Canadian Clinical Practice Guidelines for Assessing and Managing Behavioural and Psychological Symptoms of Dementia (BPSD)

2024

CCSMH Canadian Coalition for Seniors' Mental Health
CCSMPA Coalition canadienne pour la santé mentale des personnes âgées
cagp CANADIAN ACADEMY OF GERIATRIC PSYCHIATRY | acgp ACADÉMIE CANADIENNE DE GÉRONTOPSYCHIATRIE

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20 Crown Steel Drive Unit #6
Markham, ON L3R 9X9
Phone: 1-888-214-7080 extension 102
Email: info@ccsmh.ca
www.ccsmh.ca

Guideline Panel

The following individuals contributed to the development of the CCSMH Guidelines on the Assessment and Management of BPSD. Conflicts of interest statements are provided for each guideline working group member.

Co-Chairs

Dr. Dallas Seitz, MD, PhD

- Geriatric Psychiatrist, Professor, Department of Psychiatry, Cumming School of Medicine, University of Calgary; Co-Chair Canadian Coalition for Seniors' Mental Health

Dr. Jennifer Watt, MD, PhD

- Geriatrician, St. Michael's Hospital and Providence Healthcare; Assistant Professor, Department of Medicine, University of Toronto

Working Group Members

Dr. Marie-Andrée Bruneau, MD, MSc

- Geriatric Psychiatrist, Professor, Department of Psychiatry and Addictology, University of Montreal

Dr. Vivian Ewa, MD

- Family Physician and Care of the Elderly Physician, Clinical Associate Professor, Department of Family Medicine, Cumming School of Medicine, University of Calgary

Dr. Sid Feldman, MD

- Family Physician and Care of the Elderly Physician, Department of Family and Community Medicine, Baycrest and University of Toronto

Dr. Yael Goldberg, PhD, C.Psych

- Clinical Psychologist and Neuropsychologist, Neuropsychology and Cognitive Health Program, Baycrest

Dr. Zahra Goodarzi, MD, MSc

- Geriatrician, Associate Professor, Department of Medicine, Cumming School of Medicine, University of Calgary

Dr. Nathan Herrmann, MD

- Geriatric Psychiatrist, Professor, Department of Psychiatry and Sunnybrook Research Institute, University of Toronto

Debbie Hewitt Colborne, RN, MScN

- Registered Nurse, Project Advisor, Behavioral Supports Ontario Provincial Coordinating Office, North Bay Regional Health Centre

Dr. Alexandre Henri-Bhargava, MDCM, MScCH

- Neurologist, Island Health; Clinical Associate Professor, Department of Medicine, University of British Columbia; Affiliate Associate Professor, Division of Medical Sciences, University of Victoria

Dr. Zahinoor Ismail, MD

- Geriatric Psychiatrist, Professor, Department of Psychiatry, Cumming School of Medicine, University of Calgary

Dr. Julia Kirkham, MD, MSc

- Geriatric Psychiatrist, Assistant Professor, Department of Psychiatry, Cumming School of Medicine, University of Calgary

Dr. Sanjeev Kumar, MD

- Geriatric Psychiatrist, Adult Neurodevelopmental and Geriatric Psychiatry Division, Centre for Addiction and Mental Health; Associate Professor, Department of Psychiatry, University of Toronto

Dr. Krista L. Lanctôt, PhD

- Pharmacologist, Senior Scientist, Sunnybrook Research Institute; Professor, Departments of Psychiatry and Pharmacology/Toxicology, University of Toronto

Dr. Wade Thompson, PharmD, PhD

- Pharmacist, Assistant Professor, Department of Anesthesiology, Pharmacology, and Therapeutics, Faculty of Medicine, University of British Columbia

People with Lived Experience

Linda Grossman

- Caregiver, Person with Lived and Living Experience

Sogna Stipanov

- Caregiver, Person with Lived and Living Experience

Jori Warren

- Caregiver, Person with Lived and Living Experience

Trainee Contributors

We thank the following trainees for their contribution to guideline preparation:

