Canadian Geriatrics Society

LOOKING THROUGH THE LENS: REFLECTIONS ON MEDICINE, ETHICS, AND SOCIETY BY DR. MICHAEL GORDON

Book Review

Irene Turpie
Professor Emerita (Medicine and Geriatric Medicine), McMaster University

Corresponding Author:
Irene Turpie
turpiei@mcmaster.ca

This book is a must read for any Canadian geriatrician and for anyone interested in the development of health care for the elderly in Canada, as well as unique features of that care. It has vivid anecdotes of the author's early life and travels and is an anthology of historical reminiscences, clinical experiences, and reflections on medical ethical issues, particularly those affecting the health care of older adults with which the author is so familiar. Dr. Gordon is a well-known Canadian physician recognised globally for his expertise and eloquence and who, in addition to his medical skills, can write in an easy style understandable by all. Patients and families will also learn by reading the book.

He describes a journey that takes him from Michigan to a two-bedroomed apartment in Brooklyn, where he spent much of his childhood. The description is accompanied by his photographs, reflecting his early interest in using a camera. Like many geriatricians, he had a wise grandmother who shared her stories of her life in a Lithuanian village and of her early life in the United States.

His father took him and his sister to the local public library every Saturday morning. For years he was determined to study engineering, although he was also interested in English literature and writing. His parents were forward-thinkers for the mid-twentieth century and encouraged their son, who had completed high school in record time, to spend six months in Europe. On his European travels, he met some Danish medical students who inspired him to study medicine rather than engineering. This decision was confirmed by reading A.J. Cronin's The Citadel (Cronin was a Glasgow medical graduate who worked in the Welsh mining districts before the days of the British National Health Service and who described his experiences in that book).

Michael's parents encouraged him to study medicine in Europe. He chose to study in Dundee, Scotland, at St. Andrews University, where he had a traditional Scottish medical school upbringing which included lots of study, lectures, excellent teachers, and fish and chips fresh from the North Sea. He completed his internships in Aberdeen, describing well the misogynous and hierarchical learning provided to young doctors in that epoch in Scotland.

Key words:
book review,

After completing his medical studies in Scotland, he went for further studies in Israel, travelling overland in a small car through Europe to Tel Aviv Israel, where he studied obstetrics and gynecology, but where he also had a stint in the Israeli Air Force and in a hospital on the Arab Israeli border at a time of political unrest. He writes very movingly of his feelings working in that troubled area of the world. While he was in Israel, he had his first experience of Geriatric Medicine.

"*It was during this two-year residency that I became involved for the first time since medical school with geriatrics, as Shaare Zedek (in Jerusalem) had one of the first dedicated geriatric units in Israel. It was a remarkable experience and I witnessed outcomes that I had not seen in our general medical wards, and the idea of a truly multidisciplinary approach was taking shape. I also found much humour and good feeling among the staff and patients on the unit as we endeavored to improve the function and quality of life of older patients who had in many ways been dismissed as 'not likely to improve'.*"

He eventually came back to the U.S. but decided he was not going to be conscripted into a war in which he did not believe in. He came to Canada, first Montreal and then Toronto, where he began to develop his interest in the specialised care of the elderly, meeting Dr A. Rapoport.

"*I went to him (Dr. Abe Rapoport-TWH- Toronto) and after explaining what I wanted to do and how much I loved general internal medicine he asked me, 'Have you thought of geriatrics?' to which I responded, 'I did not know it was a recognized specialty in Canada.' He replied, 'No, it isn't, but there is a great institution called Baycrest' .....and the rest is history.*"

In 1981 he went on to become the first physician in Canada to obtain the specialist certification in Geriatric Medicine from the Royal College of Physicians and Surgeons and subsequently spent most of his professional life at the illustrious Baycrest Centre in Toronto.

The second and third parts of the book contain descriptions of interactions with patients, families, his work at Baycrest, and descriptions of his experiences and opinions after many years of practice. He then went back to university to obtain a degree in medical ethics, later focussing on this role as an ethicist in Toronto, both in teaching and practice. He writes about many of the issues that arose in that work. He discusses, as an example, the subject of evidence-based medicine and its relevance to the practice of Geriatric Medicine. The book also has many examples of issues which confront older adults, their families, and those caring for them in today's healthcare field.

His book is full of descriptions of his many interests, opinions, and travels, all of which make good, entertaining reading, and give insight and support to those of us who care for older patients in our everyday practice.

In summary, this is an interesting book, and I would encourage anyone with an interest in the health care of older adults to read it. Dr. Gordon supplies unique insights into what it was like to be a medical student and physician in the latter part of the 20th century and into the 21st century and all the myriad of changes that experience encompassed. He also describes his developing interest in Geriatric Medicine at a time when this speciality was in its infancy. His book provides anecdotes of travel and events that form a unique experience of medicine. It is well worth reading.

Canadian Geriatrics Society

PHARMACOLOGICAL MANAGEMENT OF INAPPROPRIATE SEXUAL BEHAVIOURS IN PATIENTS WITH DEMENTIA RESIDING IN LONG-TERM CARE: REVIEW OF THE EVIDENCE

April Kindrat
MD, CCFP
Care of the Elderly Fellow, Division of Geriatric Medicine, Providence Care Hospital, Queen's University, Kingston, Ontario

Christopher Frank
MD, FCFP
Associate Professor, Department of Medicine, Queen's University, Ontario; Clinical Lead, Specialized Geriatric Program and Attending in Palliative Care, Providence Care, Kingston, Ontario

Corresponding Author:
April Kindrat
draprilkindrat@gmail.com

Abstract

Inappropriate sexual behaviours (ISB) are an infrequent but challenging form of behavioural and psychological symptom of dementia (BPSD), particularly in the long-term care context, where shared living spaces put other residents at risk of assault. Behavioural interventions are recommended as first-line therapy, but often patients living in long-term care exhibiting ISB will require pharmacological therapy. To review the evidence for treating ISB pharmacologically within the long-term care context, a scoping review was performed. MEDLINE, EMBASE, and CINAHL were searched for literature related to dementia, long-term care, and sexual behaviour. Twenty-eight articles were included, reviewing antidepressants, antipsychotics, anticonvulsants, mood stabilizers, and hormonal agents. The available evidence is sparse, the bulk of which is from case reports of male patients. The use of any medication to treat ISB is off-label and not well studied, therefore caution should be used when initiating pharmacotherapy for this indication.

This article has been peer reviewed.

Conflict of Interest: None

This article was published in May 2023

Key words:
dementia, long-term care, inappropriate sexual behaviours

Key Points

When considering the management of inappropriate sexual behaviour (ISB) in patients with dementia residing in long-term care:

- Consider the context of the behaviour, as well as risk to staff and other residents
- Non-pharmacological behavioural interventions remain first-line, but pharmacological therapy is often necessary
- All medications used for ISB are employed off-label
- Medication classes used to treat ISB include antidepressants (SSRI, serotonin modulators, tricyclic antidepressants), antipsychotics (mostly atypical), anticonvulsants, mood stabilizers, and hormonal agents (including antiandrogens and estrogen)
- Consider dual indications for medications when deciding which agent to start

Introduction

According to the Canadian Institute for Health Information, 69% of residents in long-term care have a diagnosis of dementia. Of these individuals, 40% have severe cognitive impairment and 50% have behaviours and psychological symptoms of dementia (BPSD)[1]. Inappropriate sexual behaviour (ISB) is a particularly challenging form of BPSD. ISB presents a complex challenge for residents, their families, and staff in long-term care facilities, even though it is a less common presentation of BPSD. Unfortunately, the pharmacological management of ISB is poorly researched.

Reported frequency of ISB in those with dementia is variable, ranging from 1.8% to 25%, but is generally more common for males, in long-term care homes, and in those with severe dementia[2–4]. For vulnerable residents living in long-term care, ISB may result in high-risk situations for all involved. Many residents in long-term care may be unable to consent, refuse touch, call for help, or physically protect themselves from unwanted physical advances of their co-residents[5].

In considering the treatment of ISB, it may be helpful to consider its' potential pathophysiology. The causes of ISB are not well established. The frontal lobes, limbic system, hypothalamus, and striatum are often affected in major neurocognitive disorders and play a role in sexual drive and behaviour regulation[6,7]. The resident's previous personality characteristics and baseline need for intimacy combined with the confusion, disinhibition, and worsening judgement that often accompany major neurocognitive disorders can contribute[8]. One should always first consider acute and reversible causes with a new presentation of ISB, including delirium, medication side effect (particularly dopaminergic agents), mania, psychosis, substance use, and postictal confusion[8,9].

Most treatment approaches to ISB described in the literature appropriately start with non-pharmacological behavioural intervention. However, given the inability to constantly supervise residents living in shared spaces and the vulnerability of other residents with cognitive and functional impairments, many patients in long-term care are treated pharmacologically. There are no randomized controlled trials of medications for ISB. Instead, pharmacological agents with the side effect of reducing libido are used off-label to control ISB, including antidepressants, antipsychotics, antiseizure medications, and antiandrogens[4]. Most studies have been cohort or case studies. Given the limitations of the research, a scoping review was chosen to address this research question.

Methods

MEDLINE, EMBASE and CINAHL were used for this scoping review. All primary literature relevant to the three dimensions of interest for this topic (dementia, long-term care or institutionalized elsewhere, and inappropri-

ate sexual behaviour) were considered eligible. Each included article had to be published in or translated to English. No limitations were set for date of publication. A single reviewer performed a title screen, an abstract screen, then full text review.

Results

When generating the search terms, the decision was made to include "sex" as a key word. This greatly increased the number of articles generated from the search as it retrieved literature that stratified patients based on gender, rather than focusing on ISB. However, comparing the datasets with and without "sex" as a search term showed many articles that would have been missed by excluding this important variable. The search gathered a total of 4315 articles, 48 of which, based on title screen and/or abstract review, were potentially relevant to ISB and went on to full text review. Citations were pulled from a number of reviews and were included in the study if they met the pre-specified eligibility criteria. After full-text review, 28 articles were included in the following review. Results are summarized in Table 1.

Antidepressants

Antidepressants have been used to treat ISB due to their effects on libido and treatment of paraphilias[7]. Furthermore, they can be leveraged for a dual indication, such as irritability, depression, or apathy, common symptoms in dementia[10]. Most are generally considered safe or low risk in older adults[10]. From the studies collected, the most frequently used antidepressant was the selective serotonin reuptake inhibitor (SSRI) citalopram. Citalopram was reviewed in a case study of a single patient and a retrospective chart review with seven patients. In these eight cases, citalopram led to resolution of symptoms in one individual, a partial response in three, no response in three, and worsening of symptoms in one[5,7]. The patient who responded completely to citalopram was treated as monotherapy with resolution of behaviour[7]. The three patients that had a partial response were treated concurrently with olanzapine, risperidone, or a combination of olanzapine and medroxyprogesterone acetate (MPA)[5]. The only other SSRI studied was paroxetine, which lead to resolution of symptoms when used as monotherapy in two patients[11,12]. Other antidepressants used included the serotonin modulators mirtazapine and trazodone. In one patient, mirtazapine led to partial response when used in combination with citalopram and olanzapine. In another case, trazodone resulted in resolution of symptoms when used with risperidone and MPA[5,8]. Finally, clomipramine, an old tricyclic antidepressant, was used as monotherapy in two patients with resolution of symptoms[13]. It is worth noting that the studies using clomipramine and paroxetine were published in 1995 and 1997 respectively. The use of these medications in older adults have fallen out of favour due to their anticholinergic side effects and risk of delirium[10].

Antipsychotics

The use of antipsychotics in patients with dementia is generally not recommended due to the increased risk of mortality in this population, but they are often used with caution in patients with BPSD[10]. Antipsychotics have been postulated to be effective in reducing ISB due to their dopamine-blocking activity[14]. Aripiprazole was found to be effective in two cases studies, one female with Alzheimer's disease and one male with frontotemporal dementia[15,16]. A review of 10 patients looked at olanzapine, quetiapine, and risperidone alone or in combination with other medications in the management of ISB. Olanzapine was used in six patients in combination with other medications and found to be only partially effective. Of these cases, three patients used olanzapine with citalopram, one patient used it with both citalopram and mirtazapine, and another used olanzapine with citalopram and MPA[5]. Quetiapine was used as monotherapy in one patient, but failed to produce any response[5]. In the same study, risperidone was used for three patients, producing a partial response in only one patient when used in combination with citalopram[5]. In another case report, one patient responded favourably to risperidone in combination with trazodone and oral MPA therapy[8].

In the largest study found, risperidone and haloperidol were compared with respect to their efficacy in controlling BPSD in a double blind randomized cross-over study. The study involved 114 patients in long-term care with clinically significant BPSD on the Behavioural Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD) and Cohen-Mansfield Agitation Inventory (CMAI) scales. In this study, physical sexual advances were included as measured on the CMAI scale. The study did not report how many of the 114 patients had

ISB at baseline. At mean doses of risperidone 0.8mg and haloperidol 0.83mg, risperidone was found to be more effective in reducing physical sexual advances when compared to haloperidol. In this study, six patients stopped the trial due to somnolence (haloperidol), nausea (risperidone), and seizure (not felt to be drug related)[17].

Anticonvulsants

Gabapentin and carbamazepine have been used in cases of ISB, but the mechanisms are poorly understood. Gabapentin may result in decreased libido, erectile dysfunction, and difficulty with orgasm [4]. Carbamazepine has been shown to reduce testosterone levels in women[4]. However, side effects of these medications include dizziness, drowsiness, ataxia, confusion, and falls which are problematic in older adults[18,19]. In case reports, gabapentin was used in one patient who failed to respond to citalopram for ISB. In this case, there was improvement in ISB after four weeks of monotherapy[20]. Two other case reports found efficacy with low dose gabapentin. In one case, it was used in conjunction with quetiapine, which was eventually weaned and discontinued[21]. In another case report, carbamazepine was used in a patient who failed to respond to paroxetine. After achieving a therapeutic serum concentration, the ISB resolved[22].

Mood stabilizers

Mood stabilizers were rarely encountered in this scoping review. However, one case study used lithium in an older patient with a history of bipolar disorder with mania. In this case, lithium was used in combination with olanzapine. Treatment resulted in a partial response[5].

