INTERNATIONAL DIABETES FEDERATION, 2012
Clinical Guidelines Task Force

Global Guideline for Type 2 Diabetes

International Diabetes Federation

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Preface

There is now extensive evidence on the optimal management of diabetes, offering the opportunity of improving the immediate and long-term quality of life of those with diabetes.

Unfortunately such optimal management is not reaching many, perhaps the majority, of the people who could benefit. Reasons include the size and complexity of the evidence-base, and the complexity of diabetes care itself. One result is a lack of proven cost-effective resources for diabetes care. Another result is diversity of standards of clinical practice.

Guidelines are one part of a process which seeks to address those problems. Many guidelines have appeared internationally, nationally, and more locally in recent years, but most of these have not used the rigorous new guideline methodologies for identification and analysis of the evidence.

Many countries around the world do not have the resources, either in expertise or financially, that are needed to develop diabetes guidelines. Also such a repetitive approach would be enormously inefficient and costly. Published national guidelines come from relatively resource-rich countries, and may be of limited practical use in less well resourced countries.

In 2005 the first IDF Global Guideline for type 2 diabetes was developed. This presented a unique challenge as we tried to develop a guideline that is sensitive to resource and cost-effectiveness issues. Many national guidelines address one group of people with diabetes in the context of one health-care system, with one level of national and health-care resources. This is not true in the global context where, although every health-care system seems to be short of resources, the funding and expertise available for health-care vary widely between countries and even between localities.

Despite the challenges, we feel that we found an approach which is at least partially successful in addressing this issue which we termed 'Levels of care' (see next page).

This guideline represents an update of the first guideline and extends the evidence base by including new studies and treatments which have emerged since the original guideline was produced in 2005.

Funding is essential to an activity of this kind. IDF is grateful to a diversity of commercial partners for provision of unrestricted educational grants.

Levels of care

All people with diabetes should have access to the broad range of diabetes services and therapies and no person should be denied any element of effective diabetes care. It is recognised that in many parts of the developing world the implementation of particular standards of care is limited by lack of resources. This guideline provides a practical approach to promote the implementation of cost-effective evidence-based care in settings between which resources vary widely.

The approach adopted has been to advise on three levels of care:

Recommended care is evidence-based care which is cost-effective in most nations with a well developed service base, and with health-care funding systems consuming a significant part of national wealth.
Recommended care should be available to all people with diabetes and the aim of any health-care system should be to achieve this level of care. However, in recognition of the considerable variations in resources throughout the world, other levels of care are described which acknowledge low and high resource situations.

Limited care is the lowest level of care that anyone with diabetes should receive. It acknowledges that standard medical resources and fully-trained health professionals are often unavailable in poorly funded health-care systems. Nevertheless this level of care aims to achieve with limited and cost-effective resources a high proportion of what can be achieved by *Recommended care*. Only low cost or high cost-effectiveness interventions are included at this level.

Comprehensive care includes the most up-to-date and complete range of health technologies that can be offered to people with diabetes, with the aim of achieving best possible outcomes. However the evidence-base supporting the use of some of these expensive or new technologies is relatively weak.

SUMMARY OF THE LEVELS OF CARE STRUCTURE

Recommended care: **Evidence-based care, cost-effective in most nations with a well developed service base and with health-care funding systems consuming a significant part of their national wealth.**

Limited care: **Care that seeks to achieve the major objectives of diabetes management, but is provided in health-care settings with very limited resources – drugs, personnel, technologies and procedures.**

Comprehensive care: **Care with some evidence-base that is provided in health-care settings with considerable resources.**

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Methodology

The following methodology was used to develop the original guideline:

• A broadly based group which included people with diabetes, health-care professionals from diverse disciplines, and people from non-governmental organisations was convened (see Members of the Guidelines Group).

• Geographical representation was from all the IDF regions, and from countries in very different states of economic development (see Members of the Guidelines Group).

• Designated individuals with expertise in the topic prepared an evidence summary of the individual sections.

• The whole Group met to hear the synthesis of the evidence for each topic of diabetes care, to address what recommendations should be made, and to make recommendations over what should be in each Level of care for each section.

• The draft guideline was sent out for wider consultation to IDF member associations, IDF elected representatives globally and regionally, interested professionals, industry. Each comment received was reviewed and changes were made where the evidence-base confirmed these to be appropriate.

• A decision was made to review the guideline after 3-5 years.

This guideline represents an update of the 2005 guideline. Individuals who prepared the original sections were invited to review and update their section taking into consideration new evidence and new treatments. The updated guideline was sent out for wide consultation and was modified, where appropriate, according to comments received.

This guideline is intended to be reviewed after 5 years.

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Duality of interest:

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1 SCREENING AND DIAGNOSIS

Recommendations

Recommended care

SD1 Each health service should decide whether to have a programme to detect people with undiagnosed diabetes.

- This decision should be based on the prevalence of undiagnosed diabetes and on the resources available to conduct the detection programme and treat those who are detected.
- Universal screening for undiagnosed diabetes is not recommended.

SD2 Detection programmes are usually based on a two-step approach:

- Step 1 - Identify high-risk individuals using a risk assessment questionnaire.
- Step 2 - Glycaemic measure in high-risk individuals.

SD3 Diabetes can be diagnosed on any of the following World Health Organization (WHO) criteria:

- Fasting plasma glucose (FPG) ≥ 7.0 mmol/l (126 mg/dl) or,
- 75 g oral glucose tolerance test (OGTT) with FPG ≥ 7.0 mmol/l (126 mg/dl) and/or 2 hour plasma glucose ≥ 11.1 mmol/l (200 mg/dl) or,
- Glycated haemoglobin (HbA_{1c}) ≥ 6.5% / 48 mmol/mol, or
- Random plasma glucose ≥ 11.1 mmol/l (200 mg/dl) in the presence of classical diabetes symptoms
- Asymptomatic individuals with a single abnormal test should have the test repeated to confirm the diagnosis unless the result is unequivocally elevated.

SD4 Where a random plasma glucose level ≥ 5.6 mmol/l (≥ 100 mg/dl) and < 11.1 mmol/l (< 200 mg/dl) is detected, a FPG should be measured, or an OGTT performed, or an HbA_{1c} measured.

SD5 Use of HbA_{1c} as a diagnostic test for diabetes requires that stringent quality assurance tests are in place and assays are standardised to criteria aligned to the international reference values, and there are no conditions present which preclude its accurate measurement.

SD6 People with screen-detected diabetes should be offered treatment and care.

This guideline does not deal with lesser degrees of hyperglycaemia detected on screening.

Limited care

SD_L1 Detection programmes should be opportunistic and limited to high-risk individuals in very limited settings.

SD_L2 The principles for screening are as for *Recommended care*

SD_L3 Diagnosis should be based on fasting laboratory plasma glucose (preferred) or capillary plasma glucose if only point-of-care testing is available.

SD_L4 If blood glucose testing is not available, the presence of glycosuria, especially with classical symptoms, may be used to diagnose diabetes.

Comprehensive care

SD_C1 Resources should be available for diabetes detection programmes.

SD_C2 HbA_{1c} should be routinely available as an option to diagnose diabetes.

SD_C3 Investigations to classify type of diabetes (e.g. islet-cell related antibodies, C-peptide, genotyping) should be available.

Rationale

Screening for type 2 diabetes has important implications for individual health, day-to-day clinical practice, and public health policy. While the early detection and treatment of diabetes seems logical in terms of minimising complications, there is currently no direct evidence as to whether or not this is beneficial to individuals. Despite this lack of direct evidence, early detection through screening is taking place and is recommended by a number of organisations throughout the world.

The decision about conducting a detection programme should be based on the following considerations [1]:

- ***epidemiological*** - prevalence of undiagnosed type 2 diabetes.
- ***health systems*** - capacity to carry out the screening, provide care for those who screen positive, and implement prevention programmes in those at high risk of future development of diabetes.
- ***population*** - acceptability and likely uptake of the screening programme.
- ***economic*** - cost of early detection to the health system and to the individual, and relative cost-effectiveness of early detection compared with improving care for people with known diabetes

Evidence-base

Diabetes is associated with a range of serious complications which result in reduced quality of life and premature mortality. Early detection and treatment is one strategy for reducing this burden.

Type 2 diabetes has a long asymptomatic pre-clinical phase which frequently goes undetected. Complications are commonly present at the time of diagnosis of type 2 diabetes although the actual rates have varied between studies. In the Netherlands retinopathy was found in 7.6% of people with screen-detected diabetes, impaired foot sensitivity in 48.1% and microalbuminuria in 17.2%, myocardial infarction in 13.3%, ischaemic heart disease in 39.5% and peripheral arterial disease in 10.6% [2,3]. Since the development of retinopathy is related to duration of diabetes, it has been estimated that type 2 diabetes may have its onset up to 12 years before its clinical diagnosis [4].

Overall, for every person with diagnosed diabetes there is another who has undiagnosed diabetes, although the proportion who are undiagnosed varies between countries and ranges from 28% to 80% [5].

Although there is considerable evidence supporting the benefits of improved blood glucose, blood pressure and blood lipid control in type 2 diabetes, the potential benefits of early diagnosis on outcomes in screen-detected diabetes remain unclear. The ADDITION study compared outcomes of intensive and conventional treatment in people with screen-detected diabetes [6]. The study found that cardiovascular risk factors (HbA_{1c}, cholesterol concentrations and blood pressure) were slightly but significantly better in the intensive treatment group. These changes were associated with small non-significant reductions in the incidence of cardiovascular events (7.2% [13.5 per 1,000 person-years] in the intensive treatment group v 8.5% [15.9 per 1,000 person-years] in the routine care group (hazard ratio 0.83, 95% CI: 0.65-1.05), and all-cause mortality (6.2% [11.6 per 1,000 person-years] v 6.7% [12.5 per 1,000 person-years]; hazard ratio 0.91, 95% CI: 0.69-1.21).

There is some indirect evidence suggesting that early detection may be beneficial. The results of case-control studies which have examined possible benefits from early detection on clinical outcomes have been inconclusive [7,8]. FPG at diagnosis might serve as a surrogate for the duration of diabetes. A post-hoc analysis of UKPDS showed that the frequency of subsequent complications was related to FPG at study entry [9]. The group with an initial FPG < 7.8 mmol/l (< 140 mg/dl) had significantly lower rates of all major end-points compared with the ≥ 10.0 mmol/l (≥ 180 mg/dl) group and also had significantly lower diabetes-related death rates and myocardial infarction rates compared with the 7.8 to < 10.0 mmol/l (140 to < 180 mg/dl) group. These findings suggest a benefit of intervening either at lower FPG levels or earlier in the natural history of diabetes, and may be consistent with a benefit derived from early detection.

Screening for diabetes will also identify individuals with intermediate hyperglycaemia (impaired glucose tolerance and impaired fasting glucose) who may benefit from interventions to prevent or delay progression to diabetes, and to prevent cardiovascular disease (CVD) and other complications.

There are several options for strategies to screen for undiagnosed diabetes. The ultimate choice is based on available resources and a trade-off between sensitivity (the proportion of people with diabetes who test positive on the screening test), specificity (the proportion of people who do not have diabetes who test negative on the screening test), and the proportion of the population with a positive screening test which needs to proceed to diagnostic testing.

Most screening strategies include risk assessment and measurement of glycaemia, performed either sequentially or simultaneously. There are many risk assessment methods and scores but applicability of many is limited because they require tests not routinely available [10]. One commonly used risk score is FINDRISK [11]. This diabetes risk score is a simple, fast, inexpensive, noninvasive, and reliable tool to identify individuals at high risk for type 2 diabetes. It was developed from a large random population sample of individuals with no antidiabetic medication at baseline and who were followed for 10 years. It requires age, body mass index (BMI), waist circumference, history of antihypertensive drug treatment and high blood glucose, physical activity, and daily consumption of fruits, berries, or vegetables to calculate risk.

Screening tests are followed by diagnostic tests in order to make the diagnosis [1,12]. Combined screening strategies have a sensitivity and specificity in the order of 75%, and 25% of the population require diagnostic testing. People who screen negative should be re-tested after 3-5 years. These people should also be offered lifestyle advice to minimise their risk of developing diabetes.

Although the usefulness of urine glucose as a screening test for undiagnosed diabetes is limited because of low sensitivity (21-64%) [12], specificity is high (> 98%), so it may have a place in low-resource settings where other procedures are not available.

Following a positive screening test, diagnostic testing is required. The WHO now recommends three options for diagnosing diabetes [13,14]:

- FPG ≥ 7.0 mmol/l (≥ 126 mg/dl) or,
- 75 g OGTT with FPG ≥ 7.0 mmol/l (126 mg/dl) and / or 2 hour plasma glucose ≥ 11.1 mmol/l (200 mg/dl) or,
- HbA_{1c} ≥ 6.5% / 48 mmol/mol.

In asymptomatic individuals with a single abnormal test, the abnormal test should be repeated to confirm the diagnosis unless the result is unequivocally elevated.

In the presence of classical diabetes symptoms, diabetes can be diagnosed on the basis of a random plasma glucose ≥ 11.1 mmol/l (200 mg/dl).

Consideration

The place of screening for undiagnosed diabetes as part of an overall strategy to reduce the health burden of diabetes is not established. However, many organisations recommend it. The choice of whether to screen or not, and the screening strategy, must be made locally taking into account local considerations.

Implementation

A clear and transparent decision should be made about whether or not to endorse a screening strategy. If the decision is in favour of screening, this should be supported by local protocols and guidelines, and public and health-care professional education campaigns.

Evaluation

Number of health-care professionals and services performing screening, proportion of the population being screened, and detection rate of undiagnosed diabetes should be ascertained. Percentage of diagnosed people entering and continuing in care should be measured.

Potential indicator

Indicator	*Denominator*	*Calculation of indicator*	*Data to be collected for calculation of indicator*
Percentage of people with newly diagnosed type 2 diabetes in one year.	**Total number of people with type 2 diabetes seen in one year.**	**Number of people with newly diagnosed type 2 diabetes as a percentage of the total number of people with type 2 diabetes seen in one year.**	**Year of diagnosis of diabetes.** **Classification of diabetes.**

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2 CARE DELIVERY

Recommendations

Recommended care

CD1 Offer care to all people with diabetes, with sensitivity to cultural wishes and desires.

CD2 Encourage a collaborative relationship, by actively involving the person with diabetes in the consultation, and creating opportunities for them to ask questions and express concerns. Ensure that issues important to the person with diabetes are addressed.

CD3 Offer annual surveillance of all aspects of diabetes control and complications to all people with type 2 diabetes (see Table CD1).

CD4 Agree a care plan with each person with diabetes.
- Review this annually or more often if appropriate.
- Modify it according to changes in wishes, circumstances and medical findings.

CD5 Use protocol-driven diabetes care to deliver the care plan at scheduled routine visits between annual reviews.

CD6 Provide urgent access to diabetes health-care advice for unforeseen problems.

CD7 Organise care around the person with diabetes.

CD8 Use a multidisciplinary care team with specific diabetes expertise maintained by continuing professional education.

CD9 Ensure that each person with diabetes is recorded on a list of people with diabetes, to facilitate recall for annual complications surveillance.

CD10 Provide telephone contact between clinic visits.

CD11 Consider how people with diabetes, acting as expert patients, and knowing their limitations, together with local/regional/national associations, might be involved in supporting the care delivery of their local health-care team.

CD12 Use data gathered in routine care to support quality assurance and development activities.

Limited care

CD_L1 Offer annual surveillance, agree care plans, deliver protocol-driven care, and ensure that each person with diabetes is recorded on a local list of people with diabetes, as for *Recommended care*.

CD_L2 Organise care around the person with diabetes.

CD_L3 Use an appropriately trained health-care professional to deliver diabetes care.

Comprehensive care

CD_c1 The principles as for *Recommended care*.

CD_c2 The person with diabetes will have access to their own electronic medical record via secure technology from remote sites. They will be able to give permission for any health-care professional to access that record.

CD_c3 Decision support systems might be available to the health-care professional, and perhaps to the person with diabetes.

Table CD1

A summary of the assessments to be performed at Annual Review (or annually) for each person with type 2 diabetes

Assessment topic	*Guideline section*
Self-care knowledge and beliefs	*Education*
Lifestyle adaptation and wishes (including nutrition, physical activity, smoking)	*Lifestyle management*
Psychological status	*Psychological care*
Self-monitoring skills and equipment	*Self-monitoring*
Body weight trends	*Lifestyle management*
Blood glucose control	*Glucose control levels; Clinical monitoring; Glucose control therapy*
Blood pressure control	*Blood pressure control*
Blood lipid control	*Cardiovascular risk protection*
Cardiovascular risk	*Cardiovascular risk protection*
Erectile dysfunction, neuropathy	*Nerve damage*
Foot condition	*Foot care*
Eyes	*Eye screening*
Kidneys	*Kidney damage*
Medication review	–

Rationale

The person diagnosed with type 2 diabetes requires access to immediate and ongoing care. Who provides this care, and where and when, will depend on local circumstances, but it needs to be organised in a systematic way. General principles include: annual review of control and complications; an agreed and continually updated diabetes care plan; and involvement of the multidisciplinary team in delivering that plan, centred around the person with diabetes.

Evidence-base

Systems underlying structured organisation of care for people with diabetes do not easily lend themselves to comparison by randomised controlled trials (RCTs). Much of the literature in this area is descriptive and interventions are often multifaceted. Some aspects of care organisation which do not have a strong evidence-base have been adopted as good practice by a wide range of diabetes services across the world. Systematic reviews of the evidence were undertaken by the Canadian guideline in 2003 [1], the United Kingdom (UK) National Institute for Clinical Excellence (NICE) guideline on type 1 diabetes in 2004 [2], and by Shojania et al [3].

Evidence supports a multidisciplinary approach to diabetes care [4] including involvement of nurses with training in diabetes care, teaching skills and adult education, and of formally trained dietitians and podiatrists in specifically relevant areas of diabetes care [2,3]. Although there is no RCT evidence for annual review of control and complications, this has become the basis for many quality control structures for diabetes care [2,5]. Some of the rationale for annual surveillance in different areas of care is given in individual sections of the current guideline.

The evidence also supports organisational interventions that have been shown to improve health-care efficiencies, such as databases to provide patient and physician reminders and transfer of information [1,5], while NICE considers a database-driven recall system to be implicit in recommendations for annual surveillance [2]. Evidence for the usefulness of telemedicine (ranging from the telephone to technology for transmission of images) was reviewed by NICE, who recommended its use to improve process and outcomes [2,6], and drew attention to its potential in rural and remote situations. This has been confirmed in a systematic review [7].

Protocol-driven care is not specifically addressed by the guidelines, but Davidson has reviewed studies, including RCTs, in which nurses or pharmacists delivered diabetes care following agreed protocols, and found they achieved improved process and outcomes compared with 'usual care' within the United States health-care system [8].

The literature on care plans and patient-held/accessed records is as yet only descriptive, without useful analysis of patient-related outcomes, but the UK National Service Framework finds that these can help to empower people with diabetes [9].

A review of expert patient (lay led) education programmes for chronic disease concluded that such programmes increase patients' self efficacy and can lead to improvements in psychological health [10].

The role of community health workers in the care of people with diabetes has been the subject of a systematic review. Some of the studies reviewed reported improvements in lifestyle, in some physiological measures, and in patient knowledge [11].

In a number of countries, health economies have introduced, or are thinking of introducing, "pay for performance schemes" which provide financial incentives for providing good quality care for people with chronic diseases. There is an emerging evidence base to suggest that such incentives can improve the process and intermediate outcomes of diabetes care in most individuals [12,13,14].

Consideration

Given the diversity of health-care systems around the world, recommendations in this part of the guideline are presented in very general terms. Flexibility, adaptability, and accessibility would seem to be important principles. Redeployment of underused resources (such as leprosy clinics) or linking with other disease-specific services (such as HIV/AIDS) may offer opportunities for improved care in some countries. Where databases are not feasible, lists of people with diabetes can be established in simple book form. Telemedicine can encompass anything from telephones allowing access to health-care professional advice to sophisticated data transfer, but any advance in communications technology, or access to it, may offer opportunities for improved organisation of care. Empowering patients to find their way in the system through access to their own data and perhaps through use of decision-support tools would seem to be a logical development.

Implementation

Organisation of care to deliver the above recommendations is largely concerned with:

- Putting registration, recall and record systems in place to ensure care delivery occurs for all people with diabetes.
- Having health-care professionals trained and available to provide the appropriate advice.
- Training and using lay community health workers to support people with diabetes.

Simple communications technologies, and personnel support for those, need to be in place. More sophisticated telemedicine and other information technology approaches require not just appropriate software and hardware, but again appropriately trained staff, and continuing maintenance.

Evaluation

Evaluation should show evidence of structured records being appropriately completed as part of recall and appointment systems driven from a list of people with diabetes. Evaluation of proportions of the managed population receiving defined components of care (such as glucose control, eye screening or blood pressure checks) within a 12 month period should be made regularly. The staff providing the service should be identified, together with evidence of their continued professional training. The existence of appropriate communications equipment and protocols, and arrangements for their use, can be reviewed.

Potential indicator

Indicator	*Denominator*	*Calculation of indicator*	*Data to be collected for calculation of indicator*
Percentage of people with type 2 diabetes attending for annual review according to treatment (diet only, oral glucose lowering medications, GLP-1 RA or insulin).	**Total number of people with type 2 diabetes eligible for annual review.**	**Number of people with type 2 diabetes who have an annual review according to treatment (diet only, oral glucose lowering medications, GLP-1 RA or insulin) as a percentage of the total number of people with type 2 diabetes eligible for annual review.**	**Dates of visits in the year.** **Type of diabetes treatment.**

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3 EDUCATION

Recommendations

Recommended care

ED1 Make patient-centred, structured self-management education an integral part of the care of all people with type 2 diabetes:
- From around the time of diagnosis.
- On an ongoing basis, based on routine assessment of need.
- On request.

