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Clinical guidelines for type 1 diabetes mellitus with an emphasis on older adults: an Executive Summary

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Abstract

We present a summary of a guideline produced by an international group of experts for managing type 1 diabetes in adults with an emphasis on the special needs of older people with this condition. The rationale for delivering high-quality diabetes care for adults with type 1 diabetes, why it is important to include older people in our considerations, and the key underpinning principles of the guideline are included. The structure of the recommendations given is described and consists of 'general' recommendations followed by 'specific' recommendations according to three categories depending on the characteristics of adults addressed, such as functional level or self-management ability. Recommendations are provided in the areas of: clinical diagnosis, establishing management plans and glucose regulation, diabetes self-management education, nutritional therapy, physical activity, exercise and lifestyle modification, insulin treatments and regimens, use of technology in diabetes management, hypoglycaemia, managing cardiovascular risk, management of microvascular risk, and inpatient management of type 1 diabetes and ketoacidosis.

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Introduction to the guideline

This guideline for managing type 1 diabetes mellitus in adults addresses management concerns for the increasing numbers of adults with type 1 diabetes and the continuing shortfalls in quality diabetes care that is apparent even in well-resourced clinical care pathways. A key objective is to educate and upskill health professionals and provide clear practical advice on assessment and management for both people with type 1 diabetes and their families. We, as an international group of clinical scientists, feel it will also have value for clinical researchers and scientists, and local and national commissioners of healthcare strategies, and create a platform for enhancing the effectiveness of clinical interventions in reducing the public and personal health burden associated with this condition.

The guideline has recognized that many older adults (aged 70 years and over) have type 1 diabetes and some may also present *de novo* with type 1 diabetes in later life. With advancing age comes the increased risk of pre-disability conditions such as frailty and dementia, and the need to consider care provided predominantly by close family and informal carers. We have not included management guidelines relating to type 1 diabetes in pregnancy as we felt this subject was outside our remit for this guideline.

Rationale for high-quality diabetes care in adults with type 1 diabetes

The majority of cases of type 1 diabetes represent an autoimmune condition disease with a strong inherited background, which although seen predominantly for the first time in children and young people, is present at consistent rates in all decades of adult life. There are few studies estimating the global burden of type 1 diabetes in adults but as of 2017, the International Diabetes Federation (IDF) estimated that there were 451 million people (aged 18–99 years) with diabetes worldwide, of which type 1 diabetes accounts for between 5% and 10%. However, at present, IDF prevalence data are based on information received for those adults aged 20–79 years which limits our interpretation of type 1 prevalence in those aged 80 years and over. However, there is some indication that in high-income countries, between 10% and 15% of all diabetes is attributable to type 1 diabetes, although the estimate is likely to be lower in low- and middle-income countries. The

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What's new?

- This work represents the first diabetes guideline that makes both general and specific recommendations based on descriptive and functional characteristics of adults with type 1 diabetes.
- This is the first type 1 diabetes guideline that considers the needs of older adults with this condition.
- Recommendations are designed to provide a guide to allowing comprehensive assessment model and risk stratification approaches (including functional assessment) to be central features of management.
- The recommendations provide an individualized multidimensional integrated approach to the comprehensive management of type 1 diabetes in adults.

incidence of type 1 diabetes appears to be increasing at a rate of 2–5% per year worldwide and about 25% of such cases are diagnosed in adulthood, and some even as late as the ninth decade of life. Those affected have very particular needs and, irrespective of age, many adults with type 1 diabetes who do not receive insulin and skilled instruction after diagnosis, may die prematurely.

Many of the challenges associated with type 1 diabetes as a whole have been addressed in part by improvements in diabetes monitoring, systematic diabetes care processes and the development of new treatments during the 1980s and 1990s, and the publication of evidence on specific goals on treatment.

However, in public health terms, type 1 diabetes continues to remain a fundamental challenge to both clinicians and their employers (healthcare providers) who recognize the continuing burdens of high vascular complication rates, increased hospitalization for diabetic ketoacidosis, suboptimal care strategies that leave a majority of adults with type 1 diabetes with poor control of glucose and other risk factors, and chronic diabetes complications with consequent increasing healthcare expenditure. The personal health burden of type 1 diabetes in adults has similar disappointing effects, with lives complicated by intrusive care practices such as frequent monitoring of blood glucose, dietary restriction, worrying episodes of hypoglycaemia and treatment regimens that appear complex and difficult to manage within the context of an ordinary day in their lives.

Considering the special needs of older adults with type 1 diabetes mellitus

The working group has recognized that an important limiting factor for producing specific evidence-based clinical guidelines for adults with type 1 diabetes is the need to extrapolate evidence from earlier clinical studies carried out more than two decades ago because data from more recent large randomized controlled trials in older type 1 diabetes populations are not available. The working group has considered this implication and has attempted to seek evidence from a wide range of studies that provide enough confidence for the basis of each recommendation. This limitation has influenced our decision not to grade our recommendations at a particular level of evidence, but we have provided the rationale and key references for our recommendations in each section to offset this.

In a growing population of adults with type 1 diabetes, many of whom are now in their sixth or seventh decades of life, we also feel that it is increasingly important that modern recommendations for managing their diabetes are more closely aligned with additional individual characteristics such as functional status, presence of frailty and dependency, comorbidity profiles and life expectancy. These are likely to influence treatment goals, the care model adopted, and how the clinician plans on-going care. In response to this, the working group assessed the level of evidence available across a broad range of clinical areas but did not consider that sufficient evidence in type 1 diabetes was available in the areas of home care and diabetes or end of life diabetes care at present to justify evidenced-based recommendations in these two areas.

The working group also accepts a key limitation on developing this guideline: that is, the lack of data from published studies in type 1 diabetes in which participants included were over 70 years of age, where the risk of complex comorbidity, frailty and dependency is so often seen. This introduces an obvious weakness into this guideline relating to treatment decisions based on recommendations that include older people. However, the United Nations (UN) recognizes that people aged 60+ years are more representative of ageing populations in under-developed countries and as a consequence, we leave it to individual clinicians to decide how and why particular age thresholds for management should be applied in their local practices.

Key actions to be prompted by this guideline

The working group recognizes that shortfalls in the care of adults with type 1 diabetes are still reported in higher socioeconomic countries where diabetes services are well-developed. These deficits in care are exaggerated in those countries where there are fundamental gaps in service provision and funding for organized health care. In line with the World Health Organization (WHO), the working group has emphasized the importance of directing healthcare resources towards improving the quality of preventative care in primary care settings and public health interventions that control diabetes rates of all types.

The recommendations are designed to support clinicians to provide an individualized multidimensional integrated

approach to the comprehensive management of type 1 diabetes in adults.

Key principles underpinning the guideline

We have provided a set of guiding principles that influence the decisions taken and recommendations provided, and which describe the philosophy expressed by the working group.

The guiding principles include:

- an all-inclusive, individualized care plan written for each adult with type 1 diabetes;
- reducing distress in older adults with diabetes and maintaining safety by avoiding unnecessary hospital/emergency department attendance due to ketoacidosis or hypoglycaemia;
- increased availability of educational support for all adults with type 1 diabetes and their families/carers;
- implementation of local health strategies that minimize vascular complication rates and unnecessary surgery for diabetic foot disease;
- where possible, assisting clinicians to undertake therapeutic decisions that are based on a comprehensive assessment model and risk stratification approach, including functional assessment in those with restriction of activities of daily living (ADL) (e.g. bathing, dressing) and walking limitation, assessment of skills in insulin administration and self-blood glucose monitoring, and assessing the risk of hypoglycaemia;
- the importance of ensuring that all those with palliative care needs eventually experience a dignified death

Structure of sections with a description of categories for recommendations

Apart from the clinical diagnosis section (where 'general' recommendations only have been produced), the following chapter structure has been adopted:

- Recommendations
  - General
    - These reflect the main principles of each section in this guideline. They apply in general to all adults with type 1 diabetes where appropriate and feasible. Exceptions will be obvious for those in categories 2 and 3 below.
  - Specific
    - These are then made for each of three functional categories detailed below which have been modified to a type 1 adult perspective from the functional categories used for the IDF global guidance on managing older people with type 2 diabetes (Refs 69 and 160).

Functional category	Specific recommendations
Category 1	Independent in ADL and cognitively intact; responsible for diabetes self-management
Category 2	Degree of ADL loss or limitation of walking associated with multi-morbidity or diabetes complications; may have some features of early to moderate frailty
Category 3	Disabled due to vascular disease, or requiring carer input, or unable to self-manage*, or care home residency *includes those with cognitive impairment or dementia

Detailed guidance for clinicians on the above categories which have been used to provide the basis for the recommendations is given in the online version of the guideline (https://www.diabetes.org.uk/resources-s3/2019-05/Clinical%20Guideline%20for%20Type%201%20Diabetes%20for%20Older%20Adults%20-%20April%202019.pdf).

Additional information available in the online version of the full guidance

In the full version of the guidance, there is also a section on the evidence base and reasoning that supports the recommendations in each clinical area. The accompanying references are also provided in this Executive Summary. There are additional sections on usual clinical practice (how recommendations are implemented in routine clinical practice), and a section for each clinical topic on assessment of care and clinical audit measures.

Clinical recommendations

These are provided for each of the 11 sections in the full guidance. The full guidance is over 38 000 words in length and the authors of this Executive Summary decided to include only the key recommendations (up to five 'general' and up to three specific per category). The full guidance including the rationale and evidence base are given online (https://www.diabetes.org.uk/resources-s3/2019-05/Clinical%20Guideline%20for%20Type%201%20Diabetes%20for%20Older%20Adults%20-%20April%202019.pdf).

The references that underpin the evidence base for the recommendations in each section are provided at the end of this Executive Summary.