Dr. Manan Ahuja

Kayla Atchison

Dr. Mohammad Chowdhury

Maya Goerzen

Fardowsa Halane

Dr. Stacey Hatch

Dr. Natasha Lane

Alaia Nazir

Mkeila Sowa

Gavin Thomas

Mark Yassa

BPSD Guideline Project Staff

Jennifer Porter, MPH

- Project Research Assistant, University of Calgary

Expert Reviewers

Kathy Baker, BScN, RN

- Regional Director, Providence Care Community, Seniors Mental Health Behavioral Support Services, Trenton, Ontario

Dr. Rhonda Collins, MD

- Family Physician, Chief Medical Officer, Schlegel Villages

Dr. Vincent Dagenais-Beaulé, PharmD

- Pharmacist, Jewish General Hospital; Visiting Professor, Faculty of Pharmacy, Université de Montréal

Dr. Stewart Hutton, MD

- Family Physician, Calgary, Alberta

Theresa Iwanicki, RN

- Registered Nurse, Calgary, Alberta

Sian Lockwood

- Knowledge Transfer and Exchange Associate, Alzheimer Society of Canada

Dr. Lisa van Bussell, MD

- Geriatric Psychiatrist, St. Joseph's Health Care and Western University, London, Ontario

Dr. Laurence Villeneuve, PhD

- Psychologist, Équipe SCPD CIUSSS Centre-Sud-de-l'Ile-de-Montréal

Abbreviations Used Throughout This Guideline

AD – Alzheimer's disease

BPSD – Behavioural and Psychological Symptoms of Dementia

CI – Confidence interval

CSDD – Cornell Scale for Depression in Dementia

CMAI – Cohen-Mansfield Agitation Inventory

CPG – Clinical Practice Guidelines

DSM – Diagnostic and Statistical Manual of Mental Disorders

IPA – International Psychogeriatric Association

NPI – Neuropsychiatric Inventory

OR – Odds ratio

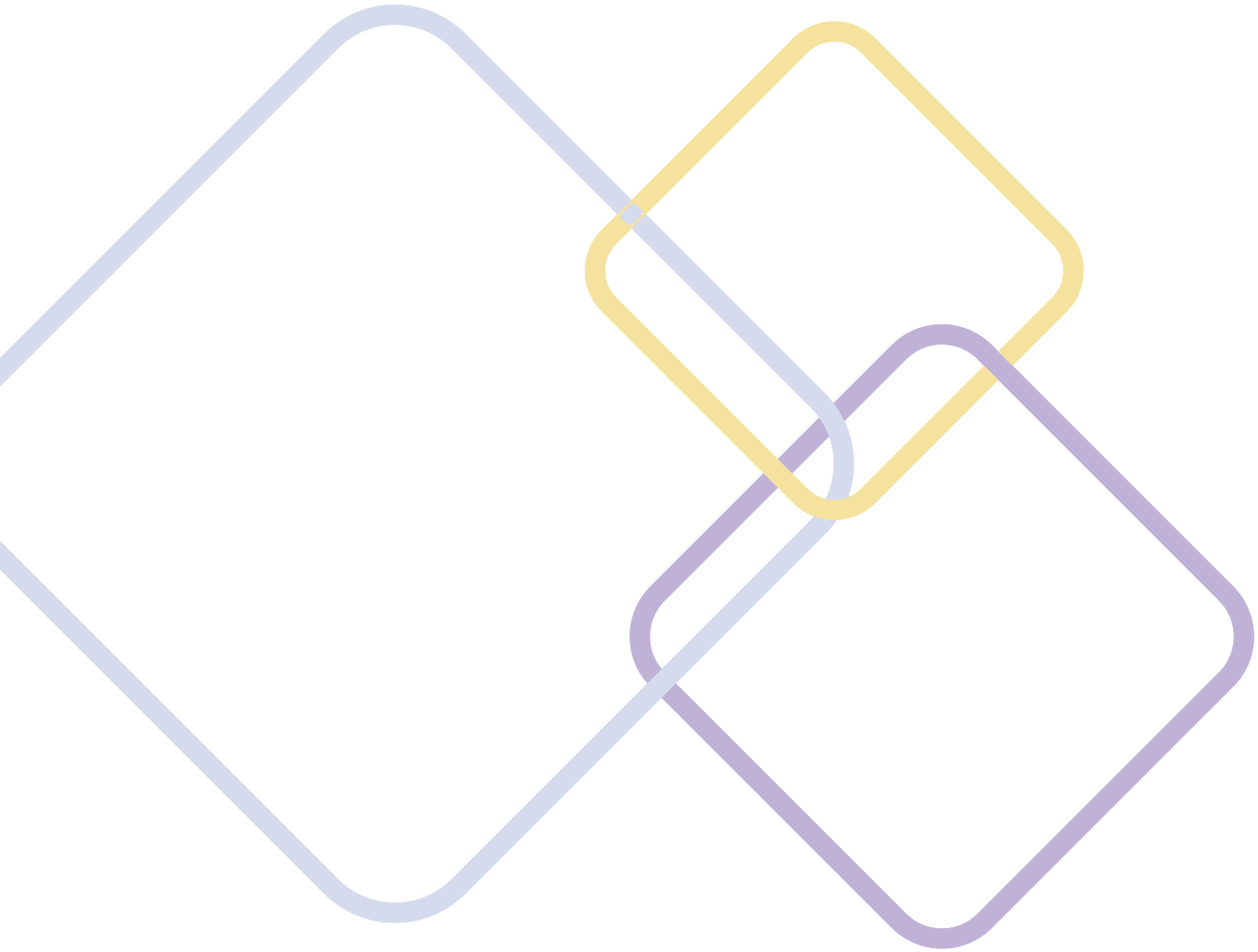
RAID – Rating Anxiety in Dementia