ED2 Use an appropriately trained multidisciplinary team to provide education to groups of people with diabetes, or individually if group work is considered unsuitable. Where desired, include a family member or friend.

ED3 Include in education teams a health-care professional with specialist training in diabetes and delivery of education for people with diabetes.

ED4 Ensure that education is accessible to all people with diabetes, taking account of culture, ethnicity, psychosocial, and disability issues. Consider delivering education in the community or at a local diabetes centre, through technology and in different languages. Include education about the potential risk of alternative medicine.

ED5 Use techniques of active learning (engagement in the process of learning and with content related to personal experience), adapted to personal choices and learning styles.

ED6 Use modern communications technologies to advance the methods of delivery of diabetes education.

ED7 Provide ongoing self-management support.

Limited care

ED_L1 The principles are as for *Recommended care* but education may be provided by a smaller team (physician and educator) or in very limited situations by an appropriately skilled individual.

ED_L2 Consider how available technologies can best be used to deliver education.

Comprehensive care

ED_C1 The principles are as for *Recommended care* but would also include the availability on demand of individual advice, through a named key contact and consideration of innovative and advanced methods for ongoing support.

Rationale

It is widely accepted that diabetes education is an important component of care [1]. Diabetes is a lifestyle disease that requires the person living with the disease to self-manage and make numerous daily decisions regarding food, activity and medications. It also necessitates that the person be proficient in a number of self-care skills, like blood glucose monitoring if appropriate, foot examination and taking medications [2]. Self-management refers to the individual's ability to manage the symptoms, treatment, physical and psychosocial consequences and lifestyle changes inherent in living with a chronic condition [3].

In order for people to learn the skills to be effective self-managers, diabetes self-management education (DSME) is critical in laying the foundation. DSME is defined as the ongoing process of facilitating the knowledge, skill and ability necessary for diabetes self-care. This process incorporates the needs, goals and life experiences of the person with diabetes and is guided by evidence-based standards [5]. The process of making and refining multi-level changes in the community and health care systems to facilitate patient self-care is referred to as self-management support (SMS), and is now considered to be important in providing ongoing support to sustain the self-management gains made by patients as a result of education [6].

Diabetes education has changed a great deal in recent years. Since diabetes education has evolved from a didactic to a more patient-centred and theoretically based model [6,7], DSME programmes should consider putting a greater emphasis on the promotion of positive behaviour change [7], with the understanding that knowledge itself is not enough to enable people to change behaviour and improve outcomes [8,9]. Incorporating SMS into programme structure is also important to sustain the benefits of the intervention [7].

Evidence-base

Education in the broadest sense underpins diabetes care, at every contact between the person with diabetes and the health-care team. This has made it difficult to isolate those aspects of education which best contribute to its effectiveness. Despite this however the evidence supporting the effectiveness of DSME has increased dramatically [1,2,10-18]. Historically, systematic reviews of the evidence have been critical of the quality of reporting and methodology in many of the studies in this field, and point out the need for further research, and possible strategies for this [1,11,15-18].

In a meta-analysis of DSME studies, Norris et al found as much as a 0.8% / 9 mmol/mol reduction in HbA_{1c} levels in the immediate time frame after DSME is delivered. Since a 1.0% / 11 mmol/mol decrease in HbA_{1c} is associated with reductions in diabetes-related complications, a 0.8% / 9 mmol/mol HbA_{1c} reduction would translate into a significant clinical benefit. Contact time with an educator was the only significant predictor of reduction in HbA_{1c}. Unfortunately the benefits are not sustained and decrease 1-3 months later indicating on-going support is necessary [1].

In the technology report informing its guidance on the use of patient-education models, NICE provided a review, rather than formal meta-analysis, due to differences in design, duration, outcome measures and reporting of studies [14].

The evidence from eight trials (six RCTs, two controlled clinical trials [CCTs]) suggested that general self-management education has a limited impact on clinical outcomes, although few long-term data were available. The evidence from eight trials (seven RCTs, one CCT) of focused self-management education (focused on one or two aspects of self-management) suggested that this may have some effect in reducing or maintaining HbA_{1c} levels, although there was little evidence of impact on other clinical outcomes, partly because of short study durations. Also reviewed were four trials (three RCTs, one CCT) that included people with type 1 or type 2 diabetes, where there was some evidence that education may improve glycaemic control and quality of life, but little evidence about the longer-term benefits of education. The Cochrane Review of individual patient education reported a significant 0.3% / 3 mmol/mol reduction in HbA_{1c} in patients with an HbA_{1c} greater than 8.0% / 64 mmol/mol at baseline [11]. The other reviews painted a similar picture of educational interventions producing modest improvements in glycaemic control [16-18]. Interestingly, both the Norris et al and NICE reports highlight the critical need for long-term follow up and study.

NICE found that costs depended on the type of programme offered, while Norris et al and others report a paucity of cost evaluation in the field and call for more investigation. Although there is little evidence regarding the cost-effectiveness of patient education in general, it was concluded that, given the relatively small costs associated with educational programmes, only small improvements in terms of morbidity or health-related quality of life were needed to make educational interventions cost effective [14].

More recently, study reviews have focused on specific diabetes education programme dynamics and ways to improve access to education in a health systems approach [19,20]. Findings suggest that attention to culture, behaviour change theory, and psychosocial criteria in evaluation of education programmes be considered. Ways to promote access include system change that includes opportunities for therapeutic patient education, ongoing self-management support, training to enhance educator skills in patient-centred and behavioural approaches and physician recognition of the importance of DSME for patient referral [20-24].

Consideration

Despite the patchy evidence, certain common principles emerge and are reflected in the recommendations. Assessment of needs, attention to psychosocial areas, and identifying barriers is fundamental to tailoring education to the perspective of the person with diabetes, while identified needs of the population served will determine the educational process. It is widely accepted that promoting knowledge is not enough and effective educational strategies require attention to behaviour change. DSME needs to be ongoing and requires continued follow-up and support. Innovative approaches for ongoing self-management support are critically important to sustain the positive impact of the education intervention. Recent studies have demonstrated the benefits of innovative approaches that include using peers, community workers, and technology to support DSME [25-27].

It is noted that diabetes education was an integral part of intensification of care in the DCCT (in type 1 diabetes), nutritional advice made a significant impact in the UKPDS cohort prior to randomisation and behaviour change was a key strategy in the diabetes prevention programmes. Accordingly diabetes education is taken as an essential part of diabetes care.

Implementation

Major components of implementing these recommendations are the recruitment of personnel and their training in the principles of both diabetes education and behaviour change strategies. These staff then need to develop theoretically based, patient centred, ongoing follow up education programmes for people with diabetes. Educational strategies and materials matched to the needs and culture of the community served with attention to health literacy are necessary. Institutional support at the practice, community and health systems is critically important.

Evaluation

Evaluation at the patient level should address behavioural, psychosocial and clinical outcomes. Programmatic measures should include numbers of people reached, patient and educator processes and outcomes and costs. Evaluation should be ongoing and programme dynamics continuously adapted based on findings.

Potential indicator

Indicator	*Denominator*	*Calculation of indicator*	*Data to be collected for calculation of indicator*
Percentage of people with type 2 diabetes receiving formal diabetes education in one year.	**Total number of people with type 2 diabetes attending the clinic in one year.**	**Number of people with type 2 diabetes receiving formal diabetes education in one year as a percentage of the number of people with type 2 diabetes attending the clinic in one year.**	**Date of receiving formal diabetes education.**

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4 PSYCHOLOGICAL CARE

Recommendations

Recommended care

PS1 In communicating with a person with diabetes, adopt a whole-person approach and respect that person's central role in their care (see Chapter 3: Education and Chapter 5: Lifestyle management). Communicate non-judgementally and independently of attitudes and beliefs.

PS2 Explore the social situation, attitudes, beliefs and worries related to diabetes and self-care issues. Assess well-being (including mood and diabetes distress), periodically, by questioning or validated measures (e.g. WHO-5 [1]). Discuss the outcomes and clinical implications with the person with diabetes, and communicate findings to other team members where appropriate.

PS3 Counsel the person with diabetes in the context of ongoing diabetes education and care.

PS4 Refer to a mental health-care professional with a knowledge of diabetes when indicated. Indications may include: severe coping problems, signs of major depression, anxiety disorder, personality disorder, addiction and cognitive decline.

Limited care

PS_L1 The communication principles as for Recommended care.

PS_L2 Be alert to signs of cognitive, emotional, behavioural and/or social problems which may negatively impact quality of life and complicate self-care, particularly where diabetes outcomes are sub-optimal.

PS_L3 Refer for mental health specialist advice according to local availability of such professionals.

Comprehensive care

PS_c1 The communication principles as for Recommended care.

PS_c2 A mental health specialist (psychologist) would be included in the multidisciplinary diabetes care team.

PS_c3 Periodic assessment and subsequent discussion would be as for *Recommended care*, but could use additional measures [2-4] and computer-based automated scoring systems. The mental health specialist in the team would be able to provide a more comprehensive (neuro)psychological assessment, if indicated.

PS_c4 Counselling would be as for *Recommended care*, but the mental health specialist in the team would be available to offer psychological counselling/ psychotherapy, to participate in team meetings, and to advise other team members regarding behavioural issues.

Rationale

Psychological well-being is itself an important goal of medical care, and psychosocial factors are relevant to nearly all aspects of diabetes management. It is important to acknowledge that well-being encompasses both physical and mental health. Being diagnosed with diabetes imposes a life-long psychological burden on the person and his/her family. Having diabetes can be seen as an additional risk factor for developing psychological problems. Indeed there is evidence that the prevalence of mental health problems in individuals with diabetes exceeds that found in the general population. Diabetes doubles the risk of developing depression [5]. Poor psychological functioning causes suffering, and can seriously interfere with daily diabetes self-management, with subsequent poor medical outcomes and high costs [6-8]. A stepped care approach, with systematic monitoring of well-being in place, can help to identify mild and serious psychological problems and offer appropriate treatment [9].

All diabetes professionals can assist patients in coping with the burden of diabetes and help resolve behavioural and psychological issue, as part of ongoing diabetes care and education. More serious psychological problems warrant referral to mental health specialists.

Evidence-base

Psychosocial aspects of diabetes care are included (to varying extents) in the guidelines from the Canadian [10], SIGN [11], NICE [12], Australia [13] and in the American Diabetes Association (ADA) standards of care [14]. Evidence-based guidelines for psychosocial care in adults with diabetes have been published under the auspices of the German Diabetes Association (DDG), indicating the level of evidence for psychological interventions in different problem areas [15]. The need for systematic evaluation of the patient's psychological status is underscored by the finding that depression is highly prevalent among people with diabetes but remains undiagnosed in 30-50% of the cases [16].

A systematic review and meta-analysis confirmed the efficacy of both anti-depressant medication and psychological therapy in people with type 1 and type 2 diabetes and co-morbid major depression, in terms of depression and glycaemic control [17]. Largest effect sizes were reported for psychological therapies, in particular cognitive behaviour therapy [18]. An RCT showed that web-based guided self-help centred on cognitive behaviour therapy for people with type 1 and type 2 diabetes with mild to moderately severe depression is effective [19]. There is growing evidence that psychological counselling can contribute to improved adherence and psychological outcomes in people with diabetes [20]. A systematic review and meta-analysis has shown that, overall, psychological interventions are effective in improving glycaemic control in type 2 diabetes [21].

Consideration

People coping with diabetes are more likely to be affected by mental health problems, and self-management is likely to be more difficult in the presence of such disorders. Detection of emotional problems in relatively brief consultations with diabetes professionals is likely to be problematic without a formal or structured approach. Lastly there is a clear need for some basic training for diabetes professionals in management issues in this area, and for appropriate referral pathways to mental health specialists with a knowledge of diabetes for people more seriously affected.

Implementation

Agreement on the importance of psychological factors, and the underpinning philosophy of empowerment of people with diabetes, implies agreement within the care team on the relevance of psychological issues in diabetes. Research has shown that with some training in communication skills and discussing psychological issues with patients, annual monitoring of well-being using short questionnaires can be successfully implemented in routine diabetes care across countries [22]. Psychological assessment tools (e.g. WHO-5 [1] are freely available to diabetes teams, and health-care professionals can be trained in applying assessment and monitoring procedures. Collaboration with mental health specialists who already have an interest in diabetes can help to extend the education and raining of other mental health specialists in relation to diabetes.

Evaluation

Evaluate by the number of psychological assessments, level of well-being and satisfaction in the managed population over a period of time (overall and by subgroups), and by number of referrals to mental health specialists, indications and outcomes. The training and continuing education of diabetes health-care team members can also be evaluated.

Potential indicator

Indicator	*Denominator*	*Calculation of indicator*	*Data to be collected for calculation of indicator*
Percentage of people with type 2 diabetes formally assessed for well-being in one year.	**Total number of people with type 2 diabetes attending the clinic in one year.**	**Number of people with type 2 diabetes formally assessed for well-being in one year as a percentage of the total number of people with type 2 diabetes attending the clinic in one year.**	**Date of receiving formal well-being assessment.**

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5 LIFESTYLE MANAGEMENT

Recommendations

Recommended care

LS1 Offer lifestyle advice to all people with type 2 diabetes around the time of diagnosis.

LS2 Review and reinforce lifestyle modification yearly and at the time of any treatment change or more frequently as indicated.

LS3 Review and provide ongoing counselling and assessment yearly as a routine, or more often as required or requested, and when changes in medication are made.

LS4 Advise people with type 2 diabetes that lifestyle modification, by changing patterns of eating and physical activity, can be effective in controlling many of the adverse risk factors found in the condition.

LS5 Provide access to a dietitian (nutritionist) or other health-care professional trained in the principles of nutrition, at or around the time of diagnosis, offering an initial consultation with follow-up sessions as required, individually or in groups.

LS6 Individualise advice on food/meals to match needs, preferences, and culture.

LS7 Advise on reducing energy intake and control of foods with high amounts of added sugars, fats or alcohol.

LS8 Match the timing of medication (including insulin) and meals.

LS9 Provide advice on the use of foods in the prevention and management of hypoglycaemia where appropriate.

LS10 Introduce physical activity gradually, based on the individual's willingness and ability, and setting individualised and specific goals.

LS11 Encourage increased duration and frequency of physical activity (where needed), up to 30-45 minutes on 3-5 days per week, or an accumulation of 150 minutes per week of moderate-intensity aerobic activity (50-70% of maximum heart rate).

LS12 In the absence of contraindications, encourage resistance training three times per week.

LS13 Provide guidance for adjusting medications (insulin) and/or adding carbohydrate for physical activity.

Limited care

LS_M1 The principles and content of lifestyle management are as for *Recommended care*.

LS_M2 Nutritional counselling may be provided by someone with training in nutrition therapy, but not necessarily a credentialed dietitian (nutritionist).

Comprehensive care

LS_c1 Advice on lifestyle management will in general be as for *Recommended care*.

LS_c2 Intensive personal counselling might be offered on a regular basis with a health-care professional specifically trained in the principles of nutrition, to facilitate maintenance of lifestyle modifications and support weight reduction or weight maintenance.

LS_c3 Aerobic and resistance training sessions might be available, with individualised testing and education by exercise specialists, and continued support from them.

Rationale

People with type 2 diabetes often have lifestyles (eating and physical activity habits) which contribute to their problem. It is essential they receive help soon after diagnosis to consider how they may modify lifestyle in ways which enable them to take control of their blood glucose, blood lipid and blood pressure, even if they also require pharmacotherapy (see Chapter 9: Glucose control therapy).

Evidence-base

Evidence supports the effectiveness of nutrition therapy and physical activity in the prevention and management of type 2 diabetes [1-4]. This is reflected in the Canadian [5], UK NICE [6] and Australian guidelines [7] as well as the ADA standards of medical care [2,8,9]. Lifestyle modification can be difficult to achieve and maintain [6]. Most lifestyle intervention studies have been short-term, however this is being addressed by the Look AHEAD study [10]. Other considerations include a lack of knowledge about the ongoing contribution of lifestyle measures once medication has been introduced, or what kind of support is required on a continuing basis. The UKPDS initial nutrition intervention was very effective in lowering blood glucose after diagnosis and some people were then able to maintain target glucose control for many years by nutrition modifications alone [11,12].

RCTs and outcomes studies of medical nutrition therapy (MNT) in the management of type 2 diabetes have reported improved glycaemic outcomes (HbA_{1c} decreases of ~1.0-2.0% / 11-22 mmol/mol; range: -0.5-2.6% / -6.5-29 mmol/mol, depending on the duration of diabetes) and level of glycaemic control [1]. MNT in these studies was provided by dietitians (nutritionists) as MNT only or as MNT in combination with diabetes self-management training. Interventions included reduced energy intake and/or reduced carbohydrate/fat intake, carbohydrate counting, and basic nutrition and healthy food choices for improved glycaemic control. Central to these interventions are multiple encounters to provide education initially and on a continued basis [5,9,13-19].

Cardioprotective nutrition therapy (saturated and trans fats less than 7% of daily energy, dietary cholesterol less than 200 mg daily, and a daily fat intake of 25-35%) can reduce total cholesterol by 7-21%, low density lipoprotein (LDL)-cholesterol by 7-22%, and triglycerides by 11-31% [20]. Energy from saturated or trans fatty acids may be replaced by energy from unsaturated fatty acids. If a reduced energy intake is a goal, reduction rather than replacement of saturated

fat energy is recommended. Pharmacological therapy should be considered if goals are not achieved between 3 and 6 months after initiating MNT.

A meta-analysis of studies of non-diabetic people reported that reductions in sodium intake to ≤ 2.4 g/day decreased blood pressure by 5/2 mmHg in hypertensive subjects. Meta-analyses, clinical trials and expert committees support the role of reduced sodium intake, modest weight loss (4-5 kg), increased physical activity, a low-fat diet that includes fruits, vegetables and low-fat dairy products, and moderate alcohol intake, in reducing blood pressure [21].

A systematic review and meta-analysis of exercise (aerobic, resistance training or both) reported an HbA_{1c} reduction of 0.7% / 8 mmol/mol, independent of changes in body weight, in people with type 2 diabetes [22]. In long-term prospective cohort studies of people with type 2 diabetes, higher physical activity levels predicted lower long-term morbidity and mortality and increases in insulin sensitivity. Interventions included both aerobic exercise (such as walking) and resistance exercise (such as weight-lifting) [2,23,24].

The Canadian Diabetes Association and ADA guidelines have a section on the management of obesity in type 2 diabetes, which addresses lifestyle measures and also pharmacotherapy and surgical options [5,9].

In addition to behavioural and medical approaches, various types of surgery on the gastrointestinal tract, originally developed to treat morbid obesity ("bariatric surgery"), constitute powerful options to ameliorate diabetes in severely obese patients, often normalising blood glucose levels, reducing or avoiding the need for medications and providing a potentially cost-effective approach to treating the disease [25]. A recent IDF position paper recommended bariatric surgery should be considered earlier in the treatment of eligible patients to help stem the serious complications that can result from diabetes [26]. Eligible patients include those who have type 2 diabetes and a BMI ≥ 35 kg/m^2; or with a BMI between 30 and 35 kg/m^2 when diabetes cannot be adequately controlled by optimal medical regimen, especially in the presence of other major CVD risk factors.

Consideration

It is noted than in general costs of educational initiatives to change lifestyle are low, because unlike pharmacotherapy they are provided on an intermittent rather than continuing basis. From a health-provider perspective many of the costs fall outside their budget, healthier foods and exercise programmes and equipment generally being a cost met directly by the person with diabetes. For these reasons, and because, for glucose control, the gain from lifestyle modification is greater than that from any individual therapy, lifestyle measures are heavily promoted. Lifestyle modification is, however, sometimes difficult for the individual to maintain in the long-term, or to develop further after early changes have been made. Where professional nutritionists are unavailable, it was noted that other health-care professionals should be trained in basic nutritional and other lifestyle education.

Implementation

Recognition of the importance and cost-effectiveness of lifestyle interventions should drive allocation of resources required for care and self-management training. Implementation demands knowledgeable and competent personnel, and dietitians/nutritionists and other health-care professionals may require training to be effective providers of lifestyle interventions.

Consistency of approach to lifestyle issues across the diabetes care team is an important principle. A process is needed to enable people to gain access to services as required.

Self-management counselling in nutrition (for individuals or groups) has four components:
1. assessment; 2. identification of the nutrition problem; 3. intervention that integrates nutrition therapy into overall diabetes management and implementation of self-management training; and 4. nutrition monitoring and evaluation of outcomes. A similar approach needs to be taken for physical activity. Development of educational materials, or adaptation of them from elsewhere, is needed.

Evaluation

Services should be able to show the availability of appropriately trained personnel, and records that individuals with diabetes have contact with them around the time of diagnosis and at regular intervals thereafter. Educational support materials should also be demonstrable. Outcomes can be assessed in terms of improvement in appropriate food choices and amounts, and responses to questioning about physical activity levels and, where appropriate, alcohol consumption. Metabolic measures are, however, likely to be confounded by changes in pharmacotherapies.

