ScotPHN report

Updating the Scottish Needs Assessment Programme Report on Type 2 Diabetes: Screening and Prevention

Part A: Project Group Conclusions on Screening and Prevention and Recommendations

November 2011

PART A – PROJECT GROUP CONCLUSIONS ON SCREENING AND PREVENTION AND RECOMMENDATIONS

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Preface

Part A of this report summarises the findings on screening and prevention described in Parts B and C. The recommendations from the health care need assessment are contained in Part A. Stakeholders have been able to comment on the draft report as part of the project process. Stakeholder comments have been taken into consideration in this final report especially with respect to the controversial issue of the relative merits of HbA_{1c} (glycated haemoglobin) versus fasting glucose as a screening test for diabetes and non–diabetic hyperglycaemia. The project group are grateful to all those stakeholders who commented on earlier drafts.

Part D of this report explores the financial considerations of the recommendations made in this Health Care Need Assessment.

Summary of Project Group Recommendations

On the basis of the current evidence, this Health Care Need Assessment (HCNA) has concluded that a case can and should be made for screening for type 2 diabetes within the context of vascular risk profiling programmes. The HCNA also concludes that there is now evidence of effectiveness of interventions to prevent diabetes that could be offered to people identified as having hyperglycaemia during screening for cardiovascular disease risk.

The following evidence-based recommendations are set out in a matter that should help NHS Boards consider how best to implement screening within the context of vascular risk programmes and to support interventions to prevent progression to diabetes. The recommendations are coherent with the aim set out in the Diabetes Action Plan 2010 " to detect and diagnose diabetes earlier in order to prevent, so far as possible complications". The Action Plan signposted our report and has recommended that the Scottish Government Health Department Directorates and NHS Boards consider it.

Recommendations on Screening (based on current evidence)

1. In Scotland screening for diabetes and non-diabetic hyperglycaemia (NDH) should be integrated into population-based vascular risk profiling programmes carried out by NHS Boards. A clear implementation plan for

vascular risk profiling in Scotland is needed and the diabetes screening element should be included in that plan.

2. All those being profiled for cardiovascular disease (CVD) risk should have HbA_{1c} measured.
3. The upper age limit of such screening would be set by the upper age limit for the vascular profiling programme as a whole.
4. HbA_{1c} should be used as the preferred screening test for diabetes and NDH. The best alternative when this is not suitable is fasting plasma glucose. Random blood glucose is not recommended for screening for diabetes and the SIGN 97 guideline should be updated accordingly. Random glucose of ≥11.1 mmol/l remains a satisfactory way of confirming a clinical diagnosis in a symptomatic patient.
5. Those patients known to have clinical conditions that interfere with the validity of HbA_{1c} testing should be screened by fasting glucose instead.
6. In those with an initial HbA_{1c} <6% (42 mmol/mol), screening with HbA_{1c} should be repeated every three years. However, earlier repetition of HbA_{1c} may be warranted for individuals with significant risk factors such as family history of diabetes and obesity.
7. In those with an initial HbA_{1c} ≥6% (42mmol/mol) a subsequent visit should be arranged to assess who has diabetes and who has non-diabetic hyperglycaemia. At this subsequent visit both fasting glucose and HbA_{1c} should be measured.
8. Asymptomatic individuals with an initial HbA_{1c} ≥6.5% (48 mmol/mol) should be diagnosed with diabetes if this repeat HbA_{1c} is also ≥6.5%.

9. If the diagnostic criteria for diabetes using HbA_{1c} have not been met (i.e. both tests ≥ 6.5% (48 mmol/mol)) but the fasting glucose is ≥7 mmol/l then a repeat fasting glucose should be arranged. Diabetes can then be diagnosed if both fasting glucose tests are ≥7 mmol/l.
10. Those with an initial elevated HbA_{1c} ≥6% (42mmol/mol) but not meeting these diagnostic criteria for diabetes at subsequent testing should be classified as having NDH and be offered intensive lifestyle intervention and repeat screening annually. Intensive lifestyle intervention needs to be funded for this policy to be feasible.
11. Further work is required to model the workload burden that would ensue, the costs, laboratory feasibility and to assess whether a phased introduction is warranted. The data from the Health Survey for Scotland 2009 suggests that there is a high prevalence of undiagnosed diabetes. Any programme of implementation needs to identify clearly what additional resources are needed. To help inform this, it is recommended that an NHS Board-wide pilot of the introduction of HbA_{1c} be undertaken within the context of a vascular risk management programme such as Keep Well to provide essential data relating to affordability and to help specify the actions needed to scale up implementation across Scotland.
12. It is also recommended that, to facilitate greater consistency in screening practice within primary care, further work be undertaken within the context of the NHSScotland Quality Strategy to encourage the adoption of the recommended approach to screening within NHS Boards.
13. The expected benefits of implementing such a programme include a reduction in cardiovascular and other complications of diabetes. Given that

there are social inequalities in these conditions prevention of these complications should also help to reduce inequalities in health. It is recommended that local approaches to monitoring these expected impacts on health inequality reduction should be developed.

Recommendations relating to prevention of diabetes and glycaemia related cardiovascular disease

1. Given that there is very good evidence that diet and physical activity changes can reduce the risk of cardiovascular disease and diabetes, a population strategy for the prevention of cardiovascular disease and type 2 diabetes should focus on lifestyle changes so that the risk factors are reduced in the whole population in all age groups. This requires coordinated policy and legislative changes in a wide range of areas including the marketing and availability of energy dense food, changes to the urban environment and transportation infrastructure and opportunities for increased physical activity as part of routine daily life. (These examples are taken from a World Health Organisation (WHO) report on evidence about the prevention of chronic disease[33].)
2. The Scottish Government Health Department should consider the health impact of all policies which influence diet and physical activity. The population strategy would focus on nutritional intervention and increased physical activity so that the risk factors for cardiovascular disease and T2DM are reduced in the whole population in all age groups. This would require coordinated policy and legislative changes with regard to such issues as food supply, labelling and marketing, the urban environment, transportation

infrastructure and workplace opportunities for physical activity. Thus a combined approach using both targeted screening (screening, detection and treatment of individual people with lifestyle interventions) and the public health model (changing the behaviour and risks of the population by public health measures such as promoting healthy eating and physical activity) is required. A number of studies of the cost-effectiveness of intervention to reduce progression to diabetes in people with impaired glucose tolerance have been published. People with non-diabetic hyperglycaemia identified by HbA_{1c}, should aim, where appropriate, to achieve weight loss or prevent further weight gain, and should increase their levels of physical activity, as part of their daily routine. Most studies conclude that supported lifestyle change is cost-effective, and in some scenarios, cost saving. One of the key factors is long-term adherence to lifestyle changes.