RCT – Randomized controlled trial

SD – Standard deviation

SMD – Standardized mean difference

SASBA – St. Andrew's Sexual Behaviour Assessment Scale



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1. Introduction

More than 55 million people in the world live with dementia, also known as major neurocognitive disorder, and approximately 10 million people are newly diagnosed each year (WHO, 2023). The number of people living with dementia is expected to rise to 131 million by 2050 (Prince et al., 2015). In Canada alone, close to 1 million people will be living with dementia by 2030, with that number expected to increase to 1.7 million people by 2050 (Alzheimer Society of Canada, 2024). Dementia is an umbrella term for several conditions that can affect memory, thinking, behaviour, and the ability to perform activities of daily living (American Psychiatric Association, 2022; Grand, 2011; WHO, 2023). The most frequently diagnosed cause of dementia is Alzheimer's disease dementia, which has been estimated to account for approximately 50% to 70% of cases (Lindeza et al., 2020; WHO, 2023). Other dementias include vascular dementia, mixed dementia, dementia with Lewy bodies, Parkinson's disease dementia, and frontotemporal dementia (Grand, 2011; WHO, 2023). Dementia may also have other causes such as alcohol or substance use disorders, malnutrition, repetitive brain injuries, and other neurological conditions (Grand, 2011; WHO, 2023). Additional risk factors for dementia may include depression, social isolation, low cognitive stimulation, low education and air pollution (WHO, 2023).

