

# Non-pharmacological interventions to reduce the risk of diabetes in people with impaired glucose regulation: a systematic review and economic evaluation

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## Executive summary

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# Executive summary

## Background

The prevalence of type 2 diabetes mellitus (T2DM) is increasing in the UK and worldwide. It is expected that the UK prevalence will increase by about 50% over the next decade. If not well managed it can have serious consequences. These include an increase in cardiovascular diseases (CVDs), such as heart disease, stroke and peripheral vascular disease, and in small vessel (microvascular) disease, which can cause blindness and renal failure. In addition to the human costs, such complications place a heavy burden on health-care resources.

Prior to the onset of T2DM, there are two conditions characterised by blood glucose levels that are above normal but below the threshold for diabetes. These are impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), known collectively as 'intermediate hyperglycaemia', and identified by measuring blood glucose levels. They are sometimes called 'pre-diabetes' but this is an unsatisfactory term because not all people with these conditions go on to develop diabetes. However, people with pre-diabetes are at increased risk of CVD, especially ischaemic heart disease.

Screening for T2DM is currently being considered by the UK Departments of Health. The National Screening Committee has recommended that it be done as part of a broader approach to reduce CVD. Depending on which screening test was used, and what threshold levels were chosen, screening would detect not only those with diabetes, but also a larger group with IGT or IFG. Therefore, it is necessary to consider how such patients would be managed.

## Objective

To review the clinical effectiveness and cost-effectiveness of non-pharmacological treatments, principally diet and physical activity, for the prevention of T2DM in people with intermediate hyperglycaemia.

## Methods

### *Clinical effectiveness*

Electronic databases were searched for systematic reviews, randomised controlled trials (RCTs) and other relevant literature on the effectiveness of diet and/or exercise for IGT or IFG. Searches were undertaken up to October 2007. Auto-alerts were kept running, and updating searches were carried out in February 2011, and selective ones in January 2012. Some more recent studies have been added to the final version.

The review of clinical effectiveness was based primarily on RCTs, which were critically appraised for internal and external validity. We also searched for recent systematic reviews and for longer-term follow-up from the RCTs.

### *Cost-effectiveness*

A recent review of screening for T2DM had included a review of five studies on the long-term costs and health outcomes associated with delaying or preventing diabetes in high-risk groups. Most of these studies concluded that screening and intervention would be cost-effective. We therefore searched for more recent studies in order to update the previous review.

Electronic databases were searched for relevant published literature on the cost-effectiveness of diet and/or exercise for IGT or IFG, and a critical review was undertaken.

We further developed the Sheffield economic model of T2DM. The model examined the cost-effectiveness of preventing or delaying T2DM in people with IGT, including the effects of interventions on CVD.

Modelling based on data from the trials may not reflect what would happen in routine care. Trials are protocol driven, and patients are supposed to stay on the treatments to which they are randomised. In normal care, if an intervention is not working then it should be stopped. We therefore created a 'real-life' scenario whereby people who did not benefit from lifestyle measures (usually because they did not adhere to diet and exercise, and, in particular, did not achieve sufficient weight loss) would be switched to alternative treatment, usually metformin.

The cost to the NHS of the implementation of any recommendations on screening and intervention would depend on the extent to which those are already provided. We therefore used data from the General Practice Research Database (GPRD) to assess the extent to which IGT and IFG were diagnosed at present, and how they were managed. We were interested not only in interventions to reduce progression to diabetes, but also those to reduce CVD, such as statins.

## Results

### *Number and quality of studies*

Nine published RCTs comparing lifestyle interventions (predominantly diet and physical activity advice, with regular reinforcement and frequent follow-up) with standard lifestyle advice or placebo were identified. They included 5875 people randomised to receive lifestyle advice, exercise programmes or combinations thereof. The trials varied in design and quality. The primary outcome for the trials was progression to T2DM. Five recent systematic reviews were identified.

### *Summary of benefits and risks*

The RCTs compared the effect of non-pharmacological lifestyle interventions with a control intervention (usually standard lifestyle advice with non-intensive follow-up) in participants with IGT. People who already had diabetes were excluded. Results from separate studies were not combined for analysis because of the heterogeneous populations, intensity of intervention and duration of follow-up of each intervention. However, progression to diabetes was quantified as a risk ratio for each study. In most of the trials, lifestyle interventions reduced progression to diabetes (risk ratio range 0.33 to 0.96).

