2021
Guideline
Update

Canadian Guidelines on Prevention, Assessment and Treatment of Depression Among Older Adults

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Canadian Guidelines on Prevention, Assessment and Treatment of Depression Among Older Adults

2021 Guideline Update Group

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1. Introduction

The proportion of Canadians who are seniors is expected to increase dramatically. Currently older adults (i.e., those aged ≥ 65) account for 18% of our country's population (Statistics Canada, 2020). Approximately 20% of those aged 65 and older are living with a mental illness. Although this figure is consistent with the prevalence of mental illness in other age groups, it does not capture the high prevalence rates seen within health and social institutions. For example, it has been reported that 80–90% of nursing home residents live with some form of mental illness and/or cognitive impairment (Seitz et al., 2010; Rovner et al., 1990). Late-life depression is common but often under-diagnosed and under-treated contributing to significant functional impairment and reduced quality of life. The Canadian Coalition for Seniors' Mental Health (CCSMH) National Guideline Project was originally created to support the development of evidence-based recommendations in 4 key areas of seniors' mental health, including depression.

The CCSMH first published national interdisciplinary best practice guidelines on the assessment and treatment of depression in older adults in 2006. Since then a number of clinical trials have been conducted that called for reinforcement or modification of the recommendations made in the initial guidelines. In 2018, CCSMH initiated an update of the guidelines. A team of interdisciplinary health care professionals from across Canada examined the latest peer-reviewed journal articles published since 2006.

In Section 3 (page 6), all new recommendations and recommendations with major modifications are described, with explanations. Some additional recommendation updates with relatively minor changes are only described in Section 4, which compares the original 2006 recommendations to the 2021 recommendations. New or modified recommendations are listed in the right-hand column. Readers are encouraged to review Sections 3 and 4.

2. Methods

A systematic search for peer-reviewed scholarly articles was performed in 5 databases including Medline, Embase, HealthStar, Cochrane, and PsychINFO from the beginning of the end date of the literature review from the previous version of the guideline—July 2006—through December 2018. The searches included and were restricted to English papers only and search terms used were the same as for the 2006 Guidelines.

Multiple phases of title and abstract review were conducted by one of the authors to identify 344 full-text articles from an initial yield of 1560 articles from database searches; those were further categorized based on types of study such as controlled trials (especially randomized), meta-analyses, reviews (especially systematic), and practice guidelines or expert committee reports potentially relevant to the subject area. Subsequently, additional relevant articles of which the members were aware were included.

A working group was assembled (listed on page 2) and participated in the evidence review followed by development of updated recommendations. Individual working group members focused on specific areas and wrote summaries with proposed recommendation updates. The working group met several times to discuss proposed changes, any gaps or controversies with proposed updated recommendations, and consensus was obtained. The proposed updates were presented at the Canadian Academy of Geriatric Psychiatry (CAGP)-CCSMH virtual conference in October 2020, providing an opportunity for feedback from our peers.

The overall grouping of the 2006 recommendations is retained with the addition of a few new categories. The strength of each recommendation was assessed using the same system utilized in the 2006 Guidelines (i.e., Shekelle et al., 1999) *Categories of Evidence and Strength of Recommendations*) summarized on the next page.

CATEGORIES OF EVIDENCE FOR CAUSAL RELATIONSHIPS AND TREATMENT

Evidence from meta-analysis of randomized controlled trials	**Ia**
Evidence from at least 1 randomized controlled trial	**Ib**
Evidence from at least 1 controlled study without randomization	**IIa**
Evidence from at least 1 other type of quasi-experimental study	**IIb**
Evidence from non-experimental descriptive studies, such as comparative studies, correlation studies, and case-control studies	**III**
Evidence from expert committees reports or opinions and/or clinical experience of respected authorities	**IV**

(Shekelle et al., 1999)

The strength of the recommendations, ranging from A to D (see below), is based on the entire body of evidence (i.e., all studies relevant to the issue) ***and the expert opinion of the Guideline Development Group regarding the available evidence***. For example, a strength level of D has been given to evidence extrapolated from literature on younger population groups or considered a good practice point by the Guideline Development Group.

It is important to interpret the rating for the strength of recommendation (A to D) as a synthesis of all the underlying evidence and not as a strict indication of the relevant importance of the recommendation for clinical practice or quality of care. Some recommendations with little empirical support, resulting in a lower rating for strength on this scale, are in fact critical components of the assessment and treatment of depression.

STRENGTH OF RECOMMENDATION

Directly based on category I evidence	**A**
Directly based on category II evidence or extrapolated recommendation from category I evidence	**B**
Directly based on category III evidence or extrapolated recommendation from category I or II evidence	**C**
Directly based on category IV evidence or extrapolated recommendation from category I, II, or III evidence	**D**

(Shekelle et al., 1999)

3. New recommendations and recommendations with major modifications with explanation of changes

The updated Guidelines include a greater emphasis on depression prevention. Historically, healthcare systems have under-funded prevention approaches, especially in the mental health arena. Although research on prevention is in its infancy, prevention may be an alternative strategy to further reduce the disease burden of depression, which has been described as a global public health priority (Reynolds et al., 2012). *Universal* prevention focuses on the general public or a whole population group regardless of risk status. *Selective* prevention targets individuals or subgroups that are at higher risk of developing mental disorders than average individuals or subgroups. *Indicated* prevention focuses on individuals who are identified as having prodromal symptoms or biological markers of mental disorders, but who do not yet meet the diagnostic criteria for a full-blown diagnosis. The recommendations below primarily focus on universal and selective prevention. Of note, there is not enough evidence to recommend the use of antidepressants for people at high risk, although 1 small study suggested a reduced risk in individuals who had suffered a stroke (Robinson et al., 2008).

NEW: PREVENTION

A variety of interventions focused on reducing social isolation and/or loneliness in older adults have demonstrated a reduction in depressive symptoms in addition to reduced loneliness. These interventions were primarily group-based and in long-term care settings. They include reminiscence therapy, physical exercise programs, videoconferences with family, horticultural therapy, and gender-based social groups. [B]

Studies of interventions for social isolation, loneliness, and depression among older adults have been conducted globally. For example, Chiang et al. (2010) investigated the effects of weekly reminiscence therapy sessions on older adults living in long-term care homes. This intervention significantly decreased feelings of loneliness and depressive symptoms among participants. Similarly, a randomized controlled trial (RCT) conducted by Westerhof et al. (2017) aimed to understand the effectiveness of an autobiographical memory discussion intervention among older adults living in residential care. Participants with clinically relevant depressive symptoms had a significant reduction in symptoms during and post-intervention. In addition, loneliness significantly decreased among intervention participants. Tse et al. (2014) investigated the effectiveness of a weekly physical exercise program on nursing home residents. The findings showed significant improvements in both loneliness and depression.

There are several published systematic reviews of social isolation and/or loneliness and/or depression interventions. Quan et al. (2019) critically reviewed the evidence of effectiveness of psychological therapies and leisure and skill development interventions among older adults living in nursing homes, assisted-living settings, and hospice. The most effective interventions at significantly reducing loneliness and depression were reminiscence therapy and horticultural therapy. Another systematic review conducted by Franck et al. (2016) aimed to assess the effects of various interventions designed to alleviate depression and social isolation among older adults receiving residential or community care services. It was reported that reminiscence therapy was successful in significantly decreasing both depression and social isolation.