Behavioural and psychological symptoms of dementia (BPSD) are non-cognitive symptoms of dementia such as changes to behaviour and mood that frequently occur in all dementias (Grand, 2011; Kwon, 2021). The prevalence of at least one BPSD has been estimated at up to 75% in community-dwelling people living with dementia in cross-sectional studies (Lyketsos et al., 2002) and over 80% among people living with dementia who reside in long-term care (LTC) (Selbaek et al., 2013). The presentation of BPSD varies depending on the type of dementia, requiring management plans to be tailored to the type of BPSD, the frequency, and severity of symptoms (Ismail, 2020; Kazui, 2016; Kim, 2017; Kogan, 2016). Common symptoms of BSPD include agitation, psychosis, depression, anxiety, apathy and changes to sleep and appetite (Cerejeira, 2012; Lyketsos et al., 2002). Many BPSD are more frequent among people living with dementia who have more advanced dementia (Lopez et al., 2003; Siafarikas, 2018). In particular, agitation, irritability and disinhibition may occur more in later stages of dementia (Kazui, 2016). The type of dementia also impacts on BPSD. For example, visual hallucinations are common to dementia with Lewy bodies (Kazui, 2016).

BPSD are associated with poor mental health outcomes for people living with dementia, increased caregiver burden, and decreased quality of life and mental health among caregivers (Cerejeira, 2012; Cummings, 1997; Grand, 2011; Kwon, 2021; Song, 2013). BPSD are associated with more rapid cognitive and physical decline, earlier admission to LTC (Kim et al., 2021; Mintzer et al., 1998; Peters et al., 2015; Toot et al., 2017), and higher mortality for people living with dementia (Bränsvik, 2021). Many common BPSD are also associated with increased costs of informal care and health care costs (Murman et al., 2002; Rattinger et al., 2019).

As there is no single cause for BPSD in any individual, a holistic biopsychosocial approach that seeks to understand BPSD is necessary. BPSD often arise due to the interactions of an individual's biology, their prior life experiences, and current social and physical environment. Appreciation of the complexity of factors contributing to BPSD is required to understand BPSD and develop an effective approach to caring for a person living with dementia experiencing these changes (Cloak, 2022). Some BPSD are associated with biological changes like changes to brain metabolism (Alves, 2017) and alterations of neurotransmitters (Ruthirakuhan, 2018), and this information can provide insights into non-pharmacological and pharmacological treatments. Addressing psychosocial contributors to BPSD, such as the person living with dementia's unmet needs for meaningful activities or interpersonal interactions, can help alleviate BPSD (Wan et al., 2021). The environment can similarly contribute to the development of BPSD and therefore, these contributors should be considered when developing individualized care strategies (Cho, 2021; Kolanowski, 2017; Wan et al., 2021). The early assessment of BPSD is recommended to inform the development of a person-centred care plan for people living with dementia and their caregivers (Cummings, 2023; Kales, 2014; Kales, 2015; Kazui, 2016; Kwon, 2021; Spring, 2024).

The Canadian Coalition for Seniors' Mental Health (CCSMH) BPSD Clinical Practice Guidelines (CPG) provide good practice statements and recommendations on assessing and managing specific BPSD among people living with dementia.

The CPG are intended to:

1. inform shared decision-making among people living with dementia, caregivers of people living with dementia and health care providers (i.e., nurses, family physicians, specialist clinicians, and providers from other health disciplines), in Canada; and,
2. support health care leaders, policymakers and researchers to understand future areas to develop health services and interventions to prevent and reduce BPSD.

2. Guideline Scope

This CPG for assessing and managing BPSD may be applied in community, outpatient, inpatient and long-term care (LTC) and other residential care settings.

In these CPG, five major BPSD have been considered:

1. agitation;
2. psychosis (including delusions and hallucinations);
3. depressive symptoms and depression;
4. anxiety;
5. sexual expressions of potential risk.

Each symptom has a section in the guideline, which includes a definition of the symptom cluster and recommendations for assessing and managing each symptom.

3. Methods

A guideline panel developed the CCSMH CPG to provide guidance on assessing and managing BPSD in the care of people living with dementia within a Canadian context. The guideline panel provided recommendations for the assessment and management of agitation, psychosis, depressive symptoms and depression, anxiety, sexual expressions of potential risk and deprescribing. The CPG provides 11 good practice statements and 63 CPG recommendations for assessing and managing BPSD, including non-pharmacological and pharmacological approaches organized according to BPSD symptom clusters.