Clinical diagnosis [1–8]

General

- Establish the diagnosis of diabetes based on recognized criteria with or without association with symptoms.
- Although adults older than 45 years of age presenting with hyperglycaemia above diagnostic thresholds are likely to have type 2 diabetes, a proportion may have an

evolving type 1 diabetes state: be particularly alert if they are thin (a BMI < 25 kg/m^2), have an atypical presentation or have a family history of autoimmune disease.

- 'Classic' presentations of type 1 diabetes in adults occur to varying degrees and may have features of an acute illness and additionally present with one or more of the following:
  - a ketotic state (ketonaemia > 3.0 mmol/l or significant ketonuria (more than 2+ on standard urine ketone sticks);
  - a sudden loss of weight;
  - a BMI of 24 kg/m^2 or below.
- The diagnosis of autoimmune type 1 diabetes may be assisted by the measurement of C-peptide and/or diabetes-selective autoantibody levels where available.
- The measurement of diabetes-selective autoantibody levels, such as glutamic acid decarboxylase autoantibodies (GAD65), islet cell cytoplasmic autoantibodies or insulin antibodies may reduce the risk of missing the diagnosis.

Establishing management plans in adults with type 1 diabetes including glucose regulation [9–20]

Education and cardiovascular risk reduction and complications screening

General

- All adults with type 1 diabetes should have a written management plan that reflects the outcome of a comprehensive and integrated assessment of need.
- Structured diabetes education should be offered to all adults with type 1 diabetes.
- Monitoring of blood glucose should only be used within an individualized care package.
- Older adults with long-standing type 1 diabetes should be regularly screened for new complications and the early features of frailty.

Specific

- **Category 1**
  - There should be a regular review of self-care behaviours and abilities that may influence goal attainment by the management plan.
  - Modifiable individual cardiovascular risk factors should be treated in all adults with type 1 diabetes irrespective of age.
  - Functionally independent people with diabetes are encouraged to maintain ADLs and mobility, and achieve and maintain a healthy body weight.
  - The blood glucose monitoring plan and the nutrition plan should be individualized with consideration of the adult's food preferences, eating habits, and physical and cognitive health status.
- **Category 2**
  The general principles are as for category 1, but additional precautions are required:
  - Health professional support for self-management education should take physical and mental functional impairments into account and be modified in adults with multiple morbidities, vascular complications and frailty.
  - Encourage light to moderate resistance training and balance training to improve physical performance, reduce falls and prevent further deterioration in functional status.
- **Category 3**
  Similar recommendations to adults in category 2 where feasible but additional areas require consideration including the need for additional family or informal or formal carer support:
  - The focus of educational support should be reassurance and preventing acute metabolic and vascular complications of diabetes.
  - The blood glucose monitoring plan should be minimized where possible, undertaken by a family member or informal care, and take into account the estimated risk of frequent hyperglycaemia (capillary blood glucose levels > 12.0 mmol/l) and hypoglycaemic episodes.

Glycaemic control

General

- Support adults with type 1 diabetes to achieve an individual target level of glycaemia taking into account their usual daily activities, occupation, current profile of vascular complications, physical and mental health status, and estimated risk of hypoglycaemia.
- The primary goals of glycaemic regulation in type 1 diabetes are: prevention of long-term vascular complications, avoidance of hyperglycaemia and diabetic ketoacidosis, avoidance of hypoglycaemia, and attainment of a maximal quality of life.
- Adults on intensive insulin therapy should be encouraged to test frequently (between four and six times per day).

- The use of continuous glucose monitoring may have a role in those adults with type 1 diabetes with hypoglycaemic unawareness.
- Where available, encourage adults with type 1 diabetes to participate in a structured diabetes education programme.

Specific

- **Category 1**
  - In general, adults with type 1 diabetes should aim for a target range of 48–53 mmol/mol (6.5–7.0%) unless there is an unacceptable risk of hypoglycaemia.
  - In adults with type 1 diabetes who are aged 70 years and over, the target range should be 53–58 mmol/mol (7–7.5%)
  - Regular pre- and postprandial capillary glucose level testing by the adult with type 1 diabetes should be asked for according to an agreed individualized plan.
- **Category 2**
  The general principles are as for category 1, but additional precautions are required:
  - A less stringent HbA_{1c} target range of 53–58 mmol/mol (7.0–7.5%) can be aimed for.
  - Older frail adults with type 1 diabetes have a high risk of acute illness and hospitalization, and may require frequent insulin dose adjustments with changes in their overall health status: in these cases, the HbA1c target range can be increased to 64 mmol/mol (7–8.0%, 53–64 mmol/mol).
- **Category 3**
  Many of the general principles in this section are not warranted, but key areas for consideration are:
  - The management target during treatment is to avoid symptomatic hyperglycaemia and hypoglycaemia.
  - An HbA_{1c} target range of 58–69 mmol/mol (7.5–8.5%) may be appropriate in those with severe disability or moderate to advanced dementia.

Cardiovascular disease management

General

- Every clinical effort should be carried out to optimize blood glucose, lipids and blood pressure to reduce cardiovascular risk. Provide advice on smoking, obesity and exercise.
- Adults with type 1 diabetes should receive an annual influenza vaccination and be considered for pneumococcal vaccination if not previously immunized against this latter infection.

Specific

- **Category 1**
  - The blood pressure goal is < 140/90 mmHg.
  - Lower blood pressure targets may be appropriate if the specific target can be achieved with an acceptable treatment burden.
  - Lipid management, should be similar in adults with either type 1 or type 2 diabetes.
- **Category 2**
  The principles are as for category 1, but additional precautions are required:
  - Carers should be provided with sufficient knowledge for safe administration of blood pressure-lowering and lipid-lowering therapy.
  - In frail older adults without end-stage chronic illness, blood pressure goals can be modified; a target blood pressure of up to 150/90 mmHg may be appropriate.
- **Category 3**
  The same overall precautions are as indicated for people in category 2.
  - Strict control of blood pressure may not be necessary, and in some circumstances withdrawal of blood pressure-lowering therapy may be appropriate.
  - Anti-hyperlipidaemic and anti-hypertensive pharmacotherapy should be approached with caution in people with advanced dementia.

Diabetes self-management education [21–25]

General

- Structured diabetes education should be offered to all adults with type 1 diabetes with the teaching strategy and learning environment modified to suit each adult and/or their carer(s) as appropriate, and must take into account learning styles and learning ability.
- Education should be individualized, include goal setting and focus on safety, risk management and complication prevention.
- All adults with type 1 diabetes require individualized plans that include:
  - insulin regimen;
  - blood glucose and blood ketone monitoring;
  - hypoglycaemia treatment and prevention;
  - sick day management.

- Education strategies focusing on monitoring blood glucose and/or blood ketones and administration of insulin by others must be considered as an integral component if self-care deficits exist.

Specific

- **Category 1**
  - The focus should be on individualized self-management education with on-going review of self-care behaviours and self-care capacity.
- **Category 2**
  The same principles as for category 1 but with additional recommendations:
  - Self-management education should take account of physical and mental functional impairments (ability to make their own choices), comorbidities, vision, hearing, manual dexterity and the social situation.
  - The characteristics of older learners need to be considered when planning, delivering and evaluation diabetes education.
- **Category 3**
  - Insulin administration, blood glucose and blood ketone testing will need to be undertaken by a family member, informal carer or healthcare professional, depending on individual circumstances.
  - Education should be provided to carers, healthcare professionals and informal carers.

Nutritional therapy [26–35]

General

- All adults with type 1 diabetes should have access to a specialist nutritional therapist to plan their individualized nutritional programmes.
- Meal planning and meal patterns should be based on advice on optimal foods to consume, snacking behaviour, content of foods that align with insulin regimen in use, safe alcohol intake, sodium intake (< 2300 mg/day) and how to reduce excessive glucose fluctuations throughout the day.

Specific

- **Category 1**
  - Functionally independent adults with type 1 diabetes should be encouraged to eat a variety of foods and maintain a healthy body weight.
  - Education on the benefits of carbohydrate counting, insulin dose adjustment and physical activity management should be part of the dietary advice given by the local healthcare or diabetes team; this may be particularly important in those on flexible insulin regimes.
- **Category 2**
  - Adults with type 1 diabetes who have moderate to severe renal impairment, or hypertension, or evidence of associated cardiovascular disease should have a revision of their nutritional plan to optimize clinical outcome.
  - Nutritional assessments using tools such as the Malnutrition Universal Screening Tool (MUST) or the Mini Nutritional Assessment (MNA), or the use of dietary software analysis, may assist in revealing important dietary shortfalls in those with frailty or excessive comorbidity.
- **Category 3**
  - All adults with type 1 diabetes in this category require nutritional assessment to exclude undernutrition, particularly those who are housebound or residing in aged care homes.
  - Carers should allow additional time for meals, snacks and drinks.
  - Individuals should be encouraged to have sufficient fluid to avoid dehydration.

Physical activity, exercise and lifestyle modification [36–50]

General

- Physical activity is recommended as an important component of diabetes care and should consist of: (1) a minimum 120–150 min of moderate aerobic activity per week; (2) a minimum of two sessions of resistance training per week, each lasting at least 20 min.
- Adults with type 1 exercise should only commence exercise when their blood glucose level is > 5.0 mmol/l; when the level of glucose is < 8.0 mmol/l before planned exercise, pre-ingestion of 10–20g of glucose may be necessary to avoid hypoglycaemia.
- In those who engage in moderate- to high-intensity exercise, advice should be sought on what levels of glycaemia are acceptable and what nutritional and/or hydration advice is needed.
- All older adults with type 1 diabetes should be encouraged to limit the daily amount of time sitting.
- Persons with diabetes and their carers should be educated about the prevention and management of hypoglycaemia that may occur during or after exercise.

