

Managing frailty and associated comorbidities in older adults with diabetes: Position Statement on behalf of the Association of British Clinical Diabetologists (ABCD)

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Abstract

This Position Statement on the management of frailty in diabetes mellitus represents a timely initiative by the Association of British Clinical Diabetologists (ABCD) to address the important issue of frailty and its association with diabetes. The authors acknowledge that frailty is emerging as a new complication of diabetes and has a significant impact in terms of increased adverse outcomes and reduced survival. The authors also recognise that little high quality research evidence exists to guide recommendations and that much of the enclosed guidance will represent best clinical practice viewpoints. In this Position Statement we have provided examples of how to detect frailty using easy to implement measures, and we emphasise that a comprehensive evaluation of physical and cognitive function is required. We have provided recommendations in eight key areas using a format previously used by the International Diabetes Federation,¹ where we provide a summary of the evidence base followed by suggestions how these recommendations can be implemented in routine clinical practice.

We have divided the document into three areas: section A: Establishing the Platform for Frailty Care; section B: Key Areas in Medical Management; and section C: Clinical Audit in Frailty. These provide a detailed introduction to the area of frailty, its definition and measurement and why frailty is important in modern day clinical care. In addition, there are over 60 clinical recommendations to guide clinical decision-making. This Position Statement will hopefully provide much needed momentum to improve the way we manage the older adult with diabetes, particularly those with frailty.

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Forward

This Position Statement on the management of frailty and associated comorbidities in diabetes mellitus is a timely development for the Association in view of: (a) several recent publications of international clinical guidelines which provide a modern but general overview of management approaches for older people with diabetes;^{1–4} and (b) the publication of the 2017 International Guidance on the Management of Frailty in Diabetes.⁵ These various documents have not only given recommendations for managing glucose control but have provided a consistent view of the importance of functional assessment, and a uniform method of dealing with frailty for the clinician dealing with these issues of management on a daily basis. The Association has produced this Position Statement in order for its recommendations to be implemented within the NHS in the UK to promote improved quality care for older people with diabetes and frailty, as well as guidance on managing the inevitable comorbidities that are present.

Whilst the International Diabetes Federation Global Guidance on managing older people with type 2 diabetes provided for the first time care recommendations for those with dependency including frailty,⁴ the Association felt that there were many areas where specific advice was still needed within local NHS settings and, indeed, would offer the clinician extra value in decision-making.

In planning the Position Statement, the Association has also acknowledged that frailty is a common finding and may be present in 32–48% of adults aged 65 years and over with diabetes,⁶ and is associated with adverse outcomes and reduced survival. At the same time, we recognise the paucity of specific studies of glucose-lowering treatments in older patients with frailty and diabetes, the varying methods of detection of frailty, and the need for clinicians to acquire new knowledge and training in managing frailty.

This Position Statement has been structured into three main section headings dealing with the definitions and clinical importance of frailty; followed by a summary of the key areas of management including glucose regulation, blood pressure and lipid management, role of exercise interventions and hypoglycaemia. It concludes with clinical audit aspects of frailty management and the development of a frailty care pathway in the NHS.

This Position Statement emphasises the importance of individualised frailty care in diabetes becoming the norm and that frailty care should be part of routine diabetes care once patients achieve the age of 70 years. Where possible, we have provided a set of evidence-based recommendations and we hope that all clinicians involved in this arena of clinical care will work collaboratively to improve the functional health status and well-being of this growing population of senior adults with diabetes and frailty.

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Section A: Establishing the Platform for Frailty Care

Introduction and background: Why is frailty important in diabetes?

With increasing ageing of the population and urbanisation of lifestyle, the epidemiology of diabetes is shifting towards old age, especially among individuals between the ages of 60 and 79 years.¹ Increasing age and diabetes are both risk factors for functional decline and disability. In older people with diabetes, geriatric syndromes, frailty and sarcopenia are emerging as a third category of complications in addition to the traditional micro- and macrovascular disease leading to considerable disability.² This is likely to lead to a considerable need for disability-related health resources increasing both direct and indirect costs.

The prevalence of physical frailty in people aged >65 years reaches up to 7% and up to 40% in those aged >80 years.³ In a systematic review of observational population-based studies, the prevalence of frailty was 14–24% and increased with age and was associated with a poor survival in a dose-response manner.⁴

Diabetes is associated with an accelerated ageing process that promotes frailty. This is likely due to an increased risk of sarcopenia which is linked to frailty.⁵ Other factors leading to frailty are associated diabetes complications, particularly renal impairment and dementia. In the analysis of the Mexican Health and Nutrition Survey of 7,164 older people of mean (SD) age 70.6 (8.1) years, diabetes was independently associated with frailty (coefficient 0.28, $p < 0.001$) with an incremental association when hypertension (0.63, $p < 0.001$) or any diabetic complication was present (0.55, $p < 0.001$).⁶ In a Japanese cross-sectional study of 9,606 participants aged ≥ 65 years, participants in the lowest quartile of renal function (estimated glomerular filtration rate (eGFR) < 30.0 mL/min/1.73m²) showed an independent higher risk of frailty (OR 1.83, 95% CI 1.01 to 3.45) compared with those in the highest quartile (eGFR ≥ 60.0 mL/min/1.73m²). Individuals with a history of hypertension or diabetes mellitus showed a significantly increased risk of frailty in the group with the lowest eGFR (OR 2.53, 95% CI 1.45 to 5.12 and 2.76, 95% CI 1.21 to 8.24, respectively) and the risk of frailty increased further when both hypertension and diabetes were present (OR 3.67, 95% CI 1.13 to 14.05).⁷ In addition to the increased risk of cerebrovascular and Alzheimer's disease dementia with diabetes, there is a dementia subgroup with characteristics predominantly associated with diabetes-related metabolic abnormalities.⁸ This type of dementia has been shown to be associated with frailty more often than diabetes-associated Alzheimer's disease. This is likely due to increased inflammatory processes and oxidative stress in these patients.⁹ In a large GP database study of older subjects with type 2 diabetes, hypoglycaemia as a consequence of treatment with antihyperglycaemic

agents has been associated with the subsequent development of dementia, with the risk increasing with the number of episodes experienced.¹⁰