Hormonal therapy

The highest number of studies collected in this review examined hormonal therapy for control of ISB. In total, 11 studies were reviewed examining 43 patients. Pharmacologic management with medroxyprogesterone acetate (MPA), cyproterone acetate (CPA), leuprolide, and estrogen are theoretically effective for ISB as they reduce levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) at the level of the pituitary, ultimately decreasing the serum testosterone level[4,14]. Finasteride is an alpha-5-reductase inhibitor that blocks the peripheral conversion of testosterone to dihydrotestosterone. While often used to treat benign prostate hyperplasia, the hormonal side effects commonly result in erectile dysfunction and decreased libido[23]. However, hormonal agents have significant side effects involving most major body systems. These are detailed below.

Medroxyprogesterone acetate

Medroxyprogesterone acetate (MPA) can be given orally or intramuscularly. The use of MPA should be avoided in patients with active or previous thromboembolic disease, including deep vein thrombosis, pulmonary embolism, myocardial infarction, stroke, and retinal vascular disease. MPA may also exacerbate hormone dependent cancers, including prostate cancers. Other side effects include osteoporosis, liver disease, adrenal suppression, depression, edema, diabetes, weight loss or gain[24]. Several case reports have shown MPA to be effective in ISB as monotherapy or in combination therapy[5,25–28]. Only one case used oral MPA, which was successful in controlling ISB when used with trazodone and risperidone[8]. The remaining studies used intramuscular MPA.

One case report described a patient who required admission to geriatric inpatient care for troublesome ISB, including sexual assault and sexual advances towards young family members. The patient had been previously treated with benzodiazepines, antipsychotics, antidepressants, and anticonvulsants with poor control of his symptoms. Once titrated to an effective dose, intramuscular MPA produced and maintained control of his ISB to the point where he could be discharged and maintained in the community[26]. Another case report described a male patient who received MPA after failing thioridazine. His behaviours resolved and he was successfully weaned off his antipsychotic[27]. Another male had failed combination therapy with antipsychotics, antidepressants, and mood stabilizers for his ISB, although the details of these therapies were not provided. He was then started on MPA and his ISB resolved within 10 injections[28].

Another case series described five patients living in either long-term care or a geriatric inpatient unit receiving MPA intramuscularly. All patients had been treated with antidepressants, antipsychotics, anticonvulsants, and/or anxiolytics for their ISB first and failed to respond adequately. In all cases, the ISB resolved once the dose of MPA was properly titrated[25]. Finally, Bardell et al reviewed five patients receiving MPA, either alone or in combination with either citalopram, olanzapine, or leuprolide. All five patients had partial response to the therapy[5].

Of note, the above was the only case in which leuprolide was encountered in this review. Leuprolide is a gonadotrophin-releasing hormone agonist, which is typically used in the management of certain hormone sensitive cancers, but is also used for males with problematic paraphilias. Leuprolide may result in thromboembolic events, prolong QT, seizures, pituitary apoplexy, and mania. It should be used cautiously and with close monitoring[29].

Cyproterone acetate

Cyproterone acetate (CPA) is a synthetic progesterone derivative with risks similar to those of MPA. The use of CPA should be avoided in patients with active or previous thromboembolic disease. Furthermore, there is a black box warning in Canada due to its' hepatoxicity[30]. One paper reviewed the use of CPA in two male patients admitted to a geriatric inpatient unit for difficult to control ISB. The first patient had a history of bipolar disorder which was managed with valproate, olanzapine, lithium, lorazepam, and L-DOPA. The authors noted that mania was not felt to be contributing to ISB, but did not mention the possible role of L-DOPA in exacerbating ISB. The patient was started on CPA with resolution of his ISB within a few days. The second patient had ISB despite trials of valproate, mirtazapine, and risperidone. He experienced resolution of his ISB within a few days of starting CPA[31].

Estrogen

Estrogen has been used in men and women to try to decrease aggression and ISB, in the forms of conjugated estrogen and diethylstilbestrol. The use of conjugated estrogen is associated with venous thromboembolic disease, dyslipidemia, breast cancer, as well as endometrial hyperplasia when used without progesterone in women with a uterus[32]. Diethylstilbestrol is no longer routinely prescribed. Conjugated estrogen was used in a 4-week randomized double blind placebo-controlled study with 14 participants. Eight of the patients received conjugated estrogen therapy titrating up to a dose of 2.5mg daily over the course of four weeks. When compared to the placebo group, there was no significant improvement in sexually aggressive behaviours, but total aggression scores were significantly lower in the estrogen group[33]. A case study reviewed a patient who was started on conjugated estrogen after failing haloperidol, risperidone, and lorazepam for ISB. With therapy, sexual aggression improved 80%, and sexual comments improved 55% as per staff observation, nursing reports, and progress notes[34]. Finally, a patient was treated with diethylstilbestrol as monotherapy with resolution of his ISB[35].

Finasteride

One study reviewed 11 male patients with known benign prostatic hyperplasia and vascular dementia with ISB. All patients were treated with finasteride for 12 weeks. In 6 of these patients, ISB resolved within 8 weeks. The other 5 patients required combination therapy: one with propranolol, two with propranolol and quetiapine, one with oxycarbamazepine, and one required gonadotropin-releasing hormone agonist for intractable ISB[36]. The mechanisms by which antipsychotics and anticonvulsants control ISB were discussed previously. Beta-blockers are thought to decrease libido by blunting adrenergic drive[4].

Antihistamines

Cimetidine is an antihistamine that has been shown to have non-hormonal antiandrogen activity, however it is not favoured in older adults due to its relatively high anticholinergic burden and subsequent risk of delirium[37]. Two studies reviewed cimetidine. One case report reviewed a patient who had resolution of ISB with cimetidine after failing to respond to memantine[3]. The other study was a retrospective chart review that found a subset of 20 patients with dementia and ISB treated with non-hormonal antiandrogen therapies, in-

cluding cimetidine, ketoconazole, and spironolactone. Patients were given cimetidine initially as monotherapy and increased to either an effective dose or the point of adverse effects (nausea, arthralgia, and headache). Fourteen of 20 patients responded to cimetidine alone. The remaining six patients required ketoconazole and/or spironolactone with resolution of their ISB[37]. While ketoconazole is an antifungal and spironolactone is a potassium-sparing diuretic, they both have non-hormonal antiandrogen activity which may decrease libido. No other details were given about those six patients.

Cholinesterase inhibitors

Cholinesterase inhibitors are often used in the management of BPSD, in addition to their function for cognitive stabilization in those with major neurocognitive disorder[14]. However, they have not been shown to be effective in managing ISB within the long-term care context. Moreover, there are a handful of case reports attributing onset of ISB with initiation of cholinesterase inhibitors as these medications can be stimulating.

Discussion

There have been several reviews published on the pharmacological treatment of ISB in dementia[4, 14, 23], but this is the first review of this topic in the context of patients living in long-term care. It is important to focus on this context due to safety concerns for other residents sharing accommodations who may be more vulnerable to assault due to their own cognitive and functional impairments. Unfortunately, the evidence supporting pharmacological management of ISB is sparse and of very poor quality.

If it has been determined that ISB is high-risk, and not responding to behavioural interventions, then a pharmacological approach can be tried. As demonstrated in this review, the evidence for pharmacotherapy is weak. With this understanding, it would be reasonable to choose an antidepressant as first-line therapy for ISB. Sertraline, citalopram, or escitalopram are excellent options given their safety profile in older adults with cognitive impairment. Another reasonable first or second-line agent for men with symptomatic BPH would be an alpha-5-reductase inhibitor, such as finasteride or dutasteride. Gabapentin could be considered as a second-line agent, particularly at low doses of 100mg twice or three times daily. However, this should be done with caution as gabapentin can cause dizziness, drowsiness, ataxia, confusion, and falls, particularly when used in combination with other sedating medications, such as opioids. Furthermore, there may be a role for cimetidine as a second-line agent, but this medication should be used with caution as it is known to have anticholinergic side effects which can cause delirium.

These suggested therapies can take several weeks to become effective, which may not be a suitable timeline in more urgent cases. If a response is required within a few days, antipsychotic medications may have a role. Risperidone, olanzapine, or aripiprazole would be reasonable options if QTc is not prolonged. If this is the case, consider initiating combination therapy with one of the safer, first or second-line therapies and use the antipsychotic as a temporary bridge. If using antipsychotic medications, caregivers should be advised of the risks and asked for consent which should be documented in the patient's record. If the ISB stabilizes, attempt to deprescribe the antipsychotic within a few months. Finally, consider an antiandrogen such as MPA, CPA, or leuprolide in refractory cases. Given the numerous dangerous side effects of these medications, this should be done in consultation with geriatric psychiatry to ensure safer medications have been appropriately considered and tried first. Other review articles studying community dwelling patients reported cases of improvement with rivastigmine, quetiapine, leuprorelin, propranolol and pindolol[4,14,23]. Studies of these medications were not found in this review of ISB in long-term care homes, but may be of value in treatment of ISB.

Given the off-label use of all these medications in the treatment of ISB, we suggest a thorough discussion of the risks and benefits with the substitute decision maker and clear documentation of that process. Considering patient comorbidities and potential secondary indications of medications (agitation, depression, benign prostatic hyperplasia) can help guide therapy. As always, part of good prescribing is deprescribing. If a medication is not effective in controlling the symptom after a reasonable trial, then it should be weaned and discontinued.

Table 1. Evidence for pharmacological management of inappropriate sexual behaviours in patients with dementia residing in long-term care.

Medication Class	Medication & Dose	Study & Patient Details	Response
Antidepressants	Citalopram 10 – 40mg once daily[5,7]	Case report, 1 male, AD	Resolution
		Retrospective chart review 6 males, 1 female AD (3), VaD (2), mixed (2)	Partial (4) None (3) Worsening (1)
	Clomipramine 150 – 200mg once daily [13]	Case report, 2 males, AD	Resolution
	Mirtazapine 15 – 30mg once daily[5]	Retrospective chart review 1 male, VaD	Partial
	Paroxetine 20mg – 40mg once daily[11,12]	Case report, 1 male Alcohol related dementia	Resolution
		Case report, 1 male, FTD	Resolution
	Trazodone 100mg once daily[8]	Case report, 1 male, AD	Resolution
Antipsychotics	Aripiprazole 2.5 – 18mg once daily[15,16]	Case report, 1 female, AD	Resolution
		Case report, 1 male, FTD	Resolution
	Olanzapine 2.5 – 15mg once daily[5]	Retrospective chart review 5 males, 1 female AD (2), VaD (2), mixed (2)	Partial (6)
	Risperidone 0.5mg – 2mg[5,8]	Case report, 1 male, AD	Resolution
		Retrospective chart review 3 males, AD (1), VaD (2)	Partial (1) None (1) Worse (1)
	Risperidone 0.5 – 1.5mg or Haloperidol 0.5 –1.5mg per day[17] (dosing interval not reported)	Randomized double blind cross over study, n = 114 AD (79), VaD (34), mixed (7)	Risperidone was "significantly more effective in treating physical sexual advances"
	Quetiapine 12.5 –150mg[5]	Retrospective chart review 1 male, VaD	None
Anticonvulsants	Gabapentin 100mg BID, 200mg BID, or 300mg TID[20,21]	Case report, 3 males NPH (1), VaD (2)	Resolution
	Carbamazepine 800mg per day[22] (dosing interval not reported)	Case report, 1 male, FTD	Resolution
Mood stabilizer	Lithium 300 – 600mg[5] once daily	Case report, 1 male VaD with history of bipolar disorder	Partial resolution

AD = Alzheimer's disease, VaD = Vascular dementia, FTD = frontotemporal dementia, NPH = normal pressure hydrocephalus

MPA = medroxyprogesterone acetate, CPA = cyproterone acetate

Medication Class	Medication & Dose	Study & Patient Details	Response
Hormonal agents	MPA 5mg orally once daily[8]	Case report, 1 male, AD	Resolution
	MPA 100mg IM once monthly to 500mg IM once weekly[5,25–28]	Case report, 1 male, AD	Resolution
		Case report, 1 male, AD	Resolution
		Case report, 1 male, FTD	Resolution
		Case report, 5 males, AD (1), VaD (2), mixed (1), unspecified (1)	Resolution
		Case report, 5 males, AD (1), VaD (3), mixed (1)	Partial
	CPA 10mg orally once daily[31]	Case report, 2 males, VaD (1) Parkinson's dementia (1)	Resolution
	Conjugated estrogen 0.625mg – 2.5mg once daily[33,34]	Randomized double blind placebo-controlled study, n = 14, Dementia subtypes not reported	No significant improved in sexually aggressive behaviours
		Case report, 1 male, VaD	Partial
	Diethylstilbestrol 1mg once to twice daily [35]	Case report, 1 male, AD	Resolution
	Finasteride 5mg once daily[36]	Case report, 11 males, VaD (11)	Resolution (6) Partial (5)
Antihistamine	Cimetidine 400 –1600mg per day[3,37] (dosing interval not reported)	Case report, 1 male, VaD	Resolution
		Retrospective chart review 17 males, 3 female, dementia subtype not specified	Resolution (14) Partial (6)
Antifungals	Ketoconazole 100 – 200mg once daily[37]	Retrospective chart review 6 of 20 patients received ketoconazole and/or spironolactone in addition to cimetidine No other details reported	Resolution

AD = Alzheimer's disease, VaD = Vascular dementia, FTD = frontotemporal dementia, NPH = normal pressure hydrocephalus

MPA = medroxyprogesterone acetate, CPA = cyproterone acetate

References

1. Canadian Institute for Health Information. Dementia in long-term care. Accessed December 13, 2022. https://www.cihi.ca/en/dementia-in-canada/dementia-care-across-the-health-system/dementia-in-long-term-care

2. Alagiakrishnan K, Lim D, Brahim A, et al. Sexually inappropriate behaviour in demented elderly people. *Postgrad Med J*. 2005;81:463-466.

3. Beri, A., Smith, A. Cimetidine treatment of sexually inappropriate behavior in dementia: A case report and literature review. *Ann Long-Term Care*. 2015;23(6):39-42.

4. De Giorgi R, Series H. Treatment of Inappropriate Sexual Behavior in Dementia. *Curr Treat Options Neurol*. 2016;18(9):41. https://link.springer.com/article/10.1007/s11940-016-0425-2

5. Bardell, A., Lau, T., Fedoroff, J. P. Inappropriate sexual behavior in a geriatric population. *Int Psychogeriatr*. 2011;23(S1):1182-1188.

6. Canevelli, M., Talarico, G., Tosto, G., Troili, F., Lenzi, G.L., Bruno G. Rivastigmine in the treatment of hypersexuality in alzheimer disease. *Alzheimer Dis Assoc Disord*. 2013;27(3):287-288.

