

SCOTTISH INTERCOLLEGIATE GUIDELINES NETWORK: MANAGEMENT OF DIABETES (SIGN 55)

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INTRODUCTION

The Scottish Intercollegiate Guidelines Network (SIGN) is a professionally-led, multi-disciplinary organisation which was established in 1993 by the Scottish Medical Royal Colleges and includes representatives from all of the medical specialties, dentistry, nursing, professions allied to medicine, pharmacy, health service managers, social workers and patients. It was established to improve the effectiveness of clinical care for patients in Scotland by developing, publishing and disseminating evidence-based guidelines which identify and promote good clinical practice and which, if implemented locally, will help to address variations in clinical practice throughout Scotland. The cost of the guideline development programme is funded by the Clinical Resource and Audit Group (CRAG) of the Scottish Executive.

The Scottish Intercollegiate Guidelines Network has published over 50 evidence-based guidelines, on a variety of clinical conditions including asthma, attention deficit and hyperkinetic disorders (ADHD), control of pain in patients with cancer, fractured hip, epilepsy, primary and secondary prevention of coronary heart disease (CHD), chlamydia, early rheumatoid arthritis, diabetes and safe sedation in children to name but a few. The Scottish Intercollegiate Guidelines Network is also now working closely on guideline development with both the World Health Organisation (WHO) and with the Council of Europe which has recently adopted the SIGN guideline development methodology as a baseline for future guideline development in over 50 member states. All SIGN guidelines can be downloaded free of charge from the SIGN website at www.sign.ac.uk.

In 2001, it was estimated that more than 150 million people worldwide had diabetes mellitus. Increases in both Type 1 and Type 2 diabetes have been seen in all strata of societies worldwide over the last 30 years. It is Type 2 diabetes that accounts for more than 85–90% of all diabetes and it is showing the greater rate of increase, with the global prevalence of diabetes predicted to exceed 220 million by 2010 and 300 million by 2025.¹

Diabetes mellitus is not just a problem because of increasing numbers but it is also a major increasing health problem for all age groups. Presently in the UK, one in 20 people >65 and one in five people >85 has diabetes.² A population of 100,000 in the UK would be expected to include between 2,000–3,000 people with diabetes, about 25–30 of whom will be children.

Guideline 55,³ launched on 14 November 2001, provides the cornerstone for the Scottish Diabetes Framework.⁴ This guideline, dealing with the management of diabetes mellitus, provides a clinical evidence base on which future standards of diabetes care in Scotland, and further afield, will be based.

BACKGROUND

The St Vincent Declaration (SVD) of 1989 formulated a series of recommendations for improvement in health in diabetic subjects, and in particular set five-year targets to prevent the costly complications of diabetes (see Table 1).⁵ In Scotland, the SVD was implemented by evidence-based medicine through SIGN which published six guidelines in the period 1996–97 (see Table 1). In addition, in 1998, SIGN published a recommended minimum dataset for collection in people with diabetes (SIGN 25). These earlier SIGN guidelines were drawn up by different subgroups, each chaired by a physician with a special interest in diabetes, but also included a wide spectrum of other professionals, medical, nursing and paramedical with public health representation, drawn together from a wide geographical background throughout Scotland to encourage 'ownership' to facilitate the local implementation of the guidelines into clinical practice.

These initial diabetic SIGN guidelines were widely accepted throughout Scotland, both in primary and secondary care. As an example, in a combined primary and secondary care setting in Fife, an audit was performed to assess the targeting of a blood pressure of 140/80 mmHg as evidence-based from SIGN guideline 19, dealing with the management of cardiovascular disease in diabetes mellitus. This study in Type 2 diabetic subjects showed a significant improvement in life expectancy compared to an earlier audit of mortality in this region of Scotland.⁶

Problems were encountered with the initial guidelines. Guideline 25 recommended a minimum dataset for diabetic subjects with the hope that this would lead to a national Scottish diabetes register. There have been problems and delays with the technology to implement a 'common' IT system in all Scottish Health Boards to achieve this ambitious goal. However, the preliminary results of an all-Scotland diabetes register were published in late 2001 in the Scottish Diabetes Survey.⁷ It is hoped to have the appropriate computer systems in place in Scotland by late 2002 and to have the first detailed results from a national diabetes register about one year later in autumn 2003.

