Screening for type 2 diabetes: a short report for the National Screening Committee

NR Waugh,* D Shyangdan, S Taylor-Phillips, G Suri and B Hall

Warwick Evidence, Warwick Medical School, University of Warwick, Coventry, UK

*Corresponding author

Declared competing interests of authors: none

Note: this is a 'short report' that has been produced with only one-third of the resources that would be available for a full technology assessment report and it cannot be as comprehensive as a full report would be.

Published August 2013
DOI: 10.3310/hta17350

Scientific summary

Screening for type 2 diabetes

Health Technology Assessment 2013; Vol. 17: No. 35
DOI: 10.3310/hta17350

NIHR Journals Library

Scientific summary

Introduction

The prevalence of type 2 diabetes mellitus (T2DM) has been increasing, owing to increases in overweight and obesity, and decreasing levels of physical activity, as well as the changing demographic structure of the population. The York and Humber Public Health Observatory estimates that about 40% of the increase in England is due to changes in age and ethnic group structure, and 60% to lifestyles, especially obesity.

The aim of this short report was to provide an update for the National Screening Committee (NSC) on screening for T2DM.

As this review was undertaken to update a previous *Health Technology Assessment* (HTA) review published in 2007 [Waugh N, Scotland G, McNamee P, Gillett M, Brennan A, Goyder E, *et al*. Screening for type 2 diabetes: literature review and economic modelling. *Health Technol Assess* 2007;11(17)], and a more recent Scottish Public Health Network review, the searches were restricted to dates from 2009 onwards, to the end of January 2012, with selected later studies added. The databases searched were MEDLINE, EMBASE, MEDLINE-in-Process & Other Non-Indexed Citations, Science Citation Index and Conference Proceedings Citation Index. The search was not restricted to a particular study type, but was restricted to English-language articles.

People can develop T2DM without symptoms. Some have symptoms without recognising them as being related to diabetes. Up to 20% of people with T2DM may be undiagnosed. They may have diabetic complications such as eye disease (diabetic retinopathy) by the time they are diagnosed, or may suffer a heart attack, without any warning. Undiagnosed diabetes can be detected by screening for elevated blood glucose levels.

In addition to diabetes, the condition of impaired glucose tolerance (IGT), where blood glucose levels are higher than normal but not yet at diabetic level, is of public health importance. This is because the risk of cardiovascular disease (CVD) is increased in people with IGT compared with people with normal glucose tolerance, and because many people with IGT will go on to develop diabetes. IGT causes no symptoms. In terms of absolute numbers of heart attacks, IGT is a greater problem than diabetes, because, although the risk of heart disease is somewhat higher with diabetes, there are far more people with IGT than with undiagnosed diabetes. However, IGT may not be a direct cause but only a marker for metabolic abnormalities.

Impaired glucose tolerance is sometimes referred to as ‘pre-diabetes’, along with increased fasting glucose (IFG). This term is unsatisfactory because only about half of people with ‘pre-diabetes’ progress to diabetes. IGT and IFG are sometimes referred to as ‘impaired glucose regulation’ or ‘non-diabetic hyperglycaemia’.

Depending on which screening strategy was used, and what cut-off levels were used, population screening for T2DM would find more, or far more, people with IGT than with diabetes.

There are arguments for avoiding categorisation, and for using a measure of blood glucose' such as glycated haemoglobin (HbA_{1c}) in a quantitative way as part of overall assessment of vascular disease, along with blood pressure (BP) and lipids. Someone with a HbA_{1c} level in the range 6.0–6.4%, the ‘IGT range’, with no other risk factor elevation, may be at low risk compared with someone with a HbA_{1c} level of 5.6% plus hypertension and raised cholesterol.

Screening policies should take into account that the prevalence of T2DM rises with age, with about 90% of those affected aged > 50 years, and about 70% aged > 60 years. In selective screening, the first stage could be identification of people at high risk by data held on general practice computer systems, or by sending out questionnaires to people at home. If general practitioner (GP) computer data were used, the QDiabetes Risk Score appears best. If it was decided to mail questionnaires out, the Finnish Diabetes Risk Score (FINDRISC) one could be used. The main risk factors would be age, body mass index (BMI) and presence of another metabolic condition, such as hypertension. Ethnicity is also important, with people of South Asian ancestry having a higher risk, including developing T2DM at a lower BMI than white people.

The second stage, in those with high scores, would be a measure of blood glucose level. There is no perfect screening test for diabetes, but there is increasing evidence to support the use of HbA_{1c} testing.

A HbA_{1c} level of $\geq 6.5\%$ indicates diabetes, but needs to be confirmed by a second test, such as a second HbA_{1c} or a fasting plasma glucose (FPG), or an oral glucose tolerance test (OGTT). A HbA_{1c} level of $\geq 6.0\%$, but $< 6.5\%$, is associated with a high risk of progression to diabetes, and such people should be followed up with annual testing. However, even using a HbA_{1c} level of 6.0% as the threshold for further testing, about 20% of people with diabetes would be missed on an OGTT.

