

SPECIAL ARTICLE

AN INTERNATIONAL POSITION STATEMENT ON THE MANAGEMENT OF FRAILTY IN DIABETES MELLITUS: SUMMARY OF RECOMMENDATIONS 2017

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Abstract: *Aim:* the the International Position Statement provides the opportunity to summarise all existing clinical trial and best practice evidence for older people with frailty and diabetes. It is the first document of its kind and is intended to support clinical decisions that will enhance safety in management and promote high quality care. *Methods:* the Review Group sought evidence from a wide range of studies that provide sufficient confidence (in the absence of grading) for the basis of each recommendation. This was supported by a given rationale and key references for our recommendations in each section, all of which have been reviewed by leading international experts. Searches for any relevant clinical evidence were generally limited to English language citations over the previous 15 years. The following databases were examined: Embase, Medline/PubMed, Cochrane Trials Register, Cinahl, and Science Citation. Hand searching of 16 key major peer-reviewed journals was undertaken by two reviewers (AJS and AA) and these included Lancet, Diabetes, Diabetologia, Diabetes Care, British Medical Journal, New England Journal of Medicine, Journal of the American Medical Association, Journal of Frailty & Aging, Journal of the American Medical Directors Association, and Journals of Gerontology - Series A Biological Sciences and Medical Sciences. *Results:* two scientific supporting statements have been provided that relate to the area of frailty and diabetes; this is accompanied by evidence-based decisions in 9 clinical domains. The Summary has been supported by diagrammatic figures and a table relating to the inter-relations between frailty and diabetes, a frailty assessment pathway, an exercise-based programme of intervention, a glucose-lowering algorithm with a description of available therapies. *Conclusions:* we have provided an up to date evidence-based approach to practical decision-making for older adults with frailty and diabetes. This Summary document includes a user-friendly set of recommendations that should be considered for implementation in primary, community-based and secondary care settings.

Key words: Diabetes mellitus, frailty, older people, sarcopenia, position statement, management.

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Introduction

Diabetes mellitus, predominantly type 2 diabetes, occurs more frequently in aging populations, and as this condition can be associated with increased healthcare expenditure in managing diabetes-related hospital admissions and the associated vascular complications, the challenge of providing focused and effective diabetes care to an aging population is daunting (1).

Diabetes mellitus has a considerable impact on our aging society and this is acknowledged by the following findings: the seventh highest cause of years lost and eight highest cause of disability adjusted life years in Western countries in those aged 60–79 years, HR of death is 1.91 (men) and 2.53 (women); the highest rates of major lower-extremity amputation, myocardial infarction (MI), visual loss, and end-stage renal disease of any age group; those aged ≥75 years also have double the rate of emergency department visits for hypoglycemia than the general

population with diabetes; and an ADL restriction increases healthcare costs of care 3-fold and admission to a care home increases costs 9-fold (2-4).

The Working Group for this Position Statement acknowledge that frailty is now increasingly seen as a new emerging complication of diabetes (5) 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 (7). Frailty has previously been identified as a key priority area for action (8), and other organisations have recognised the impact of multi-morbidity and frailty in the overall management of older people with diabetes (2, 9).

As a consequence, it is now increasingly recognised that modern day recommendations for managing diabetes in older people should be more closely-aligned with additional individual characteristics such as functional status, presence of frailty and dependency, comorbidity profiles, maintaining quality of life, and life expectancy (10). This is because the

presence of these features are likely to influence treatment goals, the care model adopted, and how the clinician plans on-going care - in this Position Statement we have placed a strong emphasis on this approach.

Main Purpose of the Position Statement

(1) Arrive at a consensus on how we approach the management of key issues of managing frailty in older people with diabetes.

(2) Identify a series of key recommendations in key areas that will support clinicians in everyday clinical practice to manage more effectively the complex issues seen in aging individuals with frailty

(3) 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

Although a helpful commissioning guide for diabetes services in older people has previously been published in the United Kingdom (11), we still observe that the syndrome of frailty has received little or no attention in the management plans of older people with diabetes. As diabetes is now also recognised as an independent risk factor for frailty, and that frailty is a major determinant of disability in diabetes populations, the review group has developed this Position Statement in a timely fashion to be the first comprehensive attempt to produce relevant and practical recommendations for managing frailty in older people with diabetes. Its clear intention is to form a significant support platform for clinicians in several clinical settings including primary and secondary healthcare, as well as in care homes.