Potential indicator

Indicator	*Denominator*	*Calculation of indicator*	*Data to be collected for calculation of indicator*
Percentage of people with type 2 diabetes receiving MNT counseling in one year.	**Total number of people with type 2 diabetes attending the clinic in one year.**	**Number of people with type 2 diabetes receiving MNT counseling in one year as a percentage of the number of people with type 2 diabetes attending the clinic in one year.**	**Date of receiving MNT counseling.**

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6 GLUCOSE CONTROL LEVELS

Recommendations

Recommended care

TT1 **Advise people with diabetes that maintaining an HbA_{1c} below 7.0% / 53 mmol/mol minimises the risk of developing complications.**

TT2 **A lower HbA_{1c} target may be considered if it is easily and safely achieved.**

TT3 **A higher HbA_{1c} target may be considered for people with co-morbidities or when previous attempts to optimise control have been associated with unacceptable hypoglycaemia.**

TT4 **An individual's HbA_{1c} target should be regularly reviewed taking into account benefits, safety and tolerability.**

TT5 **Treatment should be reviewed and modified if HbA_{1c} level is above the agreed target on two consecutive occasions.**

TT6 **Advise those in whom target HbA_{1c} levels cannot be reached that any improvement is beneficial.**

TT7 **Equivalent values for HbA_{1c} and capillary plasma glucose are as follows:**

	Normal	Target
HbA_{1c}	< 6.0% / 42 mmol/mol	< 7.0% / 53 mmol/mol
Fasting/pre-meal capillary plasma glucose	5.5 mmol/l (100 mg/dl)	6.5 mmol/l (115 mg/dl)
Post meal capillary plasma glucose	7.8 mmol/l (140 mg/dl)	9.0 mmol/l (160 mg/dl)

Limited care

TT_L1 **The principles are as for *Recommended care* including assessment of diabetes control by HbA_{1c} measurement. In very limited settings diabetes control may need to be based on measurement of plasma glucose levels alone.**

Comprehensive care

TT_C1 **The principles are as for *Recommended care* but it may be possible to devote more resources to achieving lower target levels without adverse impact on health.**

Glucose measurement

Plasma glucose is the preferred measure of most modern laboratories. Whole blood gives lower readings due to the volume occupied by haemoglobin. Capillary blood glucose strips measure the glucose in the plasma of the capillary blood sample, but may be calibrated to give results either as plasma or sometimes whole blood glucose (check meter instructions).

Rationale

The UKPDS confirmed the importance of glucose control in prevention of complications in people with type 2 diabetes [1]. The issue then arises as to the desirable level of plasma glucose control to be achieved. In an ideal world this would be 'normal', but if the available lifestyle and pharmaceutical therapies are less than optimal in terms of efficacy and adverse effects on quality of life (health gain versus health cost), or if these therapies are expensive, then some compromise (varying between individuals and health-care systems) will be needed. The chosen measures of glucose control (HbA_{1c} and self-monitoring) are discussed elsewhere (see Chapter 7: Clinical monitoring and Chapter 8: Self-monitoring). This section deals with target levels.

The concept of targets is open to criticism – they may be unattainable, they may limit what could be attained, and they may be uneconomic to attain. However, without some form of targeted control of an asymptomatic condition it becomes difficult to promote care at all. Targets are often better thought of as 'intervention levels'.

Evidence-base

Guidelines vary in their recommended general HbA_{1c} target but most recommend a target of 7.0% / 53 mmol/mol measured by a DCCT-aligned assay [1,2,3]. Other guidelines have recommended a lower HbA_{1c} target of 6.5% / 48 mmol/mol [4]. The evidence for a target level of control has infrequently been the subject of RCTs. Intervention studies which have achieved and maintained constant HbA_{1c} levels throughout the study period can inform the question of optimal HbA_{1c} targets. However results may be confounded by differences in the therapies used in different treatment arms. Epidemiological analyses of RCTs [5] can also be informative in setting targets.

The UKPDS reported that in people with newly diagnosed type 2 diabetes, the intensively treated group which achieved a median HbA_{1c} of 7.0% / 53 mmol/mol over the 10 year follow-up period, experienced significantly less microvascular complications and the composite any diabetes-related end-point but just failed to show a reduction in myocardial infarction (MI) (16% reduction, p=0.052) compared with the conventionally treated group which achieved a median HbA_{1c} of 7.9% / 63 mmol/mol [6]. The UKPDS post-trial monitoring study confirmed risk reduction persisted for another 10 years for any diabetes-related end point and microvascular disease, and significant risk reductions for MI and death from any cause emerged in the intensive sulfonylurea-insulin group [7].

The Kumamoto study [8] in non-obese insulin-requiring Japanese people with type 2 diabetes achieved and maintained during the 6 year study period a mean HbA_{1c} of 7.1% / 54 mmol/mol in the intensively treated group compared with a mean HbA_{1c} of 9.4% / 79 mmol/mol in the conventionally treated group.

Intensive treatment resulted in less retinopathy, nephropathy and neuropathy compared with the conventional treatment.

The ACCORD study [9] achieved a median HbA_{1c} of 6.4% / 46 mmol/mol and 7.5% / 58 mmol/mol in the intensive- and standard-therapy groups, respectively. No significant difference in the primary macrovascular outcome was observed. However two secondary outcomes were significant – an increase in mortality and a decrease in non-fatal MI were observed in the intensively treated group. For microvascular complications, neither the first (dialysis or renal transplantation, high serum creatinine, retinal photocoagulation or vitrectomy) nor second composite outcome (first composite outcome plus peripheral neuropathy) were significantly different. However intensive therapy delayed the onset of albuminuria and some measures of eye complications and neuropathy [10]. The ADVANCE study [11] achieved a mean HbA_{1c} of 6.5% / 48 mmol/mol in the intensive-control group and 7.3% / 56 mmol/mol in the standard-control group. There was no significant difference in major macrovascular outcomes or death between the groups, but major microvascular events were significantly reduced in the intensive-control group, primarily due to a reduction in the incidence of nephropathy. In the VADT study, the median HbA_{1c} was 6.9% / 52 mmol/mol in the intensive-therapy group and 8.4% / 68 mmol/mol in the standard-therapy group. There was no difference in the primary outcome or in microvascular complications, although there was a significant decrease in albuminuria in the intensive-therapy group [12].

Better glycaemic control is important to minimise diabetes-related microvascular and macrovascular complications. However recent studies have failed to provide conclusive results in favour of tight versus standard glycaemic control and adding additional glucose-lowering therapy below 7.0% / 53 mmol/mol is of limited efficacy and consequently cost-ineffective. Little evidence therefore supports improved outcomes to below an HbA_{1c} target of 7.0% / 53 mmol/mol. Consequently the IDF has changed the general HbA_{1c} target from 6.5% / 48 mmol/mol to 7.0% / 53 mmol/mol.

Translation of HbA_{1c} levels into self-monitored capillary plasma glucose levels is not simple. The upper level of FPG is usually taken as 5.5 mmol/l (100 mg/dl), which might then equate with a DCCT-aligned HbA_{1c} of 6.0% / 42 mmol/mol. Studies with newer insulins achieving pre-breakfast glucose levels of ~6.0 mmol/l (~110 mg/dl) typically return DCCT-aligned HbA_{1c} results of ~7.0% / 53 mmol/mol [13], but glucose profiles in these studies show rising glucose levels through the day, explaining the inconsistency. Regression equations between capillary-measured plasma glucose and HbA_{1c} are now better established [14]. These findings appear most consistent with an FPG of 6.5 mmol/l (~115 mg/dl), and post-prandial of 9.0 mmol/l (~160mg/dl).

The case for targeting post-prandial blood glucose control can be made on many grounds, none of them soundly RCT-based, but supported by careful review of the broader evidence-base [15]. Overall the case is compelling, not least by the simple logical observation that the outcome trials have established the utility of lowering blood glucose levels overall, while the highest levels of the day are generally after meals. That post-prandial levels may be particularly pathophysiological for the endothelium is generally based on arguments around 2 hour OGTT post-challenge glucose concentrations rather than post-prandial levels. However post-challenge levels seem closely related to other cardiovascular risk factors.

Consideration

The assessment/intervention level has been taken as a DCCT-aligned HbA_{1c} of 7.0% / 53 mmol/mol, with a target level less than that if easily achieved. This is taken as translating to basal self-monitored plasma glucose levels < 6.5 mmol/l (< 115 mg/dl), with post-prandial target levels of < 9.0 mmol/l (< 160 mg/dl).

A higher HbA_{1c} target may be appropriate in people with co-morbidities, when previous attempts to optimise control have been associated with unacceptable hypoglycaemia or when there is a high risk associated with possible hypoglycaemia. These situations more often apply to older people.

Implementation

These intervention levels and targets should be incorporated in local protocols and guidelines detailing methods for evaluating and advising on lifestyle and pharmaceutical therapies as the natural history of the condition evolves.

Evaluation

Glucose targets (as given above) should be present in local guidelines and protocols. Audit is of attained glucose control on different types of therapy.

Potential indicators

Indicator	*Denominator*	*Calculation of indicator*	*Data to be collected for calculation of indicator*
Percentage of people with type 2 diabetes with HbA_{1c} < 7.0% / 53 mmol/mol.	**Total number of people with type 2 diabetes attending the clinic in one year with at least one HbA_{1c} measurement.**	**Number of people with type 2 diabetes with HbA_{1c} < 7% / 53 mmol/mol as a percentage of those having at least one HbA_{1c} value measured in the past year.**	**Most recent HbA_{1c} measurement in the past year.**
Percentage of people with type 2 diabetes with HbA_{1c} ≥ 9.0% / 75 mmol/mol.	**Total number of people with type 2 diabetes attending the clinic in one year with at least one HbA_{1c} measurement.**	**Number of people with type 2 diabetes with HbA_{1c} ≥ 9.0% / 75 mmol/mol as a percentage of those having at least one HbA_{1c} value measured in the past year.**	**Most recent HbA_{1c} testing in the past year.**

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7 CLINICAL MONITORING

Recommendations

Recommended care

M01 Monitor blood glucose control by measuring HbA_{1c} using high-precision methods standardised to criteria aligned to the international reference values and subject to stringent quality assurance testing when no conditions are present in a patient that would preclude its accurate measurement.

M02 Measure HbA_{1c} every 2 to 6 months depending on level, stability of blood glucose control and changes in therapy.

M03 Report HbA_{1c} results in both DCCT-aligned units (%) and International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) units (mmol HbA_{1c} per mol unglycated haemoglobin).

M04 Provide HbA_{1c} result, measured either at site-of-care or in the laboratory, before the clinical consultation.

M05 Abnormal haemoglobins may affect the values obtained for HbA_{1c} in some assays. To determine whether abnormal haemoglobins are present, use high-performance liquid chromatography (HPLC) or mass spectrometry.

M06 If HbA_{1c} is invalid, measure blood glucose or fructosamine to monitor diabetes control. HbA_{1c} can be falsely low or high in certain patients if it is affected by abnormal haemoglobin turnover, the presence of variant haemoglobins, co-existing illnesses such as haematological disorders, renal or liver disease, or the effect of some drugs.

M07 Fructosamine should not be used as a routine substitute for HbA_{1c} measurement. It should not be used if a patient has proteinuria.

M08 Estimated average glucose ([eAG] reported in either mmol/l or mg/dl) is derived from HbA_{1c}. Only a few countries have chosen to report eAG due to its limitations and lack of applicability to all ethnic groups. It may help people with diabetes relate their HbA_{1c} to daily glucose monitoring levels or highlight when HbA_{1c} is inappropriate.

M09 Measure blood glucose when patients are hospitalised, either at site-of-care or in the laboratory. Site-of-care capillary blood glucose meters should be monitored by certified quality assurance schemes. Ascertain whether meters are calibrated against plasma or blood.

Limited care

MO_L1 If HbA_{1c} measurement is not available, blood glucose could be used for clinical monitoring measured either at site-of-care or in the laboratory.

MO_L2 Site-of-care capillary blood glucose meters should be quality controlled by certified quality assurance schemes or by reference to laboratory methods.

MO_L3 Visually read glucose test strips have a role in emergency and remote situations where maintenance of functional meters is not possible.

Comprehensive care

MO_C1 The principles are as for *Recommended care*, but continuous glucose monitoring is an additional option in the assessment of glucose profiles in people with consistent glucose control problems, or with problems of HbA_{1c} estimation.

MO_C2 HbA_{1c} measurement would be available at each visit, and provided in electronic or paper diary form to the person with diabetes.

Rationale

Type 2 diabetes results in progression of hyperglycaemia with time, and causes organ damage through controllable hyperglycaemia. Accordingly glycaemic control needs to be monitored. Some of this will be performed by the person with diabetes with glucose measurements (see Chapter 8: Self monitoring), some by site-of-care tests and some by laboratory methods.

Evidence-base

Major national guidelines now address this area in detail [1-3]. There are recommendations for patients with stable control or those requiring adjustments to their treatment regimen. Laboratory guidelines and other publications address available methods and their quality implementation [4-6].

The central role for the HbA_{1c} assay largely derives from its position in the reports of the major outcomes studies (the DCCT [7], the UKPDS [8], ACCORD [9], ADVANCE [10] and VADT [11]). HbA_{1c} provides the main method by which clinicians can relate individual blood glucose control to risk of complication development and its measurement is mandatory where affordable/available and appropriate for a particular patient.

The laboratory and site-of-care HbA_{1c} assays are precise and are now aligned to an international reference method [12]. This important development has lead to changes in the reporting of HbA_{1c}. Consensus statements from the various international, professional diabetes and clinical chemistry organisations [13,14] have recommended reporting of IFCC units (mmol HbA_{1c} per mol unglycated haemoglobin). A number of countries continue to report DCCT aligned values (%), especially in this transition period, to familiarise health care professionals with the new IFCC units.

The introduction of continuous ambulatory blood glucose monitoring technology has permitted researchers to introduce the concept of eAG, estimated average glucose [15]. A combination of results from continuous and frequent self blood glucose monitoring correlated strongly with HbA_{1c} (r = 0.92) in 507 adults (83% Caucasian). A calculator is now available for converting HbA_{1c} to eAG in both mmol/l and mg/dl. Although reporting of this measure was recommended in the 2007 consensus statement [13], it was not supported in the 2010 statement [14]. eAG reporting is being introduced in some but not all countries because of reservations about its applicability. eAG may help people with diabetes relate their HbA_{1c} to daily glucose monitoring [5] or highlight situations where HbA_{1c} is inaccurate relative to glucose due to conditions that affect the accuracy of HbA_{1c}.
Some issues still surround HbA_{1c} measurement, mostly problems affecting haemoglobin turnover or structure, but other factors can confound results [16]. Normal variation in red blood cell indices can affect HbA_{1c} in a manner that is clinically significant with regard to diabetic control [17]. Information on the extent to which abnormal haemoglobins, co-existing illnesses such as haematological, renal or liver diseases, and drugs or other factors affect the accuracy of HbA_{1c} is sparse. It is important to review haematological parameters as a high reticulocyte count leading to increased red cell turnover (e.g. in patients with polycythaemia rubra vera) can decrease HbA_{1c} [18] and iron deficiency increases HbA_{1c} [19].

HPLC-based assays are recommended in order to detect haemoglobin variants. In some laboratories HbA_{1c} is reported in a heterozygous patient with a variant haemoglobin and haemoglobin A with a comment saying that results may not be comparable to the DCCT/UKPDS and in other laboratories the HbA_{1c} result is not reported. A review of patients with fetal haemoglobin > 5% detected on HbA_{1c} measurement, showed the presence of conditions that preclude accurate HbA_{1c} [20]. Its measurement is not recommended in patients with thalassaemias [21]. Abnormal haemoglobins that co-elute with HbA_{1c} on HPLC affecting reporting have been described recently in people with diabetes [22,23].

In situations where the accuracy of HbA_{1c} is compromised, a marked discrepancy between HbA_{1c} and measured glucose will be apparent. In these situations, measurement of fructosamine should be considered. However fructosamine reflects glycation of albumin and health care professionals should be aware that it may be decreased when albumin turnover or excretion is increased although reports on the extent of this problem are scarce [24-26].

Random clinic plasma glucose testing is not seen as having a role in quality diabetes care, however in some situations it may be the only option. When HbA_{1c} is unavailable or inappropriate, timed glucose levels are often recommended as a substitute but it is important to follow recommendations on quality control for the devices used for site-of-care testing (see Chapter 8: Self-monitoring).

Continuous ambulatory blood glucose monitoring has become available in recent years and has been recommended in conjunction with intensive insulin regimen to improve glycaemic control in selected people with type 1 diabetes [27]. However, there is no good evidence-base for its routine use in people with type 2 diabetes [29].

Blood glucose measurements should be available from meters situated on hospital wards [29]. Measurement of glucose on admission is necessary to identify hypoglycaemia or hyperglycaemia and to provide appropriate patient care. Confirmation of meter values for patients with hypoglycaemia or

hyperglycaemia by laboratory measurement is necessary and fasting samples are required in some circumstances for the ongoing care of particular patients.

Consideration

HbA_{1c} measurement is pivotal to assessment of glycaemic control, performed either in the laboratory or at site-of-care. There is ongoing change to reporting of HbA_{1c} from DCCT aligned to IFCC units from the international reference method. The use of the derived eAG based on the relationship of continuous and self monitored blood glucose to HbA_{1c} remains under consideration but its reporting has not been recommended in many countries because of its limited applicability and more research has been recommended. It may be useful in particular situations. The role of continuous glucose monitoring is recommended for certain patients.

Implementation

There should be access to a laboratory or site-of-care test monitored by certified quality assurance schemes for measurement of HbA_{1c}. People in whom HbA_{1c} measurement is inappropriate must be identified by careful review of haematological parameters, detection of haemoglobinopathies and other factors that can affect HbA_{1c} values. Organisation to allow site-of-care or prior-to-visit sampling is also needed.

Provision of capillary blood glucose meters and strips needs to be assured in hospitals and clinics. It is important to ascertain whether there are contraindications for use of a meter in a particular patient e.g. conditions that affect capillary circulation. In addition, some meters cannot be used if patients are on peritoneal dialysis or intravenous [IV] solutions containing icodextrin due to interference with readings (see information accompanying meters). It is essential to establish whether meters report values for plasma or blood and to ensure that schemes for monitoring the quality of their output are in place. Blood glucose meters may use a coding chip or code entry to ensure that the meter is calibrated to the batch of strips used. Use of blood glucose meters in hospitals should be restricted to trained personnel.

Evaluation

There should be records in patient files of HbA_{1c} results obtained from site-of-care or laboratory methods with stringent quality assurance testing.

Potential indicators

Indicator	*Denominator*	*Calculation of indicator*	*Data to be collected for calculation of indicator*
Percentage of people with type 2 diabetes with at least 1 HbA_{1c} measurement in the year.	**Total number of people with type 2 diabetes seen in the year.**	**Number of people with type 2 diabetes having at least 1 HbA_{1c} measurement in the year as a percentage of the total number of people with type 2 diabetes seen in the year.**	**Dates of all HbA_{1c} measurements performed in the year.**
Percentage of people with type 2 diabetes with no HbA_{1c} measurement in the year.	**Total number of people with type 2 diabetes seen in the year.**	**Number of people with type 2 diabetes with no HbA_{1c} measurement in the year as a percentage of the total number of people with type 2 diabetes seen in the year.**	**Dates of all HbA_{1c} measurements performed in the year.**

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8 SELF-MONITORING

Recommendations

Recommended care

SM1 Self-monitoring of blood glucose (SMBG) should only be made available to people with diabetes when they have the knowledge, skills and willingness to use the information obtained through testing to actively adjust treatment, enhance understanding of diabetes and assess the effectiveness of the management plan on glycaemic control.

SM2 The purpose(s) of performing SMBG and using SMBG data should be agreed between the person with diabetes and the health-care provider.

SM3 SMBG on an ongoing basis should be available to those people with diabetes using insulin.

SM4 SMBG should be considered for people using oral glucose lowering medications as an optional component of self-management, and in association with HbA_{1c} testing:

- To provide information on, and help avoid, hypoglycaemia.
- To assess changes in blood glucose control due to medications and lifestyle changes.
- To monitor the effects of foods on postprandial glycaemia.
- To monitor changes in blood glucose levels during intercurrent illness.

SM5 Regular use of SMBG should not be considered part of routine care where diabetes is well controlled by nutrition therapy or oral medications alone.

SM6 SMBG protocols (intensity and frequency) should be individualised to address each individual's specific educational/behavioural/clinical requirements, and provider requirements for data on glycaemic patterns to monitor therapeutic decision making.

SM7 Structured assessment of self-monitoring skills, the quality and use made of the results obtained, and of the equipment used, should be made annually.

Limited care

SM_L1 SMBG using meters with strips, or visually read blood glucose strips, should be considered for people with diabetes using insulin.

Comprehensive care

SM_C1 The principles are as for *Recommended care*, but SMBG could be offered to all people with type 2 diabetes irrespective of treatment as part of a comprehensive and ongoing education and therapeutic programme.

SMc2 Continuous glucose monitoring could be considered in insulin treated people with type 2 diabetes

Rationale

SMBG is used in the care plans of many people with type 2 diabetes, although there is wide variability in access between countries [1]. SMBG has the potential to provide real-time feedback of blood glucose levels. Visually read test strips are no longer considered adequate for routine use and self testing should be carried out with blood glucose meters. Its use can be considered in relation to:

- Outcomes (achieving a decrease in HbA_{1c} with the ultimate aim of decreasing risk of complications).
- Safety (identifying hypoglycaemia).
- Process (education, self-empowerment, changes in therapy).