Research Needs

1. Further research should be undertaken to clarify the extent of any benefit from screening for diabetes and cardiovascular disease in those aged 65 years and over.
2. The cost-effectiveness of HbA_{1c} as the initial screening tool for identification of people at risk of diabetes should be compared to methods used in other national screening programmes.
3. Research on the most acceptable and cost effective methods of targeted screening is needed – whether by questionnaire based risk score, simple chart or algorithm based on electronic health records.

4. The sensitivity of the screening approach we have proposed for detecting those who have a non-diabetic level of fasting plasma glucose but have a diabetic level of post-challenge glucose and the relevance of this for subsequent micro and macrovascular disease should be evaluated in studies with data from OGTTs as well as HbA_{1c}.
5. Further cost effectiveness analyses on the optimal interval for screening are needed. We have recommended a three year interval but data on the optimal interval are lacking. It would also be useful to determine if the HbA_{1c} value could be combined with other risk measures to better define likely future trajectory and thereby better refine the time period for re-screening, particularly for people who have NDH on their first screen and normal glucose tolerance on repeat screening. Some preliminary data suggests this may well be the case. The optimal care pathway for those initially with an HbA_{1c} ≥6% who subsequently have values below this level also requires further research.
6. There is very good evidence that diet and physical activity changes can reduce the risk of diabetes in people with impaired glucose tolerance. The major gap in research is how to support people at risk to adopt and persevere with lifestyle changes. (More detailed recommendations on physical activity and weight reduction can be found in SIGN 115[21].)
7. Further research is required to better define ethnic specific lifestyle and physical activity targets, and to define best methods to help specific ethnic groups achieve such targets.
8. Any roll out of this policy requires a programme of research and evaluation to accompany it. Emphasis should be given to identifying appropriate data collection as part of this process. See for example, http://www.diabetes.fi for

the extensive evaluation of the initial Finnish Targeted Population Strategy for early detection of diabetes and those at high risk for diabetes.

Background

This report has been prepared by the Scottish Public Health Network for the Scottish Directors of Public Health but is also relevant to others in public health concerned with population screening policies.

The ScotPHN is accountable to the Directors of Public Health. Its remit is to undertake prioritised national pieces of work where there is a clearly identified need; to facilitate information exchange between all those working in public health, link with other networks and share learning; and to create effective communication amongst professionals and the public to allow efficient co-ordination of public health activity.

The prevalence of type 2 diabetes has been increasing in Scotland, due to increases in overweight and obesity, and decreasing levels of physical activity, as well as the changing demographic structure of the population. People can have type 2 diabetes, and be coming to harm because of it, without it being diagnosed. This may apply to perhaps 20% of cases – over 30,000 people - in Scotland. They may have diabetic complications such as eye disease by the time they are diagnosed, or may suffer a heart attack, without any warning. Accordingly, in October 2008, the Scottish Diabetes Group asked the Scottish Public Health Network (ScotPHN) to consider screening for diabetes and prevention of diabetes. The Scottish Needs Assessment Programme (SNAP) undertook a needs assessment of both type 1 and 2 diabetes in 1999[1]; it was thought appropriate by the Directors of Public Health that this should be updated in respect of type 2 diabetes. A lead author, Professor Norman Waugh University of Aberdeen, was

identified to undertake this work. As part of the needs assessment, a survey of current practice was undertaken, using a survey based on questionnaires to and interviews with staff in NHS Boards and Managed Clinical Networks (MCN) covering certain aspects of diabetes screening prevention and care. That was conducted and summarised by Dr Andrew Millard, ScotPHN Researcher, and the findings are included in Part C of the full report.

A Project Group was established to advise on the scope of this report, to review it and finally to make recommendations on the key public health issues arising from it. Part A of this paper summarises the key points and recommendations from the Project Group. The detailed commissioned report from Professor Waugh is contained in Part B and the survey of current practice is in Part C. Part D – the health economic analysis – was undertaken by Dr John Forbes of the University of Edinburgh.

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Definitions

Diabetes mellitus is characterised by hyperglycaemia, dyslipidaemia and an increased risk of macrovascular and microvascular disease including heart disease, stroke, peripheral vascular disease, visual loss and renal failure. Diagnostic criteria for diabetes include a fasting venous plasma glucose of ≥7mmol/l on two separate occasions or a random plasma glucose ≥11.1mmol/l on two occasions or a 2 hour glucose ≥11.1mmol/l (after a 75g anhydrous glucose challenge).[2] In a symptomatic person a single raised laboratory venous glucose reading (fasting ≥7mmol/l or a random plasma glucose ≥11.1mmol/l) establishes a diagnosis. The glucose thresholds chosen to define diabetes were mostly based on the level at which risk of diabetic retinopathy starts to rise. Recent publications from international authorities [3, 4, 5, 6, 7] recommend the use of HbA_{1c} to diagnose diabetes mellitus in the asymptomatic individual though this has not been widely adopted as yet. HbA_{1c} is used in routine clinical practice to monitor glucose control in people with established diabetes where it provides an estimate of average blood glucose over the preceding three months. Type 2 diabetes was formerly referred to as non-insulin-dependent diabetes. The new term is preferred because many people with type 2 diabetes progress to needing insulin.

Two other conditions - impaired glucose tolerance and impaired fasting glucose - are associated with an increased risk of future diabetes (see Table 1 below for definitions). Impaired glucose tolerance is also associated with an increased risk for cardiovascular disease independently of other risk factors. The magnitude of this increased risk varies between studies, but for CVD mortality was 1.34 (1.14-1.57) in the DECODE meta-analysis for example[8] Impaired fasting glycaemia appears to

exert only a slight increased risk of CVD independently of other factors. Another recent meta-analysis found that there is a stronger association between HbA_{1c} and future coronary heart disease (CHD) risk than for fasting or post load glucose[9].

Other terms are also encountered; for example "intermediate hyperglycaemia" is used by the WHO to refer to impaired glucose tolerance or impaired fasting glucose. The term pre-diabetes is sometimes used to refer to impaired glucose tolerance and/or impaired fasting glucose but is not preferred since not all such patients go on to develop diabetes. Non diabetic hyperglycaemia (NDH) is increasingly being used as a wider term that encompasses not just intermediate hyperglycaemia but also a glycated haemoglobin (HbA_{1c}) that is elevated but below the diabetic range (≥6% but <6.5%).