Diabetes and frailty have also been shown to share a common cardiovascular risk factors pathway suggesting a reciprocal relationship. The Whitehall II Prospective Cohort Study, which included 2,707 participants free of diabetes at baseline, showed that frail and pre-frail participants were more likely to be older and female, have higher body mass index, waist circumference and blood pressure, be a current smoker and less likely to be physically active or consume fruits and vegetables compared with non-frail participants. The Cambridge and Finnish diabetes risk scores were associated with frailty/pre-frailty with OR per one SD increment in the score of 1.18 (95% CI 1.09 to 1.27) and 1.27 (95% CI 1.17 to 1.37), respectively, after a mean follow-up of 10.5 years.¹¹

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Purpose of Position Statement

The Association has defined the purpose of this Position Statement as follows:

- To arrive at a consensus amongst diabetes specialists in the UK on how we approach the management of important issues of managing frailty in older people with diabetes.
- To identify a series of key recommendations in important areas

Key principles of Position Statement

We have established a set of key principles which set the scene for this Position Statement. These are based on recent international guidance in this area.¹ The principles are:

- Individualising goals of care with functional status, complexity of illness including comorbidity profiles and life expectancy
- Where possible, all therapeutic decisions should be based on a detailed geriatric assessment and risk stratification process (eg, risk of hypoglycaemia, falls risk, or risk of adverse events from treatment)
- A clear focus on patient safety, avoiding hospital/emergency department admissions and institutionalisation by recognising

that will support clinicians in everyday clinical practice to manage more effectively the complex issues seen in ageing individuals with frailty.

- To provide a platform for commissioners of healthcare and policy makers to plan and coordinate care pathways in their local regions for those older people with diabetes who are developing frailty (pre-frail), have developed frailty, and those progressing to disability.

the deterioration early and maintaining independence and quality of life to a dignified death

- An emphasis to promote locally relevant interdisciplinary diabetes care teams to develop specific pathways for frail older people with diabetes
- An encouragement to promote high quality clinical research and audit in the area of frailty management in diabetes

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Definition of frailty, diagnosis and assessment methods

Recommendations

- Requirements for screening tools are as follows: quick, no need for special equipment and time consuming measurements involving use of cut-off values, no need for administration by professional staff, validated against consensus definitions and/or clinical assessments.
- Examples of screening tools¹ that fulfil the above criteria include:
 - the FRAIL score and Frailty Index for frailty screening
 - The get up and go test
 - PRISMA 7 tool
 - the SARC-F for sarcopenia
 - MMSE and/or Clock test for cognitive impairment
- Health and social professionals engaged in direct patient care should acquire the basic skills to assess for functional status and frailty.
- Those with abnormal screening results should undergo further examination by a clinician to detect underlying reversible conditions if any, such as hypothyroidism, vitamin D deficiency, anaemia, etc.

Frailty is defined as a state of increased vulnerability to physical or psychological stressors because of decreased physiological reserve in multiple organ systems that cause limited capacity to maintain homeostasis.² Its definition was originally based on a physical phenotypic model reflected by the presence of three or more of the following: (a) difficulties in mobility such as lower extremity performance and slow gait speed; (b) muscle weakness (weak hand grip);

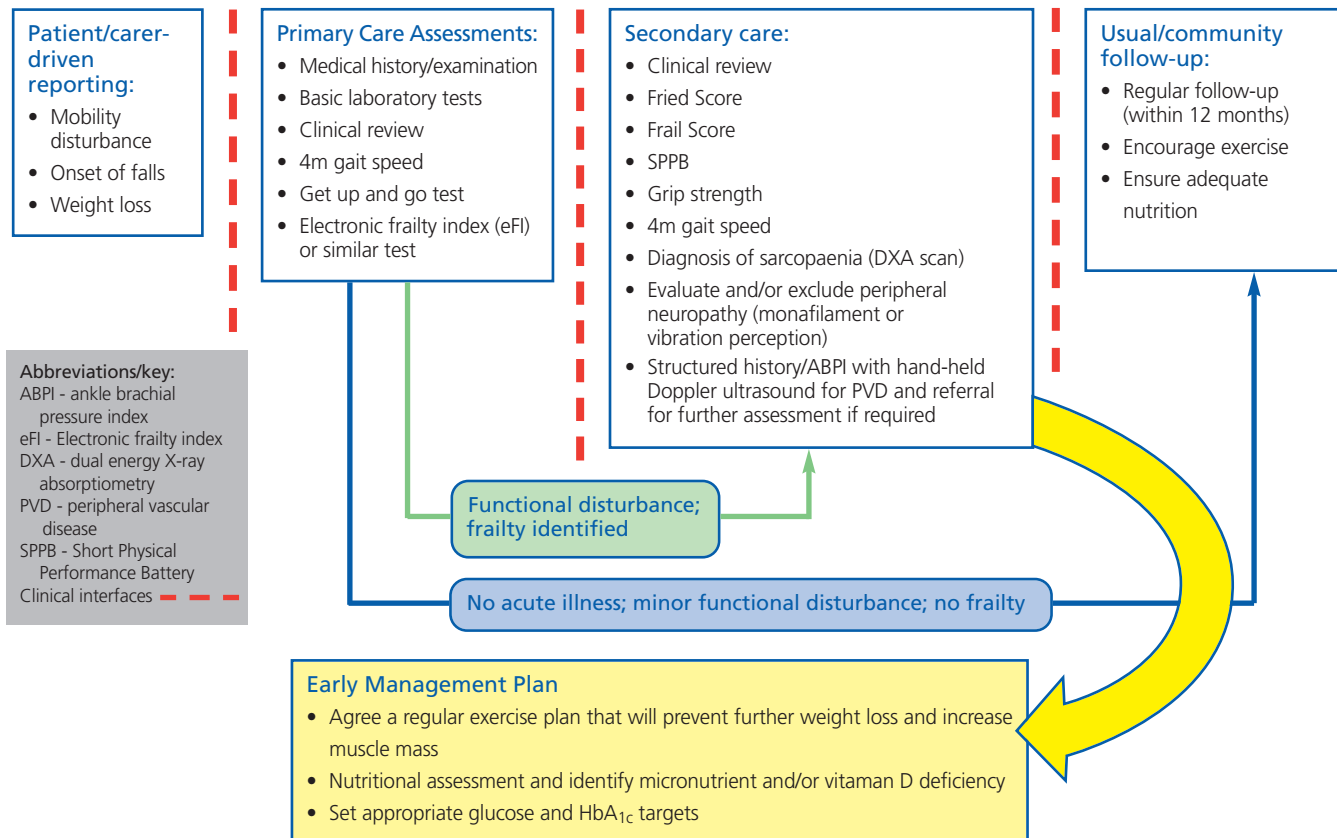
(c) decreased physical activities and poor exercise tolerance; (d) exhaustion (self-reported); and (e) unintentional weight loss.³ The presence of one or two phenotype criteria describes a pre-frail state while the absence of any positive criteria describes a robust state.

