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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

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7 Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 2000;321:405-12.
8 Guerci B, Drouin P, Grange V, Bougneres P, Fontaine P, Passa P, 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;29:587-94.
9 Davidson MB Castellanos M, Kain D, Duran P. The effect of self-monitoring of blood glucose concentrations on glycated haemoglobin levels in diabetic patients not taking insulin. *Am J Med* 2005;118:422-5.
10 Farmer A, Wade A, Goyder E, Yudkin P, French D, Craven A, et al. Impact of self monitoring of blood glucose in the management of patients with non-insulin treated diabetes: open parallel group randomised trial. *BMJ* 2007;335:132-6.
11 Gulliford M, Latinovic R. Variations in glucose self-monitoring during oral hypoglycaemic therapy in primary care. *Diabet Med* 2004;21:685-90.
12 Watkins KW, Connell CM, Fitzgerald JT, Klem L, Hickey T, Ingersoll-Dayton B. Effect of adults' self regulation of diabetes on quality of life issues. *Diabetes Care* 2000;23:1511-5.
13 Franciosi M, Pellegrini F, De Beradis G, Belfiglio M, Calviere D, Di Nardo B, et al. The impact of blood glucose self-monitoring on metabolic control and quality of life in type 2 diabetic patients: an urgent need for better educational strategies. *Diabetes Care* 2001;24:1870-7.
14 Peel E, Douglas M, Lawton J. Self monitoring of blood glucose in type 2 diabetes: longitudinal qualitative study of patients' perspectives. *BMJ* 2007;335:493.

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ABSTRACT

Objective To assess the cost effectiveness of self monitoring of blood glucose alone or with additional training in incorporating the results into self care, in addition to standardised usual care for patients with non-insulin treated type 2 diabetes.

Design Incremental cost utility analysis from a healthcare perspective. Data on resource use from the randomised controlled diabetes glycaemic education and monitoring (DiGEM) trial covered 12 months before baseline and 12 months of trial follow-up. Quality of life was measured at baseline and 12 months using the EuroQol EQ-5D questionnaire.

Setting Primary care in the United Kingdom.

Participants 453 patients with non-insulin treated type 2 diabetes.

Interventions Standardised usual care (control) compared with additional self monitoring of blood glucose alone (less intensive self monitoring) or with training in self interpretation of the results (more intensive self monitoring).

Main outcome measures Quality adjusted life years and healthcare costs (sterling in 2005-6 prices).

Results The average costs of intervention were £89 (€113; $179) for standardised usual care, £181 for less intensive self monitoring, and £173 for more intensive self monitoring, showing an additional cost per patient of £92 (95% confidence interval £80 to £103) in the less intensive group and £84 (£73 to £96) in the more intensive group. No other significant cost difference was detected between the groups. An initial negative impact of self monitoring on quality of life occurred, averaging −0.027 (95% confidence interval−0.069 to 0.015) for the less intensive self monitoring group and −0.075 (−0.119 to −0.031) for the more intensive group.

Conclusions Self monitoring of blood glucose with or without additional training in incorporating the results into self care was associated with higher costs and lower quality of life in patients with non-insulin treated type 2 diabetes. In light of this, and no clinically significant differences in other outcomes, self monitoring of blood glucose is unlikely to be cost effective in addition to standardised usual care.

Trial registration Current Controlled Trials ISRCTN47464659.

INTRODUCTION

Self monitoring of blood glucose has been shown to be the largest single component of management costs associated with implementing more intensive glycaemic control in the UK.[1] Improvements in haemoglobin A_{1c} levels are associated with reduced rates of long term complications from diabetes. Although these improvements may lead to gains in quality adjusted life expectancy and generate savings within the healthcare system, self monitoring has opportunity costs as funds could be used to finance other aspects of managing non-insulin treated type 2 diabetes. We carried out an economic evaluation of self monitoring of blood glucose using data from the diabetes glycaemic education and monitoring (DiGEM) trial.[2]

METHODS

The diabetes glycaemic education and monitoring trial was an open, randomised study of 453 patients with non-insulin treated type 2 diabetes who had haemoglobin A_{1c} levels of 6.2% or more and were self monitoring not more than once a week.[2] These patients were allocated to either standardised usual care (control, n=152), a blood glucose meter with advice for participants to contact their doctor for

interpretation of results (less intensive self monitoring, n=150), and a blood glucose meter with training in self interpretation and application of the results to diet, physical activity, and drug adherence (more intensive self monitoring, n=151). At 12 months the differences in haemoglobin A_{1c} levels between the groups were not significant (P=0.12).