Table 1: Diabetes Mellitus and Non Diabetic Hyperglycaemia – diagnostic criteria

	Fasting Plasma Glucose (FPG)	**Random Plasma Glucose (RPG)**	**Oral Glucose Tolerance test (OGTT)**	**HbA_{1c}**
Diabetes	FPG ≥7.0 mmol/L on two occasions or with symptoms†	RPG≥11.1 mmol/L on two occasions or with symptoms	2-hour glucose ≥11.1mmol/L Plus one other diagnostic glucose level	≥6.5% on two occasions (48mmol/mol)
Non diabetic Hyperglycaemia	IFG*: FG ≥6.1 and <7.0 mmol/L		IGT**: FPG <7mmol/L and 2 hour glucose ≥7.8 and <11.1 mmol/l	≥6% (42 mmol/mol) and <6.5% (48mmol/mol)
† thirst, polyuria, nocturia. * Impaired fasting glycaemia **Impaired glucose tolerance				

Introduction

In establishing the specific scope for this needs assessment, the Project Group were conscious that much had changed – both in terms of the evidence base and practice base for diabetic care – since the original Scottish Needs Assessment Programme (SNAP) report[1] had been published. An initial review of these developments was undertaken and led us to focus on the linked issues of screening for diabetes and prevention of type 2 diabetes through formal lifestyle modification programmes.

In this document (Part A of the full report), we:

i) Summarise the current policy context on screening for diabetes in the UK and Scotland.

ii) Summarise the findings from a survey of current practice on what current screening and prevention activities are currently being undertaken within the Scottish NHS Boards. (The full survey of current practice is in Part C.)

iii) Make recommendations on taking a more systematic approach to screening and prevention in Scotland, basing these on the research review conducted by Professor Waugh. (The full research review is in Part B.)

iv) Highlight areas where there is considerable uncertainty and where further research is needed.

Current Policy Context for Screening and Prevention of Type 2 Diabetes in Scotland and the UK

UK policy on screening for diabetes

The UK National Screening Committee has reviewed policy on screening for type 2 diabetes on several occasions. The last review was in July 2006. That review considered a Health Technology Assessment Report that included a comprehensive literature review and economic modelling pertaining to screening[10]. The Health Technology Assessment Report found that the case for screening for undiagnosed diabetes and for impaired glucose tolerance, while still not meeting all the criteria of the UK National Screening Committee, was becoming stronger because of greater options for the reduction of cardiovascular disease and because of the rising prevalence of obesity, and hence type 2 diabetes.

Rather than recommending a specific diabetes screening programme the National Screening Committee recommended the introduction of a Vascular Risk Management Programme in which *"the whole population would be offered a risk assessment that could include, among other risk factors, measurement of blood pressure, cholesterol and glucose."* The National Screening Committee concluded that; *"targeted screening for T2DM [Type 2 Diabetes] was feasible but should be undertaken as part of an integrated programme to detect and manage vascular risk factors in certain subgroups of the population who are at high risk of T2DM."*[11] This policy acknowledges that the relationship between glycaemia and cardiovascular disease may be a continuous one and therefore that the detection of non-diabetic hyperglycaemia followed by interventions known to reduce risk of progression to

diabetes alongside management of hypertension and dyslipidaemia can be expected to reduce CVD risk.

Following this the National Screening Committee published a Handbook on Vascular Risk Assessment[12]. The Handbook was intended as a resource rather than a policy document. It included a review of the evidence for screening for diabetes and extensive data on the sensitivity, specificity and yield of cases using various screening strategies. The Handbook emphasised that any blood glucose testing done as part of a vascular risk programme should be focused on those with other risk factors (such as obesity, family history, hypertension etc) with clear procedures.

Diabetes screening policy implementation in England

In April 2009 the Department of Health (England) produced the NHS Health Check: Vascular Risk Assessment and Management Best Practice Guidance[13] and issued revised vascular programme briefing packs to the Strategic Health Authorities. The programme includes the policy that from 2009/10, all Primary Care Trusts are being asked to implement a uniform and universal vascular risk assessment and management programme called 'NHS Health Check' for people in England aged between 40 and 74 years of age.

In brief this NHS health check includes:

- A filter for diabetes screening based on body mass index (BMI) and blood pressure.

- Followed by measurement of either fasting plasma glucose or glycated haemoglobin in those deemed at risk of diabetes with confirmation either by an oral glucose tolerance test or a repeat glycated haemoglobin.
- Those found to have diabetes then enter the diabetes care pathway.
- Those found to have either non-diabetic hyperglycaemia (either as confirmed elevated glycated haemoglobin or impaired glucose tolerance) should receive lifestyle management advice.

Diabetes screening and prevention policy in Scotland

Health policy in relation to diabetic care in Scotland is set out and described in The Scottish Diabetes Framework[14] and the Diabetes Action Plan[15]. Informed by the Scottish Intercollegiate Guidelines Network Report on the Management of Diabetes (SIGN 55, now updated by SIGN 116)[16], these set out very specific actions in relation to improving the infrastructure for the provision of diabetic care, developing services to improve the quality of care in specific areas such as eye care and foot care for people with diabetes and improving the overall standards of care. Actions to improve healthy lifestyle and psychological wellbeing were also included, though screening (apart from retinopathy screening) was not.

Progress against these actions were assessed in 2008 by NHS Quality Improvement Scotland (NHS QIS) and Diabetes UK Scotland[17]. They concluded that whilst there were significant improvements against the NHS QIS clinical standards for diabetes care, there were still opportunities to develop and improve service further.

In this regard, it should be noted that SIGN 55 has been reviewed and replaced by SIGN 116 in March 2010 and that the National Institute for Health and Clinical Excellence (NICE) published its clinical guideline (CG66[18] partially updated by CG87[19]) on the management of type 2 diabetes in 2008.

Neither the NICE guideline nor the original SIGN 55 commented on either lifestyle programmes for prevention of type 2 diabetes or the need for screening, although NICE has two relevant guidelines in development (http://guidance.nice.org.uk/PHG/Wave19/6) due for publication in 2011. The current guidance on screening is contained within the Scottish Intercollegiate Guidelines Network SIGN 97 (February 2007): Risk Estimation and The Prevention of Cardiovascular Disease[20] which has a section on estimating vascular risk. The key elements pertaining to diabetes and non-diabetic hyperglycaemia as derived from the SIGN 97 document[20] were:

1. That all those in the population aged 40 years and over should have cardiovascular disease risk assessment at least every five years.
2. "In order to screen for diabetes, impaired glucose tolerance or insulin resistance [glucose] should be measured from the same random (non-fasting) blood sample that is drawn to measure cholesterol levels. A value of ≤6.0 mmol/l indicates a normal level. A value of ≥6.1 mmol/l but ≤7.0 mmol/l requires a repeat measurement on a fasting blood sample. If the value is ≥7.0 mmol/l an oral glucose tolerance test should be performed".

3. That those with metabolic syndrome be identified, offered professional advice in relation to a cardio-protective diet, exercise and weight monitoring and followed up regularly.