However, an alternative form of a frailty state is recognised as an accumulation (during ageing) of deficits (symptoms, diseases, conditions, disabilities) that can lead to poor clinical outcomes and which requires a different assessment approach (The Frailty Index), which is now established in primary care databases as the electronic Frailty Index (eFI).⁴

The practical assessment of functional status including the detection of frailty is possible in outpatient (office) settings and only requires a set of easily learnt skills. An overall idea of functional well-being can be obtained by using simple assessment tools such as the questionnaire-based Katz (Barthel) ADL score or the Lawton IADL scale.^{5,6} These provide information ranging from basic abilities (bathing, toileting, mobility) to more complex skills such as financial or medication management. An indication of physical functioning can be obtained by measuring grip strength (using a dynamometer) or timing individuals walking a distance of 4 metres (gait speed), and a useful 'performance' measure is the SPPB (short physical performance battery) which assesses balance, gait speed and proximal lower limb strength and is predictive of future disability.⁷

Clinicians can refer patients with possible sarcopenia for a DEXA scan, but this is expensive and may not be convenient. Alternatively, a rapid screening test for sarcopenia in a clinical setting can be obtained using a simple five-question instrument called the Sarc-F which looks at falls history, ability to lift objects and difficulties with

Figure 1: ABCD Frailty Assessment Pathway in Diabetes (adapted from references 12 and 13)



mobility.⁸ It has been validated extensively and has been shown to be highly predictive of future disability and hospitalisation.⁹ Frailty can be screened for by the FRAIL scale, which is well validated and has similar sensitivity and specificity as the Fried scale. It asks five questions only, which cover fatigue, climbing stairs, walking, number of illnesses and weight loss.¹⁰ The development of biomarkers which can predict the risk of frailty and improve the accuracy of diagnosis is needed.¹¹

Other measures in the diabetes clinic scenario that assist the overall perception of functional health status and possibility of disability are standard clinical assessment for visual loss, cardiovascular health, detection of depression and the presence of neuropathy (age- or diabetes-related) by the monofilament or vibration perception test.

A practical guide to detection of frailty and overall functional status evaluation in both primary and secondary care settings is given in Figure 1 (adapted from references ¹² and ¹³).

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Section B: Key Areas in Medical Management

Glucose regulation and glucose-lowering therapies

Recommendations

- Prescribed glucose-lowering medications should have a low risk of hypoglycaemia, minor side effects profile and be cost-effective.^{1,2}
- “Start low and go slow” when dosing and titrating medications in frail older adults.
- The glycaemic goal should be individualised based on comorbid medical conditions in addition to cognitive and functional status.^{3,4} In mild to moderate frail older adults, an HbA_{1c} target range of 7–8% (53–64 mmol/mol) is appropriate depending on self-care management abilities and the presence of additional risk factors for hypoglycaemia; in severe frailty, an HbA_{1c} range of 7.5–8.5% (59–69 mmol/mol) is more protective.^{1,5}
- Many frail older adults have medical conditions that interfere with HbA_{1c} measurements. In such cases, focus on random blood glucose targets at 120–200 mg/dL (6.7–11.1 mmol/L) throughout the day instead of HbA_{1c} targets.^{6,7}
- Metformin should be used as the first line of therapy due to its low risk of hypoglycaemia, low cost and good tolerability. In frail patients, weight loss and gastrointestinal side effects should be watched for carefully.
- Dipeptidyl peptidase-4 (DPP-4) inhibitors should be considered for those older adults requiring smaller post-prandial glucose lowering, or used in combination with basal insulin.⁸
- Glucagon-like peptide-1 (GLP-1) receptor agonists should be used for post-prandial glucose lowering. They have a low risk of hypoglycaemia but are only available in injectable form. They should be considered when carer support is needed for injections due to their availability in once-a-week formulations, as well as availability in combination with basal insulin. Caution should be present where further weight loss might be an issue.
- Sulfonylurea and non-sulfonylurea secretagogues have a high risk of hypoglycaemia and should be avoided in frail older adults due to poor consequences such as traumatic falls. However, they are useful when the cost of medications is an issue or other costlier agents are not available.
- Before initiating insulin therapy, the physical and cognitive capabilities of a frail older adult should be evaluated. Once-a-day basal insulin should be used with other non-insulin agents if further glucose lowering is required.
- Intensive therapy with a complex insulin regimen is not recommended in older adults. Simplified therapies should be the goal in frail older adults with diabetes.⁹
- Carers should receive basic education and training on hypoglycaemia and its treatment.

See Table 1 for a summary of glucose-lowering therapies in managing frail older adults with diabetes.

Rationale and evidence base

Relatively few large studies have been conducted specifically assessing the use of various hypoglycaemic drugs in older adults. Meta-analyses, observations and conclusions made from smaller studies and subgroup analyses have helped to guide practical management in older adults.^{10–14} Previous guidelines by EASD/ADA describe a patient-centered approach to management in all adults with type 2 diabetes.¹⁵ The factors that are important to consider when choosing the class of glucose-lowering medications include the risk of hypoglycaemia, the efficacy of the medication, the side effect profile, its impact on weight and the cost of the medications. These factors should be considered when choosing a second or third line of agents if metformin (first-line agent) is inadequate or contraindicated.