Definition of Frailty

For the purposes of this Position Statement the review group characterises frailty as a summary concept based on:

- as a vulnerability state that leads to a range of measurable adverse outcomes such as falls or a decline in physical performance
- decline in physiological reserve and the inability to resist to physical or psychological stressors
- a pre-disability condition

The phenotypic manifestations of frailty were objectively defined by Linda Fried and colleagues in the United States in 2001 (12) which were centred around five components of exhaustion, physical activity, walk speed, hand grip strength, and weight loss. A further competing model of describing frailty based on the Canadian Health Study was introduced by Kenneth Rockwood and colleagues where a score (Frailty Index) is developed that is based on the number of deficits (or comorbidities) that are present which in turn determines the risk an individual has of an adverse outcome (13). Both measures

have been validated and have prognostic significance in terms of predicting outcomes. The Frail test developed by John Morley and colleagues, and validated in multiple populations, is increasing seen as an effective screening tool for frailty and combines components of both former approaches (14). The Working Group recognise that cognitive and psychosocial elements of frailty exist but this Position Statement has focused on the physical performance aspects in diabetic subjects only.

We have also recognised that the age-related progressive loss of muscle and function called sarcopenia may be an underlying pathophysiological process in frailty with many of the clinical recommendations logically being applicable to older patients with diabetes who are sarcopenic (6). The development/onset of diabetes leads to an acceleration of the muscle loss (15) and various factors appear to be operating including insulin resistance, AGE toxicity, changes in capillary circulation, neuropathic effects, inflammatory processes including genetic factors (16).

This Position Statement places a major emphasis on the importance of focused assessment of both physical and cognitive domains in assisting the clinician in making decisions about the functional status and comorbidity level of individuals as a guide to treatment strategies adopted. Physicians predominately working with older people often combine this series of assessments into a management tool called a comprehensive geriatric assessment (CGA) (17). This is coupled with advice on safe glucose lowering therapies, key aspects of patient safety, avoiding hospitalization and aged care home residency, and avoiding hypoglycemia.

The review group has also concluded that relevant outcome measures will also prove to have an important influence in deciding if a specific management strategy is worthwhile in routine clinical care of older people with diabetes and frailty. These should include glycaemia targets, quality of life, measures of physical performance (grip strength, walk speed) in addition to those measures more routinely measured such as rates of admission to hospital, falls rate, and changes in cognition and balance (5).

The review group has placed emphasis on how to enhance the quality of overall public health by providing recommendations for the prevention of frailty, and specific guidance in the area of primary care and in the education of health and social care professionals. This Position Statement has included sufficient information to guide providers of diabetes or geriatric medicine services on where to direct resources to manage older people with diabetes and frailty optimally and creates the opportunity for clinical care standards to be adopted

The review group has taken the decision to develop this Position Statement to address management decisions in older people aged 70 years and over with frailty and diabetes. However, these definitions can be quite arbitrary and are compounded by the lack of correlation between chronological and biological age in different continents. We feel that

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a threshold of 70+ years ensures that people with diabetes will more likely to exhibit those characteristics of functional loss associated with frailty and that these better determine the recommendations we have given. Age thresholds for management, however, can be an ad hoc viewpoint and that the clinician has the important responsibility to decide what clinical guideline is most appropriate for their older patients by determining their functional status, level of medical comorbidities, and degree of frailty. As it has been recognised elsewhere an age threshold of 70+ years also usually signifies a change in social role and the emergence of changes in dependency.

Methodology

An important limiting factor for producing specific evidence-based clinical recommendations for older people with diabetes and frailty is the relative lack of clinical evidence from randomised controlled trials involving older subjects with both index conditions. As frailty is also a specific entity and is only now emerging as a diagnosable condition, it is also not possible to extrapolate evidence from clinical studies in younger adults as the condition would have been absent in the latter in most cases. The review group has considered this implication and has sought evidence from a wide range of studies that provide sufficient confidence for the basis of each recommendation. This limitation influenced our decision not to grade our recommendations at a particular level of evidence but we have provided a rationale and key references for our recommendations in each chapter, all of which have been reviewed by leading international experts.

Searches were generally limited to English language citations over the previous 15 years. The primary strategy attempted to locate any relevant systematic reviews or meta-analyses, but randomised controlled and controlled trials were our main focus. All members provided disclosure statements to minimise bias. The following databases were examined: Embase, Medline/PubMed, Cochrane Trials Register, Cinahl, and Science Citation. Hand searching of 16 key major peer-reviewed journals was undertaken by two reviewers (AJS and AH) and these included Lancet, Diabetes, Diabetologia, Diabetes Care, British Medical Journal, New England Journal of Medicine, Journal of the American Medical Association, Journal of Frailty & Aging, Journal of the American Medical Directors Association, and Journals of Gerontology - Series A Biological Sciences and Medical Sciences.

