

Department of Primary Health Care, University of Oxford is a partner in the National Institute for Health Research School of Primary Care Research.

**Competing interests:** AG has been reimbursed by Eli Lilly 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).

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Accepted: 14 March 2008

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

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### EDITORIAL by Goyder

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BMJ 2008;336:1180-4  
doi:10.1136/bmj.39545.585289.25

### 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,<sup>1</sup> and at presentation around 20-30% have developed complications.<sup>2</sup> 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<sup>3</sup> found both lifestyle and pharmacological interventions significantly reduced the risk of type 2 diabetes in people with impaired glucose tolerance.

This article is an abridged version of a paper that was published on [bmj.com](http://bmj.com). Cite this article as: *BMJ* 2008, doi: 10.1136/bmj.39545.585289.25

Assessment of screening policies has so far been conducted through simulation studies.<sup>4-15</sup> Previous models of screening for type 2 diabetes alone have generally assessed the impact of early treatment on cardiovascular events. Overall most of the models produced favourable results for screening, but cost effectiveness varied with age group screened and the population targeted for screening.

Of the eight models assessing cost effectiveness, all compared a strategy of interventions against no interventions, rather than screening for impaired glucose tolerance followed by interventions, compared with no screening. All but one model simulated populations where all individuals had impaired glucose tolerance at the start of the model and the end state was development of diabetes, or death, hence only a limited section of the disease pathway was modelled.

We compared three active screening strategies: (a) a one-off screening for type 2 diabetes; (b) screening for impaired glucose tolerance and type 2 diabetes and intervening with lifestyle interventions in those with impaired glucose tolerance; and (c) as for (b) but with pharmacological interventions. We compared these three active screening strategies against a fourth strategy of no screening (current practice). The full pathway from screening, to interventions and treatment for type 2 diabetes, all the way through to death, was modelled.

## METHODS

The hybrid model consists of a decision tree and a Markov model (figure). The decision tree comprises three main arms, representing no screening, screening for undiagnosed type 2 diabetes, and screening for impaired glucose tolerance and undiagnosed diabetes, with either lifestyle or pharmacological interventions applied in those with impaired glucose tolerance. The decision tree uses prevalence of impaired glucose tolerance and undiagnosed type 2 diabetes and estimates sensitivity and specificity of a screening test to determine how many individuals from the population start in each state of the Markov model. The Markov model consists of seven states: normal glucose tolerance, undiagnosed impaired glucose tolerance, diagnosed impaired glucose tolerance, death, and three states for people with diabetes (undiagnosed, diagnosed clinically, or diagnosed through screening). We ran four Markov models simultaneously, one for each of the screening strategies. Each model cycle represents one year and the model is run for a time horizon of 50 years. Model results include both clinical and cost effectiveness outcomes, with cost per quality adjusted life year (QALY) being the primary outcome.

The hybrid model was implemented using a Bayesian comprehensive decision modelling approach.<sup>16</sup> Model parameters were estimated by using Markov chain Monte Carlo simulation methods.<sup>17</sup> Results are based on a sample of 20 000 simulations, following a “burn in” of 10 000. We have reported the results from the decision model with 95% credibility intervals, which are analogous to confidence intervals.

## Data for the decision tree

The base case scenario for the model was a one-off screening for a population aged 45, in whom type 2 diabetes had not previously been diagnosed. Data for the decision tree were taken from the screening those at risk (STAR) study.<sup>18</sup> The screening data included in the primary model were from a population considered to be “at risk” of type 2 diabetes.