NEW: PREVENTION

Social prescribing, which is defined as, "a means of enabling primary care services to refer patients with social, emotional, or practical needs to a range of local, non-clinical services, often provided by the voluntary and community sector", may result in reduced depressive symptoms among older adults who have experienced mild to moderate symptoms of depression, social isolation, or loneliness. [C]

The definition of social prescribing comes from Friedli and Watson (2004). Ways to Wellness, an organization located in the United Kingdom, examined the effects of social prescribing in an urban setting amongst middle-aged and older adults with chronic and multiple long-term conditions (Moffatt et al., 2017). Individuals were referred to a 'Link Worker' who identified meaningful health and wellness community and voluntary services and resources. Service users reported positive changes including reduced social isolation and improved mental health after 6 months. Age United Kingdom (UK) conducted a Social

Prescribing Pilot Project that investigated the effectiveness of general practitioners referring older adults aged 55 years and older who had mild to moderate depression or who experienced loneliness or social isolation to the social prescribing service. Older adults who participated in this study demonstrated a significant improvement in their emotional well-being. The Alliance for Healthier Communities in Ontario, Canada (2020) conducted an 18-month mixed methods pilot study on the effectiveness of social prescribing across 11 community health centres. In the *Rx: Community – Social Prescribing in Ontario* study, approximately half of participants were between the ages of 61–80 years. The most frequent reasons for referral were: (a) anxiety, (b) depression, (c) social isolation, and (d) mental health symptoms. Clients reported a significant improvement in mental well-being, reduced loneliness, and increased sense of belonging and connectedness. It should be noted that Bickerdike et al. (2017) suggested that more research was required in order to support the widespread use of this approach.

NEW: PREVENTION

A stepped-care approach (e.g., watchful waiting, cognitive behavioural therapy [CBT-based] bibliotherapy, problem-solving therapy, and referral to primary care for antidepressant medication) can reduce the incidence of depressive and anxiety disorders in community-dwelling older adults with subthreshold depression or anxiety. [B]

A stepped-care approach has been shown to reduce the incidence of depressive and anxiety disorders in community-dwelling older adults with subthreshold depression or anxiety. Van't Veer-Tazelaar et al. (2009) studied the following steps: a watchful waiting approach, CBT-based bibliotherapy, CBT-based problem-solving treatment, and referral to primary care for medication, if required. The intervention group had a 50% reduction in incidence of major depressive disorder or anxiety disorder over a 12-month period compared to usual care. Other promising approaches to preventing depression in older adults with subthreshold depression include the use of lay counsellors in middle and low-income countries (Dias et al., 2019) and the use of problem-solving therapy (Reynolds et al., 2014).

NEW: PREVENTION

Higher levels of physical activity are consistently associated with lower odds of developing future depression. This finding is consistent across all age groups including older adults. Clinicians should encourage patients with low levels of physical activity to become more active. Tools are available for clinicians to assist patients in setting health-related goals (e.g., Fountain of Health). [B]

Schuch et al. carried out a meta-analysis of 49 studies of physical activity (2018). Compared with people with low levels of physical activity, those with high levels had significantly lower odds of developing depression. Furthermore, physical activity had a protective effect against the emergence of depression across all age groups including older adults. Protective effects against depression (major depression or symptoms) were found across geographical regions, with adjusted odds ratios ranging from 0.65 to 0.84 in Asia, Europe, North America, and Oceania.

The Canadian Program entitled Fountain of Health provides clinicians and the public with tools to support behaviour change, aimed at improving lifestyle behaviours including exercise (Gough et al., 2019; Cassidy et al., 2020; www.fountainofhealth.ca).

NEW: PREVENTION

Clinicians should utilize the instilling of hope and positive thinking as important therapeutic tools in the prevention of depression and in helping individuals with depressive symptoms or disorders. [D]

The therapeutic value of hope to health, healing, wellbeing, and quality of life has been well described (Moore 2005; Wilson et al., 2010). There is increasing interest in understanding the role of hope in healing, goal-setting, coping with illness, and as an approach to combat hopelessness. When confronted with illness or loss people are highly vulnerable. Clinicians should consider the important role of instilling authentic hope and positive thinking in their interactions with patients and families in all healthcare settings. There have been a limited number of studies focused on assessing the impact of interventions specifically designed to increase hope with variable results (Kwon et al., 2015; Cheavens at al., 2006; Wilson et al., 2010). A review of 9 studies, utilizing such interventions by nurses in patients coping with cancer, concluded that it is possible to increase hope in this group (Li et al., 2018). Moore (2005) suggests that nurses are in key positions to have conversations with their clients/patients about hope and about strategies to find renewed hope in any situation. She notes that others have

stressed the importance of honouring hope as a complex and multidimensional component of people's experiences through illness and suffering (Bland & Darlington, 2002). Although more research is necessary to understand optimal interventions, we would encourage all healthcare staff to reflect on how best to incorporate the instilling of hope into their practices.

MODIFIED: TREATMENT: MAJOR DEPRESSIVE DISORDER, SINGLE OR RECURRENT EPISODE – SEVERE BUT WITHOUT PSYCHOSIS

UNCHANGED – Patients with severe unipolar depression should be offered a combination of antidepressants and concurrent psychotherapy when appropriate services are available and there is no contraindication to either treatment. [D]

MODIFIED – Electroconvulsive therapy (ECT) should be considered in the treatment of older patients with severe unipolar depression who have previously had a good response to a course of ECT and/or failed to respond to 1 or more adequate antidepressant trials plus psychotherapy, especially if their health is deteriorating rapidly due to depression. ECT is a first-line treatment in older, depressed patients who are at high risk of poor outcomes—those with suicidal ideation or intent, severe physical illness, or with psychotic features. [A]

ECT can also be useful for continuation/maintenance therapy of older patients who are partially responsive, treatment resistant, or treatment intolerant with pharmacotherapy during the acute phase of treatment. [B]

In 2006 it was recommended that ECT should be considered if adequate trials of antidepressants combined with psychotherapy have been ineffective or if the health of the patient is deteriorating rapidly due to depression. The modification above underlines the need to consider ECT in a number of different circumstances, including its potential use as a first-line treatment in some patients who are at risk of poor outcomes. Its use for continuation/maintenance treatment for some patients is also noted.

We have added repetitive transcranial magnetic stimulation (rTMS) as an additional option for patients with major depressive disorder (MDD) who have failed to respond to at least 1 adequate trial of antidepressant (see page 11).

MODIFIED: TREATMENT: MAJOR DEPRESSIVE DISORDER, SINGLE OR RECURRENT EPISODES – SEVERE WITH PSYCHOTIC FEATURES

Recently, more placebo-controlled clinical trials reported safe and effective use of combined antidepressant and antipsychotic drugs in MDD with psychotic features, so we recommend that clinicians use their judgement based on severity and patient's physical conditions to try combination pharmacotherapy first. ECT should be considered after 4–8 weeks if combination therapy fails, is poorly tolerated, or if patient develops severe health consequences. [B]

In the 2006 Guidelines it was recommended that if there is no specific contraindication to its use, patients with psychotic depression should be offered treatment with ECT when available. Alternatively, a combination of antidepressant plus antipsychotic medication was recommended. We now recommend that combined pharmacotherapy can also be considered first line. The Study of the Pharmacotherapy of Psychotic Depression (STOP-PD) trial investigated the effectiveness of combined antipsychotic medications with antidepressants (Meyers et al., 2009). The trial found higher remission rates after 12 weeks of treatment with olanzapine combined with sertraline (41.9%) as compared to olanzapine with placebo (23.9%). This was the case for patients both less than 60 and greater than 60 years of age.

NEW: PSYCHOTHERAPIES AND PSYCHOSOCIAL INTERVENTIONS

There is promising evidence for exercise and mind-body interventions (e.g., tai chi, yoga, and mindfulness-based stress reduction) in reducing depressive symptoms in late-life either alone or in combination with other therapies. Physical activity in the form of exercise is an important non-pharmacological approach to improve mood in older adults. Clinicians should use their judgement in recommending the type of exercise and duration, taking into account comorbidities, physical capacity, and level of motivation. [B]

A 2016 meta-analysis identified 8 RCTs of exercise interventions in adults aged 60 and older with depression. Adjusting for publication bias resulted in a large effect size of exercise on depressive symptoms with aerobic exercise combined with strength training, but not either alone. Benefit was also found with group-based interventions, which were of moderate but not vigorous intensity (Schuch et al., 2016). A review of previous meta-analyses examined the effects of exercise on late-life depression (symptoms or disorder) in adults older than 60 years. Three meta-analyses met eligibility criteria. A total of 1487 participants from diverse settings with ages ranging from 63.5–77.5 years were included. Depressive symptoms were significantly reduced by exercise, and the authors conclude it is

a safe and effective treatment that should be incorporated into the standard care of older adults with depression (Catalan-Matamoros et al., 2016).