The guideline panel followed the Guideline International Network (GIN)-McMaster Guideline Development Checklist in developing the CPG (Qaseem et al., 2012; Schünemann, 2014). The Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework was applied to determine recommendation strength and quality of evidence (Schünemann, 2013).

The relative importance of risks and benefits for each recommendation, in addition to equity, feasibility, and economic considerations was assessed for each recommendation (Brozek, 2009; Schunemann, 2007). Regarding the strength of recommendations, strong recommendations were made if the guideline panel was confident that benefits outweighed potential harms associated with a recommendation. Conditional recommendations were made if the guideline panel felt the benefits probably outweighed potential harms associated with a recommendation. Strong recommendations incorporate "recommend" in the text of the recommendation, whereas conditional recommendations use the term "suggest". No recommendation was made when the guideline panel felt there was insufficient evidence to judge risks and benefits associated with a recommendation statement. Throughout the CPG, the guideline panel attempted to incorporate information about feasibility, equity, patient values and preferences and resource implications with specific reference to Canadian care environments.

The quality of evidence refers to the extent to which confidence in the evidence supports a recommendation, and strength of recommendation refers to the extent that a recommendation will achieve desirable consequences and outweigh risk for the person living with dementia (Brozek, 2009). The GRADE system provides clear criteria for upgrading or downgrading the quality and strength of evidence and ranks quality of evidence as high, moderate, low, or very low (Brozek, 2009). A ranking of high indicates that any future research would be unlikely to establish further confidence in treatment effect; the moderate category indicates that future research could impact confidence in the treatment effect; a low ranking indicates that future research will very likely impact the confidence of a treatment effect; and a ranking of very low evidence suggests that the evidence for a treatment effect is uncertain (Schünemann, 2014).

Creation of the guideline panel and management of conflicts of interest

Following the GIN process (Qaseem et al, 2012), we formed a multidisciplinary panel of 15 experts in the assessment and management of BPSD led by two guideline panel co-chairs. Guideline panel members included representatives from geriatric psychiatry, geriatric medicine, family medicine, pharmacy, psychology, neurology, nursing and pharmacology. Each guideline working group member was offered an honorarium for participating in the CPG development process and conflicts-of-interest statements were completed by panel members at the beginning of the development process and again during the writing stage (Schünemann, 2014). Panel members agreed to terms of reference that included disclosure of all perceived and actual conflicts of interest. Panel members with conflicts of interest participated in panel discussions and voted without restrictions. All panel members completed INGUIDE Level 1: Guideline Group or Panel Member training for participants of guideline panels (INGUIDE, 2023).

The guideline panel met monthly during the guideline development process. Guideline panel members led the development of topics for the CPG and were involved in reviewing evidence from existing guideline evidence, recent systematic reviews, and rapid reviews of evidence to provide evidence for the guideline. Guideline panel members also participated in a Canada-wide prioritization exercise to identify preferred terminology for BPSD and prioritization of topics to include in the CPG. Guideline panel members reviewed and voted on good practice statements and recommendations.

Systematic review of existing guidelines on dementia care describing BPSD assessment and management strategies

The guideline panel conducted a systematic review of existing CPGs on BPSD to synthesize recommendations on BPSD from existing CPGs published between January 1, 2011, and October 13, 2022 (Watt et al., 2024). This review summarized information related to existing BPSD guideline recommendations, identified gaps in guideline topics, and reviewed terminology used to describe BPSD. The review also identified methodological limitations of existing guidelines (Watt et al., 2024). A medical librarian developed the literature search strategy and a second librarian peer-reviewed the strategy. Two independent reviewers completed both title and abstract screening and full-text article screening. Four independent reviewers evaluated the included guidelines using the AGREE II tool (Brouwers et al., 2010). Twenty-three moderate-to-high-quality guidelines were included in the systematic review (Watt et al., 2024). Substantial variability was noted in recommendation statements across CPGs. "BPSD" was identified as the most prevalent term used in 14 CPGs (Watt et al., 2024). This review also identified critical gaps in recommendations, particularly in sexual expressions of potential risk, as well as a lack of consensus in the terminology used in guidelines (Watt et al., 2024 manuscript under review). In addition, much of the evidence in existing guidelines includes older evidence which may not be relevant for current clinical practice.