People of African or South Asian ancestry tend to have higher HbA_{1c} levels than white people, so HbA_{1c} testing in the former is more sensitive.

One problem with HbA_{1c} and FPG tests is that they identify overlapping but different groups, with one study showing that half of those identified by HbA_{1c} as diabetic or at high risk of diabetes, were not so by FPG, and vice versa.

The OGTT is inconvenient and time-consuming, and uptake is poorer than with the HbA_{1c} test. In screening, using a more acceptable test with higher uptake but lower sensitivity may lead to more people being detected than using a less acceptable test with higher sensitivity.

The use of HbA_{1c} testing alone remains somewhat controversial. HbA_{1c} level is a stronger predictor of CVD than FPG.

One option is that the third stage should meantime involve both HbA_{1c} and FPG testing. The added value of FPG could be reviewed in the light of experience. But even using the combination of HbA_{1c} and FPG testing would not detect everyone who would be diabetic on the OGTT. However, the reproducibility of the OGTT is far from perfect – people can be diabetic in one week but not the next.

Fasting plasma glucose alone would miss up to one-third of people with diabetes diagnosed with a full OGTT, because many people have non-diabetic fasting levels but diabetic levels after a glucose load.

The role of the 50-g glucose challenge test, carried out in non-fasted people, with plasma glucose (PG) measured at 1 hour after a 50-g glucose load, needs to be evaluated in screening for T2DM but appears promising.

Hence, screening could be done in three stages: first by risk factors; then by testing with HbA_{1c}; and then, for those with levels of > 6.0%, repeat HbA_{1c} and FPG testing or the OGTT.

People found to have undiagnosed diabetes would be advised to lose weight and increase physical activity. They might also be treated for higher than desirable blood cholesterol and BP. Some patients might need glucose-lowering drug treatment soon after diagnosis. Metformin is the drug of first choice on grounds of safety, efficacy and cost.

People found to have IGT would receive similar advice, aimed at reduction of cardiovascular risk, but also at reducing progression to diabetes. This should include a period of intensive lifestyle education on diet and physical activity. Weight loss is the main key to success. The National Institute for Health and Care Excellence (NICE) has issued public health guidance on interventions for this group. The main problem is that we know what people should do to prevent diabetes but not how to persuade most to do it.

People with IGT who do not adhere to, or do not succeed on, lifestyle intervention, switching to metformin therapy after 1 year is cost-effective in preventing diabetes.

People with IGT should be monitored, probably annually, initially, for progression to diabetes.

The last HTA report on screening for T2DM noted that there had been no trials of screening and intervention. Since then the results of two trials have been reported.

The first is the ADDITION (Anglo-Danish-Dutch Study in General Practice of Intensive Treatment and Complication Prevention in Type 2 Diabetic Patients Identified by Screening) trial [Simmons RK, Echouffo-Tcheugui JB, Sharp SJ, Sargeant LA, Williams KM, Prevost AT, *et al*. Screening for type 2 diabetes and population mortality over 10 years (ADDITION-Cambridge): a cluster-randomised controlled trial. *Lancet* 2012;380:1741–8.]. This was not a trial of screening but was a trial of intensive intervention compared with standard care in people found to have undiagnosed diabetes by screening. Nevertheless, some lessons about screening can be drawn from it because of the variety of screening methods used. Uptake was lower if people had to have OGTTs, or if screening involved blood tests on more than one visit. Uptake of blood glucose testing was improved if people were made aware in advance that they were high risk. Uptake was much lower in South Asian communities.

The ADDITION trial showed that people diagnosed with diabetes through screening were at high risk of CVD, with high prevalence of modifiable risk factors, such as overweight, high BP and high cholesterol levels. However, after 5 years of follow-up, there was little difference in the frequency of cardiovascular events. The risk of cardiovascular events was reduced by 17% in the intensive group, hazard ratio (HR) 0.83, but the 95% confidence interval was 0.65 to 1.05, so the difference was not statistically significant. If it had been, to prevent one CVD event, it would be necessary to screen 1824 people to identify 76 people who would be treated for 5.3 years. The 10-year data again showed no reduction in cardiovascular, diabetes-related or total mortality events.

The reason for the non-significant difference in the ADDITION study appears to have been that standard care improved, so that improvements in BP and cholesterol levels in the standard-care arm were similar to those in the intervention arm. Much of the benefit from diagnosing and treating undiagnosed diabetes comes from treating hypertension and blood lipids, rather than blood glucose. If BP and cholesterol levels in the general population are now better controlled, the benefits of screening for diabetes will be less.

In summary, the ADDITION study shows that the combination of a risk score and screening for undiagnosed diabetes identified a group with high levels of modifiable risk factors, and led to considerable improvements in BP and blood cholesterol, with marked rises in the proportions of patients on antihypertensive drugs, statins and aspirin in the standard-care group. So the diagnosis of diabetes triggered a range of interventions.

The second is the trial of screening for diabetes from Ely. The 13-year follow-up was published in 2012. In this randomised controlled trial (RCT), one-third of the practice population, aged 40 to 65 years, was screened by OGTT in 1990–2. They were invited for repeat screening in 1994–6 and 2000–2. The other two-thirds were initially not followed up, but half (randomly selected) were then invited for screening for diabetes in 2000–2. The GPs were informed of the screening results, and could apply whatever treatment they thought appropriate.