## Transition rates and HbA<sub>1c</sub> concentrations

To estimate the annual transition rate from undiagnosed to clinically diagnosed diabetes, we used the estimated average time people have diabetes before being diagnosed.<sup>19</sup> We estimated the effects of interventions on the transition from impaired glucose tolerance to diabetes using studies identified in a recent meta-analysis.<sup>3</sup> Death rates were taken from Department of Health statistics for England and Wales for 2000 and were increased for people with diabetes compared with those without.<sup>20</sup> For the three diabetic states (undiagnosed, clinically diagnosed, and screen detected) death rates varied depending on predicted HbA<sub>1c</sub> (haemoglobin A<sub>1c</sub>) concentrations based on data from treatment groups in the UK prospective diabetes study.<sup>21-23</sup>

## Quality of life variables

For the states of normal glucose tolerance, undiagnosed impaired glucose tolerance, and diagnosed impaired glucose tolerance, we assumed the utility value to be that of full health. We calculated utilities for those with undiagnosed and screen detected diabetes from EQ-5D data from the ADDITION study.<sup>24</sup> For people with clinically diagnosed diabetes, utilities were taken from those reported by the UK prospective diabetes study.<sup>25</sup> For the states of clinically and screen detected diabetes we used reported complication rates and their estimated effect on utility values.<sup>25,26</sup>

## Economic variables

Screening costs included the costs of an initial screening test of fasting plasma glucose and a confirmatory oral glucose tolerance in those who tested positive. People with undiagnosed diabetes incur costs before diagnosis because of increased visits to the general practitioner and prescriptions.<sup>27</sup> An estimation of these costs was included.<sup>28</sup> For lifestyle interventions we included dietitian costs and costs of twice weekly group exercise sessions.<sup>5</sup> We estimated costs of antidiabetic treatment, implementation of treatment, and costs of complications for people with diagnosed diabetes, clinically diagnosed diabetes and diabetes detected at screening.<sup>28,29</sup>

## Sensitivity analyses

We carried out sensitivity analyses using a range of values of prevalence of disease, as well as compliance levels to both screening and interventions. Changing prevalence allows us to assess the effectiveness of the screening strategies for different “at risk” populations.

The effects of compliance to both screening and interventions were also important as we assumed 100% compliance to both in the base case model, which could never be achieved in practice.

To evaluate the robustness of the model we also carried out sensitivity analyses on model inputs.

**RESULTS**

The table shows clinical and cost effectiveness outcomes for an undiscounted model and a model discounted for both costs and benefits at 3.5% a year.

Discounted costs for each QALY gained, compared with no screening, were £14 150 (£17 560; \$27 860) for type 2 diabetes screening, £6242 for screening for diabetes and impaired glucose tolerance with lifestyle interventions, and £7023 for screening for both diabetes and impaired glucose tolerance with pharmacological interventions. Costs were lower in the undiscounted model: £8681, £2863, and £3429 for every QALY gained, respectively. At a willingness to pay threshold of £20 000 per QALY the probability of each strategy being cost effective was 49% for screening for type 2 diabetes only, 93% for screening for both diabetes and impaired glucose tolerance and lifestyle interventions, and 85% for screening for both diabetes and impaired glucose tolerance and pharmacological intervention.