Specific

- **Category 1**
  - Regular exercise to maintain ideal body weight is recommended.
- **Category 2**
  - Light intensity physical exercise (e.g. walking two to three times per week for 30 min) including stretching and flexibility exercises are recommended to maintain function.
  - Provide physical or occupational therapy to maximize physical function.
- **Category 3** As for category 2 with additional recommendations:
  - Exercise tailored to functional ability is recommended. For frail adults, to slow the decline in muscle strength and muscle mass, it is recommended that some form of regular resistance training be attempted up to twice per week for 15–30 min and include usual daily activities such as sit to stand or walking.
  - Carers' education about safe ways of exercise for older adults with diabetes with cognitive dysfunction.

Lifestyle modification

General

- Adequate nutrition is an essential component of diabetes care.
- Each individual should have an individualized food plan based on preferences, culture, cognitive function and the ability to adjust insulin dosage.
- Older adults with diabetes on fixed insulin dosages should have consistent daily carbohydrate consumption.
- Smoking cessation and low alcohol consumption is encouraged.

Specific

- **Category 1**
  - Achievement of ideal body weight is recommended.
- **Category 2**
  - Eating difficulties should be identified to maintain nutrition.
  - Higher calorie diets may be required in frail older adults with diabetes.
- **Category 3**
  - Adequate hydration should be maintained.
  - Carer and family education about adjusting hypoglycaemic therapy in relation to erratic eating pattern should be provided.

Insulin treatments and regimens [15,17,51–55]

General

- Preferentially offer a basal–bolus insulin regimen at the time of diagnosis for all adults with type 1 diabetes that can self-manage; if available use rapid-acting insulin analogues preferentially as prandial insulin.
- The newer basal insulins, insulin glargine-U300 and insulin degludec, may offer advantages of less nocturnal hypoglycaemia and greater flexibility.
- As an alternative basal insulin regimen in adults with type 1 diabetes, consider offering a twice-daily regimen of a longer-acting insulin such as insulin glargine or detemir.
- Educate adults with type 1 diabetes to adjust prandial insulin doses in the light of daily carbohydrate intake, pre-meal capillary glucose estimates and level of physical activity.
- In older adults with type 1 diabetes or those unable or unwilling to manage a basal–bolus insulin regiment, consider offering a twice-daily mixed insulin regimen (analogues preferentially to reduce hypoglycaemia).
- Assess for new clinical, functional or psychosocial barriers if someone suddenly feels overwhelmed, shows deterioration in glycaemic control or errors in self-care abilities.

Specific

- **Category 1**
  - If available, consider offering continuous subcutaneous insulin pump therapy as an alternative to a basal–bolus regimen when previous regimens have failed to achieved glycaemia targets or persons with type 1 diabetes are experiencing worrying hypoglycaemia.
  - Assist each adult with type 1 diabetes to minimize the risk of hypoglycaemia and explain how the consequences of hypoglycaemia such as falls, fractures or deterioration in cognitive function can impact ability to manage diabetes or live independently and may affect their quality of life.
- **Category 2**
  - Where hypoglycaemia risk is high, consider using metformin therapy adapted for renal function as an adjunct to the insulin regime to reduce daily insulin dosage.

- Assess the manual dexterity ability of each person to perform insulin injections; this may involve an assessment of their vision.

- **Category 3**
  - A less stringent glycaemic target range can be applied to avoid too low and too high glucose levels.
  - Where other insulin regimens are not acceptable or failing to meet preferred targets, consider basal insulin regimens involving insulin glargine-U300 or insulin degludec or a combination of other basal and mixed insulins which may provide reasonable control while avoiding frequent injections and /or monitoring.

Use of technology in diabetes management [56–58]

General

- Technological advances in insulin delivery and blood glucose monitoring should be implemented in local diabetes care teams to improve the range of support for adults with type 1 diabetes and lessen the adverse effects of insulin injections and monitoring.
- All members of the local diabetes team should become aware of the newer automated injection devices such as insulin pens and pumps, as well as the latest durable insulin delivery devices for adults with type 1 diabetes.

Specific

- **Category 1**
  - Where feasible, all adults with type 1 diabetes in category 1 should be made aware of the latest technological developments in insulin delivery (including insulin pens and pumps) and considered if current insulin regimens are failing to achieve objectives and targets.
  - It is important to assess coping skills periodically, as a functionally independent individual may become dependent, or develop cognitive decline, and become unable to handle the use of technology over time.
- **Category 2**
  - These individuals may benefit from the use of auto-controlled technologies such as continuous glucose monitoring and smart-phone based apps that allow participation by carers. Carers can assist by receiving glucose data on their smart phones and following up with reminders to take insulin doses or eat on time.
  - Some of the technologies requiring complex decision-making may not be appropriate for use by this group.
- **Category 3**
  - Many technologies are not useful at this stage of life and should be avoided to prevent unnecessary cost, stress, and burden on both older people with diabetes and their families. The use of new technologies, however, must be adapted to the actual needs of patients and carer with the aim to simplify the care and increase quality of life where feasible.

Hypoglycaemia [59–67]

General

- Assessment of risk factors and the modifying factors for hypoglycaemia should be undertaken at each visit.
- All adults with type 1 diabetes should be carefully reviewed for hypoglycaemic unawareness at review procedures (at least annually).
- In the presence of impaired awareness of hypoglycaemia, ensure that the individual receives appropriate education about its importance and implications (preferably through a structured diabetes education programme).
- In adults with type 1 diabetes who remain persistently troubled by hypoglycaemic episodes exacerbated by impaired awareness, consider management with continuous subcutaneous insulin infusion or continuous glucose monitoring.
- After each episode of hypoglycaemia, a careful review of likely causes, identification of any new risk factors and an assessment of the treatment given to assist recovery from hypoglycaemia is recommended.

Specific

- **Category 1**
  - All general recommendations apply to this category.
- **Category 2**
  - All of the recommendations apply as for category 1.
  - Risk assessment for hypoglycaemia with regular review of risk and modifying factors is essential: adults with under nutrition or erratic meal plans, presence of frailty, or the onset of memory difficulties are at particular risk.
- **Category 3**
  - Adults with type1 diabetes in this category (such as aged care home residents) will be at the highest risk of hypoglycaemia and consideration should be given to relaxing strict glucose targets and reviewing insulin doses and associated regimens.
  - Adults in this category are at risk of hypoglycaemia may present similarly with behavioural symptoms or other symptoms of cognitive impairment. Carers

should have a low threshold for measuring capillary blood glucose levels whenever any potential symptom or sign is present.

Managing cardiovascular risk including blood pressure and lipid management [14,68–94]

Cardiovascular risk

General

- The approach strategies to preventing and identifying cardiovascular disease in adults with type 1 diabetes are the same used in the general population.
- All adults with type 1 diabetes aged 70 years and over should already be considered to be at high cardiovascular risk (10 year atherosclerotic cardiovascular disease risk >15%).

Specific

- **Category 1**
  - Each modifiable cardiovascular risk factor (e.g. atrial fibrillation, blood pressure, lipids, glycaemia, albuminuria and smoking) should be optimally treated.
- **Category 2**
  As for category 1 with additional measures according to the health status of the individual:
  - For those adults with some features of frailty less aggressive risk factor modification may be appropriate.
- **Category 3**
  - Those who are severely disabled with limited life expectancy, or who are fully dependent living in an aged care home, or at end of life, the detection and management of risk factors is usually unnecessary.

Blood pressure management

General

- In older adults with type 1 diabetes, the systolic blood pressure target range should be 130–140 mmHg if tolerated.
- Angiotensin-converting enzyme inhibitors should be the first choice for initiating therapy, particularly in the presence of diabetic nephropathy.
- Anti-hypertensives should be began at the lowest dose and be increased gradually.
- Down-titration of medications may be necessary, especially in the presence of polypharmacy and declining renal function.

Specific

- **Category 1**
  - All general recommendations apply.
- **Category 2**
  As for category 1 but with added measures:
  - Diuretics and alpha-blockers should be prescribed with caution in those who are frail or have mobility disorders.
  - Less-aggressive goals may be appropriate in those whose functional health is irreversibly compromised.
- **Category 3**
  - A target blood pressure of up to 150/90 mmHg may be appropriate.
  - In those with dementia, a lower blood pressure target (140/90 mmHg) may aimed for to optimize remaining cognitive performance.
  - Among individuals with advanced dementia, strict control of blood pressure may not have any added advantage, and for those at end of life, withdrawal of therapy may become appropriate.

Management of dyslipidaemia

Adults with type 1 diabetes demonstrate a lesser risk of dyslipidaemia than adults with type 2 diabetes and lipid profiles of those adults with well-controlled diabetes are similar to non-diabetic individuals.

General

- Total cholesterol, LDL-cholesterol, HDL-cholesterol and triglyceride levels should be assessed at diabetes diagnosis and at clinically relevant intervals.
- In the absence of definitive data, similar statin treatment approaches should be considered for those with type 1 or type 2 diabetes, particularly in the presence of other cardiovascular risk factors.
- Additional LDL-lowering therapy such as ezetimibe or a proprotein convertase subtilisin/kexin type 9 inhibitor may be of benefit in those with high atherosclerotic cardiovascular disease risk where levels of LDL remain > 1.8 mmol/l on other therapy.
- In adults with type 1 diabetes and high triglyceride levels (> 4.5 mmol/l) optimize glucose regulation, exclude other causes such as excess alcohol, and if necessary consider treatment with a fibric acid derivative or a fish oil if levels of triglycerides remain in excess of 10.0 mmol/l, which is general advice given to adults with type 2 diabetes including older adults.
- Lipid targets are as follows: LDL-cholesterol < 2.0 mmol/l; triglyceride < 2.3 mmol/l; HDL-cholesterol > 1.0 mmol/l;

non-HDL-cholesterol < 2.5 mmol/l. LDL-cholesterol should be < 1.8 mmol/l in established cardiovascular disease.