MODIFIED:	PSYCHOTHERAPIES AND PSYCHOSOCIAL INTERVENTIONS

Psychotherapies with the most evidence for effectiveness in older adults include: cognitive behaviour therapies (CBT; individual and group) and problem-solving therapy (PST). PST can be provided to older adults with cognitive impairment and executive dysfunction; CBT and PST have also shown benefit for older adults with depression and medical comorbidity. [B]

Psychotherapies and psychosocial treatments should be made available to older adults with depression (symptoms and disorder) in diverse settings (community, hospital, long-term care) across all regions of Canada. [A]

There is also evidence to support behaviour therapy, behavioural activation, reminiscence, and other psychotherapies including psychodynamic psychotherapy and interpersonal psychotherapy (IPT). [B]

Internet-delivered therapies may be comparable to face-to-face treatment, and may improve access to services for individuals in under-serviced areas and those with mobility issues. [C]

We emphasize the vital need for psychotherapies and psychosocial treatments to be made available for older adults with depression in diverse settings in all regions of the country.

Although many forms of psychotherapy have demonstrated benefits for older adults with depression, we note that the most evidence for effectiveness is for CBT (individual and group) and PST. Numerous meta-analyses support CBT as an effective treatment for late-life depression (Cuijpers et al., 2006; Pinquart et al., 2007; Peng et al., 2009) when provided in both individual and group formats. Some of these meta-analyses also found evidence in support of other psychotherapies such as reminiscence therapy. Emerging studies also suggest CBT is an effective intervention for depressed older adults with medical comorbidities such as chronic pain (Ehde et al., 2014) and heart failure (Jeyanantham et al., 2017). Meta-analyses of psychotherapeutic interventions also support the effectiveness of PST for late-life depression showing moderate to high effect sizes (Cuipjers et al., 2016 Kirkham et al., 2016), including among frail older adults (Jonsson et al., 2016).

Internet-delivered cognitive behavioural therapy (iCBT) has been piloted with depressed older adults with favourable results (Titov et al., 2015). Such interventions can improve access to psychotherapy, especially for older adults in under-serviced areas, and/or those who face mobility challenges. One RCT comparing online or iCBT to usual care among depressed older adults with knee osteoarthritis showed benefit compared to usual care (O'Moore et al., 2018). This approach is highly relevant during the expansion of virtual care related to the COVID-19 pandemic.

MODIFIED:	SELECTING AN ANTIDEPRESSANT/MONITORING FOR SIDE EFFECTS AND DRUG INTERACTIONS

It is recommended that clinicians consider sertraline or duloxetine as first-line medications for an acute episode of major depression in older adults. Alternatives include escitalopram and citalopram based on the low possibility of drug interactions but concern about QTc interval may limit dosage to sub-therapeutic levels. [A]

In addition, we suggest clinicians should choose an antidepressant with lowest risk of anticholinergic side effects and drug-drug interactions, as well as being relatively safe in the case of cardiovascular comorbidity. Patients need to be closely monitored for medication compliance, substance use, suicidal ideation, and development of drug toxicity. [D]

Because of concerns about QTc prolongation with citalopram and escitalopram, and incorporating level of evidence, we are recommending sertraline or duloxetine as first-line medications for an acute episode of major depression in older adults. Citalopram and escitalopram remain useful options. There are a variety of other appropriate antidepressants for older adults such as venlafaxine, bupropion, and mirtazapine. In addition vortioxetine is a relatively new antidepressant, which has shown benefit for older adults, including some evidence of improvement in depression-related cognitive dysfunction (McIntyre et al., 2014; Nomikos et al., 2017; McIntyre et al., 2016). In most cases, fluoxetine is not recommended due to its long biological half-life, paroxetine is not recommended due to higher anticholinergic effects, and first generation monoamine oxidase inhibitors are not recommended due to higher risk of serious drug-drug and drug-food interactions. Tricyclic antidepressants should only be considered as third-line agents with due consideration of their potentially serious side effects.

A number of systematic reviews and meta-analyses have been conducted since the last iteration of these guidelines. Overall, the meta-analyses have found that antidepressants are efficacious for geriatric depression. A systematic review and meta-analysis of non-tricyclic "second generation" antidepressants found that these antidepressants were superior to placebo for MDD in adults over 60 years of age. The mean pooled response rates for antidepressant and placebo were 44.4% and 34.7%, respectively. The therapeutic effects were found to be modest and vary according to study and medication (Nelson et al., 2008). Of interest, it was found that

longer trials of 10–12 weeks were needed for older adult to achieve a response. A meta-analysis of 51 double-blind RCTs of antidepressants in older patients found that all classes of antidepressant (tricyclic antidepressants [TCAs], selective serotonin reuptake inhibitors [SSRIs], and other antidepressants) were superior to placebo to achieve response, with less robust findings for remission. There were no differences in remission or response rates between classes of antidepressants. The numbers needed to treat (NNT) were 14.4 and 6.7 for response and remission, respectively (Kok et al., 2012). The efficacy of duloxetine was supported by a systematic review and meta-analysis of 12 trials of antidepressants for geriatric major depression, with less convincing outcomes for SSRIs (Tham et al., 2016).

MODIFIED: TITRATION AND DURATION OF THERAPY (FREQUENCY OF FOLLOW-UP)

When starting antidepressants, patients should initially be seen every 1–2 weeks (in-person or virtually) to assess response, side effects, and to titrate the dose. Visits should include, at a minimum, supportive psychosocial interventions and monitoring for worsening of depression, agitation, and suicide risk. [D]

The 2006 Guidelines recommended weekly visits after starting an antidepressant. Although ideal, this has been deemed often unrealistic (e.g., in primary care and in many mental health ambulatory settings). A brief check-in by phone may be helpful for some patients who are experiencing side effects and may encourage patients to continue taking the medication as the initial side effects frequently diminish.

MODIFIED: TITRATION AND DURATION OF THERAPY (INADEQUATE RESPONSE)

When significant improvement has occurred but recovery is not complete after an adequate trial, the clinician should consider:

- **a further 4 weeks of monotherapy or consider augmentation with another antidepressant or lithium or an antipsychotic (e.g., aripiprazole) or specific psychotherapy (e.g., IPT, CBT, PST).**
- **a switch to another antidepressant (same or another class) after discussing with the patient the potential risk of losing any significant improvements made with the first treatment. [C]**
- **augmentation with lithium remains a viable option but needs to be used carefully due to the risk of lithium toxicity; the clinician must be aware of how to monitor the patient on lithium over time through investigations.**

NOTE: 2006 recommendation did not include augmentation with an antipsychotic.

The atypical antipsychotic aripiprazole has been investigated for treatment-refractory depression with promising results. A post hoc examination of 3 RCTs for patients 18–67 years of age demonstrated that augmentation with aripiprazole was superior to placebo in reducing depression and achieving remission in the 61–67 year-old subgroup (Steffens et al., 2011). A subsequent randomized, placebo-controlled trial of aripiprazole for older adults (average age 66) who did not respond to venlafaxine found that augmentation with aripiprazole (average daily dose 7 mg) resulted in remission significantly more often than placebo (44% vs 29%) (Lenze et al., 2015). The NNT to achieve remission with aripiprazole augmentation was 6. Extended-release quetiapine has demonstrated efficacy as monotherapy for geriatric depression (Katila et al., 2013). It must be noted that atypical antipsychotic medications have significant potential side effects such as tardive dyskinesia, akathisia, extrapyramidal side effects, and prolongation of QTc, and there may be an increased risk of death and stroke, based on the dementia literature.

In attempting to achieve optimal outcomes, some experts favour an approach that utilizes a treatment algorithm. One Canadian example of this approach was described by Mulsant et al. (2014). In this algorithm, the first-line antidepressant was escitalopram, with sertraline and duloxetine as alternatives. For non-responders, duloxetine is the preferred second-line antidepressant, with venlafaxine and desvenlafaxine as alternatives. Duloxetine was favoured partly due to the impact on the management of several pain syndromes that are quite common in older adults. If the patient fails an SSRI and a serotonin and norepinephrine reuptake inhibitor (SNRI); i.e., no response despite an adequate trial at a therapeutic dose) the

next step is the use of the TCA nortriptyline, with bupropion as an alternative. For those patients who achieve a partial response to a first- or second-line antidepressant (SSRI or SNRI), the algorithm recommends augmentation with either lithium or an atypical antipsychotic. An alternative is combining the SSRI or SNRI with mirtazapine or bupropion.