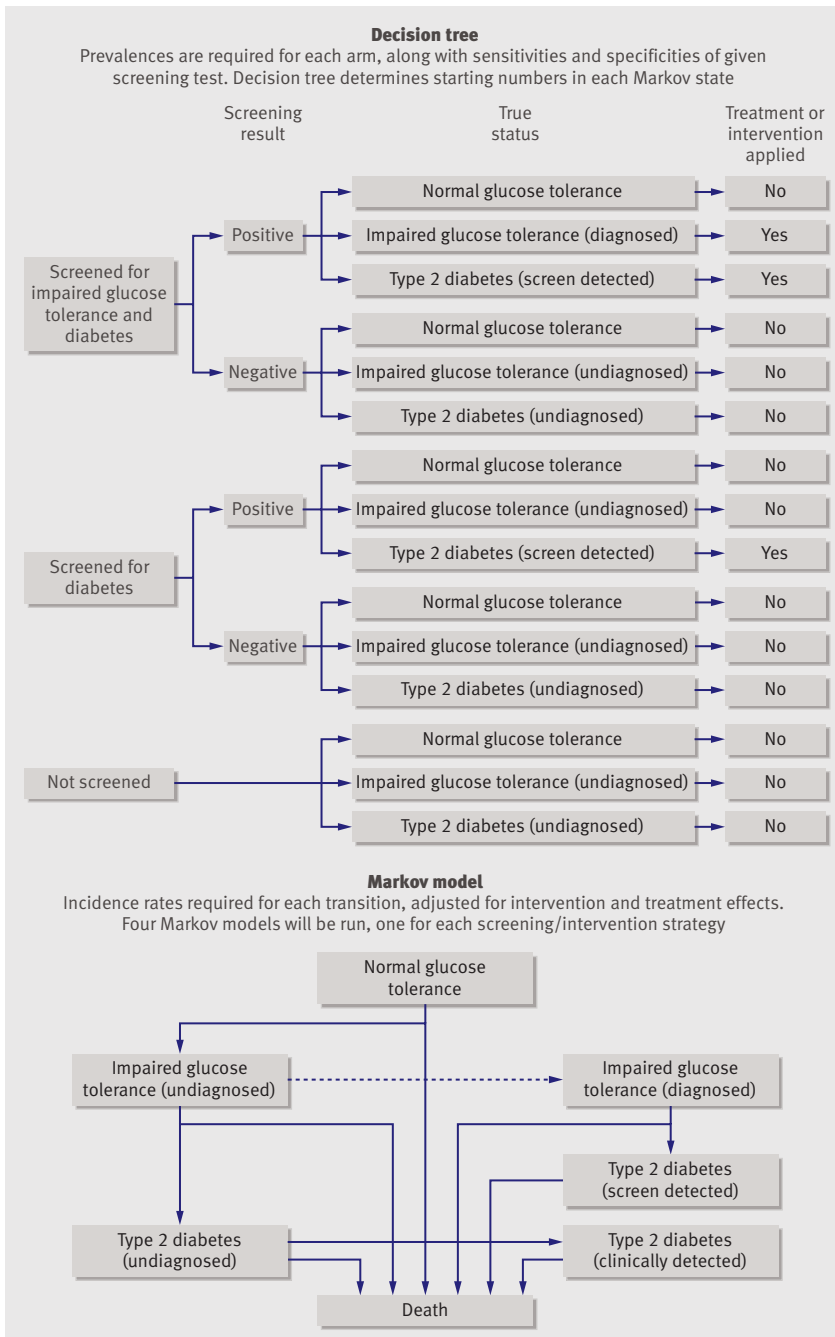
Discounted QALYs gained compared with no screening were 0.03 (-0.02 to 0.09) for diabetes screening, 0.09 (0.03 to 0.17) for screening and lifestyle interventions, and 0.07 (0.01 to 0.15) for screening with pharmacological interventions. Both the intervention strategies showed potential benefits in terms of average years spent without diabetes and cases of diabetes prevented.

In sensitivity analyses, increasing the prevalence of impaired glucose tolerance and type 2 diabetes decreased the QALYs and increased total costs of each screening strategy. The comparisons of the three active screening/intervention strategies compared with no screening remained fairly constant in terms of costs per QALY and probability of cost effectiveness. When we lowered compliance with screening, the impact on results was also minimal. Reducing compliance with interventions had a greater impact in that the total costs and cost per QALY gained increased for both the screening/intervention strategies. The probability that these strategies were cost effective compared with no screening still remained high, with an estimated probability of 88% for screening with lifestyle interventions and 84% for screening with pharmacological interventions at the willingness to pay threshold of £20 000.

Increasing the costs of both lifestyle and pharmacological interventions (by a factor of 10) and increasing the costs of diabetes (by a factor of two) did not change the results enough to alter the conclusions of the model. As we increased the time horizon the model was run for, the probability of the three active screening strategies being cost effective compared with no screening increased. This is because the benefits of screening or interventions are not all immediate. The intervention strategies became cost effective when we considered a time horizon of at least 30 years (probability of being cost effective of 0.97 for lifestyle and 0.91 for pharmacological interventions at the willingness to pay threshold of £20 000).