TABLE 1
The five-year European targets outlined in the St Vincent Declaration
and the corresponding original six diabetic SIGN guidelines.

| The St Vincent Declaration targets (1989) | SIGN guidelines (1996–97) |
|--------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> • To reduce new blindness due to diabetes mellitus by 30 per cent or more | <ul style="list-style-type: none"> • SIGN 4: Prevention of Visual Impairment |
| <ul style="list-style-type: none"> • To achieve a pregnancy outcome in diabetic women that approximates to that in non-diabetic women | <ul style="list-style-type: none"> • SIGN 9: Management of Diabetes in Pregnancy |
| <ul style="list-style-type: none"> • To reduce the number of patients entering end-stage diabetic renal failure by at least 30 per cent | <ul style="list-style-type: none"> • SIGN 10: Good Practice in the Care of Children and for Young People with Diabetes |
| <ul style="list-style-type: none"> • To reduce the rate of limb amputations for diabetic gangrene by 50 per cent | <ul style="list-style-type: none"> • SIGN 11: Management of Diabetic Renal Disease |
| <ul style="list-style-type: none"> • To cut morbidity and mortality from coronary artery disease | <ul style="list-style-type: none"> • SIGN 12: Management of Diabetic Foot Disease |
| | <ul style="list-style-type: none"> • SIGN 19: Management of Diabetic Cardiovascular disease and stroke by vigorous programmes of risk factor reduction |

RECENT DEVELOPMENTS

The new SIGN guideline, SIGN 55, dealing with the management of diabetes mellitus, updates the six previous guidelines and includes a seventh, a new section on life-style management. These revised guidelines encompass all the advances made in the four-year period since the earlier guidelines were introduced. The aim was to provide an updated evidence-based approach to influence current practice in diabetes mellitus in order to reduce the burden of long-term micro- and macrovascular complications, as well as to improve pregnancy outcome for the mother with diabetes. As with the earlier guidelines, SIGN 55 was developed by seven multi-disciplinary groups, each with a diabetologist as chairperson, each with at least one diabetic patient representative; Dr Moray Nairn, SIGN Programme Manager, acted as a facilitator for all the groups. Almost 100 people from all over Scotland, with a widespread interest in diabetes management, were involved with these subgroups.

The systematic literature review was synthesised in accordance with SIGN methodology.⁸ The grading system for levels of evidence and grades of recommendations are fully documented in the SIGN 55 guideline and are available on the SIGN website. Almost 400 references were cited in the guideline production. As part of the consultation process, a national open meeting was held in the Royal College of Physicians of Edinburgh in December 2000, where approximately 400 people from all branches of diabetes and healthcare attended. In addition, the draft guideline was on the website for a limited period to allow those unable to attend the meeting to contribute to the development of the guideline. The

guideline was reviewed by a panel of independent expert referees who were asked to comment primarily on the comprehensiveness and accuracy of the interpretation of the evidence-base supporting the recommendations in SIGN 55. The different aspects of diabetes covered within the guideline have been reviewed in two other recent publications.^{9, 10}

KEY POINTS IN SIGN 55

The key to evidence statements and grades of recommendations is summarised in Table 2.¹¹ Guideline 55 is a comprehensive 50-page document with recommendations arranged in seven sections with a short introductory summary regarding diagnosis and screening for diabetes mellitus. All of this information is on the SIGN website but, in addition, a quick reference guide (QRG) in the form of a 16-page booklet has been produced to provide a summary of the main recommendations contained in the full guideline. As an example of how the recommendations are given, the QRGs for (a) children and young people with diabetes, (b) management of diabetic nephropathy, (c) diabetic cardiovascular disease, (d) prevention of visual impairment, and (e) diabetes in pregnancy are shown in Tables 3–7.

THE FUTURE

In December 2000, the Scottish Executive made a commitment in the Scottish Health Plan¹² to develop a *Scottish Diabetes Framework* which would lead to improved standards of care in Scotland. The Clinical Standards Board for Scotland has identified key clinical standards for diabetes services.¹³ *The Scottish Diabetes Framework* aims to draw together existing guidance and best practice, including plans to establish a national screening strategy

TABLE 2
Levels of evidence and grades of recommendations.

| KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS | |
|----------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| LEVELS OF EVIDENCE | |
| 1 ⁺⁺ | High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias |
| 1 ⁺ | Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias |
| 1 | Meta-analyses, systematic reviews, or RCTs with a high risk of bias |
| 2 ⁺⁺ | High quality systematic reviews of case-control or cohort studies High quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal |
| 2 ⁺ | Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal |
| 2 | Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal |
| 3 | Non-analytic studies, e.g. case reports, case series |
| 4 | Expert opinion |
| GRADES OF RECOMMENDATION | |
| A | All (or one) meta-analysis, systematic review, or RCT rated as 1 ⁺⁺ and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 2 ⁺⁺ , directly applicable to the target population, and demonstrating overall consistency of results |
| B | A body of evidence including studies rated as 2 ⁺ , directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1 ⁺⁺ or 1 ⁺ |
| C | A body of evidence including studies rated as 2 ⁻ , directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2 ⁺⁺ |
| D | Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2 ⁻ |
| GOOD PRACTICE POINTS | |
| ☑ | Recommended best practice based on the clinical experience of the guideline development group |