Insulin can be used safely and effectively in older adults when used as part of the right strategy.¹⁶ The availability of basal insulin has helped to improve glycaemic control with a lower risk of hypoglycaemia than multiple daily insulin therapies. In general, de-intensification is recommended for frail older adults who are on complex insulin regimens. The simplification of the insulin regimen can decrease the risk of hypoglycaemia without worsening glycaemic control in older adults with diabetes.¹⁷ Recent guidance has been released that offers alternative approaches on combining injectable therapies with and without oral agents.¹⁸

How to implement the recommendations into routine clinical practice

Algorithms that provide direction for choosing hyperglycaemia-lowering medications in frail older adults should be provided to improve existing clinical practice.¹⁹ Guidelines specifically addressing the patient-centered approach have been available from various organisations such as IDF, EASD/ADA.¹⁵ The risk of hypoglycaemia and its impact on morbidity and mortality in frail older adults should be stressed when glycaemic goals are determined.²⁰ Clinicians should also be made aware of a ‘reverse algorithm’ to de-intensify complex insulin regimens in frail older adults who are not coping well with their multi-dose insulin therapy.

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Table 1 Summary of glucose-lowering therapies in managing frail older adults with diabetes. Each class of agent can be used in frail people with diabetes but cautions are present. Numerous factors must be taken into account in prescribing a safe but effective glucose-lowering agent.

	HbA_{1c} reduction	Advantages	Disadvantages	Vignette in frail population
Metformin	1% (11 mmol/mol)	Low hypoglycaemia risk Low cost Well tolerated generally	Many contraindications in population with high comorbidity burden. May cause weight loss, GI upset in frail patients	Can be used until eGFR <30 mL/min Use with caution if previous episode of acute kidney injury Extended release formulation has lower complexity and fewer GI side effects Assess and replace vitamin B12
Sulfonylureas	1% (11 mmol/mol)	Low cost Established glucose-lowering medication Can be used in moderate to severe renal impairment	High risk of hypoglycaemia Avoid glibenclamide (glyburide)	Avoid in patients with inconsistent eating pattern such as in advanced dementia and malignancy High risk of hypoglycaemia during acute illness or weight loss Consider discontinuing if already receiving substantial amount of insulin (approximately >40 units/day) Have a high threshold for use with insulin in frail older adults
Meglitinides	0.4–0.9% (4.4–9.9 mmol/mol)	Shorter duration of action compared with sulfonylurea	Higher cost than sulfonylurea Increased regimen complexity due to multiple daily doses with meals	Can be withheld if patient refuses to eat any particular meal
TZDs, Pioglitazone	1% (11 mmol/mol)	Low hypoglycaemia risk Low cost Once a day dosing Can be used in moderate to severe renal impairment	Many contraindications in population with high comorbidity burden such as CHF, leg oedema, anaemia, fractures Use with caution in combination with insulin	Good efficacy in older patients with high insulin resistance
DPP-4 inhibitors	0.5–0.8% (6–9 mmol/mol)	Low hypoglycaemia risk Once a day oral medication Well tolerated Can be used in renal impairment but dose adjustment required (except linagliptin)	Medium/high cost HbA _{1c} reduction modest compared with other agents Potential risk of heart failure in at-risk individuals	Can be combined with basal insulin for a low complexity regimen
SGLT-2 inhibitors	0.8–1.0% (9–11 mmol/mol)	Low hypoglycaemia risk Reasonable efficacy Risk of other adverse effects moderate Diuretic, blood pressure-lowering effect	High cost Limited experience in older population but evidence increasing Low risk of diabetic ketoacidosis which may be euglycaemic and unrecognised	In frail adults, watch for increased urinary frequency, incontinence, lower BP, genital infections, dehydration; do not initiate if eGFR is <60 mL/min; dose reduction required in the presence of renal impairment Withhold SGLT-2 inhibitors at times of acute illness or major surgery
GLP-1 receptor agonists	0.8–1.0% (9–11 mmol/mol)	Low hypoglycaemia risk Once a day and once a week formulation New formulations available in combination with basal insulin	High cost Injectable GI side effects	Monitor for anorexia, weight loss; do not use in severe renal impairment (eGFR <30 mL/min); dose reduction needed in moderate impairment (except for liraglutide and dulaglutide) Once-weekly formulations may be helpful if carer support is necessary to deliver injectable therapy
Insulin	>1% (>11 mmol/mol)	No ceiling effect Many different types including high concentrated forms have variable serum half-life and can be used to target hyperglycaemia at different times of the day; can be used in renal impairment	High risk of hypoglycaemia Need for matching carbohydrate content in patients with variable appetite when using prandial insulin Carer education and training needed if involved in administration Blood glucose testing necessary adding to cost	Use of basal insulin with other agents to lower post-prandial glucose can lower complexity of management and reduce the risk of hypoglycaemia

HbA_{1c}, glycosylated haemoglobin; eGFR, estimated glomerular filtration rate; GI, gastrointestinal; TZDs, thiazolidinediones; DPP-4, dipeptidyl peptidase-4; SGLT-2, sodium-glucose cotransporter 2; GLP-1, glucagon-like peptide-1.

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Blood pressure management

Recommendations

- Target blood pressure in older people with diabetes, including those with dementia, is below 140/90 mmHg. A blood pressure target of below 150/90 mmHg may be appropriate in frail, dependent older individuals with diabetes.¹
- If possible, lying and standing blood pressure should be measured.
- Non-pharmacological interventions may not be possible or appropriate.
- “Start low and go slow” when dosing and titrating blood pressure-lowering medication in frail older adults.
- Renal function and electrolytes should be monitored.
- The first-line treatment of hypertension in older people with diabetes is an ACE-inhibitor, particularly in the presence of diabetic nephropathy or cardiac failure. An aldosterone receptor antagonist may be substituted if an ACE-inhibitor is not tolerated.
- Either a thiazide-like diuretic or dihydropyridine calcium channel blocker can be added to an ACE-inhibitor to achieve target blood pressure.
- All major classes of blood pressure-lowering medication can be used to achieve blood pressure target.
- Reduction or withdrawal of blood pressure-lowering medication may be necessary with increasing frailty and dependence.

