

Psychological impact of screening for type 2 diabetes: controlled trial and comparative study embedded in the ADDITION (Cambridge) randomised controlled trial

Helen C Eborall,¹ Simon J Griffin,² A Toby Prevost,¹ Ann-Louise Kinmonth,¹ David P French,³ Stephen Sutton¹

EDITORIAL by Stolk
RESEARCH p490

¹General Practice and Primary Care Research Unit, Department of Public Health and Primary Care, University of Cambridge, Cambridge CB2 0SR

²Medical Research Council Epidemiology Unit, Strangeways Research Laboratory, Cambridge

³Applied Research Centre in Health and Lifestyle Interventions, Coventry University, Coventry

Correspondence to: H C Eborall
hce21@medschl.cam.ac.uk

BMJ 2007;335:486-9
[doi:10.1136/bmj.39303.723449.55](https://doi.org/10.1136/bmj.39303.723449.55)

ABSTRACT

Objective To quantify the psychological impact of primary care based stepwise screening for type 2 diabetes.

Design Controlled trial and comparative study embedded in a randomised controlled trial.

Setting 15 practices (10 screening, five control) in the ADDITION (Cambridge) trial in the east of England.

Participants 7380 adults (aged 40-69) in the top fourth for risk of having undiagnosed type 2 diabetes (6416 invited for screening, 964 controls).

Interventions Invited for screening for type 2 diabetes or not invited (controls), incorporating a comparative study of subgroups of screening attenders. Attenders completed questionnaires after a random blood glucose test and at 3-6 months and 12-15 months later. Controls were sent questionnaires at corresponding time points. Non-attenders were sent questionnaires at 3-6 months and 12-15 months.

Main outcome measures State anxiety (Spielberger state anxiety inventory), anxiety and depression (hospital anxiety and depression scale), worry about diabetes, and self rated health.

Results No significant differences were found between the screening and control participants at any time—for example, difference in means (95% confidence intervals) for state anxiety after the initial blood glucose test was -0.53, -2.60 to 1.54, at 3-6 months was 1.51 (-0.17 to 3.20), and at 12-15 months was 0.57, -1.11 to 2.24. After the initial test, compared with participants who screened negative, those who screened positive reported significantly poorer general health (difference in means -0.19, -0.25 to -0.13), higher state anxiety (0.93, -0.02 to 1.88), higher depression (0.32, 0.08 to 0.56), and higher worry about diabetes (0.25, 0.09 to 0.41), although effect sizes were small. Small but significant trends were found for self rated health across the screening subgroups at 3-6 months ($P=0.047$) and for worry about diabetes across the screen negative groups at 3-6 months and 12-15 months ($P=0.001$).

Conclusions Screening for type 2 diabetes has limited psychological impact on patients. Implementing a national screening programme based on the stepwise screening procedure used in the ADDITION (Cambridge) trial is unlikely to have significant consequences for patients' psychological health.

Trial registration Current Controlled Trials
ISRCTN99175498.

INTRODUCTION

Type 2 diabetes fulfils many of the criteria for screening yet important uncertainties remain.¹ The current study was embedded in the Anglo-Danish-Dutch study of intensive treatment in people with screen detected diabetes in primary care (ADDITION) trial,² which includes 54 general practices in the Cambridge arm. We investigated the psychological impact of inviting people at high risk of developing type 2 diabetes to attend for screening at a general practice and of the screening tests and results.

METHODS

The study design was a controlled trial comparing those invited for screening with non-invited controls, incorporating additional comparisons between subgroups of screening attenders, embedded in the ADDITION (Cambridge) trial. In that trial, practices were randomly allocated to screening or control arms. The psychological impact substudy (see bmj.com) included all five control practices in the main trial and a sample of 10 of the screening practices.

Participants in the screening practices who attended the initial glucose test ($n=4370$) were given a questionnaire to complete and return to the study centre; subsequent questionnaires were sent 3-6 months and 12-15 months later. Screening non-attenders ($n=2046$) were sent the questionnaire at 3-6 months and 12-15 months after the date of their scheduled random blood glucose test.

In each of the five control practices 25% ($n=964$) of those with a high risk score were randomly sampled to be sent questionnaires at equivalent times to 3-6 months and 12-15 months.

At the initial time point screening attenders were classified according to their initial test result. At 3-6 months and 12-15 months participants were classified according to the point at which they had tested negative or positive or failed to attend (see bmj.com).