Clinical practice guideline topic prioritization exercises

A Canada-wide prioritization exercise was conducted from February to March 2023 to identify topics of interest for the CCSMH CPG for assessing and managing BPSD. Responses were received from 254 individuals including health care providers, people living with dementia, caregivers of people living with dementia, managers, and policymakers. They prioritized preferred language to describe behaviours in dementia. The survey respondents identified BPSD as the preferred title for the CPG from several potential options which included neuropsychiatric symptoms, responsive behaviours, and others.

Additional topics addressed in the survey included best approaches to managing BPSD; detection of prodromal symptoms and effective approaches to screening for BPSD; identification of effective non-pharmacological and pharmacological interventions; and training or capacity building in caregivers and health care providers. A thematic analysis of the open-text section of the survey was conducted to identify common themes for free-text responses. Guideline panel members also voted on specific BPSD symptoms and topics that were to be prioritized as topics for the CCSMH CPG. All BPSD syndromes and topic areas were prioritized as either "critical" or "important but not critical".

BPSD that had a median rating above the critical importance threshold included agitation, psychosis, depression, anxiety, and sexual expressions of potential risk. Within these topic areas the following questions were developed:

1. What are the best reference standard criteria for diagnosing specific BPSD or BPSD syndromes among people living with dementia?
2. What tools have the best diagnostic test accuracy for assessing these BPSD among people living with dementia compared to a reference standard?
3. What is the effectiveness and safety of non-pharmacologic and pharmacological interventions for managing these BPSD in people living with dementia?

Throughout the CPG, recommendations are provided on the suggested diagnostic criteria for the BPSD syndrome, tools that may be considered for the detection of symptoms, and management strategies categorized as non-pharmacological and pharmacological. The term "management" was used in recommendations related to non-pharmacological strategies and "treatment" for pharmacological strategies. The guideline panel acknowledges that the majority of recommendations related to pharmacological treatment for BPSD refer to treatments that are ***not*** Health Canada approved for treatment of BPSD, unless stated as such in the CPG. The evidence supporting recommendations is presented by setting, including primary care, tertiary or specialty care, or LTC where this information is available.

In addition to the guideline recommendations related to BPSD, an additional topic area related to deprescribing medications was identified in the survey. The topic of deprescribing was also rated as high priority by our guideline panel. The deprescribing section of the CPG addressed the following guideline questions:

1. Which medications prescribed for the management of BPSD should be considered for deprescribing?
2. What are clinical factors that should be considered when deciding whether to deprescribe medications used for BPSD or not?
3. What are the organizational approaches that have been found to be effective in supporting deprescribing?

Rapid overview of systematic reviews on BPSD assessment and management

A rapid overview of systematic reviews (CRD42023437242) was undertaken to identify systematic reviews conducted since 2017 relevant to the CCSMH CPG development. This review included studies describing: (1) the effectiveness and safety of non-pharmacologic and pharmacologic interventions for reducing symptoms of agitation, psychosis, depression, anxiety and sexual expressions of potential risk; and, (2) the diagnostic test accuracy of tools for assessing agitation, depression, anxiety, psychosis, and sexual expressions of potential risk in people living with dementia. An experienced librarian developed a literature search strategy and a second librarian peer-reviewed the strategy. Two independent

reviewers screened all (1) titles and abstracts and (2) full-text articles. A single reviewer appraised each systematic review with the AMSTAR 2 tool (Shea, 2017). A single reviewer extracted data from 246 systematic reviews to inform CCSMH CPG recommendations. The results of this rapid overview of systematic reviews were used to identify evidence for recommendations related to agitation, psychosis, depression, anxiety and deprescribing.