7. Tosto, G., Talarico, G., Lenzi, G. L., Bruno, G. Effect of citalopram in treating hypersexuality in an Alzheimer's Disease case. *Neurol Sci*. 2008;29(4):269-270.

8. Kuhn, D. R., Greiner, D., Arseneau, L. Addressing hypersexuality in Alzheimer's disease. *J Gerontol Nurs*. 1998;24(4):44-50.

9. Alkhalil C, Tanvir F, Alkhalil B, Lowenthal DT. Treatment of Sexual Disinhibition in Dementia: Case Reports and Review of the Literature. *Am J Ther*. 2004;11(3):231-235.

10. McKeith I, Cummings J. Behavioural changes and psychological symptoms in dementia disorders. *Lancet Neurol*. 2005;4(11):735-742.

11. Jazi AN, Shebak SS, Kim KY. Treatment of Hypersexuality in an Elderly Patient With Frontotemporal Dementia in a Long-Term Care Setting. *Prim Care Companion CNS Disord*. 2017;19(3).

12. Stewart JT, Shin KJ. Paroxetine treatment of sexual disinhibition in dementia. *Am J Psychiatry*. 1997;154:1474.

13. Leo RJ, Kim KY. Clomipramine Treatment of Paraphilias in Elderly Demented Patients. *J Geriatr Psychiatry Neurol*. 1995;8:123-124.

14. De Sousa A, Lodha P. Sexual issues in dementia: An overview. *Telangana J Psychiatry*. 2019;5(1):7-11. https://www.researchgate.net/publication/333803918_Sexual_issues_in_dementia_An_overview

15. Sarikaya, S., Sarikaya, B. Aripiprazole for the Treatment of Inappropriate Sexual Behavior: Case Report of an Alzheimer's Disease Patient Known as Heterosexual with Recently Shifted Sexual Orientation to Same Gender. *J Alzheimers Dis Rep*. 2018;2(1):117-121.

16. Nomoto H, Matsubara Y, Ichimiya Y, Arai H. A case of frontotemporal dementia with sexual disinhibition controlled by aripiprazole. *Psychogeriatrics*. 2017;17(6):509-510.

17. Suh, G., Greenspan, A. J., Choi, S. Comparative efficacy of risperidone versus haloperidol on behavioural and psychological symptoms of dementia. *Int J Geriatr Psychiatry*. 2006;21(7):654-660.

18. Gabapentin: Drug information. Accessed February 3, 2023. https://www.uptodate.com/contents/gabapentin-drug-information?search=gabapentin&selectedTitle=1~146&usage_type=panel&display_rank=1&kp_tab=drug_general&source=panel_search_result

19. Carbamazepine: Drug information. https://www.uptodate.com/contents/carbamazepine-drug-information?sectionName=Adult&anchor=F145593&source=auto_suggest&selectedTitle=1~1---2~4---carbama&showDrugLabel=true&search=carbamazepine#

20. Mufti, M. A., Schneider S., Solberg, L. M. Inappropriate sexual behaviors in dementia treated with gabapentin. *J Am Geriatr Soc*. 2019;67(Supplement 1):S111.

21. Cooney, C., Murphy, S., Tessema, H., Freyne, A. Use of low-dose gabapentin for aggressive behavior in vascular and Mixed Vascular/Alzheimer Dementia. *J Neuropsychiatry Clin Neurosci*. 2013;25(2):120-125.

22. Poetter CE, Stewart JT. Treatment of Indiscriminate, Inappropriate Sexual Behavior in Frontotemporal Dementia With Carbamazepine. *J Clin Psychopharmacol*. 2012;32(1):137-138.

23. Joller P, Gupta N, Seitz DP, Frank C, Gibson M, Gill SS. Approach to inappropriate sexual behaviour in people with dementia. *Can Fam Physician*. 2013;59:255-260. https://www.cfp.ca/content/cfp/59/3/255.full.pdf

24. Medroxyprogesterone acetate: Drug information. Accessed February 3, 2023. https://www.uptodate.com/contents/medroxyprogesterone-acetate-drug-information?search=medroxyprogesterone%20ace-tate&source=panel_search_result&selectedTitle=1~148&usage_type=panel&kp_tab=drug_general&display_rank=1

25. Light, S. A., Holroyd, S. The use of medroxyprogesterone acetate for the treatment of sexually inappropriate behaviour in patients with dementia. *J Psychiatry Neurosci*. 2006;31(2):132-134.

26. Amadeo M. Antiandrogen Treatment of Aggressivity in Men Suffering from Dementia. *J Geriatr Psychiatry Neurol*. 1996;9:142-145.

27. Weiner M, Denke M, Williams K, Guzman R. Intramuscular Medroxyprogesterone Acetate for Sexual Aggression in Elderly Men. *The Lancet*. 1992;339(8801):1121.

28. Balasubramaniam, M., Jensen, T. P., Alici Y. Successful treatment of inappropriate sexual behavior in fronto-temporal dementia with MPA: A case report. *Am J Geriatr Psychiatry*. 2013;21(1, S3):S92-S93.

29. Leuprolide: Drug information - UpToDate. Accessed February 3, 2023. https://www.uptodate.com/contents/leuprolide-drug-information?search=leuprolide&source=panel_search_result&selectedTitle=1~74&usage_type=panel&kp_tab=drug_general&display_rank=1#references

30. Cyproterone (United States: Not available): Drug information. Accessed February 3, 2023. https://www.uptodate.com/contents/cyproterone-united-states-not-available-drug-information?source=auto_suggest&selectedTitle=1~2---1~2---cyproteron&search=cyproterone

31. Haussermann P, Goecker D, Beier K, Schroeder S. Low-Dose Cyproterone Acetate Treatment of Sexual Acting Out in Men With Dementia. *Int Psychogeriatr*. 2003;15(2):181-186.

32. Conjugated equine estrogens (systemic): Drug information. Accessed February 3, 2023. https://www.uptodate.com/contents/conjugated-equine-estrogens-systemic-drug-information?search=conjugated%20estrogens&selectedTitle=1~78&usage_type=panel&display_rank=1&kp_tab=drug_general&source=panel_search_result

33. Kyomen HH, Satlin A, Hennen J, Wei JY. Estrogen Therapy and Aggressive Behavior in Elderly Patients With Moderate-to-Severe Dementia: Results From a Short-Term, Randomized, Double-Blind Trial. *Am J Geriatr Psychiatry*. 1999;7(4):339-348.

34. Shelton, P. S., Brooks, V. G. Estrogen for dementia-related aggression in elderly men. *Ann Pharmacother*. 1999;33:808-812.

35. Kyomen HH, Nobel KW, Wei JY. The Use of Estrogen to Decrease Aggressive Physical Behavior in Elderly Men with Dementia. *J Am Geriatr Soc*. 1991;39(11):1110-1112.

36. Na HR, Lee JW, Park SM, Ko SB, Kim SY, Cho ST. Inappropriate Sexual Behaviors in Patients with Vascular Dementia: Possible Response to Finasteride. *J Am Geriatr Soc*. 2009;57(11):2161-2162.

37. Wiseman SV, McAuley JW, Freidenberg GR, Freidenberg DO. Hypersexuality in patients with dementia: Possible response to cimetidine. *Neurology*. 2000;54(10):2024.

Canadian Geriatrics Society

DIABETES MANAGEMENT IN OLDER ADULTS WITH A SPECIAL FOCUS ON SODIUM GLUCOSE COTRANSPORTER 2 INHIBITORS (SGLT2is)

Abstract

Treatment of type 2 diabetes mellitus (T2DM) should be individualized, particularly in older adults who may be frail, functionally dependent, cognitively impaired, or have a short life expectancy. Frail older adults are more vulnerable to hypoglycemia and are more likely to suffer from hypoglycemia-related adverse effects. As such, a more flexible HbA1c target may be necessary, as aggressive glycemic control in older adults may lead to net harm. Newer clinical practice guidelines now recommend use of sodium glucose cotransporter 2 inhibitors (SGLT2is) in patients without diabetes due to proven cardiorenal benefits. What does this mean for the frail older adult? In this article we acknowledge the benefits of the newer oral antihyperglycemic agents with particular focus on the SGLT2i and potential harms associated with SGLT2i use with a hypothetical but plausible case presentation.

Kara Hawker
MD
Internal Medicine Resident (PGY2), Department of Medicine, University of Ottawa, ON

Ripa Akter
MD, FRCPC
Department of Medicine, University of Ottawa; Division of Geriatric Medicine, The Ottawa Hospital; Ottawa Hospital Research Institute

Corresponding Author:
Dr. Ripa Akter
rakter@toh.ca

This article has been peer reviewed.

Conflict of Interest: None

This article was published in May 2023.

Key words:
Diabetes, older adults, polypharmacy

KEY POINTS

1. Newer agents, such as GLP1-RAs, DPP4is, and SGLT2is, are effective, safe, and tolerable in older persons and can be considered for use in older patients.

2. SGLT2is should be considered for use in older patients with cardiovascular and/or renal disease, however, caution and close follow-up should be practiced in frail older adults, especially those with history of falls, orthostatic hypotension, malnutrition, and weight loss.

3. Antihyperglycemic agents with high risk of hypoglycemia should be avoided in older persons.

4. Addition and/or substitution of different antihyperglycemic agents depends on the older patient's functional status, comorbidities, current medications, and risks and benefits of the side effects associated with that drug – an individualized approach that will vary for each older patient.

CASE

Mrs. X is an 80-year-old single female who lives alone in an apartment with minimal social supports. She receives home care supports for bathing, otherwise she is independent for all other basic activities of daily living. Her close friend is her power of attorney who assists with finances and transportation. She manages her medications independently, however, she finds this task overwhelming. She has a history of mild dementia on donepezil, hypertension, myocardial infarction (MI), heart failure with reduced ejection fraction (HFrEF) on furosemide, bisoprolol, and perindopril, dyslipidemia on atorvastatin, T2DM with hemoglobin A1c (HbA1c) level of 7.0% on canagliflozin and saxagliptin. She had two falls in the past year related to orthostatic hypotension and mobilizes with a walker. She has also lost interest in cooking, relying on simple pre-cooked meals. She has lost 15 pounds in the past year. She presented to the hospital with acute cholecystitis and underwent an urgent, uncomplicated cholecystectomy. Post-operatively, she developed euglycemic diabetic ketoacidosis (DKA). She has no previous history of hyperglycemic emergency.

INTRODUCTION

People with T2DM form a heterogenous group, therefore, therapeutic regimens and targets should be individualized, especially in older patients with dementia, functional dependency, and frailty.[1] Numerous factors predispose older adults to hypoglycemia, one of the most feared complications in this group, including isolation, erratic appetite, skipped meals, undernutrition, polypharmacy that favors drug-drug interactions, declining renal function that increases drug levels, and more frequent intercurrent illnesses.[2] One benefit of the newer antihyperglycemic agents highlighted in the updated Diabetes Canada Clinical Practice Guidelines (CPG) is their negligible to low risk of hypoglycemia. Furthermore, some agents have proven benefit in patients with cardiovascular (CV) comorbidities. Theoretically, these agents would be preferred for the older population, as they have improved the ability to cope with the risk of hypoglycemia and CV events, the two most important drawbacks in treating older people with diabetes.[3] Unfortunately, clinical trials examining the efficacy and safety of these drugs often fail to include older adults, especially those with limited life expectancy and/or frailty.

This article aims to review the benefits, efficacy, safety, and tolerability of SGLT2i use with a specific focus on their applicability to older adults, as compared to other new agents including the glucagon-like peptide-1 receptor agonists (GLP1-RA), and dipeptidyl peptidase 4 inhibitors (DPP4is).

REVIEW OF AVAILABLE ORAL ANTIHYPERGLYCEMICS

The Diabetes Canada CPG outlines an approach to prescribing antihyperglycemic therapy in patients with diabetes and reviews the currently available oral antihyperglycemic agents, available at: Diabetes Canada | Clinical Practice Guidelines - Chapter 13: Pharmacologic Glycemic Management of Type 2 Diabetes in Adults: 2020 Update. Table 1, adapted from the Diabetes Canada CPG[4] and Koufakis et al.[5], outlines the advantages and disadvantages of these agents in older adults specifically.

Table 1. Advantages and disadvantages of antihyperglycemic agents in older patients

Class and mechanism of action	Name of drug	Advantages in older adults	Disadvantages in older adults
Biguanide: Enhances liver and peripheral insulin sensitivity, reduces gluconeogenesis, excreted by urine	Metformin	Low risk of hypoglycemia Possible anti-aging effects[6]	No randomized trials in older patients Increased probability of GI adverse events and lactic acidosis[5] Frequent monitoring of renal function[5] Increased risk of vitamin B12 deficiency which can predispose to falls
Thiazolidinedione: Enhances liver and peripheral insulin sensitivity	Rosiglitazone Pioglitazone	Low risk of hypoglycemia	Increased incidence of edema and HF[7] Increased risk of HF, acute MI, and mortality with rosiglitazone[7] Increased risk of bone fractures in females[8]
Insulin secretagogue: Stimulates endogenous insulin production	Sulfonylureas: Gliclazide Glyburide Glimepiride Meglitinides: Repaglinide	Strong hypoglycemic effect	High risk of hypoglycemia Increased mortality risk has been reported[9] Debatable CV safety[5]
Alpha-glucosidase inhibitor: Inhibits pancreatic alpha-amylase and intestinal alpha-glucosidase	Acarbose	Modest efficacy Relatively safe	Lack of studies in older patients No studies with outcomes that show a protection against diabetic complications[2] Increased probability of GI adverse events[2]
Incretin: Increases glucose-dependent insulin release, slows gastric emptying, inhibits glucagon release	GLP1-RA: Exenatide Lixisenatide Dulaglutide Liraglutide Semaglutide	GLP1-RA: Low risk of hypoglycemia Cardiorenal benefits Potential to improve neurological outcomes[10-11] Weekly administration available	Mostly injectable therapies Increased probability of GI adverse events[5] Potential to induce significant weight loss High cost
	DPP4i: Alogliptin Linagliptin Saxagliptin Sitagliptin	DPP4i: RCTs demonstrate efficacy and safety in elderly CV and renal safety Improved sarcopenic parameters[12] Good tolerability	Increased risk of bullous pemphigoid[13-14] Risk of pancreatitis and pancreatic cancer debatable[15] Specific agents contraindicated in HF
Sodium glucose cotransporter 2 inhibitor: Reduces renal glucose reabsorption causing increased glucosuria	Canagliflozin Empagliflozin Dapagliflozin	Phase III studies show safety in elderly[16] Low risk of hypoglycemia Cardiorenal benefits	Concerns regarding increased risk of euglycemic DKA, genitourinary infections, dehydration, and fractures High cost

Abbreviations: GI: gastrointestinal; HF: heart failure; MI: myocardial infarction; RCTs: randomized controlled trials; CV: cardiovascular; GLP1-RA: glucagon-like peptide-1 receptor agonists; DPP4i: dipeptidyl peptidase 4 inhibitors; DKA: diabetic ketoacidosis.