In Scotland the preferred risk profiling score for cardiovascular risk assessment is the ASSIGN score, which was developed as part of SIGN 97[20]. While based on the Framingham risk score, ASSIGN includes a measure of social deprivation, – the Scottish Index of Multiple Deprivation. Among other risk factors it includes whether or not the person has been diagnosed with diabetes. –. The use of the risk score is being implemented and assessed initially through GP practices involved in the *Keep Well* programme. A web-based tool already exists to allow access to ASSIGN in clinical settings.

It was in the context of the above that Professor Waugh, supported by Dr Millard from ScotPHN:

- assessed the current extent of systematic screening for and prevention of type 2 diabetes in Scotland; and
- considered the research evidence for making recommendations on the glycaemia-related components of any vascular screening programme under implementation.

Their findings are contained in Parts B and C of this report and summarised in this next section. The review was specifically concerned with type 2 diabetes (and not gestational or type 1 diabetes). Since the key issue of the prevention and management of obesity is already the subject of considerable current Scottish

Government work and the recently updated SIGN guideline on obesity[21] our focus with respect to prevention was specifically on the identification of those at most risk for diabetes over a short time horizon and targeted intervention in this group.

Current screening and prevention activities within the Scottish NHS Boards: Findings from the Survey of Current Practice
(Full report in Parts B and C)

Current Practice

The review of current practice in Scotland highlighted that, at the present time, there are no systematic screening and prevention programmes for type 2 diabetes known to any of the diabetes MCNs.

Population screening for diabetes and impaired fasting glycaemia (IFG)/impaired glucose tolerance (IGT) from the perspective of both Managed Clinical Networks and the Directors of Public Health had partial coverage and was part of a more general health promotion initiative rather than being only diabetes-focused. Where used, screening was targeted at high risk groups and opportunistic rather than based on a systematic call and recall approach, apart from in practices participating in Keep Well[1] or Well North. Five of the seven areas involved in Keep Well in 2009 mentioned an example of systematic population screening for diabetes. Systematic screening was mentioned less frequently in connection with IFG/IGT screening.

No diabetes-specific measures (for example, the use of metformin) were reported for primary prevention of type 2 diabetes or secondary prevention in people who

[1]Keep Well (http://www.keepwellscotland.com/) is a national Scottish project aiming to reduce health inequalities by providing practice based cardiovascular health checks to people aged 45 to 64 years in areas of deprivation. Four NHS Boards took part in wave 1, recruiting volunteer GP practices in areas with the largest numbers of patients living in deprived data zones. One board (NHS Tayside) recruited practices more widely but limited checks to people in those practices living in the most deprived datazones. Wave 1 started health checks early in 2007. A second wave extended activities to three additional NHS boards and the programme is now being extended to all Scottish boards. At the end of 2009, 67,712 patients had received checks out of a total eligible population of 139,192 people.)

were identified as having IFG/IGT. Prevention advice was *ad hoc* (except for cases identified through Keep Well or Well North) through general lifestyle advice and obesity prevention and treatment for high risk individuals. Patients with known IGT were systematically retested annually or as required dependent on age and progression rate to diabetes in six boards.

Eight MCNs wanted to shift the balance of care further to primary care but mentioned that resources for training staff in diabetes care, for example in delivering Structured Patient Education (SPE) were a barrier. The Scottish Diabetes Survey (2009) found that the proportion of people on patients with diabetes registers with (both type 1 and type 2) who had HbA_{1c} <7.5%, varied from 59.4% to 70.8% between Scottish NHS Boards. An equity audit carried out in NHS Lothian found that that similar proportions of patients from less affluent areas had HbA_{1c} <7.5% to those from more affluent areas, but less affluent people with diabetes were more likely to be overweight and to smoke than more affluent people with diabetes. South Asians had less good diabetic control than the white population.

At present within Scotland there is little systematic screening for diabetes. Screening activity for diabetes appears to be *ad hoc,* part of the Keep Well programme that targets specific but small sections of the population or part of the primary care Local Enhanced Service (LES) for diabetes and CHD/stroke.

There is lack of clarity with regard to the current stage of implementation of cardiovascular risk factor screening in the general population.

Prevention of Diabetes

The questionnaire to NHS Boards found that the prevention methods in the general population were not restricted to those at risk of diabetes, or targeted specifically to prevention of diabetes, but comprised general healthy lifestyle advice on diet, exercise, obesity management and (less often) referral for specific intervention measures involving for example physical activity, weight management or bariatric surgery. Bariatric surgery was seen as a method of preventing or treating diabetes of recent onset by treating obesity. SIGN 115 recommends that 'Bariatric surgery should be considered on an individual case basis following assessment of risk/benefit in patients who fulfil the following criteria:

- BMI ≥35 kg/m^2
- Presence of one or more severe co-morbidities which are expected to improve significantly with weight reduction (e.g. severe mobility problems, arthritis, type 2 diabetes).'[21]

Professionals mentioned as delivering the healthy lifestyle advice included practice nurses, health promotion specialists and community pharmacists. Some of the advice was targeted at children and young people, and some was supported by a strategy or strategic framework such as a Healthy Weight strategy, although resource issues were mentioned as a barrier to implementation.

Summary of evidence base for systematic screening from the Research Review
(Part B)

On the basis of the above review of current activities, the Project Group concludes that current screening and prevention programmes for type 2 diabetes across Scotland are not being implemented in a systematic way. Yet the policy context summarised above clearly indicates that some form of systematic screening for glycaemia should be undertaken *within a setting of vascular risk assessment*. The Project Group also concluded that there is a need for clearer guidelines on the tests that should be used for systematic detection of diabetes and non-diabetic hyperglycaemia and the subsequent care pathways to be followed in Scotland. In formulating such guidelines the Project Group next considered the evidence for each step in such care pathways as detailed in Professor Waugh's Report (Part B) and summarised in this section. Here we attempt to summarise some of the key points only and refer the reader to Part B, to Professor Waugh's comprehensive Health Technology Assessment Report 2007[10] and to the Handbook on Vascular Risk Assessment[12] for a detailed review of the issues in screening for glycaemia and diabetes.

What are the aims of screening for diabetes and non diabetic hyperglycaemia?

