smith A, *et al*.

No. 3
Equity and the economic evaluation of
healthcare.
By Sassi F, Archard L, Le Grand J.

No. 4
Quality-of-life measures in chronic
diseases of childhood.
By Eiser C, Morse R.

No. 5
Eliciting public preferences for
healthcare: a systematic review of
techniques.
By Ryan M, Scott DA, Reeves C, Bate
A, van Teijlingen ER, Russell EM, *et al*.

No. 6
General health status measures for
people with cognitive impairment:
learning disability and acquired brain
injury.
By Riemsma RP, Forbes CA,
Glanville JM, Eastwood AJ, Kleijnen J.

No. 7
An assessment of screening strategies
for fragile X syndrome in the UK.
By Pembrey ME, Barnicoat AJ,
Carmichael B, Bobrow M, Turner G.

No. 8
Issues in methodological research:
perspectives from researchers and
commissioners.
By Lilford RJ, Richardson A, Stevens
A, Fitzpatrick R, Edwards S, Rock F, *et al*.

No. 9
Systematic reviews of wound
care management: (5) beds;
(6) compression; (7) laser therapy,
therapeutic ultrasound, electrotherapy
and electromagnetic therapy.
By Cullum N, Nelson EA,
Flemming K, Sheldon T.

No. 10
Effects of educational and psychosocial
interventions for adolescents with
diabetes mellitus: a systematic review.
By Hampson SE, Skinner TC, Hart J,
Storey L, Gage H, Foxcroft D, *et al*.

No. 11
Effectiveness of autologous chondrocyte
transplantation for hyaline cartilage
defects in knees: a rapid and systematic
review.
By Jobanputra P, Parry D, Fry-Smith
A, Burls A.

No. 12
Statistical assessment of the learning
curves of health technologies.
By Ramsay CR, Grant AM, Wallace
SA, Garthwaite PH, Monk AF, Russell IT.

No. 13
The effectiveness and cost-effectiveness
of temozolomide for the treatment of
recurrent malignant glioma: a rapid
and systematic review.
By Dinnes J, Cave C, Huang S,
Major K, Milne R.

No. 14
A rapid and systematic review of
the clinical effectiveness and cost-
effectiveness of debriding agents in
treating surgical wounds healing by
secondary intention.
By Lewis R, Whiting P, ter Riet G,
O'Meara S, Glanville J.

No. 15
Home treatment for mental health
problems: a systematic review.
By Burns T, Knapp M, Catty J,
Healey A, Henderson J, Watt H, *et al*.

No. 16
How to develop cost-conscious
guidelines.
By Eccles M, Mason J.

No. 17
The role of specialist nurses in multiple
sclerosis: a rapid and systematic review.
By De Broe S, Christopher F,
Waugh N.

No. 18
A rapid and systematic review
of the clinical effectiveness and
cost-effectiveness of orlistat in the
management of obesity.
By O'Meara S, Riemsma R,
Shirran L, Mather L, ter Riet G.

No. 19
The clinical effectiveness and cost-
effectiveness of pioglitazone for
type 2 diabetes mellitus: a rapid and
systematic review.
By Chilcott J, Wight J, Lloyd Jones
M, Tappenden P.

No. 20
Extended scope of nursing practice:
a multicentre randomised controlled
trial of appropriately trained nurses
and preregistration house officers in
preoperative assessment in elective
general surgery.
By Kinley H, Czoski-Murray C,
George S, McCabe C, Primrose J,
Reilly C, *et al*.

No. 21
Systematic reviews of the effectiveness of day care for people with severe mental disorders: (1) Acute day hospital versus admission; (2) Vocational rehabilitation; (3) Day hospital versus outpatient care.
By Marshall M, Crowther R, Almaraz- Serrano A, Creed F, Sledge W, Kluiter H, *et al.*

No. 22
The measurement and monitoring of surgical adverse events.
By Bruce J, Russell EM, Mollison J, Krukowski ZH.

No. 23
Action research: a systematic review and guidance for assessment.
By Waterman H, Tillen D, Dickson R, de Koning K.

No. 24
A rapid and systematic review of the clinical effectiveness and cost-effectiveness of gemcitabine for the treatment of pancreatic cancer.
By Ward S, Morris E, Bansback N, Calvert N, Crellin A, Forman D, *et al.*

No. 25
A rapid and systematic review of the evidence for the clinical effectiveness and cost-effectiveness of irinotecan, oxaliplatin and raltitrexed for the treatment of advanced colorectal cancer.
By Lloyd Jones M, Hummel S, Bansback N, Orr B, Seymour M.

No. 26
Comparison of the effectiveness of inhaler devices in asthma and chronic obstructive airways disease: a systematic review of the literature.
By Brocklebank D, Ram F, Wright J, Barry P, Cates C, Davies L, *et al.*

No. 27
The cost-effectiveness of magnetic resonance imaging for investigation of the knee joint.
By Bryan S, Weatherburn G, Bungay H, Hatrick C, Salas C, Parry D, *et al.*

No. 28
A rapid and systematic review of the clinical effectiveness and cost-effectiveness of topotecan for ovarian cancer.
By Forbes C, Shirran L, Bagnall A-M, Duffy S, ter Riet G.

No. 29
Superseded by a report published in a later volume.

No. 30
The role of radiography in primary care patients with low back pain of at least 6 weeks duration: a randomised (unblinded) controlled trial.
By Kendrick D, Fielding K, Bentley E, Miller P, Kerslake R, Pringle M.

No. 31
Design and use of questionnaires: a review of best practice applicable to surveys of health service staff and patients.
By McColl E, Jacoby A, Thomas L, Soutter J, Bamford C, Steen N, *et al.*

No. 32
A rapid and systematic review of the clinical effectiveness and cost-effectiveness of paclitaxel, docetaxel, gemcitabine and vinorelbine in non-small-cell lung cancer.
By Clegg A, Scott DA, Sidhu M, Hewitson P, Waugh N.

No. 33
Subgroup analyses in randomised controlled trials: quantifying the risks of false-positives and false-negatives.
By Brookes ST, Whitley E, Peters TJ, Mulheran PA, Egger M, Davey Smith G.

No. 34
Depot antipsychotic medication in the treatment of patients with schizophrenia: (1) Meta-review; (2) Patient and nurse attitudes.
By David AS, Adams C.

No. 35
A systematic review of controlled trials of the effectiveness and cost-effectiveness of brief psychological treatments for depression.
By Churchill R, Hunot V, Corney R, Knapp M, McGuire H, Tylee A, *et al.*

No. 36
Cost analysis of child health surveillance.
By Sanderson D, Wright D, Acton C, Duree D.

Volume 6, 2002

No. 1
A study of the methods used to select review criteria for clinical audit.
By Hearnshaw H, Harker R, Cheater F, Baker R, Grimshaw G.

No. 2
Fludarabine as second-line therapy for B cell chronic lymphocytic leukaemia: a technology assessment.
By Hyde C, Wake B, Bryan S, Barton P, Fry-Smith A, Davenport C, *et al.*

No. 3
Rituximab as third-line treatment for refractory or recurrent Stage III or IV follicular non-Hodgkin's lymphoma: a systematic review and economic evaluation.
By Wake B, Hyde C, Bryan S, Barton P, Song F, Fry-Smith A, *et al.*

No. 4
A systematic review of discharge arrangements for older people.
By Parker SG, Peet SM, McPherson A, Cannaby AM, Baker R, Wilson A, *et al.*

No. 5
The clinical effectiveness and cost-effectiveness of inhaler devices used in the routine management of chronic asthma in older children: a systematic review and economic evaluation.
By Peters J, Stevenson M, Beverley C, Lim J, Smith S.

No. 6
The clinical effectiveness and cost-effectiveness of sibutramine in the management of obesity: a technology assessment.
By O'Meara S, Riemsma R, Shirran L, Mather L, ter Riet G.

No. 7
The cost-effectiveness of magnetic resonance angiography for carotid artery stenosis and peripheral vascular disease: a systematic review.
By Berry E, Kelly S, Westwood ME, Davies LM, Gough MJ, Bamford JM, *et al.*

No. 8
Promoting physical activity in South Asian Muslim women through 'exercise on prescription'.
By Carroll B, Ali N, Azam N.

No. 9
Zanamivir for the treatment of influenza in adults: a systematic review and economic evaluation.
By Burls A, Clark W, Stewart T, Preston C, Bryan S, Jefferson T, *et al.*

No. 10
A review of the natural history and epidemiology of multiple sclerosis: implications for resource allocation and health economic models.
By Richards RG, Sampson FC, Beard SM, Tappenden P.

No. 11
Screening for gestational diabetes: a systematic review and economic evaluation.
By Scott DA, Loveman E, McIntyre L, Waugh N.

No. 12
The clinical effectiveness and cost-effectiveness of surgery for people with morbid obesity: a systematic review and economic evaluation.
By Clegg AJ, Colquitt J, Sidhu MK, Royle P, Loveman E, Walker A.

No. 13
The clinical effectiveness of trastuzumab for breast cancer: a systematic review.
By Lewis R, Bagnall A-M, Forbes C, Shirran E, Duffy S, Kleijnen J, *et al.*

No. 14
The clinical effectiveness and cost-effectiveness of vinorelbine for breast cancer: a systematic review and economic evaluation.
By Lewis R, Bagnall A-M, King S, Woolacott N, Forbes C, Shirran L, *et al.*

No. 15
A systematic review of the effectiveness and cost-effectiveness of metal-on-metal hip resurfacing arthroplasty for treatment of hip disease.
By Vale L, Wyness L, McCormack K, McKenzie L, Brazzelli M, Stearns SC.

No. 16
The clinical effectiveness and cost-effectiveness of bupropion and nicotine replacement therapy for smoking cessation: a systematic review and economic evaluation.
By Woolacott NF, Jones L, Forbes CA, Mather LC, Sowden AJ, Song FJ, *et al*.

No. 17
A systematic review of effectiveness and economic evaluation of new drug treatments for juvenile idiopathic arthritis: etanercept.
By Cummins C, Connock M, Fry-Smith A, Burls A.

No. 18
Clinical effectiveness and cost-effectiveness of growth hormone in children: a systematic review and economic evaluation.
By Bryant J, Cave C, Mihaylova B, Chase D, McIntyre L, Gerard K, *et al*.

No. 19
Clinical effectiveness and cost-effectiveness of growth hormone in adults in relation to impact on quality of life: a systematic review and economic evaluation.
By Bryant J, Loveman E, Chase D, Mihaylova B, Cave C, Gerard K, *et al*.

No. 20
Clinical medication review by a pharmacist of patients on repeat prescriptions in general practice: a randomised controlled trial.
By Zermansky AG, Petty DR, Raynor DK, Lowe CJ, Freementle N, Vail A.

No. 21
The effectiveness of infliximab and etanercept for the treatment of rheumatoid arthritis: a systematic review and economic evaluation.
By Jobanputra P, Barton P, Bryan S, Burls A.

No. 22
A systematic review and economic evaluation of computerised cognitive behaviour therapy for depression and anxiety.
By Kaltenthaler E, Shackley P, Stevens K, Beverley C, Parry G, Chilcott J.

No. 23
A systematic review and economic evaluation of pegylated liposomal doxorubicin hydrochloride for ovarian cancer.
By Forbes C, Wilby J, Richardson G, Sculpher M, Mather L, Reimsma R.

No. 24
A systematic review of the effectiveness of interventions based on a stages-of-change approach to promote individual behaviour change.
By Riemsma RP, Pattenden J, Bridle C, Sowden AJ, Mather L, Watt IS, *et al*.

No. 25
A systematic review update of the clinical effectiveness and cost-effectiveness of glycoprotein IIb/IIIa antagonists.
By Robinson M, Ginnelly L, Sculpher M, Jones L, Riemsma R, Palmer S, *et al*.

No. 26
A systematic review of the effectiveness, cost-effectiveness and barriers to implementation of thrombolytic and neuroprotective therapy for acute ischaemic stroke in the NHS.
By Sandercock P, Berge E, Dennis M, Forbes J, Hand P, Kwan J, *et al*.

No. 27
A randomised controlled crossover trial of nurse practitioner versus doctor-led outpatient care in a bronchiectasis clinic.
By Caine N, Sharples LD, Hollingworth W, French J, Keogan M, Exley A, *et al*.

No. 28
Clinical effectiveness and cost – consequences of selective serotonin reuptake inhibitors in the treatment of sex offenders.
By Adi Y, Ashcroft D, Browne K, Beech A, Fry-Smith A, Hyde C.

No. 29
Treatment of established osteoporosis: a systematic review and cost–utility analysis.
By Kanis JA, Brazier JE, Stevenson M, Calvert NW, Lloyd Jones M.

No. 30
Which anaesthetic agents are cost-effective in day surgery? Literature review, national survey of practice and randomised controlled trial.
By Elliott RA Payne K, Moore JK, Davies LM, Harper NJN, St Leger AS, *et al*.

No. 31
Screening for hepatitis C among injecting drug users and in genitourinary medicine clinics: systematic reviews of effectiveness, modelling study and national survey of current practice.
By Stein K, Dalziel K, Walker A, McIntyre L, Jenkins B, Horne J, *et al*.

No. 32
The measurement of satisfaction with healthcare: implications for practice from a systematic review of the literature.
By Crow R, Gage H, Hampson S, Hart J, Kimber A, Storey L, *et al*.

No. 33
The effectiveness and cost-effectiveness of imatinib in chronic myeloid leukaemia: a systematic review.
By Garside R, Round A, Dalziel K, Stein K, Royle R.

No. 34
A comparative study of hypertonic saline, daily and alternate-day rhDNase in children with cystic fibrosis.
By Suri R, Wallis C, Bush A, Thompson S, Normand C, Flather M, *et al*.

No. 35
A systematic review of the costs and effectiveness of different models of paediatric home care.
By Parker G, Bhakta P, Lovett CA, Paisley S, Olsen R, Turner D, *et al*.

Volume 7, 2003

No. 1
How important are comprehensive literature searches and the assessment of trial quality in systematic reviews? Empirical study.
By Egger M, Jüni P, Bartlett C, Holenstein F, Sterne J.

No. 2
Systematic review of the effectiveness and cost-effectiveness, and economic evaluation, of home versus hospital or satellite unit haemodialysis for people with end-stage renal failure.
By Mowatt G, Vale L, Perez J, Wyness L, Fraser C, MacLeod A, *et al*.

No. 3
Systematic review and economic evaluation of the effectiveness of infliximab for the treatment of Crohn's disease.
By Clark W, Raftery J, Barton P, Song F, Fry-Smith A, Burls A.

No. 4
A review of the clinical effectiveness and cost-effectiveness of routine anti-D prophylaxis for pregnant women who are rhesus negative.
By Chilcott J, Lloyd Jones M, Wight J, Forman K, Wray J, Beverley C, *et al*.

No. 5
Systematic review and evaluation of the use of tumour markers in paediatric oncology: Ewing's sarcoma and neuroblastoma.
By Riley RD, Burchill SA, Abrams KR, Heney D, Lambert PC, Jones DR, *et al*.

No. 6
The cost-effectiveness of screening for *Helicobacter pylori* to reduce mortality and morbidity from gastric cancer and peptic ulcer disease: a discrete-event simulation model.
By Roderick P, Davies R, Raftery J, Crabbe D, Pearce R, Bhandari P, *et al*.

No. 7

The clinical effectiveness and cost-effectiveness of routine dental checks: a systematic review and economic evaluation.

By Davenport C, Elley K, Salas C, Taylor-Weetman CL, Fry-Smith A, Bryan S, *et al*.

No. 8

A multicentre randomised controlled trial assessing the costs and benefits of using structured information and analysis of women's preferences in the management of menorrhagia.

By Kennedy ADM, Sculpher MJ, Coulter A, Dwyer N, Rees M, Horsley S, *et al*.

No. 9

Clinical effectiveness and cost–utility of photodynamic therapy for wet age-related macular degeneration: a systematic review and economic evaluation.

By Meads C, Salas C, Roberts T, Moore D, Fry-Smith A, Hyde C.

No. 10

Evaluation of molecular tests for prenatal diagnosis of chromosome abnormalities.

By Grimshaw GM, Szczepura A, Hultén M, MacDonald F, Nevin NC, Sutton F, *et al*.

No. 11

First and second trimester antenatal screening for Down's syndrome: the results of the Serum, Urine and Ultrasound Screening Study (SURUSS).

By Wald NJ, Rodeck C, Hackshaw AK, Walters J, Chitty L, Mackinson AM.

No. 12

The effectiveness and cost-effectiveness of ultrasound locating devices for central venous access: a systematic review and economic evaluation.

By Calvert N, Hind D, McWilliams RG, Thomas SM, Beverley C, Davidson A.

No. 13

A systematic review of atypical antipsychotics in schizophrenia.

By Bagnall A-M, Jones L, Lewis R, Ginnelly L, Glanville J, Torgerson D, *et al*.

No. 14

Prostate Testing for Cancer and Treatment (ProtecT) feasibility study.

By Donovan J, Hamdy F, Neal D, Peters T, Oliver S, Brindle L, *et al*.

No. 15

Early thrombolysis for the treatment of acute myocardial infarction: a systematic review and economic evaluation.

By Boland A, Dundar Y, Bagust A, Haycox A, Hill R, Mujica Mota R, *et al*.

No. 16

Screening for fragile X syndrome: a literature review and modelling.

By Song FJ, Barton P, Sleightholme V, Yao GL, Fry-Smith A.

No. 17

Systematic review of endoscopic sinus surgery for nasal polyps.

By Dalziel K, Stein K, Round A, Garside R, Royle P.

No. 18

Towards efficient guidelines: how to monitor guideline use in primary care.

By Hutchinson A, McIntosh A, Cox S, Gilbert C.

No. 19

Effectiveness and cost-effectiveness of acute hospital-based spinal cord injuries services: systematic review.

By Bagnall A-M, Jones L, Richardson G, Duffy S, Riemsma R.

No. 20

Prioritisation of health technology assessment. The PATHS model: methods and case studies.

By Townsend J, Buxton M, Harper G.

No. 21

Systematic review of the clinical effectiveness and cost-effectiveness of tension-free vaginal tape for treatment of urinary stress incontinence.

By Cody J, Wyness L, Wallace S, Glazener C, Kilonzo M, Stearns S, *et al*.

No. 22

The clinical and cost-effectiveness of patient education models for diabetes: a systematic review and economic evaluation.

By Loveman E, Cave C, Green C, Royle P, Dunn N, Waugh N.

No. 23

The role of modelling in prioritising and planning clinical trials.

By Chilcott J, Brennan A, Booth A, Karnon J, Tappenden P.

No. 24

Cost–benefit evaluation of routine influenza immunisation in people 65–74 years of age.

By Allsup S, Gosney M, Haycox A, Regan M.

No. 25

The clinical and cost-effectiveness of pulsatile machine perfusion versus cold storage of kidneys for transplantation retrieved from heart-beating and non-heart-beating donors.

By Wight J, Chilcott J, Holmes M, Brewer N.

No. 26

Can randomised trials rely on existing electronic data? A feasibility study to explore the value of routine data in health technology assessment.

By Williams JG, Cheung WY, Cohen DR, Hutchings HA, Longo MF, Russell IT.

No. 27

Evaluating non-randomised intervention studies.

By Deeks JJ, Dinnes J, D'Amico R, Sowden AJ, Sakarovitch C, Song F, *et al*.

No. 28

A randomised controlled trial to assess the impact of a package comprising a patient-orientated, evidence-based self-help guidebook and patient-centred consultations on disease management and satisfaction in inflammatory bowel disease.

By Kennedy A, Nelson E, Reeves D, Richardson G, Roberts C, Robinson A, *et al*.

No. 29

The effectiveness of diagnostic tests for the assessment of shoulder pain due to soft tissue disorders: a systematic review.

By Dinnes J, Loveman E, McIntyre L, Waugh N.

No. 30

The value of digital imaging in diabetic retinopathy.

By Sharp PF, Olson J, Strachan F, Hipwell J, Ludbrook A, O'Donnell M, *et al*.

No. 31

Lowering blood pressure to prevent myocardial infarction and stroke: a new preventive strategy.

By Law M, Wald N, Morris J.

No. 32

Clinical and cost-effectiveness of capecitabine and tegafur with uracil for the treatment of metastatic colorectal cancer: systematic review and economic evaluation.

By Ward S, Kaltenthaler E, Cowan J, Brewer N.

No. 33

Clinical and cost-effectiveness of new and emerging technologies for early localised prostate cancer: a systematic review.

By Hummel S, Paisley S, Morgan A, Currie E, Brewer N.

No. 34

Literature searching for clinical and cost-effectiveness studies used in health technology assessment reports carried out for the National Institute for Clinical Excellence appraisal system.

By Royle P, Waugh N.

57

No. 19
A rapid and systematic review and economic evaluation of the clinical and cost-effectiveness of newer drugs for treatment of mania associated with bipolar affective disorder.
By Bridle C, Palmer S, Bagnall A-M, Darba J, Duffy S, Sculpher M, *et al*.

No. 20
Liquid-based cytology in cervical screening: an updated rapid and systematic review and economic analysis.
By Karnon J, Peters J, Platt J, Chilcott J, McGoogan E, Brewer N.

No. 21
Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement.
By Avenell A, Broom J, Brown TJ, Poobalan A, Aucott L, Stearns SC, *et al*.

No. 22
Autoantibody testing in children with newly diagnosed type 1 diabetes mellitus.
By Dretzke J, Cummins C, Sandercock J, Fry-Smith A, Barrett T, Burls A.

No. 23
Clinical effectiveness and cost-effectiveness of prehospital intravenous fluids in trauma patients.
By Dretzke J, Sandercock J, Bayliss S, Burls A.

No. 24
Newer hypnotic drugs for the short-term management of insomnia: a systematic review and economic evaluation.
By Dündar Y, Boland A, Strobl J, Dodd S, Haycox A, Bagust A, *et al*.

No. 25
Development and validation of methods for assessing the quality of diagnostic accuracy studies.
By Whiting P, Rutjes AWS, Dinnes J, Reitsma JB, Bossuyt PMM, Kleijnen J.

No. 26
EVALUATE hysterectomy trial: a multicentre randomised trial comparing abdominal, vaginal and laparoscopic methods of hysterectomy.
By Garry R, Fountain J, Brown J, Manca A, Mason S, Sculpher M, *et al*.

No. 27
Methods for expected value of information analysis in complex health economic models: developments on the health economics of interferon-β and glatiramer acetate for multiple sclerosis.
By Tappenden P, Chilcott JB, Eggington S, Oakley J, McCabe C.

No. 28
Effectiveness and cost-effectiveness of imatinib for first-line treatment of chronic myeloid leukaemia in chronic phase: a systematic review and economic analysis.
By Dalziel K, Round A, Stein K, Garside R, Price A.

No. 29
VenUS I: a randomised controlled trial of two types of bandage for treating venous leg ulcers.
By Iglesias C, Nelson EA, Cullum NA, Torgerson DJ, on behalf of the VenUS Team.

No. 30
Systematic review of the effectiveness and cost-effectiveness, and economic evaluation, of myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction.
By Mowatt G, Vale L, Brazzelli M, Hernandez R, Murray A, Scott N, *et al*.

No. 31
A pilot study on the use of decision theory and value of information analysis as part of the NHS Health Technology Assessment programme.
By Claxton K, Ginnelly L, Sculpher M, Philips Z, Palmer S.

No. 32
The Social Support and Family Health Study: a randomised controlled trial and economic evaluation of two alternative forms of postnatal support for mothers living in disadvantaged inner-city areas.
By Wiggins M, Oakley A, Roberts I, Turner H, Rajan L, Austerberry H, *et al*.

No. 33
Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review.
By Green JM, Hewison J, Bekker HL, Bryant, Cuckle HS.

No. 34
Evaluation of abnormal uterine bleeding: comparison of three outpatient procedures within cohorts defined by age and menopausal status.
By Critchley HOD, Warner P, Lee AJ, Brechin S, Guise J, Graham B.

No. 35
Coronary artery stents: a rapid systematic review and economic evaluation.
By Hill R, Bagust A, Bakhai A, Dickson R, Dündar Y, Haycox A, *et al*.

No. 36
Review of guidelines for good practice in decision-analytic modelling in health technology assessment.
By Philips Z, Ginnelly L, Sculpher M, Claxton K, Golder S, Riemsma R, *et al*.

No. 37
Rituximab (MabThera®) for aggressive non-Hodgkin's lymphoma: systematic review and economic evaluation.
By Knight C, Hind D, Brewer N, Abbott V.

No. 38
Clinical effectiveness and cost-effectiveness of clopidogrel and modified-release dipyridamole in the secondary prevention of occlusive vascular events: a systematic review and economic evaluation.
By Jones L, Griffin S, Palmer S, Main C, Orton V, Sculpher M, *et al*.

No. 39
Pegylated interferon α-2a and -2b in combination with ribavirin in the treatment of chronic hepatitis C: a systematic review and economic evaluation.
By Shepherd J, Brodin H, Cave C, Waugh N, Price A, Gabbay J.

No. 40
Clopidogrel used in combination with aspirin compared with aspirin alone in the treatment of non-ST-segment-elevation acute coronary syndromes: a systematic review and economic evaluation.
By Main C, Palmer S, Griffin S, Jones L, Orton V, Sculpher M, *et al*.

No. 41
Provision, uptake and cost of cardiac rehabilitation programmes: improving services to under-represented groups.
By Beswick AD, Rees K, Griebsch I, Taylor FC, Burke M, West RR, *et al*.

No. 42
Involving South Asian patients in clinical trials.
By Hussain-Gambles M, Leese B, Atkin K, Brown J, Mason S, Tovey P.

No. 43
Clinical and cost-effectiveness of continuous subcutaneous insulin infusion for diabetes.
By Colquitt JL, Green C, Sidhu MK, Hartwell D, Waugh N.

No. 44
Identification and assessment of ongoing trials in health technology assessment reviews.
By Song FJ, Fry-Smith A, Davenport C, Bayliss S, Adi Y, Wilson JS, *et al*.

No. 45
Systematic review and economic evaluation of a long-acting insulin analogue, insulin glargine
By Warren E, Weatherley-Jones E, Chilcott J, Beverley C.

59

No. 46

Supplementation of a home-based exercise programme with a class-based programme for people with osteoarthritis of the knees: a randomised controlled trial and health economic analysis.

By McCarthy CJ, Mills PM, Pullen R, Richardson G, Hawkins N, Roberts CR, *et al*.

No. 47

Clinical and cost-effectiveness of once-daily versus more frequent use of same potency topical corticosteroids for atopic eczema: a systematic review and economic evaluation.

By Green C, Colquitt JL, Kirby J, Davidson P, Payne E.

No. 48

Acupuncture of chronic headache disorders in primary care: randomised controlled trial and economic analysis.

By Vickers AJ, Rees RW, Zollman CE, McCarney R, Smith CM, Ellis N, *et al*.

No. 49

Generalisability in economic evaluation studies in healthcare: a review and case studies.

By Sculpher MJ, Pang FS, Manca A, Drummond MF, Golder S, Urdahl H, *et al*.

No. 50

Virtual outreach: a randomised controlled trial and economic evaluation of joint teleconferenced medical consultations.

By Wallace P, Barber J, Clayton W, Currell R, Fleming K, Garner P, *et al*.

Volume 9, 2005

No. 1

Randomised controlled multiple treatment comparison to provide a cost-effectiveness rationale for the selection of antimicrobial therapy in acne.

By Ozolins M, Eady EA, Avery A, Cunliffe WJ, O'Neill C, Simpson NB, *et al*.

No. 2

Do the findings of case series studies vary significantly according to methodological characteristics?

By Dalziel K, Round A, Stein K, Garside R, Castelnuovo E, Payne L.

No. 3

Improving the referral process for familial breast cancer genetic counselling: findings of three randomised controlled trials of two interventions.

By Wilson BJ, Torrance N, Mollison J, Wordsworth S, Gray JR, Haites NE, *et al*.

No. 4

Randomised evaluation of alternative electrosurgical modalities to treat bladder outflow obstruction in men with benign prostatic hyperplasia.

By Fowler C, McAllister W, Plail R, Karim O, Yang Q.

No. 5

A pragmatic randomised controlled trial of the cost-effectiveness of palliative therapies for patients with inoperable oesophageal cancer.

By Shenfine J, McNamee P, Steen N, Bond J, Griffin SM.

No. 6

Impact of computer-aided detection prompts on the sensitivity and specificity of screening mammography.

By Taylor P, Champness J, Given-Wilson R, Johnston K, Potts H.

No. 7

Issues in data monitoring and interim analysis of trials.

By Grant AM, Altman DG, Babiker AB, Campbell MK, Clemens FJ, Darbyshire JH, *et al*.

No. 8

Lay public's understanding of equipoise and randomisation in randomised controlled trials.

By Robinson EJ, Kerr CEP, Stevens AJ, Lilford RJ, Braunholtz DA, Edwards SJ, *et al*.

No. 9

Clinical and cost-effectiveness of electroconvulsive therapy for depressive illness, schizophrenia, catatonia and mania: systematic reviews and economic modelling studies.

By Greenhalgh J, Knight C, Hind D, Beverley C, Walters S.

No. 10

Measurement of health-related quality of life for people with dementia: development of a new instrument (DEMQOL) and an evaluation of current methodology.

By Smith SC, Lamping DL, Banerjee S, Harwood R, Foley B, Smith P, *et al*.

No. 11

Clinical effectiveness and cost-effectiveness of drotrecogin alfa (activated) (Xigris®) for the treatment of severe sepsis in adults: a systematic review and economic evaluation.

By Green C, Dinnes J, Takeda A, Shepherd J, Hartwell D, Cave C, *et al*.

No. 12

A methodological review of how heterogeneity has been examined in systematic reviews of diagnostic test accuracy.

By Dinnes J, Deeks J, Kirby J, Roderick P.

No. 13

Cervical screening programmes: can automation help? Evidence from systematic reviews, an economic analysis and a simulation modelling exercise applied to the UK.

By Willis BH, Barton P, Pearmain P, Bryan S, Hyde C.

No. 14

Laparoscopic surgery for inguinal hernia repair: systematic review of effectiveness and economic evaluation.

By McCormack K, Wake B, Perez J, Fraser C, Cook J, McIntosh E, *et al*.

No. 15

Clinical effectiveness, tolerability and cost-effectiveness of newer drugs for epilepsy in adults: a systematic review and economic evaluation.

By Wilby J, Kainth A, Hawkins N, Epstein D, McIntosh H, McDaid C, *et al*.

No. 16

A randomised controlled trial to compare the cost-effectiveness of tricyclic antidepressants, selective serotonin reuptake inhibitors and lofepramine.

By Peveler R, Kendrick T, Buxton M, Longworth L, Baldwin D, Moore M, *et al*.

No. 17

Clinical effectiveness and cost-effectiveness of immediate angioplasty for acute myocardial infarction: systematic review and economic evaluation.

By Hartwell D, Colquitt J, Loveman E, Clegg AJ, Brodin H, Waugh N, *et al*.

No. 18

A randomised controlled comparison of alternative strategies in stroke care.

By Kalra L, Evans A, Perez I, Knapp M, Swift C, Donaldson N.

No. 19

The investigation and analysis of critical incidents and adverse events in healthcare.

By Woloshynowych M, Rogers S, Taylor-Adams S, Vincent C.

No. 20

Potential use of routine databases in health technology assessment.

By Raftery J, Roderick P, Stevens A.

No. 21

Clinical and cost-effectiveness of newer immunosuppressive regimens in renal transplantation: a systematic review and modelling study.

By Woodroffe R, Yao GL, Meads C, Bayliss S, Ready A, Raftery J, *et al*.

No. 22

A systematic review and economic evaluation of alendronate, etidronate, risedronate, raloxifene and teriparatide for the prevention and treatment of postmenopausal osteoporosis.

By Stevenson M, Lloyd Jones M, De Nigris E, Brewer N, Davis S, Oakley J.

No. 23
A systematic review to examine the impact of psycho-educational interventions on health outcomes and costs in adults and children with difficult asthma.
By Smith JR, Mugford M, Holland R, Candy B, Noble MJ, Harrison BDW, *et al*.

No. 24
An evaluation of the costs, effectiveness and quality of renal replacement therapy provision in renal satellite units in England and Wales.
By Roderick P, Nicholson T, Armitage A, Mehta R, Mullee M, Gerard K, *et al*.

No. 25
Imatinib for the treatment of patients with unresectable and/or metastatic gastrointestinal stromal tumours: systematic review and economic evaluation.
By Wilson J, Connock M, Song F, Yao G, Fry-Smith A, Raftery J, *et al*.

No. 26
Indirect comparisons of competing interventions.
By Glenny AM, Altman DG, Song F, Sakarovitch C, Deeks JJ, D'Amico R, *et al*.

No. 27
Cost-effectiveness of alternative strategies for the initial medical management of non-ST elevation acute coronary syndrome: systematic review and decision-analytical modelling.
By Robinson M, Palmer S, Sculpher M, Philips Z, Ginnelly L, Bowens A, *et al*.

No. 28
Outcomes of electrically stimulated gracilis neosphincter surgery.
By Tillin T, Chambers M, Feldman R.

No. 29
The effectiveness and cost-effectiveness of pimecrolimus and tacrolimus for atopic eczema: a systematic review and economic evaluation.
By Garside R, Stein K, Castelnuovo E, Pitt M, Ashcroft D, Dimmock P, *et al*.

No. 30
Systematic review on urine albumin testing for early detection of diabetic complications.
By Newman DJ, Mattock MB, Dawnay ABS, Kerry S, McGuire A, Yaqoob M, *et al*.

No. 31
Randomised controlled trial of the cost-effectiveness of water-based therapy for lower limb osteoarthritis.
By Cochrane T, Davey RC, Matthes Edwards SM.

No. 32
Longer term clinical and economic benefits of offering acupuncture care to patients with chronic low back pain.
By Thomas KJ, MacPherson H, Ratcliffe J, Thorpe L, Brazier J, Campbell M, *et al*.

No. 33
Cost-effectiveness and safety of epidural steroids in the management of sciatica.
By Price C, Arden N, Coglan L, Rogers P.

No. 34
The British Rheumatoid Outcome Study Group (BROSG) randomised controlled trial to compare the effectiveness and cost-effectiveness of aggressive versus symptomatic therapy in established rheumatoid arthritis.
By Symmons D, Tricker K, Roberts C, Davies L, Dawes P, Scott DL.

No. 35
Conceptual framework and systematic review of the effects of participants' and professionals' preferences in randomised controlled trials.
By King M, Nazareth I, Lampe F, Bower P, Chandler M, Morou M, *et al*.

No. 36
The clinical and cost-effectiveness of implantable cardioverter defibrillators: a systematic review.
By Bryant J, Brodin H, Loveman E, Payne E, Clegg A.

No. 37
A trial of problem-solving by community mental health nurses for anxiety, depression and life difficulties among general practice patients. The CPN-GP study.
By Kendrick T, Simons L, Mynors-Wallis L, Gray A, Lathlean J, Pickering R, *et al*.

No. 38
The causes and effects of socio-demographic exclusions from clinical trials.
By Bartlett C, Doyal L, Ebrahim S, Davey P, Bachmann M, Egger M, *et al*.

No. 39
Is hydrotherapy cost-effective? A randomised controlled trial of combined hydrotherapy programmes compared with physiotherapy land techniques in children with juvenile idiopathic arthritis.
By Epps H, Ginnelly L, Utley M, Southwood T, Gallivan S, Sculpher M, *et al*.

No. 40
A randomised controlled trial and cost-effectiveness study of systematic screening (targeted and total population screening) versus routine practice for the detection of atrial fibrillation in people aged 65 and over. The SAFE study.
By Hobbs FDR, Fitzmaurice DA, Mant J, Murray E, Jowett S, Bryan S, *et al*.

No. 41
Displaced intracapsular hip fractures in fit, older people: a randomised comparison of reduction and fixation, bipolar hemiarthroplasty and total hip arthroplasty.
By Keating JF, Grant A, Masson M, Scott NW, Forbes JF.

No. 42
Long-term outcome of cognitive behaviour therapy clinical trials in central Scotland.
By Durham RC, Chambers JA, Power KG, Sharp DM, Macdonald RR, Major KA, *et al*.

No. 43
The effectiveness and cost-effectiveness of dual-chamber pacemakers compared with single-chamber pacemakers for bradycardia due to atrioventricular block or sick sinus syndrome: systematic review and economic evaluation.
By Castelnuovo E, Stein K, Pitt M, Garside R, Payne E.

No. 44
Newborn screening for congenital heart defects: a systematic review and cost-effectiveness analysis.
By Knowles R, Griebsch I, Dezateux C, Brown J, Bull C, Wren C.

No. 45
The clinical and cost-effectiveness of left ventricular assist devices for end-stage heart failure: a systematic review and economic evaluation.
By Clegg AJ, Scott DA, Loveman E, Colquitt J, Hutchinson J, Royle P, *et al*.

No. 46
The effectiveness of the Heidelberg Retina Tomograph and laser diagnostic glaucoma scanning system (GDx) in detecting and monitoring glaucoma.
By Kwartz AJ, Henson DB, Harper RA, Spencer AF, McLeod D.

No. 47
Clinical and cost-effectiveness of autologous chondrocyte implantation for cartilage defects in knee joints: systematic review and economic evaluation.
By Clar C, Cummins E, McIntyre L, Thomas S, Lamb J, Bain L, *et al*.

No. 48
Systematic review of effectiveness of
different treatments for childhood
retinoblastoma.
By McDaid C, Hartley S, Bagnall
A-M, Ritchie G, Light K, Riemsma R.

No. 49
Towards evidence-based guidelines
for the prevention of venous
thromboembolism: systematic
reviews of mechanical methods, oral
anticoagulation, dextran and regional
anaesthesia as thromboprophylaxis.
By Roderick P, Ferris G, Wilson K,
Halls H, Jackson D, Collins R, *et al.*

No. 50
The effectiveness and cost-effectiveness
of parent training/education
programmes for the treatment
of conduct disorder, including
oppositional defiant disorder, in
children.
By Dretzke J, Frew E, Davenport C,
Barlow J, Stewart-Brown S, Sandercock J,
et al.

Volume 10, 2006

No. 1
The clinical and cost-effectiveness of
donepezil, rivastigmine, galantamine
and memantine for Alzheimer's
disease.
By Loveman E, Green C, Kirby J,
Takeda A, Picot J, Payne E, *et al.*

No. 2
FOOD: a multicentre randomised trial
evaluating feeding policies in patients
admitted to hospital with a recent
stroke.
By Dennis M, Lewis S, Cranswick G,
Forbes J.

No. 3
The clinical effectiveness and cost-
effectiveness of computed tomography
screening for lung cancer: systematic
reviews.
By Black C, Bagust A, Boland A,
Walker S, McLeod C, De Verteuil R, *et al.*

No. 4
A systematic review of the effectiveness
and cost-effectiveness of neuroimaging
assessments used to visualise the seizure
focus in people with refractory epilepsy
being considered for surgery.
By Whiting P, Gupta R, Burch J,
Mujica Mota RE, Wright K, Marson A,
et al.

No. 5
Comparison of conference abstracts
and presentations with full-text articles
in the health technology assessments of
rapidly evolving technologies.
By Dundar Y, Dodd S, Dickson R,
Walley T, Haycox A, Williamson PR.

No. 6
Systematic review and evaluation
of methods of assessing urinary
incontinence.
By Martin JL, Williams KS, Abrams
KR, Turner DA, Sutton AJ, Chapple C,
et al.

No. 7
The clinical effectiveness and cost-
effectiveness of newer drugs for
children with epilepsy. A systematic
review.
By Connock M, Frew E, Evans B-W,
Bryan S, Cummins C, Fry-Smith A, *et al.*

No. 8
Surveillance of Barrett's oesophagus:
exploring the uncertainty through
systematic review, expert workshop and
economic modelling.
By Garside R, Pitt M, Somerville M,
Stein K, Price A, Gilbert N.

No. 9
Topotecan, pegylated liposomal
doxorubicin hydrochloride and
paclitaxel for second-line or subsequent
treatment of advanced ovarian cancer:
a systematic review and economic
evaluation.
By Main C, Bojke L, Griffin S,
Norman G, Barbieri M, Mather L, *et al.*

No. 10
Evaluation of molecular techniques
in prediction and diagnosis
of cytomegalovirus disease in
immunocompromised patients.
By Szczepura A, Westmoreland D,
Vinogradova Y, Fox J, Clark M.

No. 11
Screening for thrombophilia in high-
risk situations: systematic review
and cost-effectiveness analysis. The
Thrombosis: Risk and Economic
Assessment of Thrombophilia
Screening (TREATS) study.
By Wu O, Robertson L, Twaddle S,
Lowe GDO, Clark P, Greaves M, *et al.*

No. 12
A series of systematic reviews to inform
a decision analysis for sampling and
treating infected diabetic foot ulcers.
By Nelson EA, O'Meara S, Craig D,
Iglesias C, Golder S, Dalton J, *et al.*

No. 13
Randomised clinical trial, observational
study and assessment of cost-
effectiveness of the treatment of
varicose veins (REACTIV trial).
By Michaels JA, Campbell WB,
Brazier JE, MacIntyre JB, Palfreyman SJ,
Ratcliffe J, *et al.*

No. 14
The cost-effectiveness of screening for
oral cancer in primary care.
By Speight PM, Palmer S, Moles DR,
Downer MC, Smith DH, Henriksson M,
et al.

No. 15
Measurement of the clinical and cost-
effectiveness of non-invasive diagnostic
testing strategies for deep vein
thrombosis.
By Goodacre S, Sampson F,
Stevenson M, Wailoo A, Sutton A,
Thomas S, *et al.*

No. 16
Systematic review of the effectiveness
and cost-effectiveness of HealOzone®
for the treatment of occlusal pit/fissure
caries and root caries.
By Brazzelli M, McKenzie L, Fielding
S, Fraser C, Clarkson J, Kilonzo M, *et al.*

No. 17
Randomised controlled trials of
conventional antipsychotic versus
new atypical drugs, and new atypical
drugs versus clozapine, in people with
schizophrenia responding poorly to, or
intolerant of, current drug treatment.
By Lewis SW, Davies L, Jones PB,
Barnes TRE, Murray RM, Kerwin R,
et al.

No. 18
Diagnostic tests and algorithms used
in the investigation of haematuria:
systematic reviews and economic
evaluation.
By Rodgers M, Nixon J, Hempel S,
Aho T, Kelly J, Neal D, *et al.*

No. 19
Cognitive behavioural therapy in
addition to antispasmodic therapy for
irritable bowel syndrome in primary
care: randomised controlled trial.
By Kennedy TM, Chalder T,
McCrone P, Darnley S, Knapp M,
Jones RH, *et al.*

No. 20
A systematic review of the
clinical effectiveness and cost-
effectiveness of enzyme replacement
therapies for Fabry's disease and
mucopolysaccharidosis type 1.
By Connock M, Juarez-Garcia A,
Frew E, Mans A, Dretzke J, Fry-Smith A,
et al.

No. 21
Health benefits of antiviral therapy for
mild chronic hepatitis C: randomised
controlled trial and economic
evaluation.
By Wright M, Grieve R, Roberts J,
Main J, Thomas HC, on behalf of the
UK Mild Hepatitis C Trial Investigators.

No. 22
Pressure relieving support surfaces: a
randomised evaluation.
By Nixon J, Nelson EA, Cranny G,
Iglesias CP, Hawkins K, Cullum NA, *et al.*

No. 23
A systematic review and economic model of the effectiveness and cost-effectiveness of methylphenidate, dexamfetamine and atomoxetine for the treatment of attention deficit hyperactivity disorder in children and adolescents.
By King S, Griffin S, Hodges Z, Weatherly H, Asseburg C, Richardson G, *et al.*

No. 24
The clinical effectiveness and cost-effectiveness of enzyme replacement therapy for Gaucher's disease: a systematic review.
By Connock M, Burls A, Frew E, Fry-Smith A, Juarez-Garcia A, McCabe C, *et al.*

No. 25
Effectiveness and cost-effectiveness of salicylic acid and cryotherapy for cutaneous warts. An economic decision model.
By Thomas KS, Keogh-Brown MR, Chalmers JR, Fordham RJ, Holland RC, Armstrong SJ, *et al.*

No. 26
A systematic literature review of the effectiveness of non-pharmacological interventions to prevent wandering in dementia and evaluation of the ethical implications and acceptability of their use.
By Robinson L, Hutchings D, Corner L, Beyer F, Dickinson H, Vanoli A, *et al.*

No. 27
A review of the evidence on the effects and costs of implantable cardioverter defibrillator therapy in different patient groups, and modelling of cost-effectiveness and cost–utility for these groups in a UK context.
By Buxton M, Caine N, Chase D, Connelly D, Grace A, Jackson C, *et al.*

No. 28
Adefovir dipivoxil and pegylated interferon alfa-2a for the treatment of chronic hepatitis B: a systematic review and economic evaluation.
By Shepherd J, Jones J, Takeda A, Davidson P, Price A.

