

The cost-effectiveness of testing strategies for type 2 diabetes: a modelling study

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Scientific summary

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Background

In 2011, a NHS Health Checks programme was introduced in England for people of 40–70 years of age, to identify and modify risk factors for cardiovascular disease (CVD) and, ultimately, reduce the risk of future CVD events. Having diabetes or being at high risk of diabetes (HRD) is a risk factor for CVD; therefore, identifying these is one component of a health check.

In 2012, the National Institute for Health and Care Excellence (NICE) published guidance on risk assessment to identify individuals with HRD who should be offered an intensive lifestyle intervention to reduce their risk of diabetes. The NICE guidance recommends either a glycated haemoglobin (HbA_{1c}) test or a fasting plasma glucose (FPG) test for diabetes testing, and also recommends cut-off points for categorising individuals with HRD as HbA_{1c} 6.0–6.4% or FPG 5.5–7.0 mmol/l.

The two main objectives of this report are (1) to compare the cost-effectiveness of HbA_{1c} and FPG as alternative screening tests for diabetes and HRD within the NHS Health Checks programme, following the NICE guidance; and (2) to compare the cost-effectiveness of a 'finger-prick' random capillary glucose (RCG) test with that of a diabetes risk score, for the purpose of identifying individuals at highest risk of diabetes who should be offered a blood test (HbA_{1c} or FPG).

The majority of the report deals with issues concerning the cost-effectiveness of a HbA_{1c} test versus a FPG test, specifically variation in prevalence of diabetes and HRD across different localities of England, discordance between the two sets of individuals defined as having diabetes or HRD according to a HbA_{1c} test versus a FPG test, and the impact of uptake of blood tests.

Methods

The economic analysis comprised two stages. The first stage involved constructing a model of individual screening outcomes of alternative strategies. A screening strategy is a combination of (1) a 'prescreening' approach (a risk score or an RCG test or no 'prescreen') and (2) a HbA_{1c} or FPG test with a defined cut-off point for HRD.

The risk score evaluated is the Leicester Practice Database Score (LPDS), which is a general practice computer-based score, and a cut-off point of 4.75 was chosen so that approximately one-quarter of the population in the Leicester Ethnic Atherosclerosis and Diabetes Risk (LEADER) data set would not require blood testing.

For the base case analysis, the cut-off points on the HbA_{1c} and FPG tests for offering a lifestyle intervention for individuals with HRD were 6.0% and 5.5 mmol/l, respectively, per the 2012 NICE guidance.

To populate the base case model of screening outcomes, we used individual patient data from the LEADER data set to quantify:

- the prevalence of undiagnosed diabetes and undiagnosed HRD in a multiethnic population
- the proportion of individuals who would exceed the LPDS risk score cut-off point (or RCG cut-off point as applicable) for receiving a blood glucose test

- taking account of uptake rates of blood testing, the proportion of individuals who would be:
 - newly diagnosed with HbA_{1c}-defined, or FPG-defined, diabetes
 - detected with a HbA_{1c} of 6.0–6.4% or a FPG of 5.5–6.9 mmol/l, thereby being eligible for a preventative intervention.

For uptake rates, direct evidence from NHS health checks was lacking so, based on clinical advice, HbA_{1c} test uptake rates were assumed to be 20% higher than for FPG (95% and 75%, respectively) because people having a FPG test need to fast and are offered a morning-only appointment.

Unit costs of screening (including consumables, staff time and laboratory processing costs) were estimated as LPDS risk score £0.24, FPG £12.18, HbA_{1c} £14.40 and RCG £3.34.

As the LEADER data set does not include an RCG measure, we used data from the Anglo-Danish–Dutch Study of Intensive Treatment In People with Screen Detected Diabetes in Primary Care (ADDITION)-Cambridge study to inform sampled RCG values and incorporate them into the LEADER data set using a mapping between HbA_{1c} and RCG.

The second stage entailed economic modelling using an adaptation of the Sheffield Type 2 Diabetes Model. The model simulates changes in individuals' glucose tolerance status, treatment pathways, incidence of complications of diabetes (coronary heart disease, stroke, retinopathy, nephropathy and neuropathy) and mortality over an 80-year horizon. Costs of medication and treatments and health utility measures were applied to incident events to estimate the lifetime discounted costs and quality-adjusted life-years (QALYs), the incremental cost-effectiveness ratio (ICER) and expected net monetary benefit (NMB) for each screening strategy, assuming 1 QALY value = £20,000. The 'optimal' strategy is that with highest expected NMB. Uncertainty analysis entailed probabilistic sensitivity analysis (PSA) and one-way sensitivity analyses.

Individuals follow model pathways determined by their screening outcome:

- Cases of diagnosed diabetes identified through screening are treated in line with routine care pathways for type 2 diabetes.
- Cases identified as HRD are offered a preventative group-based intensive lifestyle intervention adapted for 'real-world' practice.
- Cases of diabetes not detected through screening (either because of a low LPDS or because blood glucose testing has not been taken up) initially follow a glucose trajectory for undiagnosed diabetes.
- Undetected HRD cases are modelled according to their associated risk of progressing to diabetes.