CURRENT MANAGEMENT OF DIABETES MELLITUS IN OLDER ADULTS

In general, in those with obesity and T2DM, the primary metabolic defect is insulin resistance, but insulin secretion remains intact; appropriate initial therapy for this group should involve agents that target insulin resistance, such as metformin.[1] In a patient with T2DM who is lean, the metabolic defect is impaired glucose-induced insulin secretion; initial therapy for this group should involve agents that stimulate insulin secretion without causing hypoglycemia. DPP4is are ideal in this case, particularly in older patients.[1] Still, metformin remains the first line agent when initiating antihyperglycemic agents, according to the Diabetes Canada CPG, due to its low risk of hypoglycemia and weight gain and long-term experience with the agent.[4]

SGLT2is are a game-changing addition to the therapeutic arsenal of T2DM. In addition to lowering HbA1c with minimal hypoglycemic risk, they have been shown to have cardiorenal protective properties in large scale cardiovascular outcome trials (CVOTs).[5] The efficacy profile of SGLT2is versus placebo is unchanged by age.[17]

Table 2. Major possible side effects/adverse events and benefits with the use of SGLT2i agents in older patients

Possible side effects/adverse events	Considerations in older adults
Volume depletion	May cause orthostatic hypotension Adjust antihypertensive therapies, especially loop diuretics, before starting SGLT2i therapy[18]
Amputation	Canagliflozin associated with higher risk of lower limb amputations in CANVAS trial[19] Overall, SGLT2is are not associated with increased risk of amputation operations, even among high-risk groups, including elderly aged 65 years or older and those with peripheral arterial disease[20]
Fractures	Canagliflozin associated with higher risk of bone fractures in CANVAS trial[19] – high CV risk and use of diuretics in this trial suggests fracture incidence may be related to fall events[21]
Renal function	Transient decline in eGFR with initiation similar in younger patients[21] Compromised renal function may contraindicate SGLT2i use[22] May be slightly less effective at reducing HbA1c in setting of CKD, but efficacy and safety profiles have been demonstrated in mild to moderate CKD[18] Delays progression of CKD and reduces clinically significant renal events[19,23-24] Superior in reducing risk of albuminuria and risk of ESRD compared to DPP4is[25]
Genitourinary infections	Tend to occur more frequently in females[22] Increased risk of genital mycotic infections, but not UTIs, compared to DPP4is[26]
Gastrointestinal events	Not associated with increased risk of GI side effects, even when used with metformin[27]

Possible side effects/adverse events	Considerations in older adults
Cancer	Debatable risk of bladder cancer[28]
Euglycemic DKA	Higher rate of DKA compared to DPP4is[29] Overall, DKA incidence in clinical trials was low and did not appear to increase according to age[21] Strategies to help prevent DKA occurrence include avoiding excessive reduction or interruption of insulin; suspending SLGT2i use at least 72 hours before surgery or during times of illness or infection; avoiding alcohol consumption or ketogenic diets

Abbreviations: SGLT2i: sodium glucose cotransporter 2 inhibitor; CANVAS: CANagliflozin cardioVascular Assessment Study; CV: cardiovascular; eGFR: estimated glomerular filtration rate; HbA1c: glycated hemoglobin; CKD: chronic kidney disease; ESRD: end-stage renal disease; DPP4i: dipeptidyl peptidase 4 inhibitor; UTI: urinary tract infection; GI: gastrointestinal; DKA: diabetic ketoacidosis.

While the safety profiles of SGLT2is (e.g., empagliflozin,[30] dapagliflozin,[31] canagliflozin,[32] and ertugliflozin[16]) in those aged 65 years or older are considered good,[33] there remains hesitance in prescribing these drugs to older adults in clinical practice, which may be due to the concern for increased potential for adverse events.[34] Table 2 reports some of these possible adverse events to be aware of. However, pooled analysis results from phase II/III studies have demonstrated that two-year long treatment with dapagliflozin was well tolerated in older people with T2DM; between older and younger populations, the rates of hypoglycemia, genital infections, and urinary tract infections were comparable, there were low rates of volume depletion for older patients, and there was no increased risk of bone fractures in older patients.[35]

SGLT2is can be used as add-on therapy in select and relatively healthy older patients with T2DM but dedicated randomized controlled trials (RCTs) assessing both efficacy and safety of this drug class in older patients, aged 75 years or older specifically, are lacking. The studies use participants without complex comorbidities, so the outcomes in frailer older patients are unclear. Due to a larger body of evidence with DPP4is (e.g., alogliptin, linagliptin, saxagliptin, and sitagliptin) in this older group, the Diabetes Canada CPG recommends they should generally be used before SGLT2is as add-on therapy after metformin in older patients.[1] However, there is one scenario where an SGLT2i can be considered as second-line after metformin; if the patient is an older adult younger than 75 years old with evidence of CV disease, adequate renal function, and no other complex comorbidities, then empagliflozin can be considered.[1] Considering the recently updated NICE clinical guidelines for management of T2DM in adults, which recommends SGLT2i as first-line treatment in certain individuals with heart failure (HF), established atherosclerotic cardiovascular disease (ASCVD), or are at high risk of developing CV disease, it is likely SGLT2is will be more widely prescribed.[36]

GLP1-RAs are also included in the Canadian guidelines and can be considered in older adults aged 60 years or older with at least two CV risk factors, with the strongest evidence for dulaglutide, then liraglutide and subcutaneous semaglutide.[4] Unfortunately, this drug class is mostly available as injectables, a potential challenge for use in older adults. All SGLT2is are available as oral medications and can be taken at any time of the day.[34]

CARDIORENAL EFFECTS OF NEWER AGENTS

The Diabetes Canada CPG reviews the evidence for cardiorenal benefits of SGLT2is, GLP1-RAs, and DPP4is, available at: Diabetes Canada | Clinical Practice Guidelines - Chapter 13: Pharmacologic Glycemic Management of Type 2 Diabetes in Adults: 2020 Update.

The SGLTI2i- and GLP1-RA-mediated cardiovascular and renal protection demonstrated in CVOTs has led to a paradigm shift in the care of patients with diabetes, encouraging health care providers to use these antihyperglycemics in patients with high cardiorenal risk, regardless of glucose control.[37] The benefits of SGLT2is

and GLP1-RAs are well recognized even in patients without diabetes. The 2022 Canadian Cardiovascular Society (CCS) guidelines now recommend using SGLT2is in non-diabetic patients.[38] In adults with HF and left ventricular ejection fraction (LVEF) 40% or below, SGLT2i reduces all-cause and CV mortality, hospitalization for heart failure (HHF), and a composite endpoint of significant decline in estimated glomerular filtration rate (eGFR), progression to end-stage renal disease (ESRD), or death due to kidney disease.[38] This risk reduction in CV death and HHF remains consistent for patients aged 75 years or older.[22,39] In adults with HF and LVEF above 40%, SGLT2i reduces HHF.[38] In adults with chronic kidney disease (CKD), SGLT2i reduces a composite endpoint of significant decline in eGFR, progression to ESRD, or death due to kidney disease, all-cause and CV mortality, nonfatal MI, and HHF.[38]

If utilizing SGLT2is to treat CV disease in a non-diabetic patient, caution should be used with respect to volume depletion, hypotension, active genital mycotic infection (GMI), previous critical limb ischemia; initiation of therapy should be delayed until the condition is resolved, or therapies are modified to reduce risk.[38] Ongoing monitoring for GMIs, concomitant dehydrating illnesses, volume depletion, and renal function is recommended.[38] If considering using SGLT2i in a diabetic patient, additional consideration should be given for DKA (i.e., an SGLT2i should not be started in a patient with a history of DKA) and concomitant use of insulin or an insulin secretagogue (i.e., dose reduction or drug cessation may be required).[38]

The use of GLP1-RAs is associated with a significant benefit on composite CV outcomes, major adverse cardiovascular events (MACE), all-cause mortality, MI, stroke, CV disease, peripheral artery disease, and HF, compared to other antihyperglycemic agents, except the SGLT2is.[40] They also have significant benefit on eGFR and hard renal outcomes versus other glucose-lowering drugs, except the SGLT2is.[40]

Patorno et al. notably enrolled older adults with a mean age of 72 years, approximately 10 years older than those enrolled in the CVOTs that most of the data and recommendations above are derived from.[41] This study compared SGLT2i and GLP1-RA efficacy and safety in this often-neglected subgroup of type 2 diabetic patients, and found that older adults taking an SGLT2i had a similar MACE risk but decreased HHF risk versus those taking a GLP1-RA.[41]

SHOULD WE BE ADDING OR SUBSTITUTING SGLT2i IN EVERYONE?

In the general population, metformin remains the first-line agent in the treatment of T2DM and the Diabetes Canada CPG recommends SGLT2i as second-line if therapeutic advancement or adjustment is required in adults with T2DM and ASCVD or HFrEF or CKD with an eGFR > 30 mL/min/1.73m^2, and in adults with T2DM aged 60 years or older with at least two CV risk factors.[4] A GLP1-RA could also be considered, except for those with history of HF.[4]

According to the CCS, in patients with T2DM and either ASCVD or multiple risk factors for ASCVD without HF or CKD and irrespective of HbA1c, integration of SGLT2i or GLP1-RA is recommended to reduce cardiorenal risk.[38] Therefore, replacing, rather than adding an agent with cardiorenal benefit, would be most appropriate in the general population at or near HbA1c target.[38]

The European Society of Cardiology diabetes guideline recommends SGLT2i or GLP1-RA as first-line therapy, instead of metformin, for the general population in patients with ASCVD or at high or very high CV risk.[42] No specific trials exist showing cardiorenal benefit with these agents used as first-line therapy or as monotherapy or in newly diagnosed T2DM, but the benefit seen in CVOTs does not vary with diabetes duration, suggesting these benefits may be seen in early diabetes.[40] Furthermore, the benefits are not dependent on the presence of metformin.[38]

It should be noted, however, that these recommendations are for the general population, which does not specifically include older adults. However, post-hoc analyses of the large CVOTs examining the efficacy and safety of the SGLT2i according to age have been performed. Dapagliflozin reduces the risk of death and worsening HF and improved symptoms across all ages, even in those 75 years or older.[43] Similarly, empagli-

flozin was found to reduce the risk of CV mortality, HF, and renal outcomes across all ages.[44] Meta-analysis of EMPA-REG OUTCOMES, DECLARE TIMI 58, and CANVAS trials show that the effect of SGLT2i on CV outcomes among patients with T2DM was consistent across all age groups, with no subgroup differences.[17] Similar results were seen in another meta-analysis of EMPRA-REG OUTCOMES, DECLARE TIMI 58, and CREDENCE trials where the reduction on MACE outcomes associated with SGLT2i use was far greater in older adults than younger individuals.[45] Clearly the SGLT2is confer cardiorenal benefits in older individuals. Furthermore, the outcome benefits can be realized quickly following initiation of the drug. Dapagliflozin was associated with a reduction in the risk of CV death and HHF as early as 28 days,[46] and in another study as early as 24 days.[47] This supports the early addition of SGLT2i in patients where clinical benefits are important. On the other hand, the DAPA-CKD trial showed that in patients with CKD, regardless of the presence of T2DM or not, dapagliflozin did cause significant risk reduction in the composite endpoints, including both cardiac and renal outcome benefits, compared to placebo, but the time to outcome benefits was approximately 13 months.[48] For older adults, the benefits would likely be realized within their anticipated life expectancy, but for those who are severely frail, the benefit is unlikely to be seen within their anticipated life expectancy.[34]

CAN WE ROUTINELY APPLY THE ABOVE RECOMMENDATIONS AND EVIDENCE IN THE FRAIL OLDER ADULT?

There is a common perception that evidence-based therapies are less effective in frail individuals in addition to concerns that these patients experience more treatment intolerance and adverse side effects, often leading to discontinuation of the drug.[49] The anticipation of a less favorable risk versus benefit profile in frail individuals may cause clinicians to hesitate to initiate these therapies in these individuals. However, there is little evidence to support this assumption.[49]

SGLT2is are a desirable option in the older patient due to their potent antihyperglycemic effect with low hypoglycemic risk and cardiorenal benefits but certainly there are numerous side effects to consider in an older patient (see Table 2). Post-hoc analysis of the DAPA-HF trial examined the efficacy of dapagliflozin according to frailty status and found that dapagliflozin reduced the risk of worsening HF or CV death in all frailty groups, with the largest absolute reductions seen in the frailer patients, and that adverse events were not higher than for placebo regardless of frailty status.[50] The DELIVER trial examined efficacy and safety of dapagliflozin according to frailty status, utilizing The Clinical Frailty Scale developed by Rockwood et al.,[51] in patients with HF with mildly reduced or preserved ejection fraction.[49] Treatment efficacy was not diminished in patients with the greatest degree of frailty and the improvement in health-related quality of life with dapagliflozin was greater in patients with greater frailty.[49] The proportion of patients who discontinued SLGT2i treatment or experienced adverse events increased with increasing frailty, but adverse events were not more common in those taking dapagliflozin compared to placebo irrespective of frailty class. Ultimately, the risk versus benefit balance related to frailty was favorable for dapagliflozin and this finding could challenge the reluctance to initiate this drug in frail patients.[49]

Weight loss is one side effect that must be strongly considered in older patients as it can be associated with falls, disability, increased morbidity, and mortality. The EMPA-ELDERLY trial will be the first RCT in older patients 65 years or older with T2DM to evaluate the effect of an SGLT2i on skeletal muscle mass, muscle strength, and physical performance.[52] SGLT2is may also be associated with volume loss due to their diuretic action. The overall incidence of volume depletion-related events is low but increases as renal function worsens in CKD[53] and may occur more frequently in patients 75 years or older.[44] This effect may be more pronounced in older adults due to their increased number of comorbidities, concomitant use of antihypertensive medications, altered thirst response, and changes in water and sodium balance that occur with ageing.[34] Special attention must be paid to orthostatic hypotension (for more on this entity see 4D-AID+-+A+Practical+Approach+to+the+Assessment+of+Orthostatic.pdf (squarespace.com)), especially in patients on antihypertensive or diuretic medication that may require dosage reduction.[54-55] The consensus on fracture risk is conflicting. Only canagliflozin has been associated with non-significant higher rates of low trauma fractures, though this may be due to a higher fall incidence, as volume-related adverse events were more frequent with canagliflozin than placebo.[56] SGLT2i use does not increase genitourinary (GU) infection incidence

in older individuals, though precaution is recommended for female patients with poorly controlled diabetes due to their high infectious risk.[55]

Though the incidence of euglycemic DKA during SGLT2i treatment is low and does not appear to increase according to age, the frequency may be double that compared to other antihyperglycemics.[53] Among reported cases, a high proportion of patients had comorbidities which may increase their susceptibility, like autoimmune diabetes (type 1 diabetes or late autoimmune diabetes of adulthood), reduction of background insulin therapy, and acute illness.[53] This risk should not preclude their use in older adults. However, avoiding predisposing factors, like carbohydrate intake restriction, excessive alcohol consumption, ketogenic diets, severe dehydration, or inappropriate reduction of insulin doses, is important.