Rationale and evidence base

Hypertension is a common and significant comorbidity in older people with diabetes, resulting in a high risk of cardiovascular and cerebrovascular disease as well as the microvascular complications of nephropathy and retinopathy.² Hypertension, like diabetes, can also be considered to be a risk factor for frailty.³

There is much evidence to show that blood pressure reduction is associated with improved diabetes-related and cardiovascular outcomes including death.^{2,4,5} However, a blood pressure target of less than 140/90 mmHg may not always be beneficial in type 2 diabetes.^{6,7}

There is a lack of randomised controlled trials to guide the setting of blood pressure targets in frail older people. Nonetheless, it is clear that the concept of “the lower the better” is not applicable to frail older patients with diabetes where over-treatment of hypertension has the potential to cause significant harm.^{6,8} An individualised approach using different blood pressure targets in older people with diabetes according to functional status and comorbidity is recommended.

A blood pressure target of less than 140/90 mmHg is appropriate for most people with diabetes and hypertension, including older adults who are functionally independent.^{1,9}

Table 2 Antihypertensive medications - indications and cautions in frail older adults with diabetes

Drug class	Indication	Caution	Vignette in frail population
ACE-inhibitor	Recommended first-line treatment in older people with diabetes and hypertension, particularly if co-existent cardiac failure or diabetic nephropathy	Hyperkalaemia: avoid concurrent use with potassium-sparing diuretics ¹⁰ Hypotension Dry cough Angioedema (rare)	Orthostatic hypotension can increase risk of falls Withhold during intercurrent illness or acute kidney injury
Angiotensin-receptor blocker (ARB)	Use as first-line treatment if intolerance to ACE-inhibitor	Hyperkalaemia: avoid concurrent use with potassium-sparing diuretics Hypotension ACE-inhibitor and ARB combination should be avoided ¹⁰	See ACE-inhibitor section
Diuretic	Use added on to ACE-inhibitor or ARB to achieve BP target, particularly if fluid retention present Use thiazide-like diuretic such as chlorthalidone or indapamide; avoid bendroflumethiazide		May precipitate fluid depletion and falls Withhold during intercurrent illness with risk of acute kidney injury Administer in morning to avoid inconvenient and nocturnal micturition
Dihydropyridine calcium channel blocker	Use added on to ACE-inhibitor or ARB to achieve BP target		May cause peripheral oedema and constipation
Beta-blockers	Can be considered particularly if co-existing ischaemic heart disease, cardiac failure or tachycardia	Avoid if hypoglycaemic awareness impaired Use with caution in the presence of bronchospasm	
Alpha-blockers	Can be considered particularly in men with symptoms of benign prostatic hyperplasia		Can precipitate orthostatic hypotension

In frail older adults with diabetes a blood pressure target of 150/90 mmHg or less is recommended. In this group, blood pressure lowering may be limited by the presence of concomitant disease, polypharmacy including psychotropic medications and orthostatic hypotension. In older adults with diabetes and dementia, a blood pressure target of 140/90 mmHg is advocated if blood pressure lowering is considered clinically appropriate.¹ In Table 2 of this Position Statement we have listed the blood pressure-lowering classes with additional comments.

How to implement the recommendations into routine clinical practice

Blood pressure measurement should take place as part of routine diabetes consultations, in clinic or care home if feasible and on at least two occasions before the introduction of pharmacological therapy. Both lying and sitting or standing blood pressure should be measured and treatment offered which will not impact adversely on orthostatic hypotension. A holistic and individualised approach should be used to decide target blood pressure, taking into consideration the patient’s level of dependency and place of residence, comorbidities and concurrent medication. The use of blood pressure-lowering medication that might be expected to benefit other comorbidities should be considered. Renal function and electrolytes should be monitored after initiation of new blood pressure-lowering treatment and periodically thereafter.

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Use of lipid-lowering agents

Recommendations

- A full lipid profile should be included in the assessment of older people with diabetes.
- Other secondary causes of hyperlipidaemia should be excluded including primary hypothyroidism, liver disease and alcohol excess.
- Diet and lifestyle interventions may not be possible.
- All older people with diabetes are considered at high cardiovascular risk and statins are considered the treatment of choice provided this is clinically appropriate.
- Statin myopathy is more common in older patients due to sarcopenia and low or moderate dose statin therapy should be used.
- Correction of vitamin D depletion may improve statin-associated myalgia.
- With increasing frailty and dependence, withdrawal of lipid-lowering treatment should be considered.

Rationale and evidence base

All older people with diabetes are at high cardiovascular risk and statin therapy should be routinely considered to improve cardiovascular outcome.¹ Although epidemiological studies suggest that the relative risk of coronary heart disease associated with raised cholesterol decreases with age,² given the high prevalence of cardiovascular disease in older people with diabetes the absolute benefits of lipid lowering are greater in this population.

Whilst statins are most beneficial in secondary prevention in older people,³ a recent retrospective cohort study also supported the use of statins for primary prevention in people with diabetes up to the age of 85.⁴ Statin use is also associated with a reduction in ischaemic stroke,⁵ although with an increase in haemorrhagic stroke.⁶

The addition of fenofibrate to statin therapy in high-risk patients with diabetes has not been shown to confer additional benefit,⁷ and fibrate treatment is not recommended unless marked hypertriglyceridaemia is present.

There is limited evidence looking at the effects of statins over the age of 80. However, up to 10% of patients develop muscle-related symptoms with the use of statins which is more common in older people and in the presence of chronic kidney disease, frailty and multi-morbidity.⁸ As 80% of cholesterol-lowering effect is seen at

50% of maximal statin dose⁹ and the side effects of statins are dose dependent, low or moderate doses of statins are recommended in older people. In Table 3 of this Position Statement we have listed the lipid-lowering classes with additional comments.

How to implement the recommendations into routine clinical practice

Measurement of a full lipid profile should be incorporated into the routine assessment of older people with diabetes and statin therapy initiated as the lipid-lowering treatment of choice to reduce cardiovascular risk. Lipid-lowering treatment goals should be individualised; functionally independent older people with diabetes should be actively managed and, in more dependent older individuals, statin therapy should be contemplated provided this is clinically meaningful.