Specific

- **Category 1**
  All general recommendations apply including the following emphasis:
  - These individuals should be actively managed to reach agreed lipid targets.
  - Statins should be considered as first-line therapy.
- **Category 2**
  - Lipid-lowering therapy should be prescribed with caution in the frail or those with significant medical comorbidity and less aggressive goals may be more appropriate.
- **Category 3**
  - The threshold for prescribing lipid-lowering therapy in those with dementia or residing in an aged care home should be high.
  - Lipid-lowering therapy in those at end of life is not usually necessary, and withdrawal of therapy may be appropriate.

Management of microvascular risk and associated pathologies

Section A: diabetic eye disease [95–105]

General

- Where feasible, all adults with type 1 diabetes should have their eyes examined at the time of diagnosis and at least every 1–2 years thereafter.
- Depending on available resources, the eye examination could be done by direct fundoscopy through dilated pupils (using tropicamide) or fundus photography.
- All adults with type 1 diabetes and evidence of proliferative or severe non-proliferative retinopathy should be considered for laser photocoagulation to minimize visual loss.
- **Category 1**
  - All general recommendations apply to this category.
- **Categoy 2**
  As for category 1 but with the following added recommendations:
  - Primary care clinicians should ensure that all adults in category 2 are not lost to diabetic eye service follow up and that domiciliary assessment is offered where available.
  - Every endeavour should be made to ensure frail, housebound and aged care home residents with type 1 diabetes receive clinically appropriate eye examination and care.
- **Category 3**
  - Routine eye examinations for detecting diabetic retinopathy will not usually be warranted, but eye health should be assessed as a part of regular general health assessments and scheduled physical examinations.
  - In view of a future risk of blindness, a person with diabetes who lacks the mental capacity to consent to having an eye examination should not be permanently or automatically removed from a screening recall programme unless a 'best interest decision' to do so has been taken on his or her behalf.

Section B: diabetic renal disease [71,106–118]

General

- Screening for kidney disease should be performed at diabetes diagnosis and annually by measuring:
  - serum creatinine and determining the estimated eGFR;
  - a urine test for albuminuria (albumin to creatinine ratio). Urinary albumin to creatinine ratio measurement as a first morning void is the preferred method. If this is not possible, a random urine sample is appropriate.
- Persons with type 1 diabetes with more advanced chronic kidney disease (CKD) may have reduced insulin requirements and insulin regimens must adapt accordingly.
- Individuals with CKD should be managed as follows:
  - use of renin-angiotensin-aldosterone system blockade (angiotensin converting enzyme inhibitor or angiotensin receptor blocker) in persons with diabetes with albuminuria;
  - management of modifiable risk factors for cardiovascular disease;
  - avoid a high-protein diet;
  - adjust medications for level of kidney function;
  - referral to a nephrology specialist service when indicated.

Specific

Specific recommendations made for each of the categories detailed as follows:

- **Category 1**
  All general recommendations are pertinent to this category. A lower blood pressure or glycaemic goal

should be considered in this category compared with other categories.

- **Category 2**
  All general recommendations to prevent and treat CKD are pertinent to this category.
  - Those with CKD develop frailty at a younger age so interventions to maintain appropriate ADL should be started earlier.
  - Interventions to decrease sarcopenia include exercise as well as treatment of acidosis.
- **Category 3**
  All general recommendations to prevent and treat CKD are pertinent to this category.
  - Conservative management rather than dialysis should be considered for those with limited life expectancy.
  - Palliative care should be considered for those with severe CKD or who are at end of life.

Section C: diabetic foot disease [119–131]

General

- All adults with type 1 diabetes should receive a comprehensive assessment of their feet annually which includes a detailed history of their functional health, comorbidities, treatment and risk factor identification for prevention of ulcers and amputations; in cases with vascular insufficiency or loss of protective sensation, or previous history of ulceration or amputation, foot examination is recommendation at each visit.
- Foot examination should include: a detailed inspection of footwear, presence of infection, callus and deformities; assess risk for neuropathy using 10 g monofilament, 128 Hz tuning fork for vibration or biothesiometer; assess peripheral vascular circulation through palpation of foot pulses or by ankle–brachial pressure index. Note: an ankle–brachial pressure index < 0.9 may be indicative of vascular insufficiency but readings may be misleading in severe atherosclerotic stiffness.
- In people who are at high risk of a foot ulcer or amputation an integrated approach to foot care is recommended using a skilled multidisciplinary team.
- All adults with type 1 diabetes should receive education about preventative foot care from their local diabetes or healthcare team; ideally, this should be part of a structured diabetes education programme.
- All adults with type 1 diabetes should have access to specialist teams to assess worsening lower limb vascular function.

Specific

- **Category 1**
  All general recommendations apply with added measures:
  - Annual reviews should make an assessment of future risk by continued risk factor detection and management.
  - In cases of moderate (one or two risk factors – neuropathy or ischaemia) to high risk (more than two risk factors or previous ulcer or amputation), increase reviews by the clinician or foot care team to 3–6-monthly, and consider specialist referral as appropriate.
  - In cases of active ulceration, with or without infection, refer swiftly to the multidisciplinary specialist team.
- **Category 2**
  As for category 1 with added measures:
  - Assess for undernutrition, review comorbidity profile, detect features of frailty if present, and assess visual loss and a history of falls.
  - Ensure that carers have received education in the basics of diabetes foot care and have knowledge of how to prevent foot injury.
- **Category 3**
  As for category 2 with added measures:
  - Consider conservative measures in severe disability or dependency concentrating on symptomatic management if life expectancy < 6 months.
  - Take into account the person's quality of life and overall health status, particularly when any invasive vascular or surgical procedures are being considered.

Section D: diabetic neuropathy [132–151]

General

All adults with type 1 diabetes should undergo examination of the peripheral nerves at the initial visit and as part of the annual review using a 10 g monofilament or 128 Hz tuning fork, a biothesiometer (cut-off point for ulcer risk > 25 V) or non-traumatic pin-prick.

- Management of adults with type 1 diabetes and peripheral neuropathy includes:
  - optimizing glucose control;
  - regular foot care;
  - management of cardiovascular risk factors (hypertension, hyperlipidaemia, smoking cessation, etc.);
  - pain relief (if indicated),

- exclude other causes of pain in the limbs,
- therapeutic options include antidepressants, opiates, capsaicin cream, lidocaine patch, alpha-lipoic acid and transcutaneous electrical nerve stimulation,
- antidepressants, anticonvulsants and opiates may adversely affect stability, balance and cause cognitive problems, and careful titration is essential.

- Consider the presence of cardiovascular autonomic neuropathy if indicated clinically.
- Enquire about erectile dysfunction as part of the annual review.

Specific

- **Category 1**
  - All general recommendations apply to this category.
- **Category 2**
  - As for category 1 but with added measures:
  - In the presence of frailty, treatment approaches will in general be cautious and tailored to a prediction of likely benefits, use limited procedures for evaluation, and an optimal and safe dosage regimen of therapeutic agents.
- **Category 3**
  - Residents of aged care homes have a high prevalence of untreated pain and every effort should be made to detect and treat this symptom.
  - In cases of dementia, pain assessment is particularly important and should be formally evaluated in people with neuropathy.
  - Opiates should be used with great care because they may produce confusion in older adults with existing cognitive problems.
  - For those at end of life, detailed assessment procedures are not usually warranted and conservative management is recommended.

Inpatient management of type 1 diabetes and ketoacidosis [114,152–170]

General

- Admitting institutions and hospitals should make provisions to allow adults with type 1 diabetes to diabetes self-manage if they are well enough to do so.
- All admitting institutions and hospitals should have evidence of regular mandatory staff education in insulin management, and carbohydrate content displayed on menus.
- Glycaemic targets for inpatients vary; for those undergoing surgery or who are admitted acutely unwell, a target level of glucose in line with the Joint British Diabetes Society (JBDS) guidance is 6.0–10.0 mmol/l if it is not associated with hypoglycaemia; for those who are non-critically ill persons with type 1 diabetes, a target of 7.0–12.0 mmol/l is reasonable and acceptable, particularly in older adults, as long as these targets can be achieved safely.
- For inpatients who are not critically unwell, are able to eat, and where subcutaneous insulin administration is feasible and safe, consider using a subcutaneous basal–bolus insulin regimen to main satisfactory glucose levels.
- For inpatients who are acutely unwell, or who are scheduled for major surgery, or who are demonstrating wide fluctuations in glucose, use an agreed intravenous insulin regimen which is familiar to the clinical team managing the person.

Specific

- **Category 1**
  - All general recommendations apply.
- **Category 2**
  As for category 1 with added measures:
  - The diabetes specialist team and dietetic team should work collaboratively on developing agreed pathways with ward teams, for all insulin-treated inpatients whose functional level has changed adversely.
  - Frail older inpatients with type 1 diabetes are at particular risk of hypoglycaemia, with an increased risk of falls and cognitive impairment, and hypoglycaemia avoidance should be an important concern.
  - Older vulnerable adults with ketoacidosis require immediate specialist medical and nursing care to reduce adverse clinical outcomes.
- **Category 3**
  - In those adults with marked cognitive impairment or dementia, early involvement of the specialist diabetes inpatient team to implement the most effective insulin regimen during the inpatient stay and plans following discharge is important.
  - Adults with reduced life expectancy who develop features of ketoacidosis should be assessed for fluid replacement, insulin therapy, their tolerability for regular close monitoring, and the goals of treatment promptly agreed by the admitting team and patient/family where possible.

Conclusion

The effective management of type 1 diabetes in adults requires a multidisciplinary integrated approach to care, Individualized programmes, consideration of all factors that may influence outcome, and the expectations of those with the condition should be paramount in the strategy adopted by the diabetes care team.