The aims of screening can include:

i) *detection of undiagnosed diabetes with a view to initiating treatment strategies aimed at lowering blood glucose and initiating screening for microvascular complications including retinopathy.* People can have type 2 diabetes, and be coming to harm because of it, without it being diagnosed. They may have diabetic

complications such as eye disease by the time they are diagnosed, or may suffer a heart attack without any warning. The current crude prevalence of diagnosed type 2 diabetes in Scotland is approximately 3.9% of the population based on data for 199,264 people included in a population-based database in 2009 (Scottish Diabetes Survey, 2009). The prevalence of undiagnosed diabetes is uncertain but has been estimated to be at least 20,000 or approximately 0.4% of the population {http://www.scotpho.org.uk/} with other estimates being up to 1% of the population. The estimate of the delay in diagnosing diabetes through not screening is not known with certainty but modelling studies suggest that the average delay is probably of the order of six years (HTA report: p8 and p68).

ii) detection of people at high risk of developing diabetes with a view to initiating measures to prevent progression. In addition to diabetes, non-diabetic hyperglycaemia (NDH: this term includes impaired fasting glycaemia, impaired glucose tolerance and elevated HbA_{1c} ≥6.0% (42mmol/mol) but <6.5% (48mmol/mol) is of public health importance since it is associated with a increased risk of progression to diabetes compared to people with normal glucose tolerance. The exact progression rate is not known with certainty but estimates range from about 4-9% per year among those with IGT with lower rates of progression for people with IFG (HTA Report: p10).

iii) *detection of a group at increased risk of macrovascular disease with a view to initiating both measures to reduce glycaemia and other CVD risk factor*s. Key points here are that the increase in risk of macrovascular disease starts at levels of glycaemia below those diagnostic for diabetes (Part B: p14, 15, 16). However, even for elevated HbA_{1c} and IGT, which are more strongly associated with macrovascular

disease than is IFG, it is not clear whether testing for glycaemia improves CVD risk prediction beyond other CVD risk factors. Whilst independent associations between HbA_{1c} and CHD have been reported, reclassification of risk category with HbA_{1c} result is, at best, modest [22],[23],[24]. In addition, the evidence base that reducing glycaemia reduces macrovascular risk, even in diabetes is still sparse, being mainly limited to UKPDS observational data. On the other hand it has been argued that even among those already categorised as at elevated risk for CVD the knowledge that they have NDH could be an additional motivating factor for lifestyle change/medication adherence (HTA Report: p85). In any case the project group accept the view of the National Screening Committee that screening for diabetes is best achieved within a context of screening for overall vascular risk.

Should we screen for diabetes?

Definitive trial data on the clinical effectiveness of screening for diabetes are lacking but such trials are underway; for example the ADDITION trial[25]. The HTA report included a modeling exercise and reviews of the existing data and concluded that screening for diabetes leading to increased intervention for micro- and macrovascular disease prevention is likely to be cost effective in those aged 40-70 years (HTA Report: p iii) and that screening aimed at reducing progression to diabetes can also be cost effective (Part B: p30) but of course many of the parameters and assumptions in modeling contain considerable uncertainty. In the end, there remains a lack of randomised trial data to inform screening for diabetes. The cost effectiveness depends on many specific aspects of a given strategy to be implemented and many of these are not known with certainty, including such major issues as the optimal screening interval. Beyond cost effectiveness, the wider issue

of whether diabetes screening meets other National Screening Committee criteria have also been reviewed (HTA Report: p iv) with the conclusion that most of the criteria other than availability of RCT data and optimisation of current service provision have been met. On the basis of the existing data as described above the National Screening Committee (NSC) have advocated screening for diabetes in the context of a vascular risk programme, so the challenge for Scotland is not so much *whether* this should be done, but *how*. It is clear that there should be a combined, individual approach (screening, detection and treatment of individual people with lifestyle intervention advice and, if appropriate, drugs) and population approach (changing the behaviour and risks of the population by public health measures such as promoting healthy eating and physical activity, and hence weight control).

What sections of the population should be screened?

This report does not address the clinical issue of which patients presenting to clinical services should be tested for diabetes but refers to active and systematic screening of asymptomatic people. The recommendations are not intended to preclude *ad hoc* screening of patients in other specific clinical contexts associated with higher diabetes risk, for example, obese women with polycystic ovary disease or individuals with dyslipidaemia involving high triglycerides, or evidence of non-alcoholic fatty liver disease etc. Recommendations already exist for other situations such as for women with a history of gestational diabetes (GDM) where the current SIGN 116 guideline recommends an annual assessment of glycaemia using fasting glucose or HbA_{1c} if assessment at six weeks post-partum does not show diabetes[15].

It is already established policy that people with diagnosed CVD be screened for diabetes. (For example, SIGN 97 recommends that glucose measurement forms part of the clinical assessment of people with stable angina. Our recommendations do not refer to the diagnosis of type 1 diabetes[19] where screening is not necessary.)

As stated the NSC has already recommended screening take place within the context of vascular risk screening. Thus our recommendations are specifically about what measure of glycaemia should be used *in such a vascular screening programme* and what care pathways should follow.

Clearly the cost effectiveness of any screening programme can be increased by targeting those at higher risk. The issue is then how to identify those at higher risk and what threshold of risk to use. Any targeting approach needs to minimise the numbers of people with diabetes missed by targeting and the number of normal individuals needlessly referred for further assessment, though most approaches involve a trade off between these two risks. The key risk factors for type 2 diabetes and vascular disease that could be used for targeting screening include: age, BMI, co-morbidities (eg hyperlipidaemia and hypertension, and known vascular disease), family history of diabetes, smoking and ethnicity. The approaches that are currently being evaluated are discussed in Part B and are extensively reviewed in The Handbook on Vascular Risk Assessment (p085)[11] though we note that no specific recommendation is made in the Handbook. In a recent abstract from the ADDITION trial, initial use of the Cambridge Diabetes Risk score, followed by OGTT resulted in confirmed diabetes in 0.64% of the target population and 3.5% of those who actually attended for blood tests[25]. The use of risk scores would either require

implementation in GP information systems across Scotland and is therefore not an immediate solution, or would require those attending for vascular risk assessment to complete data items or have measurements such as waist circumference specifically done as these are not routinely available on primary care databases. In the English vascular risk assessment programme age, sex, ethnicity specific BMI and blood pressure data are used to target which individuals should have blood tests for glycaemia[26]. There does not appear to be a consensus on the optimal approach to targeting screening and the current risk scores have imperfect agreement between each other[27]. The Project Group regards this area of optimal approaches to targeting to be a major evidence gap that needs to be addressed, with any diabetes screening programme being modified to reflect future evidence. The Project Group considers that ideally some targeting of those warranting a blood test should occur but at the present time the evidence for which approach is best is lacking. Accordingly the Project Group has taken the pragmatic view that ALL those being called for CVD screening should have an HbA_{1c} measurement. It should then be possible to review and refine the targeting when several years of such screening data are available.

Given that there are social inequalities and ethic differences in the prevalence of diabetes and its complications early detection of diabetes, diabetes prevention and prevention of diabetic complications should also help to reduce socioeconomic and ethnic inequalities in health.