We used five outcome measures. State anxiety was measured using the Spielberger state anxiety inventory.³ General anxiety and depression were

This article is an abridged version of a paper that was published on bmj.com on 31 August 2007. Cite this version as: *BMJ* 31 August 2007, doi: 10.1136/bmj.39303.723449.55 (abridged text, in print: *BMJ* 2007;335:486-9).

measured with the hospital anxiety and depression scale.⁴ Disease specific worry was measured using the Lerman cancer worry scale.⁵ A single item was used to measure self reported general health.

The study size was based on the Spielberger state anxiety inventory, informed by a pilot study⁶ providing a standard deviation of 12, an intrapractice correlation coefficient of 0.048, and plausible effect differences of 3 to 7 units from state anxiety scores of 34.1 (control), 37.6 (screening), 33.1 (negative at first test), and 41.7 (after further testing). Allowing for 20-40% dropout (depending on group and wave), the study had 80% power, with two sided tests at the 5% level of significance, to detect a difference in mean state anxiety between screening and control (hypothesis 1) of 3.2 units, between screen negative and screen positive groups (hypothesis 2) of 1.4 units, and between the two smallest fully screened groups of 5.7 units at 3-6 months and 5.4 units at 12-15 months (for hypothesis 3). A difference of 3.2 units equates to a difference between adjacent response categories—for example, “not at all” and “somewhat”—on three of the 20 items on the full form of the scale.

We assessed cross sectional comparisons between groups and dose-response trends across testing groups using a linear mixed effects model, with practice as random effect to account for clustering. Effect sizes were summarised with 95% confidence intervals, and we assessed hypotheses using two sided tests at the 5% level of significance. These were adjusted for clustering and for age and comorbidity (use of antihypertensives). The size of the difference in means between groups was interpreted in terms of the response categories of the scale and by comparison with the standard deviation, using Cohen's guidelines.⁷ Analysis was primarily by intention to treat although we followed the explanatory nature of the hypotheses by excluding those who did not return a questionnaire until after their subsequent test in the screening programme.

RESULTS

The screening and control groups were comparable at baseline on the measures used to calculate diabetes risk⁸ and for practice size (see bmj.com). The response rates are on bmj.com.

Impact of being invited to screening

At the time of the random blood glucose test no significant differences were found between the screening attenders and controls on any of the five outcome measures (state anxiety, difference in means -0.53 (95% confidence interval -2.60 to 1.54 ; $P=0.62$; table 1). At 3-6 months and 12-15 months no significant differences were found between those invited for screening (attenders and non-attenders) and controls (state anxiety, difference in means at 3-6 months 1.51 (-0.17 to 3.20 ; $P=0.10$) and at 12-15 months 0.57 (-1.11 to 2.24 ; $P=0.52$, table 2).

Immediate impact of initial screening test results

After the initial test the participants who screened positive reported significantly poorer general health (difference in means -0.19 , -0.25 to -0.13 ; $P<0.001$), higher state anxiety (0.93 , -0.02 to 1.88 ; $P=0.05$), higher depression (0.32 , 0.08 to 0.56 ; $P=0.01$), and higher diabetes specific worry (0.25 , 0.09 to 0.41 ; $P=0.002$) than those who screened negative (table 1). The effect sizes were, however, small. No significant difference was found on general anxiety.

Impact of a recent diagnosis of type 2 diabetes

A significant linear trend across the subgroups of screening attenders was found on two measures (see bmj.com). At 3-6 months self reported health declined across groups according to the number of tests before testing negative, with the poorest general health reported by those testing positive at the final test—that is, those with newly diagnosed type 2 diabetes ($P=0.047$). The effect was no longer evident at 12-15 months. The more screening tests that a participant underwent before testing negative, the higher the