Key Principles of Position Statement

These principles incorporate the important elements of managing older adults with frailty and diabetes which include:

- 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 comprehensive geriatric assessment and risk stratification
- Identifying and subsequent assessment of key risks in frail older adults with diabetes: hypoglycemia, worsening ADL and IADL with mobility disorder, falls, and adverse events from treatment
- A clear focus on patient safety, avoiding hospital/emergency department admissions and institutionalization by recognizing the deterioration early and maintaining independence and quality of life to a dignified death
- A management plan that incorporates educational support for families and carers, and health and social care professionals
- 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

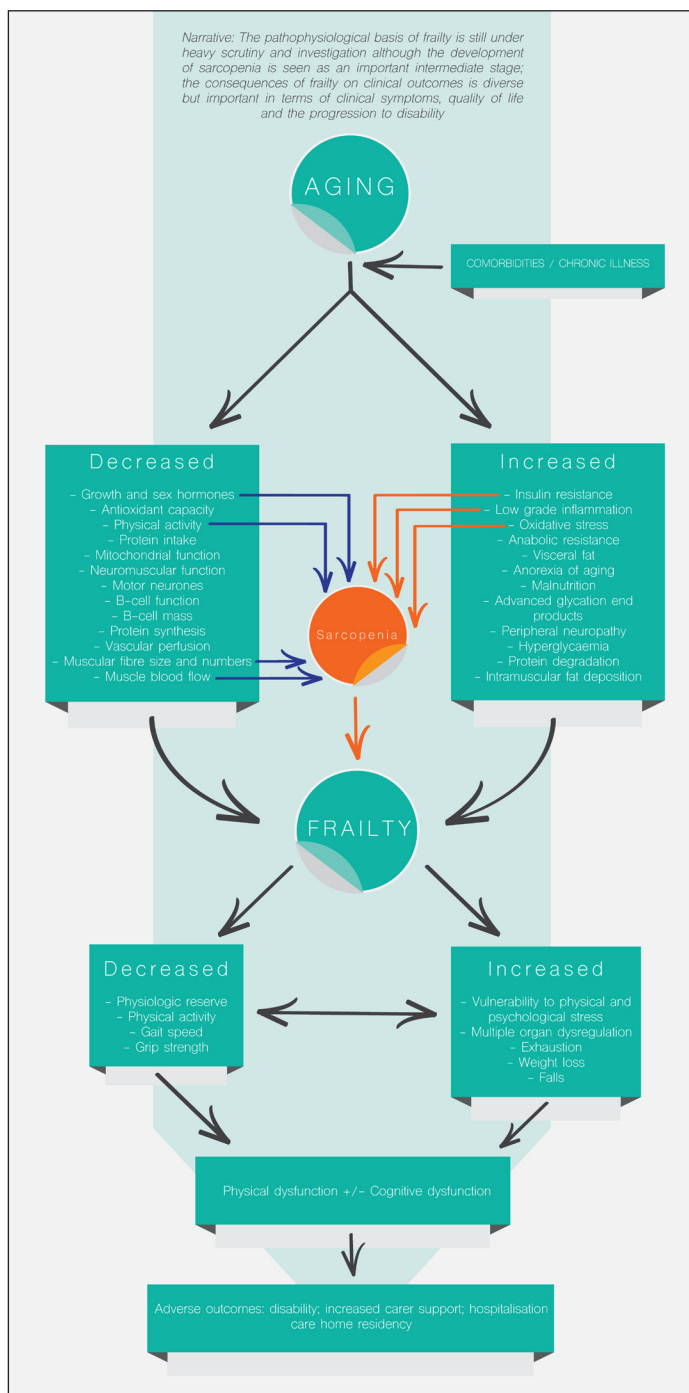
We hope that this Position Statement will form a platform for all clinicians as part of renewed emphasis on specific management approaches to those who are frail and have diabetes.