Rapid review of non-pharmacological and pharmacological interventions for reducing sexual expressions of potential risk in people living with dementia

No systematic reviews on the treatment of sexual expressions of potential risk were identified in the rapid overview of systematic reviews although one scoping review was identified on pharmacological management of sexual expressions of potential risk (Klindrat, 2023). Therefore, a separate rapid review on this topic was undertaken to review studies reporting the effectiveness and safety of non-pharmacologic and pharmacologic interventions for reducing sexual expressions of potential risk in people living with dementia (CRD42023469625) (Lane, et al., In Preparation). An experienced librarian developed the literature search strategy and a second librarian peer-reviewed the strategy. Two independent reviewers screened all (1) titles and abstracts and (2) full-text articles. One reviewer abstracted data from included studies and appraised study quality with the JBI tools for case reports and case series (Moola et al., 2017). The search retrieved only case reports and case series.

Guideline recommendation development process

Topic working group leads developed the CCSMH CPG recommendations, including the assignment of preliminary strength of each recommendation and quality of evidence. CPG topic working groups revised draft recommendations, which were presented to and voted on by the full CPG working group panel at a hybrid in-person and virtual meeting held on November 1, 2023, in Toronto, Canada. The voting process for each recommendation consisted of a review of evidence-to-decision tables informing the strength and quality of evidence for each recommendation, a review and discussion of each recommendation, and voting by guideline panel members. Additional voting occurred during virtual meetings on November 27, 2023, for recommendations that were not voted on during the initial meeting and any recommendations that required revisions. Recommendations were revised by the CPG co-chairs based on discussions with guideline panel members, which provided an opportunity to modify recommendations based on group discussion prior to voting. Recommendations were approved if at least 80% of guideline panel members voted in favour of the recommendation. Recommendations were shared with external reviewers and people with lived experience of dementia for additional feedback.

Process for updating the CCSMH BPSD CPG

Updating outdated recommendations within the CPG is anticipated in three to four years. The CCMSH will re-survey health care providers, people living with dementia, and care partners of people living with dementia to identify new priorities for CPG recommendations. Key informants (e.g., clinical experts, researchers, and people with lived experience of dementia) will be asked about key evidence developments in the field. Of note, although apathy and sleep disturbances were not identified as critical outcomes during the CPG development prioritization process, stakeholders later voiced their concern about the omission of recommendations for these two symptoms in the current CPG. Recommendations on these topics could not be included at the current time because of resource constraints, but the feasibility of including these (and potentially other) BPSD in future CPG updates will be revisited. The CCSMH will also make recommendations on how to support caregivers of people living with dementia in a future CPG iteration. The rapid overview of systematic reviews will be updated to identify recent and relevant literature to inform recommendations and conduct new reviews where relevant reviews could not be found.

Knowledge mobilization strategy and barriers to CPG implementation

The BPSD CPG will be hosted on the CCSMH website, which will also include information on resources relevant to the assessment and management of BPSD. The following user metrics will be collected from the CCSMH website: number of users; session length; resources accessed; and approximate geolocation of users. Knowledge mobilization strategies include English and French language webinars, presentations at related scientific conferences, and publications in academic journals. The CCSMH developed the Behaviours in Dementia online toolkit, which contains over 280 free resources for health care providers and care partners to help them better understand, assess and compassionately respond to dementia-related changes in mood and behaviour, and for people with lived experience of dementia. (*www.behavioursindementia.ca*). The toolkit was developed with leadership from an interdisciplinary working group in consultation with individual stakeholders, focus groups, a usability study, and a webinar. A post-launch evaluation of this toolkit will be conducted. As adherence to clinical practice guidelines improves outcomes for patients (Aakhus et al. 2015), a scoping review was conducted to inform knowledge mobilization of our CPG (*https://doi.org/10.17605/OSF.IO/VXRZM*).