At the 13-year follow-up, there were no differences in cardiovascular outcomes or self-reported health status.

Does screening for type 2 diabetes mellitus yet meet the National Screening Committee criteria?

Criterion 12, on optimisation of existing management of the condition, has not been met. The recent report of the National Audit Office (NAO) gives details of shortcomings.

Criterion 13 requires evidence from high-quality RCTs that screening is beneficial. This has not been met. The Ely trial of screening showed no benefit. The ADDITION trial was not a trial of screening, but showed no cardiovascular outcomes benefit from applying intensive management.

Criterion 18 on staffing and facilities does not appear to have been met, according to the NAO report, which gives details on very marked variations in care among primary care trusts.

Criterion 19 requires that all other options, including prevention, should have been considered. In theory, a large proportion of cases of T2DM could be prevented if people avoided becoming overweight or obese. However, there is a difference between what is theoretically possible and what can be achieved in reality. Prevention has so far failed, so the issue is whether or not more efforts should be made. It has been considered, so the criterion could be deemed to have been met.

Summary

Arguments in favour of screening include:

- Type 2 diabetes is becoming more common and many people with the condition are undiagnosed.
- Health promotion measures to prevent T2DM by persuading people to adopt healthy lifestyles and avoid obesity and overweight have failed.
- There have been advances in screening methods, including refinements in risk scoring, and more convenient blood glucose testing using HbA_{1c} levels in non-fasting people.
- There have been advances in diabetes care, including retinal screening and a wider range of treatments both for glycaemic control and reduction of cardiovascular risk. So it is more advantageous to be diagnosed than a decade or two ago.
- It has been shown, for example, by the ADDITION trial, that people identified by screening to have T2DM or lesser degrees of hyperglycaemia have significant, but treatable, cardiovascular risk factors.
- Depending on which test is used and what cut-off is chosen, more people with lesser degrees of hyperglycaemia will be found than people with diabetes. NICE has recently issued guidance for this group.
- Some people with undiagnosed diabetes will develop retinopathy.

Arguments against population screening:

- Some of the NSC criteria for a screening programme are not met.
- In particular, we now have a trial of screening for diabetes but it found no advantage in health measures or cardiovascular morbidity after a 13-year follow-up.
- Identifying people at high risk of CVD and applying intensified management, as done in the ADDITION trial, did not result in any benefit.
- There is no perfect screening test. The OGTT is inconvenient and time-consuming, requires fasting overnight, and acceptance may be poor. The FPG lacks sensitivity. HbA_{1c} testing costs more than a simple PG test and will miss some people who are identified as diabetic by an OGTT.

- If other cardiovascular risk factors are assessed and addressed, the benefits of screening for hyperglycaemia are modest in terms of further reducing cardiovascular risk.
- The proportion undiagnosed has probably been reduced by opportunistic screening.

Conclusions

The case for universal screening of those aged > 40 years is not proven.

There is a case for selective screening as part of overall vascular risk assessment.

The first stage of selection would use risk factors. This could be done using data held on GP computer systems, using QDiabetes Risk Score, or by sending out questionnaires, using the FINDRISC. (The diabetes filter used in the NHS Health Check programme has shortcomings.)

Those at high risk would have a measure of blood glucose.

Glycated haemoglobin has advantages in not requiring a fasting sample and it is a predictor of vascular disease across a wider range than just the diabetic one. However, it lacks sensitivity and would miss some people with diabetes.

The OGTT is more sensitive, but inconvenient, more costly, with imperfect reproducibility, and less popular, meaning that uptake would be lower.

Some important NSC criteria are not met.

Decisions on screening for T2DM, with or without IGT, will be taken in the context of what other screening is being done in each of the four territories of the UK. In England, determination of diabetes status might be carried out in the context of the vascular screening programme, although it might add little to the overall vascular risk score. Absolute values of, for example, HbA_{1c}, may be more useful as part of overall risk than a dichotomous diabetes or not diabetes diagnosis.

Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research.

Health Technology Assessment

HTA/HTA TAR

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Five-year impact factor: 5.804

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the ISI Science Citation Index and is assessed for inclusion in the Database of Abstracts of Reviews of Effects.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: nihredit@southampton.ac.uk

The full HTA archive is freely available to view online at www.journalslibrary.nihr.ac.uk/hta. Print-on-demand copies can be purchased from the report pages of the NIHR Journals Library website: www.journalslibrary.nihr.ac.uk

Criteria for inclusion in the *Health Technology Assessment* journal

Reports are published in *Health Technology Assessment* (HTA) 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 reviewers 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.

HTA programme

The 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 journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

For more information about the HTA programme please visit the website: www.hta.ac.uk/

This report

The research reported in this issue of the journal was funded by the HTA programme as project number 11/18/01. The contractual start date was in August 2011. The draft report began editorial review in September 2012 and was accepted for publication in April 2013. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk).