Screening for diabetes: what are we really doing?

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Screening for non-insulin dependent diabetes is supported by a raft of international and national recommendations from authoritative bodies.¹⁻⁵ The assumption is that the benefits of early diagnosis in asymptomatic individuals will outweigh any harm associated with screening,⁶ earlier diagnosis,⁷ or the side effects. We have examined the research evidence for screening for diabetes and suggest a move from screening for the disease itself to screening for risk factors.

Methods

With no direct evidence of long term benefit from randomised controlled trials in screened populations, we used Medline and the Cochrane Library to identify randomised controlled trials that included populations with clinical diabetes and reported long term outcomes. We also used a model of clinical non-insulin dependent diabetes to estimate outcomes in the absence of screening.⁸⁻⁹

Screening for disease

Most current screening guidelines and recommendations use a model of disease screening when they suggest screening for diabetes. Research has focused on establishing the sensitivity and specificity of different tests, and tends to measure the success of a diabetes screening programme in terms of the number of new cases identified.¹⁰⁻¹²

One problem with focusing on case detection is that the potential benefit of screening is not similar for all cases. The risk of microvascular complications increases with the plasma glucose concentration and the duration of diabetes, while the risk of macrovascular disease depends on age, sex, genes, and lifestyle, as well as hyperglycaemia. As an increased risk of macrovascular disease may occur in people whose plasma glucose concentration is lower than values found in diabetes, it is difficult to identify a single screening cut off point for case ascertainment.¹³ Within the model of disease screening, a disorder which would never be diagnosed clinically without screening during the person's lifetime is considered "pseudo disease," and someone with a pseudo disease cannot benefit from screening. Yet detection of asymptomatic hyperglycaemia during life could lead to more effective management of cardiovascular risk.

Screening for risk factors

We suggest that screening for hyperglycaemia should be regarded more appropriately as screening for risk

Summary points

Current recommendations for diabetes screening suggest that screening decisions should be based on the risk of diabetes itself

However, it is more logical to base screening and treatment decisions on the risk of microvascular and macrovascular complications that can be prevented effectively by early intervention

People with diabetes detected by screening are at high risk of macrovascular disease and comparatively low risk of microvascular complications

Early treatment for other macrovascular risk factors may be more important than early treatment for diabetes itself

factors, with the aim of preventing both microvascular and macrovascular complications. Whether we screen people on the basis of an increased risk of microvascular complications (that is, screen preferentially younger people who will have a longer mean duration of disease) or of macrovascular complications (that is, screen preferentially older people and those with other cardiovascular risk factors) depends on the relative importance of these two distinct potential sources of benefit. This depends on the likely benefits in terms of reduced relative risks of microvascular and macrovascular complications and on the absolute risks of microvascular and macrovascular complications in the population we identify by screening.

That screening and treatment are more likely to be beneficial in those at greatest risk of microvascular complications is already acknowledged implicitly by guidelines that place an upper age limit on screening.⁴ Few guidelines currently consider screening in those at increased risk of cardiovascular disease except in the presence of risk factors that are also predictors of diabetes (for example, hypertension).³⁻⁵ Yet treating macrovascular risk factors will probably produce a greater net benefit than preventing the specific microvascular complications of diabetes.

Benefits of early intervention

There is no direct evidence from randomised trials of reduced complications after earlier intervention in people with asymptomatic non-insulin dependent diabetes. Trials have shown a short term impact on cardiovascular risk factors and hyperglycaemia from intervention in early diabetes.¹⁴ They have had insufficient power to detect measurable reductions in microvascular disease and have indicated either no important effect or an increase in cardiovascular complications.^{15–17}

Benefit has therefore been calculated by extrapolating results from treatment trials in populations with clinically diagnosed diabetes. For microvascular complications, the evidence comes from a trial in patients with insulin dependent diabetes treated intensively with insulin¹⁸ and a small trial in a population with clinically diagnosed non-insulin dependent diabetes, also treated intensively with insulin.¹⁹ A problem with extrapolating from this result is that this type of treatment is rarely considered appropriate for people with asymptomatic disease detected by screening, who are likely to have a lower blood glucose concentration.²⁰

For macrovascular complications, there are three distinct ways in which early diagnosis may influence risk. Firstly, an individual may be put into a higher risk category for cardiovascular disease, so that treatment of other risk factors is initiated. If hyperglycaemia doubles the five year risk of a cardiovascular event²¹ and the threshold for considering drug treatment for hypertension or hyperlipidaemia is a five year risk of 10%,²² then in the subgroup whose risk is initially estimated at between 5% and 10%, a diagnosis of hyperglycaemia may lead directly to starting drug treatment.