The Diabetes Prevention Program (DPP) from North America (which had higher risk recruits than most other trials) reported that the prevalence of diabetes at 3 years was 29% in the control group compared with 14% in the lifestyle intervention arm. The Finnish Diabetes Prevention Study (DPS) had the longest follow-up, to 7 years, which included the 4 years of intervention and then 3 years of post-intervention follow-up. After 4 years, 4% of the lifestyle group and 7.4% of the control group had developed diabetes, roughly a halving of risk. At 7 years, the difference had diminished slightly, but the intervention group retained most of the benefit, suggesting that 4 years of the lifestyle intervention had resulted in a sustained change in lifestyle habits.

The benefits of the lifestyle intervention were greatest in those with the highest compliance and who achieved more of the targets (such as weight loss and dietary change). For example, in the

Finnish study, those who achieved four or five of the five targets had a risk of developing diabetes that was only 23% of the figure for those who achieved none.

However, even among the volunteers in the trials, many did not succeed, and others succeeded in the short term (such as the first 6 months) but not in the longer term. The key to success is sustained lifestyle change, especially weight loss.

### Cost-effectiveness

Our aim was to update a previous review in the *Health Technology Assessment* (HTA) monograph [Vaughan 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)] on screening for diabetes published in 2007. Several new studies were found. One was a further analysis by the authors of one of the studies in the screening review, and was set in a North American context of multiple providers and funders of care. The study was based on a Markov model, using data from the DPP, and concluded that intervention to delay or prevent diabetes would be cost-effective. Another was from the Indian DPS; although a good-quality trial, the economics of care are very different and not applicable to the UK. It also concluded, as did previous studies, that prevention by lifestyle means was cost-effective. Another new study from the USA used an entirely different type of model, the Archimedes Diabetes Model, which is based on the physiological mechanisms that underlie the development of diabetes and its complications. It also used data from the DPP. The authors concluded that the lifestyle intervention would not be cost-effective. This analysis assumed that over a 30-year period, the cumulative incidence of diabetes would fall by only 11%, from 72% to 61%. This was based on a linear model of diabetes incidence over 30 years.

However, our analysis of GPRD data suggested that most of those who were going to progress would do so in the first 10 years. That analysis also suggested that most practices were not seeking, recording, or intervening in IGT. This suggests that any programme of screening and intervention for people with that condition would be starting from a low baseline.

Our modelling assumed that people with IGT would initially be treated with a structured lifestyle intervention similar to that in the Finnish trial, but that those who did not comply would be switched to metformin after 12 months. Metformin is now a very cheap drug, and reduces the risk of progression to diabetes, although not by as much as adherence to lifestyle measures does. Applying an early switch to metformin in the non-adherers means that the adherers remaining on diet and physical activity will do better than seen in the lifestyle arms of the trials. We assumed that the non-adherers to lifestyle modifications will have better adherence to metformin, so that they will also do better than if left on the lifestyle interventions.

Using the switching assumption, intervention is highly cost-effective, and, in certain scenarios, cost-saving.

### Suggested research priorities

There is very good evidence that diet and physical activity changes can reduce the risk of diabetes. We know what people should do to reduce the risk of progression to diabetes. However, we do not know how best to persuade them to do it. The research most needed is how to persuade people at risk to adopt and persevere with lifestyle changes.

## Conclusion

In people with IGT, lifestyle change (diet and physical activity) is clinically effective and cost-effective in reducing progression to diabetes.

## Funding

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## Publication

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# 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 needed 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.

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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.

The research reported in this issue of the journal was commissioned by the HTA programme as project number 06/11/01. The contractual start date was in July 2006. The draft report began editorial review in March 2008 and was accepted for publication in March 2012. As the funder, by devising a commissioning brief, the HTA programme specified the research question and study design. 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 referees 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.

The views expressed in this publication are those of the authors and not necessarily those of the HTA programme or the Department of Health.

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