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References

The reference list for the full guideline is available online.

1 American Diabetes Association. Classification and diagnosis of diabetes: standards of medical care in diabetes - 2019. *Diabetes Care* 2019; **42**(Suppl 1): S13–S28.
2 Handelsman Y, Bloomgarden ZT, Grunberger G, Umpierrez G, Zimmerman RS, Bailet TS *et al*. American Association of Clinical Endocrinologists and American College of Endocrinology – clinical practice guidelines for developing a diabetes mellitus comprehensive care plan – 2015. *Endocr Pract* 2015; **21**(Suppl 1): 1–87.
3 National Institute for Health and Care Excellence. Type 1 Diabetes in Adults: Diagnosis and Management [NG17]. Available at https://www.nice.org.uk/guidance/ng17 Last accessed 19 September 2019.
4 Pihoker C, Gilliam LK, Hampe CS, Lernmark A. Autoantibodies in diabetes. *Diabetes* 2005; **54**(Suppl 2): S52–S61.
5 Pinero-Pilona A, Litonjua P, Aviles-Santa L, Raskin P. Idiopathic type 1 diabetes in Dallas, Texas. *Diabetes Care* 2001; **24**: 1014–1018.
6 American Diabetes Association. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 1997; **20**: 1183–1197.
7 Mulukutla SN, Acevedo-Calado M, Hampe CS, Pietropaolo M, Balasubramanyam A. Autoantibodies to the IA-2 extracellular domain refine the definition of 'A+' subtypes of ketosis-prone diabetes. *Diabetes Care* 2018; **41**: 2637–2640.
8 Umpierrez GE, Smiley D, Kitabchi AE. Narrative review: ketosis-prone type 2 diabetes mellitus. *Ann Intern Med* 2006; **144**: 350–357.
9 Bansal N, Dhaliwal R, Weinstock RS. Management of diabetes in the elderly. *Med Clin North Am* 2015; **99**: 351–377.
10 Munshi MN, Segal AR, Suhl E, Ryan C, Sternthal A, Giusti J *et al*. Assessment of barriers to improve diabetes management in older adults. *Diabetes Care* 2013; **36**: 543–549.
11 Sullivan DH, Bopp MM, Robertson PK. Protein–energy undernutrition and life-threatening complications among the hospitalized elderly. *J Gen Intern Med* 2002; **17**: 923–932.
12 Wells JL, Dumbrell AC. Nutrition and aging: assessment and treatment of compromised nutritional status in frail elderly patients. *Clin Interv Aging* 2019; **1**: 67–79.
13 Conway B, Miller RG, Costacou T, Fried L, Kelsey S, Evans RW *et al*. Adiposity and mortality in type 1 diabetes. *Int J Obes* 2009; **33**: 796–805.
14 de Ferranti SD, de Boer IH, Fonseca V, Fox CS, Golden SH, Lavie CJ *et al*. Type 1 diabetes mellitus and cardiovascular disease: a scientific statement from the American Heart Association and American Diabetes Association. *Circulation* 2014; **130**: 1110–1130.
15 The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993; **329**: 977–986.
16 Nathan DM, for the DCCT/EDIC Research Group. The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study at 30 years: overview. *Diabetes Care* 2014; **37**: 9–16.
17 DCCT/EDIC Research Group. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *N Engl J Med* 2005; **353**: 2643–2653.
18 Writing Group for the DCCT/EDIC Research Group. Association between 7 years of intensive treatment of type 1 diabetes and long-term mortality. *JAMA* 2015; **313**: 45–53.
19 Schnell O, Cappuccio F, Genovese S, Standl E, Valensi P, Ceriello A. Type 1 diabetes and cardiovascular disease. *Cardiovasc Diabetol* 2013; **12**: 156.
20 Lee SI, Patel M, Jones CM, Narendran P. Cardiovascular disease and type 1 diabetes: prevalence, prediction and management in an ageing population. *Ther Adv Chronic Dis* 2015; **6**: 347–374.
21 Marrero DG, Ard J, Delamater AM, Peragallo-Dittko V, Mayer-Davies EJ, Nwankwo R *et al*. Twenty-first century behavioral medicine: a context for empowering clinicians and patients with diabetes. *Diabetes Care* 2013; **36**: 463–470.
22 Cooke D, Bond R, Lawton J, Rankin D, Heller S, Clark M *et al*. Structured type 1 diabetes education delivered within routine care. *Diabetes Care* 2013; **36**: 270–272.

23 Steinsbekk A, Rygg L, Lisulo M, Rise MB, Fretheim A. Group based diabetes self-management education compared to routine treatment for people with type 2 diabetes mellitus. A systematic review with meta-analysis. *BMC Health Serv Res* 2012; **12**: 213.

24 Robbins JM, Thatcher GE, Webb DA, Valdmanis VG. Nutritionist visits, diabetes classes, and hospitalization rates and charges. *Diabetes Care* 2008; **31**: 655–660.

25 May C, Montori VM, Mair FS. We need minimally disruptive medicine. *BMJ* 2009; **339**: 485–487.

26 American Diabetes Association. Lifestyle management. *Diabetes Care* 2019; **42**(Suppl 1): S46–S60.

27 Franz MJ, Powers MA, Leontos C, Holzmeister LA, Kulkarni K, Monk A *et al*. The evidence for medical nutrition therapy for type 1 and type 2 diabetes in adults. *J Am Diet Assoc* 2010; **110**: 1852–1889.

28 Reedy J, Krebs-Smith SM, Miller PE, Liese AD, Kahle LL, Park P *et al*. Higher diet quality is associated with decreased risk of all-cause, cardiovascular disease, and cancer mortality among older adults. *J Nutr* 2014; **144**: 881–889.

29 McNaughton SA, Bates CJ, Mishra GD. Diet quality is associated with all-cause mortality in adults aged 65 years and older. *J Nutr* 2011; **142**: 320–325.

30 Murton AJ. Muscle protein turnover in the elderly and its potential contribution to the development of sarcopenia. *Proc Nutr Soc* 2015; **74**: 387–396.

31 Burger C, Kiesswetter E, Gietl A, Pfannes U, Arens-Azevedo U, Sieber CC *et al*. Size matters! Differences in nutritional care between small, medium and large nursing homes in Germany. *J Nutr Health Aging* 2017; **21**: 464–472.

32 Saarela RK, Lindroos E, Soini H, Hiltunen K, Muurinen S, Suominen MH *et al*. Dentition, nutritional status and adequacy of dietary intake among older residents in assisted living facilities. *Gerodontology* 2016; **33**: 225–232.

33 British Association of Parenteral and Enteral Nutrition. Malnutrition Universal Screening Tool. Available at http://www.bapen.org.uk/pdfs/must/must_full.pdf Last accessed 19 September 2019.

34 Vellas B, Guigoz Y, Garry PJ, Nourhashashemi F, Bennahum D, Laugue S *et al*. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. *Nutrition* 1999; **15**: 116–122.

35 Nutritics. Nutritics Professional Nutrition Analysis Software. Available at https://www.nutritics.com/p/home Last accessed 19 September 2019.

36 Colberg SR, Sigal RJ, Yardley JE, Riddell MC, Dunstan DW, Dempsey PC *et al*. Physical activity/exercise and diabetes: a position statement of the American Diabetes Association. *Diabetes Care* 2016; **39**: 2065–2079.

37 Davidson LE, Hudson R, Kilpatrick K, Kuk JL, McMillan K, Janiszewski PM *et al*. Effects of exercise modality on insulin resistance and functional limitation in older adults: a randomized controlled trial. *Arch Intern Med* 2009; **169**: 122–131.

38 Rabasa-Lhoret R, Garon J, Langelier H, Poisson D, Chiasson JL. Effects of meal carbohydrate content on insulin requirements in type 1 diabetic patients treated intensively with the basal-bolus (ultralente-regular) insulin regimen. *Diabetes Care* 1999; **22**: 667–673.

39 McMahon SK, Ferreira LD, Ratnam N, Davey RJ, Youngs LM, Davis EA *et al*. Glucose requirements to maintain euglycemia after moderate-intensity afternoon exercise in adolescents with type 1 diabetes are increased in a biphasic manner. *J Clin Endocrinol Metab* 2007; **92**: 963–968.

40 Ramalho AC, de Lourdes Lima M, Nunes F, Cambuí Z, Barbosa C, Andrade A *et al*. The effect of resistance versus aerobic training on metabolic control in patients with type-1 diabetes mellitus. *Diabetes Res Clin Pract* 2006; **72**: 271–276.

41 Laaksonen DE, Atalay M, Niskanen LK, Mustonen J, Sen CK, Lakka TA *et al*. Aerobic exercise and the lipid profile in type 1 diabetic men: a randomized controlled trial. *Med Sci Sports Exerc* 2000; **32**: 1541–1548.

42 Mason NJ, Jenkins AJ, Best JD, Rowley KG. Exercise frequency and arterial compliance in non-diabetic and type 1 diabetic individuals. *Eur J Cardiovasc Prev Rehab* 2006; **13**: 598–603.

43 Kriska AM, Laporte RE, Patrick SL, Kuller LH, Orchard TJ. The association of physical activity and diabetic complications in individuals with insulin-dependent diabetes mellitus: the epidemiology of diabetes complications study – VII. *J Clin Epidemiol* 1991; **44**: 1207–1214.

44 Dempsey PC, Larsen RN, Sethi P, Scare JW, Straznicky NE, Cohen ND *et al*. Benefits for type 2 diabetes of interrupting prolonged sitting with brief bouts of light walking or simple resistance activities. *Diabetes Care* 2016; **39**: 964–972.

45 Zoppini G, Carlini M, Muggeo M. Self-reported exercise and quality of life in young type 1 diabetic subjects. *Diabetes Nutr Metab* 2003; **16**: 77–80.