No. 29
An evaluation of the clinical and cost-effectiveness of pulmonary artery catheters in patient management in intensive care: a systematic review and a randomised controlled trial.
By Harvey S, Stevens K, Harrison D, Young D, Brampton W, McCabe C, *et al.*

No. 30
Accurate, practical and cost-effective assessment of carotid stenosis in the UK.
By Wardlaw JM, Chappell FM, Stevenson M, De Nigris E, Thomas S, Gillard J, *et al.*

No. 31
Etanercept and infliximab for the treatment of psoriatic arthritis: a systematic review and economic evaluation.
By Woolacott N, Bravo Vergel Y, Hawkins N, Kainth A, Khadjesari Z, Misso K, *et al.*

No. 32
The cost-effectiveness of testing for hepatitis C in former injecting drug users.
By Castelnuovo E, Thompson-Coon J, Pitt M, Cramp M, Siebert U, Price A, *et al.*

No. 33
Computerised cognitive behaviour therapy for depression and anxiety update: a systematic review and economic evaluation.
By Kaltenthaler E, Brazier J, De Nigris E, Tumur I, Ferriter M, Beverley C, *et al.*

No. 34
Cost-effectiveness of using prognostic information to select women with breast cancer for adjuvant systemic therapy.
By Williams C, Brunskill S, Altman D, Briggs A, Campbell H, Clarke M, *et al.*

No. 35
Psychological therapies including dialectical behaviour therapy for borderline personality disorder: a systematic review and preliminary economic evaluation.
By Brazier J, Tumur I, Holmes M, Ferriter M, Parry G, Dent-Brown K, *et al.*

No. 36
Clinical effectiveness and cost-effectiveness of tests for the diagnosis and investigation of urinary tract infection in children: a systematic review and economic model.
By Whiting P, Westwood M, Bojke L, Palmer S, Richardson G, Cooper J, *et al.*

No. 37
Cognitive behavioural therapy in chronic fatigue syndrome: a randomised controlled trial of an outpatient group programme.
By O'Dowd H, Gladwell P, Rogers CA, Hollinghurst S, Gregory A.

No. 38
A comparison of the cost-effectiveness of five strategies for the prevention of nonsteroidal anti-inflammatory drug-induced gastrointestinal toxicity: a systematic review with economic modelling.
By Brown TJ, Hooper L, Elliott RA, Payne K, Webb R, Roberts C, et al.

No. 39
The effectiveness and cost-effectiveness of computed tomography screening for coronary artery disease: systematic review.
By Waugh N, Black C, Walker S, McIntyre L, Cummins E, Hillis G.

No. 40
What are the clinical outcome and cost-effectiveness of endoscopy undertaken by nurses when compared with doctors? A Multi-Institution Nurse Endoscopy Trial (MINuET).
By Williams J, Russell I, Durai D, Cheung W-Y, Farrin A, Bloor K, *et al.*

No. 41
The clinical and cost-effectiveness of oxaliplatin and capecitabine for the adjuvant treatment of colon cancer: systematic review and economic evaluation.
By Pandor A, Eggington S, Paisley S, Tappenden P, Sutcliffe P.

No. 42
A systematic review of the effectiveness of adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis in adults and an economic evaluation of their cost-effectiveness.
By Chen Y-F, Jobanputra P, Barton P, Jowett S, Bryan S, Clark W, *et al.*

No. 43
Telemedicine in dermatology: a randomised controlled trial.
By Bowns IR, Collins K, Walters SJ, McDonagh AJG.

No. 44
Cost-effectiveness of cell salvage and alternative methods of minimising perioperative allogeneic blood transfusion: a systematic review and economic model.
By Davies L, Brown TJ, Haynes S, Payne K, Elliott RA, McCollum C.

No. 45
Clinical effectiveness and cost-effectiveness of laparoscopic surgery for colorectal cancer: systematic reviews and economic evaluation.
By Murray A, Lourenco T, de Verteuil R, Hernandez R, Fraser C, McKinley A, *et al.*

No. 46
Etanercept and efalizumab for the treatment of psoriasis: a systematic review.
By Woolacott N, Hawkins N, Mason A, Kainth A, Khadjesari Z, Bravo Vergel Y, *et al.*

No. 47
Systematic reviews of clinical decision tools for acute abdominal pain.
By Liu JLY, Wyatt JC, Deeks JJ, Clamp S, Keen J, Verde P, *et al.*

No. 48
Evaluation of the ventricular assist device programme in the UK.
By Sharples L, Buxton M, Caine N, Cafferty F, Demiris N, Dyer M, *et al.*

No. 49
A systematic review and economic model of the clinical and cost-effectiveness of immunosuppressive therapy for renal transplantation in children.
By Yao G, Albon E, Adi Y, Milford D, Bayliss S, Ready A, *et al*.

No. 50
Amniocentesis results: investigation of anxiety. The ARIA trial.
By Hewison J, Nixon J, Fountain J, Cocks K, Jones C, Mason G, *et al*.

Volume 11, 2007

No. 1
Pemetrexed disodium for the treatment of malignant pleural mesothelioma: a systematic review and economic evaluation.
By Dundar Y, Bagust A, Dickson R, Dodd S, Green J, Haycox A, *et al*.

No. 2
A systematic review and economic model of the clinical effectiveness and cost-effectiveness of docetaxel in combination with prednisone or prednisolone for the treatment of hormone-refractory metastatic prostate cancer.
By Collins R, Fenwick E, Trowman R, Perard R, Norman G, Light K, *et al*.

No. 3
A systematic review of rapid diagnostic tests for the detection of tuberculosis infection.
By Dinnes J, Deeks J, Kunst H, Gibson A, Cummins E, Waugh N, *et al*.

No. 4
The clinical effectiveness and cost-effectiveness of strontium ranelate for the prevention of osteoporotic fragility fractures in postmenopausal women.
By Stevenson M, Davis S, Lloyd-Jones M, Beverley C.

No. 5
A systematic review of quantitative and qualitative research on the role and effectiveness of written information available to patients about individual medicines.
By Raynor DK, Blenkinsopp A, Knapp P, Grime J, Nicolson DJ, Pollock K, *et al*.

No. 6
Oral naltrexone as a treatment for relapse prevention in formerly opioid-dependent drug users: a systematic review and economic evaluation.
By Adi Y, Juarez-Garcia A, Wang D, Jowett S, Frew E, Day E, *et al*.

No. 7
Glucocorticoid-induced osteoporosis: a systematic review and cost–utility analysis.
By Kanis JA, Stevenson M, McCloskey EV, Davis S, Lloyd-Jones M.

No. 8
Epidemiological, social, diagnostic and economic evaluation of population screening for genital chlamydial infection.
By Low N, McCarthy A, Macleod J, Salisbury C, Campbell R, Roberts TE, *et al*.

No. 9
Methadone and buprenorphine for the management of opioid dependence: a systematic review and economic evaluation.
By Connock M, Juarez-Garcia A, Jowett S, Frew E, Liu Z, Taylor RJ, *et al*.

No. 10
Exercise Evaluation Randomised Trial (EXERT): a randomised trial comparing GP referral for leisure centre-based exercise, community-based walking and advice only.
By Isaacs AJ, Critchley JA, See Tai S, Buckingham K, Westley D, Harridge SDR, *et al*.

No. 11
Interferon alfa (pegylated and non-pegylated) and ribavirin for the treatment of mild chronic hepatitis C: a systematic review and economic evaluation.
By Shepherd J, Jones J, Hartwell D, Davidson P, Price A, Waugh N.

No. 12
Systematic review and economic evaluation of bevacizumab and cetuximab for the treatment of metastatic colorectal cancer.
By Tappenden P, Jones R, Paisley S, Carroll C.

No. 13
A systematic review and economic evaluation of epoetin alfa, epoetin beta and darbepoetin alfa in anaemia associated with cancer, especially that attributable to cancer treatment.
By Wilson J, Yao GL, Raftery J, Bohlius J, Brunskill S, Sandercock J, *et al*.

No. 14
A systematic review and economic evaluation of statins for the prevention of coronary events.
By Ward S, Lloyd Jones M, Pandor A, Holmes M, Ara R, Ryan A, *et al*.

No. 15
A systematic review of the effectiveness and cost-effectiveness of different models of community-based respite care for frail older people and their carers.
By Mason A, Weatherly H, Spilsbury K, Arksey H, Golder S, Adamson J, *et al*.

No. 16
Additional therapy for young children with spastic cerebral palsy: a randomised controlled trial.
By Weindling AM, Cunningham CC, Glenn SM, Edwards RT, Reeves DJ.

No. 17
Screening for type 2 diabetes: literature review and economic modelling.
By Waugh N, Scotland G, McNamee P, Gillett M, Brennan A, Goyder E, *et al*.

No. 18
The effectiveness and cost-effectiveness of cinacalcet for secondary hyperparathyroidism in end-stage renal disease patients on dialysis: a systematic review and economic evaluation.
By Garside R, Pitt M, Anderson R, Mealing S, Roome C, Snaith A, *et al*.

No. 19
The clinical effectiveness and cost-effectiveness of gemcitabine for metastatic breast cancer: a systematic review and economic evaluation.
By Takeda AL, Jones J, Loveman E, Tan SC, Clegg AJ.

No. 20
A systematic review of duplex ultrasound, magnetic resonance angiography and computed tomography angiography for the diagnosis and assessment of symptomatic, lower limb peripheral arterial disease.
By Collins R, Cranny G, Burch J, Aguiar-Ibáñez R, Craig D, Wright K, *et al*.

No. 21
The clinical effectiveness and cost-effectiveness of treatments for children with idiopathic steroid-resistant nephrotic syndrome: a systematic review.
By Colquitt JL, Kirby J, Green C, Cooper K, Trompeter RS.

No. 22
A systematic review of the routine monitoring of growth in children of primary school age to identify growth-related conditions.
By Fayter D, Nixon J, Hartley S, Rithalia A, Butler G, Rudolf M, *et al*.

No. 23
Systematic review of the effectiveness of preventing and treating *Staphylococcus aureus* carriage in reducing peritoneal catheter-related infections.
By McCormack K, Rabindranath K, Kilonzo M, Vale L, Fraser C, McIntyre L, *et al*.

No. 24
The clinical effectiveness and cost of repetitive transcranial magnetic stimulation versus electroconvulsive therapy in severe depression: a multicentre pragmatic randomised controlled trial and economic analysis.
By McLoughlin DM, Mogg A, Eranti S, Pluck G, Purvis R, Edwards D, *et al.*

No. 25
A randomised controlled trial and economic evaluation of direct versus indirect and individual versus group modes of speech and language therapy for children with primary language impairment.
By Boyle J, McCartney E, Forbes J, O'Hare A.

No. 26
Hormonal therapies for early breast cancer: systematic review and economic evaluation.
By Hind D, Ward S, De Nigris E, Simpson E, Carroll C, Wyld L.

No. 27
Cardioprotection against the toxic effects of anthracyclines given to children with cancer: a systematic review.
By Bryant J, Picot J, Levitt G, Sullivan I, Baxter L, Clegg A.

No. 28
Adalimumab, etanercept and infliximab for the treatment of ankylosing spondylitis: a systematic review and economic evaluation.
By McLeod C, Bagust A, Boland A, Dagenais P, Dickson R, Dundar Y, *et al.*

No. 29
Prenatal screening and treatment strategies to prevent group B streptococcal and other bacterial infections in early infancy: cost-effectiveness and expected value of information analyses.
By Colbourn T, Asseburg C, Bojke L, Philips Z, Claxton K, Ades AE, *et al.*

No. 30
Clinical effectiveness and cost-effectiveness of bone morphogenetic proteins in the non-healing of fractures and spinal fusion: a systematic review.
By Garrison KR, Donell S, Ryder J, Shemilt I, Mugford M, Harvey I, *et al.*

No. 31
A randomised controlled trial of postoperative radiotherapy following breast-conserving surgery in a minimum-risk older population. The PRIME trial.
By Prescott RJ, Kunkler IH, Williams LJ, King CC, Jack W, van der Pol M, *et al.*

No. 32
Current practice, accuracy, effectiveness and cost-effectiveness of the school entry hearing screen.
By Bamford J, Fortnum H, Bristow K, Smith J, Vamvakas G, Davies L, *et al.*

No. 33
The clinical effectiveness and cost-effectiveness of inhaled insulin in diabetes mellitus: a systematic review and economic evaluation.
By Black C, Cummins E, Royle P, Philip S, Waugh N.