TABLE 3
Children and young people with diabetes.

| CHILDREN AND YOUNG PEOPLE WITH DIABETES | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>Table 3 (continued) recommends that 75% of children in young people in 20 years.</p> <ul style="list-style-type: none"> 10-15% of young people in 20 years will have diabetes due to affected first degree relatives. Diabetes in young people under 15 is a chronic disease. It may affect the future course of the disease. 90% of patients with type 1 diabetes will develop 2 diabetes by the age of 50 and the remaining 10% will develop it by age 70 years. | |
| DIAGNOSIS & SCREENING | PSYCHOLOGICAL INTERVENTIONS |
| <p>B Screening for pre-type 1 diabetes is not recommended in either the general population or high-risk children and young people.</p> <p>C Patients with ID should be screened annually for diabetes from 10 years of age.</p> | <p>B Psychological or educational interventions have positive effects on psychological outcomes, knowledge about diabetes and glycaemic control.</p> <p>C Regular assessment for psychological outcomes, especially psychological coping strategies, and eating disorder is recommended.</p> |
| INITIATING THERAPY AT DIAGNOSIS | THE USE OF COGNITIVE-BEHAVIOURAL STRATEGIES |
| <p>C A structured programme for initial management and education of children with diabetes and their families is an appropriate alternative to a hospital-based programme.</p> | <p>B The use of cognitive-behavioural strategies to support adherence to the guidelines is recommended.</p> |
| CONTINUING MANAGEMENT | LONG TERM COMPLICATIONS |
| INSULIN THERAPY | RETINOPATHY |
| <p>B Insulin therapy should be delivered as part of a comprehensive support package.</p> <p>C The insulin regimen should be tailored to the individual child to achieve the best possible glycaemic control without causing hypoglycaemia.</p> <p>D <ul style="list-style-type: none"> Phenylalanine-free insulin analogues may safely be used in very young children with severely labile fasting patterns. Insulin analogues other than insulin have no effect on the management of type 1 diabetes in the young. </p> | <p>A To reduce the risk of long-term complications, target HbA1c for all young people with diabetes to the equivalent of glycaemic control towards a normal level.</p> <p>B From the age of 11 years, all people with diabetes should have the following annual checks: <ul style="list-style-type: none"> measurement of the retina measurement of microalbuminuria annual ACE or first morning UCE blood pressure </p> <p>D There is no evidence that routine screening for retinopathy in hyperlipidaemia are of benefit.</p> |
| DIETARY MANAGEMENT | RISKS AND CONSEQUENCES |
| <p>B Dietary advice as part of a comprehensive management plan significantly improves glycaemic control.</p> | <p>B Young people with diabetes should be screened for thyroid and cardiovascular at onset of diabetes and at intervals throughout their lives.</p> |

TABLE 4
Management of diabetic nephropathy.