Scientific Supporting Statements

Inter-relationships between Frailty, Sarcopenia and Diabetes Mellitus

Sarcopenia, frailty and diabetes seem to be reciprocally related and may share a similar pathogenetic pathway (see Figure 1). As diabetes leads to sarcopenia, it is also plausible that sarcopenia leads to lower muscle glucose uptake, hyperglycemia and hyperinsulinaemia and eventually insulin resistance which are the precursor to diabetes development (18). Muscle weakness has been shown to be associated with increased risk of diabetes (OR 1.69, 95% CI 1.37 to 2.10). (19, 20) Muscle fat infiltration or myosteatosis may also alter glucose metabolism setting off insulin resistance and promoting the development of sarcopenia and diabetes (21). Chronic low grade inflammation is another link or contributing factor to the occurrence of chronic diseases associated with aging such as diabetes, sarcopenia and frailty (22). Diabetes and frailty have also been shown to share a common cardiovascular risk factors pathway suggesting a reciprocal relationship (23). Obesity is another factor associated with inflammation, oxidative stress and insulin resistance and may have a pathophysiological burden potentiating sarcopenia, frailty and diabetes. The term sarcopenic obesity has been used to describe sarcopenia plus increased visceral fat and has been shown to be associated with increased risk of atherosclerosis more than obesity alone. This suggests that sarcopenia combined with visceral obesity may have a synergistic effect increasing the risk of vascular complications and metabolic syndrome that lead to diabetes and frailty (24).

Figure 1
Frailty – Sarcopenia – Diabetes Inter-Relations



Sinclair AJ, Abdelhafiz AH, Rodriguez-Manas L. Frailty and sarcopenia – newly emerging and high impact complications of diabetes. J Diabetes Complications 2017; online: doi.org/10.1016/j.jdiacomp.2017.05.003

(25-27). Major contributing factors during the aging process include partial functional muscle denervation following by re-innervation of abandoned fibres, decreased maximal voluntary activation of the agonist muscles or changes in degree of agonist-antagonist co-activation (28), and the loss of spinal motor neurones leads to a decline in in the size and/or number of individual muscle fibres, especially of fast-twitch fibres. The consequences are related with an impaired mechanical muscle performance (i.e reduced maximal muscle strength, power) that can adversely affect the ability of an older person to remain functionally independent to perform daily activity tasks (29) (i.e. walking, stair walking, rising from a chair). Along with a decrease in muscle size, aging is also associated with a decrease in muscle quality as a consequence of increased amount of intramyocellular adipose tissue (i.e., muscle fat infiltration) and connective tissue (30, 31).

Sarcopenia is a hallmark sign of frailty syndrome, which results in loss of muscle strength, poor mobility and balance and, consequently, an increased risk of falls, adverse health outcomes, dependency, institutionalisation and death (32). Sarcopenia not only has been related with substantial reorganization in the neuromuscular system and the central nervous system, but also is associated with numerous factors, many of which are biological mechanisms contributory of aging, such as low-grade chronic inflammation (33), decline in mitochondrial function and biogenesis (34), reduced satellite cell numbers that impaired regenerative capacity, apoptosis activation and decline in hormones that are important in muscle mass maintenance (i.e. IGF-1, DHEA, testosterone and estrogens) (27, 29, 35).

Sections with Recommendations

Please note that the key references per domain of recommendations are provided online and the full set of recommendations that relate to the rationale, evidence base and implementation in routine clinical care of the International Position Statement are available at EDWPOP website (<http://edwpop.org>).

Assessment Processes for Frailty

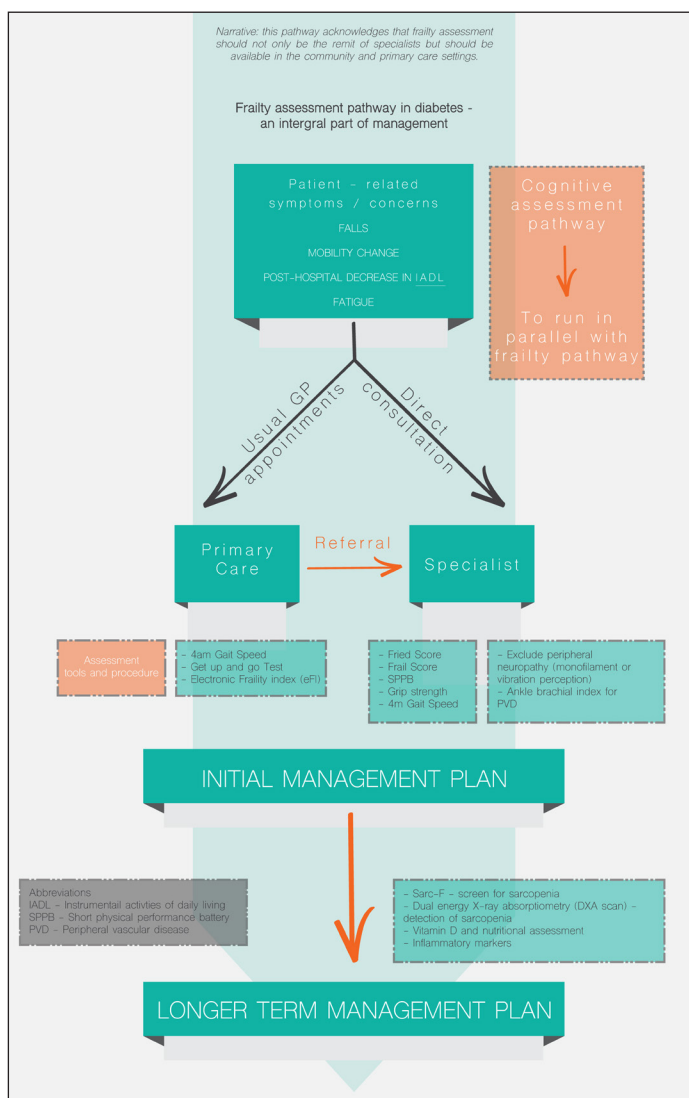
Narrative: Screening for geriatric syndromes including frailty should be part of stepped care approach in older people with diabetes particularly in primary and community care settings. Where there is evidence of physical or cognitive impairment, or functional loss, referral to geriatricians or other skilled clinicians for a comprehensive assessment is needed. (see Figure 2);