SGLT2is act favorably on blood pressure, even in CKD patients, and may help control hypertension burden in older individuals.[57]

IF AN OLDER ADULT PATIENT WITH T2DM IS NOT ON AN SGLT2I, IS IT NECESSARY TO START ONE GIVEN THE ABOVE BENEFITS?

This raises the concern of polypharmacy, which may result in net harm in the older adult. Most patients with T2DM also have hypertension and dyslipidemia and take medications for all three conditions concurrently, where the effect of one drug could be confounded with that of another. The studies of the effect of each class of medication on survival exist, but unfortunately are not adjusted for the concurrent use of other drugs.[9]

Robust evidence supporting cardiorenal benefit of SGLT2is has led to more emphatic recommendations in diabetes treatment guidelines to prioritize using this drug class over others. The frequency of adverse events suggests there are no absolute contraindications for SGLT2i use in older patients. However, extra caution is required in real-life conditions where older individuals may be less robust than those recruited in RCTs.[18] Custódio et al. proposes an algorithm for introducing SGLT2i therapy in older patients with T2DM.[21] The "SGLT2 Rx Tool" may also be used to further understand the risks and benefits in various patient profiles.[58]

WHAT HBA1C LEVELS SHOULD WE BE TARGETING WITH THESE MEDICATIONS IN OLDER PATIENTS?

The strong association between poor glycemic control, risk of complications, and increased mortality remains consistent across all age groups, with some data suggesting a trend towards greater all-cause and cause-specific mortality among patients aged 65 years or older with HbA1c 8.0% or greater.[5] On the other hand, a U-shaped relationship between mortality and HbA1c was demonstrated in diabetic patients aged 80 to 89 years old, with the lowest mortality observed among those with HbA1c 7.0 to 7.4% and significantly higher mortality rates in subjects with strict glycemic control (HbA1c 6.0% or less) or poor glycemic control (HbA1c 8.5% or more).[59] Attempts to achieve intensive glycemic control may lead to net harm in older adults with T2DM.[60]

In functionally independent older patients with normal cognition and life expectancy long enough to benefit from treatment, HbA1c target should be 7.0% or below, just like the younger population. In those with multiple chronic diseases, mild to moderate cognitive impairment, or shortened life expectancy, HbA1c target should be 7.1 to 8.0%. In older patients with diabetes and advanced diabetic complications, significant health problems, short life expectancy, fragility, less functionality, or have limited cognitive capacity, the target should remain flexible, but still an HbA1c 8.5% or below is recommended.[3] The Diabetes Canada CPG Chapter 37 emphasizes considering functional status in determining target HbA1c in older people with T2DM.[1] In fact, the guidelines incorporate The Clinical Frailty Scale, briefly mentioned above, to recommend glycemic targets based on the patient's frailty index; a more flexible target of 7.1 to 8.0% is recommended for a patient with a frailty index of 4-5, a target of 7.1 to 8.5% is recommended for a patient with a frailty index of 6-7, and measuring HbA1c at all is not recommended for those with a frailty index of 8-9.[1]

SUMMARY

The GLP1-RAs, DPP4is, and SGLT2is, with their unique characteristics of cardiorenal benefits, independent of glycemic control, efficacy in patients with or without cardiorenal disease, and low hypoglycemic risk, offer ideal therapeutic choices for older patients. The cardiorenal benefit extends to include even very old patients aged 75 years or older.[54] This may supersede the choice to use metformin as a first-line agent. Age should not be a barrier to using these agents and, SGLT2is in particular should be considered as a valid therapeutic option for older frail adults with T2DM, HF, or CKD.[34]

Safety considerations for these drugs are essential. All individuals with T2DM currently using or starting therapy with insulin secretagogues (GLP1-RA or DPP4i) must be counselled on the prevention, recognition, and treatment of hypoglycemia.[4] If an individual develops an acute illness associated with dehydration or has an upcoming procedure associated with risk of acute kidney injury, their metformin and/or SGLT2i should be temporarily held and their insulin secretagogue dose should be reduced or held entirely if oral intake is reduced.[4] SGLT2i must be held before major surgeries and/or during acute infections or serious illnesses to reduce the risk of DKA, particularly in people who follow low carbohydrate diets or with suspected insulin deficiency[4]. Implementation of these safety considerations is imperative in our vulnerable older population.

Ultimately, selection of therapy depends on the patient, their preferences, comorbidities and current medications, tolerability, and the individualized glycemic target. In the older person with T2DM, functional status is key in determining the HbA1c target. Management beyond pharmacotherapy, including self-management education and support programs, are also vital aspects of diabetes care in this population. Further dedicated studies involving this older population with these new antihyperglycemic therapies are warranted.

CASE CONCLUSION

Mrs. X had reduced oral intake leading to an admission to the hospital. She was kept on nil per os (NPO) status prior to surgery, followed by suboptimal oral intake post-operatively. Dehydration in combination with surgery and canagliflozin use likely precipitated euglycemic DKA. She was also found to have postural hypotension. Given her frail status, history of weight loss, poor nutrition, orthostatic hypotension, increased fall risk, recent HbA1c of 7.0%, canagliflozin was discontinued as associated risks of SGLT2i would outweigh benefits in her case.

REFERENCES

1. Meneilly GS, Knip A, Miller DB, et al. *Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada*: Diabetes in Older People. Can J Diabetes. 2018;42:S283-S295.

2. Scheen AJ. Careful use to minimize adverse events of oral antidiabetic medications in the elderly. Expert Opin Pharmacother. 2021 Nov;22(16):2149-2165. doi: 10.1080/14656566.2021.1912735. Epub 2021 Apr 13. PMID: 33823723.

3. Altuntaş Y. Approach Toward Diabetes Treatment in the Elderly. Sisli Etfal Hastan Tip Bul. 2019 Jun 25;53(2):96-102. doi: 10.14744/SEMB.2019.00868. PMID: 32377065; PMCID: PMC7199825.

4. Lipscombe L, Butalia S, Dasgupta K, et al. *Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada*: Pharmacologic Glycemic Management of Type 2 Diabetes in Adults: 2020 Update. 2020;44:575-591.

5. Koufakis T, Grammatiki M, Kotsa K. Type 2 diabetes management in people aged over seventy-five years: targets and treatment strategies. Maturitas. 2021 Jan;143:118-126. doi: 10.1016/j.maturitas.2020.10.005. Epub 2020 Oct 16. PMID: 33308617.

6. Kulkarni AS, Gubbi S, Barzilai N. Benefits of Metformin in Attenuating the Hallmarks of Aging. Cell Metab. 2020 Jul 7;32(1):15-30. doi: 10.1016/j.cmet.2020.04.001. Epub 2020 Apr 24. PMID: 32333835; PMCID: PMC7347426.

7. Lipscombe LL, Gomes T, Lévesque LE, Hux JE, Juurlink DN, Alter DA. Thiazolidinediones and cardiovascular outcomes in older patients with diabetes. JAMA. 2007 Dec 12;298(22):2634-43. doi: 10.1001/jama.298.22.2634. PMID: 18073359.

8. Guja C, Guja L, Miulescu RD. Effect of type 2 diabetes medications on fracture risk. Ann Transl Med. 2019 Oct;7(20):580. doi: 10.21037/atm.2019.09.51. PMID: 31807561; PMCID: PMC6861738.

9. Baik SH, McDonald CJ. Independent effects of 15 commonly prescribed drugs on all-cause mortality among US elderly patients with type 2 diabetes mellitus. BMJ Open Diabetes Res Care. 2020 Apr;8(1):e000940. doi: 10.1136/bmjdrc-2019-000940. PMID: 32341050; PMCID: PMC7202731.

10. McClean PL, Hölscher C. Liraglutide can reverse memory impairment, synaptic loss and reduce plaque load in aged APP/PS1 mice, a model of Alzheimer's disease. Neuropharmacology. 2014 Jan;76 Pt A:57-67. doi: 10.1016/j.neuropharm.2013.08.005. Epub 2013 Aug 21. PMID: 23973293.

11. Bomba M, Granzotto A, Castelli V, Massetti N, Silvestri E, Canzoniero LMT, Cimini A, Sensi SL. Exenatide exerts cognitive effects by modulating the BDNF-TrkB neurotrophic axis in adult mice. Neurobiol Aging. 2018 Apr;64:33-43. doi: 10.1016/j.neurobiolaging.2017.12.009. Epub 2017 Dec 19. PMID: 29331730.

12. Rizzo MR, Barbieri M, Fava I, Desiderio M, Coppola C, Marfella R, Paolisso G. Sarcopenia in Elderly Diabetic Patients: Role of Dipeptidyl Peptidase 4 Inhibitors. J Am Med Dir Assoc. 2016 Oct 1;17(10):896-901. doi: 10.1016/j.jamda.2016.04.016. Epub 2016 Jun 2. PMID: 27262494.

13. Hung CT, Liu JS, Cheng CY, Chung CH, Chiang CP, Chien WC, Wang WM. Increased risk of bullous pemphigoid in dipeptidyl peptidase 4 inhibitors: A nationwide, population-based, cohort study in Taiwan. J Dermatol. 2020 Mar;47(3):245-250. doi: 10.1111/1346-8138.15195. Epub 2019 Dec 29. PMID: 31885117.

14. Sun L, Wang C, Wu C, Zhou Y, Wang C. Analysis of the Clinical Characteristics of Dipeptidyl Peptidase-4 Inhibitor-Induced Bullous Pemphigoid. Ann Pharmacother. 2022 Feb;56(2):205-212. doi: 10.1177/10600280211022722. Epub 2021 Jun 9. PMID: 34105395.

15. Dicembrini I, Montereggi C, Nreu B, Mannucci E, Monami M. Pancreatitis and pancreatic cancer in patientes treated with Dipeptidyl Peptidase-4 inhibitors: An extensive and updated meta-analysis of randomized controlled trials. Diabetes Res Clin Pract. 2020 Jan;159:107981. doi: 10.1016/j.diabres.2019.107981. Epub 2019 Dec 20. PMID: 31870827.

16. Pratley R, Dagogo-Jack S, Charbonnel B, Patel S, Hickman A, Liu J, Tarasenko L, Pong A, Ellison MC, Huyck S, Gantz I, Terra SG. Efficacy and safety of ertugliflozin in older patients with type 2 diabetes: A pooled analysis of phase III studies. Diabetes Obes Metab. 2020 Dec;22(12):2276-2286. doi: 10.1111/dom.14150. Epub 2020 Aug 31. PMID: 32700421.

17. Giugliano D, Longo M, Maiorino MI, Bellastella G, Chiodini P, Solerte SB, Esposito K. Efficacy of SGLT-2 inhibitors in older adults with diabetes: Systematic review with meta-analysis of cardiovascular outcome trials. Diabetes Res Clin Pract. 2020 Apr;162:108114. doi: 10.1016/j.diabres.2020.108114. Epub 2020 Mar 9. PMID: 32165164.

18. Scheen AJ. Efficacy / safety balance of DPP-4 inhibitors versus SGLT2 inhibitors in elderly patients with type 2 diabetes. Diabetes Metab. 2021 Nov;47(6):101275. doi: 10.1016/j.diabet.2021.101275. Epub 2021 Sep 2. PMID: 34481962.

19. Neal B, Perkovic V, Mahaffey KW, de Zeeuw D, Fulcher G, Erondu N, Shaw W, Law G, Desai M, Matthews DR; CANVAS Program Collaborative Group. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. N Engl J Med. 2017 Aug 17;377(7):644-657. doi: 10.1056/NEJMoa1611925. Epub 2017 Jun 12. PMID: 28605608.

20. Huang CY, Lee JK. Sodium-glucose co-transporter-2 inhibitors and major adverse limb events: A trial-level meta-analysis including 51 713 individuals. Diabetes Obes Metab. 2020 Dec;22(12):2348-2355. doi: 10.1111/dom.14159. Epub 2020 Sep 9. PMID: 32744411.

21. Custódio JS Jr, Roriz-Filho J, Cavalcanti CAJ, Martins A, Salles JEN. Use of SGLT2 Inhibitors in Older Adults: Scientific Evidence and Practical Aspects. Drugs Aging. 2020 Jun;37(6):399-409. doi: 10.1007/s40266-020-00757-y. PMID: 32239461.

22. Sciacqua A, Succurro E, Armentaro G, Miceli S, Pastori D, Rengo G, Sesti G. Pharmacological treatment of type 2 diabetes in elderly patients with heart failure: randomized trials and beyond. Heart Fail Rev. 2021 Dec 2. doi: 10.1007/s10741-021-10182-x. Epub ahead of print. PMID: 34859336.

23. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, Mattheus M, Devins T, Johansen OE, Woerle HJ, Broedl UC, Inzucchi SE; EMPA-REG OUTCOME Investigators. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. N Engl J Med. 2015 Nov 26;373(22):2117-28. doi: 10.1056/NEJMoa1504720. Epub 2015 Sep 17. PMID: 26378978.

24. Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, Silverman MG, Zelniker TA, Kuder JF, Murphy SA, Bhatt DL, Leiter LA, McGuire DK, Wilding JPH, Ruff CT, Gause-Nilsson IAM, Fredriksson M, Johansson PA, Langkilde AM, Sabatine MS; DECLARE–TIMI 58 Investigators. Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2019 Jan 24;380(4):347-357. doi: 10.1056/NEJMoa1812389. Epub 2018 Nov 10. PMID: 30415602.

25. Bae JH, Park EG, Kim S, Kim SG, Hahn S, Kim NH. Comparative Renal Effects of Dipeptidyl Peptidase-4 Inhibitors and Sodium-Glucose Cotransporter 2 Inhibitors on Individual Outcomes in Patients with Type

2 Diabetes: A Systematic Review and Network Meta-Analysis. Endocrinol Metab (Seoul). 2021 Apr;36 (2):388-400. doi: 10.3803/EnM.2020.912. Epub 2021 Mar 31. PMID: 33789035; PMCID: PMC8090474.

26. Lega IC, Bronskill SE, Campitelli MA, Guan J, Stall NM, Lam K, McCarthy LM, Gruneir A, Rochon PA. Sodium glucose cotransporter 2 inhibitors and risk of genital mycotic and urinary tract infection: A population-based study of older women and men with diabetes. Diabetes Obes Metab. 2019 Nov;21(11):2394 -2404. doi: 10.1111/dom.13820. Epub 2019 Jul 21. PMID: 31264755.

27. Bonnet F, Scheen A. Understanding and overcoming metformin gastrointestinal intolerance. Diabetes Obes Metab. 2017 Apr;19(4):473-481. doi: 10.1111/dom.12854. Epub 2017 Feb 22. PMID: 27987248.

28. Tang H, Dai Q, Shi W, Zhai S, Song Y, Han J. SGLT2 inhibitors and risk of cancer in type 2 diabetes: a systematic review and meta-analysis of randomised controlled trials. Diabetologia. 2017 Oct;60 (10):1862-1872. doi: 10.1007/s00125-017-4370-8. Epub 2017 Jul 19. PMID: 28725912.

29. Fralick M, Colacci M, Thiruchelvam D, Gomes T, Redelmeier DA. Sodium-glucose co-transporter-2 inhibitors versus dipeptidyl peptidase-4 inhibitors and the risk of heart failure: A nationwide cohort study of older adults with diabetes mellitus. Diabetes Obes Metab. 2021 Apr;23(4):950-960. doi: 10.1111/ dom.14300. Epub 2021 Jan 13. PMID: 33336894.

30. Kinduryte Schorling O, Clark D, Zwiener I, Kaspers S, Lee J, Iliev H. Pooled Safety and Tolerability Analysis of Empagliflozin in Patients with Type 2 Diabetes Mellitus. Adv Ther. 2020 Aug;37(8):3463-3484. doi: 10.1007/s12325-020-01329-7. Epub 2020 May 5. PMID: 32372290; PMCID: PMC7370973.

31. Fioretto P, Mansfield TA, Ptaszynska A, Yavin Y, Johnsson E, Parikh S. Long-Term Safety of Dapagliflozin in Older Patients with Type 2 Diabetes Mellitus: A Pooled Analysis of Phase IIb/III Studies. Drugs Aging. 2016 Jul;33(7):511-22. doi: 10.1007/s40266-016-0382-1. PMID: 27357173; PMCID: PMC4937081.

32. Sinclair AJ, Bode B, Harris S, Vijapurkar U, Shaw W, Desai M, Meininger G. Efficacy and Safety of Canagliflozin in Individuals Aged 75 and Older with Type 2 Diabetes Mellitus: A Pooled Analysis. J Am Geriatr Soc. 2016 Mar;64(3):543-52. doi: 10.1111/jgs.14028. PMID: 27000327; PMCID: PMC4819884.

33. Scheen AJ. Pharmacodynamics, efficacy and safety of sodium-glucose co-transporter type 2 (SGLT2) inhibitors for the treatment of type 2 diabetes mellitus. Drugs. 2015 Jan;75(1):33-59. doi: 10.1007/ s40265-014-0337-y. PMID: 25488697.

34. Evans M, Morgan AR, Davies S, Beba H, Strain WD. The role of sodium-glucose co-transporter-2 inhibitors in frail older adults with or without type 2 diabetes mellitus. Age Ageing. 2022 Oct 6;51 (10):afac201. doi: 10.1093/ageing/afac201. PMID: 36201329; PMCID: PMC9536439.

35. Fioretto P, Mansfield TA, Ptaszynska A, Yavin Y, Johnsson E, Parikh S. Long-Term Safety of Dapagliflozin in Older Patients with Type 2 Diabetes Mellitus: A Pooled Analysis of Phase IIb/III Studies. Drugs Aging. 2016 Jul;33(7):511-22. doi: 10.1007/s40266-016-0382-1. PMID: 27357173; PMCID: PMC4937081.

36. National Institute for Health and Care Excellence. NICE Guideline [NG28]: Type 2 Diabetes in Adults: Management. 2022. https://www.nice.org.uk/guidance/ng28 (10 April 2023, date last accessed).

37. Jacob S, Krentz AJ, Deanfield J, Rydén L. Evolution of Type 2 Diabetes Management from a Glucocentric Approach to Cardio-Renal Risk Reduction: The New Paradigm of Care. Drugs. 2021 Aug;81(12):1373-1379. doi: 10.1007/s40265-021-01554-6. Epub 2021 Jul 24. PMID: 34302636.

38. Mancini GBJ, O'Meara E, Zieroth S, Bernier M, Cheng AYY, Cherney DZI, Connelly KA, Ezekowitz J, Goldenberg RM, Leiter LA, Nesrallah G, Paty BW, Piché ME, Senior P, Sharma A, Verma S, Woo V, Darras P, Grégoire J, Lonn E, Stone JA, Yale JF, Yeung C, Zimmerman D. 2022 Canadian Cardiovascular Society Guideline for Use of GLP-1 Receptor Agonists and SGLT2 Inhibitors for Cardiorenal Risk Reduction in Adults. Can J Cardiol. 2022 Aug;38(8):1153-1167. doi: 10.1016/j.cjca.2022.04.029. Erratum in: Can J Cardiol. 2022 Oct 25;: PMID: 35961754.

39. Zannad F, Ferreira JP, Pocock SJ, Anker SD, Butler J, Filippatos G, Brueckmann M, Ofstad AP, Pfarr E, Jamal W, Packer M. SGLT2 inhibitors in patients with heart failure with reduced ejection fraction: a meta-analysis of the EMPEROR-Reduced and DAPA-HF trials. Lancet. 2020 Sep 19;396(10254):819-829. doi: 10.1016/S0140-6736(20)31824-9. Epub 2020 Aug 30. PMID: 32877652.

40. Caruso I, Cignarelli A, Sorice GP, Natalicchio A, Perrini S, Laviola L, Giorgino F. Cardiovascular and Renal Effectiveness of GLP-1 Receptor Agonists vs. Other Glucose-Lowering Drugs in Type 2 Diabetes: A Systematic Review and Meta-Analysis of Real-World Studies. Metabolites. 2022 Feb 15;12(2):183. doi: 10.3390/metabo12020183. PMID: 35208256; PMCID: PMC8879165.

41. Patorno E, Pawar A, Bessette LG, Kim DH, Dave C, Glynn RJ, Munshi MN, Schneeweiss S, Wexler DJ, Kim SC. Comparative Effectiveness and Safety of Sodium-Glucose Cotransporter 2 Inhibitors Versus Glucagon-Like Peptide 1 Receptor Agonists in Older Adults. Diabetes Care. 2021 Mar;44(3):826-835. doi: 10.2337/dc20-1464. Epub 2021 Jan 25. PMID: 33495295; PMCID: PMC7896266.

42. Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V, Federici M, Filippatos G, Grobbee DE, Hansen TB, Huikuri HV, Johansson I, Jüni P, Lettino M, Marx N, Mellbin LG, Östgren CJ, Rocca B, Roffi M, Sattar N, Seferović PM, Sousa-Uva M, Valensi P, Wheeler DC; ESC Scientific Document Group. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. Eur Heart J. 2020 Jan 7;41(2):255-323. doi: 10.1093/eurheartj/ehz486. Erratum in: Eur Heart J. 2020 Dec 1;41(45):4317. PMID: 31497854.

43. Martinez FA, Serenelli M, Nicolau JC, Petrie MC, Chiang CE, Tereshchenko S, Solomon SD, Inzucchi SE, Køber L, Kosiborod MN, Ponikowski P, Sabatine MS, DeMets DL, Dutkiewicz-Piasecka M, Bengtsson O, Sjöstrand M, Langkilde AM, Jhund PS, McMurray JJV. Efficacy and Safety of Dapagliflozin in Heart Failure With Reduced Ejection Fraction According to Age: Insights From DAPA-HF. Circulation. 2020 Jan 14;141(2):100-111. doi: 10.1161/CIRCULATIONAHA.119.044133. Epub 2019 Nov 17. PMID: 31736328.

44. Monteiro P, Bergenstal RM, Toural E, Inzucchi SE, Zinman B, Hantel S, Kiš SG, Kaspers S, George JT, Fitchett D. Efficacy and safety of empagliflozin in older patients in the EMPA-REG OUTCOME® trial. Age Ageing. 2019 Nov 1;48(6):859-866. doi: 10.1093/ageing/afz096. PMID: 31579904; PMCID: PMC7963112.

45. Strain WD, Griffiths J. A systematic review and meta-analysis of the impact of GLP-1 receptor agonists and SGLT-2 inhibitors on cardiovascular outcomes in biologically healthy older adults. Br J Diabetes 2021; 21: 30–5.

46. Berg DD, Jhund PS, Docherty KF, Murphy SA, Verma S, Inzucchi SE, Køber L, Kosiborod MN, Langkilde AM, Martinez FA, Bengtsson O, Ponikowski P, Sjöstrand M, Solomon SD, McMurray JJV, Sabatine MS. Time to Clinical Benefit of Dapagliflozin and Significance of Prior Heart Failure Hospitalization in Patients With Heart Failure With Reduced Ejection Fraction. JAMA Cardiol. 2021 May 1;6(5):499-507. doi: 10.1001/jamacardio.2020.7585. PMID: 33595593; PMCID: PMC7890451.

47. Packer M, Anker SD, Butler J, Filippatos G, Ferreira JP, Pocock SJ, Carson P, Anand I, Doehner W, Haass M, Komajda M, Miller A, Pehrson S, Teerlink JR, Brueckmann M, Jamal W, Zeller C, Schnaidt S,

Zannad F. Effect of Empagliflozin on the Clinical Stability of Patients With Heart Failure and a Reduced Ejection Fraction: The EMPEROR-Reduced Trial. Circulation. 2021 Jan 26;143(4):326-336. doi: 10.1161/CIRCULATIONAHA.120.051783. Epub 2020 Oct 21. Erratum in: Circulation. 2021 Jan 26;143 (4):e30. PMID: 33081531; PMCID: PMC7834905.

48. Heerspink HJL, Stefánsson BV, Correa-Rotter R, Chertow GM, Greene T, Hou FF, Mann JFE, McMurray JJV, Lindberg M, Rossing P, Sjöström CD, Toto RD, Langkilde AM, Wheeler DC; DAPA-CKD Trial Committees and Investigators. Dapagliflozin in Patients with Chronic Kidney Disease. N Engl J Med. 2020 Oct 8;383(15):1436-1446. doi: 10.1056/NEJMoa2024816. Epub 2020 Sep 24. PMID: 32970396.

49. Butt JH, Jhund PS, Belohlávek J, de Boer RA, Chiang CE, Desai AS, Drożdż J, Hernandez AF, Inzucchi SE, Katova T, Kitakaze M, Kosiborod MN, Lam CSP, Maria Langkilde A, Lindholm D, Bachus E, Martinez F, Merkely B, Petersson M, Saraiva JFK, Shah SJ, Vaduganathan M, Vardeny O, Wilderäng U, Claggett BL, Solomon SD, McMurray JJV. Efficacy and Safety of Dapagliflozin According to Frailty in Patients With Heart Failure: A Prespecified Analysis of the DELIVER Trial. Circulation. 2022 Oct 18;146(16):1210-1224. doi: 10.1161/CIRCULATIONAHA.122.061754. Epub 2022 Aug 27. PMID: 36029465; PMCID: PMC9815819.

50. Butt JH, Dewan P, Merkely B, Belohlávek J, Drożdż J, Kitakaze M, Inzucchi SE, Kosiborod MN, Martinez FA, Tereshchenko S, Ponikowski P, Bengtsson O, Lindholm D, Langkilde AM, Schou M, Sjöstrand M, Solomon SD, Sabatine MS, Chiang CE, Docherty KF, Jhund PS, Køber L, McMurray JJV. Efficacy and Safety of Dapagliflozin According to Frailty in Heart Failure With Reduced Ejection Fraction : A Post Hoc Analysis of the DAPA-HF Trial. Ann Intern Med. 2022 Jun;175(6):820-830. doi: 10.7326/M21-4776. Epub 2022 Apr 26. PMID: 35467935.

51. Moorhouse P, Rockwood K. Frailty and its quantitative clinical evaluation. J R Coll Physicians Edinb. 2012;42(4):333-40. doi: 10.4997/JRCPE.2012.412. PMID: 23240122.

52. Yabe D, Shiki K, Suzaki K, Meinicke T, Kotobuki Y, Nishida K, Clark D, Yasui A, Seino Y. Rationale and design of the EMPA-ELDERLY trial: a randomised, double-blind, placebo-controlled, 52-week clinical trial of the efficacy and safety of the sodium-glucose cotransporter-2 inhibitor empagliflozin in elderly Japanese patients with type 2 diabetes. BMJ Open. 2021 Apr 7;11(4):e045844. doi: 10.1136/bmjopen-2020-045844. PMID: 33827843; PMCID: PMC8031078.

53. Erondu N, Desai M, Ways K, Meininger G. Diabetic Ketoacidosis and Related Events in the Canagliflozin Type 2 Diabetes Clinical Program. Diabetes Care. 2015 Sep;38(9):1680-6. doi: 10.2337/dc15-1251. Epub 2015 Jul 22. PMID: 26203064; PMCID: PMC4542268.

54. Abdelhafiz AH, Sinclair AJ. Cardio-renal protection in older people with diabetes with frailty and medical comorbidities - A focus on the new hypoglycaemic therapy. J Diabetes Complications. 2020 Sep;34 (9):107639. doi: 10.1016/j.jdiacomp.2020.107639. Epub 2020 May 26. PMID: 32595017.