MODIFIED: MONITORING FOR SIDE EFFECTS AND DRUG INTERACTIONS (SODIUM)

When prescribing SSRI or SNRI antidepressants to older adults, the prescriber should screen for a history of hyponatremia before prescribing, as part of the consent process and then consider getting a sodium level prior to starting the antidepressant if there is a history of hyponatremia. [C]

A serum sodium level should be done within 2–4 weeks of initiating SSRI or SNRI antidepressants. Prescribers may consider checking the level after 2 weeks for those patients on diuretics or who have a history of hyponatremia. There is a lower of risk of hyponatremia with TCAs, bupropion, and mirtazapine. [C]

The 2006 Guidelines recommended that a sodium level be done after 1 month, especially if the patient was taking a medication known to cause hyponatremia. Reports suggest that hyponatremia often occurs with the first 2 weeks of treatment (Leth-Møller et al., 2016; Lien, 2018).

A review of 21 studies and over 100 case reports revealed a relatively higher risk of hyponatremia with SSRIs and venlafaxine, particularly when combined with patient risk factors for hyponatremia (De Picker et al., 2014). The risks associated with mirtazapine were lower. A recent commentary compared 4 population-based studies, revealing that SSRIs and SNRIs are most likely to cause hyponatremia in older adults, with TCAs and mirtazapine having lower risk. There are case reports for bupropion possibly causing hyponatremia as well (Lien, 2018).

NEW: REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (rTMS)

We recommend repetitive transcranial magnetic stimulation (rTMS; left-sided only or sequential bilateral or deep rTMS) for older adults (> 60 years) with unipolar depression who have failed to respond to at least 1 adequate trial of antidepressant. rTMS is not recommended in patients who have failed a course of ECT or who have a seizure disorder. [B]

rTMS is a brain stimulation method that uses magnetic field pulses, rather than an electrical current, and does not induce a seizure. The procedure requires a stimulator and coil to produce an electromagnetic field. A typical treatment course is 5 days per week for between 4–6 weeks. In general, the treatment has a favourable adverse effect profile with common side effects including scalp discomfort and transient headache. There are no cognitive adverse effects reported with rTMS. In 2008, the FDA approved rTMS as a treatment for depression for patients not responding to at least 1 antidepressant medication with a maximum age of 69 (Manepalli et al., 2014).

Despite the relatively large number of rTMS studies completed to date, there is a paucity of studies evaluating the efficacy of rTMS in treatment-resistant late-life depression specifically. A number of older reports have suggested that older age is a negative predictor of response to rTMS (Figiel et al., 1998; Fregni et al., 2006; Manes et al., 2001; Mosimann et al., 2002). However, these studies were limited in several important ways: short treatment courses and suboptimal stimulation parameters, particularly with respect to the stimulation intensity needed to overcome the prefrontal atrophy that occurs with advancing age. The proposed mechanism for these negative findings is likely related to the increased scalp-to-cortex distance in the elderly (Figiel et al. 1998). Imaging studies (Mosimann et al., 2004; Kozel et al., 2000) and a small uncontrolled clinical pilot study (Nahas et al., 2004) have suggested a correlation between antidepressant effect of rTMS and scalp-to-cortex distance. Nahas et al. (2004) used an open design in which they adjusted stimulus intensity based on the distance of the scalp to the cortex and used magnetic resonance imaging (MRI) co-registration to target the dorsolateral prefrontal cortex (DLPFC), in 18 older subjects. The average intensity required was 114%; significantly higher than the intensity used in other treatment trials at the time. Interestingly, a more recent RCT in an elderly sample with depression and cerebrovascular damage found unilateral rTMS at 110% stimulation intensity resulted in a significant, but modest 27.3% remission rate (Jorge et al., 2008).

The rTMS field has moved to using 120% of the motor threshold intensity across the age range of subjects and as a result, meta-analyses of more recent DLPFC rTMS have not found that older age is a negative predictor of response (Berlim et al., 2014; Gross et al., 2007). Some preliminary data suggest that older adults may respond better to a sequential bilateral form of rTMS where low frequency (i.e., 1 Hz) right-sided stimulation is immediately followed by high frequency (i.e., 10 Hz) left-sided stimulation, using 120% stimulation intensity (Blumberger et al., 2012; Blumberger et al., 2016; Trevizol et al.,2019). Other data suggest that older adults may respond better with a coil that generates a larger induced electrical field than the standard figure of 8 coils (Levkovitz et al., 2009). A controlled trial in older adults aged 60–80 demonstrated that deep rTMS led to a statistically significant higher remission rate compared to sham (Kaster et al., 2018).

Further study of rTMS in older adults is warranted given that optimal treatment parameters have demonstrated more promising results than earlier studies. Controlled studies across the age spectrum of older adults (i.e., over age 70) are needed to confirm efficacy and tolerability in this subgroup of older adults. Older adults may be particularly able to benefit from rTMS as daily schedules may be more conducive to the 5 days weekly treatment schedule. rTMS has good patient acceptability due to the favourable adverse effect profile, in particular the lack of cognitive side effects.

NEW: PHARMACOGENETIC TESTING

At present we do not recommend the broad use of pharmacogenetic testing in older adults with late-life depression. Patients with recurrent severe side effects to several anti-depressant drugs may benefit from pursuing a pharmacogenetic test to see if CYP450 metabolism is contributing. [C]

There is some recent evidence that pharmacogenetic testing might improve outcomes among older adults with MDD who had failed a trial of at least 1 antidepressant. In a controlled trial of 206 adults (aged 65 or older) participants receiving care guided by pharmacogenetic testing showed significantly improved response and rates of remission compared to usual care (Forester et al., 2020). However, this testing is not widely available and is expensive. We do not recommend its use in routine practice, although some patients who are intolerant of several antidepressants may benefit from a pharmacogenetic test.

MODIFIED: SPECIAL POPULATIONS: DEMENTIA

UNCHANGED: Patients who have mild depressive symptoms or symptoms of short duration should be treated with psychosocial supportive interventions first. [D]

MODIFIED: There is limited evidence to recommend antidepressant therapy for mild or moderate depression associated with dementia at this time. Behavioural interventions may be utilized as a first-line intervention and antidepressant medication could be offered if symptoms are severe and persistent, understanding that efficacy is not well established and that side effects could occur. [D]

A number of meta-analyses and systematic reviews have investigated the efficacy of antidepressants for depression associated with dementia. The initial Cochrane review in 2002 was negative (Bains et al., 2002). This was followed by a positive meta-analysis of 5 studies, which showed a NNT of 5 to achieve remission (Thompson et al., 2007). Subsequently, 4 more meta-analyses, including another Cochrane review in 2018, were negative (Nelson et al., 2011, Sepehry et al., 2012, Orgeta et al., 2017, Dudas et al., 2018). We would still suggest that antidepressant medication could be offered if symptoms are severe and persistent.

NEW: SPECIAL POPULATIONS: PARKINSON'S DISEASE

We recommend SSRIs as first line for the treatment of depression in patients with Parkinson's disease with SNRIs as an alternative. CBT can also be considered. [B]

The 2006 Guidelines did not make a recommendation for patients with depression associated with Parkinson's disease. A meta-analysis of 20 RCTs compared pharmacologic, behavioural, or rTMS with a placebo/other drugs or methods. There were 13 medication trials, 9 of 13 were placebo-controlled and most were studies involving antidepressants. Two studies examined dopamine agonists and 1 study examined memantine. Antidepressant medications were found to be efficacious, specifically SSRIs and SNRIs. Non-antidepressant medications (e.g., dopamine agonists) did not have positive results. CBT was also beneficial (Bomasang-Layno et al., 2015). Another meta-analysis assessed the efficacy of antidepressants for depression in Parkinson's disease compared to placebo or a control group. This involved 20 studies and of those, 12 were randomized, placebo-controlled trials, while the others were either comparative studies or antidepressant versus no treatment. The results demonstrated efficacy for SSRIs, MAOIs, and TCAs when compared with placebo. The antidepressants were well-tolerated overall (Mills et al., 2018). Given equal efficacy among antidepressants, we recommend SSRIs or SNRIs, as they are generally better tolerated than older antidepressants such as TCAs.