Muscle Changes in Frailty and Diabetes Mellitus

Aging is associated with declines in muscle function and cardiorespiratory fitness, resulting in an impaired capacity to perform daily activities and maintain independent functioning

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Figure 2
Frailty Assessment Pathway



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 tools* that fulfil the above criteria include the FRAIL score for frailty screening; the SARC-F for sarcopenia; the Rapid Cognitive screen (RCS) for cognitive impairment; and the simplified nutrition questionnaire (SNAQ).
- 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.

- Optimal Group nutrition plus resistance exercise classes should be prescribed as a continuing regular activity
- Management of diabetes should be individualized based on the presence/absence of these syndromes, using re-ablement and goal setting as targets in addition to blood parameters.

Glucose Regulation

Narrative: The overarching principle of management of glucose levels in frail older adults with diabetes is to aim for the best glycemic control that can be achieved without increasing the risk of hypoglycemia and without lowering their quality of life through additional treatment-burden effects (see Table 1, Figure 3).

Recommendations

- Prescribed glucose-lowering medications should have a low risk of hypoglycemia, minor side effects profile and be cost-effective .
- “Start low and go slow” when dosing and titrating medications in frail older adults.
- The glycemic goal should be individualized based on comorbid medical conditions in addition to cognitive and functional status. In mild to moderate frail older adults, an A1C target range of 7 – 8.0% (53 – 64 mmol/mol) is appropriate depending on self-care management abilities and presence of additional risk factors for hypoglycemia; in severe frailty, a HbA1c range of 7.5 – 8.5% (59 – 69 mmol/mol) is more protective.
- Many frail older adults have medical conditions that interfere with HbA1c 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 HbA1c targets.
- Metformin should be used as the first line of therapy due to its low risk of hypoglycemia, low cost, and good tolerability. In frail patients, weight loss and gastrointestinal side effects should be watched for carefully.
- DPP-4 inhibitors should be considered for those older adults requiring smaller post-prandial glucose lowering, or used in combination with basal insulin.
- GLP-1 agonists should be used for post-prandial glucose lowering. They have a low risk of hypoglycemia 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 hypoglycemia 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.

*refer to Morley JE and Adams EV (2010) for a description of the tools (online access)

- 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.
- Carers should receive basic education and training on hypoglycemia and its treatment

Exercise Intervention

Narrative: Along with pharmacological and dietary interventions, physical training including resistance and endurance training is required for effective benefits to be realised in the management of frailty in older adults with diabetes (see Figure 4 which is available online at: <http://www.jfrailtyaging.com/all-issues.html?article=609>).

Recommendations

- In addition to the beneficial effects of exercise interventions on glycemic 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 older 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 with diabetes should include the following :
 - Resistance-training programs 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.
 - To optimise the functional capacity of individuals, resistance training programs 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 optimize 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 program. The intensity should start between 40 and 50 % of HRmax and progress to 70–80 % of HRmax.
 - The Rate of Perceived Exertion (Borg) 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 programs should include gradual increases in the volume, intensity, and complexity of the exercises, along with the simultaneous performance of resistance, endurance, and balance exercises.

Management of Multimorbidities

Narrative: All frail older people with diabetes require a comprehensive assessment to include identifying all relevant co-morbidities including diabetes-related vascular complications.