Self-monitoring should only be considered when the person with diabetes is prepared to learn the skills, record the findings, understand the data and act appropriately on the data.

The IFCC have proposed that plasma rather than blood glucose values should be reported by blood glucose meters (blood glucose x 1.1 = plasma glucose). The same type of meter may be calibrated to report blood glucose in one country and plasma values in another. Until this issue is resolved, the calibration of a meter should be checked and the thresholds for action set accordingly.

Urine glucose testing is cheap but has limitations. Urine free of glucose is an indication that the blood glucose level is below the renal threshold, which usually corresponds to a plasma glucose level of about 11.0 mmol/l (198 mg/dl). Positive results do not distinguish between moderately and grossly elevated levels, and a negative result does not distinguish between normoglycaemia and hypoglycaemia.

Evidence-base

The evidence-base for SMBG is summarised in IDF and national guidelines [2-6]. Major clinical trials of people with insulin-treated diabetes demonstrating improvements in diabetic complications from intensive glycaemic control have included SMBG as part of a multifactorial intervention. SMBG is thus an integral component of effective therapy for type 1 diabetes [7]. Studies in insulin treated people with type 2 diabetes also suggest that SMBG is required to titrate the insulin dose whilst avoiding hypoglycaemia, although the optimal regimen is not clear [8]. For most people with type 1 diabetes and pregnant women taking insulin, SMBG is recommended three or more times daily when intensive glycaemic control is required. More frequent testing may be required to reach HbA_{1c} targets safely without hypoglycaemia.

Optimal use of SMBG for people with non-insulin treated type 2 diabetes remains unclear [2]. A recent meta-analysis of non-insulin treated people with type 2 diabetes concluded that SMBG was associated with a reduction in HbA_{1c} of 0.2% / 2 mmol/mol [9]. However, many of the studies included in this analysis also included patient education with diet and exercise counselling and in some cases pharmacologic intervention. Some [10], but not all [11], observational studies have also found evidence for improvements in glycaemic control with more frequent monitoring, but these studies are also unable to separate out the impact of patient motivation from testing. Recent trials have called into question the clinical utility and cost-effectiveness of routine SMBG in well-controlled non-insulin treated patients [12-14].

There are many unresolved questions about SMBG, including frequency and timing of testing, its value in new users and ongoing users, and if and how users act on the results. It is clear however, that SMBG should only be used as part of a structured self-management programme and when it serves an identified purpose in self management. For example, a recent trial demonstrated an improvement of 0.3% / 3mmol/mol in HbA_{1c} over six months in a group using SMBG to titrate oral glucose lowering medication, compared with a group receiving usual care [15]. In patients unable to achieve target HbA_{1c}, characterising the extent of hyperglycaemia 1 to 2 hours after a meal should aim to reduce post-meal levels below 9.0mmol/l (160mg/dl) [16].

There are limited data on the impact of SMBG on quality of life and treatment satisfaction. No differences were found in diabetes treatment satisfaction between groups using or not using SMBG [17,18]. One study found a significant increase in depression [14] and another noted a negative impact on overall quality of life [13]. Patients carrying out SMBG can become discouraged and less motivated, particularly if health professionals do not take an interest in the test results [19].

There are few data on self-monitoring using urine glucose testing. A meta-analysis from 2005 [20] included two studies which compared SMBG and self-monitoring of urine glucose and reported a non-significant reduction in HbA_{1c} of 0.2% / 2 mmol/mol in favour of SMBG. Urine testing may have a place for some people where there is limited availability of SMBG.

Consideration

SMBG is accepted as an integral part of self-management of people on insulin therapy. However, the data are less clear for people who are not being treated with insulin, and therefore the decision as to whether to recommend SMBG for individuals in this group will largely be determined by personal preferences, cost and individual and health-care system resources. Priority lists may be needed to decide which individuals should be offered SMBG. These might include people recently diagnosed with diabetes, those with more erratic lifestyles, people having problems of hypoglycaemia and those particularly keen to tighten their blood glucose control. There is no evidence to support routine use of SMBG in well controlled patients using lifestyle management alone. There is little evidence to support the use of urine testing.

Implementation

Provision should be made for the supply of glucose strips on a continuing basis to people with diabetes. When providing meters, education in their use and in interpretation of the results should be given. Review of technique, data interpretation and meter function should be a part of the Annual Review (see Chapter 2: Care delivery).

Evaluation

Provision of self-monitoring education and equipment should be assessed, and protocols and a record of review as part of the Annual Review should be available. There should be evidence of the results being made use of by the person with diabetes and in other clinical consultations with health-care professionals.

Potential indicator

Indicator	*Denominator*	*Calculation of indicator*	*Data to be collected for calculation of indicator*
Percentage of people with insulin treated diabetes routinely performing SMBG.	**Total number of people with insulin treated type 2 diabetes seen in the year.**	**Number of people with insulin treated type 2 diabetes routinely performing SMBG as a percentage of the total number of people with insulin treated type 2 diabetes seen in the year.**	**Routine use of SMBG by people with insulin treated diabetes.**

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9 GLUCOSE CONTROL THERAPY

Recommendations

Recommended care

GC1 Begin oral glucose lowering medications when lifestyle interventions alone are unable to maintain blood glucose control at target levels (see Chapter 6: Glucose control levels).
Maintain support for lifestyle measures throughout the use of these medications.
Consider each initiation or dose increase of an oral glucose lowering medications as a trial, monitoring the response in 3 months.
Consider cost and benefit:risk ratio when choosing a medication.
Consider discontinuing ineffective therapies.

GC2 FIRST-LINE THERAPY
Begin with metformin unless there is evidence of renal impairment or other contraindication.
Titrate the dose over early weeks to minimise discontinuation due to gastrointestinal intolerance.
Monitor renal function and use metformin with caution if estimated glomerular filtration rate (eGFR) < 45 ml/min/1.73 m^2.
Other options include a sulfonylurea (or glinide) for rapid response where glucose levels are high, or a-glucosidase inhibitors in some populations; these agents can also be used initially where metformin cannot.
In some circumstances dual therapy may be indicated initially if it is considered unlikely that single agent therapy will achieve glucose targets.

GC3 SECOND-LINE THERAPY
When glucose control targets are not being achieved, add a sulfonylurea.
Other options include adding metformin if not used first-line, an a-glucosidase inhibitor, a dipeptidyl peptidase 4 (DPP-4) inhibitor or a thiazolidinedione.
A rapid-acting insulin secretagogue is an alternative option to sulfonylureas.

GC4 THIRD-LINE THERAPY
When glucose control targets are no longer being achieved, start insulin or add a third oral agent.
If starting insulin, add basal insulin or use premix insulin (see below).
If adding a third oral agent options include an a-glucosidase inhibitor, a DPP-4 inhibitor or a thiazolidinedione.
Another option is to add a glucagon-like peptide-1 receptor agonist (GLP-1 RA).

GC5 FOURTH-LINE THERAPY
Begin insulin therapy when optimised oral blood

glucose lowering medications (and/or GLP-1 RA) and lifestyle interventions are unable to maintain target glucose control.
Intensify insulin therapy is already using insulin.

GC6 INSULIN THERAPY

Do not unduly delay the commencement of insulin.
Maintain lifestyle measures, support for work and activities of daily living and after introduction of insulin.
Consider every initiation or dose increase of insulin as a trial, monitoring the response.
Explain to the person with diabetes from the time of diagnosis that insulin is one of the options available to manage their diabetes, and that it may turn out to be the best, and eventually necessary, way of maintaining glucose control, especially in the longer term.
Provide education (see Chapter 3: Education) and appropriate self-monitoring (see Chapter 8: Self-monitoring).
Explain that starting doses of insulin are low, for safety reasons, but that eventual dose requirement is expected to be 30-100 units/day.
Continue metformin. Other oral agents may also be continued.
Begin with:

- A basal insulin once daily such as neutral protamine Hagedorn (NPH) insulin, insulin glargine or insulin determir;
- Once or twice daily premix insulin (biphasic insulin).

Initiate insulin using a self-titration regimen (dose increases of two units every 3 days) or with biweekly or more frequent contact with a health-care professional.
Aim for pre-meal glucose levels of < 6.5 mmol/l (< 115 mg/dl).
Monitor glucose control for deterioration and increase dose to maintain target levels or consider transfer to a basal plus mealtime insulin regimen.

Limited care

GCL1 The principles are as for *Recommended care* taking particular note of cost and availability of generic therapies.

GCL2 Less expensive human insulins can give most of the health care gains achievable with insulin therapy.

GCL3 Insulin supplies should be assured and be of consistent quality and type.

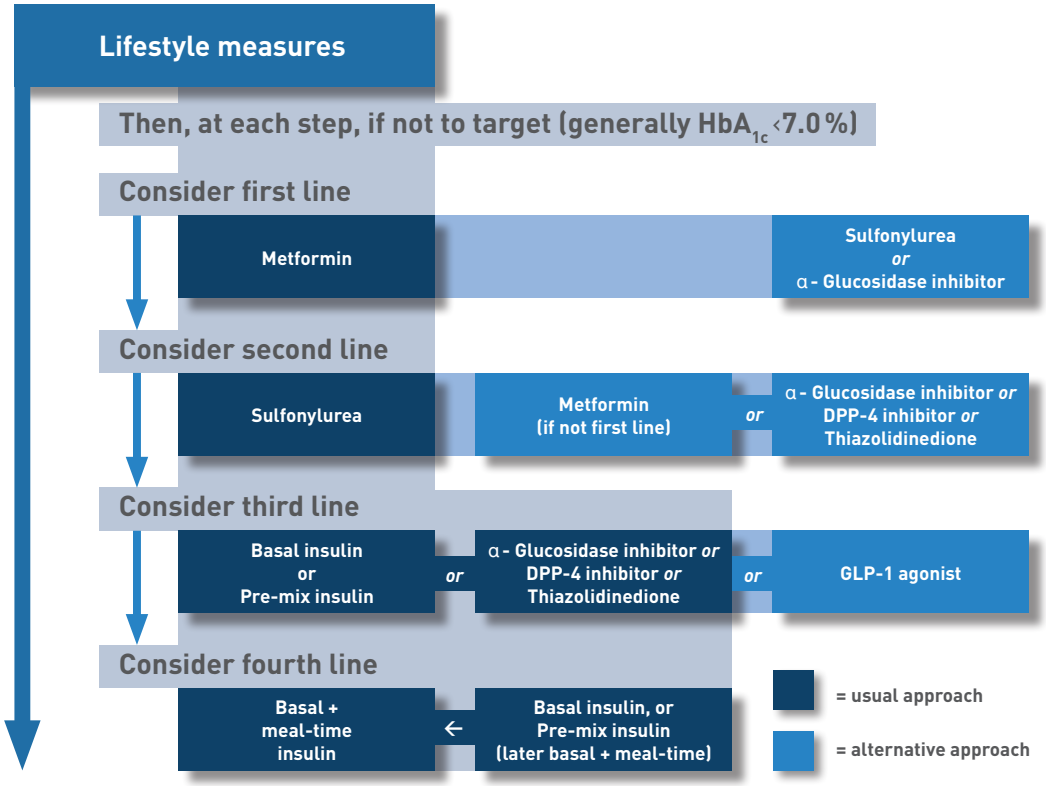
Comprehensive care

GC_c1 The principles are as for *Recommended care*.

GC_c2 Metformin remains the first-line therapy choice, unless contraindicated. More expensive therapies, and insulin, may be considered earlier in the treatment sequence.

GC_c3 Insulin pump therapy is an additional option.

Treatment algorithm for people with type 2 diabetes



Rationale

The evidence that elevated blood glucose levels can result in various forms of vascular damage is discussed elsewhere in this guideline (see Chapter 6: Glucose control levels). Lifestyle modification (see Chapter 5: Lifestyle management) by itself can only provide control of blood glucose concentrations to target levels in a minority of people with diabetes, and then usually only for a limited period after diagnosis. Accordingly, supplementary pharmaceutical measures are needed, and these can be oral glucose lowering medications, GLP-1 RAs or insulin injection therapy, separately or in combination.

The natural history of type 2 diabetes is of progression of islet β-cell failure. Ultimately insulin remains the only glucose-lowering therapy which can maintain blood glucose control despite such progression.

Evidence-base

There are a wide range of pharmacological agents available to treat hyperglycaemia, however availability and access to many of these options is limited in many middle and low income countries.

Many guidelines provide guidance on ways in which glucose-lowering agents can be used either alone or in combination. These national treatment algorithms are based on available evidence and local availability and prescribing regulations [1-8]. In its 2005 global guideline for type 2 diabetes [6], IDF gave guidance on treatment options but did not formulate a treatment algorithm, mainly because of the differences in availability, access and cost of medications between countries. However this updated guideline includes a generic algorithm which is intended for adaptation by countries for local use.

Lifestyle changes including diet modification, increase in physical activity, weight reduction in the overweight and smoking cessation are essential components of the management of type 2 diabetes. This is recommended as the initial step in diabetes management. Subsequent treatment changes are based on failure to achieve target HbA_{1c} after a 3 month period taking in account tolerability and hypoglycaemia. For each subsequent step the IDF algorithm recommends both a usual approach and an alternative approach. The response to each medication initiation or dose increase should be monitored and ineffective therapies should be discontinued.

A recent update of a previous systematic review compared effectiveness and safety of medications for type 2 diabetes, excluding α-glucosidase inhibitors and insulin [9]. Most diabetes medications were similarly efficacious when used as monotherapy and decreased HbA_{1c} levels by 1% point / 11mmol/mol although there were some exceptions. Differences in other clinical outcomes were observed - metformin was more efficacious than other agents in weight reduction (although limited data on GLP-1 RA were included); sulfonylureas (or glinides) increased risk of mild or moderate hypoglycaemia; and thiazolidinediones increased risk of fluid retention/congestive heart failure and bone fractures. The strength of evidence was low or insufficient to support conclusions about the comparative effectiveness of diabetes medications on all-cause mortality, cardiovascular morbidity and mortality, and microvascular outcomes.

Metformin is generally considered the first choice oral medication, unless contraindicated e.g. in the presence of renal impairment. This recommendation is based on metformin's favourable effects on weight, low risk of hypoglycaemia, and low cost, however gastro-intestinal intolerance is common and the need to monitor renal function can be problematic in many health systems. Long-term outcome data are limited. In a sub-study of the UKPDS in 342 overweight people [10], metformin resulted in a significantly greater risk reduction than those assigned intensive therapy with sulfonylurea or insulin for any diabetes-related endpoint and all-cause mortality. However a possible macrovascular benefit of metformin was not found in a recent meta-analysis of randomised clinical trials which examined the effect of metformin on cardiovascular events and mortality [11].

Global alternatives to metformin as first-line therapy include sulfonylureas or α-glucosidase inhibitors. Sulfonylureas are commonly used and efficacious but can be associated with weight gain and an increased risk of hypoglycaemia.

Outcomes studies compared with other agents are limited [9] but both the UKPDS [12] and ADVANCE study [13] showed that intensive therapy with sulfonylurea-based treatment improved long-term outcomes. The ADVANCE study achieved this without weight gain and with low rates of hypoglycaemia [13].

a-glucosidase inhibitors are widely used and are popular in many, especially Asian, countries [14]. Gastrointestinal side effects such as flatulence and diarrhoea are frequent. Hanefeld et al performed a meta-analysis on the effect of the a-glucosidase inhibitor acarbose on cardiovascular events in seven randomized placebo-controlled studies of at least 52 weeks duration and found significantly reduced risk for myocardial infarction and any cardiovascular event [15].
When monotherapy fails to achieve target glycaemia, a second agent is required. Of the many options, the addition of a sulfonylurea is recommended as the usual approach for people on metformin. Alternatives include addition of an α-glucosidase inhibitor, DPP-4 inhibitor or thiazolidinedione. There is little to choose between options based on efficacy alone. Combination therapy decreases HbA_{1c} levels more than monotherapy by about 1% point / 11mmol/mol, with most combinations providing similar reductions [9]. Therefore choices are driven by availability, cost and untoward effects and combined metformin and sulfonylurea therapy remains widely used throughout the world. Probably because of this, few studies have specifically examined long-term outcomes with this combination.

Other options as second-line therapy should be considered if the use of either metformin or sulfonylurea is associated with side effects or contraindicated. An α-glucosidase inhibitor is effective in combination with metformin or sulfonylurea and is an option in countries where it is commonly prescribed.

DPP-4 inhibitors act to increase levels of endogenous incretin hormones. A meta-analysis by Amori et al [16] reported that compared with placebo DPP-4 inhibitors lowered HbA_{1c} by approximately 0.7% / 8 mmol/mol and were weight neutral. DPP-4 inhibitors have proven efficacy when combined with metformin, sulfonylurea or both metformin and sulfonylurea. There are a lack of studies evaluating long-term efficacy and safety but a number of outcome studies are currently underway. These agents are relatively expensive in many countries.

Thiazolidinedione (peroxisome proliferator-activated receptor-g agonist) effectively lower blood glucose when used as monotherapy, dual or triple therapy. However their side effects and increasing safety concerns have seen their use decrease. The most common adverse effects are weight gain and fluid retention which may result in peripheral oedema and congestive heart failure. Increasingly recognised is the increased incidence of fractures, especially in females [17]. Some meta-analyses suggest an increased risk of myocardial infarction with rosiglitazone [18,19], although this was not apparent in the RECORD study [20]. Pioglitazone has not been associated with an increase in cardiovascular risk and the PROactive study reported some improved outcomes [21]. However recent concerns have been raised about a possible link with bladder cancer when used for more than a year. Although thiazolidinediones are included as an option in the IDF algorithm, other choices are favoured and the situation with respect to safety continues to be monitored by IDF, especially with respect to any further regulatory restrictions.

If diabetes control remains unsatisfactory and a third agent is required, the usual approach options include either adding a third oral agent or commencing insulin. Options for a third oral agent include a DPP-4 inhibitor, an α-glucosidase

inhibitor or a thiazolidinedione. Few studies have compared these options but those which have, show similar short-term effects on glycaemic control [22].

The UKPDS established the effectiveness of intensive therapy based on insulin treatment in reducing vascular complications compared with conventional therapy [10]. The options for insulin therapy (preparations, delivery) have expanded considerably since the UKPDS and have been reviewed in a number of guidelines [2-5].

Comparisons of older insulins and the newer insulin analogues have provided variable findings. A Cochrane review of short-acting insulins found that analogue and regular human insulin were almost identically effective in long term glycaemic control and were associated with similar episodes of hypoglycaemia. There was no information available on effects on late complications [23]. Another Cochrane review compared NPH insulin, insulin glargine and insulin detemir. HbA_{1c} results were almost identical, although fewer people experienced symptomatic overall or nocturnal hypoglycaemic episodes with treatment with either of the two analogues. No conclusive information on late complications was found and therefore no firm conclusions about relative cost effectiveness could be determined [24]. However the Canadian guidelines found indications for use of analogues in relation to postprandial glucose excursions, risk of hypoglycaemia and weight gain [2]. Insulin glargine was the subject of specific guidance from NICE [25] including a recommendation for use where once-daily injections would suffice or NPH insulin gave troublesome hypoglycaemia.

Insulin options include adding once daily basal insulin or twice daily premixed insulin. A recent systematic review reported the percentage of people reaching an HbA_{1c} target of < 7.0% / 53 mmol/mol was similar using basal or premixed insulins [26].

There is supporting evidence for insulin use in combination with metformin, insulin secretagogues (sulfonylureas), metformin plus sulfonylurea, a-glucosidase inhibitors, thiazolidinediones [27]. The NICE review found that for people on insulin therapy, glucose control was improved and body weight and hypoglycaemia risk reduced when metformin was used in combination with insulin [1].

GLP-1 RAs are considered as an alternate approach at this time mainly on the basis of their availability and cost. GLP-1 RAs lower HbA_{1c} by approximately 1.0% / 11 mmol/mol compared with placebo and result in moderate and continuous weight loss, low rates of hypoglycaemia but are associated with gastrointestinal side effects, especially nausea and vomiting [16]. There is some poorly supported data that the use of GLP-1 RAs may predispose to pancreatitis.

The final step in the algorithm is to use insulin if triple oral therapy has failed to achieve target glycaemic control or to intensify insulin therapy with basal and meal-time insulins. Intensified insulin therapy in type 2 diabetes has been shown to improve metabolic control [27] and improve clinical outcomes [28]. Evidence on insulin pump therapy in type 2 diabetes is still insufficient to support a recommendation for use in general, although it is a potential option in highly selected patients or in very individual settings [29].

The generic IDF treatment algorithm takes into consideration differences in availability, access and cost of medications between countries. The algorithm is not proscriptive but rather is formulated to encourage adaptation by individual countries for local use. The algorithm will be continuously updated

as new evidence, particularly the results of current outcomes studies, becomes available.

Considerations

A major limitation in developing algorithms is the relatively limited evidence base for choosing particular treatment options or combinations of medications. Given the range of available treatment options, not all options have been compared. Therefore treatment algorithms cannot be truly evidence-based due to a lack of studies comparing all available treatment combination options. However it is possible to reach evidence-informed consensus by carefully balancing available evidence and consensus in order to avoid the potential for bias.

Generic metformin and sulfonylureas are available at very low cost. Proprietary blood glucose lowering medications are considerably more expensive, with limited evidence of extra benefit. The newer treatments are usually expensive. Where this impacts on its use, NPH insulin and human insulin mixes are still very useful and effective alternatives. Consistency of supply (quality, availability, insulin type) requires careful organisation.

During periods of regular change in food consumption (e.g. Ramadan), the dose of blood glucose lowering therapies will usually need to be adjusted, especially insulin. The total amount of insulin should not be reduced but redistributed according to the amount and timing of carbohydrate intake. However, if the total calorie intake is reduced, the daily amount of insulin for meals usually needs to be reduced.

Implementation

Contracts should be in place for uninterrupted availability of metformin and at least one sulfonylurea, as well as insulin and supporting materials (including for self-monitoring and education).

Availability is needed of an HbA_{1c} assay and visits to health-care professionals at a frequency (sometimes 3 monthly) sufficient to titrate therapy where glucose control is deteriorating. Lifestyle measures, self-monitoring and education, as discussed elsewhere in this guideline (see Chapter 5: Lifestyle management, Chapter 8: Self-monitoring and Chapter 3: Education), are integral parts of maintaining glucose control to target, and will enhance the effectiveness of blood-glucose lowering therapies.

These recommendations should be the basis for developing local clinical protocols.

Avoiding delay in starting insulin therapy has been problematic in nearly all diabetes services. Structured guidelines and protocols and audit of glucose control of people on oral medications are an integral part of dealing with this problem.

Evaluation

Evaluation of achieved blood glucose control should be by reference to the documented use of blood glucose lowering therapies and insulin in different combinations to identify appropriately early use of these treatments. Local protocols should be identifiable.

Potential indicators

Indicator	*Denominator*	*Calculation of indicator*	*Data to be collected for calculation of indicator*
Percentage of people with type 2 diabetes on diet alone with HbA_{1c} ≥ 7.0% / 53 mmol/mol.	**Number of people with type 2 diabetes on diet alone seen in the year and having at least one HbA_{1c} measurement in the year.**	**Number of people with type 2 diabetes on diet alone with HbA_{1c} ≥ 7.0% / 53 mmol/mol as a percentage of people with type 2 diabetes on diet alone seen in the year and having at least one HbA_{1c} measurement in the year.**	**Diabetes management and most recent HbA_{1c} measurement in the past year.**
Percentage of people with type 2 diabetes not treated with insulin with HbA_{1c} ≥ 9.0% / 75 mmol/mol.	**Number of people with type 2 diabetes not treated with insulin seen in the year and having at least one HbA_{1c} measurement in the year.**	**Number of people with type 2 diabetes not treated with insulin with HbA_{1c} ≥ 9.0% / 75 mmol/mol as a percentage of people not treated with insulin seen in the year and having at least one HbA_{1c} measurement in the year.**	**Diabetes management and most recent HbA_{1c} measurement in the past year.**

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10 BLOOD PRESSURE CONTROL

Recommendations

Recommended care

BP1 Measure blood pressure at least annually, and at every routine clinic visit in people with known CVD, if found to be above target blood pressure levels at previous visits (see below), or if on blood pressure lowering treatment.

BP2 Measure blood pressure with a validated meter in good working order and an appropriately sized cuff (large or normal depending on arm size).
Measure blood pressure after sitting for at least 5 minutes, with arm at heart level, using first and fifth phases of Korotkoff sounds.
Use 24 hour ambulatory blood pressure monitoring (ABPM) if 'white coat' hypertension suspected, but adjust targets down by 10/5 mmHg.

BP3 Consider secondary causes of raised blood pressure if there is evidence of renal disease, electrolyte disturbance or other specific features.

BP4 Consider blood pressure lowering treatment if blood pressure is consistently above 130/80 mmHg.

BP5 All people with known CVD should receive blood pressure lowering therapy unless contraindicated or not tolerated.

BP6 Aim to maintain blood pressure ≤ 130/80 mmHg, if therapy is well tolerated. Revise individual targets upwards if there is significant risk of postural hypotension and falls. Higher targets should be used in the elderly (see Chapter 16: Older People).

BP7 Initiate a trial of lifestyle modification with appropriate education (see Chapter 5: Lifestyle management), aiming to reduce energy intake, salt intake, alcohol intake and inactivity.

BP8 In diabetes not complicated by raised albumin excretion rate any agent can be used as first line therapy except for a-adrenergic blockers, with consideration of costs, and actively titrating dose according to response.

- Angiotensin converting enzyme-inhibitors (ACE-inhibitors) and angiotensin-II receptor blockers (ARBs) may offer some advantages over other agents in some situations, but do not use the two together (see Chapter 11: Cardiovascular risk protection and Chapter 13: Kidney damage).
  They are less effective in people of African extraction.
- Calcium channel blockers (CCBs) should be avoided in congestive heart failure.
- Use β-adrenergic blockers in people with

angina; β-adrenergic blockers and ACE-inhibitors in people with coronary artery disease; ACE-inhibitors or diuretics in those with heart failure; ACE-inhibitor plus low dose thiazide or thiazide-like diuretic (indapamide or chlorthalidone), or ACE-inhibitor plus CCB in people with cerebrovascular disease.
Care should be taken with combined thiazide and β-adrenergic blockers because of risk of deterioration in metabolic control.

BP9 **Add further medications from a different class if targets are not reached on maximal doses of current medications, reviewing for adverse effects and likely adherence problems as tablet numbers increase. The preferred combinations are:**

- **ACE-inhibitor plus CCB.**
- **ACE-inhibitor plus low dose thiazide or thiazide-like diuretic (indapamide or chlorthalidone).**

Accept that blood pressure target may not be achievable with three or more anti-hypertensive medications in some people.

Limited care

BP_L1 **Principles for measurement and targets as for *Recommended care*.**

BP_L2 **Initiate a trial of lifestyle modification as for *Recommended care* with appropriate education (see Chapter 5: Lifestyle management).**

BP_L3 **Initiate medications for lowering blood pressure in diabetes not complicated by proteinuria, using generic ACE-inhibitors, ARBs, CCBs, diuretics or β-adrenergic blockers, according to availability and cost.**

Comprehensive care

BP_C1 **The principles as for *Recommended care*, but with the additional option of self-monitoring of blood pressure on validated semi-automatic devices to provide additional information and educational feedback.**

Rationale

Blood pressure is elevated in many people with type 2 diabetes. Increasing blood pressure levels are associated with a spectrum of adverse outcomes, including premature mortality, CVD (cardiac disease and stroke), eye damage and kidney damage and treatment to lower blood pressure reduces these adverse outcomes. Blood pressure lowering in people with type 2 diabetes is highly cost-effective [1].

Evidence-base

The evidence-base on this topic is spread among guidelines primarily addressing diabetes, elevated blood pressure, CVD or kidney disease and the evidence may derive from trials involving primarily people with diabetes or people with elevated blood pressure.

Recommendations on thresholds for intervention and targets of therapy are generally similar across guidelines [2-4]. There is a strong association between blood pressure levels and incidence of adverse outcomes but no clear blood pressure threshold. This relationship appears linear for stroke but some studies suggest a J-shaped curve for mortality and cardiac events. This raises the question of whether blood pressure should be reduced using a treat to target approach or reduced as far as possible.

Law et al pooled data from 147 trials involving 464,164 people and reported a significant reduction in risk of coronary events and stroke with blood pressure lowering therapy with the risk reduction being similar regardless of blood pressure level [5]. Two meta-analyses have examined the question of blood pressure targets. Bangalore et al found that intensive blood pressure control (systolic blood pressure [SBP] ≤ 135 v ≤ 140 mmHg) was associated with a reduction in all-cause mortality and stroke but increased serious adverse effects while other outcomes (cardiac, renal and retinal) were similar. More intensive control (SBP ≤ 130 mm Hg) was associated with further reduction in stroke only and a 40% increase in serious adverse events [6]. The other reported that intensive therapy (mean achieved SBP 129 mmHg) significantly reduced the risk of stroke but not myocardial infarction [7]. The ACCORD study compared a more tight (< 120 mmHg) with a less tight (< 140 mmHg) SBP goal in people with type 2 diabetes. Achieved SBP with intensive therapy was 119.3 mmHg and 133.5 mmHg with less tight control. The incidence of the primary endpoint and MI did not differ between the two groups. In the more intensively treated subjects the incidence of stroke was lower but there were more serious adverse events [8]. The ADVANCE study compared combination blood pressure lowering to placebo in people with type 2 diabetes and achieved a mean SBP with perindopril/indapamide versus placebo of 135 and 140 mmHg respectively. Significant reductions in the composite outcome and total coronary and renal events, and all-cause and cardiovascular mortality were observed with combination therapy compared with placebo [9].

There is continuing controversy and debate about blood pressure targets in people with diabetes. Overall the evidence suggests that treatment achieving a SBP of 130-135 mmHg reduces the risk of premature death and stroke. While IDF and other organisations continue further discussion and review of emerging evidence, the consensus view is to maintain the general blood pressure target for people with diabetes at ≤ 130/80 mmHg. A lower target may be considered in people at higher risk of stroke but any potential benefit must be balanced against an increased risk of adverse events and lack of established benefit for cardiac, renal and retinal outcomes.

At the initial assessment, blood pressure should be measured at least twice using a validated device. Sitting and standing blood pressure should both be measured if orthostatic hypotension is suspected. 24 hour ABPM should be considered, especially if 'white coat hypertension' is suspected.

Lifestyle modification (including weight reduction, reducing salt intake, increasing physical activity, reducing alcohol intake) can reduce SBP by 4-10 mmHg (see Chapter 5: Lifestyle management).

Many randomised trials have shown that blood-pressure-lowering therapy reduces CVD morbidity and mortality in people with diabetes. Two large systematic reviews of blood pressure-lowering medications versus placebo in people without a history of CVD demonstrate that pharmacological lowering of blood pressure reduces the incidence of coronary heart disease events and stroke in the order of 20-25% and 30-45%, respectively [5] and across young to very old age groups [10].

There is strong evidence that all people with type 2 diabetes and CVD should be on blood pressure lowering therapy irrespective of their baseline blood pressure level, provided it is not contraindicated or not tolerated [11,12].

Many blood pressure lowering agents (ACE-inhibitors, ARBs, CCBs, low dose thiazide, thiazide-like diuretics and β-blockers) are effective in improving outcomes when blood pressure lowering is achieved [5]. The choice of agent for a person with diabetes may be influenced by a number of factors including their risk profile (cardiovascular, renal, end-organ damage), preferences, and previous experience of therapy, as well as costs. In general ACE-inhibitors or ARBs are the agents of choice but they should not be used together. The ONTARGET study compared an ARB plus an ACE-inhibitor to an ARB alone or an ACE-inhibitor alone. There were no significant differences in the risks of the combined endpoints but significantly more patients receiving combination therapy discontinued treatment because of adverse events [13]. Thiazide diuretics may adversely affect glucose, lipid and potassium levels, and β-adrenergic blockers may adversely affect glucose and lipid levels, but no RCTs have shown these drugs increase cardiovascular mortality in type 2 diabetes. Avoidance of a-adrenergic blockers as first-line therapy is based on evidence from ALLHAT [14].

Most people with diabetes will require more than one agent to control blood pressure. While many combinations can be used and not all have been compared in head-to-head studies, some studies point to preferred combinations. The ACCOMPLISH study compared an ACE-inhibitor combined with a CCB or a diuretic and reported significantly fewer fatal and non-fatal CVD events in the CCB group [15]. The ASCOT-BPLA compared a CCB ± an ACE-inhibitor or a β-blockers ± a diuretic and reported significantly fewer CVD events with the CCB ± ACE-inhibitor combination [16]. Based on current evidence, if monotherapy with an ACE-inhibitor or ARB does not adequately control blood pressure, a CCB or low dose thiazide or thiazide-like diuretic should be added. Some combinations should generally be avoided – ACE-inhibitors and ARBs, potassium-sparing diuretic plus either an ACE-inhibitor or ARB, and β-blocker plus verapamil. Any intensification of therapy and polypharmacy are associated with greater risks of side effects, thus the balance of benefits and risks must be determined for each patient.

Achieving effective control of blood pressure, and consequent therapeutic benefits, is influenced by adherence to therapy. A recent meta-analysis assessed adherence to ARBs, ACE-inhibitors, CCBs, β-blockers and diuretics and found adherence lowest for diuretics and β-blockers, and highest in ARBs and then ACE-inhibitors [17]. Cultural health beliefs, complex therapeutic regimens, adverse effects, tablet number burden and poor social support are reported predictors of poor concordance with therapy. These issues need to be discussed with the person concerned, where response to medications is poor.

Consideration

Blood pressure management is among the most cost-effective methods of prevention of vascular complications in people with type 2 diabetes. Lifestyle measures are generally preferred as a trial before therapeutic intervention, but alone are generally insufficient. Because individual therapies are not particularly effective even in full dosage, the experience of the need for multiple therapies found in UKPDS is reflected in the guideline recommendations. However, this also implies the need for frequent monitoring and dose titration until targets, or the limits of therapeutic effect, are reached.

Implementation

There is need for equipment for measurement of blood pressure, maintenance of that equipment and training of personnel in its use. Protocols using locally available medication should be drawn up and followed to ensure appropriate medication prescribing and dose titration to target. Lifestyle education is described elsewhere (see Chapter 5: Lifestyle management).

Evaluation

A record of measurement of blood pressure in clinical records in the last 12 months should be found. Where blood pressure is elevated there should be evidence of action to lower it. The percentage of people in whom blood pressure achieves the target level of 130/80 mmHg can be ascertained, and the percentage of those with blood pressure above target who are receiving treatment involving lifestyle modification and medications. Availability of sphygmomanometers in working order, and appropriate cuffs can be ascertained, as can training and proficiency of staff measuring blood pressure.

Potential indicators

Indicator	*Denominator*	*Calculation of indicator*	*Data to be collected for calculation of indicator*
Percentage of people with type 2 diabetes with BP ≤ 130/80 mmHg.	**Number of people with type 2 diabetes seen in the past year and having at least one BP measurement in the year.**	**Number of people with type 2 diabetes and both SBP and DBP with a BP ≤ 130/80 mmHg as a percentage of people seen in the past year and having at least one BP measurement in the year.**	**Most recent SBP and DBP measurement in the past year.**
Percentage of people with type 2 diabetes not treated with anti-hypertensive medications with BP > 140/90 mmHg.	**Number of people with type 2 diabetes with at least one BP measurement in the year.**	**Number of people with type 2 diabetes not treated with anti-hypertensive medications with BP > 140/90 mmHg as a percentage of people seen in the past year and having at least one BP measurement in the year.**	**Most recent SBP and DBP measurement in the past year.** **Record of anti-hypertensive treatment.**

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11 CARDIOVASCULAR RISK PROTECTION

Cardiovascular risk protection through blood glucose control, blood pressure control, and lifestyle interventions is dealt with elsewhere in this guideline (see Chapter 5: Lifestyle management, Chapter 6: Glucose control levels and Chapter 10: Blood pressure control). This section deals with cardiovascular risk assessment, lipid modifying therapy and anti-platelet therapy.

Recommendations

Recommended care

CV1 Assess cardiovascular risk factors at diagnosis and at least annually thereafter including:
- Current or previous CVD.
- Age and BMI (abdominal adiposity).
- Conventional CVD risk factors including smoking, blood pressure, serum lipids and family history of premature CVD.
- Renal damage (particularly albuminuria).
- Atrial fibrillation (for stroke).

CV2 Assessment of absolute CVD risk is an option for stratifying risk. Use of risk equations developed for people with diabetes is preferred.

CV3 People with a previous CVD event should be treated with lifestyle modification, low-dose aspirin (or clopidigrel), statins and blood pressure lowering medications, unless contraindicated or considered clinically inappropriate.

CV4 High risk individuals should be actively treated to reduce CVD risk with lifestyle modification and pharmacotherapy. Anti-platelet therapy is not routinely recommended in high risk individuals who have not had a CVD event.

CV5 Ensure optimal management through lifestyle measures (see Chapter 5: Lifestyle management), and measures directed at good blood glucose and blood pressure control (see Chapter 6: Glucose control levels and Chapter 10: Blood pressure control).

CV6 Arrange smoking cessation advice in smokers contemplative of reducing or stopping tobacco consumption.

CV7 Treat high risk individuals with statins unless contraindicated or considered clinically inappropriate.

CV8 Consider the addition of fenofibrate where serum triglycerides are > 2.3 mmol/l (> 200 mg/dl) and high density lipoprotein (HDL) cholesterol is low, especially when retinopathy is present. Combination of gemfibrizol with a statin is not recommended.

CV9 Consider other medications for dyslipidaemia (bile acid binding resins, ezetimibe, sustained release nicotinic acid, concentrated omega-3 fatty acids) in those failing to reach lipid lowering targets or intolerant of conventional medications.

CV10 Lipid targets are as follows: LDL cholesterol < 2.0 mmol/l (< 80 mg/dl), triglyceride < 2.3 mmol/l (< 200 mg/dl), HDL cholesterol > 1.0 mmol/l (> 39 mg/dl), non-HDL cholesterol < 2.5 mmol/l (< 97 mg/dl). LDL cholesterol should be < 1.8 mmol/l (< 70 mg/dl) in established CVD.

CV11 Refer early for further investigation and consideration of revascularisation those with problematic or symptomatic peripheral arterial disease, those with problems from coronary artery disease, and those with evidence of carotid disease.

Limited care

CV_L1 The assessment principles are as for *Recommended care*, with lipid profile measures if available.

CV_L2 The management principles as for *Recommended care*, but using lowest acquisition cost generic statins.

CV_L3 Statins should be used in high risk individuals even if the serum lipid profile cannot be measured.

CV_L4 Revascularisation procedures will generally not be available, but where possible those limited by symptoms should be referred.

Comprehensive care

CV_C1 The assessment principles are as for *Recommended care*, but with more aggressive investigation of asymptomatic peripheral arterial disease, coronary artery disease and carotid disease. Lipid profiles may be investigated more extensively to give better direct assessments of LDL cholesterol and apolipoproteins. A specialist lipidologist may be consulted. Serum levels of ultrasensitive C-reactive protein may be helpful to assess risk beyond LDL cholesterol.

CV_C2 The intervention principles are as for *Recommended care* but with aggressive lipid lowering for all, using multiple therapies and more expensive/efficacious statins except where LDL cholesterol, triglycerides and HDL cholesterol are all within target ranges. Serum levels of ultrasensitive C-reactive protein > 2 mg/l may call for more aggressive statin treatment.

CV_C3 Anti-platelet agents to consider might include clopidogrel substituted for aspirin, in particular for those with multiple CVD events/problems, peripheral arterial disease, or previous coronary bypass grafting.

Rationale

CVD is the major cause of mortality and morbidity in people with type 2 diabetes. All adults with diabetes are at increased risk of recurrent cardiovascular events. Some, but not all studies have suggested a risk similar to that of people without diabetes who have had a CVD event. Assessment and aggressive management of CVD risk factors in type 2 diabetes is a core part of care.

Some of the CVD risk relates to blood pressure control and blood glucose control and is addressed elsewhere in this guideline, as are the lifestyle interventions which generally benefit the whole spectrum of CVD risk factors.

Evidence-base

The epidemiological evidence that CVD is the major cause of mortality in people with type 2 diabetes is extensive, as is the evidence that the risk is considerably high than the non-diabetic population. More controversy surrounds the extent of the increased risk. A much quoted paper by Haffner et al [1] suggested that people with type 2 diabetes have a CVD risk equivalent to non-diabetic people with previous CVD, but this is not supported by other data [2].

There is a lack of consensus on how to assess CVD risk in people with type 2 diabetes. Some guidelines consider people with diabetes (usually based on age alone or in combination with other risk factors) to be high risk while others recommend a risk assessment using a risk calculator, or a combination of both approaches.

There is general agreement that the following people with type 2 diabetes are at high CVD risk and do not require formal risk assessment:

- Those who have had a previous cardiovascular event.
- Micro and macroalbuminuria.
- Markedly elevated single risk factors.

CVD risk factors tend to cluster and assessment of CVD risk on the basis of the combined effect of multiple risk factors is considered more accurate than the use of individual risk factors because the cumulative effects of multiple factors are additive or synergistic. Furthermore moderate reductions in several risk factors may be more effective in reducing overall CVD risk than a major reduction in one risk factor. Many guidelines for the prevention of CVD have moved from an approach based on identifying and correcting individual risk factors to a focus on the individual's overall risk through multiple risk factor assessment. While this approach is generally accepted for people without diabetes, some argue that type 2 diabetes per se is a sufficiently high risk factor as to make risk assessment redundant. Furthermore there is controversy about the validity of calculators for CVD risk assessment and their application to people with diabetes. Consequently there are significant differences in guideline recommendations to risk stratification in people with type 2 diabetes. The NICE guideline recommends CVD risk assessment annually using the UKPDS risk engine [3] if the person is considered not to be at high CVD risk (i.e. not overweight, normotensive, non-smoker, no high-risk lipid profile, no family history of CVD) [4].

The European cardiovascular prevention guidelines recommend risk calculation in people with diabetes who are not at high risk (see above) using the SCORE charts [5].

The Australian guidelines recommend using the Framingham risk equation unless the person with diabetes is in a high risk category which include previous CVD event; age > 60 years; microalbuminuria; moderate or severe chronic kidney disease (CKD) (persistent proteinuria or eGFR < 45); extreme level of a single risk factor [6].

The New Zealand guideline recommends annual risk assessment in people with diabetes from the time of diagnosis and calculation of CVD risk using the New Zealand Cardiovascular Risk Charts. People with diabetes with microalbuminuria, diabetes duration of 10 or more years or with HbA_{1c} consistently ≥ 8% / 64 mmol/mol are moved up one risk category [7].