55. Cintra R, Moura FA, Carvalho LSF, Barreto J, Tambascia M, Pecoits-Filho R, Sposito AC. Inhibition of the sodium-glucose co-transporter 2 in the elderly: clinical and mechanistic insights into safety and efficacy. Rev Assoc Med Bras (1992). 2019 Jan;65(1):70-86. doi: 10.1590/1806-9282.65.1.70. PMID: 30758423.

56. Watts NB, Bilezikian JP, Usiskin K, Edwards R, Desai M, Law G, Meininger G. Effects of Canagliflozin on Fracture Risk in Patients With Type 2 Diabetes Mellitus. J Clin Endocrinol Metab. 2016 Jan;101(1):157-66. doi: 10.1210/jc.2015-3167. Epub 2015 Nov 18. PMID: 26580237; PMCID: PMC4701850.

57. Kohan DE, Fioretto P, Tang W, List JF. Long-term study of patients with type 2 diabetes and moderate renal impairment shows that dapagliflozin reduces weight and blood pressure but does not improve gly-

cemic control. Kidney Int. 2014 Apr;85(4):962-71. doi: 10.1038/ki.2013.356. Epub 2013 Sep 25. PMID: 24067431; PMCID: PMC3973038.

58. Fralick M, Gyenes M, Zhao A. SGLT2 Rx Tool. 2022. https://www.slgt2rx.com/.

59. Lipska KJ, Krumholz H, Soones T, Lee SJ. Polypharmacy in the Aging Patient: A Review of Glycemic Control in Older Adults With Type 2 Diabetes. JAMA. 2016 Mar 8;315(10):1034-45. doi: 10.1001/jama.2016.0299. PMID: 26954412; PMCID: PMC4823136.

60. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group. Lancet. 1998 Sep 12;352 (9131):854-65. Erratum in: Lancet 1998 Nov 7;352(9139):1558. PMID: 9742977.

Canadian Geriatrics Society

PRINCIPLES OF REHABILITATION POTENTIAL IN THE OLDER ADULT

Sandrine Couture, MDCM
Division of Geriatric Medicine, Department of Medicine, McGill University, Montreal, QC

Sofia Nene, MD
Division of Geriatric Medicine, Department of Medicine, McGill University, Montreal, QC

Corresponding Author:
Sofia Nene
sofia.nene@mcgill.ca

Abstract

Older adults are at risk of developing functional decline and disability following hospitalization. Rehabilitation is an intervention aimed at restoring physical and mental abilities that have been lost, and to help attain the highest possible function and quality of life. Assessing rehabilitation potential is a complex decision-making process that allows one to identify older adults who are likely to benefit from rehabilitation interventions, which is often defined as returning to community living after rehabilitation. This assessment is multidisciplinary and must consider physical, cognitive, psychological, social, and environmental factors. Predictors of community discharge after rehabilitation in older adults include higher level of cognition, better mobility at admission to rehabilitation, higher level of functional independence at baseline, lower multimorbidity, fewer acute care hospitalization days, and greater social support.

This article has been peer reviewed.

Conflict of Interest: None of the authors have conflicts of interest or funding sources to disclose.

This article was published in February 2024

Key words:
models of care, frailty, rehabilitation

Key Points

Factors associated with a community discharge in older adults admitted to inpatient rehabilitation include higher level of cognition, better mobility at admission to rehabilitation, higher level of functional independence at baseline, lower multimorbidity, fewer acute care hospitalization days, and greater social support.

In patients over age 90, higher functional independence at admission to rehabilitation and fewer prescribed medications at admission to rehabilitation are associated with community discharge, while multiple comorbidities, previous hospital admissions in the past year, and lack of social work involvement are associated with readmission.

In the stroke population, older adults are more likely to be discharged in the community if they have a higher level of functional independence at admission to rehabilitation and higher Functional Independence Measure (FIM) at discharge.

Introduction

Population aging is a defining demographic trend in Canada. Older adults (over 65 years old) currently represent 18.5% of the population. This percentage is expected to increase to approximately 22% by 2030.[1] Older adults are at risk of developing functional decline and disability following hospitalization.[2] Rehabilitation interventions are necessary to support them in their recovery from acute illness or injury.[3] Healthcare professionals are frequently required to make recommendations regarding a patient's likelihood of benefitting from rehabilitation interventions: to determine the "rehabilitation potential." Decisions about rehabilitation potential can significantly impact patient care and functional trajectory, dictate the type and amount of rehabilitation they will receive, and determine resource allocation.[4,]

This article reviews predictors for successful outcomes following rehabilitation for older adults, the process and components of the evaluation of rehabilitation potential and presents criteria that can be used in clinical practice to make decisions regarding admission to rehabilitation.

What is geriatric rehabilitation?

Rehabilitation is an intervention aimed at restoring a person's physical and mental abilities that have been lost due to an illness or injury, and to help attain the highest possible degree of functioning and quality of life.[6] Younger individuals usually require rehabilitation in the context of an acute event leading to disability and benefit from disease-specific rehabilitation. Older adults are more likely to have pre-existing disabilities due to underlying comorbidities and geriatric syndromes, and require a rehabilitation approach that is comprehensive and considers their complexity.[7] Goals of rehabilitation in younger adults are commonly centered around reentering the workforce or studies, while the focus in older adults is often recovery of autonomy and mobility.[6]

Geriatric rehabilitation was recently defined by the Geriatric Rehabilitation Special Interest Group of the European Geriatric Medicine Society (EuGMS) as "a multidimensional approach of diagnostic and therapeutic interventions, the purpose of which is to optimize functional capacity, promote activity and preserve functional reserve and social participation in older people with disabling impairments."[8] This definition follows the World Health Organization's (WHO) international classification of functioning, disability, and health (ICF) framework, and considers not only the medical aspects of functional impairment, but also the social impact of disability.[9]

Geriatric rehabilitation is available in various care settings, both inpatient and outpatient, and can be administered in acute care hospitals, rehabilitation centers, and long-term care.[10, 11] Common admission diagnoses include stroke, hip fracture, post orthopedic surgery, musculoskeletal diseases such as osteoarthritis, movement disorders, oncological diseases, and cardiopulmonary conditions.[10, 12]

Geriatric rehabilitation is carried out by a multidisciplinary team, led by a geriatric rehabilitation skilled physician.[8, 13] Core members include skilled nurses, physiotherapists, occupational therapists, and social workers.

Extended team members may include pharmacists, psychologists, dieticians, and speech language pathologists, depending on the needs of the patients and local rehabilitation resources and models.[8, 13]

What are successful outcomes of rehabilitation?

Returning to community living from rehabilitation is considered a successful outcome and is used in studies of rehabilitation programs as an indicator of quality of care.[14, 15] Admission to long-term care facilities from rehabilitation is considered an unsuccessful outcome.[14, 15]

Kus et al. assessed patient perspectives for defining rehabilitation success and identified "walking," "getting rid of pain," "autonomy," and "returning home" as the most important patient centered goals.[16]

The Functional Independence Measure (FIM) (https://www.va.gov/vdl/documents/Clinical/Func_Indep_Meas/fim_user_manual.pdf) Th Functional Independence Measure (FIM) is an 18-item score that is frequently used at admission and discharge from inpatient rehabilitation and is employed in the literature to characterize patients' functional trajectory in rehabilitation.[17, 18] It assesses 6 areas of function: self-care, sphincter control, transfers, locomotion, communication, and social cognition.[18] Higher scores on the FIM signify better function and therefore can be an indicator of successful rehabilitation. A positive change in FIM score between admission and discharge, as well as FIM efficiency, which is the total FIM change during admission divided by the length of stay, are also used to measure rehabilitation success.[19, 20] The minimal clinically importance difference (MCID) in FIM instrument varies depending on the population in which it is used. The FIM as a tool is well established in the stroke population.[21, 22] The MCID of the FIM in adults of all ages admitted to inpatient rehabilitation was estimated at 22 points.[23] It was also determined to be 22 points in a population of older adults admitted to inpatient rehabilitation with hip fractures.[24]

What are predictors for successful outcomes of geriatric rehabilitation?

Factors associated with discharge back to the community in older adults admitted to inpatient rehabilitation include; higher level of cognition, better mobility at admission to rehabilitation, higher level of functional independence at baseline, lower multimorbidity, fewer acute care hospitalization days, and having greater social support.[25-28] In patients above age 90, higher functional independence at admission to rehabilitation and fewer medications prescribed at the time of admission to rehabilitation are associated with community discharge, while multiple comorbidities, previous hospital admission in the past year, and lack of social work involvement are associated with readmission to hospital.[29] In the stroke population, older adults are more likely to be discharged to the community if they have a higher level of independence at admission to rehabilitation and higher FIM at discharge.[30, 31]

What is the process and the components of the assessment of rehabilitation potential?

Rehabilitation potential assessments are typically completed by a multidisciplinary team of rehabilitation professionals, including physiotherapists, occupational therapists, physicians, and rehabilitation nurses.[32, 33] The assessment can occur in different settings including outpatient clinics, intermediate care units, acute care units, day hospitals, and long-term care.[32] The assessment of rehabilitation potential should be performed over multiple time points, and ideally, when acute medical issues are approaching resolution given that acute medical issues, such as delirium, may affect a patient's ability to participate in rehabilitation interventions.[33] Components of assessments of rehabilitation are presented in Table 1.[32, 33]

Table 1. Components of and tools for the assessment of rehabilitation potential

Component	Details of the evaluation	Tools
Diagnoses and medications	Active diagnoses and comorbidities Medical stability Medication review Nutritional status Continence Communication abilities: vision and hearing	Charlson Comorbidity Index (https://www.mdcalc.com/calc/3917/charlson-comorbidity-index-cci) Cumulative Illness Rating Scale (https://www.mdcalc.com/calc/10088/cumulative-illness-rating-scale-geriatric-cirs-g)
Functional ability (baseline and current)	Activities of daily living Instrumental activities of daily living Mobility Transfers	Barthel Index (https://www.albertahealthservices.ca/assets/about/scn/ahs-scn-bjh-hf-barthel-index-of-adls.pdf) Functional Independence Measure (FIM) (https://www.va.gov/vdl/documents/Clinical/Func_Indep_Meas/fim_user_manual.pdf) Grip Strength (https://www.jospt.org/doi/epdf/10.2519/jospt.2018.7851) Timed Up and Go Test (https://strokengine.ca/en/assessments/timed-up-and-go-tug/) Short Physical Performance Battery (https://geriatrictoolkit.missouri.edu/SPPB-Score-Tool.pdf) Berg Balance Scale (https://www.physio-pedia.com/images/b/bd/Berg_balance_scale_with_instructions.pdf)
Cognition and psychological ability	Cognition* Behaviors Motivation	Mini Mental State Examination (MMSE) Montreal Cognitive Assessment Geriatric Depression Scale (https://geriatrictoolkit.missouri.edu/cog/GDS_SHORT_FORM.PDF)
Nutrition	Nutritional status	Mini Nutritional Assessment (https://www.mna-elderly.com/sites/default/files/2021-10/mna-mini-english.pdf) Malnutrition Screening Tool (https://sscbc.ca/sites/default/files/SPH%20Malnutrition%20Screening%20Tool%20%28MST%29%20pdf%20%28ID%20315681%29.pdf)
Environment	Usual place of residence Proposed rehabilitation venue Projected realistic discharge destination that can support anticipated needs	
Social	Social support mechanisms	

*Cognitive testing performed in the acute setting may result in falsely low scores due to acute illness and may not reflect the true cognitive baseline.

Are there comprehensive rehabilitation potential assessment tools?

Multiple assessment tools exist to inform decisions regarding rehabilitation potential in older adults. Examples are presented below. While optional, these instruments, together with those listed in Table 1, may assist the clinician in providing additional objective measures to the rehabilitation potential assessment. They may also aid clinicians in systematically structuring their assessments. It should, nevertheless, be noted that these tools primarily consider physical function and do not capture the entire complexity of psychological, social, and economic circumstances. Therefore, the clinical team's judgement and holistic evaluation remain essential in this multifaceted decision-making process.

The Minimum Data Set for Post-Acute Care (MDS-PAC) (https://www.aapacn.org/resources/rai-manual/) is a comprehensive, standardized instrument designed to guide care planning in the rehabilitation setting. It incorporates the needs, strengths, and preferences of older patients admitted to rehabilitation. The assessment includes evaluation of multiple key domains in older adults requiring rehabilitation: cognition, communication/hearing, vision, mood and behavior, social function, physical performance, continence, comorbidities, nutritional status, dental status, skin integrity, and medications.[27] The cognitive performance scale and the performance in ADL scale of the MDS instruments demonstrate good validity compared to commonly used scales, such as the MMSE and Barthel Index (https://www.albertahealthservices.ca/assets/about/scn/ahs-scn-bjh-hf-barthel-index-of-adls.pdf). [34] The instrument also demonstrates good interrater reliability.[35]

The Rehabilitation Potential Assessment Tool (RePAT) (https://bmcgeriatr.biomedcentral.com/articles/10.1186/s12877-022-03420-w#MOESM1) is a 15-item questionnaire developed at Nottingham University to promote structured patient-centered rehabilitation assessments in the acute care setting.[36] The tool was specifically designed for older adults. A feasibility study conducted amongst physiotherapists, occupational therapists, patients, and caregivers demonstrated that its implementation in clinical practice was feasible and acceptable in addition to usual care. [36] Further research will aim to determine how well the tool can predict rehabilitation success.

The Gait, Eyesight, Mobility, Mental state, Sedation (GEMS) tool (https://onlinelibrary.wiley.com/doi/10.1111/j.1447-0594.2010.00626.x) and the Hospital Admission Risk Profile (HARP) (https://agsjournals.onlinelibrary.wiley.com/doi/abs/10.1111/j.1532-5415.1996.tb00910.x?sid=nlm%3Apubmed) are two instruments designed to identify older adults at risk of functional decline and discharge to a facility following an acute care admission.[37, 38] They allow early identification of patients who could benefit from targeted interventions or a more prolonged rehabilitation course to avoid the outcome of discharge to long-term care.

What criteria can be used in clinical practice to determine rehabilitation potential?

A recent study aimed to develop criteria that can be applied in clinical practice to guide decisions regarding rehabilitation potential.[39] We reviewed their recommendations and suggest the practical criteria listed in Table 2. The purpose of these criteria is to structure the decision-making process of clinical teams around a patient's rehabilitation potential. While meeting all criteria is not necessary for a patient to be considered for rehabilitation, the evaluation should demonstrate that the patient can tolerate rehabilitation, is motivated to participate in such a program, and that the prognosis of rehabilitation is favorable.