Recommendations

- Screening for dementia and cognitive problems is recommended to implement safe and quality care and to provide support for carers.
- Targets for care for comorbidities should be established in each case and adapted according to the patient's health status: this should form part of an individualised care plan.
- The glycaemic goal should be individualised based on the presence or not of frailty and other comorbid medical conditions in addition to cognitive and functional status.
- In mild to moderate frail older adults, an A1C target range of 7 – 8.0% (53 – 64 mmol/mol) is appropriate depending on self-care management abilities and presence of additional risk factors for hypoglycemia; in severe frailty, a HbA1c range of 7.5 – 8.5% (59 – 69 mmol/mol) is more protective.
- Many frail older adults have medical conditions that interfere with HbA1c 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 HbA1c targets.
- Hypertension is commonly associated with type 2 diabetes and adds to the increased risk for cardiovascular disease. Therefore, screening and treating hypertension in older people with diabetes is essential.
- A target of 140/90 mmHg is reasonable but systolic blood pressure <140mmHg may be associated with adverse events. All major antihypertensive drug classes can be used to achieve the target.
- Dyslipidaemia often co-exists with diabetes and statin therapy is recommended in order to reduce cardiovascular risk unless specifically contraindicated.
- The addition of fibrate or niacin to statin therapy has no benefit and should not be considered for older people with diabetes.
- In those with a frequent history of urinary or chest infections, reduce infection risk by adjusting the HbA1c to be $\leq 8.5\%$ (≤ 69 mmol/mol).

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- Bladder control may be improved by aiming for a HbA1c of $\leq 8.5\%$ (≤ 69 mmol/mol) owing to the resulting decrease of polyuria linked to hyperglycemia
- Nutritional status and oral health should be assessed with the purpose to optimise nutrition and physical function
- The patient with both cancer and diabetes requires integrative care to lower the potential toxicities during cancer treatment and to continue to favor active treatment and outcomes.

Hypoglycemia Management

Narrative: Risk factors for hypoglycemia (defined as a state when blood glucose levels fall below 4 mmol/L (72mg/dL) are highly prevalent among older people with diabetes and carry both short term and longer term risks.

Recommendations

- Frail older people with diabetes should have their hypoglycemia risk regularly assessed.
- Educational programmes should be available to patients and their carers that suit their cognitive abilities.
- A care plan that includes an individualised optimum blood glucose range should be in place.
- Cognitive function and instrumental daily activities ability should be regularly checked especially in patients on insulin therapy.
- Blood glucose monitoring is useful in certain patients at risk of hypoglycemia such as those on insulin.
- A relaxed HbA1c target of 59-69 mmol/mol (7.5-8.5%) is appropriate in moderate to severe frailty.
- Hypoglycaemic medications with lower hypoglycaemic potential should be used if there are no contraindications.
- Simplification of insulin regimens from multiple to once daily basal insulin injection is recommended when feasible.
- Regular review and de-intensification of hypoglycaemic medications in patients with tight glycaemic control is recommended.
- Complete withdrawal of hypoglycaemic medications may be considered in patients with significant weight loss and recurrent hypoglycemia.
- Patients on end of life or palliative care will require an approach that focuses on comfort and symptom control.

Primary and Community Care

Narrative: Multidisciplinary care is required for optimal management of frail older people with diabetes in the community: this requires all those with direct care responsibilities learn the key assessment procedures for the early identification and diagnosis of frailty (see Figure 2).

Recommendations

- Care must be individualized in terms of setting appropriate glycaemic, blood pressure, and lipid targets and choice of medication.
- Older patients with both diabetes and frailty may have significant co-morbidities or reduced life expectancy that alters the risk–benefit balance of aggressive management of cardiovascular risk: optimal management of these co-morbidities and risks requires a broad range of health practitioner expertise and is ideally suited to a primary and community health environment
- Additional issues such as polypharmacy, mental illness, risk of falls, urinary incontinence, social isolation, persistent pain, and medication adherence all need to be considered as part of the management plan.
- Primary health practitioners are also best placed to advise and assist their patients in relation to those lifestyle behaviours most likely to prevent or delay the development of type 2 diabetes and/or frailty: this requires a public health perspective that includes attention to the social determinants of health and strong collaboration with public health and social services.
- Older people with diabetes in care homes are often frail and thus are highly vulnerable and require complex nursing and medical care in addition to assistance with personal hygiene.
- Risk factors for hypoglycemia are highly prevalent in residents of care homes.
- Maintaining health status and functional capacity, and eventually a dignified end of life using individualized care plans are key care goals for all residents with diabetes and frailty
- Where possible, primary and community care teams need to work with local care homes to ensure that each care home with diabetes residents should have an agreed Diabetes Care Policy or Protocol

Inpatient Care

Narrative: at any one time point, a large number of hospital beds are occupied by older people with diabetes and the presence of frailty increases the length of stay, and delays recovery. The majority of hospital admissions due diabetes are associated with emergencies such as hypoglycemia and the presence of frailty increases these risks.