The Canadian guidelines consider the following with diabetes at high CVD risk: men aged ≥ 45 years, women aged ≥ 50 years; men < 45 years and women < 50 years with ≥ 1 of the following: macrovascular disease; microvascular disease; multiple additional risk factors; extreme level of a single risk factor; duration of diabetes > 15 years with age > 30 years [8]. A risk calculator is not used to assess CVD risk.

The Scottish SIGN guideline considers all people with diabetes over the age of 40 years to be at high risk and do not require a risk assessment with a scoring system [9].

WHO recommends decisions about whether to initiate specific CVD preventive action, and with what degree of intensity, should be guided by estimation of the risk of vascular events using risk prediction charts. Individuals who do not need risk stratification because they are already at high CVD risk include those who have already experienced a CVD event or have very high levels of individual risk factors which includes people with 2 diabetes with overt nephropathy or other significant renal disease [10].

Ultimately the choice of risk assessment strategy must be made at a country level taking into account country-specific CVD and risk factor epidemiological data, availability and cost of CVD preventive treatments, and resource implications of the size of the population identified at high risk and requiring intervention.

There is an evidence-base for integrated multiple risk factor intensive intervention, particularly in high-risk people with type 2 diabetes with microalbuminuria, showing powerful absolute and relative risk reductions in the Steno-2 study [11] and in its subsequent 5.5 years follow-up which showed a further benefit in the reduction of mortality rates [12].

People with diabetes identified at increased CVD risk require interventions to reduce risk. High risk individuals should be encouraged to modify lifestyle (see Chapter 5: Lifestyle management), smokers should cease smoking, the overweight should reduce weight and blood glucose control should be optimised. These individuals should also be treated with blood pressure lowering medications (see Chapter 10: Blood pressure control) and statins, unless contraindicated, not tolerated or clinically inappropriate. The wide availability of low cost generic statins is likely to make them cost effective in most parts of the world.

There is strong and consistent evidence that statins reduce the risk of death or CVD events irrespective of age and gender, and across a wide range of cholesterol levels [13-18].

The guidelines also address the issue of management of serum triglyceride and HDL cholesterol levels, an area where the evidence-base is softer, but all conclude that management with fibrates is indicated if serum triglyceride levels are raised and HDL cholesterol is low. However, there is no consensus on the levels at which fibrates should be introduced, or on how they should be introduced in combination with statins.

Fibrates significantly reduce non-fatal MI but have no significant effect on CVD or all-cause mortality, fatal MI or stroke, all of which are significantly reduced by statins. Jun et al found overall benefit of fibrates in preventing major CVD events primarily due to a reduction in coronary disease with no effect on stroke, CVD or all-cause mortality [19]. A meta-analysis specific to people with diabetes also found a significant reduction in non-fatal coronary events but no effect on stroke or mortality outcomes [20]. Interestingly fibrates significantly reduced retinopathy and amputations [21,22]. In general, fibrates are safe and easy to use and fenofibrate can be co-administered with a statin [23]. The benefit of combination therapy is not clear with the ACCORD study reporting no benefit of adding fibrates to statins, rather than statin therapy alone, to reduce cardiovascular risk in people with type 2 diabetes at high-risk of CVD [24]. It should be noted that co-administration of statins with gemfibrozil is not recommended due to the increased risk of myopathy.

The evidence-base for other lipid-lowering medications (extended-acting nicotinic acid, concentrated omega-3 fatty acids, ezetimibe, bile acid binding resins) is weaker and there are very few quality outcomes studies [6]. The use of these agents is generally reserved for uncontrolled hyperlipidaemia when taking first-line agents, or intolerance of these.

For people with established CVD the benefit of long-term aspirin for reducing the risk of MI, stroke and vascular death is well established [25,26]. However guidelines generally do not support the routine use of aspirin (or other anti-platetet agents) in CVD prevention in people who have not had a CVD event [4,6,8]. Evidence from three meta-analyses [26-28] indicates that aspirin does not affect all-cause or CVD-related mortality, but does have a small benefit in reducing non-fatal vascular events (e.g., MI or stroke), a benefit driven largely by a reduction in non-fatal MI among men. Aspirin increases the relative risk for gastrointestinal and extracranial bleeds by 54%. Based on the absolute benefits and risks observed the Calvin et al analysis [29], aspirin therapy for an average of 6.4 years prevents approximately three CVD events per 1,000 women and results in 2.5 major bleeding events and in 1,000 men aspirin prevents four cardiovascular events and results in three major bleeding events. The findings of four systematic reviews [26,28-30] are consistent and report that the effects of aspirin therapy in people with diabetes are smaller than those for the general population, which has lead to a conservative approach about aspirin therapy for CVD prevention in people with diabetes.

Dual anti-platelet therapy is also not recommended for primary prevention of CVD. The CHARISMA study examined the efficacy and safety of dual anti-platelet therapy with clopidogrel and aspirin versus aspirin alone. In the primary prevention cohort (2,289 of the 15,603 participants), cardiovascular death was non-significantly increased with dual therapy (single 1.8% versus dual 3.0%, p=0.07) [31].

Consideration

Cardiovascular risk protection for people with type 2 diabetes is an area of high need with good and strong evidence of interventions to meet that need. One obvious problem is the need to extrapolate evidence in some areas from groups of people who do not have diabetes, for example regarding smoking cessation. However, because event rates are much higher in people with diabetes (particularly with regard to primary prevention) the gains and cost-effectiveness are also potentially much better, so that the risks of extrapolation of evidence are relatively low. This is especially true because the processes of arterial damage in people with type 2 diabetes are similar pathologically to those occurring in the general population, though usually present to a more abnormal degree.

Accordingly, the recommendations are for very active management. Statin use is given prominence, as best founded in evidence. Although hypertriglyceridaemia and low HDL cholesterol are associated with poor outcomes, recommendations over use of fibrates for dyslipidaemia are still controversial because the evidence is either limited or the findings inconclusive. Aspirin is warranted for secondary prevention but its benefit in primary prevention is unclear. The results of the ongoing ASCEND trial, which is randomising 10,000 people with diabetes without pre-existing CVD to aspirin 100 mg and omega-3 fatty acids in a 2 x 2 factorial trial, should clarify its role in primary prevention [32].

Implementation

The recommendations require access to measurement of a full lipid profile and supporting biochemistry, and to aspirin and statins as a minimum. Structured annual assessment and record-keeping should be instituted.

Evaluation

Evaluation is by achieved lipid levels, especially LDL cholesterol and triglycerides, and numbers of high risk people treated with statins and if appropriate, aspirin. In general, CVD outcome rates are difficult to assess except in very large populations.

Potential indicators

Indicator	*Denominator*	*Calculation of indicator*	*Data to be collected for calculation of indicator*
Percentage of people with type 2 diabetes with serum lipid measurement during past year.	Total number of people with type 2 diabetes seen in the past year.	Number of people with type 2 diabetes with serum lipid measurement during past year as a percentage of people with type 2 diabetes seen in the past year.	Documentation and date of serum lipid measurement.
Percentage of people with type 2 diabetes with LDL cholesterol < 2.0 mmol/l (80 mg/dl).	Number of people with type 2 diabetes seen in the past year and having at least one lipid profile measurement in the year.	Number of people with type 2 diabetes with LDL cholesterol < 2.0 mmol/l (80 mg/dl) as a percentage of people seen in the past year, and with at least one lipid profile measured in the past year.	Most recent lipid profile including an LDL cholesterol result in the past year.
Percentage of people with type 2 diabetes with LDL cholesterol ≥ 3.0 mmol/l (115 mg/dl) not treated with lipid-lowering medications.	Number of people with type 2 diabetes with at least one lipid profile measurement in the past year and not on lipid-lowering treatment.	Number of people with type 2 diabetes seen in the past year not treated with lipid-lowering medications and as a percentage of people with type 2 diabetes having at least one lipid profile measurement in the past year and a with an LDL cholesterol ≥ 3.0 mmol/l (115 mg/dl) .	Documentation and date of lipid profile measurement and lipid lowering medications.
Percentage of people with type 2 diabetes who smoke.	Total number of people with type 2 seen in the past year.	Number of people with type 2 diabetes seen in the past year who smoke as a percentage of the number of people with type 2 seen in the past year.	Documentation of smoking status.

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12 EYE SCREENING

Recommendations

These guidelines are concerned with preventative diabetes care. No advice is given on the further investigation of retinopathy by an ophthalmic specialist, or the subsequent use of laser or other retinal therapy, of vitrectomy, or other tertiary care. It is noted that a substantive evidence-base does exist for these techniques in the prevention of visual loss.

Recommended care

ES1 Ensure that examination of the eyes of people with type 2 diabetes is performed around the time of diagnosis and then routinely every 1-2 years as part of a formal recall process:

- Measure and document visual acuity, corrected with glasses or pinhole.
- Assess retinopathy:
  - ** Using retinal photography through dilated pupils, performed by an appropriately trained health-care professional, or
  - ** By examination by an ophthalmic specialist.

ES2 Discuss the reasons for eye examination with the person with diabetes.

ES3 Use tropicamide to dilate pupils, unless contraindicated, after discussing the implications and obtaining agreement of the person with diabetes.

ES4 Classify the findings of eye examination as requiring: routine review, earlier review or referral to an ophthalmologist (if not making the examination). The following frequency of screening is suggested:

- 1-2 years if no retinopathy.
- 12 months if minimal unchanged retinopathy.
- 3 to 6 months if worsening since last examination.
- More often during pregnancy.

ES5 The following situations require specialist referral:

- The same day:
  - ** Sudden loss of vision.
  - ** Evidence of retinal detachment.
- Within 1 week:
  - ** Evidence of pre-retinal and/or vitreous haemorrhage.
  - ** New vessel formation or rubeosis iridis.
- Within 1-2 months:
  - ** Advanced retinal lesions (4:2:1 rule).
    - •• Microaneurysms or retinal haemorrhages in 4 quadrants.
    - •• Venous beading in 2 quadrants.
    - •• IRMAs in 1 quadrant.
  - ** Unexplained deterioration of visual acuity.
  - ** Macular oedema.

** Unexplained retinal findings.
** Cataract.
** Inability to visualise fundus.

ES6 Advise that good control of blood glucose, blood pressure and blood lipids (see Chapter 6: Glucose control levels, Chapter 10: Blood pressure control and Chapter 11: Cardiovascular risk protection) can help to reduce the risk of eye damage developing or worsening.

ES7 Advise that diabetic retinopathy is not a contraindication for use of aspirin if this is indicated for prevention of CVD.

ES8 Advise that tests of intra-ocular pressure should be made periodically.

Limited care

ES_L1 Use direct fundoscopy through dilated pupils, performed by a member of the health-care team who is properly trained and has appropriate experience to assess retinopathy.

ES_L2 Check visual acuity.

ES_L3 Repeat review, referral and preventative therapy are as for *Recommended care*.

Comprehensive care

ES_C1 Retinal screening will be as for *Recommended care* in most respects, but could use seven-standard field stereoscopic colour fundus photography interpreted by a trained reader (where a retinal ophthalmological specialist is not performing the eye check).

Rationale

Diabetic retinopathy is the most common complication of diabetes and a major cause of visual loss. Damage (maculopathy) to the area of the retina used for fine and central vision (the macular area around the fovea) is the most significant problem in people with type 2 diabetes, though classical retinopathy with new vessels and consequent problems is also important. Interventions to control blood glucose, blood pressure and blood lipids (discussed elsewhere) can help to prevent or delay the onset of retinopathy and slow its progression, but most people with retinopathy will be asymptomatic until the damage is advanced. Early detection by regular surveillance is thus essential if people with sight-threatening retinopathy are to be identified in time to offer laser treatment to prevent visual loss.

New therapies are being developed for retinopathy although current and improved laser photocoagulation and vitrectomy will continue as essential interventions to reduce severe visual loss from focal and diffuse diabetic macular oedema and proliferative diabetic retinopthy. Promising therapies for diabetic retinopathy include intraocular corticosteroids, inhibitors of growth

hormone, anti-vascular endothelial growth fact agents and oral protein kinase inhibitors. Inhibitors of androgen receptors, anti-inflammatory agents and inhibitors of leukostasis could also prove effective medications to prevent early diabetic retinopathy. Combination therapy aimed at different targets may prove more effective in delaying or preventing diabetic retinopathy [1].

Evidence-base

Guidelines which address the subject of eye screening for diabetic retinopathy draw on an evidence-base going back to the 1970s, including the findings of the WESDR, DRS and ETDRS studies which provide the framework for retinal screening and laser treatment [2-4]. The 'gold standard' screening test of seven-standard field stereoscopic colour fundus photography and associated grading scheme were established by these studies. An international grading system has also been developed [5]. In recent years technological developments in digital photography have offered expanding opportunities for recording and transmitting images, with potential for automated grading [6].

The importance of screening people with type 2 diabetes at diagnosis relates to the finding that between 21 and 39% already have some retinopathy [2,7] and is sight-threatening in about 3% [8]. In the WESDR study,1.6% of people with type 2 diabetes were legally blind [2]. For people who have no retinopathy at diagnosis of type 2 diabetes, there is a very small chance of developing sight-threatening retinopathy. The Liverpool Diabetic Eye Study reported the 1 year cumulative incidence of sight-threatening diabetic retinopathy in people with type 2 diabetes who at baseline had no diabetic retinopathy, had background retinopathy, or had mild pre-proliferative retinopathy. The annual incidence in these groups of sight threatening retinopathy was 0.3, 5.0 and 15.0%, respectively [9].

Guidelines are divided about the frequency of screening in people found not to have retinopathy at the initial examination. The NICE guideline recommends annual screening [10] and the ADA recommends initial annual screening but also suggests less-frequent examinations (every 2-3 years) may be considered following one or more normal eye examinations [11].The Canadian guideline recommends screening every 1 to 2 years [12], the Australian guideline recommends screening at least every 2 years [13] and the SIGN guideline recommends screening every 2 years [14]. Cataract is another important cause of visual loss in people with diabetes, being twice as common as in people without diabetes.

Support for optimised glucose control and tighter blood pressure control derives from the reduction in risk of microvascular complications found in the UKPDS [15,16]. The ACCORD study found that the rate of progression of diabetic retinopathy was reduced with intensive glycaemic control and with intensive combination treatment of dyslipidemia with statins and fenofibrate, but not with intensive blood pressure control [17]. The ADVANCE study reported additive effects of combined improved blood glucose and blood pressure control [18]. The Steno-2 study demonstrated that subjects receiving intensive multifactorial treatment had a significantly lower risk of retinopathy (hazard ratio, 0.42; 95% CI: 0.21-0.86) [19].

Quality screening procedures are crucial to ensure timely detection of retinopathy and intervention to prevent or minimise visual loss [13]. Screening options include ophthalmologists, optometrists and other trained medical examiners using dilated ophthalmoscopy or slit lamp biomicroscopy. In the

absence of a dilated fundus examination by a trained examiner, non-mydriatic (or mydriatic) photography can be used. The level of sensitivity needed for the screening test cannot be defined unequivocally. Screening examinations or tests should aim for a sensitivity of at least 60%, though higher levels are usually achievable. It is considered that mild diabetic retinopathy missed at one visit would likely be detected at the next. Specificity levels of 90-95% and technical failure rates of 5-10% are considered appropriate. Cost-effectiveness of screening is dependent on the sensitivity and specificity of screening tests, attendance and prevalence of diabetic retinopathy.

Consideration

The core issue is how to provide regular structured review using either ophthalmological expertise or camera technologies. With regard to the latter, use of digital cameras with eyes dilated to reduce the incidence of screen failures is cost-effective. However, camera technologies cannot detect macular oedema, so visual acuity testing must accompany photography. Where neither camera technologies nor ophthalmologists are available, ophthalmoscopy by a trained observer can detect many problems (though with significantly poorer sensitivity).

The availability of laser therapy is currently limited in many parts of the world due to cost and lack of trained expertise. It is noted that raising awareness of eye problems by examination and recording of detected problems can both help individual preventative care (blood glucose and blood pressure control) and provide the necessary evidence for establishment of a laser service.

Implementation

Staff requirements are sufficient numbers of experienced ophthalmologists, optometrists and other health-care professionals to perform the screening, and sufficient ophthalmologists to perform laser therapy, and training of such staff. Equipment for screening and treatment will be required, as will a structured recall system and record. All screening modalities require quality assurance checks; for retinal photography it has been suggested this should happen for around 1% of photographs.

A national or regional advisory group, including representation of ophthalmologists, optometrists, internists and people with diabetes, can work with health funders to define such issues as: criteria for screening and treatment; training and education programmes; provision of accessible facilities; awareness programmes; strategies for programme implementation and guideline dissemination; information systems (for monitoring diabetic eye disease, follow-up and recall, collection of baseline and annual data); annual reports based on defined indicators.

Evaluation

The percentage of records containing the results of eye examination within a 12 month period is easily evaluated. Where such records are of sight-threatening retinopathy or decrease of visual acuity, evidence of review by (or referral to) an ophthalmological specialist should be present. Eye screening services can be checked for appropriately trained personnel and facilities sufficient to ensure

diabetes population coverage. Evidence of quality checks should be assessed. Evidence of control of rates of visual loss is more difficult to gather unless the records of ophthalmological services can be linked to those of diabetes services.

Potential indicator

Indicator	*Denominator*	*Calculation of indicator*	*Data to be collected for calculation of indicator*
Percentage of people with type 2 diabetes having an eye examination in the past year.	**Number of people with type 2 diabetes seen in the past year.**	**Number of people with type 2 diabetes having at least one eye examination during the past year as a percentage of the number of people with type 2 diabetes seen in the past year.**	**Documentation and date of the most recent eye examination.**

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13 KIDNEY DAMAGE

Recommendations

These guidelines are concerned with preventative diabetes care. No advice is given on further investigation of kidney disease by a renal specialist, or subsequent tertiary care.

Recommended care

KD1 Kidney function should be assessed at diagnosis and annually by:

- Urine test for albuminuria.
- Measurement of serum creatinine and calculation of eGFR.

KD2 Urinary albumin:creatinine ratio (ACR) measurement in an early morning first void spot specimen is the preferred method for assessment of albuminuria/ proteinuria Where a first void specimen is not possible or practical, a random spot urine specimen is acceptable. ACR can be measured in the laboratory or at site-of-care.

KD3 If ACR is raised (microalbuminuria ACR > 2.5 mg/ mmol in men, > 3.5 mg/mmol in women), repeat ACR twice over the following 4 months.
Microalbuminuria is confirmed if ACR is elevated in two out of three tests, in the absence of infection or overt proteinuria.
If both repeat tests are not raised, check again annually.
An ACR > 30 mg/mmol indicates macroalbuminuria.

KD4 Chronic kidney disease is diagnosed on the basis of a raised urine albumin/protein or a reduced eGFR (< 60 ml/min/1.73 m^2) calculated from the MDRD formula and using a standardised creatinine assay.

KD5 Individuals with chronic kidney disease should be managed as follows:

- Use ACE-inhibitors or ARBs in individuals with micro- or macroalbuminuria, titrated to maximum tolerated dose.
- Intensify management of blood pressure (target ≤ 130/80 mmHg) using blood pressure lowering medications and dietary modification (low salt intake) (see Chapter 10: Blood pressure control).
- Intensify management of blood glucose (see Chapter 6: Glucose control levels and Chapter 9: Glocose control therapy).
- Monitor ACR, eGFR and serum potassium.
- Advise limiting protein intake to 1 g/kg daily if proteinuric.
- Intensify other renal and cardiovascular protection measures (see Chapter 13: Kidney damage and Chapter 11: Cardiovascular risk protection).

KD6 **Agree referral criteria for specialist renal care between local diabetes specialists and nephrologists. Referral criteria might include eGFR < 30 ml/min/1.73 m^2, progressive deterioration of kidney function, persistent proteinuria, biochemical or fluid retention problems.**

Limited care

KD_L1 **Check annually for proteinuria in an early morning urine sample (or a random sample) using a dipstick. If test is positive exclude urinary tract infection by microscopy (and culture if possible). Measure serum creatinine and calculate eGFR annually.**

KD_L2 **Manage those with proteinuria as follows:**

- **If available consider use of ACE-inhibitors or ARBs taking into account cost.**
- **Aim for blood pressure ≤ 130/80 mmHg using any blood pressure lowering medication and control of salt intake.**
- **Aim to achieve targets for blood glucose control.**
- **Aim to improve lipid profile using available medications.**
- **Check proteinuric status annually.**
- **Measure serum creatinine and calculate eGFR annually.**

Comprehensive care

KD_C1 **The principles as for *Recommended care*, but assessment of albuminuria would always be by a laboratory quantitative method (ACR).**

KD_C2 **Investigations to exclude other possible causes of renal disease for all with raised ACR or protein:creatinine ratio might include auto-antibodies, ultrasound, biopsy.**

Rationale

Diabetes is now the leading cause of CKD in many developed countries. The prevalence of CKD in people with type 2 diabetes varies between 25 and 50% and it is associated with increased risk of morbidity and premature mortality. With increasing numbers of people with type 2 diabetes, younger age of onset, and better cardiovascular protection measures, the health impact of CKD in individuals with diabetes is growing. While the major effort of management must go to primary prevention (good blood glucose and blood pressure control from early diagnosis), the success of interventions at a later stage suggests that detection of developing kidney damage is useful.