46 Ahmed AT, Karter AJ, Liu J. Alcohol consumption is inversely associated with adherence to diabetes self-care behaviours. *Diabet Med* 2006; **23**: 795–802.

47 Moy CS, Laporte RE, Dorman JS, Songer TJ, Orchard TJ, Kuller LH *et al*. Insulin-dependent diabetes mellitus mortality. The risk of cigarette smoking. *Circulation* 1990; **82**: 37–43.

48 Seet RC, Loke WM, Khoo CM, Chew SE, Chong L, Quek AM *et al*. Acute effects of cigarette smoking on insulin resistance and arterial stiffness in young adults. *Atherosclerosis* 2012; **224**: 195–200.

49 Yoshikawa H, Hellstrom-Lindahl E, Grill V. Evidence for functional nicotinic receptors on pancreatic β cells. *Metabolism* 2005; **54**: 247–254.

50 Mühlhauser I, Bender R, Bott U, Jörgens V, Grüsser M, Wagener W *et al*. Cigarette smoking and progression of retinopathy and nephropathy in type 1 diabetes. *Diabet Med* 1996; **13**: 536–543.

51 DeWitt DE, Hirsch IB. Outpatient insulin therapy in type 1 and type 2 diabetes mellitus: scientific review. *JAMA* 2003; **289**: 2254–2264.

52 Rosenstock J, Dailey G, Massi-Benedetti M, Fritsche A, Lin Z, Salzman A. Reduced hypoglycemia risk with insulin glargine: a meta-anysis comparing insulin glargine with human NPH insulin in type 2 diabetes. *Diabetes Care* 2005; **28**: 950–955.

53 Yeh HC, Brown TT, Maruthur N, Ranasinghe P, Berger Z, Suh YD *et al*. Comparative effectiveness and safety of methods of insulin delivery and glucose monitoring for diabetes mellitus: a systematic review and meta-analysis. *Ann Intern Med* 2012; **157**: 336–347.

54 Mathieu C, Dandona P, Gillard P, Senior P, Hasslacher C, Araki E *et al*. Efficacy and safety of dapagliflozin in patients with inadequately controlled type 1 diabetes (the DEPICT-2 Study): 24-week results from a randomized controlled trial. *Diabetes Care* 2018; **41**: 1938–1946.

55 Garg SK, Henry RR, Banks P, Buse JB, Davies MJ, Fulcher GR *et al*. Effects of sotagliflozin added to insulin in patients with type 1 diabetes. *N Engl J Med* 2017; **377**: 2337–2348.

56 Munshi MN, Segal AR, Suhl E, Staum E, Desrichers L, Sternthal G *et al*. Frequent hypoglycemia among elderly patients with poor glycemic control. *Arch Intern Med* 2011; **171**: 362–364.

57 Munshi MN, Slyne C, Segal AR, Saul N, Lyons C, Weinger K. Simplification of insulin regimen in older adults and risk of hypoglycemia. *JAMA Intern Med* 2016; **176**: 1023–1025.

58 Diabetes UK. Diabetes UK Consensus Guideline for Flash Glucose Monitoring. Available at https://www.diabetes.org.uk/resources-s3/2017-09/1190_Flash%20glucose%20monitoring%20guideline_SB_V9%5B4%5D.pdf Last accessed 19 September 2019.

59 Alvarez-Guisasola F, Yin DD, Nocea G, Qiu Y, Mavros P. Association of hypoglycemic symptoms with patients' rating of their health-related quality of life state: a cross sectional study. *Health Qual Life Outcome* 2010; **8**: 86.

60 Di Battista AM, Hart TA, Greco L, Gloizer J. Type 1 diabetes among adolescents. *Diabetes Educ* 2009; **35**: 465–475.

61 Brod M, Christensen T, Thomsen TL, Bushnell DM. The impact of non-severe hypoglycemic events on work productivity and diabetes management. *Value Health* 2011; **14**: 665–671.

62 Signorovitch JE, Macaulay D, Diener M, Yan Y, Wu EQ, Gruenberger JB *et al*. Hypoglycaemia and accident risk in people with type 2 diabetes mellitus treated with non-insulin antidiabetes drugs. *Diabetes Obes Metab* 2013; **15**: 335–341.

63 Chen LK, Lin MH, Lai HY, Hwang SJ. Care of patients with diabetes mellitus in long-term care facilities in Taiwan: diagnosis, glycemic control, hypoglycemia, and functional status. *J Am Geriatr Soc* 2008; **56**: 1975–1976.

64 Jaap AJ, Jones GC, McCrimmon RJ, Deary IJ, Frier BM. Perceived symptoms of hypoglycaemia in elderly Type 2 diabetic patients treated with insulin. *Diabet Med* 1998; **15**: 398–401.

65 Bonds DE, Miller ME, Dudl J, Feinglos M, Ismail-Beigi F, Malozowski S *et al*. Severe hypoglycemia symptoms, antecedent behaviors, immediate consequences and association with glycemia medication usage: secondary analysis of the ACCORD clinical trial data. *BMC Endocr Disord* 2012; **12**: 5.

66 Seaquist ER, Anderson J, Childs B, Cryer P, Dagogo-Jack S, Fish L *et al*. Hypoglycemia and diabetes: a report of a workgroup of the American Diabetes Association and The Endocrine Society. *Diabetes Care* 2013; **36**: 1384–1395.

67 Munshi M. Hypoglycemia. Sinclair AJ, Dunning T, Manas LR, Munshi M eds. *Diabetes in Old Age*. Chichester: Wiley Blackwell, 2017; 350–359.

68 Soedamah-Muthu SS, Fuller JH, Mulnier HE, Rayleigh VS, Lawrenson RA, Colhoun HM. High risk of cardiovascular disease in patients with type 1 diabetes in the U.K.: a chort study using the general practice research database. *Diabetes Care* 2006; **29**: 798–804.

69 Dunning T, Sinclair A, Colagiuri S. New IDF guideline for managing type 2 diabetes in older people. *Diabetes Res Clin Pract* 2014; **103**: 538–540.

70 Schwab KO, Doerfer J, Hallermann K, Krebs A, Schorb E, Krebs K *et al*. Marked smoking-associated increase of cardiovascular risk in childhood type 1 diabetes. *Int J Adolesc Med Health* 2008; **20**: 285–292.

71 Groop PH, Thomas MC, Moran JL, Wadèn J, Thom LM, Mäkinen VP *et al*. The presence and severity of chronic kidney disease predicts all-cause mortality in type 1 diabetes. *Diabetes* 2009; **58**: 1651–1658.

72 American Diabetes Association. Summary of revisions. *Diabetes Care* 2019; **42**(Suppl 1): S4–S6.

73 Fisher L, Hessler DM, Polonsky WH, Masharani U, Peters AL, Blumer I *et al*. Prevalence of depression in Type 1 diabetes and the problem of over-diagnosis. *Diabet Med* 2016; **33**: 1590–1597.

74 van Dijk M, Donga E, van Dijk JG, Lammers GJ, van Kralingen KW, Dekkers OM *et al*. Disturbed subjective sleep characteristics in adult patients with long-standing type 1 diabetes mellitus. *Diabetologia* 2011; **54**: 1967–1976.

75 Silva MF, Barbosa KG, Pereira JV, Bento PM, Godoy GP, Gomes DQ. Prevalence of oral mucosal lesions among patients with diabetes mellitus types 1 and 2. *An Bras Dermatol* 2015; **90**: 49–53.

76 Calixto OJ, Anaya JM. Socioeconomic status. The relationship with health and autoimmune diseases. *Autoimmun Rev* 2014; **13**: 641–654.

77 Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M *et al*. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *Eur Heart J* 2018; **39**: 3021–3104.

78 Collado-Mesa F, Colhoun HM, Stevens LK, Boavida J, Ferriss JB, Karamanos B *et al*. Prevalence and management of hypertension in Type 1 diabetes mellitus in Europe: the EURODIAB IDDM Complications Study. *Diabet Med* 1999; **16**: 41–48.

79 The European Study for the Prevention of Renal Disease in Type 1 Diabetes ESPRIT Study Group. Effect of 3 years of antihypertensive therapy on renal structure in type 1 diabetic patients with albuminuria. *Diabetes* 2001; **50**: 843–850.

80 Moreno G, Mangione CM. Management of cardiovascular disease risk factors in older adults with type 2 diabetes mellitus: 2002-2012 literature review. *J Am Geriatr Soc* 2013; **61**: 2027–2037.

81 Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. *Lancet* 2010; **376**: 1670–1681.

82 Maahs DM, Nadeau K, Snell-Bergeon JK, Schauter I, Bergman B, West NA *et al*. Association of insulin sensitivity to lipids across the lifespan in people with Type 1 diabetes. *Diabet Med* 2011; **28**: 148–155.

83 Livingstone SJ, Looker HC, Hothersall EJ, Wild SH, Lindsay RS, Chalmers J *et al*. Risk of cardiovascular disease and total mortality in adults with type 1 diabetes: Scottish registry linkage study. *PLoS Med* 2012; **9**: e1001321.

84 Prospective Studies Collaboration. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55000 vascular deaths. *The Lancet* 2007; **370**: 1829–1839.

85 Barry AR, O'Neill DE, Graham MM. Primary prevention of cardiovascular disease in older adults. *Can J Cardiol* 2016; **32**: 1074–1081.

86 Miettinen TA, Pyorala K, Olsson AG, Musliner TA, Cook TJ, Faergeman O *et al*. Cholesterol-lowering therapy in women and elderly patients with myocardial infarction or angina pectoris. *Circulation* 1997; **96**: 4211–4218.