Table 1 Differences in outcome between screening attenders and control participants, and between participants who screened positive and those who screened negative (random blood glucose test), at initial time point*. Values are means (standard deviations) unless stated otherwise

| Variables | Control, non-screening n=253 | Screening attenders n=3199 | Difference† (95% CI), P value‡ | Screen negative at RBG n=2057 | Screen positive at RBG n=1142 | Difference§ (95% CI), P value‡ |
|----------------------|---------------------------------|-------------------------------|-----------------------------------|----------------------------------|----------------------------------|-----------------------------------|
| Self reported health | 3.14 (0.85) | 3.10 (0.88) | -0.02 (-0.18 to 0.14), 0.81 | 3.17 (0.87) | 2.97 (0.89) | -0.19 (-0.25 to -0.13), <0.001 |
| State anxiety | 32.7 (11.5) | 32.7 (11.6) | -0.53 (-2.60 to 1.54), 0.62 | 32.4 (11.4) | 33.1 (11.9) | 0.93 (-0.02 to 1.88), 0.05 |
| HADS anxiety | 6.42 (4.39) | 6.04 (3.79) | -0.46 (-0.99 to 0.07), 0.12 | 6.07 (3.75) | 5.97 (3.87) | -0.00 (-0.28 to 0.27), 0.99 |
| HADS depression | 4.52 (3.48) | 4.24 (3.31) | -0.37 (-0.93 to 0.18), 0.21 | 4.14 (3.24) | 4.41 (3.43) | 0.32 (0.08 to 0.56), 0.01 |
| Worry about diabetes | 7.95 (2.44) | 8.04 (2.20) | 0.03 (-0.36 to 0.42), 0.90 | 7.97 (2.19) | 8.18 (2.21) | 0.25 (0.09 to 0.41), 0.002 |

HADS=hospital anxiety and depression scale; RBG=random blood glucose test.

*Immediately after initial (random blood glucose) test for screening attenders, first contact for control participants.

†Screening attenders minus controls.

‡Adjusted for age and comorbidity (use of antihypertensives).

§Participants who screened positive minus participants who screened negative.

diabetes specific worry reported at 3-6 months and 12-15 months ($P=0.001$ for both). No significant trend was found across groups for anxiety and depression.

Non-attenders

Those invited for screening included two further groups (see bmj.com): screening non-attenders (for the initial test) and dropouts (those testing positive at the initial test but not attending for further tests). Compared with screening attenders, non-attenders had significantly higher scores on diabetes specific worry at 3-6 months (difference in means 0.26, 0.01 to 0.50; $P=0.04$) and 12-15 months (0.35, 0.03 to 0.66; $P=0.03$), but the effect sizes were small. Dropouts had significantly poorer self reported health at 12-15 months (-0.26, -0.46 to -0.06; $P=0.01$) and significantly higher diabetes specific worry at 12-15 months (1.25, 0.66 to 1.83; $P<0.001$), a medium sized effect.

Sensitivity to missing data

Sensitivity analyses examining the influence of missing data and possible bias arising from study attrition did not change the main conclusions.

DISCUSSION

Our finding that the psychological impact of screening for type 2 diabetes seems to be limited is in line with previous research.⁹⁻¹⁴ Firstly, no significant differences were found for state anxiety, anxiety, depression, diabetes specific worry, and self rated health between the screening attenders and controls at the initial random blood glucose test or between those invited for screening and controls at 3-6 months and 12-15 months.

Those who screened positive at the initial test reported significantly poorer general health and higher state anxiety and depression and diabetes specific worry than those who screened negative. These effects were, however, small and the mean scores were not clinically relevant (anxiety and depression)^{3,4} or relatively high (worry).^{5,15} Being required to return for further tests after an initial positive test result seems to have a small negative psychological impact that is unlikely to be of clinical significance.

At 3-6 months rather than comparing those with and without screen detected type 2 diabetes we compared participants according to the point in the screening process at which they screened negative or positive, to examine the impact of the tests as well as the diagnosis. A marginally significant dose-response effect was found on self reported health in the hypothesised direction—those screening negative at the initial test reported the best health and those with a diagnosis of diabetes reported the poorest health; the trend was, however, no longer evident at 12-15 months. Within the screen negative group the more screening tests that participants had before screening negative the higher was their worry at 3-6 months about developing type 2 diabetes; this trend was maintained at 12-15 months. Although this trend is in the direction hypothesised the level of worry was relatively low^{15,16}: the mean score for those screening negative after three tests equated to being “sometimes” worried on three items and “not at all or rarely” worried on the other three items on the scale. No trends were found for anxiety and depression. Thus the hypothesis of a dose-response