What is the optimal test for screening?

At present there is considerable controversy over the diagnostic tests and cut-offs for diagnosing diabetes and frequent changes in international guidelines. With improved standardisation of HbA_{1c} assays there is now increasing data to support the use of HbA_{1c} for diagnosing diabetes though this remains somewhat controversial. In July 2009 an expert committee appointed by the European Association for the Study of Diabetes, International Diabetes Federation and American Diabetes Association published an International Expert Committee Report on the Role of the A1C Assay in the Diagnosis of Diabetes[5] recommending its use for diagnosis (Part B: p22) and this has now been adopted by various bodies including the American Diabetes Association[30] and the American Endocrine Society. A full discussion of this issue is contained in Part B and is covered in brief here. A randomly measured HbA_{1c}, though more expensive than measuring glucose is at least as informative for future microvascular disease risk as fasting glucose measured under controlled fasting conditions that are not always achievable in clinical practice. HbA_{1c} can be measured on a non-fasting sample and has low biological variability making it easier to implement as a screening test than fasting blood glucose or oral glucose tolerance tests. In the non diabetic range, it can capture much of the risk of CVD associated with non diabetic hyperglycaemia (Part B: pg22-27). On the other hand analyses of National Health and Nutrition Examination Survey (NHANES) data in the United States indicate that, assuming universal screening of the undiagnosed, the HbA_{1c} cut off point of ≥6.5% identifies one-third fewer cases of undiagnosed diabetes than a fasting glucose cut point of ≥126 mg/dl (7.0 mmol/l).[31] Furthermore it is clear that there are differences in the relationship between HbA_{1c} levels and fasting glucose and post load glucose levels

between ethnic groups that are not fully understood or characterised as yet. This issue of whether HbA_{1c} could be used for screening raised most comments from stakeholders, including the Scottish Clinical Biochemistry Managed Diagnostic Network. On the basis of the logistical ease of use of $HbA_{1c,}$ its performance characteristics in predicting both diabetes and CVD risk, and that those with near diabetic levels will have regular re-screening, the Project Group recommends the use of HbA_{1c} as the initial screening test for diabetes in any vascular risk screening programme if appropriate resources can be made available. We recommend that those with an initial screening HbA_{1c} ≥6% (42 mmol/mol) should have both HbA_{1c} and a fasting glucose measured at a subsequent visit with a final diagnosis of diabetes comprising either two HbA_{1c} or two fasting glucose measurements meeting the criteria for diabetes. In this way the advantages of HbA_{1c} for assessing CVD risk and for gaining coverage of the population to be screened by not requiring fasting initially can be maintained whilst some of the concern regarding its sensitivity may be dealt with. However, our recommendation is also intended to yield better data on this controversial issue so as to refine policy in this area in future.

Clinicians will already be aware that there are several circumstances in which HbA_{1c} testing would not be optimal and here fasting glucose should be used as the initial screening test. These include for example i) Abnormal Haemoglobins ii) any condition where there is known disturbance of red cell survival iii) some anaemias iv) renal failure. In people known to have haemoglobinopathies or other conditions that affect the validity of HbA_{1c}, testing fasting glucose should be used as the screening test instead.

What are optimal test result cut-offs for screening and diagnosis?

The European Association for Study Diabetes (EASD)/International Diabetes Federation (IDF)/American Diabetic Association (ADA) Joint Expert Committee{reference} mentioned above recommended[32] a cut off for diagnosing diabetes of 6.5% using HbA_{1c} with a threshold of 6.0% identifying those at highest risk of developing diabetes warranting preventive action (Part B: pg23-25). More recently the American Diabetes Association have recommended a lower threshold of HbA_{1c} of 5.7% as indicating "pre-diabetes" on the basis of an NHANES analysis that among the adult population without diabetes an FPG of 110 mg/dl (6.05 mmol/L) corresponds to an HbA_{1c} of 5.6%, and that an HbA_{1c} cut off of 5.7%, had the best combination of sensitivity (39%) and specificity (91%) to identify cases of IFG (FPG ≥100 mg/dl [5.6 mmol/l]). The Project Group recognise that the risk of diabetes is continuously increasing across the range of HbA_{1c} but recommends that a cut-off of ≥6% (42 mmol/mol) for defining NDH and ≥6.5% (48 mmol/mol) for defining diabetes should be used as proposed in the EASD/IDF/ADA Joint Expert Committee statement. It is expected that the clinician will tailor their advice and their interval for re-screening in those with HbA_{1c} below but near to the NDH level of 6% to take account of this continuous relationship and should be careful to avoid reassuring such patients that they are not at risk of diabetes or cardiovascular disease. In December 2010 the WHO published a report of a WHO consultation that concluded that HbA_{1c} can be used as a diagnostic test for diabetes and endorsed the recommendation that an HbA_{1c} of 6.5% is recommended as the cut point for diagnosing diabetes[33]. They noted that a value less than 6.5% does not exclude diabetes diagnosed using glucose tests. The expert group concluded that

there is currently insufficient evidence to make any formal recommendation on the interpretation of HbA_{1c} levels below 6.5%.

An important question is the expected prevalence of undiagnosed diabetes and NDH in the Scottish population using these HbA_{1c} criteria and estimates of this vary. The recently published Scottish Health Survey (2009) showed that a very high proportion (3.8%) of the adult population aged 40 years and upwards without a prior diagnosis of diabetes had an HbA_{1c} of 6.5% or above[28]. Of the non-diabetic adult population aged 40 years and upwards who took part in the Scottish Health Survey in 2009, 21.7% had an HbA_{1c} of 6.0% or above (personal communication from the Scottish Health Survey Team, 6 December 2010). In Orkney data for 1441 people of 40 years of age and older not known to have diabetes were collected between 2005 and 2010. The prevalence of DCCT aligned HbA_{1c} 6-6.4% was 12.8% and of HbA_{1c} ≥6.5% was 3.3% (personal communication Dr Jim Wilson and Dr Sarah Wild, 6 December 2010). In contrast in England data from the EPIC-Norfolk study[34] reported that just 6% of those without known diabetes had an HbA_{1c} 6-6.4%. Even the lower estimates from these studies suggest that any screening for diabetes is likely to create a significant additional burden on diabetes care resources and is likely to yield large numbers of people with NDH, also creating a resource burden. Clearly evaluation of the feasibility and opportunity cost of meeting any such burden on resources is required before any screening policy is implemented.

What intervention should be offered to people found to have diabetes?

In those diagnosed with type 2 diabetes, the recommended interventions are set out in the SIGN guidance.

What intervention should be offered to people found to have NDH?