Secondary causes of dyslipidaemia should be excluded, particularly hypothyroidism, and a fibrate initiated in the presence of significant hypertriglyceridaemia. Otherwise, addition of a fibrate or niacinic acid is not indicated in the management of dyslipidaemia in older individuals.

Statin-associated myopathy is more common in older people and lower doses of statin therapy should be considered in older individuals. Patients and their carers should be counselled about the risk and symptoms of statin-associated myopathy.

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Table 3 Lipid-lowering agents - indications and cautions in frail older adults with diabetes

Drug class	Indication	Caution	Vignette in frail population
Statin	All older adults with diabetes are considered at increased cardiovascular risk and statin therapy should be considered provided clinically appropriate Risk reduction in recurrent ischaemic stroke	Risk of myalgia, myositis and rhabdomyolysis (rare) Maximum simvastatin dose 20 mg when administered with amlodipine ¹⁰ Avoid using in primary haemorrhagic stroke ⁶	Increased risk of statin myopathy in older adults due to reduced muscle mass in addition to decreased renal and liver function. Low dose statin therapy advised
Fibrate	Hypertriglyceridaemia		Use with caution in chronic kidney disease and in combination with statin therapy due to increased risk of myopathy, particularly if sarcopenia present

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Frailty and chronic kidney disease

Recommendations

- All individuals with chronic kidney disease (CKD) and diabetes require a functional assessment to detect frailty or functional impairment at an early stage.
- Frailty assessment can be undertaken using the assessment tools indicated in Section A (Definition of frailty, diagnosis and assessment methods).
- In order to improve clinical outcomes, those identified as frail require a frailty management plan that includes:
 - minimising hypoglycaemia
 - agreeing a regular exercise plan that will prevent further weight loss and increase muscle mass
 - a nutritional status assessment and identifying micronutrient and/or vitamin D deficiency
 - and setting appropriate glucose and HbA_{1c} targets.
- In moderate to severe frailty, glucose and blood pressure targets may need revision to be less strict and advance care planning may be required.
- In moderate to severe frailty, protein restriction and aggressive salt restriction may not be appropriate.

Rationale and evidence base

Frailty is a common co-existing state in those with CKD, and whilst the prevalence of frailty in older people living in the community may be of the order of 11%, the prevalence of frailty exceeds 60% in CKD patients on dialysis.^{1–3} Among community-dwelling older people, the Cardiovascular Health Study (CHS) demonstrated that mild to moderate elevation in serum creatinine was associated with a greater prevalence of frailty.⁴ A recent review of the area concluded that frailty was independently linked with poor outcomes in all stages of CKD including increased risk of mortality and hospitalisation.^{2,5,6} Physical inactivity is more marked for individuals with CKD⁷ and is associated with increased mortality in those with CKD,⁸ and may be a pathogenetic basis for the development of sarcopenia and frailty in patients with CKD. Frailty with associated protein-energy wasting are also common findings in older people with end-stage renal disease undergoing dialysis.⁹ emphasising the importance of both functional and nutritional assessment in these individuals.

Diabetes mellitus remains the leading cause of CKD in Western countries and diabetic nephropathy leads to increased mortality and accounts for 20% of people commencing renal replacement therapy.¹⁰ There is little published work on diabetic CKD and frailty, but frailty management must be added to the list of other key actions

including early recognition of both diabetic kidney disease and frailty, aggressive management of cardiovascular risk factors and control of blood pressure and glucose regulation to worthwhile levels. In those with moderate to severe frailty, discussion with the nephrologist, patient and family should take place to agree more realistic and appropriate metabolic targets and, in some cases, the issue of advance care planning should be raised.

How to implement the recommendations into routine clinical practice

Frailty assessment should form part of the routine comprehensive evaluation of all older people with CKD, particularly those with diabetes. For those with diagnosed frailty or functional impairment, a feasible exercise schedule should be part of their routine management plan. All health professionals directly engaged in managing older people with both diabetes kidney disease and frailty should be familiar with the basic assessments required to measure functional loss and detect frailty.

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Avoiding and managing hypoglycaemia

Recommendations

- Healthcare professionals caring for older people with diabetes should evaluate their risk of hypoglycaemia and develop individualised HbA_{1c} and blood glucose goals as part of care planning.
- Older people with chronic kidney disease and dementia are at particular risk of hypoglycaemia and review of dietary intake is critical.
- Blood glucose levels should be greater than 6 mmol/L and HbA_{1c} greater than 7% in frail older people with diabetes to minimise the risk of hypoglycaemia. An HbA_{1c} level below 7% is likely to indicate overtreatment of hyperglycaemia.
- A severe episode of hypoglycaemia should trigger a comprehensive diabetes review including assessment of blood glucose-lowering treatment and dietary intake.
- De-intensification of blood glucose-lowering agents and regimens should take place in response to overtreatment of hypoglycaemia.
- The use of newer blood glucose-lowering treatments with lower hypoglycaemic potential should be considered to manage hyperglycaemia in frail older people.
- If insulin therapy is necessary, a basal insulin regimen has the lowest risk of hypoglycaemia. Intensive basal-bolus insulin regimens should be avoided in frail older people.
- The person with diabetes or their carer should have an evaluation of their abilities to inject, conduct blood glucose monitoring and insulin dose adjustment.
- Amongst hospital inpatients, bedtime snacks and “hypo boxes” are recommended to reduce risk and treat episodes of hypoglycaemia.

Rationale and evidence base

In older adults, hypoglycaemia is defined as a blood glucose level of 4 mmol/L or below.¹ Hypoglycaemia is common but under-reported in older people due in part to reduced counter-regulatory hormonal responses to low blood glucose levels which diminish with age.² The lack of adrenergic symptoms and increased symptoms of neuroglycopenia in older people can result in a delayed diagnosis of hypoglycaemia, increasing the potential for harm to occur.³

Amongst older people in particular, hypoglycaemia has the potential to cause adverse consequences including falls, fractures and admission to hospital. Hypoglycaemia has been shown to be associated with increased cardiovascular events and mortality,⁴ whilst severe episodes of hypoglycaemia are associated with accelerated cognitive decline.^{5,6} It is also acknowledged that recurrent hypoglycaemia, especially if associated with hospital admission, is a risk factor for frailty.⁷

Older people are at higher risk of hypoglycaemia, particularly if cognitive impairment is present.⁸ Other risk factors for hypoglycaemia include duration of diabetes, treatment with insulin or sulfonylureas,⁹ the presence of multiple comorbidities¹⁰ and renal impairment.