Table 2. Appropriate criteria for admission to geriatric rehabilitation

	Criteria
1.	The patient is medically stable. There are no active or unresolved medical issues that may affect or interfere with rehabilitation. The patient could safely withstand a rehabilitation program.*
2.	The patient demonstrates motivation to participate in a rehabilitation program.
3.	The patient experienced an acute episode of functional decline, which resulted in diminished ability to care for IADLS and/or ADLs. The patient is no longer at their functional and/or mobility baseline.
4.	The patient requires an integrated multidisciplinary approach to optimize their function.
5.	Functional improvement with rehabilitation is conceivable. The proposed rehabilitation program is likely to be effective.
6.	If there is limited potential for functional recovery, a rehabilitation program is likely to reduce the patient's degree of disability.
7.	Social support mechanisms can be put in place for the patient's needs to be met in the community following rehabilitation.

*Rehabilitation streams of different intensities for older adults may exist depending on the province and city. The multidisciplinary team will issue recommendations regarding the most appropriate stream.

Conclusion

Geriatric rehabilitation is a multidimensional intervention aimed at optimizing functional capacity, functional reserve, and social participation of older adults following illness, or injury. The assessment of rehabilitation potential allows clinicians to select patients who are most likely to have a successful course in rehabilitation, experience functional improvement, and be discharged back to the community. The assessment relies on a careful multidisciplinary evaluation that considers cognition, motivation, social supports, mobility, and current and baseline function. Table 2 can be used to frame that assessment.

References

1. Chagnon J. Population projections for Canada (2018 to 2068), Provinces and Territories (2018 to 2043): Technical report on methodology and assumptions: Statistics Canada= Statistique Canada; 2020.

2. McCusker J, Kakuma R, Abrahamowicz M. Predictors of Functional Decline in Hospitalized Elderly Patients: A Systematic Review. The Journals of Gerontology: Series A. 2002;57(9):M569-M77. doi: 10.1093/gerona/57.9.M569.

3. Andrew MK, Rockwood K. Making our health and care systems fit for an ageing population: considerations for Canada. Can Geriatr J. 2014;17(4):133-5. Epub 2014/12/03. doi: 10.5770/cgj.17.163. PubMed PMID: 25452826; PubMed Central PMCID: PMCPMC4244127.

4. Goodwin VA, Allan LM. 'Mrs Smith has no rehab potential': does rehabilitation have a role in the management of people with dementia? Age Ageing. 2019;48(1):5-7. Epub 2018/09/25. doi: 10.1093/ageing/afy152. PubMed PMID: 30247498.

5. Enderby P, Pandyan A, Bowen A, Hearnden D, Ashburn A, Conroy P, et al. Accessing rehabilitation after stroke - a guessing game? Disabil Rehabil. 2017;39(7):709-13. Epub 2016/05/03. doi: 10.3109/09638288.2016.1160448. PubMed PMID: 27133783.

6. Halter JB. Hazzard's geriatric medicine and gerontology. New York: McGraw Hill; 2022.

7. Achterberg WP, Cameron ID, Bauer JM, Schols JM. Geriatric Rehabilitation-State of the Art and Future Priorities. J Am Med Dir Assoc. 2019;20(4):396-8. Epub 2019/04/08. doi: 10.1016/j.jamda.2019.02.014. PubMed PMID: 30954132.

8. Grund S, Gordon AL, van Balen R, Bachmann S, Cherubini A, Landi F, et al. European consensus on core principles and future priorities for geriatric rehabilitation: consensus statement. Eur Geriatr Med. 2020;11(2):233-8. Epub 2020/04/17. doi: 10.1007/s41999-019-00274-1. PubMed PMID: 32297191.

9. Organization WH. Disability prevention and rehabilitation: report of the WHO Expert Committee on Disability Prevention and Rehabilitation [meeting held in Geneva from 17 to 23 February 1981]. 1981.

10. Grund S, van Wijngaarden JP, Gordon AL, Schols J, Bauer JM. EuGMS survey on structures of geriatric rehabilitation across Europe. Eur Geriatr Med. 2020;11(2):217-32. Epub 2020/04/17. doi: 10.1007/s41999-019-00273-2. PubMed PMID: 32297190.

11. van Balen R, Gordon AL, Schols J, Drewes YM, Achterberg WP. What is geriatric rehabilitation and how should it be organized? A Delphi study aimed at reaching European consensus. Eur Geriatr Med. 2019;10(6):977-87. Epub 2019/12/01. doi: 10.1007/s41999-019-00244-7. PubMed PMID: 34652774.

12. Holstege MS, Caljouw MA, Zekveld IG, van Balen R, de Groot AJ, van Haastregt JC, et al. Changes in geriatric rehabilitation: a national programme to improve quality of care. The Synergy and Innovation in Geriatric Rehabilitation study. Int J Integr Care. 2015;15:e045. Epub 2016/04/28. doi: 10.5334/ijic.2200. PubMed PMID: 27118962; PubMed Central PMCID: PMCPMC4843176.

13. Wells JL, Seabrook JA, Stolee P, Borrie MJ, Knoefel F. State of the art in geriatric rehabilitation. Part I: review of frailty and comprehensive geriatric assessment. Arch Phys Med Rehabil. 2003;84(6):890-7. Epub 2003/06/17. doi: 10.1016/s0003-9993(02)04929-8. PubMed PMID: 12808544.

14. van der Laag PJ, Arends SAM, Bosma MS, van den Hoogen A. Factors associated with successful rehabilitation in older adults: A systematic review and best evidence synthesis. Geriatr Nurs. 2021;42(1):83-93. Epub 2021/01/03. doi: 10.1016/j.gerinurse.2020.11.010. PubMed PMID: 33387828.

15. Everink IH, van Haastregt JC, van Hoof SJ, Schols JM, Kempen GI. Factors influencing home discharge after inpatient rehabilitation of older patients: a systematic review. BMC Geriatr. 2016;16:5. Epub 2016/01/13. doi: 10.1186/s12877-016-0187-4. PubMed PMID: 26755206; PubMed Central PMCID: PMCPMC4709872.

16. Kus S, Müller M, Strobl R, Grill E. Patient goals in post-acute geriatric rehabilitation--goal attainment is an indicator for improved functioning. J Rehabil Med. 2011;43(2):156-61. Epub 2011/01/15. doi: 10.2340/16501977-0636. PubMed PMID: 21234516.

17. Dodds TA, Martin DP, Stolov WC, Deyo RA. A validation of the functional independence measurement and its performance among rehabilitation inpatients. Arch Phys Med Rehabil. 1993;74(5):531-6. Epub 1993/05/01. doi: 10.1016/0003-9993(93)90119-u. PubMed PMID: 8489365.

18. Keith RA, Granger CV, Hamilton BB, Sherwin FS. The functional independence measure: a new tool for rehabilitation. Adv Clin Rehabil. 1987;1:6-18. Epub 1987/01/01. PubMed PMID: 3503663.

19. MacDonald SL, Linkewich E, Bayley M, Jeong IJ, Fang J, Fleet JL. The association between inpatient rehabilitation intensity and outcomes after stroke in Ontario, Canada. Int J Stroke. 2023:17474930231215005. Epub 2023/12/11. doi: 10.1177/17474930231215005. PubMed PMID: 38078378.

20. Mendelson G, Katz Y, Shahar DR, Bar O, Lehman Y, Spiegel D, et al. Nutritional Status and Osteoporotic Fracture Rehabilitation Outcomes in Older Adults. J Nutr Gerontol Geriatr. 2018;37(3-4):231-40. Epub 2018/10/31. doi: 10.1080/21551197.2018.1496513. PubMed PMID: 30376425.

21. Granger CV, Cotter AC, Hamilton BB, Fiedler RC. Functional assessment scales: a study of persons after stroke. Arch Phys Med Rehabil. 1993;74(2):133-8. Epub 1993/02/01. PubMed PMID: 8431095.

22. Bottemiller KL, Bieber PL, Basford JR, Harris M. FIM score, FIM efficiency, and discharge disposition following inpatient stroke rehabilitation. Rehabil Nurs. 2006;31(1):22-5. Epub 2006/01/21. doi: 10.1002/j.2048-7940.2006.tb00006.x. PubMed PMID: 16422041.

23. Beninato M, Gill-Body KM, Salles S, Stark PC, Black-Schaffer RM, Stein J. Determination of the minimal clinically important difference in the FIM instrument in patients with stroke. Arch Phys Med Rehabil. 2006;87(1):32-9. Epub 2006/01/13. doi: 10.1016/j.apmr.2005.08.130. PubMed PMID: 16401435.

24. Arcolin I, Godi M, Giardini M, Guglielmetti S, Bellotti L, Corna S. Minimal clinically important difference of the functional independence measure in older adults with hip fracture. Disabil Rehabil. 2023:1-8. Epub 2023/02/09. doi: 10.1080/09638288.2023.2175386. PubMed PMID: 36750763.

25. Kool J, Oesch P, Bachmann S. Predictors for living at home after geriatric inpatient rehabilitation: A prospective cohort study. J Rehabil Med. 2017;49(2):185-90. Epub 2017/01/20. doi: 10.2340/16501977-2182. PubMed PMID: 28101555.

26. Cary MP, Jr., Prvu Bettger J, Jarvis JM, Ottenbacher KJ, Graham JE. Successful Community Discharge Following Postacute Rehabilitation for Medicare Beneficiaries: Analysis of a Patient-Centered Quality Measure. Health Serv Res. 2018;53(4):2470-82. Epub 2017/11/15. doi: 10.1111/1475-6773.12796. PubMed PMID: 29134630; PubMed Central PMCID: PMCPMC6052014.

27. Landi F, Bernabei R, Russo A, Zuccalà G, Onder G, Carosella L, et al. Predictors of rehabilitation outcomes in frail patients treated in a geriatric hospital. J Am Geriatr Soc. 2002;50(4):679-84. Epub 2002/05/02. doi: 10.1046/j.1532-5415.2002.50162.x. PubMed PMID: 11982668.

28. Lindenberg K, Nitz JC, Rahmann A, Bew P. Predictors of discharge destination in a geriatric population after undergoing rehabilitation. J Geriatr Phys Ther. 2014;37(2):92-8. Epub 2014/01/11. doi: 10.1519/JPT.0b013e3182abe79e. PubMed PMID: 24406715.

29. Elphick HL, Mankad K, Madan S, Parker C, Liddle BJ. The determinants of successful in-hospital rehabilitation in people aged 90 years and older. Gerontology. 2007;53(2):116-20. Epub 2007/01/05. doi: 10.1159/000098414. PubMed PMID: 17202818.

30. O'Brien SR, Xue Y. Inpatient Rehabilitation Outcomes in Patients With Stroke Aged 85 Years or Older. Phys Ther. 2016;96(9):1381-8. Epub 2016/02/27. doi: 10.2522/ptj.20150364. PubMed PMID: 26916929.

31. Vluggen T, van Haastregt JCM, Tan FES, Kempen G, Schols J, Verbunt JA. Factors associated with successful home discharge after inpatient rehabilitation in frail older stroke patients. BMC Geriatr. 2020;20 (1):25. Epub 2020/01/25. doi: 10.1186/s12877-020-1422-6. PubMed PMID: 31973729; PubMed Central PMCID: PMCPMC6979374.

32. Cowley A, Goldberg SE, Gordon AL, Logan PA. Rehabilitation potential in older people living with frailty: a systematic mapping review. BMC Geriatr. 2021;21(1):533. Epub 2021/10/09. doi: 10.1186/s12877-021-02498-y. PubMed PMID: 34620112; PubMed Central PMCID: PMCPMC8496021.

33. Muscat F, Camilleri L, Attard C, Lungaro Mifsud S. Assessment Tools for the Admission of Older Adults to Inpatient Rehabilitation: A Scoping Review. J Clin Med. 2023;12(3). Epub 2023/02/12. doi: 10.3390/jcm12030919. PubMed PMID: 36769567; PubMed Central PMCID: PMCPMC9918169.

34. Landi F, Tua E, Onder G, Carrara B, Sgadari A, Rinaldi C, et al. Minimum data set for home care: a valid instrument to assess frail older people living in the community. Med Care. 2000;38(12):1184-90. Epub 2001/02/24. doi: 10.1097/00005650-200012000-00005. PubMed PMID: 11186297.

35. Hawes C, Morris JN, Phillips CD, Mor V, Fries BE, Nonemaker S. Reliability estimates for the Minimum Data Set for nursing home resident assessment and care screening (MDS). Gerontologist. 1995;35(2):172-8. Epub 1995/04/01. doi: 10.1093/geront/35.2.172. PubMed PMID: 7750773.

36. Cowley A, Goldberg SE, Gordon AL, Logan PA. A non-randomised feasibility study of the Rehabilitation Potential Assessment Tool (RePAT) in frail older people in the acute healthcare setting. BMC Geriatr. 2022;22 (1):785. Epub 2022/10/08. doi: 10.1186/s12877-022-03420-w. PubMed PMID: 36207681; PubMed Central PMCID: PMCPMC9541000.

37. Jupp BJ, Mallela SK, Kwan J, Allen S, Sharma JC, Vassallo M. Development and evaluation of the GEMS (gait, eyesight, mental state, sedation) tool as an aid to predict outcome after hospitalization. Geriatr Gerontol Int. 2011;11(1):8-15. Epub 2010/06/16. doi: 10.1111/j.1447-0594.2010.00626.x. PubMed PMID: 20546025.

38. Liu SK, Montgomery J, Yan Y, Mecchella JN, Bartels SJ, Masutani R, et al. Association Between Hospital Admission Risk Profile Score and Skilled Nursing or Acute Rehabilitation Facility Discharges in Hospitalized Older Adults. J Am Geriatr Soc. 2016;64(10):2095-100. Epub 2016/10/21. doi: 10.1111/jgs.14345. PubMed PMID: 27602551; PubMed Central PMCID: PMCPMC5073021.

39. Muscat F, Camilleri L, Attard C, Lungaro Mifsud S. Inpatient Geriatric Rehabilitation: Definitions and Appropriate Admission Criteria, as Established by Maltese National Experts. J Clin Med. 2022;11(23). Epub 2022/12/12. doi: 10.3390/jcm11237230. PubMed PMID: 36498804; PubMed Central PMCID: PMCPMC9736396.