Evidence-base

CKD is defined as a glomerular filtration rate (GFR) < 60ml/min/1.73 m^2 or evidence of kidney damage with or without a decreased GFR as evidenced by microalbuminuria; macroalbuminuria/proteinuria; glomerular haematuria; pathological abnormalities; anatomical abnormalities [1]. The two main manifestations of CKD in people with type 2 diabetes are a reduction in eGFR or the presence of albuminuria/proteinuria. A number of evidence-based guidelines specifically address CKD in people with type 2 diabetes [2-6]. There is a strong evidence base that treatment in the early stages of CKD reduces progression of kidney damage. Therefore there is general agreement that people with type 2 diabetes should be screened regularly (at diagnosis and then annually) to detect early indications of kidney damage and receive treatment.
The ACR is the preferred method of detecting albuminuria but cut-off values differ somewhat between guidelines with microalbuminuria being defined as 2.0-20.0 mg/mmol (men) and 2.8-28.0 (women) in Canada [6], 2.5-30.0 mg/mmol (men) and 3.5-30.0 mg/mmol (women) in Europe [3,5], and 2.5-25.0 mg/mmol (men) and 3.5-35.0 (women) in Australia [4] and macroalbuminuria as > 20/28 mg/mmol, > 30 mg/mmol and > 25/35 mg/mmol respectively. Issues surrounding screening tests are reviewed in detail in the NICE and Australian type 2 guidelines [4,5], with attention drawn to the day-to-day variation in albumin excretion which underlines the need for confirmatory testing. Monitoring of changes in GFR is emphasised in all guidelines, which recommend serum creatinine measurement and calculation of estimated GFR [2-6]. Assessment of both ACR and eGFR are necessary in order to stage CKD.

The UKPDS provided clear evidence for the benefits of blood glucose control and blood pressure control in delaying the development of kidney disease [7,8]. More recent studies have also demonstrated renal benefits of intensive blood glucose control [9,10]. Other evidence for the importance of blood pressure control in prevention comes from trials of various blood pressure lowering medications [2-6]. Choice of agent stems from evidence on the additional benefits of agents which target the renin-angiotensin system in offering renal and cardiovascular (see Chapter 11: Cardiovascular risk protection) protection, over and above the blood pressure-lowering effect. Both ACE-inhibitors and ARBs delay progression from micro- to macro-albuminuria in people with type 2 diabetes and hypertension. ARBs have been shown to delay progression of nephropathy in those who have macroalbuminuria and renal insufficiency (serum creatinine > 1.5 mg/dl [> 130 µmol/l]).

Advice to treat to tighter targets those with albuminuria is now a minority view, with general advice converging towards a target of 130/80 mmHg [2-6].

Cardiovascular risk is increased in people with microalbuminuria, and further increased in those with proteinuria and/or reduced GFR. The issue of cardiovascular risk is addressed elsewhere in this guideline (see Chapter 11: Cardiovascular risk protection).

Consideration

Although it is possible to treat kidney failure by dialysis or transplantation, availability of these very expensive treatments is severely limited in a global context. This makes efforts at prevention all the more important. It has been estimated that once a dipstick test is positive, time to kidney failure is

about 9 years, but that this time-interval can be doubled through appropriate treatment of blood pressure. The issue of targets can be a particular problem in people with type 2 diabetes who are often elderly, and in whom attainment of 140/80 mmHg or less is challenging even with multiple medications and reasonable lifestyle intervention.

Implementation

Management of blood pressure overlaps with the advice given in Chapter 10: Blood pressure control. Repeat blood pressure measurement and dose titration of medications requires good access to health services for people with evidence of renal damage. Management of CKD requires access to laboratory for ACR and creatinine estimations, and availability of multiple blood-pressure-lowering medications in particular renin-angiotensin system blockers.

Evaluation

The percentage of people with appropriate urine albumin and serum creatinine measurements should be ascertained. Where abnormalities are detected, evidence of action to ensure tight blood pressure control is required, together with achieved blood pressure. Level of eGFR at which referral to nephrologists occurred may also be determined.

Potential indicators

Indicator	*Denominator*	*Calculation of indicator*	*Data to be collected for calculation of indicator*
Percentage of people with type 2 diabetes having at least one measurement for microalbuminuria in the past year.	**Number of people with type 2 diabetes seen in the past year.**	**Number of people with type 2 diabetes having at least one measurement for microalbuminuria in the past year as a percentage of the number of people with type 2 diabetes seen in the past year.**	**Documentation and date of the microalbuminuria measurement.**
Percentage of people with type 2 diabetes having at least one creatinine measurement (and eGFR calculated) in the past year.	**Number of people with type 2 diabetes seen in the past year.**	**Number of people with type 2 diabetes having at least one creatinine measurement (and eGFR calculated) in the past year as a percentage of the number of people with type 2 diabetes seen in the past year.**	**Documentation and date of the creatinine measurement (and calculated eGFR).**

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14 FOOT CARE

Recommendations

Recommended care

FT1 **Assess feet of people with diabetes as part of an annual review for lesions which require active treatment and for risk factors for ulcer and amputation:**

1. **History of previous foot ulceration or amputation, symptoms of peripheral arterial disease, physical or visual difficulty in self-foot-care.**
2. **Foot deformity (hammer or clawed toes, bone prominences); visual evidence of neuropathy (dry skin, dilated veins) or incipient ischaemia; callus; nail deformity or damage; footwear.**
3. **Detection of neuropathy by 10 g monofilament (or 128 Hz tuning fork); a biothesiometer is an option for quantitative assessment (cut-off point for ulcer risk > 25 volts); non-traumatic pin-prick.**
4. **Palpation of foot pulses (dorsalis pedis and posterior tibial). Doppler ankle:brachial pressure ratio (< 0.9 for occlusive vascular disease) may be used where pulses are diminished to quantify the abnormality.**

FT2 **Discuss the reasons for foot review with each person with diabetes as part of the foot-care educational process.**

FT3 **Agree a foot-care plan based on the findings of annual foot review with each person with diabetes.**
Assess and provide necessary foot-care education according to individual need and risks of ulcer and amputation.

FT4 **Classify risk of ulcer or amputation according to findings of the foot assessment:**

1. **NO ADDED RISK: no risk factors and no previous history of foot ulcer or amputation.**
2. **AT RISK: one risk factor and no previous history of foot ulcer or amputation.**
3. **HIGH RISK:**
   - **Two or more risk factors.**
   - **Previous ulcer or amputation (very high risk).**

FT5 **Manage according to risk classification level:**
NO ADDED RISK:
Provide foot-care education.
AT RISK:
Arrange regular review, approximately 6 monthly, by foot-care team.
At each review:

1. **Inspect both feet – ensure provision of local management as indicated.**

2. Evaluate footwear – provide appropriate advice.
3. Enhance foot-care education.

HIGH RISK:

Arrange frequent review every 3-6 months by foot-care team.

At each review:

1. Inspect both feet – ensure provision of local management as indicated.
2. Evaluate footwear – provide advice and specialist insoles and shoes if indicated.
3. Consider need for vascular assessment or referral if indicated.
4. Evaluate and ensure the appropriate provision of intensified foot-care education.

FT6 People with foot ulceration or infection require the following management:

Refer to multidisciplinary foot-care team within 24 hours for:

1. Appropriate wound management, dressings and debridement as indicated.
2. Infections should be classified as mild (superficial with minimal cellulitis), moderate (deeper than skin or more extensive cellultis), or severe (accompanied by systemic signs of sepsis). Consideration of systemic antibiotic therapy (often longer term) for extensive cellulitis or bone infection as indicated; generic penicillins, macrolides, clindamycin and/or metronidazole as indicated as first-line medications, with ciprofloxacin or co-amoxicllin as examples of second-line medications.
3. Probing to bone, radiology and scans, magnetic resonance imaging, and biopsy where indicated for suspected osteomyelitis.
4. Reduce weight bearing, relief of pressure (walking with crutches, rest) and optimal pressure distribution (casting if indicated and not contraindicated)
5. Investigation and treatment (referral) for vascular insufficiency.
6. Specialist footwear and orthotic care (e.g. insoles), and individualised discussion of prevention of recurrence, when ulcer has healed.
7. Optimal blood glucose control.

FT7 Amputation should not be considered unless:

1. A detailed vascular evaluation has been performed by the vascular staff.
2. Ischaemic rest pain cannot be managed by analgesia or revascularisation.
3. A life-threatening foot infection cannot be treated by other measures.
4. A non-healing ulcer is accompanied by a higher burden of disease than would result from amputation.

A specialist foot-care team will include doctors with a special interest in diabetes foot care, people with educational skills, and people with formal training in foot care (usually podiatrists or trained nurses).

Limited care

FT_L1 **Risk assessment and classification would be as for *Recommended care* but with sensory assessment by 10 g monofilament or tuning fork, with or without non-traumatic disposable pin-prick only, and peripheral circulation assessment by palpation of pedal pulses.**

FT_L2 **Classification of infection would be as for *Recommended care* but antibiotic therapy would be with generic penicillins, macrolides and/or metronidazole, given intravenously for deep tissue infections, and adjusted by response or culture results.**

FT_L3 **Vascular referral would be according to findings and local revascularisation facilities.**

Comprehensive care

FT_C1 **The principles are as for *Recommended care*, but the multidisciplinary foot-care team can be enhanced by on-site inclusion of vascular surgeons, orthopaedic surgeons, orthotists, social workers and psychologists.**

FT_C2 **Foot pressure distribution measurements might be made. Sophisticated vascular scanning and angiography could be available to the foot-care team.**

Rationale

Foot ulceration and limb amputation are among the major drivers of impaired health and of health-care costs in people with diabetes. While primary prevention of the underlying damage to nerves and vessels is addressed elsewhere in this guideline (see Chapter 15: Nerve damage), secondary intervention in those developing such risk factors can reduce this burden and cost on both the person with diabetes and society. Amputation is usually preceded by a foot ulcer. A strategy that includes prevention, patient and staff education, multidisciplinary treatment of foot ulcers, and close monitoring can substantially reduce amputation rates.

Evidence-base

Because of the potential for improvement of health and reduction of health-care costs, the evidence surrounding diabetes foot-care has been extensively and formally reviewed in many guidelines [1-6].

The output from these documents is very consistent in suggesting that formal regular review to detect people at risk, more regular review of those found to be at risk, and intensive management of those developing foot ulceration and infection can produce major returns in avoiding the health and monetary costs of amputation. Providing foot-care education for all patients, with increased intensity for those at higher risk [7], and vascular interventions where critical ischaemia is identified (or is contributing to ulceration), are also common recommendations arising from the evidence-base.

Diabetes foot care is predicated on regular examination of the feet for lesions which require treatment and for risk factors for future ulceration and amputation. The main risk factors include a past history of foot ulcer or amputation, peripheral neuropathy, peripheral vascular disease and foot deformity. In the majority, inappropriate footwear is the final event in the causal pathway to ulceration. Risk can be stratified according to the presence or absence of risk factors and risk classification schemes are generally similar across guidelines. Although assessment methods vary in their sophistication, accurate risk classification can be achieved with simple procedures available in routine primary care.

Interventions are based on risk level and should focus on individuals with an elevated risk. All people with diabetes require foot care education and regular assessment with the intensity increasing according to level of risk. Appropriate footwear is important in preventing foot problems.

Ideally patients with a foot ulcer should be referred to a multidisciplinary foot care team consisting of a diabetologist, surgeon (general and/or vascular and/or orthopaedic), podiatrist and diabetic nurse. Involvement of a multidisciplinary team can reduce amputations by 50-80% [8].

Consideration

There is little controversy over the system and needs of diabetes foot-care provision. Most recommendations of formal evidence-based guidelines can be implemented with little modification in situations where minimal health-care funding resources are available, as simply removing shoes and examining feet can usefully prevent serious foot problems and save people from becoming disabled and unproductive members of their communities.

Implementation

The availability of basic equipment, appropriate protocols, structured records and recall systems need to be supported by appropriate training for professionals providing screening and management services. In particular the training and provision of non-medically qualified foot-care assistants (podiatrists or people fulfilling that role) need to be assured. Liaison needs to be established with orthotists, footwear suppliers and cast technicians. Facilities for vascular scanning and vascular interventions will be by agreement with vascular surgical staff. Policy makers should be approached to consider the socio-economic burden of diabetes foot problems and assure structural and financial support for preventative strategies.

Evaluation

Evaluation is by annual incidence of foot ulceration, foot hospitalisation, foot ulceration healing rates within defined time-periods and amputation rates at different levels of the limb.

Potential indicator

Indicator	*Denominator*	*Calculation of indicator*	*Data to be collected for calculation of indicator*
Percentage of people with type 2 diabetes having at least one foot examination in the past year.	**Number of people with type 2 diabetes seen in the past year.**	**Number of people with type 2 diabetes having at least one foot examination in the past year as a percentage of the number of people with type 2 diabetes seen in the past year.**	**Documentation and date of the most recent foot examination.**

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15 NERVE DAMAGE

Recommendations

Recommended care

NU1 Diagnose sensorimotor nerve damage by history and examination (monofilament with or without temperature, non-traumatic pin-prick, vibration [tuning fork], ankle reflexes), and/or simple quantitative testing (e.g. biothesiometer vibration perception).
Use serum B12, thyroid function tests, creatinine/urea and medication history to exclude other causes.

NU2 Diagnose symptomatic (painful) diabetic neuropathy by excluding other possible causes of the symptoms.
Manage by stabilising blood glucose control, and treatment with tricyclic antidepressants if simple analgesia is not successful.
If a one month trial of tricyclic therapy is not successful, further treatment options include pregabalin/gabapentin and duloxetine, then tramadol and oxycodone. Further management normally requires referral to a pain control team.
Be aware of the psychological impact of continuing symptoms, particularly if sleep is disturbed.

NU3 Diagnose erectile dysfunction by history (including medication history), exclusion of endocrine conditions (measure prolactin and testosterone), and a trial of a phosphodiesterase type-5 (PDE5) inhibitor (where not contraindicated by nitrate therapy).
Consider other approaches such as intra-urethral or intracavernosal drugs and sexual and relationship counselling, where PDE5 inhibitors fail or cannot be used.

NU4 Diagnose gastroparesis by history, trial of a prokinetic drug (metoclopramide, domperidone) and if troublesome by gastric emptying studies.

NU5 Diagnose cardiovascular autonomic neuropathy by resting heart rate and heart rate response to provocation tests (lying-standing, Valsalva, deep breathing), and by lying and standing blood pressure.
Advise anaesthetists when relevant where this is present.

Limited care

NU_L1 Screen and diagnose sensorimotor nerve damage by history of symptoms, and sensory assessment by 10 g monofilament or tuning fork with/without non-traumatic disposable pin-prick (see Chapter 14: Foot care).

NU_L2 Manage symptomatic (painful) diabetic neuropathy by excluding other causes, stabilising glycaemic control, and treatment with tricyclic antidepressants if simple analgesia is not successful. Opiate analgesia may be necessary as locally available.

NU_L3 Assess erectile dysfunction by history and examination and consider possible contributions of other medication or disease.

Comprehensive care

NU_C1 The principles are as for *Recommended care*, but screening and diagnostic testing could also include quantitative sensory testing (vibration and temperature), electrophysiology and autonomic function tests.

Rationale

Neuropathy (nerve damage) is a common complication of type 2 diabetes. It contributes not only to foot problems (see Chapter 14: Foot care) but also to a range of troublesome symptoms including pain/paraesthesia and (where the autonomic nervous system is involved) gastro-intestinal, bladder and sexual problems. New therapeutic options have emerged in recent years.

Evidence-base

Aspects of neuropathy which do not relate directly to foot care have received increasing attention in evidence-based guidelines [1-4]. In addition, treatment options are expanding, especially for painful neuropathy [5-7].

Exclusion of non-diabetic causes of neuropathy is important because these may account for 10% of cases of neuropathy in people with diabetes [8]. These include assessment for vitamin B12 deficiency, hypothyroidism and renal insufficiency as well as enquiry about neurotoxic medications and excessive alcohol consumption. The range of tests available in clinical and research settings is detailed in two technical reviews [9,10].

There is general agreement that stabilising glycaemic control is important in the medium and longer term, and that tricyclic medications should be used as first-line therapy for painful neuropathy, although side-effects are common.

The evidence base for direct comparison of different agents is limited. Newer antidepressants such as duloxetine can reduce pain intensity and improve quality of life. Anticonvulsants such as gabapentin and pregabalin are more effective than placebo in reducing symptoms of painful neuropathy. Finally opiate analgesia (tramadol, oxycodone) either alone or in combination with other agents, can improve symptom control in individuals not controlled with other agents or monotherapy [1-7].

There are a variety of manifestations of autonomic neuropathy including gastroparesis, diarrhoea, faecal incontinence, erectile dysfunction, bladder

disturbance, orthostatic hypotension, gustatory and other sweating disorders, dry feet and unexplained ankle oedema.
Erectile dysfunction is a common but often overlooked complication of diabetes and specific enquiry should be included as part of the annual review. Treatment options include PDE5 inhibitors, intracorporeal or intraurethral prostaglandins, vacuum devices or penile prostheses. Men with erectile dysfunction should receive education about contributory factors. PDE5 inhibitors are the usual first-line therapy in the absence of contraindications. Referral for other medical or surgical management is indicated if PDE5 inhibitors are ineffective.

Gastroparesis symptoms may improve with dietary changes and prokinetic agents such as metoclopramide or erythromycin. Although there is limited research on specific dietary changes for improving gastroparetic symptoms, recommendations for low-fibre, and small, frequent meals, with a greater proportion of liquid energy have be helpful for some individuals [11].

Cardiovascular autonomic neuropathy should be suspected by resting tachycardia (> 100 bpm) or orthostatic reduction in blood pressure (a fall in SBP > 20 mmHg on standing without an appropriate heart rate response). It is associated with increased cardiac event rates.

Consideration

Manifestations of polyneuropathy and autonomic neuropathy often require specific enquiry and should be a part of the routine annual review. A diagnosis can usually be established by taking a history and a simple examination. Neuropathies can be very troublesome but a range of therapies is available. Some therapies are costly which argues against their use in situations where resources could be better directed to prevention by measures aimed at improving and stabilising glycaemic control.

Implementation

Appropriate protocols should be developed for sensory testing and may include formal assessment using the neuropathy disability score. Recommended medications should be available according to level of resources. Medical teams need to remain trained in the diverse manifestations of autonomic neuropathy.

Evaluation

Evidence should be available of records of regular surveillance for neuropathic symptoms, usually as part of direct questioning in programmed annual review. Where appropriate, record should also be available of direct questioning for erectile dysfunction. The availability of simple equipment for surveillance, and of drug supplies, can be evaluated.

Potential indicator

Indicator	*Denominator*	*Calculation of indicator*	*Data to be collected for calculation of indicator*
Percentage of people with type 2 diabetes assessed for symptomatic neuropathy in the past year.	**Number of people with type 2 diabetes seen in the past year.**	**Number of people with type 2 diabetes assessed for symptomatic neuropathy in the past year as a percentage of the number of people with type 2 diabetes seen in the past year.**	**Documentation and date of the most recent assessment.**

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16 OLDER PEOPLE

Recommendations

This chapter addresses aspects of diabetes care for older people (70 years and over) which are amenable to an evidence-informed intervention and have the potential to improve clinical outcome and quality of life.

Recommended care

OP1 Diagnosis of diabetes in older people should be in accordance with WHO criteria which apply to all age groups (see Chapter 1: Screening and diagnosis).
Asymptomatic older people should be screened for undiagnosed diabetes as outlined in Chapter 1: Screening and diagnosis.
Clinicians should be alert to isolated post-challenge hyperglycaemia which is common in older people.

OP2 An agreement should be negotiated between the clinician and the patient or principal carer on treatment aims and goals of care designed to optimise patient empowerment.

OP3 Glucose-lowering interventions should aim to achieve an HbA_{1c} of 7.0-7.5% / 53-59 mmol/mol.
A higher target may be appropriate in the presence of modifying factors such as vulnerability to hypoglycaemia, presence of co-morbidities, cognitive and mood status, and limited life expectancy.
Care should be taken in commencing blood glucose lowering medications unless FPG is consistently 6 mmol/l or higher.
As a precaution to reduce the risk of hypoglycaemia, particular care should be taken to avoid FPG < 6.0 mmol/l on treatment.

OP4 At initial assessment, all older people with diabetes should have a:

- Basic assessment of walking and activities of daily living abilities including the use of walking aids and special footwear, and a history taken enquiring about falls.
- History taken of any recent memory problems.
- Nutritional evaluation using a recognised assessment tool (e.g. the Malnutrition Universal Screening Tool [1]).
- Cardiovascular risk assessment and review/ discussion of modifiable risk factors including smoking cessation.

OP5 Structured patient educational should be accessible to all older people and take into account culture, language, nutritional preferences, ethnicity, level of disability, geographical factors and needs of carers.

OP6 Provide continuing care and support including:

- Promoting self-management including SMBG if indicated (see Chapter 8: Self-monitoring) within the context of the family and clinical setting.
- Annual Review including weight and height, BMI, blood pressure, falls risk assessment, assessment for foot (see Chapter 14: Foot care) and eye (see Chapter 12: Eye screening) problems, eGFR and urine albumin and lipid profile.

OP7 Regularly review those on oral agents taking into consideration the often increased risk of hypoglycaemia, renal dysfunction, polypharmacy and difficulties in adherence to treatment.
Metformin can be considered as first-line glucose-lowering therapy, and as an adjunct to insulin therapy in those requiring insulin.
Sulfonylurea is suitable as second-line therapy but is best avoided in those at higher risk of hypoglycaemia (the frail, housebound, or resident of a care home).
Where risk of hypoglycaemia is moderate and an insulin secretagogue is being considered, an agent with a lower hypoglycaemic potential should be used.
A DPP-4 inhibitor may be considered as second-line therapy.
A GLP-1 RA may be considered in obese non-frail older subjects as third-line therapy with metformin and a sulfonylurea.
Insulin treatment should not be delayed but offered as an option when clinical features are appropriate.
A basal insulin regimen may be safer in terms of hypoglycaemia risk than a pre-mixed insulin regimen.