No. 34
Surveillance of cirrhosis for hepatocellular carcinoma: systematic review and economic analysis.
By Thompson Coon J, Rogers G, Hewson P, Wright D, Anderson R, Cramp M, *et al.*

No. 35
The Birmingham Rehabilitation Uptake Maximisation Study (BRUM). Homebased compared with hospital-based cardiac rehabilitation in a multi-ethnic population: cost-effectiveness and patient adherence.
By Jolly K, Taylor R, Lip GYH, Greenfield S, Raftery J, Mant J, *et al.*

No. 36
A systematic review of the clinical, public health and cost-effectiveness of rapid diagnostic tests for the detection and identification of bacterial intestinal pathogens in faeces and food.
By Abubakar I, Irvine L, Aldus CF, Wyatt GM, Fordham R, Schelenz S, *et al.*

No. 37
A randomised controlled trial examining the longer-term outcomes of standard versus new antiepileptic drugs. The SANAD trial.
By Marson AG, Appleton R, Baker GA, Chadwick DW, Doughty J, Eaton B, *et al.*

No. 38
Clinical effectiveness and cost-effectiveness of different models of managing long-term oral anti-coagulation therapy: a systematic review and economic modelling.
By Connock M, Stevens C, Fry-Smith A, Jowett S, Fitzmaurice D, Moore D, *et al.*

No. 39
A systematic review and economic model of the clinical effectiveness and cost-effectiveness of interventions for preventing relapse in people with bipolar disorder.
By Soares-Weiser K, Bravo Vergel Y, Beynon S, Dunn G, Barbieri M, Duffy S, *et al.*

No. 40
Taxanes for the adjuvant treatment of early breast cancer: systematic review and economic evaluation.
By Ward S, Simpson E, Davis S, Hind D, Rees A, Wilkinson A.

No. 41
The clinical effectiveness and cost-effectiveness of screening for open angle glaucoma: a systematic review and economic evaluation.
By Burr JM, Mowatt G, Hernández R, Siddiqui MAR, Cook J, Lourenco T, *et al.*

No. 42
Acceptability, benefit and costs of early screening for hearing disability: a study of potential screening tests and models.
By Davis A, Smith P, Ferguson M, Stephens D, Gianopoulos I.

No. 43
Contamination in trials of educational interventions.
By Keogh-Brown MR, Bachmann MO, Shepstone L, Hewitt C, Howe A, Ramsay CR, *et al.*

No. 44
Overview of the clinical effectiveness of positron emission tomography imaging in selected cancers.
By Facey K, Bradbury I, Laking G, Payne E.

No. 45
The effectiveness and cost-effectiveness of carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma: a systematic review and economic evaluation.
By Garside R, Pitt M, Anderson R, Rogers G, Dyer M, Mealing S, *et al.*

No. 46
Drug-eluting stents: a systematic review and economic evaluation.
By Hill RA, Boland A, Dickson R, Dündar Y, Haycox A, McLeod C, *et al.*

No. 47
The clinical effectiveness and cost-effectiveness of cardiac resynchronisation (biventricular pacing) for heart failure: systematic review and economic model.
By Fox M, Mealing S, Anderson R, Dean J, Stein K, Price A, *et al.*

No. 48
Recruitment to randomised trials: strategies for trial enrolment and participation study. The STEPS study.
By Campbell MK, Snowdon C, Francis D, Elbourne D, McDonald AM, Knight R, *et al.*

No. 49
Cost-effectiveness of functional cardiac testing in the diagnosis and management of coronary artery disease: a randomised controlled trial. The CECaT trial.

By Sharples L, Hughes V, Crean A, Dyer M, Buxton M, Goldsmith K, *et al*.

No. 50
Evaluation of diagnostic tests when there is no gold standard. A review of methods.

By Rutjes AWS, Reitsma JB, Coomarasamy A, Khan KS, Bossuyt PMM.

No. 51
Systematic reviews of the clinical effectiveness and cost-effectiveness of proton pump inhibitors in acute upper gastrointestinal bleeding.

By Leontiadis GI, Sreedharan A, Dorward S, Barton P, Delaney B, Howden CW, *et al*.

No. 52
A review and critique of modelling in prioritising and designing screening programmes.

By Karnon J, Goyder E, Tappenden P, McPhie S, Towers I, Brazier J, *et al*.

No. 53
An assessment of the impact of the NHS Health Technology Assessment Programme.

By Hanney S, Buxton M, Green C, Coulson D, Raftery J.

Volume 12, 2008

No. 1
A systematic review and economic model of switching from nonglycopeptide to glycopeptide antibiotic prophylaxis for surgery.

By Cranny G, Elliott R, Weatherly H, Chambers D, Hawkins N, Myers L, *et al*.

No. 2
'Cut down to quit' with nicotine replacement therapies in smoking cessation: a systematic review of effectiveness and economic analysis.

By Wang D, Connock M, Barton P, Fry-Smith A, Aveyard P, Moore D.

No. 3
A systematic review of the effectiveness of strategies for reducing fracture risk in children with juvenile idiopathic arthritis with additional data on long-term risk of fracture and cost of disease management.

By Thornton J, Ashcroft D, O'Neill T, Elliott R, Adams J, Roberts C, *et al*.

No. 4
Does befriending by trained lay workers improve psychological well-being and quality of life for carers of people with dementia, and at what cost? A randomised controlled trial.

By Charlesworth G, Shepstone L, Wilson E, Thalanany M, Mugford M, Poland F.

No. 5
A multi-centre retrospective cohort study comparing the efficacy, safety and cost-effectiveness of hysterectomy and uterine artery embolisation for the treatment of symptomatic uterine fibroids. The HOPEFUL study.

By Hirst A, Dutton S, Wu O, Briggs A, Edwards C, Waldenmaier L, *et al*.

No. 6
Methods of prediction and prevention of pre-eclampsia: systematic reviews of accuracy and effectiveness literature with economic modelling.

By Meads CA, Cnossen JS, Meher S, Juarez-Garcia A, ter Riet G, Duley L, *et al*.

No. 7
The use of economic evaluations in NHS decision-making: a review and empirical investigation.

By Williams I, McIver S, Moore D, Bryan S.

No. 8
Stapled haemorrhoidectomy (haemorrhoidopexy) for the treatment of haemorrhoids: a systematic review and economic evaluation.

By Burch J, Epstein D, Baba-Akbari A, Weatherly H, Fox D, Golder S, *et al*.

No. 9
The clinical effectiveness of diabetes education models for Type 2 diabetes: a systematic review.

By Loveman E, Frampton GK, Clegg AJ.

No. 10
Payment to healthcare professionals for patient recruitment to trials: systematic review and qualitative study.

By Raftery J, Bryant J, Powell J, Kerr C, Hawker S.

No. 11
Cyclooxygenase-2 selective non-steroidal anti-inflammatory drugs (etodolac, meloxicam, celecoxib, rofecoxib, etoricoxib, valdecoxib and lumiracoxib) for osteoarthritis and rheumatoid arthritis: a systematic review and economic evaluation.

By Chen Y-F, Jobanputra P, Barton P, Bryan S, Fry-Smith A, Harris G, *et al*.

No. 12
The clinical effectiveness and cost-effectiveness of central venous catheters treated with anti-infective agents in preventing bloodstream infections: a systematic review and economic evaluation.

By Hockenhull JC, Dwan K, Boland A, Smith G, Bagust A, Dundar Y, *et al*.

No. 13
Stepped treatment of older adults on laxatives. The STOOL trial.

By Mihaylov S, Stark C, McColl E, Steen N, Vanoli A, Rubin G, *et al*.

No. 14
A randomised controlled trial of cognitive behaviour therapy in adolescents with major depression treated by selective serotonin reuptake inhibitors. The ADAPT trial.

By Goodyer IM, Dubicka B, Wilkinson P, Kelvin R, Roberts C, Byford S, *et al*.

No. 15
The use of irinotecan, oxaliplatin and raltitrexed for the treatment of advanced colorectal cancer: systematic review and economic evaluation.

By Hind D, Tappenden P, Tumur I, Eggington E, Sutcliffe P, Ryan A.

No. 16
Ranibizumab and pegaptanib for the treatment of age-related macular degeneration: a systematic review and economic evaluation.

By Colquitt JL, Jones J, Tan SC, Takeda A, Clegg AJ, Price A.

No. 17
Systematic review of the clinical effectiveness and cost-effectiveness of 64-slice or higher computed tomography angiography as an alternative to invasive coronary angiography in the investigation of coronary artery disease.

By Mowatt G, Cummins E, Waugh N, Walker S, Cook J, Jia X, *et al*.

No. 18
Structural neuroimaging in psychosis: a systematic review and economic evaluation.

By Albon E, Tsourapas A, Frew E, Davenport C, Oyebode F, Bayliss S, *et al*.

No. 19
Systematic review and economic analysis of the comparative effectiveness of different inhaled corticosteroids and their usage with long-acting beta$_2$ agonists for the treatment of chronic asthma in adults and children aged 12 years and over.

By Shepherd J, Rogers G, Anderson R, Main C, Thompson-Coon J, Hartwell D, *et al*.

No. 20

Systematic review and economic analysis of the comparative effectiveness of different inhaled corticosteroids and their usage with long-acting beta$_2$ agonists for the treatment of chronic asthma in children under the age of 12 years.

By Main C, Shepherd J, Anderson R, Rogers G, Thompson-Coon J, Liu Z, *et al*.

No. 21

Ezetimibe for the treatment of hypercholesterolaemia: a systematic review and economic evaluation.

By Ara R, Tumur I, Pandor A, Duenas A, Williams R, Wilkinson A, *et al*.

No. 22

Topical or oral ibuprofen for chronic knee pain in older people. The TOIB study.

By Underwood M, Ashby D, Carnes D, Castelnuovo E, Cross P, Harding G, *et al*.

No. 23

A prospective randomised comparison of minor surgery in primary and secondary care. The MiSTIC trial.

By George S, Pockney P, Primrose J, Smith H, Little P, Kinley H, *et al*.

No. 24

A review and critical appraisal of measures of therapist–patient interactions in mental health settings.

By Cahill J, Barkham M, Hardy G, Gilbody S, Richards D, Bower P, *et al*.

No. 25

The clinical effectiveness and cost-effectiveness of screening programmes for amblyopia and strabismus in children up to the age of 4–5 years: a systematic review and economic evaluation.

By Carlton J, Karnon J, Czoski-Murray C, Smith KJ, Marr J.

No. 26

A systematic review of the clinical effectiveness and cost-effectiveness and economic modelling of minimal incision total hip replacement approaches in the management of arthritic disease of the hip.

By de Verteuil R, Imamura M, Zhu S, Glazener C, Fraser C, Munro N, *et al*.

No. 27

A preliminary model-based assessment of the cost–utility of a screening programme for early age-related macular degeneration.

By Karnon J, Czoski-Murray C, Smith K, Brand C, Chakravarthy U, Davis S, *et al*.

No. 28

Intravenous magnesium sulphate and sotalol for prevention of atrial fibrillation after coronary artery bypass surgery: a systematic review and economic evaluation.

By Shepherd J, Jones J, Frampton GK, Tanajewski L, Turner D, Price A.

No. 29

Absorbent products for urinary/faecal incontinence: a comparative evaluation of key product categories.

By Fader M, Cottenden A, Getliffe K, Gage H, Clarke-O'Neill S, Jamieson K, *et al*.

No. 30

A systematic review of repetitive functional task practice with modelling of resource use, costs and effectiveness.

By French B, Leathley M, Sutton C, McAdam J, Thomas L, Forster A, *et al*.