For those with NDH the research evidence suggests that intervention to change lifestyle factors can reduce the progression to type 2 diabetes (Part B: p29-30). Although some drug therapies have been shown to reduce progression rate to diabetes and metformin has been shown to be cost effective, it is not yet licensed for this purpose and there is no consensus on using it for this purpose at present. Therefore those with NDH should be offered intensive lifestyle intervention.

What is the optimal interval for screening and should screening be risk profiled?

The HTA report considered the issue of the optimal interval for screening for diabetes and whether it should be tailored to the initial test result since clearly the progression rate to diabetes is not uniform in all those with NDH. It concluded that there are insufficient data on which to base a screening interval but that a fixed screening interval should be used for at least the first two rounds (HTA Report p86). In the US a screening interval of every year in those with "pre-diabetes" and three years for those with screening tests below this threshold is used, on the basis that those with diabetes missed at screening or who progress early to diabetes within this interval would have a low risk of microvascular complications supervening within three years. Data on the prevalence of microvascular disease close to diagnosis of diabetes using current practice would be useful in this regard. We have suggested a one year interval for those with NDH since some patients in this category may progress rapidly, but this approach will need evaluation of its cost-effectiveness. Below this level we have recommended re-screening at a minimum of every three years. Similarly we acknowledge that the algorithm for returning someone with NDH on one test followed by regression to normoglycaemia to a three year interval is not

evidence based but pragmatic. The Project Group considers that consideration of optimal intervals be included in any evaluation plan.

Summary of Project Group Recommendations

Recommendations on Screening (based on current evidence)

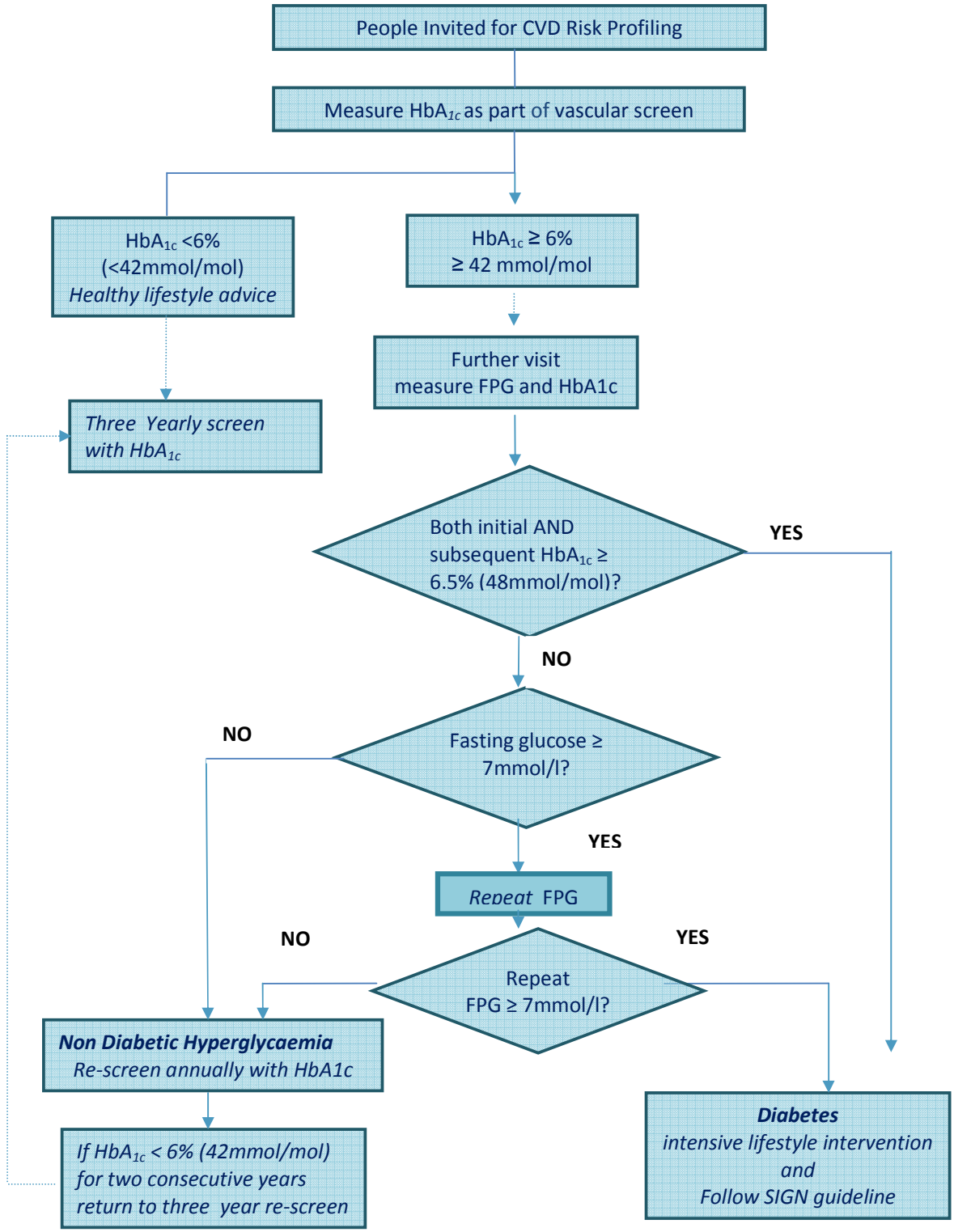
1. In Scotland if resources permit, screening for diabetes and non-diabetic hyperglycaemia (NDH) should be integrated into population-based vascular risk profiling programmes carried out by NHS Boards. A clear implementation plan for vascular risk profiling in Scotland is needed and the diabetes screening element should be included in that plan.
2. All those being profiled for cardiovascular disease (CVD) risk should have HbA_{1c} measured.
3. The upper age limit of such screening would be set by the upper age limit for the vascular profiling programme as a whole.
4. HbA_{1c} should be used as the preferred initial screening test for diabetes and NDH. The best alternative when this is not suitable is fasting plasma glucose. Random blood glucose is not recommended for screening for diabetes and the SIGN 97 guideline should be updated accordingly. Random glucose of ≥11.1 mmol/l remains a satisfactory way of confirming a clinical diagnosis in a symptomatic patient.
5. Those patients known to have clinical conditions that interfere with the validity of HbA_{1c} testing should be screened by fasting glucose instead.
6. In those with an initial HbA_{1c} <6% (42 mmol/mol) screening with HbA_{1c} should be repeated every three years. However, earlier repetition of HbA_{1c} may be warranted for individuals with significant risk factors such as family history of diabetes and obesity.
7. In those with an initial HbA_{1c} ≥6% (42mmol/mol) a subsequent visit should be arranged to assess who has diabetes and who has non-diabetic

hyperglycaemia. At this subsequent visit both fasting glucose and HbA_{1c} should be measured.