In addition to the base case analysis, the sensitivity of the results was examined in four contexts:

1. Alternative assumptions for prevalence of diabetes and HRD, and for uptake rates: the base case analyses described are based on the multiethnic LEADER cohort from Leicestershire. Other regional subpopulations can have quite different relative prevalence of HbA_{1c}-defined versus FPG-defined diabetes and HRD, the University of East Anglia-Impaired Fasting Glucose (UEA-IFG) study being the one differing most from LEADER. In UEA-IFG, the prevalence of HbA_{1c}- and FPG-defined diabetes was 2.3% and 2.1%, respectively, whereas in LEADER the prevalence was 5.7% and 1.8%, respectively. To test how sensitive the results and conclusions were to alternative glucose distributions, we repeated the modelling with four cohorts with alternative glucose distributions. One of these closely mirrors the prevalence according to the UEA-IFG study; the other three represent scenarios in between the prevalence of LEADER and UEA-IFG.

In parallel with the above, four alternative scenarios were adopted for the difference in uptake rates for first HbA_{1c} and first FPG tests, the difference varying from 10% to 40% (HbA_{1c} less FPG). Each of the four prevalence scenarios was run adopting each of the four uptake scenarios separately to create a set of 16 scenario analyses.

2. Alternative non-prevalence parameter assumptions.
3. Undertaking blood tests in everyone, that is not using a prescreening step (LPDS or RCG test).
4. Potential alternative future cut-off points for preventative intervention.

Previous modelling suggests that offering preventative interventions to those with $HbA_{1c} < 6\%$ could be cost-effective. As this is a theoretically possible option at some point in the future, subject to supporting evidence on a number of related issues, we decided to examine HbA_{1c} versus FPG screening at alternative thresholds (below HbA_{1c} 6.0% or FPG 5.5 mmol/l) for defining HRD and receiving an intervention. To enable fair comparisons between HbA_{1c} - and FPG-based testing, we compute, for each HbA_{1c} threshold, a comparable FPG 'cut-off point' at which the number of people identified as at HRD (and hence the resource implications for commissioners) would be the same. We refer to these proportions as 'ISO-resource' for a pair of strategies.

Findings

Findings from base case analyses using the Leicester Ethnic Atherosclerosis and Diabetes Risk data set around strategies recommended in National Institute for Health and Care Excellence guidance 2012 (figures are per person attending health checks)

The first finding was that, if LPDS risk score ≥ 4.75 is used for prescreening, then screening using HbA_{1c} testing alongside offering prevention intervention to those with HbA_{1c} 6.0–6.4% is more cost-effective than screening using FPG testing and offering prevention to those with FPG 5.5–6.9 mmol/l. HbA_{1c} tests have slightly higher cost per test than FPG (£14.40 vs. £12.18), but the incremental discounted lifetime cost of the HbA_{1c} strategy versus FPG is estimated as –£12 per person (£66 vs. £78), that is a cost saving. The incremental discounted QALYs for HbA_{1c} versus FPG are 0.0220 (0.0513 vs. 0.0293). HbA_{1c} testing therefore appears to marginally dominate FPG testing. PSA indicates a 98% probability that HbA_{1c} testing is more cost-effective than FPG at these cut-off points.

The second finding was that screening everyone using a HbA_{1c} test and screening everyone using a FPG test would each identify 16% of individuals as at HRD but HbA_{1c} testing identifies a larger number of people with undiagnosed diabetes (4.4% vs. 1.2%).

Sensitivity of results to alternative prevalence assumptions and uptake rates of blood tests

For the majority of scenario combinations of prevalence and uptake, HbA_{1c} testing is very or highly likely to be more cost-effective than FPG testing. The exceptions occur where HbA_{1c} -based prevalence of undiagnosed diabetes is much lower than in the LEADER cohort and at a similar level to FPG-based prevalence, as in the UEA-IFG study, but it still depends on the relative prevalence of HRD and relative uptake rates. These exceptions can be broken down into two cases:

- i. If the prevalence of HbA_{1c} -based HRD is very low compared with that for FPG (as in UEA-IFG), then FPG testing is more likely to be cost-effective than HbA_{1c} testing, unless there is a very large difference in uptake of the tests (at least of the order 35%).
- ii. If the prevalence of HbA_{1c} -based HRD is lower than for FPG but higher than in UEA-IFG, then only if there is a small difference in uptake rates (less than 20%) is it likely that FPG testing is more cost-effective than HbA_{1c} testing.

Sensitivity of the Leicester Ethnic Atherosclerosis and Diabetes Risk-based results to alternative non-prevalence assumptions

Sensitivity analyses around the LEADER cohort all indicate that HbA_{1c} testing appears to be more cost-effective than FPG.