Whilst an HbA_{1c} level of 7% (53 mmol/mol) or less is acknowledged as a sign of potential overtreatment in frail older adults with diabetes, the risk of severe episodes of hypoglycaemia has been found to be greatest in those with either near normal (HbA_{1c} <6.0%; <42 mmol/mol) or poor control (HbA_{1c} >9.0%; >75 mmol/mol),¹¹ and glycaemic variability has been identified as an important factor when considering mortality risk in older people with diabetes.¹²

In recent years there has been an increasing focus and recognition of the overtreatment of hyperglycaemia in frail older people with diabetes and the potential for this to cause harm.¹³ As older people with diabetes form a heterogeneous group of differing degrees of dependence and frailty, there is need for individualisation of glycaemic treatment goals and therapeutic options.¹⁴ This is recognised in national and international guidelines which advocate the introduction of individualised HbA_{1c} goals in older people to minimise the risk of hypoglycaemia.^{15,16}

The concept of deintensification describes the simplification of blood glucose-lowering treatment regimens to achieve an individualised HbA_{1c} goal and reduce the risk of hypoglycaemia.¹⁷ This process might incorporate the use of glucose-lowering therapies with lower hypoglycaemic potential, rather than sulfonylurea and insulin treatment, to achieve treatment goals in dependent older people. In the IMPERIUM Study, Heller and colleagues demonstrated that similar glycaemic goals could be achieved in vulnerable older people with type 2 diabetes with less hypoglycaemia using newer glucose-dependent therapies compared with a more traditional sulfonylurea and insulin-based approach.¹⁸

How to implement the recommendations into routine clinical practice

All older people with diabetes should have an appropriate individualised HbA_{1c} goal taking into account functional status, cognitive ability, comorbidities including renal function and duration of diabetes. If HbA_{1c} is unreliable, capillary blood glucose goals can be used. Optimal HbA_{1c} in older people should be reviewed annually as part of their care, or more frequently if there is a change in functional status or the development of new comorbidities such as malignancy which increase the risk of hypoglycaemia.

Overtreatment of hyperglycaemia is common in frail older people with diabetes and deintensification of treatment should be undertaken to meet an appropriate HbA_{1c} goal, particularly in response to episodes of hypoglycaemia.

Routine care of older people with diabetes should include assessment of the individual's ability to self-manage diabetes incorporating blood glucose testing, administration of insulin or alternative blood glucose-lowering therapy and insulin dose titration. If carer support is necessary, then appropriate education of the carer should occur.

All patients or their carers should be educated about the risk, recognition and treatment of hypoglycaemia ideally as part of an educational programme. Care homes should have a protocol covering the prevention, recognition and treatment of hypoglycaemia.

Box 1: Strategies to avoid hospital admission due to hypoglycaemia

- Adoption of the use of individualised HbA_{1c} goals and blood glucose targets reflecting level of dependence, frailty and presence of dementia.
 - An HbA_{1c} level of <7%/53 mmol/mol should serve as a warning of possible overtreatment and trigger review of blood glucose-lowering treatment.
 - Blood glucose levels below 6 mmol/L should be avoided.
- A severe episode of hypoglycaemia should trigger a detailed diabetes review including structured medication review.
- Deintensification of blood glucose-lowering treatment should be undertaken in response to overtreatment of hyperglycaemia incorporating simplification of insulin regimen, withdrawal of non-glucose dependent medication and the use of glucose-dependent therapies where necessary to lower hyperglycaemia.
- The presence of dementia or malignancy with poor appetite should trigger dietary review and a switch to basal insulin if necessary and glucose-dependent therapies.
- Older frail individuals or their carers should undergo assessment of blood glucose testing, insulin administration and ability to undertake insulin dose titration.
- Development of an educational programme for people with diabetes or their carers to minimise the risk of hypoglycaemia.

All diabetes care teams should have in place a hospital avoidance scheme agreed with primary and community care colleagues (see Box 1).

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Exercise interventions

Recommendations

- Along with pharmacological and dietary interventions, physical training including resistance and endurance training is required for effective benefits to be realised.
- In addition to the beneficial effects of exercise interventions on glycaemic control and on the cardiovascular risk factors associated with diabetes, physical exercise should be employed as an effective intervention to improve neuromuscular and cardiorespiratory function as well as functional capacity and quality of life in elderly diabetic patients.
- The combination of resistance and endurance training should be considered to be the most effective exercise intervention to promote overall physical fitness in older diabetic patients.
- On the basis of recent evidence, exercise strategies to improve neuromuscular and cardiovascular parameters and functional performance in frail older individuals should include the following:
 - Resistance-training programmes should be performed two to three times per week, with two to three sets of 8–12 repetitions at an intensity that starts at 30–40% and progresses to 80% of 1RM (one-repetition maximum, the maximum force that can be generated in one maximal contraction).
- To optimise the functional capacity of individuals, resistance training programmes should include exercises in which daily activities are simulated, such as the sit-to-stand exercise. Part of resistance training exercises (especially lower limbs) should be performed as fast as possible (muscle power training) in order to optimise skeletal power output and, consequently, functional capacity.
- Endurance training should include walking with changes in pace and direction, treadmill walking, step-ups, stair climbing and stationary cycling. Endurance exercise may start at 5–10 min during the first weeks of training and progress to 15–30 min for the remainder of the programme. The intensity should start between 40% and 50% of HRmax (maximum heart rate, the highest heart rate that an individual can achieve before an individual experiences severe problems due to exercise) and progress to 70–80% of HRmax.
- The Rate of Perceived Exertion scale is an alternative method for prescribing the exercise intensity, and an intensity of 12–14 on the Borg scale appears to be well tolerated. This method can be applied to multi-directional weight lifts, heel-toe walking, line walking, stepping practice, standing on one leg, weight transfers (from one leg to the other) and modified Tai Chi exercises.
- Multi-component training programmes should include gradual increases in the volume, intensity and complexity of the exercises, along with the simultaneous performance of resistance, endurance and balance exercises.