8. Asymptomatic individuals with an initial HbA_{1c} ≥6.5% (48 mmol/mol) should be diagnosed with diabetes if this repeat HbA_{1c} is also ≥6.5%.
9. If the diagnostic criteria for diabetes using HbA_{1c} have not been met (ie both HbA_{1c} results ≥6.5% (48 mmol/mol)) but the fasting glucose is ≥7 mmol/l then the fasting glucose should be repeated. Diabetes can then be diagnosed if both fasting glucose tests are ≥7 mmol/l.
10. Those with an initial elevated HbA_{1c} ≥6% (42mmol/mol) but not meeting diagnostic criteria for diabetes at subsequent testing should be classified as having NDH and be offered intensive lifestyle intervention and repeat screening annually. Intensive lifestyle intervention needs to be funded for this policy to be feasible.
11. Should our recommendations for screening for diabetes and NDH be accepted in principle, then further work is required to model the workload burden that would ensue, the costs, laboratory feasibility and to assess whether a phased introduction is warranted. Estimates from other studies of the expected prevalence of undiagnosed diabetes and non-diabetic hyperglycaemia vary widely but all indicate a substantial prevalence. Any programme of implementation needs to identify clearly what additional resources are needed. To help inform this is recommended that an NHS Board-wide pilot of the introduction of HbA_{1c} be undertaken within the context of a vascular risk management programme such as Keep Well to provide essential data relating to affordability and the help specify the actions needed to scale up implementation across Scotland.

12. It is also recommended that, to facilitate greater consistency in screening practice within primary care, further work be undertaken within the context of the NHSScotland Quality Strategy to encourage the adoption of the recommended approach to screening within NHS Boards.
13. The expected benefits of implementing such a programme include a reduction in cardiovascular and other complications of diabetes. Given that there are social inequalities in these conditions prevention of these complications should also help to reduce inequalities in health. It is recommended that local approaches to monitoring these expected impacts on health inequality reduction should be developed.

Figure 1:
Screening for asymptomatic diabetes and non-diabetic hyperglycaemia using HbA_{1c} within a Scottish screening programme for cardiovascular disease;



Recommendations relating to prevention of diabetes and cardiovascular disease

1. Given that there is very good evidence that diet and physical activity changes can reduce the risk of cardiovascular disease and diabetes, a population strategy for the prevention of cardiovascular disease and type 2 diabetes should focus on lifestyle changes so that the risk factors are reduced in the whole population in all age groups. This requires coordinated policy and legislative changes in a wide range of areas including the marketing and availability of energy dense food, changes to the urban environment and transportation infrastructure and opportunities for increased physical activity as part of routine daily life. (These examples are taken from a WHO report on evidence about the prevention of chronic disease[35].) The IMAGE Toolkit for the Prevention of Type 2 Diabetes in Europe provides a comprehensive summary of the many approaches that might be adopted for the prevention of diabetes[36].
2. The Scottish Government Health Department should consider the health impact of all policies which influence diet and physical activity. The population strategy would focus on nutritional intervention and increased physical activity so that the risk factors for cardiovascular disease and T2DM are reduced in the whole population in all age groups. This would require coordinated policy and legislative changes with regard to such issues as food supply, labelling and marketing, the urban environment, transportation infrastructure and workplace opportunities for physical activity. Thus a combined approach using both targeted screening (screening, detection and treatment of individual people with lifestyle interventions) and the public health model (changing the behaviour and risks of the population by public

health measures such as promoting healthy eating and physical activity and reducing excess alcohol consumption) is required. A number of studies of the cost-effectiveness of intervention to reduce progression to diabetes in people with impaired glucose tolerance have been published. People with non-diabetic hyperglycaemia identified by HbA_{1c}, should aim, where appropriate, to achieve weight loss or prevent further weight gain, and should increase their levels of physical activity, most feasibly as part of their daily routine. Most studies conclude that supported lifestyle change is cost-effective, and in some scenarios, cost saving. One of the key factors is adherence to lifestyle changes.

The full report from Andrew Millard (Part C) is available from ScotPHN (www.scotphn.net). A Health Technology Assessment Report on screening for type 2 diabetes was published in 2007 and can be downloaded from http://www.hta.ac.uk/execsumm/summ1117.shtml. A second report from the HTA on non-pharmacological prevention of type 2 diabetes in people with impaired glucose tolerance will also be available in due course.

Research Needs

As indicated above there are many aspects of the screening programme we have recommended about which there is considerable uncertainty and where further research is needed.

1. Further research should be undertaken to clarify the extent of any benefit from screening for diabetes and cardiovascular disease in those aged 65 years and over.

2. The cost-effectiveness of HbA_{1c} as the initial screening tool for identification of people at risk of diabetes should be compared to methods used by other national screening programmes.
3. Research on the most acceptable and cost effective methods of targeting screening is needed – ie whether by questionnaire-based risk score, simple chart or algorithm based on electric health records.
4. The sensitivity and specificity of the screening approach we have proposed for detecting those who have a non-diabetic level of fasting plasma glucose but have a diabetic level of post-challenge glucose and the relevance of this for subsequent micro and macrovascular disease should be evaluated in studies with data from OGTTs as well as HbA_{1c}.
5. Further cost effectiveness analyses on the optimal interval for screening are needed. We have recommended a three year interval but data on the optimal interval are lacking. It would also be useful to determine if the HbA_{1c} value could be combined with other risk measures to better define likely future trajectory and thereby better refine the time period for re-screening, particularly for people who have NDH on their first screen and normal glucose tolerance on repeat screening. Some preliminary data suggests this may well be the case[37]. The optimal care pathway for those initially with an HbA_{1c} ≥6% who subsequently have values below this level also requires further research.
6. There is very good evidence that diet and physical activity changes can reduce the risk of diabetes in people with impaired glucose. The research most needed is how to persuade people at risk to adopt and persevere with the lifestyle changes. (More detailed recommendations on physical activity and weight reduction can be found in SIGN 115[21].)

7. Further research is required to better define ethnic specific lifestyle and physical activity targets, and to define best methods to help specific ethnic groups achieve such targets.
8. Any roll out of this policy requires a programme of research and evaluation to accompany it. Emphasis should be given to identifying appropriate data collection as part of this process. See for example, http://www.diabetes.fi for the extensive evaluation of the initial Finnish Targeted Population Strategy for early detection of diabetes and those at high risk for diabetes.

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Part B (Research report), Part C (Survey of Current Practice) and Part D (Cost-effectiveness and budget impact analysis) are provided as separate documents.

ScotPHN report

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