Sensitivity of results to undertaking blood tests in everyone without using a prescreening step

If no risk score is used, the incremental costs and QALYs of using HbA_{1c} 6.0% versus FPG 5.5 mmol/l (as cut-off points for HRD) are –£30 (£75 vs. £105), that is a saving, and 0.0224 (0.0566 vs. 0.0342), respectively. Again, HbA_{1c} appears to marginally dominate FPG. PSA indicates a 95% probability that HbA_{1c} testing is more cost-effective than FPG.

With no risk score, fewer cases of HRD are identified using HbA_{1c} testing than FPG (17.6% vs. 23.1%), which partially offsets the benefits of HbA_{1c} identifying more cases of undiagnosed diabetes (4.6% vs. 1.2%).

It is the higher prevalence of diabetes and the higher uptake of testing with HbA_{1c} versus FPG that cause the difference in long-term cost-effectiveness because these factors drive fewer long-term clinical events when using HbA_{1c} testing.

Sensitivity of results to potential alternative future cut-off points for offering preventative interventions (our purpose here was to test if the conclusion that glycated haemoglobin appears more cost-effective than fasting plasma glucose holds at lower cut-off points)

Using LEADER prevalence rates, lowering the thresholds for defining HRD and offering preventative intervention does not change the finding that HbA_{1c} testing appears more cost-effective than FPG testing. This same finding was found for several 'ISO-resource' comparisons.

Use of random capillary glucose test versus the Leicester Practice Database Score to prescreen

Where capacity dictates that blood glucose testing cannot be undertaken for everyone (as likely in most localities), then using the LPDS risk score (together with HbA_{1c} cut-off point of 6.0%) appears more cost-effective than using RCG. The estimated incremental costs and QALYs of LPDS versus RCG testing are –£1 and 0.0029, respectively, with an 88% probability that LPDS is more cost-effective. For a lower HRD cut-off point of HbA_{1c} 5.7%, the incremental costs and QALYs are –£18 and –0.0004, respectively (a more marginal result with NMB of £9 in favour of LPDS and 59% probability that LPDS is more cost-effective).

Conclusions relevant to policy and practice

Based on available evidence, especially around the prevalence of undiagnosed diabetes and HRD and the uptake of blood tests, it appears that under most scenarios HbA_{1c}-based testing is very likely to be more cost-effective than FPG-based testing (regardless of whether or not there is prescreening).

In absolute terms, the expected differences in total costs and QALYs between the two tests are, however, small as per the first finding from the base case analyses using the LEADER data set around strategies recommended in the 2012 NICE guidance.

A change to this conclusion would require either:

- (a) (1) a very different prevalence of undiagnosed diabetes and HRD from what is found in the multiethnic LEADER cohort, that is a smaller excess of cases of undiagnosed diabetes using HbA_{1c}-defined diabetes relative to FPG-defined diabetes, and/or a higher excess of FPG-defined cases of HRD with FPG testing relative to HbA_{1c} testing and (2) difference in uptake of HbA_{1c} testing and FPG testing at the lower end of the range of tested scenarios

or

- (b) some new evidence that has a highly favourable impact for FPG testing, for example evidence of differential natural history.

Variations in ethnicity as well as in deprivation are likely to be key determinants of variations between localities in prevalence of diabetes and HRD.

The conclusions are likely to hold if, at some point in the future, consideration were given to offering preventative interventions to some individuals at lower HbA_{1c} or FPG thresholds than those recommended in current NICE guidance.

Using the LPDS risk score appeared more cost-effective than using a RCG test to prescreen individuals.

Conclusions in relation to further research

1. In most scenarios examined, there is a very high probability that HbA_{1c}-based testing is more cost-effective than FPG. We would, therefore, not recommend any large primary data collection research, for example a national RCT of HbA_{1c} versus FPG.
2. The issues which affect the choice between HbA_{1c} and FPG relate more to (1) the local relative prevalence of diabetes and HRD according to each measure and (2) the potential difference in uptake rates between the two tests. If local stakeholders are interested in undertaking research locally to aid their decision about which test to use, these would be the two priorities for local data collection. If local data reveal a markedly different relative prevalence from the scenarios analysed here, it may be useful for the model to be rerun to examine what difference this evidence would make.
3. We have been unable to model alternative options for the time interval between a first test and retesting because there are important evidence gaps.
4. Looking beyond the current context, it is possible that relative prevalence of undiagnosed HbA_{1c}- and FPG-defined diabetes (5.7% vs. 1.8% using LEADER data) might change over time. The current difference may be partly a result of historical opportunistic screening using an oral glucose tolerance test (OGTT) which includes a FPG test. Research to track prevalence over time would be useful.
5. There are other uncertainties around the evidence used in the model. However, it is difficult to make firm research recommendations without a value-of-information analysis to assess the expected resulting benefits. Reducing the uncertainty around model parameters may have little impact on the relative cost-effectiveness.

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