MODIFIED: **SPECIAL POPULATIONS: VASCULAR DEPRESSION/ POST-STROKE DEPRESSION**

Consider SSRIs as first-line treatment for post-stroke depression (PSD) regardless of whether or not the stroke is ischemic or hemorrhagic. Second-line treatments can include SNRIs and mirtazapine. Methylphenidate may also be considered, especially if apathy is significant. [B]

NOTE: The 2006 recommendations suggested that venlafaxine be avoided. Methylphenidate was not mentioned.

Several meta-analyses have demonstrated that a variety of antidepressants are superior to placebo in PSD (Xu et al., 2016; Deng et al. 2017; Qin et al., 2018). We favour SSRIs as first line based on overall risk of side effects, although they are associated with an increased risk of bleeding when combined with non-steroidal anti-inflammatory medication (Shin 2015). Methylphenidate may be efficacious based on 1 placebo-controlled RCT (Grade et al., 1998).

NEW: **MODELS OF CARE (COLLABORATIVE, INTERPROFESSIONAL MODELS)**

Core elements of evidence-based models for treating late-life depression in primary care include improved patient education, and incorporating interprofessional staff as depression care managers who routinely assess and follow patients clinically, utilizing a stepped-care approach. Treatment prescriptions are provided by a primary care physician or nurse practitioner, with as needed psychiatric consultation. An individualized plan of care should be developed using a collaborative approach. [A]

Interventions that integrate mental health services into primary care have increased the number of patients who are treated for depression and the quality of that treatment. The most effective models involve systematic depression screening and monitoring, interprofessional teams that include primary care providers and mental health specialists, a depression care manager to work directly with patients over time, and the use of guideline-based depression treatment (Bruce & Sirey, 2018). Three major studies have demonstrated the effectiveness of integrated approaches (PRISM-E, IMPACT, and PROSPECT) in the care of older adults. Thota et al., (2012) carried out an extensive review and meta-analysis of collaborative care to improve the management of depressive disorders across multiple patient populations. The results from their meta-analyses suggest robust evidence of effectiveness of collaborative care in improving depression symptoms, adherence to treatment; response to treatment, remission of symptoms, recovery from symptoms, quality of life/functional status, and satisfaction with care for patients diagnosed with depression.

NEW: **MODELS OF CARE (VIRTUAL CARE)**

To optimize access to clinical services, "senior-friendly" virtual care options (e.g., videoconferencing) should be available. Older adult patients should have appropriate equipment and support to ensure effective and efficient communication to optimize virtual care encounters. [C]

The use of telepsychiatry for care of older adults has been shown to be feasible and effective (Conn et al., 2013; Ramos-Ríos et al., 2012). A systematic review of studies demonstrated that telehealth care is feasible and well-accepted in the areas of inpatient and nursing home consultation, cognitive testing, dementia diagnosis and treatment of depression in integrated and collaborative care models and psychotherapy (Gentry et al., 2019). However, the use of telepsychiatry in Canada has been quite limited prior to the COVID-19 pandemic. Since then the use of virtual care approaches has dramatically increased across multiple areas of healthcare. Older adults are often at a disadvantage with many having limited capacity to utilize newer technologies. As such we strongly advocate for senior-friendly virtual care options with appropriate equipment and support.

4. Summary of 2006 recommendations with new and updated 2021 recommendations

PREVENTION

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
	A variety of interventions focused on reducing social isolation and/or loneliness in older adults have demonstrated a reduction in depressive symptoms in addition to reduced loneliness. These interventions were primarily group-based and in long-term care settings. They include reminiscence therapy, physical exercise programs, videoconferences with family, horticultural therapy, and gender-based social groups. **[B]**
	Social prescribing, which is defined as "a means of enabling primary care services to refer patients with social, emotional, or practical needs to a range of local, non-clinical services, often provided by the voluntary and community sector," may result in reduced depressive symptoms among older adults who have experienced mild to moderate symptoms of depression, social isolation, or loneliness. **[C]**
	A stepped-care approach (e.g., watchful waiting, cognitive behavioural therapy [CBT-based] bibliotherapy, problem-solving therapy, and referral to primary care for antidepressant medication) can reduce the incidence of depressive and anxiety disorders in community-dwelling older adults with subthreshold depression or anxiety. **[B]**
	Higher levels of physical activity are consistently associated with lower odds of developing future depression. This finding is consistent across all age groups including older adults. Clinicians should encourage patients with low levels of physical activity to become more active. Tools are available for clinicians to assist patients in setting health-related goals (e.g., Fountain of Health). **[B]**
Public education efforts should focus on the prevention of depression and suicide in older adults. **[D]**	Unchanged

SCREENING & ASSESSMENT

Recommendations: Screening and Assessment – Risk Factors

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Health care providers should be familiar with the physical, psychological, and social risk factors for depressive disorders in older adults and include a screening for depression for their clients/ patients who present with some of these risk factors. **[D]**	Unchanged
We recommend targeted screening of those elderly at higher risk for depression due to the following situations: • Recently bereaved with unusual symptoms (e.g., active suicidal ideation, guilt not related to the deceased, psychomotor retardation, mood congruent delusions, marked functional impairment after 2 months of the loss, reaction that seems out of proportion with the loss) • Bereaved individuals, 3 to 6 months after the loss • Socially isolated • Persistent complaints of memory difficulties • Chronic disabling illness • Recent major physical illness (e.g., within 3 months) • Persistent sleep difficulties • Significant somatic concerns or recent onset anxiety • Refusal to eat or neglect of personal care • Recurrent or prolonged hospitalization • Diagnosis of dementia, Parkinson disease or stroke • Recent placement in a nursing/Long Term Care (LTC) home **[B]**	Essentially unchanged, but note that the exclusion of major depression in the first 2 months after the loss and in bereavement was removed in Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-V).

Recommendations: Screening and Assessment – Screening and Screening Tools

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Health care providers should have knowledge and skills in the application of age-appropriate screening and assessment tools for depression in older adults. **[D]**	Unchanged
In hospital settings, we recommend screening high risk elderly upon intake, or as soon as the acute condition has stabilized. **[D]**	Unchanged
Appropriate depression screening tools for elderly persons without significant cognitive impairment in general medical or geriatric settings include the self-rating *Geriatric Depression Scale (GDS)*, *the SELFCARE self-rating scale*, and the *Brief Assessment Schedule Depression Cards (BASDEC)* for hospitalized patients. **[B]**	We recommend using the GDS or the Patient Health Questionnaire-9 (PHQ-9). **[B]**
For patients with moderate to severe cognitive impairment, an observer-rated instrument, such as the Cornell Scale for Depression in Dementia is recommended instead of the GDS. **[B]**	Unchanged

SCREENING & ASSESSMENT (CONT'D)

Recommendations: Screening and Assessment – Further Assessment

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Following a positive screen for depression, a complete bio-psycho-social assessment should be conducted, including: • A review of diagnostic criteria outlined in DSM-IV -TR or ICD 10 diagnostic manuals • An estimate of severity, including the presence of psychotic or catatonic symptoms • Risk assessment for suicide • Personal and family history of mood disorder • Review of medication use and substance use • Review of current stresses and life situation • Level of functioning and/or disability • Family situation, social integration/support and personal strengths • Mental status examination, including assessment of cognitive functions • Physical examination and laboratory investigations looking for evidence of medical problems that could contribute to or mimic depressive symptoms **[D]**	No change except for new version of DSM (DSM-5).
LTC homes' assessment protocols should specify that screening for depressive and behavioural symptoms will occur both in the early post-admission phase and subsequently, at regular intervals, as well as in response to significant change. **[D]**	Unchanged

Recommendations: Screening and Assessment – Suicide

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Clinicians should always assess the risk of suicide in patients with suspected depression by directly asking patients about suicidal ideation, intent and plan. Those at high risk for suicide should be referred to a specialized mental health professional and/or service as a priority for further assessment, treatment, and suicide prevention strategies. **[D]**	Unchanged

TREATMENT OPTIONS FOR TYPE AND SEVERITY OF DEPRESSION

Recommendation: Treatment: Adjustment Disorder with Depressed Mood

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
We recommend initial treatment with supportive psychosocial interventions or psychotherapy. If symptoms become severe enough to meet DSM-IV diagnostic criteria for a depressive disorder or persist after resolution of the stressor, more specific therapies in keeping with the revised diagnosis should be considered (e.g., medication, more intensive/ specific psychotherapy). **[D]**	No change except for new version of DSM (DSM-5).