87 Sacks FM, Pfeffer MA, Moye LA, Rouleau JL, Rutherford JD, Cole TG *et al*. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators. *N Engl J Med* 1996; **335**: 1001–1009.

88 Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. *N Engl J Med* 1998; **339**: 1349–1357.

89 Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002; **360**: 7–22.

90 Cholesterol Treatment Trialists' (CTT) Collaborators. Efficacy of cholesterol-lowering therapy in 18,686 people with diabetes in 14 randomised trials of statins: a meta-analysis. *Lancet* 2008; **371**: 117–125.

91 McGuinness B, Craig D, Bullock R, Passmore P. Statins for the prevention of dementia. *Cochrane Database of Systematic Reviews* 2016; (1)CD003160. Available at https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD003160.pub3/epdf Last accessed 19 September 2019.

92 Murphy SA, Cannon CP, Blazing MA, Giugliano RP, White JA, Lokhnygina Y *et al*. Reduction in total cardiovascular events with Ezetimibe/Simvastatin post-acute coronary syndrome: The IMPROVE-IT trial. *J Am Coll Cardiol* 2016; **67**: 353–361.

93 Giugliano RP, Pedersen TR, Park JG, De Ferrari GM, Gaciong ZA, Ceska R *et al*. Clinical efficacy and safety of achieving very low LDL-cholesterol concentrations with the PCSK9 inhibitor

evolocumab: a prespecified secondary analysis of the FOURIER trial. *Lancet* 2017; **390**: 1962–1971.
94 ASCEND study group. Effects of aspirin for primary prevention in persons with diabetes mellitus. *N Engl J Med* 2018; **379**: 1529–1539.
95 Quartilho A, Simkiss P, Zekite A, Xing W, Wormald R, Bunce C. Leading causes of certifiable visual loss in England and Wales during the year ending 31 March 2013. *Eye* 2016; **30**: 602–607.
96 Klein R, Knudtson MD, Lee KE, Gangnon R, Klein BE. The Wisconsin Epidemiologic Study of Diabetic Retinopathy XXII: The twenty-five-year progression of retinopathy in persons with type 1 diabetes. *Ophthalmology* 2008; **115**: 1859–1868.
97 Stratton IM, Aldington SJ, Taylor DJ, Adler AI, Scanlon PH. A simple risk stratification for time to development of sight-threatening diabetic retinopathy. *Diabetes Care* 2013; **36**: 580–585.
98 Hooper P, Boucher MC, Cruess A, Dawson KG, Delpero W, Greve M *et al*. Canadian Ophthalmological Society evidence-based clinical practice guidelines for the management of diabetic retinopathy – Executive summary. *Can J Ophthalmol* 2012; **47**: 91–101.
99 Klein R, Klein BE, Moss SE, Davis MD, DeMets D. The Wisconsin Epidemiologic Study of Diabetic Retinopathy: II. Prevalence and risk of diabetic retinopathy when age at diagnosis is less than 30 years. *Arch Ophthalmol* 1984; **102**: 520–526.
100 Varma R, Torres M, Pena F, Klein R, Azen SP. Prevalence of diabetic retinopathy in adult Latinos: The Los Angeles Latino Eye Study. *Ophthalmology* 2004; **111**: 1298–1306.
101 Diabetes Control and Complications Trial Research Group. Progression of retinopathy with intensive versus conventional treatment in the Diabetes Control and Complications Trial. *Ophthalmology* 1995; **102**: 647–661.
102 Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group. Prolonged effect of intensive therapy on the risk of retinopathy complications in patients with type 1 diabetes mellitus10 years after the Diabetes Control and Complications Trial. *Arch Ophthalmol* 2008; **126**: 1707–1715.
103 Diabetic Retinopathy Study Research Group. Preliminary report on effects of photocoagulation therapy. *Am J Ophthalmol* 1976; **81**: 383–396.
104 Early Treatment Diabetic Retinopathy Study Research Group. Photocoagulation for diabetic macular edema: Early Treatment Diabetic Retinopathy study report number 1. *Arch Ophthalmol* 1985; **103**: 1796–1806.
105 Vashist P, Singh S, Gupta N, Saxena R. Role of early screening for diabetic retinopathy in patients with diabetes mellitus: an overview. *Indian J Commun Med* 2011; **36**: 247–252.
106 Orchard TJ, Secrest AM, Miller RG, Costacou T. In the absence of renal disease, 20-áyear mortality risk in type 1 diabetes is comparable to that of the general population: a report from the Pittsburgh Epidemiology of Diabetes Complications Study. *Diabetologia* 2010; **53**: 2312–2319.
107 Yeung E, Astor BC, Miller ER, Coresh J, Hallan SI. Glomerular filtration rate, albuminuria, and risk of cardiovascular and all-cause mortality in the US population. *Am J Epidemiol* 2008; **167**: 1226–1234.
108 Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 2004; **351**: 1296–1305.
109 Costacou T, Ellis D, Fried L, Orchard TJ. Sequence of progression of albuminuria and decreased GFR in persons with type 1 diabetes: A cohort study. *Am J Kidney Dis* 2007; **50**: 721–732.
110 de Boer IH, Katz R, Cao JJ, Fried LF, Kestenbaum B, Mukamal K *et al*. Cystatin C, albuminuria, and mortality among older adults with diabetes. *Diabetes Care* 2009; **32**: 1833–1838.
111 United States Renal Data System. 2015 USRDS Annual Data Report: Epidemiology of Kidney Disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2015. Available at https://www.usrds.org/2015/view/Default.aspx Last accessed 19 September 2019.
112 Jassal SV, Watson D. Dialysis in late life: Benefit or burden. *Clin J Am Soc Nephrol* 2009; **4**: 2008–2012.
113 Perkins BA, Ficociello LH, Ostrander BE, Silva KH, Weinberg J, Warram JH *et al*. Microalbuminuria and the risk for early progressive renal function decline in type 1 diabetes. *J Am Soc Nephrol* 2007; **18**: 1353–1361.
114 Davis TM, Brown SG, Jacobs IG, Bulsara M, Bruce DG, Davis WA. Determinants of severe hypoglycemia complicating type 2 diabetes: The Fremantle Diabetes Study. *J Clin Endocrinol Metab* 2010; **95**: 2240–2247.
115 Huang ES, Laiteerapong N, Liu JY, John PM, Moffet HH, Karter AJ. Rates of complications and mortality in older patients with diabetes mellitus. The diabetes and aging study. *JAMA Intern Med* 2013; **174**: 251–258.
116 Moen MF, Zhan M, Hsu VD, Walker LD, Einhorn LM, Seliger SL *et al*. Frequency of hypoglycemia and its significance in chronic kidney disease. *Clin J Am Soc Nephrol* 2009; **4**: 1121–1127.
117 Perkins BA, Ficociello LH, Silva KH, Finkelstein DM, Warram JH, Krolewski AS. Regression of microalbuminuria in type 1 diabetes. *N Engl J Med* 2003; **348**: 2285–2293.
118 Molitch ME, Steffes M, Sun W, Rutledge B, Cleary P, de Boer IH *et al*. Development and progression of renal insufficiency with and without albuminuria in adults with type 1 diabetes in the Diabetes Control and Complications Trial and the Epidemiology of Diabetes Interventions and Complications study. *Diabetes Care* 2010; **33**: 1536–1543.
119 Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. *JAMA* 2005; **293**: 217–228.
120 Yazdanpanah L, Nasiri M, Adarvishi S. Literature review on the management of diabetic foot ulcer. *World J Diabetes* 2015; **6**: 37–53.
121 Prompers L, Huijberts M, Schaper N, Apelqvist J, Bakker K, Edmonds M *et al*. Resource utilisation and costs associated with the treatment of diabetic foot ulcers. Prospective data from the Eurodiale Study. *Diabetologia* 2008; **51**: 1826–1834.
122 Morley JE, Malmstrom TK, Rodriguez-Manas L, Sinclair AJ. Frailty, sarcopenia and siabetes. *J Am Med Dir Assoc* 2014; **12**: 853–859.
123 Vinik AI, Strotmeyer ES, Nakave AA, Patel CV. Diabetic neuropathy in older adults. *Clin Geriatr Med* 2008; **24**: 407–435.
124 Prompers L, Huijberts M, Apelqvist J, Jude E, Piaggesi A, Bakker K *et al*. High prevalence of ischaemia, infection and serious comorbidity in patients with diabetic foot disease in Europe. Baseline results from the Eurodiale study. *Diabetologia* 2007; **50**: 18–25.
125 MacFarlane RM, Jeffcoate WJ. Factors contributing to the presentation of diabetic foot ulcers. *Diabet Med* 1997; **14**: 867–870.
126 Valk GD, Kriegsman DM, Assendelft WJ. Patient education for preventing diabetic foot ulceration. A systematic review. *Endocrinol Metab Clin North Am* 2002; **31**: 633–658.
127 Brownrigg JR, Schaper NC, Hinchliffe RJ. Diagnosis and assessment of peripheral arterial disease in the diabetic foot. *Diabet Med* 2015; **32**: 738–747.
128 Boulton AJ, Armstrong DG, Albert SF, Frykberg RG, Hellman R, Kirkman MS *et al*. Comprehensive foot examination and risk assessment: A report of the Task Force of the Foot Care Interest Group of the American Diabetes Association, with endorsement by the American Association of Clinical Endocrinologists. *Diabetes Care* 2008; **31**: 1679–1685.

129 Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJ, Armstrong DG *et al*. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis* 2012; **54**: e132–e173.

130 Lebrun E, Tomic-Canic M, Kirsner RS. The role of surgical debridement in healing of diabetic foot ulcers. *Wound Rep Reg* 2010; **18**: 433–438.

131 National Institute for Health and Care Excellence. Diabetic Foot Problems: Prevention and Management [NG19]. Available at http://www.nice.org.uk/guidance/ng19 Last accessed 19 September 2019.