No. 31

The effectiveness and cost-effectivness of minimal access surgery amongst people with gastro-oesophageal reflux disease – a UK collaborative study. The REFLUX trial.

By Grant A, Wileman S, Ramsay C, Bojke L, Epstein D, Sculpher M, *et al*.

No. 32

Time to full publication of studies of anti-cancer medicines for breast cancer and the potential for publication bias: a short systematic review.

By Takeda A, Loveman E, Harris P, Hartwell D, Welch K.

No. 33

Performance of screening tests for child physical abuse in accident and emergency departments.

By Woodman J, Pitt M, Wentz R, Taylor B, Hodes D, Gilbert RE.

No. 34

Curative catheter ablation in atrial fibrillation and typical atrial flutter: systematic review and economic evaluation.

By Rodgers M, McKenna C, Palmer S, Chambers D, Van Hout S, Golder S, *et al*.

No. 35

Systematic review and economic modelling of effectiveness and cost utility of surgical treatments for men with benign prostatic enlargement.

By Lourenco T, Armstrong N, N'Dow J, Nabi G, Deverill M, Pickard R, *et al*.

No. 36

Immunoprophylaxis against respiratory syncytial virus (RSV) with palivizumab in children: a systematic review and economic evaluation.

By Wang D, Cummins C, Bayliss S, Sandercock J, Burls A.

Volume 13, 2009

No. 1

Deferasirox for the treatment of iron overload associated with regular blood transfusions (transfusional haemosiderosis) in patients suffering with chronic anaemia: a systematic review and economic evaluation.

By McLeod C, Fleeman N, Kirkham J, Bagust A, Boland A, Chu P, *et al*.

No. 2

Thrombophilia testing in people with venous thromboembolism: systematic review and cost-effectiveness analysis.

By Simpson EL, Stevenson MD, Rawdin A, Papaioannou D.

No. 3

Surgical procedures and non-surgical devices for the management of non-apnoeic snoring: a systematic review of clinical effects and associated treatment costs.

By Main C, Liu Z, Welch K, Weiner G, Quentin Jones S, Stein K.

No. 4

Continuous positive airway pressure devices for the treatment of obstructive sleep apnoea–hypopnoea syndrome: a systematic review and economic analysis.

By McDaid C, Griffin S, Weatherly H, Durée K, van der Burgt M, van Hout S, Akers J, *et al*.

No. 5

Use of classical and novel biomarkers as prognostic risk factors for localised prostate cancer: a systematic review.

By Sutcliffe P, Hummel S, Simpson E, Young T, Rees A, Wilkinson A, *et al*.

No. 6

The harmful health effects of recreational ecstasy: a systematic review of observational evidence.

By Rogers G, Elston J, Garside R, Roome C, Taylor R, Younger P, *et al*.

No. 7

Systematic review of the clinical effectiveness and cost-effectiveness of oesophageal Doppler monitoring in critically ill and high-risk surgical patients.

By Mowatt G, Houston G, Hernández R, de Verteuil R, Fraser C, Cuthbertson B, *et al*.

No. 8

The use of surrogate outcomes in model-based cost-effectiveness analyses: a survey of UK Health Technology Assessment reports.

By Taylor RS, Elston J.

No. 9

Controlling Hypertension and Hypotension Immediately Post Stroke (CHHIPS) – a randomised controlled trial.

By Potter J, Mistri A, Brodie F, Chernova J, Wilson E, Jagger C, *et al*.

No. 10
Routine antenatal anti-D prophylaxis for RhD-negative women: a systematic review and economic evaluation.
By Pilgrim H, Lloyd-Jones M, Rees A.

No. 11
Amantadine, oseltamivir and zanamivir for the prophylaxis of influenza (including a review of existing guidance no. 67): a systematic review and economic evaluation.
By Tappenden P, Jackson R, Cooper K, Rees A, Simpson E, Read R, *et al*

No. 12
Improving the evaluation of therapeutic interventions in multiple sclerosis: the role of new psychometric methods.
By Hobart J, Cano S.

No. 13
Treatment of severe ankle sprain: a pragmatic randomised controlled trial comparing the clinical effectiveness and cost-effectiveness of three types of mechanical ankle support with tubular bandage. The CAST trial.
By Cooke MW, Marsh JL, Clark M, Nakash R, Jarvis RM, Hutton JL, *et al*., on behalf of the CAST trial group.

No. 14
Non-occupational postexposure prophylaxis for HIV: a systematic review.
By Bryant J, Baxter L, Hird S.

Health Technology Assessment Programme

Director,
Professor Tom Walley,
Director, NIHR HTA
Programme, Professor of
Clinical Pharmacology,
University of Liverpool

Deputy Director,
Professor Jon Nicholl,
Director, Medical Care Research
Unit, University of Sheffield

Prioritisation Strategy Group

Members

Chair,
Professor Tom Walley,
Director, NIHR HTA
Programme, Professor of
Clinical Pharmacology,
University of Liverpool

Deputy Chair,
Professor Jon Nicholl,
Director, Medical Care Research
Unit, University of Sheffield

Dr Bob Coates,
Consultant Advisor, NCCHTA

Dr Andrew Cook,
Consultant Advisor, NCCHTA

Dr Peter Davidson,
Director of Science Support,
NCCHTA

Professor Robin E Ferner,
Consultant Physician and
Director, West Midlands Centre
for Adverse Drug Reactions,
City Hospital NHS Trust,
Birmingham

Professor Paul Glasziou,
Professor of Evidence-Based
Medicine, University of Oxford

Dr Nick Hicks,
Director of NHS Support,
NCCHTA

Dr Edmund Jessop,
Medical Adviser, National
Specialist, National
Commissioning Group (NCG),
Department of Health, London

Ms Lynn Kerridge,
Chief Executive Officer,
NETSCC and NCCHTA

Dr Ruairidh Milne,
Director of Strategy and
Development, NETSCC

Ms Kay Pattison,
Section Head, NHS R&D
Programme, Department of
Health

Ms Pamela Young,
Specialist Programme Manager,
NCCHTA

HTA Commissioning Board

Members

Programme Director,
Professor Tom Walley,
Director, NIHR HTA
Programme, Professor of
Clinical Pharmacology,
University of Liverpool

Chair,
Professor Jon Nicholl,
Director, Medical Care Research
Unit, University of Sheffield

Deputy Chair,
Dr Andrew Farmer,
Senior Lecturer in General
Practice, Department of
Primary Health Care,
University of Oxford

Professor Ann Ashburn,
Professor of Rehabilitation
and Head of Research,
Southampton General Hospital

Professor Deborah Ashby,
Professor of Medical Statistics,
Queen Mary, University of
London

Professor John Cairns,
Professor of Health Economics,
London School of Hygiene and
Tropical Medicine

Professor Peter Croft,
Director of Primary Care
Sciences Research Centre, Keele
University

Professor Nicky Cullum,
Director of Centre for Evidence-
Based Nursing, University of
York

Professor Jenny Donovan,
Professor of Social Medicine,
University of Bristol

Professor Steve Halligan,
Professor of Gastrointestinal
Radiology, University College
Hospital, London

Professor Freddie Hamdy,
Professor of Urology,
University of Sheffield

Professor Allan House,
Professor of Liaison Psychiatry,
University of Leeds

Dr Martin J Landray,
Reader in Epidemiology,
Honorary Consultant Physician,
Clinical Trial Service Unit,
University of Oxford

Professor Stuart Logan,
Director of Health & Social
Care Research, The Peninsula
Medical School, Universities of
Exeter and Plymouth

Dr Rafael Perera,
Lecturer in Medical Statisitics,
Department of Primary Health
Care, Univeristy of Oxford

Professor Ian Roberts,
Professor of Epidemiology &
Public Health, London School
of Hygiene and Tropical
Medicine

Professor Mark Sculpher,
Professor of Health Economics,
University of York

Professor Helen Smith,
Professor of Primary Care,
University of Brighton

Professor Kate Thomas,
Professor of Complementary &
Alternative Medicine Research,
University of Leeds

Professor David John
Torgerson,
Director of York Trials Unit,
University of York

Professor Hywel Williams,
Professor of Dermato-
Epidemiology, University of
Nottingham

Observers

Ms Kay Pattison,
Section Head, NHS R&D
Programmes, Research and
Development Directorate,
Department of Health

Dr Morven Roberts,
Clinical Trials Manager,
Medical Research Council

Diagnostic Technologies & Screening Panel

Members

Chair,
Professor Paul Glasziou,
Professor of Evidence-Based Medicine, University of Oxford

Deputy Chair,
Dr David Elliman,
Consultant Paediatrician and Honorary Senior Lecturer, Great Ormond Street Hospital, London

Professor Judith E Adams,
Consultant Radiologist, Manchester Royal Infirmary, Central Manchester & Manchester Children's University Hospitals NHS Trust, and Professor of Diagnostic Radiology, Imaging Science and Biomedical Engineering, Cancer & Imaging Sciences, University of Manchester

Ms Jane Bates,
Consultant Ultrasound Practitioner, Ultrasound Department, Leeds Teaching Hospital NHS Trust

Dr Stephanie Dancer,
Consultant Microbiologist, Hairmyres Hospital, East Kilbride

Professor Glyn Elwyn,
Primary Medical Care Research Group, Swansea Clinical School, University of Wales

Dr Ron Gray,
Consultant Clinical Epidemiologist, Department of Public Health, University of Oxford

Professor Paul D Griffiths,
Professor of Radiology, University of Sheffield

Dr Jennifer J Kurinczuk,
Consultant Clinical Epidemiologist, National Perinatal Epidemiology Unit, Oxford

Dr Susanne M Ludgate,
Medical Director, Medicines & Healthcare Products Regulatory Agency, London

Dr Anne Mackie,
Director of Programmes, UK National Screening Committee

Dr Michael Millar,
Consultant Senior Lecturer in Microbiology, Barts and The London NHS Trust, Royal London Hospital

Mr Stephen Pilling,
Director, Centre for Outcomes, Research & Effectiveness, Joint Director, National Collaborating Centre for Mental Health, University College London

Mrs Una Rennard,
Service User Representative

Dr Phil Shackley,
Senior Lecturer in Health Economics, School of Population and Health Sciences, University of Newcastle upon Tyne

Dr W Stuart A Smellie,
Consultant in Chemical Pathology, Bishop Auckland General Hospital

Dr Nicholas Summerton,
Consultant Clinical and Public Health Advisor, NICE

Ms Dawn Talbot,
Service User Representative

Dr Graham Taylor,
Scientific Advisor, Regional DNA Laboratory, St James's University Hospital, Leeds

Professor Lindsay Wilson Turnbull,
Scientific Director of the Centre for Magnetic Resonance Investigations and YCR Professor of Radiology, Hull Royal Infirmary

Observers

Dr Tim Elliott,
Team Leader, Cancer Screening, Department of Health

Dr Catherine Moody,
Programme Manager, Neuroscience and Mental Health Board

Dr Ursula Wells,
Principal Research Officer, Department of Health

Pharmaceuticals Panel

Members

Chair,
Professor Robin Ferner,
Consultant Physician and Director, West Midlands Centre for Adverse Drug Reactions, City Hospital NHS Trust, Birmingham

Deputy Chair,
Professor Imti Choonara,
Professor in Child Health, University of Nottingham

Mrs Nicola Carey,
Senior Research Fellow, School of Health and Social Care, The University of Reading

Mr John Chapman,
Service User Representative

Dr Peter Elton,
Director of Public Health, Bury Primary Care Trust

Dr Ben Goldacre,
Research Fellow, Division of Psychological Medicine and Psychiatry, King's College London