Recommendations: Treatment: Minor Depressive Disorder

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Patients with minor depression of less than 4 weeks duration should be treated with supportive psychotherapy or psychosocial interventions. **[D]**	Unchanged
Pharmacological treatment or evidence-based psychotherapy should be considered if symptoms persist for more than 4 weeks after psychosocial interventions have been initiated. **[D]**	Unchanged

Recommendations: Treatment: Dysthymic Disorder – Persistent Depressive Disorder

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Patients with dysthymic disorder should be treated with pharmacological therapy, with or without psychotherapy, with periodic reassessment to measure response. **[B]**	Clinicians may consider non-pharmacological approaches as first-line in persistent depressive disorder, with pharmacotherapy recommended for those who have persistent or worsening symptoms despite psychosocial interventions. **[C]**
In specific clinical situations, for example where patients do not wish to take antidepressants, psychotherapy may be used alone with periodic reassessment to measure response. **[D]**	Unchanged

Recommendation: Treatment: Major Depressive Disorder, Single or Recurrent Episode – Mild to Moderate Severity

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Mild or moderate unipolar major depression should be treated pharmacologically using antidepressants or with psychotherapy or a combination of both. **[A]**	Unchanged

TREATMENT OPTIONS FOR TYPE AND SEVERITY OF DEPRESSION (CONT'D)

Recommendations: Treatment: Major Depressive Disorder, Single or Recurrent Episode – Severe but Without Psychosis

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Patients with severe unipolar depression should be offered a combination of antidepressants and concurrent psychotherapy when appropriate services are available and there is no contra-indication to either treatment. **[D]**	Unchanged
ECT should be considered if adequate trials of antidepressants combined with psychotherapy have been ineffective or if the health of the patient is deteriorating rapidly due to depression. **[D]**	Electroconvulsive therapy (ECT) should be considered in the treatment of older patients with severe unipolar depression who have previously had a good response to a course of ECT and/or failed to respond to 1 or more adequate antidepressant trials plus psychotherapy, especially if their health is deteriorating rapidly due to depression. ECT is a first-line treatment in older, depressed patients who are at high risk of poor outcomes—those with suicidal ideation or intent, severe physical illness, or with psychotic features. **[A]** ECT can also be useful for continuation/maintenance therapy of older patients who are partially responsive, treatment resistant, or treatment intolerant with pharmacotherapy during the acute phase of treatment. **[B]**

Recommendation: Treatment: Major Depressive Disorder, Single or Recurrent Episodes – Severe with Psychotic Features

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
If there is no specific contraindication to its use, patients with psychotic depression should be offered treatment with ECT when available. Alternatively, a combination of antidepressant plus antipsychotic medication should be used. If this combination is not effective (e.g., poorly tolerated, no improvement in at least some of the symptoms within 4-8 weeks of treatment, or lack of remission despite optimisation of dose and duration of treatment over more than 8-12 weeks), ECT needs to be offered. ECT should also be considered if severe health consequences (e.g., suicide, metabolic derangement) are imminent because pharmacological treatment has been poorly tolerated or would be too slow to provide needed improvements. **[D]**	Recently, more placebo-controlled clinical trials reported safe and effective use of combined antidepressant and antipsychotic drugs in MDD with psychotic features, so we recommend that clinicians use their judgement based on severity and patient's physical conditions to try combination pharmacotherapy first. ECT should be considered after 4–8 weeks if combination therapy fails, is poorly tolerated, or if patient develops severe health consequences. **[B]**

Recommendation: Treatment: Referrals for Psychiatric Care at Time of Diagnosis

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Clinicians should refer patients with the following to available psychiatry services: • Psychotic depression • Bipolar disorder • Depression with suicidal ideation or intent (cont'd on next page)	Change of terminology from depression with co-morbid substance abuse to depression with co-morbid substance use disorder.

TREATMENT OPTIONS FOR TYPE AND SEVERITY OF DEPRESSION (CONT'D)

Recommendation: Treatment: Referrals for Psychiatric Care at Time of Diagnosis (cont'd)

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Additionally, patients with the following conditions may benefit from such referral: • Depression with co-morbid substance abuse • Major depressive episode, severe • Depression with co-morbid dementia **[D]**	Change of terminology from depression with co-morbid substance abuse to depression with co-morbid substance use disorder.

Recommendations: Transcranial Magnetic Stimulation

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
	We recommend rTMS (left-sided only or sequential bilateral or deep rTMS) for older adults (> 60 years) with unipolar depression who have failed to respond to at least 1 adequate trial of antidepressant. rTMS is not recommended in patients who have failed a course of ECT or who have a seizure disorder. **[B]**

Recommendations: Pharmacogenetic Testing

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
	At present we do not recommend the broad use of pharmacogenetic testing in older adults with late-life depression. Patients with recurrent severe side effects to several antidepressant drugs may benefit from pursuing a pharmacogenetic test to see if CYP450 metabolism is contributing. **[C]**

Recommendations: Psychotherapies and Psychosocial Interventions

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Supportive care should be offered to all patients with depression **[B]** Psychotherapies and/or psychosocial treatments should be made available to patients with dysthymic disorder, minor depression or depressive symptoms of normal grief reactions during bereavement **[B]**	Psychotherapies and/or psychosocial treatments should be made available to older adults with depression (symptoms or disorder) in all settings (community, hospital, long-term care). **[A]**
Evidence-based psychotherapies recommended for geriatric depressions include: behaviour therapy; cognitive-behaviour therapy; problem-solving therapy; brief dynamic therapy; interpersonal therapy; and reminiscence therapy. **[A]**	Psychotherapies with the most evidence for effectiveness in older adults include: cognitive behavioural therapy (CBT) – individual and group, and problem-solving therapy (PST). PST can be provided to older adults with cognitive impairment and executive dysfunction; CBT and PST have also been studied in older adults with medical comorbidity. **[B]** There is also evidence to support behaviour therapy, behavioural activation, reminiscence, and other psychotherapies including psychodynamic psychotherapy and interpersonal therapy. **[B]** Internet-delivered therapies may be comparable to face-to-face treatment, and may improve access to services for individuals in under-serviced areas and those with mobility issues. **[C]**

TREATMENT OPTIONS FOR TYPE AND SEVERITY OF DEPRESSION (CONT'D)

Recommendations: Psychotherapies and Psychosocial Interventions (cont'd)

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
	New: There is promising evidence for exercise and mind-body interventions (e.g., tai chi, yoga, and mindfulness-based stress reduction) in reducing depressive symptoms in late-life either alone or in combination with other therapies. Physical activity in the form of exercise is an important non-pharmacological approach to improve mood in older adults. Clinicians should use their judgement in recommending the type of exercise and duration, taking into account comorbidities, physical capacity, and level of motivation. **[B]**
Psychotherapy should be available to patients suffering from major depression, either alone as first line treatment or in combination with antidepressant medication, for individuals who prefer this treatment modality and are able to safely participate in treatment (e.g., no severe cognitive impairment, no psychotic symptoms). **[A]** Psychotherapy in combination with antidepressant medication should be available to patients with severe major depression, or chronic or recurrent depression. **[A]**	Unchanged
At least one form of psychosocial intervention should be offered to the patient depending upon the patient's needs and preferences, and available resources. These interventions should be delivered by professionals who have had some training in the provision of geriatric care. **[C]**	Unchanged
Psychotherapies should be delivered by trained mental health professionals. It is recommended that health care teams and professionals treating elderly depressed patients have access to personnel with training and competence in delivering psychotherapies which have demonstrated efficacy. When psychotherapy is not available, supportive care should be offered and other psychosocial interventions should be considered. **[D]**	Unchanged