We carried out an incremental cost utility analysis for both self monitoring groups, with difference in costs and in effects calculated in relation to standardised usual care. The study perspective was that of the healthcare purchaser. We adopted the quality adjusted life year (QALY) as the effectiveness measure to capture changes in life expectancy and quality of life.[3]

Data collection

We collected data on use of healthcare resources for 12 months before baseline and during the trial at three, six, nine, and 12 months. Information was obtained on the frequency of self monitoring, number and duration of visits to a nurse, daily doses of drugs, and the variable of "other healthcare resource use" (see bmj.com). These data were collected from patients' monitoring diaries, nurses' notes, and health service use questionnaires.

We included all 453 patients in the base case analysis. For missing information on self monitoring and drug use we carried forward the last known value. We calculated data missing for any reason other than loss to follow-up in the categories for other resource use in Stata 9 by imputation, which was conditional on randomisation group, age, sex, duration of diabetes, and comorbidity.[4] Our imputation of missing data on length of contacts with nurses was based on values adjusted for strictly trial related activities and was conditional on type of contact and randomisation group.

Costs and effects

We calculated costs by multiplying the volume of resource use in each category by the associated UK national level unit cost in 2005-6 prices (see bmj.com). Average costs were estimated in each arm for 12 months before baseline and 12 months of follow-up. We categorised each item for resource use as part of the cost of the intervention (including nurse intervention and self monitoring), cost of drugs, or cost of other healthcare resource use (see bmj.com). We calculated the mean costs of the intervention and drugs across all patients in each arm. To account for patients lost to follow-up we adjusted the mean costs of other healthcare use for censoring.[5] Differences in costs between the groups during the 12 months of the trial were adjusted for variations in the costs that occurred during the 12 months before baseline.

We estimated the impact of the interventions on quality of life using the EuroQol EQ-5D.[6] The distribution of responses across the different levels of each dimension was calculated for complete cases, and we used a *t* test to compare changes in the distribution between baseline and 12 months between the groups. Mean utility values were derived from EQ-5D responses using the UK tariff.[6] In the base case analysis we replaced missing values by conditional multiple imputation in Stata 9.[4] We assumed changes in mean utility values between baseline and 12 month follow-up to be straight line transitions. To estimate QALYs gained during the study period we weighted survival times within the trial by the average change in quality of life between baseline and 12 months for each patient.[3]

Analysis

We undertook a within trial economic analysis, with total healthcare costs and QALYs gained per patient calculated for the 12 months of the trial in each of the three groups. All analyses were carried out on an intention to treat basis. We report results as means with standard deviations or standard errors or as mean differences with 95% confidence intervals. We used sensitivity analyses to examine the effects of imputing missing data and of deaths on the main results.

RESULTS

Costs

The cost of monitoring in both self monitoring groups at 12 months was similar (£96 in less intensive group, £89 in more intensive group). Nurse time spent on standardised patient care was significantly greater in both self monitoring groups than in the control group (see bmj.com). The additional cost per patient over one year, however, was minor: £6 (95% confidence interval £1 to £11) in the less intensive group and £5 (£0 to £10) in the more intensive group. The differences in overall costs for intervention were statistically significant: £92 (£80 to £103) between the less intensive group and control group and £84 (£73 to £96) between the more intensive group and control group (see bmj.com).

Compared with baseline a substantial increase in overall drug costs (£70 to £98) was evident in all three groups. Although there was some indication that more patients started using insulin in the self monitoring groups than in the control group, no significant differences were found between the groups in the overall cost of diabetes drugs (see bmj.com).

A non-significant increase occurred in other healthcare costs between the period before baseline and follow-up, averaging about £100-£150 per patient in each group, which was mainly attributable to additional admissions to hospital (see bmj.com). During the 12 months before baseline the total mean healthcare costs per patient averaged £1042 for standardised usual care, £1048 for less intensive self monitoring, and £1145 for more intensive self monitoring. The costs increased by about £300-£400 over the trial period to £1371, £1434, and £1482. No statistically significant differences were found between the groups.