Recommendations

- Random blood glucose level should be checked in all older patients acutely admitted to hospital to screen for undiagnosed cases.
- Diabetes status for older people with diabetes including diabetes-related complications and hypoglycaemic medications should be clearly documented in medical records on admission.
- Routine blood testing should include renal and liver functions along with blood glucose and HbA1c check.

Table 1
Glucose-lowering therapies in Frail Older Adults with Diabetes

	HbA1c reduction	Advantages	Disadvantages	Vignette in Frail Population
Metformin	1% (11 mmol/mol)	Low hypoglycemia 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 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 hypoglycemia Avoid glibenclamide (glyburide)	Avoid in patients with inconsistent eating pattern High risk of hypoglycemia during acute illness or weight loss Consider discontinuing if already receiving substantial amount of insulin (approximately >40 units/day)
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 hypoglycemia 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 edema, anemia Possible risk of bladder cancer, fractures	Good efficacy in older patients with high insulin resistance
DPP-4 inhibitors	0.5-0.8% (6-9 mmol/mol)	Low hypoglycemia risk Once a day oral medication Well tolerated Can be used in renal impairment but dose adjustment required (except linagliptin) No additional cardiovascular adverse effects	Medium / high cost	Can be combined with basal insulin for a low complexity regimen
SGLT-2 inhibitors	0.8-1.0% (9-11 mmol/mol)	Low hypoglycemia risk Reasonable efficacy Risk of other adverse effects moderate	High cost Limited experience in older population but evidence increasing	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
GLP-1 agonists	0.8-1.0% (9-11 mmol/mol)	Low hypoglycemia risk Once a day and once a week formulation New formulations available in combination with basal insulin	High cost Injectable	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)
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 hyperglycemia at different times of the day; can be used in renal impairment	High risk of hypoglycemia Need for matching carbohydrate content in patients with variable appetite when using prandial insulin Carer education and training needed if involved in administration	Use of basal insulin with other agents to lower post-prandial glucose can lower complexity and reduce the risk of hypoglycemia

Narrative: 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; Abbreviations: HbA1c: 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 glucose should be regularly monitored during hospital admission to help adjust hypoglycaemic therapy.
- Random blood glucose levels should be maintained above 6mmol (108 mg/dl) (to minimise hypoglycemia) but below 15 mmol/L (270 mg/dl) to avoid osmotic symptoms.
- Patients should have access to diabetes specialist multidisciplinary team assessment when needed.
- Hospitals should have clearly written medical guidelines for the treatment of diabetes-related emergencies such as diabetic ketoacidosis and hypoglycemia.
- A Hypoglycemia Treatment Kit should be available in each ward and staff should be familiar with its use.
- Patients who can self-administer their insulin should be encouraged with minimal supervision from the staff.
- The routine use of sliding scale insulin is not encouraged due to its complications and inconsistent messages.
- Patients should be well hydrated and their renal function checked before having any radiologic investigation that includes contrast injection.
- At discharge, patients should have clear documentations of any change of medications and future care plans smoothly communicated to primary care teams.

Educational Aspects for Health Professionals in Clinical Settings

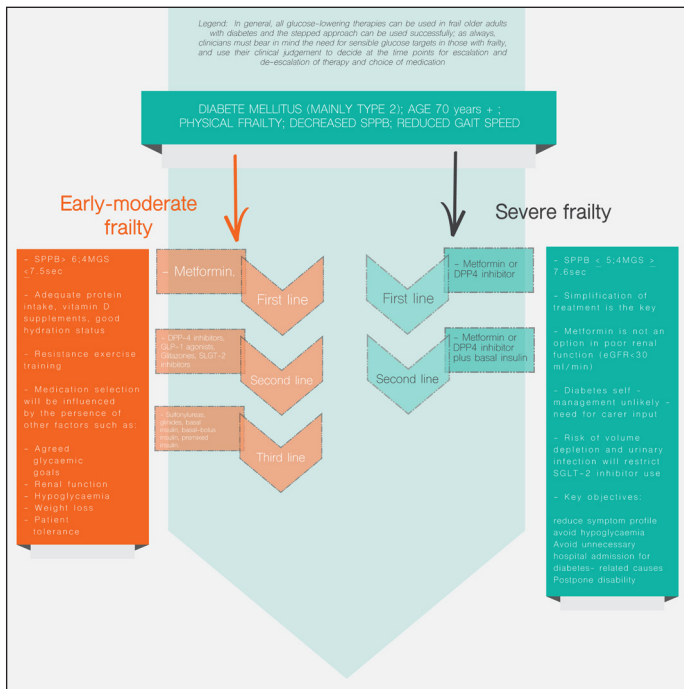
Narrative: The theoretical framework and associated clinical practice should be incorporated in frailty education programs in diabetes. A sound educational platform should form the basis of an integrated care system that provides continuity of care and interdisciplinary team care.