PHARMACOLOGICAL TREATMENT

Recommendations: Selecting an Appropriate Antidepressant (also see section that follows)

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Older patients have a response rate with antidepressant therapy similar to younger adults. Clinicians should approach elderly depressed individuals with therapeutic optimism. **[A]**	Unchanged
Antidepressants should be used when indicated, even in patients with multiple co-morbidities and serious illnesses, as they have similar efficacy rates compared with use in well elderly. Adverse events in patients with multiple co-morbidities can be minimized by careful selection of drugs that are not likely to worsen or complicate patient-specific medical problems. **[B]**	Unchanged
Co-morbid psychiatric disorders, particularly generalized anxiety disorders and substance abuse, should be identified and appropriately treated as they will adversely influence the outcome of depression. In cases where benzodiazepines have to be used to prevent acute withdrawal or as a temporary measure until antidepressants or psychotherapeutic interventions take effect, there should be a review and gradual discontinuation when feasible. Clinicians should avoid the use of benzodiazepines for treatment of depressive symptoms with elderly patients. **[B]**	Unchanged

Recommendations: Monitoring for Side Effects and Drug Interactions

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Clinicians should choose an antidepressant with the lowest risk of drug-drug interactions when patients are taking multiple medications. Good choices include citalopram, sertraline, venlafaxine, bupropion and mirtazapine. **[C]**	It is recommended that clinicians consider duloxetine or sertraline as first-line medications for an acute episode of major depression in older adults. Alternatives include escitalopram and citalopram based on the low possibility of drug interactions but concern about QTc interval may limit dosage to sub-therapeutic levels. **[A]**
When choosing agents from a specific class, clinicians should select those found to be safer with the elderly (e.g., selecting drugs with the lowest anti-cholinergic properties amongst available antidepressants). **[D]**	We suggest clinicians choose an antidepressant with the lowest risk of anticholinergic side effects and drug-drug interactions as well as being relatively safe in the case of cardiovascular comorbidity. Patients need to be closely monitored for medication compliance, substance use, suicidal ideation, and development of drug toxicity. **[D]**
We recommend that physicians and pharmacists consult up-to-date drug interaction data bases when a new antidepressant is prescribed to patients taking multiple medications. **[C]**	Unchanged

PHARMACOLOGICAL TREATMENT (CONT'D)

Recommendations: Monitoring for Side Effects and Drug Interactions (cont'd)

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
When starting antidepressant therapy (e.g., SSRI or venlafaxine), clinicians should monitor for serotonin-related side effects (such as agitation) and for short-term worsening of symptoms. **[B]**	Unchanged
When starting an antidepressant we recommend monitoring for suicidal ideation and risk. **[C]**	TCAs should only be considered as third-line agents with due consideration of the potentially serious side effects. **[C]**
If TCAs are used, clinicians should monitor for postural hypotension, cardiac symptoms and anti-cholinergic side effects and blood levels. **[D]**	Side effects of TCAs include: postural hypotension (fall/fracture), cardiac conduction defects, anticholinergic effects (delirium, dry mouth, urinary retention, constipation). If used, nortriptyline and desipramine have the lowest anticholinergic effects. **[D]**
We recommend checking sodium blood levels after one month of treatment with SSRIs, especially with patients taking other medications that can cause hyponatremia (e.g., diuretics). **[C]** We recommend checking sodium levels before switching to another agent due to poor response or tolerance or when patients display symptoms of hyponatremia (e.g., fatigue, malaise, delirium). **[C]**	When prescribing SSRI or SNRI antidepressants to older adults, the prescriber should screen for a history of hyponatremia before prescribing, as part of the consent process and then consider getting a sodium level prior to starting the antidepressant if there is a history of hyponatremia. **[C]** A serum sodium level should be done within 2–4 weeks of initiating SSRI or SNRI antidepressants. Prescribers may consider checking the level after 2 weeks for those patients on diuretics or who have a history of hyponatremia. There is a lower of risk of hyponatremia with TCAs, bupropion, and mirtazapine. **[C]**

Recommendations: Titration and Duration of Therapy

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
When starting antidepressants, patients should be seen at weekly intervals for several weeks to assess response, side effects, and to titrate the dose. Visits should include, at a minimum, supportive psychosocial interventions and monitoring for worsening of depression, agitation and suicide risk. **[D]**	When starting antidepressants, patients should initially be seen every 1–2 weeks (in-person or virtually) to assess response, side effects, and to titrate the dose. Visits should include, at a minimum, supportive psychosocial interventions and monitoring for worsening of depression, agitation, and suicide risk. **[D]**
Clinicians should start at half of the recommended dose for younger adults, but aim at reaching an average dose within one month if the medication is well tolerated at weekly reassessments **[D]**	Unchanged
If there is no sign of improvement after at least 2 weeks on an average dose, further gradual increases are recommended until there is either some clinical improvement, limiting side effects, or one has reached the maximum recommended dose. **[D]**	Unchanged

PHARMACOLOGICAL TREATMENT (CONT'D)

Recommendations: Titration and Duration of Therapy (cont'd)

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Before considering a change in medication, it is important to ensure an adequate trial. Change should be made if: there is no improvement in symptoms after at least 4 weeks at the maximum tolerated or recommended dose; there is insufficient improvement after 8 weeks at the maximum tolerated or recommended dose. **[C]**	Unchanged
When significant improvement has occurred but recovery is not complete after an adequate trial, the clinician should consider: • a further 4 weeks of treatment with or without augmentation with another antidepressant or lithium or specific psychotherapy (e.g., IPT, CBT, PST); • a switch to another antidepressant (same or another class) after discussing with the patient the potential risk of losing any significant improvements made with the first treatment. **[C]**	When significant improvement has occurred but recovery is not complete after an adequate trial, the clinician should consider: • a further 4 weeks of monotherapy or consider augmentation with another antidepressant or lithium or an antipsychotic (e.g., aripiprazole) or specific psychotherapy (e.g., IPT, CBT, PST). • a switch to another antidepressant (same or another class) after discussing with the patient the potential risk of losing any significant improvements made with the first treatment. • augmentation with lithium remains a viable option, but needs to be used carefully due to the risk of lithium toxicity. The clinician must be aware of how to monitor the patient on lithium over time through investigations. **[C]**
When switching agents, it is generally safe to reduce the current medication while starting low doses of the alternate agent. Specific drug interaction profiles need to be checked for both drugs involved during this overlap since antidepressants commonly interact with each other. **[C]**	Unchanged
Augmentation strategies require supervision by experienced physicians. **[D]**	Unchanged
Given its long half-life and risk of interaction with many of the drugs prescribed for the elderly, we do not recommend the use of fluoxetine as first-line treatment despite its documented efficacy. **[C]**	Fluoxetine is not recommended due to long biological half-life, paroxetine is not recommended due to higher anticholinergic effects, and first generation MAOIs are not recommended due to higher risk of serious drug-drug or drug-food interactions. **[D]**
Antidepressants, especially SSRIs, should not be abruptly discontinued but should be tapered off over a 7 to10 day period when possible. **[C]**	Unchanged

PHARMACOLOGICAL TREATMENT (CONT'D)