Effects

The control group showed no significant change in mean utility per patient during the trial. By contrast, patients in both self monitoring groups showed reductions in quality of life, which reached statistical

WHAT IS ALREADY KNOWN ON THIS TOPIC

The clinical effects of blood glucose testing in non-insulin treated type 2 diabetes are unclear

Self monitoring of blood glucose is costly

A previous study suggesting that routine self monitoring could be cost effective for non-insulin treated diabetes was potentially confounded by heterogeneity

WHAT THIS STUDY ADDS

Self monitoring in non-insulin treated type 2 diabetes is unlikely to be cost effective and should not be recommended for routine use

The additional intervention costs of self monitoring of blood glucose are between £84 and £92 per patient over 12 months

Self monitoring has an initial negative impact on quality of life, in part associated with increased reported anxiety

significance for the more intensive self monitoring group compared with the control group (difference −0.072, 95% confidence interval −0.127 to −0.017). QALYs gained during the trial showed similar pattern with a significant difference of −0.036 (−0.056 to −0.015) between the more intensive self monitoring group and the control group (see bmj.com). The EQ-5D questionnaire was fully completed by 313 patients (69%) both at baseline and the 12 month follow-up. Analysis of the distribution of responses across the different levels of each dimension indicated that worsening of patients' quality of life in the self monitoring groups was likely owing to significant increases in the levels of anxiety and depression compared with standardised usual care (see bmj.com).

Sensitivity analysis

Changes in quality of life in the self monitoring groups on the basis of complete cases showed similar negative trends to the base case analysis: −0.037 (95% confidence interval −0.080 to 0.005) for the less intensive self monitoring group and −0.056 (−0.099 to −0.013) for the more intensive self monitoring group. Other healthcare costs based on available cases only also remained similar to those in the base case analysis. QALYs gained during the trial were not affected significantly in any group when people who died during the trial were excluded from the analysis (see bmj.com).

DISCUSSION

Self monitoring of blood glucose was significantly more expensive than standardised usual care for non-insulin treated type 2 diabetes. Although the mean lengths of visits to a nurse were longer, the average intervention cost was lower in the more intensive self monitoring group than in the less intensive self monitoring group (£84 *v* £92) owing to the higher losses to follow-up in the more intensive group. Furthermore, the analysis showed an initial negative impact of self monitoring on quality of life. Overall, the analysis implies that neither type of self monitoring is likely to be cost effective if added to standardised usual care.

The higher costs of visits to a primary care surgery for the more intensive self monitoring group than for standardised usual care may relate to the observed changes in health status between the groups, with a need to seek further support or advice, or may be a chance finding.

This study is a prospectively designed economic evaluation of information collected on relevant items of healthcare resource use and quality of life in a randomised controlled trial. The base case analysis used the full imputed dataset but we also did available and complete case analyses on costs and effects, respectively. We adjusted the incremental costs and outcomes for baseline variations between the groups and we used sensitivity analysis to assess the effect of uncertainty surrounding some aspects of the costs and effects.

The estimates of costs and effects reported here are averages for the routine recommendation to use self monitoring across reasonably well controlled patients with non-insulin treated type 2 diabetes. These results may not reflect the costs and benefits in other specific groups, or where usual care has not been standardised to recommended levels. Also, although the EuroQol is a widely applied instrument for measuring quality of life, it may not capture all aspects of quality of life changes.[7]

One modelling study using aggregated data from a meta-analysis of randomised trials estimated the cost effectiveness of self monitoring to be between £4500 and £15 515 per QALY gained.[8] The meta-analysis concluded that the level of clinical evidence showing that self monitoring could improve haemoglobin A_{1c} levels was only moderate. Problems with included trials were low rates of follow-up, use of per protocol rather than intention to treat analyses, and cointervention with both education and self monitoring compared with usual care.[9]

The results of this analysis, and the reported lack of convincing evidence for an impact on haemoglobin A_{1c} levels,[2] indicate that self monitoring (less and more intensive) of blood glucose is unlikely to have significant lifetime health benefits or to be cost effective in addition to standardised usual care. It is possible that subgroups of patients exist for whom self monitoring may be cost effective—patients who adhere closely to treatment and who may have been excluded from the trial.

These results are based on a prospective trial over 12 months. Given this time horizon we may not have captured all relevant costs and effects. Therefore we also did a secondary analysis predicting the lifetime quality adjusted life expectancy and costs of complications from diabetes by extrapolating main risk factors beyond the trial period using modelling techniques (see bmj.com).

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Competing interests: AG has been reimbursed by Eli Lily for attending several advisory meetings.
Ethical approval: The diabetes glycaemic education and monitoring study was approved by the Oxfordshire Research Ethics Committee B (002.059).