Recommendations for education providers

- Education programs should encompass reflection in and on practice, and use individual experiences to enhance learning.
- Health professionals involved in diabetes care should adopt positive proactive approaches to older age to help dispel ageist attitudes and stereotypes.
- Frail older people with diabetes should be engaged in education programmes for clinicians when possible and relevant. People’s stories are powerful teaching/learning tools.
- Traditional teaching and modern technology such as simulation, short podcasts, and online learning resources should be used to deliver frailty education e.g. Geriatric E-learning Modules (MiniGEMS,) Camden Education Module-frailty, and De Villiers Continuing Medical

Figure 3

Treatment Strategies for Frail Older Adults with type 2 Diabetes



Abbreviations: SPPB, Short Physical Performance Battery; 4 MGS - 4 metre gait speed Based on Sinclair AJ, Abdelhafiz A, Rodriguez Manans L (2017) (5)

Education Program

Recommendations for clinicians

- Clinicians should provide coordinated interdisciplinary team care.
- Clinicians should not use ageist language and stereotypes of older people. Older people are not a homogenous group. Obese and thin older people can be frail.
- Clinicians should provide frailty care within an holistic person-centred model of care and decide the care plan with the individual.
- Clinicians should commence screening older people with diabetes for pre-frailty and frailty before age 70.
- Clinicians should undertake frailty assessments during diabetes complication screening programs, when health status changes and before hospital admissions.
- Clinicians should undertake medicine reviews before prescribing new medicines and at regular intervals to determine whether any medicines or medicine combinations might contribute to frailty.
- Clinicians should include light to moderate resilience training to improve function and reduce falls risk soon after admission to hospital or aged care home.
- Clinicians should use self-administered questionnaires to complement physical assessments e.g. The Flourishing Scale.
- Clinicians should include frailty education in the individual’s diabetes education and care plan.
- Clinicians should tailor frailty education to suit older people

with diabetes health literacy/education level and their pre- and frailty risk, social situation and life expectancy.

- Clinicians should consult family carers; they can provide very useful information about the individual's social situation, functional changes and health status.

Recommendations for service providers

- Service providers should ensure clinicians have access to relevant technology to support optimal frailty care and education.
- Service providers should ensure guidelines, algorithms, policies and referral pathways are based on the best available evidence and are accessible.
- Service providers must ensure resources are available to support clinicians to deliver quality care and frailty education.
- Service providers should promote frailty education resources for older people with diabetes and their family carers that meet readability standards.

Research Directions

Narrative: Knowledge of many topics pertaining to the fields of frailty and diabetes show many gaps of knowledge - the role of insulin resistance, mechanisms of target organ damage, relationship between sarcopenia glucose metabolism and frailty, clinical targets in subpopulations, screening and diagnosis of frailty in older people with diabetes, usefulness of technology in the management of older frail people with diabetes, selection of drug regimes, usefulness of new drugs taking into account the therapeutic objectives in these patients, cost-effectiveness analysis, models of care: all raising many targets and opportunities for research.

Recommendations

- A multidisciplinary approach is required to produce effective worthwhile research: participants from basic science, pharmacologists, geriatricians, endocrinologists, nurses, health economists, physiotherapists, epidemiologists, and engineers.
- Basic science approaches need to examine the key underlying interrelationships: insulin resistance, endothelial dysfunction, low-grade pro-inflammatory activity, low testosterone levels, impairments in the bioenergetics response to exercise, the role of different signalling routes such as PGC1-alpha between both entities (diabetes and frailty).
- The development of aging models should be of help to study in depth some of these underlying mechanisms, and be used to raise hypotheses that fit clinical observations
- Clinical and epidemiological science should provide new knowledge on the components of frailty and diabetes that have prognostic value in terms of clinical outcomes, modulation of health trajectories, and survival

- The design and implementation of information and communication platforms to screen, early diagnose and manage patients with frailty and diabetes is needed; this will enable patients (and their families) to be empowered; validation of such platforms in real clinical settings is an important requirement
- The development of Randomised Clinical Trials, going beyond traditional outcome assessments is needed with a focus on changes in function (physical and cognitive), quality of life, use of resources, costs, and survival

All authors listed as part of the Expert Working Group have met full authorship criteria in this manuscript.

Full version, including rationale, evidence base and implementation in routine clinical care and associated citations for each set of recommendations of this International Position Statement is available at: <http://edwpop.org>

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