Recommendations: Monitoring and Long-Term Treatment

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Health care providers should monitor the older adult for re-occurrence of depression for the first 2 years after treatment. Ongoing monitoring should focus on depressive symptoms that were present during the initial (index) episode. **[B]**	Unchanged
Assistance from specialists may be required for the long-term treatment of patients with severe symptoms affecting function and overall health, psychotic depression, depression with active suicidal ideation, depression with bipolar disorder, and depression that has not responded to treatment trials. **[D]**	Unchanged
Older patients who achieve remission of symptoms following treatment of their first episode of depression should be treated for a minimum of one year (and up to 2 years) with their full therapeutic dose. **[B]**	Unchanged
When discontinuing antidepressant treatment after remission of symptoms, we recommend a slow taper over months, monitoring closely for recurrence of symptoms and resuming full therapeutic dose if there is any sign of relapse or recurrence. **[D]**	Unchanged
An evidence-based psychotherapy represents a treatment option for patients who present with relapse and incomplete remission. **[B]**	Unchanged
Older patients with partial resolution of symptoms should receive indefinite maintenance therapy and ongoing efforts at a complete resolution of symptoms through the use of augmentation or combination strategies, as well as consideration for ECT. **[B]**	Clinicians are strongly encouraged to assess medication adherence as an initial step in managing partial response or treatment-resistant depression. Other considerations include the use of alcohol, substances, and medications that may promote depressive symptoms. Medical conditions should be reviewed, especially the possibility of antidepressant-induced hyponatremia. The working diagnosis should also be reviewed. ECT can also be useful for continuation/ maintenance therapy of older patients who are partially responsive, treatment resistant, or treatment intolerant to pharmacotherapy during the acute phase of treatment. **[B]**
Older patients who have had more than 2 depressive episodes, had particularly severe or difficult-to-treat depressions or required ECT should continue to take antidepressant maintenance treatment indefinitely, unless there is a specific contraindication to its use. **[D]**	Unchanged
For those patients who fail to remain well with traditional maintenance therapy but have responded well to ECT, maintenance ECT may be a useful option. **[D]**	Unchanged

PHARMACOLOGICAL TREATMENT (CONT'D)

Recommendations: Monitoring and Long-Term Treatment

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
In LTC homes, the response to antidepressant therapy should be evaluated monthly after initial improvement and at quarterly care conferences, as well as at the annual assessment after remission of symptoms. A decision to continue or discontinue the antidepressant therapy should be based on: • whether the depression has been treated long enough to allow sustained remission of symptoms (e.g., now one year of full remission); or • whether the treatment is still tolerated well in the context of their health problems; and • the risks of discontinuation (i.e., return of original depressive symptoms) are less than those associated with continuation of medication. **[D]**	Unchanged

Recommendations: Education

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Specialized content in regards to assessment and treatment of depression in older adults should be included as part of the basic education and continuing education programs of all health care professionals. **[D]**	Specialized content in regards to prevention, assessment, and treatment of depression in older adults should be included as part of the basic education and continuing education programs of all healthcare professionals. **[D]**
Specific training on geriatric mental health issues should be provided for personnel caring for depressed older adults. **[D]**	Unchanged
Health care professionals should provide older depressed adults with education regarding the nature of depression, its biological, psychological and social aspects, effective coping strategies, and lifestyle changes that will assist their recovery, while being mindful of the individual's stresses and strengths. **[B]**	Unchanged
Families of depressed older adults should be provided with information regarding the signs and symptoms of depression, attitudes and behaviours of the depressed person and their own reaction to them, and depression coping strategies, as well as available treatment options and the benefits of treatment. **[D]**	Unchanged

SPECIAL POPULATIONS

Recommendations: Special Populations: Bipolar Disorder

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Elderly individuals who present with manic or hypomanic symptoms for the first time after age 65 need a thorough assessment for possible underlying medical causes. **[C]**	Unchanged
A mood stabilizer (e.g. lithium) should be the first line treatment of bipolar disorder. When depressive episodes occur despite prior stabilization with a mood stabilizer, antidepressant medication needs to be added. **[B]**	Unchanged
The choice of mood stabilizer should be based on prior response to treatment, type of illness (e.g., rapid-cycling or not), medical contraindications to the use of specific mood stabilizers (i.e., side effects that could worsen pre-existing medical problems), and potential interactions with other drugs required by the patient. **[C]**	Unchanged
All mood stabilizers require monitoring over time for possible short-term and longer-term adverse events. **[B]**	All mood stabilizers require monitoring over time for possible short-term and longer-term adverse events. Using lithium requires the patient, family, and healthcare team to understand the factors that may increase lithium levels leading to potential toxicity. Lithium can cause hypothyroidism, hypercalcemia through hyperparathyroidism, and renal dysfunction. The clinician must regularly monitor the patient on lithium, including laboratory investigations. **[B]**

Recommendations: Special Populations: Dementia

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Patients who have mild depressive symptoms or symptoms of short duration should be treated with psychosocial supportive interventions first. **[D]**	Unchanged
Pharmacological treatment is recommended for patients who have major depression co-existing with dementia. **[B]**	There is limited evidence to recommend antidepressant therapy for mild or moderate depression associated with dementia. Behavioural interventions may be utilized as a first-line intervention and antidepressant medication could be offered if symptoms are severe and persistent, understanding that efficacy is not well established and that side effects could occur. **[D]**
In selecting pharmacological treatment for depression with dementia, clinicians should select drugs that have low anticholinergic properties, such as citalopram and escitalopram, sertraline, moclobemide, venlafaxine, or bupropion. **[C]**	As noted above, we recommend duloxetine and sertraline as first-line antidepressants, while recognizing that other antidepressants are also appropriate. Limiting exposure to anticholinergic properties remains an important consideration in patients with both dementia and depression.

SPECIAL POPULATIONS (CONT'D)

Recommendations: Special Populations: Dementia

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Psychosocial treatment should be part of the treatment of depression co-existing with dementia. This treatment should be flexible to account for the decline in functioning as well as multifaceted to provide help with the diversity of problems facing the patient and caregiver. It should be delivered by clinicians sensitized to the vulnerabilities and frailties of older adults with dementia. This treatment should include helping caregivers deal with the disease in a skill-oriented manner. **[A]**	Unchanged
For patients who have psychotic depression and dementia, a combination of antidepressant and antipsychotic medication is usually the first choice, although ECT may be used if medications are ineffective or rapid response is required to maintain safety. **[D]**	Unchanged

Recommendations: Special Populations: Vascular Depression/Post-Stroke Depression

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Patients who have had strokes should be monitored closely for the possible development of depression as a common complication of stroke, even in those who do not report depressed mood. **[B]**	Unchanged
Patients who have depression following single or multiple cerebral vascular injury should be treated following the guidelines outlined in *Section 8.3*, *Vascular Depression*, but taking care not to worsen their ongoing vascular risk factors. **[D]** (avoid antidepressants with high anticholinergic properties and those that can cause hypertension or severe hypotension)	Consider SSRIs as first-line treatment for post-stroke depression whether or not the stroke is ischemic or hemorrhagic. Second-line treatments can include SNRIs and mirtazapine. Methylphenidate may also be considered, especially if apathy is significant. **[B]**

Recommendations: Special Populations: Parkinson's Disease

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
	We recommend SSRIs as first-line for the treatment of depression in patients with Parkinson's disease with SNRIs as an alternative **[B]**. CBT can also be considered. **[B]**

MODELS OF CARE

Recommendations: Models of Care

2006 RECOMMENDATIONS	2021 NEW OR UPDATED RECOMMENDATIONS
Health care professionals and organizations should implement a model of care that addresses the physical/ functional as well as the psychosocial needs of older depressed adults. Given the complex care needs of older adults, these are most likely to require interdisciplinary involvement in care, whether in primary care or specialized mental health settings. **[B]**	Unchanged
Health care professionals and organizations should implement a model of care that promotes continuity of care as older adults appear to respond better to consistent primary care providers. **[B]**	Unchanged
	New: Core elements of evidence-based models for treating late-life depression in primary care include: improved patient education, incorporating interprofessional staff as depression care managers who routinely assess and follow patients clinically, utilizing a stepped-care approach. Treatment prescriptions are provided by a primary care physician or nurse practitioner, with as needed psychiatric consultation. An individualized plan of care should be developed using a collaborative approach. **[A]**
	New: To optimize access to clinical services, "senior-friendly" virtual care options (e.g., videoconferencing) should be available. Older adult patients should have appropriate equipment and support, to ensure effective and efficient communication to optimize virtual care encounters. **[C]**

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