1 Gray A, Clarke P, Farmer A, Holman R, on behalf of the United Kingdom Prospective Diabetes Study (UKPDS) Group. Implementing intensive control of blood glucose concentration and blood pressure in type 2 diabetes in England: cost analysis (UKPDS 63). *BMJ* 2002;325:860-5.
2 Farmer A, Wade A, Goyder E, Yudkin P, French D, Craven A, et al. Impact of self-monitoring of blood glucose in the management of patients with non-insulin treated diabetes: open parallel group randomised trial. *BMJ* 2007;335:132-9.
3 Drummond MF, O'Brien B, Stoddart GL, Torrance GW. *Methods for the economic evaluation of health care programmes.* Oxford: Oxford University Press, 1997.
4 Royston P. Multiple imputation of missing values: update of ice. *Stata J* 2005;5:527-36.
5 Bang J, Tsiatis AA. Estimating medical costs with censored data. *Biometrika* 2000;87:329-43.
6 Dolan P, Gudex C, Kind P, Williams A. *A social tariff for EuroQol: results from a UK population survey*. York: Centre for Health Economics, University of York, 1995.
7 Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Ann Med* 2001;33:337-43.
8 Palmer AJ, Dinneen S, Gavin JR, Gary A, Herman WH, Karter AJ. Cost-utility analysis in a UK setting of self-monitoring of blood glucose in patients with type 2 diabetes. *Curr Med Res Opin* 2006;22:861-72.
9 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;28:1510-7.

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Different strategies for screening and prevention of type 2 diabetes in adults: cost effectiveness analysis

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ABSTRACT

Objective To compare four potential screening strategies, and subsequent interventions, for the prevention and treatment of type 2 diabetes: (*a*) screening for type 2 diabetes to enable early detection and treatment, (*b*) screening for type 2 diabetes and impaired glucose tolerance, intervening with lifestyle interventions in those with a diagnosis of impaired glucose tolerance to delay or prevent diabetes, (*c*) as for (*b*) but with pharmacological interventions, and (*d*) no screening.

Design Cost effectiveness analysis based on development and evaluation of probabilistic, comprehensive economic decision analytic model, from screening to death.

Setting A hypothetical population, aged 45 at time of screening, with above average risk of diabetes.

Data sources Published clinical trials and epidemiological studies retrieved from electronic bibliographic databases; supplementary data obtained from the Department of Health statistics for England and Wales, the screening those at risk (STAR) study, and the Leicester division of the ADDITION study.

Methods A hybrid decision tree/Markov model was developed to simulate the long term effects of each screening strategy, in terms of both clinical and cost effectiveness outcomes. The base case model assumed a 50 year time horizon with discounting of both costs and benefits at 3.5%. Sensitivity analyses were carried out to investigate assumptions of the model and to identify which model inputs had most impact on the results.

Results Estimated costs for each quality adjusted life year (QALY) gained (discounted at 3.5% a year for both costs and benefits) were £14 150 (€17 560; $27 860›)for screening for type 2 diabetes, £6242 for screening for diabetes and impaired glucose tolerance followed by lifestyle interventions, and £7023 for screening for diabetes and impaired glucose tolerance followed by pharmacological interventions, all compared with no screening. At a willingness-to-pay threshold of £20 000 the probability of the intervention being cost effective was 49%, 93%, and 85% for each of the active screening strategies respectively.

Conclusions Screening for type 2 diabetes and impaired glucose tolerance, with appropriate intervention for those with impaired glucose tolerance, in an above average risk population aged 45, seems to be cost effective. The cost effectiveness of a policy of screening for diabetes alone, which offered no intervention to those with impaired glucose tolerance, is still uncertain, and further research on the impact of early detection of diabetes is needed.

INTRODUCTION

Currently there is no systematic screening policy for type 2 diabetes in the United Kingdom. One approach would be to screen only for type 2 diabetes, which will allow for early diagnosis and treatment. An estimated 50% of people with diabetes are currently undiagnosed,[1] and at presentation around 20-30% have developed complications.[2] An alternative approach would be to lower the threshold of the screening test and to screen for impaired glucose tolerance and type 2 diabetes together. As well as allowing for earlier diagnosis of type 2 diabetes, interventions can be administered to those identified with impaired glucose tolerance to delay the onset of type 2 diabetes. A recent systematic review and meta-analysis of intervention trials for prevention of type 2 diabetes[3] found both lifestyle and pharmacological interventions significantly reduced the risk of type 2 diabetes in people with impaired glucose tolerance.