| MANAGEMENT OF DIABETIC NEPHROPATHY | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| RISK FACTORS | SCREENING |
| <ul style="list-style-type: none"> hypertension total blood protein baseline urinary albumin excretion insulin use duration of diabetes presence of retinopathy smoking genetic factors renal dysfunction and glycaemic levels malnutrition cardiac disease/vascular health | <p>B All patients with diabetes should have their urinary albumin concentration and serum creatinine measured at diagnosis and at regular intervals, usually annually.</p> <p>B Urinary albumin concentration should be measured using a first morning urine sample and the urinary albumin:creatinine ratio should be measured by a laboratory method of a microalbumin test specific for albumin at low concentrations.</p> <p>B An abnormal result should be confirmed by a further sample without delay.</p> |
| DEFINITIONS | PREVENTION OF DIABETIC NEPHROPATHY |
| <p>Microalbuminuria – a rise in urinary albumin loss to between 30 and 300 mg/day. Alternatively, in a spot urine collection, a urinary albumin:creatinine ratio (UACR) of 3.3 mg/mmol (in men and > 3.5 mg/mmol) in women or a urinary albumin concentration of 30 mg/L albumin microalbuminuria.</p> <p>It is the earliest sign of diabetic nephropathy and predicts increased renal mortality, cardiovascular mortality and morbidity, and end-stage renal failure.</p> <p>Diabetic nephropathy – the presence of a raised urinary albumin:creatinine ratio (> 3 mg/day) with or without a raised serum creatinine level in a patient with existing diabetic retinopathy.</p> <p>Therapies to slow disease and stabilised form at renal disease and a more strongly predictive of total mortality, cardiovascular morbidity and end-stage renal failure than microalbuminuria.</p> | <p>A Good glycaemic control (HbA1c around 7%) in all patients with diabetes and type 1 blood pressure control (< 140/90 mm Hg) in patients with type 2 diabetes should be maintained to reduce the risk of developing diabetic nephropathy.</p> |
| | TREATMENT OF DIABETIC NEPHROPATHY |
| | <p>A Blood pressure should be maintained < 140/90 mm Hg in all patients with diabetes.</p> <p>A Patients with microalbuminuria or proteinuria should be: <ul style="list-style-type: none"> commenced on an ACE inhibitor continued on angiotensin II antagonist therapy. </p> <p>B Patients with type 1 diabetes, proteinuria and a reduced GFR should reduce dietary protein intake to 0.8-1.0 g/kg/day.</p> <p>C Patients should be referred to a renal clinic if serum creatinine exceeds 130 μmol/L.</p> |

TABLE 5
Diabetic cardiovascular disease.

| DIABETIC CARDIOVASCULAR DISEASE | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| RISK FACTORS | <p>Morbidity and mortality from cardiovascular disease (CVD) are 2-5 times higher in people with diabetes than the general population.</p> <p>Current assessment methods may underestimate risk in people with type 1 diabetes or type 2 diabetes with retinopathy.</p> |
| PRIMARY PREVENTION | |
| SMOKING CESSATION | <p>B Treat aggressively with lifestyle measures and drug therapy.</p> |
| BP CONTROL | <p>A Control ACE inhibitors as first line therapy for most diabetes.</p> |
| GLYCAEMIC CONTROL | <p>B Consider metformin as first treatment hypoglycaemia in overweight patients (> 100% ideal body weight).</p> |
| LPD (LOWERING TRIGLYCERIDE) THERAPY | <p>B Consider lipid lowering drug therapy in type 2 diabetes if 90 year risk of a major coronary event is ≥ 20%.</p> <p>Consider as a lower risk treatment in people with type 1 diabetes and type 2 diabetes with nephropathy.</p> |
| ANTIPLATELET THERAPY | <p>B Consider aspirin (75 mg) for all patients who have diabetes and well-controlled hypertension when risk of a coronary event is ≥ 20% over 10 years.</p> |
| <p>Coronary heart disease in patients with diabetes is the first of the general population. Diabetes patients have often serious with a coronary heart disease.</p> | |
| MANAGEMENT OF ESTABLISHED CVD | |
| INTERVENCIVE TREATMENT | <p>B Statins should not be withheld due to concerns about diabetic retinopathy.</p> |
| THROMBOLYTIC THERAPY | <p>B Primary angioplasty may be more effective than thrombolytic therapy in diabetic patients with acute MI.</p> |
| CONTROL PRIMARY ANGIOPLASTY | <p>B Diabetes is not a contraindication to use of 2 diabetes.</p> |
| LONG TERM ASPIRIN + clopidogrel (75 mg/day) | <p>B Indications for secondary angioplasty in patients with diabetes are similar to the general population, excepting the increased risk of mortality following CABG and angioplasty.</p> |
| BLOCKER THERAPY | |
| ACE INHIBITOR (within 48 hours in patients with CVD) | |
| STATIN THERAPY (if total cholesterol > 3 mmol/L) | |
| DIABETIC PATIENTS UNDERGOING ANGIOPLASTY | <p>should be treated with double or triple therapy, and avoid alternative therapy with alcohol.</p> |

- 10 Campbell IW. New SIGN guideline addresses seven major areas of diabetes care. *Guidelines in Practice* 2002; **5**:23–31.
 - 11 Harbour R, Miller J. A new system for grading recommendations in evidence-based guidelines. *BMJ* 2001; **323**:334–6.
 - 12 *Our National Health. A plan for action, a plan for change.* Edinburgh: Scottish Executive; 2000.
 - 13 Clinical Standards Board for Scotland. *Clinical Standards Diabetes.* Edinburgh: Scottish Executive; 2002. (www.clinicalstandards.org/pdf/Diabetes.pdf).
 - 14 *Organisation of services for diabetic retinopathy screening.* Glasgow: Health Technology Board for Scotland; 2002.
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