**DISCUSSION**

Screening for impaired glucose tolerance in people at risk of diabetes and intervening with either lifestyle or pharmacological interventions is a cost effective health



Decision model comparing no screening, screening for type 2 diabetes, and screening for impaired glucose tolerance and diabetes and intervening to delay or prevent type 2 diabetes with either lifestyle or pharmacological interventions

policy. Although screening for type 2 diabetes alone gave a relatively low predicted incremental cost per QALY of £14 150, because of uncertainty in the model the probability of this strategy being cost effective was only 49% at the willingness to pay threshold of £20 000.

### Strengths and weaknesses

Previous studies have compared the cost and clinical effectiveness of intervening in people with impaired glucose to delay onset of type 2 diabetes but all models assumed management of diabetes started as soon as the disease developed.<sup>5-11</sup> Our model considered the whole screening and intervention pathway from screening to death.

Differences in clinical outcomes between the no screening strategy and the three active screening strategies were small, partly because they were reported as an average for a screened population with mixed glucose tolerance. Also microvascular and macrovascular outcomes were not measured individually in this model, which might show benefits from the early detection or delay of type 2 diabetes.

Our model makes several assumptions. No transition was allowed from normal glucose tolerance to diabetes without first passing through impaired glucose tolerance. No transition was allowed from diabetes back to impaired glucose tolerance or from impaired to normal glucose tolerance. Once an individual has a diagnosis of type 2 diabetes, even if their glucose

tolerance improves, they are still clinically defined as having diabetes.

Another assumption was that the HbA<sub>1c</sub> concentration of those with diabetes who were clinically diagnosed would be similar to the 10 year average of an intensively treated group of people with diabetes from the UK prospective diabetes study.<sup>24</sup> Further data are needed on how HbA<sub>1c</sub> concentration could be expected to increase over time.

Screening costs incorporated within the model included only costs of opportunistic screening. When modelling costs of treatment and complications associated with diabetes, we used the average yearly costs taken from the UK prospective diabetes study. As costs would be expected to start off low and then increase, this means that costs of diabetes might be initially overestimated when an individual receives the diagnosis, and eventually underestimated by this model.

Although compliance was high in the intervention trials from which estimates of their effectiveness were obtained, it is still to be determined whether compliance could be maintained outside a trial setting. Sensitivity analyses found that even with compliance rates as low as 50%, the screening strategies involving either lifestyle or pharmacological interventions were still cost effective when compared with a strategy of no screening.

**Clinical and cost outcomes from decision model, where prevalence of impaired glucose tolerance was 15% and type 2 diabetes 7.5%, and sensitivity and specificity of screening tests was 85% and 80%, respectively. Figures are mean values per person (95% credible intervals) for no screening and mean difference from, or compared with, no screening (95% credible intervals) for all other strategies**

|   | No screening            | Screening for diabetes only | Screening for diabetes and impaired glucose tolerance |                               |
|---|-------------------------|-----------------------------|---|-------------------------------|
|   |                         |                             | Lifestyle interventions                               | Pharmacological interventions |
| <b>Undiscounted</b>   |                         |                             |   |                               |
| Total life years  | 30.34 (27.75 to 32.86)  | 0.06 (0.02 to 0.12)         | 0.15 (0.08 to 0.22)                                   | 0.13 (0.06 to 0.20)           |
| QALYs   | 28.06 (23.49 to 32.01)  | 0.07 (-0.03 to 0.18)        | 0.22 (0.08 to 0.36)                                   | 0.17 (0.03 to 0.32)           |
| Years spent without diabetes  | 20.85 (10.36 to 29.45)  | —                           | 0.33 (0.21 to 0.43)                                   | 0.20 (0.10 to 0.37)           |
| Lifetime risk of diabetes (%)   | 64.55 (18.02 to 91.83)  | —                           | -0.98 (-0.50 to -1.42)                                | -0.54 (-0.21 to -1.17)        |
| Total cost  | 17 290 (5746 to 39 580) | 730 (-9 to 2341)            | 610 (-373 to 2693)                                    | 579 (-428 to 2658)            |
| Cost per life year gained   | —                       | 11 460                      | 4179  | 4768                          |
| Cost per QALY gained  | —                       | 8681                        | 2863  | 3429                          |
| Cost per case prevented   | —                       | —                           | 62 810  | 105 000                       |
| Probability of cost effectiveness at willingness to pay threshold per QALY (%): |                         |                             |   |                               |
| £20 000   |                         | 68.1                        | 98.6  | 94.7                          |
| £30 000   |                         | 76.5                        | 99.6  | 97.3                          |
| <b>Discounted at 3.5% a year for both costs and benefits</b>                    |                         |                             |   |                               |
| Total life years  | 18.19 (17.25 to 18.98)  | 0.02 (-0.01 to 0.05)        | 0.05 (0.03 to 0.08)                                   | 0.05 (0.02 to 0.07)           |
| QALYs   | 17.13 (15.02 to 18.49)  | 0.03 (-0.02 to 0.09)        | 0.09 (0.03 to 0.17)                                   | 0.07 (0.01 to 0.15)           |
| Years spent diabetes free   | 13.69 (7.99 to 17.08)   | —                           | 0.17 (0.11 to 0.23)                                   | 0.11 (0.06 to 0.19)           |
| Total cost  | 7636 (2636 to 19 370)   | 587 (61 to 1525)            | 580 (-103 to 1760)                                    | 528 (-163 to 1,719)           |
| Cost per life year gained   | —                       | 23 710                      | 10 900  | 11 690                        |
| Cost per QALY gained  | —                       | 14 150                      | 6242  | 7023                          |
| Probability of cost effectiveness at willingness to pay threshold per QALY (%): |                         |                             |   |                               |
| £20 000   |                         | 48.6                        | 93.0  | 85.0                          |
| £30 000   |                         | 60.8                        | 97.4  | 91.6                          |

### WHAT IS ALREADY KNOWN ON THIS TOPIC

In people with impaired glucose tolerance interventions are clinically and cost effective  
Screening for type 2 diabetes to allow early detection might be cost effective in certain groups

### WHAT THIS STUDY ADDS

Modelling the whole screening and intervention pathway from screening to death shows that screening for type 2 diabetes and impaired glucose tolerance, followed by interventions, seems to be cost effective compared with no screening

Uncertainty still exists concerning the cost effectiveness of screening for type 2 diabetes alone

Screening populations with a higher prevalence of glucose intolerance might result in better clinical outcomes, although cost effectiveness seems unaffected

### Conclusions

A policy of a one-off screening for type 2 diabetes and impaired glucose tolerance, with appropriate intervention for those identified with impaired glucose tolerance, seems to be cost effective in an “at risk” population. Changing compliance with screening or interventions did not change the conclusions of the model. Given the uncertainty in the results presented here for screening for diabetes alone, further research is needed on the long term clinical effects of early diagnosis.

We thank the STAR study, in particular Jenny Tringham, and the Leicester arm of the ADDITION study, for providing the data on individual patients that were used for the analyses. We also thank Philip Clarke for advice on the UKPDS outcomes model.

**Contributors:** See bmj.com.

**Funding:** CLG is funded jointly by the UK Medical Research Council and the Economic and Social Research Council, under an interdisciplinary postgraduate research studentship in the social and medical sciences. NJC is funded by a Medical Research Council training fellowship in health services research.

**Competing interests:** MJD and KK have received sponsorship for attending conferences and small honorariums and funding for research from pharmaceutical companies that manufacture hypoglycaemic and anti-obesity drugs. KRA has also received funding for research from pharmaceutical companies that manufacture hypoglycaemic and anti-obesity drugs and has acted as a paid consultant to consultancy companies who undertake work for the healthcare industry generally.

**Ethical approval:** Not required.

**Provenance and peer review:** Not commissioned; externally peer reviewed.

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Accepted: 25 March 2008