Table 2 Differences in outcome between screening and control participants at 3-6 months* and 12-15 months†. Values are means (standard deviations) unless stated otherwise

| Time | Control, non-screening | Screening group (attenders and non-attenders) | Difference‡ (95% CI), P value§ |
|-----------------------|------------------------|---|--------------------------------|
| Self reported health: | | | |
| 3-6 months | 3.14 (0.80), n=443 | 3.13 (0.88), n=3211 | 0.02 (-0.13 to 0.18), 0.78 |
| 12-15 months | 3.21 (0.81), n=383 | 3.15 (0.87), n=3093 | -0.03 (-0.20 to 0.13), 0.70 |
| State anxiety: | | | |
| 3-6 months | 31.8 (11.4), n=358 | 33.5 (12.0), n=2504 | 1.51 (-0.17 to 3.20), 0.10 |
| 12-15 months | 32.8 (11.8), n=304 | 33.5 (12.2), n=2377 | 0.57 (-1.11 to 2.24), 0.52 |
| HADS anxiety: | | | |
| 3-6 months | 5.97 (3.86), n=442 | 5.91 (3.89), n=3159 | -0.12 (-0.55 to 0.32), 0.61 |
| 12-15 months | 5.81 (3.87), n=377 | 5.85 (3.87), n=3034 | -0.01 (-0.47 to 0.45), 0.98 |
| HADS depression: | | | |
| 3-6 months | 4.18 (3.38), n=444 | 4.24 (3.40), n=3177 | 0.01 (-0.51 to 0.54), 0.96 |
| 12-15 months | 4.03 (3.35), n=378 | 4.28 (3.40), n=3049 | 0.22 (-0.31 to 0.74), 0.44 |
| Worry about diabetes: | | | |
| 3-6 months | 7.87 (2.35), n=428 | 7.79 (2.15), n=3041 | -0.11 (-0.42 to 0.19), 0.48 |
| 12-15 months | 8.08 (2.30), n=365 | 7.75 (2.21), n=2889 | -0.33 (-0.67 to 0.01), 0.08 |

HADS=hospital anxiety and depression scale.

*Time since initial or scheduled (random blood glucose) test for screening group, 3-6 months since first contact or equivalent for control group.

†Time since initial or scheduled (random blood glucose) test for screening group, 12-15 months since first contact or equivalent for control group.

‡Screening group minus control group.

§Adjusted for age and comorbidity (use of antihypertensives).

WHAT IS ALREADY KNOWN ON THIS TOPIC

Observational studies suggest that the psychological impact of screening for type 2 diabetes is limited

No evidence is available from controlled trials

WHAT THIS STUDY ADDS

Screening for type 2 diabetes does not seem to have an adverse psychological impact

A national screening programme based on the ADDITION (Cambridge) model is unlikely to have important psychological costs

effect across the screening groups was only partially supported.

Only a small proportion of non-attenders for the initial test returned questionnaires but those who did had higher scores on diabetes specific worry than the attenders. The non-attender group comprised 32% of those invited for screening, so an adverse impact in this group is a potential concern. The effect size was, however, small. Another important group of non-attenders was the 11% of participants who screened positive at the initial test but who failed to attend for further tests. These dropouts were more worried about diabetes at 12-15 months than those who completed subsequent tests.

Most comparisons in this study provided no statistically significant differences between groups. As a consequence of the large sample size, the estimates of differences in means had narrow confidence intervals and these can be interpreted as robust negative findings. When significant differences between groups were observed, in almost every case the effect size was small. The largest effect we observed was for diabetes specific worry at 12-15 months between participants who screened positive at the initial test but dropped out and those who attended for subsequent tests (see bmj.com).

The current study had several limitations. Firstly, the screening practices were not randomly selected from the main trial. Nevertheless, the screening and control groups were comparable at baseline for diabetes risk score and practice size. Secondly, the study did not include a true baseline measure of anxiety and other psychological measures assessed before participants were invited for screening. This was a deliberate decision to avoid the possibility that the uptake of screening would be influenced by sending patients a questionnaire. It means, however, that to attribute the observed differences between groups to differences in their screening experience, it is necessary to assume similarity at baseline for psychological measures. Even without a true baseline, the findings are informative.

A third limitation is the low response rates among the screening non-attenders. This affects the comparison between those invited for screening and controls. If screening non-attenders who do not return questionnaires are more anxious (as a result of receiving an invitation) than those who do, we may be

underestimating the adverse impact of being invited for screening.

Despite these limitations this study provides strong evidence on the psychological impact of screening for type 2 diabetes. Implementing a national screening programme based on the stepwise screening procedure used in the ADDITION (Cambridge) trial is unlikely to have significant consequences for patients' psychological health.