132 Tesfaye S, Boulton AJ, Dyck PJ, Freeman R, Horowitz M, Kempler P *et al*. Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments. *Diabetes Care* 2010; **33**: 2285–2293.

133 Spallone V, Ziegler D, Freeman R, Bernardi L, Frontoni S, Pop-Busui R *et al*. Cardiovascular autonomic neuropathy in diabetes: clinical impact, assessment, diagnosis, and management. *Diabetes Metab Res Rev* 2011; **27**: 639–653.

134 Tesfaye S, Vileikyte L, Rayman G, Sindrup SH, Perkins BA, Baconja M *et al*. Painful diabetic peripheral neuropathy: consensus recommendations on diagnosis, assessment and management. *Diabetes Metab Res Rev* 2011; **27**: 629–638.

135 The Diabetes Control and Complications Trial Research Group. The effect of intensive diabetes therapy on the development and progression of neuropathy. *Ann Intern Med* 1995; **122**: 561–568.

136 Tesfaye S, Boulton AJ, Dickenson AH. Mechanisms and management of diabetic painful distal symmetrical polyneuropathy. *Diabetes Care* 2013; **36**: 2456–2465.

137 Moore R, Derry S, Adlington D, Cole P, Wiffen PJ. Amitriptyline for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2015; (7)CD008242. Available at https://www.cochrane.org/CD008242/SYMPT_amitriptyline-neuropathic-pain-adults Last accessed 19 September 2019.

138 Lunn MP, Hughes RA, Wiffen PJ. Duloxetine for treating painful neuropathy, chronic pain or fibromyalgia. *Cochrane Database of Systematic Reviews* 2014; (1)CD007115. Available at https://www.cochrane.org/CD007115/NEUROMUSC_duloxetine-treating-painful-neuropathy-chronic-pain-or-fibromyalgia Last accessed 19 September 2019.

139 Derry S, Bell R, Straube S, Wiffen PJ, Adlington D, Moore R. Pregabalin for chronic neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2019; (1)CD007076. Available at https://www.cochrane.org/CD007076/SYMPT_pregabalin-chronic-neuropathic-pain-adults Last accessed 19 September 2019.

140 Wiffen PJ, Derry S, Bell R, Rice ASC, Tölle T, Phillips T *et al*. Gabapentin for chronic neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2017; (6)007938. Available at https://www.cochrane.org/CD007938/SYMPT_gabapentin-chronic-neuropathic-pain-adults Last accessed 19 September 2019.

141 Freeman R, Durso-DeCruz E, Emir B. Efficacy, safety, and tolerability of pregabalin treatment for painful diabetic peripheral neuropathy. *Diabetes Care* 2008; **31**: 1448–1454.

142 Sultan A, Gaskell H, Derry S, Moore RA. Duloxetine for painful diabetic neuropathy and fibromyalgia pain: systematic review of randomised trials. *BMC Neurology* 2008; **8**: 29.

143 Wong MC, Chung JW, Wong TK. Effects of treatments for symptoms of painful diabetic neuropathy: systematic review. *BMJ* 2007; **335**: 87.

144 Dworkin RH, O'Connor AB, Audette J, Baron R, Gourlay GK, Haanpää ML *et al*. Recommendations for the pharmacological management of neuropathic pain: An overview and literature update. *Mayo Clin Proc* 2010; **85**(Suppl): S3–S14.

145 Attal N, Cruccu G, Baron R, Haanpää ML, Hansson P, Jensen TS *et al*. EFNS guidelines on the pharmacological treatment of neuropathic pain: 2010 revision. *European Journal of Neurology* 2010; **17**: 1113–e88.

146 National Institute for Health and Care Excellence. Neuropathic Pain in Adults: Pharmacological Management in Non-Specialist Settings [CG173]. Available at https://www.nice.org.uk/guidance/CG173 Last accessed 19 September 2019.

147 Dubinsky RM, Miyasaki J. Assessment: efficacy of transcutaneous electric nerve stimulation in the treatment of pain in neurologic disorders (an evidence-based review). *Neurology* 2010; **74**: 173–176.

148 Tesfaye S, Watt J, Benbow SJ, Pang KA, Miles J, MacFarlane IA. Electrical spinal-cord stimulation for painful diabetic peripheral neuropathy. *Lancet* 1996; **348**: 1698–1701.

149 Abell T, McCallum R, Hocking M, Koch K, Abrahamsson H, Leblanc I *et al*. Gastric electrical stimulation for medically refractory gastroparesis. *Gastroenterology* 2003; **125**: 421–428.

150 Chong K, Dhatariya K. A case of severe, refractory diabetic gastroparesis managed by prolonged use of aprepitant. *Nat Rev Endocrinol* 2009; **5**: 285–288.

151 American Diabetes Association. Microvascular complications and foot care: standards of medical care in diabetes 2019. *Diabetes Care* 2019; **42**(Suppl 1): S124–S138.

152 Roberts A, James J, Dhatariya K, on behalf of the Joint British Diabetes Societies (JBDS) for Inpatient Care group and guidelines writing group. Management of hyperglycaemia and steroid (glucocorticoid) therapy: a guideline from the Joint British Diabetes Societies (JBDS) for Inpatient Care group. *Diabet Med* 2018; **35**: 1011–1017.

153 Health and Social Care Information Centre. National Diabetes Inpatient Audit (NaDIA) –2015. Available at http://www.hscic.gov.uk/catalogue/PUB20206 Last accessed 19 September 2019.

154 Barranco RJ, Gomez-Peralta F, Abreu C, Delgado M, Palomares R, Romero F *et al*. Incidence and care-related costs of severe hypoglycaemia requiring emergency treatment in Andalusia (Spain): the PAUEPAD project. *Diabet Med* 2015; **32**: 1520–1526.

155 Edridge CL, Dunkley AJ, Bodicoat DH, Rose TC, Gray LJ, Davies MJ *et al*. Prevalence and incidence of hypoglycaemia in 532,542 people with type 2 diabetes on oral therapies and insulin: a systematic review and meta-analysis of population based studies. *PLoS ONE* 2015; **10**: e0126427.

156 Prinz N, Stingl J, Dapp A, Denkinger MD, Fasching P, Jehle PM *et al*. High rate of hypoglycemia in 6770 type 2 diabetes patients with comorbid dementia: A multicenter cohort study on 215,932 patients from the German/Austrian diabetes registry. *Diabetes Res Clin Pract* 2016; **112**: 73–81.

157 Bruce DG, Davis WA, Casey GP, Clarnette RM, Brown SG, Jacobs IG *et al*. Severe hypoglycaemia and cognitive impairment in older patients with diabetes: the Fremantle Diabetes Study. *Diabetologia* 2009; **52**: 1808–1815.

158 Elwen FR, Huskinson A, Clapham L, Bottomley MJ, Heller SR, James C *et al*. An observational study of patient characteristics and mortality following hypoglycemia in the community. *BMJ Open Diabetes Res Care* 2015; **3**: e000094.

159 Lu CL, Hsu PC, Shen HN, Chang YH, Chen HF, Li CY. Association between history of severe hypoglycemia and risk of falls in younger and older patients with diabetes. *Medicine (Baltimore)* 2015; **94**(33: e1339.

160 International Diabetes Federation. Managing Older People with Type 2 Diabetes. A Global Guideline. Available at http://www.idf.org/sites/default/files/IDF-Guideline-for-older-people-T2D.pdf Last accessed 19 September 2019.

161 Rodriguez-Gutierrez R, Lipska KJ, McCoy RG, Ospina NS, Ting HH, Montori VM; Hypoglycemia as a Quality Measure in Diabetes Study Group. Hypoglycemia as an indicator of good diabetes care. *BMJ* 2016; **352**: i1084.

162 Malone ML, Gennis V, Goodwin JS. Characteristics of diabetic ketoacidosis in older versus younger adults. *J Am Geriatr Soc* 1992; **40**: 1100–1104.
163 Nyenwe EA, Kitabchi AE. The evolution of diabetic ketoacidosis: an update of its etiology, pathogenesis and management. *Metabolism* 2016; **65**: 507–521.
164 Dhatariya KK, Nunney I, Higgins K, Sampson MJ, Iceton G. A national survey of the management of diabetic ketoacidosis in the UK in 2014. *Diabet Med* 2016; **33**: 252–260.
165 National Patient Safety Agency. Safety in Doses: Improving the Use of Medicines in the NHS. Available at http://www.nrls.npsa.nhs.uk/resources/patient-safety-topics/medication-safety/?entryid45=61625&q=0%c2%acsafety+in+doses%c2%ac Last accessed 19 September 2019.
166 National Patient Safety Agency. Insulin Safety. Reducing Harm Associated with the Unsafe Use of Insulin Products. Available at http://www.patientsafetyfirst.nhs.uk/Content.aspx?path=/interventions/relatedprogrammes/medicationsafety/insulin/ Last accessed 19 September 2019.
167 NHS England. Never Events List 2015/16. Available at https://www.england.nhs.uk/wp-content/uploads/2015/03/never-evnts-list-15-16.pdf Last accessed 19 September 2019.
168 Wang J, Williams DE, Narayan KM, Geiss LS. Declining death rates from hyperglycemic crisis among adults with diabetes, U.S., 1985–2002. *Diabetes Care* 2006; **29**: 2018–2022.
169 Lin SF, Lin JD, Huang YY. Diabetic ketoacidosis: comparisons of patient characteristics, clinical presentations and outcomes today and 20 years ago. *Chang Gung Med J* 2005; **28**: 24–30.
170 Otieno CF, Kayima JK, Omonge EO, Oyoo GO. Diabetic ketoacidosis: risk factors, mechanisms and management strategies in sub-Saharan Africa: a review. *E Afr Med J* 2005; **82**(Suppl): S197–S203.