The second way in which early diagnosis may influence risk is by changing the choice of treatment—for example, changing an antihypertensive drug to one specifically recommended in diabetes.²³ Evidence is accruing that lipid lowering agents and antihypertensive medication benefit populations with diabetes.^{21 24–26} These results are from post hoc subgroup analyses of large trials. Although trials in diabetic populations are in progress, these populations are still generally clinically diagnosed and not detected by screening. However, since cardiovascular risk is high in both clinically diagnosed and undiagnosed populations,²⁰ extrapolation of results to screening detected cases may be more easily justified than for trials of improved glycaemic control.

Lastly, treatment to control the blood glucose concentration may influence risk directly.²⁷ Evidence on whether treatment to improve glycaemic control can reduce the risk of macrovascular complications will come from the United Kingdom prospective diabetes study.

Absolute versus relative risk

The importance of the absolute, rather than relative, risk of macrovascular disease in determining treatment of hypertension²⁸ has been debated extensively over the past few years.^{29–33} The importance of absolute risk is generally accepted and favours treating older people because their absolute risk of adverse outcomes is

higher. Similarly, in diabetes, the benefit of early intervention will be the product of the baseline risk of complications and the relative risk reduction associated with earlier treatment.

The availability of an effective treatment after clinical diagnosis will actually reduce the potential benefits of screening by reducing the baseline risk of complications in unscreened people. Using modelling based on results of the diabetes control and complications trial,¹⁸ “comprehensive treatment” is predicted to reduce the lifetime risk of blindness from 19% to 5.3% in a population with clinically diagnosed non-insulin dependent diabetes.^{8 9} The risk of blindness in a population identified by screening for hyperglycaemia (some of whom would never develop symptomatic diabetes) will be lower than this and there is little room for further reduction. The same model predicts that 39% of a population with clinically diagnosed diabetes will develop cardiovascular disease and the risk is likely to be similar in those whose diabetes remains undiagnosed.²⁰ So the lifetime risk of macrovascular complications is much higher than that of microvascular complications. It would be even higher if screening were restricted to people already at increased risk of cardiovascular disease.

Implications of risk factor screening

A risk factor approach means that screening for hyperglycaemia needs to be considered in the context of screening for other cardiovascular risk factors. Evidence that treating cardiovascular risk factors in populations with hyperglycaemia is beneficial means that asymptomatic hyperglycaemia becomes increasingly important in providing a rational basis for the choice of treatment of other cardiovascular risk factors. In practice, some interventions (increased exercise, weight loss) may benefit both cardiovascular risk and glycaemic control.

The real value of screening can only be determined on the basis of an overall net benefit for all outcomes that matter to the people screened, as judged by information from randomised controlled trials. We have discussed trials that provide some of this information: is it now time to consider major randomised controlled trials to establish the benefit and harms of screening?

IAN BARRACLOUGH

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A memorable mistake

Please come back—the patient won't take her cotton wool

Back in 1967, hospital cardiopulmonary resuscitation teams were new, almost as new as my medical degree. My preregistration houseman duties included coronary care, directed by a highly regarded general physician of legendary wisdom and humanity. It was accepted by all that it was inappropriate to admit patients over the age of 70 to coronary care or to resuscitate them on the ward. After all, the bible indicated that a life span of three score years and ten was normal. No ethics committees in those days.

This particular cardiac arrest call came from the general women's medical ward, the patient was in asystole and because of her age—72—resuscitation was ceased shortly after I arrived. The monitor, correctly connected, continued to show asystole; there were no heart sounds, and the pupils were fixed and dilated. An ophthalmoscope showed trucking in the retinal vessels and life was pronounced extinct.

I left the ward, in company with a colleague, only to be paged urgently: "Please come back, Mrs A won't take her cotton wool." During the ritual of preparing the body for the undertaker, cotton wool was inserted into her mouth. This had been unexpectedly expelled by an active tongue. A few minutes later, the electrocardiograph showed a reasonable rate and rhythm, the blood pressure was adequate, and consciousness was returning.

My question: "Have the relatives been told?" was answered by the sister in charge: "Oh no doctor, they don't have the phone—I had to send a police message."

Nervously I asked: "What did you say?" Sister replied: "I asked for them to phone the hospital at once, she had had a turn."

The patient went on to make an uneventful recovery, and the relatives were unaware of my error; the bacon had been duly saved. But, ever since then on the few occasions that I have had to declare that death has occurred I invoke a half hour rule: always find a reason to delay telling the family for half an hour. If they are waiting outside I go and talk with them, guiding their expectations and gently steering them to the inevitability of death. Then I go back to check the patient, and finally return to deliver the now expected news.

The diagnosis in my heart-stop patient? Prolonged sinus arrest.

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We welcome articles of up to 600 words on topics such as *A memorable patient*, *A paper that changed my practice*, *My most unfortunate mistake*, or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk. Permission is needed from the patient or a relative if an identifiable patient is referred to.