We thank the participants and the practices; the Cambridge ADDITION trial coordination team, in particular Kate Williams (trial manager), Lincoln Sargeant (clinical epidemiologist), Ryan Butler (data manager), Tom Fanshawe (medical statistician), Lewis Moore, Pesheya Doubleday, Ros Barling, and Nick Wareham (principal investigator, ADDITION trial); and the Medical Research Council field epidemiology team, in particular Sandra Bovan, Liz White, Christine May-Hall, Rozi Robbins, Muriel Hood, Georgina Lewis, Kate Westgate, and Ros Stevenson (leads Suzie Hennings and Paul Roberts).

Contributors: See bmj.com.

Funding: This study was funded by a project grant from the Wellcome trust (reference No 071200/Z/03/Z). NHS Research and Development provided support for science funding to cover the NHS costs of hosting the research. The Cambridge ADDITION trial was funded by the Wellcome trust (reference No G0000753). HCE is funded by post doctoral fellowship from the Economic and Social Research Council/Medical Research Council.

Competing interests: None declared.

Ethical approval: Ethical approval was granted by the eastern multicentre research ethics committee (reference No 02/5/54).

- 1 Wareham NJ, Griffin SJ. Should we screen for type 2 diabetes? Evaluation against national screening committee criteria. *BMJ* 2001;322:986-8.
- 2 Lauritzen T, Griffin S, Borch-Johnsen K, Wareham N, Wolffenbuttel BHR, Rutten G. The ADDITION study: proposed trial of the cost-effectiveness of an intensive multifactorial intervention on morbidity and mortality among people with type 2 diabetes detected by screening. *Int J Obes* 2000;(suppl 3):S6-11.
- 3 Marteau TM, Bekker H. The development of six-item short-form of the state scale of the Spielberger state-trait anxiety inventory (STAI). *Br J Clin Psychol* 1992;31:301-6.
- 4 Zigmond AS, Smaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361-70.
- 5 Lerman C, Trock B, Rimer BK, Jepson C, Brody D, Boyce A. Psychological side effects of breast cancer screening. *Health Psychol* 1991;10:259-67.
- 6 Park P. Informing decision-making about screening for type 2 diabetes. University of Cambridge, 2001. (Unpublished PhD thesis.)
- 7 Cohen J. *Statistical power analysis for the behavioral sciences*, 2 ed. Hillsdale, NJ: Erlbaum, 1989.
- 8 Griffin SJ, Little PS, Kinmonth AL, Hales CN, Wareham NJ. Diabetes risk score: towards earlier detection of type 2 diabetes in general practice. *Diabetes Metab Res Rev* 2000;16:164-71.
- 9 Adriaanse MC, Snoek FJ. The psychological impact of screening for type 2 diabetes. *Diabetes Metab Res Rev* 2006;22:20-5.
- 10 Skinner TC, Davies MJ, Farooqi AM, Jarvis J, Tringham JR, Khunti K. Diabetes screening anxiety and beliefs. *Diabet Med* 2005;22:1497-502.
- 11 Farmer AJ, Doll H, Levy JC, Salkovskis PM. The impact of screening for type 2 diabetes in siblings of patients with established diabetes. *Diabet Med* 2003;20:996-1004.
- 12 Thoolen BJ, de Ridder DT, Besing JM, Gorter KJ, Rutten GE. Psychological outcomes of patients with screen-detected type 2 diabetes: the influence of time since diagnosis and treatment intensity. *Diabetes Care* 2005;29:2257-62.
- 13 Edelman D, Harris AC, Olsen MK, Oddone EZ, Dudley TK. Impact of diabetes screening on quality of life. *Diabetes Care* 2002;25:1022-6.
- 14 Adriaanse MC, Snoek FJ, Dekker JM, Spijkerman AMW, Nijpels G, Twisk JWR, et al. No substantial psychological impact of the diagnosis of type 2 diabetes following targeted population screening: the Hoom screening study. *Diabet Med* 2004;21:992-8.
- 15 Bish A, Sutton S, Jacobs C, Levene S, Ramirez A, Hodgson S. Changes in psychological distress after cancer genetic counselling: a comparison of affected and unaffected women. *Br J Cancer* 2002;86:43-50.
- 16 Sutton S, Saidi G, Bickler G, Hunter J. Does routine screening for breast cancer raise anxiety? Results from a three wave prospective study in England. *J Epidemiol Community Health* 1995;49:413-8.