Rationale and evidence base

Loss of muscle mass in older adults with diabetes may be a part explanation why diabetes is associated with an increased risk of disability¹ and, along with changes in muscle quality (eg, by fat

infiltration), may explain the observation of an association between diabetes and gait speed.²

Physical inactivity is a key factor contributing to the onset of muscle mass and function decline (ie, sarcopenia), which in turn appears to be a vital aspect related to frailty.³ Poor health, disability and dependency are not inevitable consequences of ageing. Individuals that are more likely to remain healthy and live independently and incur fewer health-related costs are those who engage in a healthy lifestyle and physical exercise, and avoid excessive sedentariness, and continue to socially engage with family and friends. Recently, it has also been proven that physical activity, as an intervention, is one of the most important components in improving the functional capacity of frail seniors.^{4–8} Furthermore, physical exercise administration is relatively free of potential unwanted side effects caused by common medications that are prescribed in patients with multiple comorbidities.

Among the several comorbidities that may coexist in frailty syndrome, diabetes is one of the most prevalent.⁹ In frail patients with diabetes, enhancement in functional capacity is crucial and may be more beneficial than attention to metabolic control alone.⁹ Accordingly, an important conceptual idea for frailty is that the focus should be on functionality and not on the diagnosis of disease for older patients.

Exercise interventions, including resistance training, together with pharmacological and dietary interventions, represent the cornerstones of type 2 diabetes mellitus management.^{10–12} Exercise intervention in older people with diabetes has important benefits in improving glycaemic control,^{10–12} increasing insulin sensitivity, decreasing intra-abdominal adipose tissue and muscle fat infiltration,¹³ as well as modifying cardiovascular risk factors associated with diabetes. In addition, physical exercise is an effective intervention to improve muscle mass, strength, power output, cardiovascular function and functional capacity in older people with diabetes.¹³ Another aspect that should be taken into consideration with respect to the benefits of exercise to older diabetic patients is the role of exercise in the prevention of cognitive impairment and dementia. In this regard, exercise may also help to prevent dementia and to improve muscle functional capacity in older patients with dementia and these characteristics may be a consequence of diabetes complications.^{5,14}

Combined resistance and endurance training appears to serve as an effective exercise intervention to promote overall physical fitness in older patients with diabetes.^{4,5} In addition, in the frail elderly diabetic with severe functional decline, multicomponent exercise programmes composed of resistance, endurance, balance and gait retraining should be employed to increase functional capacity and quality of life and to avoid falls, institutionalisation and disability. However, the studies in which systematic resistance training was performed (either alone or as part of multi-component exercise programmes) revealed greater strength gains in the older individual with physical frailty or severe functional decline. Exercise prescription, especially in older frail patients with diabetes, must be carefully

adapted to provide a sufficient stimulus for improving the functional capacity.⁷ Furthermore, because muscle power is an important predictor of functional capacity, strategies to develop skeletal muscle power in this population must be included to prevent or postpone functional limitations and subsequent disability.^{4,5,7}

How to implement the recommendations into routine clinical practice

The above findings are especially important because they suggest that physical training can prevent or slow the progression of functional decline in older people with diabetes.

Health professional educational programmes on the importance of exercise in promoting functional independence and preventing decline in physical performance should be commissioned by local healthcare services.

Recently, the Vivifrail Project, a European Union funded project (part of the Erasmus+ programme), focuses on provide training for health professionals in the management of frail older people through exercise and designs materials on how to promote and prescribe physical exercise in older adults (www.vivifrail.com).¹⁵

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Section C: Clinical Audit in Frailty

As part of reviewing local clinical practice, observing the effects of various interventions or change in procedures in a clinical pathway, identifying gaps in treatment and promoting the drive to enhanced diabetes care, clinical multidisciplinary audit is an important tool. This Position Statement will have provided sufficient ideas for clinical audit activity in the area of diabetes and frailty and these can be undertaken as part of an annual process of reviewing if frailty is being looked for in people with diabetes, if appropriate assessment tools are being used, and if clinical decision-making has been influenced by the detection of frailty.

In Panel A we have identified five areas for audit activity from which to choose as local diabetes care teams start to take on board the importance of frailty in the routine care of older adults with frailty and diabetes. Other areas for audit can be chosen during multidisciplinary meetings of the diabetes care team. Targets are recorded as 75% but can be adjusted upwards to 100% as the experience of the local team in developing frailty pathways increas their multi-dose insulin therapy.

Panel A: Selection of Audit Areas in Diabetes and Frailty			
Clinical setting or area of activity	Nature of audit indicator and suggested initial target	Lead for audit activity in this area	Data collection
Frailty assessment: inpatients, outpatients, community	Percentage of all patients receiving a frailty assessment in the past month or year; target 75%	Diabetes specialist nurse or practice nurse or dietician	Documentation of assessment in clinical/medical records*
Medicines review	Percentage of all patients with frailty receiving a medicines review in the past month or year; target 75%	Doctor or diabetes specialist nurse or pharmacist	Documentation of assessment in clinical/medical records*
Falls risk	Percentage of all patients with frailty receiving a falls risk assessment in the past month or year; target 75%	Diabetes specialist nurse or doctor or podiatrist	Documentation of assessment in clinical/medical records*
Hypoglycaemia risk assessment	Percentage of all patients with frailty receiving a hypoglycaemia risk assessment in the past month or year; target 75%	Diabetes specialist nurse or doctor or pharmacist	Documentation of assessment in clinical/medical records*
Individualised care plan in place: inpatients, outpatients, community	Percentage of all patients with frailty who have an individualised care plan in place in each setting including discharge from hospital. Time frame: 1 month or 1 year; target 75%	All members of the diabetes care team	Documentation of assessment/plan in clinical/medical records*

*Will include assessment tool/procedure used and healthcare professional involved

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