OP8 Blood pressure lowering treatment should be commenced when blood pressure is consistently 140/90 mmHg or higher in people aged 70 to 80 years and if consistently 150/90 or higher in people aged over 80 years.
Aim for a target clinic blood pressure below 140/90 mmHg in people aged 70 to 80 years.
Aim for a target clinic blood pressure below 150/90 mmHg in people aged over 80 years.
Caution should be exercised in implementing aggressive blood pressure lowering therapy in older people.

OP9 Policies supported by enforcement should be in place for ensuring dignity, respect and freedom from age discrimination for all older people with diabetes.

Limited care

OPL1 **The principles are as for *Recommended care* and an Annual Review is mandatory.**

OPL2 **Medication options for control of blood glucose, blood pressure and lipids may be limited according to local availability (as per other sections of this Guideline).**

OPL3 **All older hospital in-patients with hyperglycaemia should be screened for diabetes and treatment to reduce glucose levels should not be delayed.**

Comprehensive care

OP_c1 **The principles are as for *Recommended care*, but all health and social care professionals engaged in the diabetes care of older people should be encouraged (and trained as necessary) to maintain a knowledge and skills base that considers the special characteristics and needs of the elderly.**

OP_c2 **Assessment of functional status by a multidisciplinary team skilled in evaluation using well-validated assessment tools should include a measure of three major domains of function – global/physical, cognitive and affective.**

OP_c3 **A multidisciplinary Falls Intervention programme should be offered to all people with a history of a fall or who by virtue of other risk factors have a high risk of falling.**

OP_c4 **To avoid excessive carer burden, support should be available in the areas of education, access to medical and nursing care, financial assistance, transport facilities and networking with other carers and support groups.**

OP_c5 **In the setting of an assisted facility or care home:**

- **A distinct Diabetes Care policy or protocol should be operating.**
- **At the time of admission, each resident should be screened for diabetes.**
- **Each resident with diabetes should have an individualised diabetes care plan with the following minimum details:**
  dietary plan, medication list, glycaemic and blood pressure targets, weight and nursing plan.

Rationale

Diabetes is a highly prevalent chronic disease in ageing populations often characterised by complexity of illness due to multiple co-morbidities and medications, and a substantially increased risk of functional and cognitive impairment, and disability. Diagnosis may be delayed, vascular complications undetected, and clinical care systems sub-optimal and uncoordinated.

Modern diabetes care systems for older people require integrated care between general practitioners, hospital specialists and other members of the health-care team.

The terms 'elderly' and 'older people' are often interchangeable, but for this guideline, they refer to individuals aged 70 years and over irrespective of the degree of independency or presence of other co-existing disease. The term 'frailty' is used to describe those with multiple co-morbidities (including dementia) and/or functional impairments who have an increased vulnerability in the short-term (usually within 2 years) to an adverse event such as a protracted hospital admission, institutionalisation, significant mobility disorder and need for carer support.

Diabetes care should include a multi-dimensional approach with an emphasis on prevention of and early intervention for vascular disease, tailored and individual metabolic goal setting, and assessment of disability due to physical and cognitive dysfunction. In subjects with functional impairment, facilitating subjects to take an active part in rehabilitation can foster autonomy, improve self-esteem and coping skills, and reduce anxiety and depression. Variations in clinical practice are common in most health-care systems resulting in inequalities of care. For older people with diabetes, this may be manifest as lack of access to services, inadequate specialist provision, poorer clinical outcomes and patient and family dissatisfaction. Clinician care should promote the highest level of health status and quality of life, and ensure patient safety.

Evidence-base

Despite the increasing number of older people with diabetes, few guidelines have addressed the special needs of older people [2-6].

In older people, there is a disproportionate increase in postprandial hyperglycaemia and FPG alone may be inadequate for diagnosing diabetes [7].

Few studies address the importance of diabetes education in the elderly although the empowerment approach showed significant improvements in various patient-centred outcomes including level of depression and significant reductions in HbA_{1c} and hospital admissions [8].

Advancing age and male sex are risk factors for lower limb complications and amputation in older people with diabetes and justify an aggressive approach to the identification and prompt intervention in early diabetic foot disease. Visual loss has a significant impact on quality of life in the elderly and those with diabetes are significantly more likely to have both corrected and uncorrected visual impairment. Increasing age and duration of diabetes are also risk factors for the development of diabetic retinopathy in elderly subjects with diabetes.

Diabetes in older people is often associated with marked declines in physical performance and lower limb disability and multiple underlying factors have been implicated [9]. Disability, falls risk and co-morbidities are often interrelated in older people with diabetes and diabetes in post-menopausal women is associated with a significant increased risk of fractures [10]. Structured exercise programmes including resistance training alone or as part of an activity plan may improve functional capacity and glycaemic control in older people with diabetes [11].

Diabetes is associated with an increased risk of both cognitive impairment and dementia (both Alzheimer's Disease and vascular dementia) [12] which are likely to adversely influence management and clinical outcomes, and their early detection is needed. Poor glycaemic control is associated with changes in mental performance and improving glycaemic control may lead to better working memory [13]. Diabetes increases the likelihood of mood disturbances including depressive illness in older people which can lead to poor adherence to medication and self-management [14]. Details of age-related and relevant functional assessment tools for older people with diabetes are available [15].

The prevalence of diabetes within care homes and extended facilities exceeds 20% [16]. Residents with diabetes may be particularly prone to hypoglycaemia and their associated frailty and high prevalence of cognitive impairment pose numerous problems for care, nutritional planning and medication use [3]. Data from major RCTs of interventions in this area are not available and current recommendations follow good practice observations [2-6].

In general, advanced age is not a barrier to the use of any glucose-, blood pressure- or lipid-lowering agent used in the treatment of adults with type 2 diabetes. The evidence-base for the benefit of glucose-lowering in people aged 70 years and over is minimal and the presence of co-morbid illness and functional impairments lessen any expected long-term benefits of better glycaemic control [17]. Newer treatments such as DPP-4 inhibitors appear to be effective and well tolerated in older patients [18]. Compared with the use of pre-mixed insulin, addition of a once-daily long-acting insulin to oral agents in older subjects can lead to less hypoglycaemia and a greater HbA_{1c} decrease [19]. Glucose control targets are usually set higher and are influenced by risk of hypoglycaemia, co-morbidities and life expectancy.

The benefits of treating older people with elevated blood pressure are widely published and even in very elderly patients (> 80 years), treatment with relatively simple regimens can lead to clinically relevant reductions in fatal and non-fatal stroke and death from any cause [20]. Blood pressure targets in older people with diabetes usually increase with advancing age, and targets are less stringent in the frail [2-6].

Statins appear to reduce cardiovascular risk similarly in both younger and older people irrespective of whether or not diabetes is present [21] with benefits generally observed up to the age of 80 years. Important reductions in major cardiovascular events, stroke and death rates have also been seen in a primary prevention trial in type 2 diabetes using atorvastatin versus placebo in subjects aged 40-75 years [21]. Studies of fibrate use in older people with diabetes are more limited. Although the FIELD study in subjects aged 50-75 years showed no fenofibrate benefit on the primary composite outcome, significant reductions in albuminuria progression, amputations and requirement for laser therapy for retinopathy were observed [23].

Consideration

Health-care professionals involved in the care of older people need to be alert to their wide variation in health status and functional and cognitive ability, and that medical management may be complex requiring an understanding of the physiology and complications of ageing. Many older people can self-manage and participate actively in diabetes education but for others where their independence is compromised, greater levels of support will be needed by both

formal and informal carer input. The importance of family must be emphasised, with good cooperation between the care giver and family.

Weight reduction and energy restriction are not encouraged in older people with diabetes and should only be considered with caution. Unintentional weight loss in older people has been shown to increase morbidity and mortality [24,25].

Implementation

A continuing integrated package of care should be offered by multidisciplinary diabetes teams in both hospital settings and in the community, trained in recognising special issues in older people such as multiple co-morbidities, functional impairments including cognitive and mood disturbances, and frailty. Access to specialist care and structured follow-up systems including recall for annual assessment are essential, as is the need to address the transition from empowered self-care to dependency and institutionalisation.

Evaluation

This should follow similar guidance recommended for diabetes care services for all adults but the focus must be on the inclusion of older people in audits, surveys and diabetes register data collection, irrespective of their level of dependency or domicile.

Items for evaluation can include annual surveillance rates, hospital admission rates, rates of amputation and visual loss, numbers being institutionalised and quality of life. Different diabetes care models which seek to optimise care of older people should include cost-effectiveness data.

Potential Indicator

Indicator	*Denominator*	*Calculation of indicator*	*Data to be collected for calculation of indicator*
Percentage of people with type 2 diabetes 70 years and older who have had a comprehensive assessment in the past year.	**Number of people with type 2 diabetes aged 70 and older seen in the past year.**	**Number of people with type 2 diabetes 70 years and older who have had a comprehensive assessment in the past year as a percentage of people with type 2 diabetes aged 70 years and older seen in the past year.**	**Documentation and date of the most comprehensive assessment.**

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17 IN-PATIENT CARE
Recommendations

Recommended care

IN-PATIENT CARE ORGANISATION

HO1 All patients with diabetes admitted to the hospital should have their diabetes clearly identified in the medical record.
All patients with diabetes should have an order for blood glucose monitoring, with results available to all members of the health care team.

HO2 Designate a diabetes-trained health-care professional to:
- Manage and co-ordinate systems of care related to diabetes management of in-patients.
- Co-ordinate training of hospital staff in awareness of the needs of people with diabetes.
- Implement strategies to prevent disempowerment of those who could self-manage their diabetes.
- Plan for discharge and follow-up.

HO3 Provide access for people with diabetes and hospital staff to a multidisciplinary diabetes team.

HO4 Ensure laboratory/service support for:
- Assays including plasma glucose, HbA_{1c}, basic haematology and biochemistry, and lipid profile.
- Microbiological investigation.
- Radiology and other imaging.

HO5 Patients with hyperglycaemia in the hospital who do not have a prior diagnosis of diabetes should have appropriate plans for follow-up testing and care documented at discharge.

GENERAL WARD CARE

HO6 Encourage self-management of diabetes (food choice, self-monitoring, insulin dose adjustment where appropriate) integrated into usual ward care.

MANAGEMENT DURING IN-PATIENT PROCEDURES

HO7 Evaluate blood glucose control and metabolic and vascular complications (in particular renal and cardiac status) prior to planned procedures; provide advice on the management of diabetes on the day or days prior to the procedure.

HO8 Ensure the provision and use of an agreed protocol for in-patient procedures and surgical operations.

HO9 Aim to maintain premeal blood glucose targets < 8.0 mmol/l (140mg/dl) and random blood glucose < 10 mmol/l (180 mg/dl), provided these targets can be safely achieved.

HO10 IV insulin delivery where needed, would generally be given as a glucose/insulin/potassium infusion.

HO11 Ensure awareness of special risks to people with diabetes during hospital procedures, including risks

from:

- Neuropathy (heel ulceration, cardiac arrest).
- Intra-ocular bleeding from new vessels (vascular and other surgery requiring anticoagulation).
- Medication (risks of acute renal failure causing lactic acidosis in people on metformin, for example with radiological contrast media).

CRITICAL CARE SITUATIONS

HO12 Provide access to intensive care units (ICU) for life-threatening illness, including blood glucose control usually with IV insulin therapy.

HO13 Provide protocol-driven care to ensure detection and immediate control of hyperglycaemia for anyone with a presumed acute coronary event or stroke, normally using IV insulin therapy with transfer to subcutaneous insulin therapy once stable and eating.

HO13 Once insulin therapy is started, a glucose range of 8.0-10 mmol/l (140-180 mg/dl) is recommended for the majority of critically ill patients while avoiding hypoglycaeamia.

HO15 Emergency rooms must have clearly visable standing orders stating all critically ill patients must have their blood glucose checked.

Limited care

HO_L1 The principles are as for *Recommended care*, but hospitals should designate an individual in charge of matters relating to in-patient diabetes, to co-ordinate training in awareness of the needs and provision of in-patient care for people with diabetes, and the provision and use of guidelines and protocols.

HO_L2 Laboratory assays should include plasma glucose and basic biochemistry; basic radiology should be available.

HO_L3 Management of plasma glucose levels during in-patient procedures will generally be as for *Recommended care*. Where this is not possible or carries special risk, frequent subcutaneous short acting insulin with frequent monitoring may be used in emergency situations, or longer acting insulin (e.g. NPH insulin) for minor procedures or more stable health states.

Comprehensive care

HO_c1 The principles are as for *Recommended care*, but would include repeated review by a diabetes specialist where general health state is changing or glucose control is problematic.

HO_c2 Maintain staff trained in aspects of diabetes management on any ward or procedure area with a significant throughput of people with diabetes.

HO_c3 Use telematic review of blood glucose control to a specialist's office for people in critical situations.

Rationale

Hyperglycaemia is found, and requires management, in hospital settings not only in people with known diabetes but also in people with previously unrecognised diabetes and in people with hospital-related hyperglycaemia which reverts to normal after discharge. Prevalence of diabetes in hospitalised adult patients is of the order of 10-20%. Hospital care for people with diabetes may be required for metabolic emergencies, in-patient stabilisation of diabetes, diabetes-related complications, intercurrent illnesses, surgical procedures, and labour and delivery.

Evidence-base

Some guidelines and recent publications have addressed in-patient management of hyperglycaemia [1-4]. There are three situations in which hyperglycaemia can occur in hospital – people with known diabetes, previously undiagnosed diabetes, or transient hospital-related hyperglycaemia. There is an established association between hyperglycaemia in hospitalised patients and poor outcomes. In general evidence supports targeted glucose control in the hospital setting to improve clinical outcomes. However there is some uncertainty as to how low the glucose targets should be since recent studies in critically ill patients have not shown a significant improvement in mortality with intensive glycaemic control and some have reported increased mortality [5] and increased risk of severe hypoglycaemia. The NICE-SUGAR RCT compared intensive glycaemic control (target 4.5-6.0 mmol/l [81-108mg/dl]) with standard glycaemic control (target 8.0-10.0 mmol/l [144-180 mg/dl]) in 6,104 critically ill participants, most of whom required mechanical ventilation [5]. Mortality was significantly higher in the intensive versus the conventional group in both surgical and medical patients and severe hypoglycaemia was more common in the intensively treated group. This suggests that it may not be necessary to target blood glucose values < 7.8mmol/l (140mg/dl), and that a highly stringent target of 6.1 mmol/l (110mg/dl) may actually be dangerous.

In a recent meta-analysis of 26 trials, pooled relative risk of death with intensive insulin therapy was 0.93 compared with conventional therapy (95% CI: 0.83-1.04) [6]. The pooled relative risk of hypoglycaemia with intensive therapy was 6.0 (95% CI: 4.5-8.0). The overall conclusion was that intensive insulin therapy increased the risk of hypoglycaemia but provided no overall benefit on mortality in the critically ill, but there was a possible mortality benefit for patients admitted to the surgical ICU.

The ADA [1] recommends that critically ill patients in ICU would normally be treated with an insulin infusion aiming to maintain glucose level between 7.8 and 10 mmol/l (140-180 mg/dl). Glucose targets < 6.1 mmol/l (110 mg/dl) are not recommended. Insulin infusion should also be considered during other illness requiring prompt glycaemic control, or prolonged fasting. There is a lack of studies on non-critically ill patients but the general glucose target range is also 7.8 to 10 mmol/l (140-180 mg/dl), as long as these can be achieved safely. Insulin is the preferred therapy in the hospital setting in the majority of clinical situations. This would usually comprise scheduled subcutaneous basal insulin with supplemental short acting insulin if required. Prolonged therapy with sliding scale insulin is not routinely recommended. Continuation of oral agents may be appropriate in selected stable patients who are expected to consume meals at regular intervals. Specific caution is required with metformin due to the possibility that a contraindication may develop during the hospitalisation, such as renal insufficiency, unstable haemodynamic status, or need for an imaging study that requires a radio-contrast dye.

Self-management in the hospital may be appropriate for competent adult patients who are medically stable and successfully self-managing their diabetes at home. The patient and physician, in consultation with nursing staff, must agree that patient self management is appropriate under the conditions of hospitalisation.

Consideration

It is important that hospitals designate a 'diabetes lead' individual who would be in charge of matters relating to diabetes, and could co-ordinate training of staff in awareness of the needs of those with diabetes, and develop strategies to prevent disempowerment of those who could self-manage their diabetes. Major considerations include that diabetes should not complicate the management of whatever condition resulted in admission to hospital, and that a person's diabetes should not emerge from hospital worse than when they were admitted. While the evidence over use of protocol-driven IV insulin regimens is not conclusive, the widespread and general adoption of these regimens globally appears telling.

Implementation

Systems of care and protocols need to be put in place and staff trained to ensure their effectiveness. Standardised protocols, developed by multidisciplinary teams, should specify insulin dose, include guidelines for identifying patients at risk for hypoglycaemia, and actions to be taken to prevent and treat hypoglycaemia. Bedside glucose monitoring requires defined administrative responsibility, a procedure manual, training, policies regarding frequency and procedures for alert values, quality control and regular maintenance of equipment.

Evaluation

Evaluation should consider evidence of the availability of trained staff (and training courses) and of protocols as above. Audits can be made of ward blood glucose control, and blood glucose control during surgery, after MI and in intensive care. Admissions to coronary care can be reviewed to ensure

measurement of blood glucose is occurring, and appropriate actions are then taken while in the unit and during follow-up.

Potential Indicator

Indicator	*Denominator*	*Calculation of indicator*	*Data to be collected for calculation of indicator*
Percentage of people with type 2 diabetes admitted to hospital with a care plan for the hospitalisation.	**Number of people with type 2 admitted to hospital over a given period of time.**	**Number of people with type 2 diabetes admitted to hospital with a care plan for the hospitalisation as a percentage of the number of people with type 2 admitted to hospital over a given period of time.**	**Documentation of presence of diabetes and of a care plan.**

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Acronyms and abbreviations

ABPM	ambulatory blood pressure monitoring
ACCOMPLISH	Avoiding Cardiovascular events in COmbination therapy in Patients LIving with Systolic Hypertension
ACCORD	Action to Control CardiOvascular Risk in Diabetes
ACE-inhibitor	angiotensin converting enzyme-inhibitor
ACR	albumin:creatinine ratio
ADA	American Diabetes Association
ADDITION	Anglo-Danish-Dutch study of Intensive Treatment In peOple with screeN detected diabetes in primary care
ADVANCE	Action in Diabetes and Vascular disease; preterax And diamicroN-MR Controlled Evaluation
AIDS	acquired immunodeficiency syndrome
ALLHAT	Antihypertensive and Lipid-Lowering treatment to prevent Heart Attack Trial
ARB	angiotensin-II receptor blocker
ASCEND	Acute Study of Clinical Effectiveness of Nesiritide in Decompensated heart failure
ASCOT-BPLA	Anglo-Scandinavian Cardiac Outcomes Trial – Blood Pressure Lowering Arm
BMI	body mass index
BP	blood pressure
bpm	beats per minute
CCB	calcium channel blocker
CCT	controlled clinical trial
CHARISMA	Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance
CKD	chronic kidney disease
CVD	cardiovascular disease
DBP	diastolic blood pressure
DCCT	Diabetes Control and Complications Trial
DDG	German Diabetes Association
DPP-4	dipeptidyl peptidase 4
DRS	Diabetic Retinopathy Study
DSME	diabetes self-management education
eAG	estimated average glucose
eGFR	estimated glomerular filtration rate
ETDRS	Early Treatment Diabetic Retinopathy Study
FIELD	Fenofibrate Intervention and Event Lowering in Diabetes
FPG	fasting plasma glucose
GFR	glomerular filtration rate
GLP-1 RA	glucagon-like peptide-1 receptor antagonist
HbA_{1c}	glycated haemoglobin
HDL	high density lipoprotein
HIV	human immunodeficiency virus infection
HPLC	high-performance liquid chromatography
ICU	intensive care unit
IDF	International Diabetes Federtion
IFCC	International Federation of Clinical Chemistry and Laboratory Medicine
IRMA	intra retinal microvascular abnormalities
IV	intravenous
LDL	low density lipoprotein
Look AHEAD	Action for HEAlth in Diabetes

MDRD	modification of diet in renal disease formula
MI	myocardial infarction
MNT	medical nutrition therapy
NICE	National Institute for Clinical Excellence
NICE-SUGAR	Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation
NPH insulin	neutral protamine Hagedorn insulin
OGTT	oral glucose tolerance test
ONTARGET	ONgoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial
PDE5	phosphodiesterase type-5
PROactive	PROspective pioglitAzone Clinical Trial In macroVascular Events
RCT	randomised controlled trial
RECORD	Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycaemia in Diabetes
SIGN	Scottish Intercollegiate Guidelines Network
SMBG	self-monitoring of blood glucose
SMS	self-management support
SBP	systolic blood pressure
UK	United Kingdom
UKPDS	United Kingdom Prospective Diabetes Study
USA	United States of America
VADT	Veterans Affairs Diabetes Trial
WESDR	Wisconsin Epidemiologic Study of Diabetic Retinopathy
WHO	World Health Organization
WHO-5	World Health Organization (five) well-being index

Disclaimer

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