Mrs Barbara Greggains,
Service User Representative

Dr Bill Gutteridge,
Medical Adviser, London Strategic Health Authority

Dr Dyfrig Hughes,
Reader in Pharmacoeconomics and Deputy Director, Centre for Economics and Policy in Health, IMSCaR, Bangor University

Professor Jonathan Ledermann,
Professor of Medical Oncology and Director of the Cancer Research UK and University College London Cancer Trials Centre

Dr Yoon K Loke,
Senior Lecturer in Clinical Pharmacology, University of East Anglia

Professor Femi Oyebode,
Consultant Psychiatrist and Head of Department, University of Birmingham

Dr Andrew Prentice,
Senior Lecturer and Consultant Obstetrician and Gynaecologist, The Rosie Hospital, University of Cambridge

Dr Martin Shelly,
General Practitioner, Leeds, and Associate Director, NHS Clinical Governance Support Team, Leicester

Dr Gillian Shepherd,
Director, Health and Clinical Excellence, Merck Serono Ltd

Mrs Katrina Simister,
Assistant Director New Medicines, National Prescribing Centre, Liverpool

Mr David Symes,
Service User Representative

Dr Lesley Wise,
Unit Manager, Pharmacoepidemiology Research Unit, VRMM, Medicines & Healthcare Products Regulatory Agency

Observers

Ms Kay Pattison,
Section Head, NHS R&D Programme, Department of Health

Mr Simon Reeve,
Head of Clinical and Cost-Effectiveness, Medicines, Pharmacy and Industry Group, Department of Health

Dr Heike Weber,
Programme Manager, Medical Research Council

Dr Ursula Wells,
Principal Research Officer, Department of Health

Current and past membership details of all HTA Programme 'committees' are available from the HTA website (www.hta.ac.uk)

Therapeutic Procedures Panel

Members

Chair,
Dr John C Pounsford,
Consultant Physician, North
Bristol NHS Trust

Deputy Chair,
Professor Scott Weich,
Professor of Psychiatry, Division
of Health in the Community,
University of Warwick, Coventry

Professor Jane Barlow,
Professor of Public Health in
the Early Years, Health Sciences
Research Institute, Warwick
Medical School, Coventry

Ms Maree Barnett,
Acting Branch Head of Vascular
Programme, Department of
Health

Mrs Val Carlill,
Service User Representative

Mrs Anthea De Barton-Watson,
Service User Representative

Mr Mark Emberton,
Senior Lecturer in Oncological
Urology, Institute of Urology,
University College Hospital,
London

Professor Steve Goodacre,
Professor of Emergency
Medicine, University of
Sheffield

Professor Christopher Griffiths,
Professor of Primary Care, Barts
and The London School of
Medicine and Dentistry

Mr Paul Hilton,
Consultant Gynaecologist
and Urogynaecologist, Royal
Victoria Infirmary, Newcastle
upon Tyne

Professor Nicholas James,
Professor of Clinical Oncology,
University of Birmingham,
and Consultant in Clinical
Oncology, Queen Elizabeth
Hospital

Dr Peter Martin,
Consultant Neurologist,
Addenbrooke's Hospital,
Cambridge

Dr Kate Radford,
Senior Lecturer (Research),
Clinical Practice Research
Unit, University of Central
Lancashire, Preston

Mr Jim Reece
Service User Representative

Dr Karen Roberts,
Nurse Consultant, Dunston Hill
Hospital Cottages

Observers

Dr Phillip Leech,
Principal Medical Officer for
Primary Care, Department of
Health

Ms Kay Pattison,
Section Head, NHS R&D
Programme, Department of
Health

Dr Morven Roberts,
Clinical Trials Manager,
Medical Research Council

Professor Tom Walley,
Director, NIHR HTA
Programme, Professor of
Clinical Pharmacology,
University of Liverpool

Dr Ursula Wells,
Principal Research Officer,
Department of Health

Disease Prevention Panel

Members

Chair,
Dr Edmund Jessop,
Medical Adviser, National
Specialist, National
Commissioning Group (NCG),
London

Deputy Chair,
Dr David Pencheon,
Director, NHS Sustainable
Development Unit, Cambridge

Dr Elizabeth Fellow-Smith,
Medical Director, West London
Mental Health Trust, Middlesex

Dr John Jackson,
General Practitioner, Parkway
Medical Centre, Newcastle
upon Tyne

Professor Mike Kelly,
Director, Centre for Public
Health Excellence, NICE,
London

Dr Chris McCall,
General Practitioner, The
Hadleigh Practice, Corfe
Mullen, Dorset

Ms Jeanett Martin,
Director of Nursing, BarnDoc
Limited, Lewisham Primary
Care Trust

Dr Julie Mytton,
Locum Consultant in Public
Health Medicine, Bristol
Primary Care Trust

Miss Nicky Mullany,
Service User Representative

Professor Ian Roberts,
Professor of Epidemiology
and Public Health, London
School of Hygiene & Tropical
Medicine

Professor Ken Stein,
Senior Clinical Lecturer in
Public Health, University of
Exeter

Dr Kieran Sweeney,
Honorary Clinical Senior
Lecturer, Peninsula College
of Medicine and Dentistry,
Universities of Exeter and
Plymouth

Professor Carol Tannahill,
Glasgow Centre for Population
Health

Professor Margaret Thorogood,
Professor of Epidemiology,
University of Warwick Medical
School, Coventry

Observers

Ms Christine McGuire,
Research & Development,
Department of Health

Dr Caroline Stone,
Programme Manager, Medical
Research Council

Expert Advisory Network

Members

Professor Douglas Altman,
Professor of Statistics in Medicine, Centre for Statistics in Medicine, University of Oxford

Professor John Bond,
Professor of Social Gerontology & Health Services Research, University of Newcastle upon Tyne

Professor Andrew Bradbury,
Professor of Vascular Surgery, Solihull Hospital, Birmingham

Mr Shaun Brogan,
Chief Executive, Ridgeway Primary Care Group, Aylesbury

Mrs Stella Burnside OBE,
Chief Executive, Regulation and Improvement Authority, Belfast

Ms Tracy Bury,
Project Manager, World Confederation for Physical Therapy, London

Professor Iain T Cameron,
Professor of Obstetrics and Gynaecology and Head of the School of Medicine, University of Southampton

Dr Christine Clark,
Medical Writer and Consultant Pharmacist, Rossendale

Professor Collette Clifford,
Professor of Nursing and Head of Research, The Medical School, University of Birmingham

Professor Barry Cookson,
Director, Laboratory of Hospital Infection, Public Health Laboratory Service, London

Dr Carl Counsell,
Clinical Senior Lecturer in Neurology, University of Aberdeen

Professor Howard Cuckle,
Professor of Reproductive Epidemiology, Department of Paediatrics, Obstetrics & Gynaecology, University of Leeds

Dr Katherine Darton,
Information Unit, MIND – The Mental Health Charity, London

Professor Carol Dezateux,
Professor of Paediatric Epidemiology, Institute of Child Health, London

Mr John Dunning,
Consultant Cardiothoracic Surgeon, Papworth Hospital NHS Trust, Cambridge

Mr Jonothan Earnshaw,
Consultant Vascular Surgeon, Gloucestershire Royal Hospital, Gloucester

Professor Martin Eccles,
Professor of Clinical Effectiveness, Centre for Health Services Research, University of Newcastle upon Tyne

Professor Pam Enderby,
Dean of Faculty of Medicine, Institute of General Practice and Primary Care, University of Sheffield

Professor Gene Feder,
Professor of Primary Care Research & Development, Centre for Health Sciences, Barts and The London School of Medicine and Dentistry

Mr Leonard R Fenwick,
Chief Executive, Freeman Hospital, Newcastle upon Tyne

Mrs Gillian Fletcher,
Antenatal Teacher and Tutor and President, National Childbirth Trust, Henfield

Professor Jayne Franklyn,
Professor of Medicine, University of Birmingham

Mr Tam Fry,
Honorary Chairman, Child Growth Foundation, London

Professor Fiona Gilbert,
Consultant Radiologist and NCRN Member, University of Aberdeen

Professor Paul Gregg,
Professor of Orthopaedic Surgical Science, South Tees Hospital NHS Trust

Bec Hanley,
Co-director, TwoCan Associates, West Sussex

Dr Maryann L Hardy,
Senior Lecturer, University of Bradford

Mrs Sharon Hart,
Healthcare Management Consultant, Reading

Professor Robert E Hawkins,
CRC Professor and Director of Medical Oncology, Christie CRC Research Centre, Christie Hospital NHS Trust, Manchester

Professor Richard Hobbs,
Head of Department of Primary Care & General Practice, University of Birmingham

Professor Alan Horwich,
Dean and Section Chairman, The Institute of Cancer Research, London

Professor Allen Hutchinson,
Director of Public Health and Deputy Dean of ScHARR, University of Sheffield

Professor Peter Jones,
Professor of Psychiatry, University of Cambridge, Cambridge

Professor Stan Kaye,
Cancer Research UK Professor of Medical Oncology, Royal Marsden Hospital and Institute of Cancer Research, Surrey

Dr Duncan Keeley,
General Practitioner (Dr Burch & Ptnrs), The Health Centre, Thame

Dr Donna Lamping,
Research Degrees Programme Director and Reader in Psychology, Health Services Research Unit, London School of Hygiene and Tropical Medicine, London

Mr George Levvy,
Chief Executive, Motor Neurone Disease Association, Northampton

Professor James Lindesay,
Professor of Psychiatry for the Elderly, University of Leicester

Professor Julian Little,
Professor of Human Genome Epidemiology, University of Ottawa

Professor Alistaire McGuire,
Professor of Health Economics, London School of Economics

Professor Rajan Madhok,
Medical Director and Director of Public Health, Directorate of Clinical Strategy & Public Health, North & East Yorkshire & Northern Lincolnshire Health Authority, York

Professor Alexander Markham,
Director, Molecular Medicine Unit, St James's University Hospital, Leeds

Dr Peter Moore,
Freelance Science Writer, Ashtead

Dr Andrew Mortimore,
Public Health Director, Southampton City Primary Care Trust

Dr Sue Moss,
Associate Director, Cancer Screening Evaluation Unit, Institute of Cancer Research, Sutton

Professor Miranda Mugford,
Professor of Health Economics and Group Co-ordinator, University of East Anglia

Professor Jim Neilson,
Head of School of Reproductive & Developmental Medicine and Professor of Obstetrics and Gynaecology, University of Liverpool

Mrs Julietta Patnick,
National Co-ordinator, NHS Cancer Screening Programmes, Sheffield

Professor Robert Peveler,
Professor of Liaison Psychiatry, Royal South Hants Hospital, Southampton

Professor Chris Price,
Director of Clinical Research, Bayer Diagnostics Europe, Stoke Poges

Professor William Rosenberg,
Professor of Hepatology and Consultant Physician, University of Southampton

Professor Peter Sandercock,
Professor of Medical Neurology, Department of Clinical Neurosciences, University of Edinburgh

Dr Susan Schonfield,
Consultant in Public Health, Hillingdon Primary Care Trust, Middlesex

Dr Eamonn Sheridan,
Consultant in Clinical Genetics, St James's University Hospital, Leeds

Dr Margaret Somerville,
Director of Public Health Learning, Peninsula Medical School, University of Plymouth

Professor Sarah Stewart-Brown,
Professor of Public Health, Division of Health in the Community, University of Warwick, Coventry

Professor Ala Szczepura,
Professor of Health Service Research, Centre for Health Services Studies, University of Warwick, Coventry

Mrs Joan Webster,
Consumer Member, Southern Derbyshire Community Health Council

Professor Martin Whittle,
Clinical Co-director, National Co-ordinating Centre for Women's and Children's Health, Lymington