4. General Principles for Assessing and Managing BPSD Good Practice Statements

Good Practice Statement #1

Provide health care providers and caregivers with the education and organizational system of support needed to implement a structured approach for assessing and managing BPSD.

A critical component to the effective assessment and management of BPSD involves the development of organizational systems to address the educational needs of caregivers and health care providers to develop skills needed to implement structured approaches to BPSD care. Examples of these approaches include the PIECES approach™ (PIECES Canada, 2020), U-first!® (Alzheimer Society of Ontario, 2024), The DICE Approach™ (Kales et al., 2014; Kales et al., 2015), and the approach proposed in the International Psychogeriatrics Association (IPA) consensus algorithm for the prevention and reduction of agitation (Cummings et al., 2023).

Providing education to friend and family caregivers and health care providers is effective in reducing BPSD and improving caregiver outcomes (Savaskan et al., 2014). Programs providing psychoeducation about dementia, along with skills training in behavioural strategies and problem-solving are key components of most educational programs (Poon, 2022). The development of comprehensive educational programs at the level of individual organizations and practice settings should include adequate training for all health care providers who are supporting people living with dementia on how to conduct structured approaches to the assessment and treatment of BPSD. Aligning organizational values and processes to facilitate the integration of these approaches in care settings, such as providing adequate time and support to participate in training, is critical to a successful implementation (Grinspun, 2016).

The guideline panel recognizes that developing organizational systems of support required to implement best practices in the assessment and management of BPSD involves additional time for health care providers who are currently working in resource constrained environments. Building capacity by identifying and supporting champions within the organization can help support implementation and sustainability of educational efforts (Grinspun, 2016; Lee et al., 2018). Educational organizations including colleges and universities involved in the training of health care providers should also ensure that educational curricula incorporate appropriate education related to the care of people with dementia, including training on the assessment and management of BPSD.

Good Practice Statement #2

Obtain informed consent for the assessment and management of BPSD.

Supporting the person living with dementia to make voluntary choices about their health is fundamental in respecting their autonomy and underpins collaborative decision making between the person living with dementia, their caregivers, and health care providers involved in their care (Faden, 1986). Informed consent related to the assessment and management of BPSD and other decisions is defined as the person's ability to understand and appreciate the importance of information; reasonably use the information for decision making; and, express choices (Dunn et al., 2006; Karlawish et al., 2013; Lai, 2007; Marson et al., 1994). Capacity to consent to decisions is assumed for all individuals unless a determination of incapacity is made. The guideline panel concluded that the capacity to consent should be assumed to be present at the initial evaluation of BPSD unless the person living with dementia has been deemed to lack capacity for a specific decision during previous assessments.

Prior to discussing any health care decision with any person living with dementia, capacity to consent should be evaluated by the clinicians involved. While capacity may become progressively impaired with neurodegenerative dementias, the capacity to make certain decisions about health care may remain intact for prolonged periods of time (Lai & Karlawish, 2007). Decision-making capacity will need to be evaluated over time for people living with dementia using both clinical assessment and possibly formal-capacity evaluation tools.

Capacity to consent is most commonly evaluated in clinical care through verbal discussions between the person living with dementia and the health care provider proposing the health care assessment or treatment. There are also more formal tools that can be used to assist with assessments related to decision-making capacity (Amaral, 2022). The MacArthur Competence Assessment Tool (MacCAT-T) has been validated for use with people with dementia to determine capacity to consent (Amaral, 2022; Grisso & Appelbaum, 1998). The MacCAT-T is a semi-structured interview that requires 15-20 minutes to administer and measures outcomes of understanding, reasoning, and ability to express choice (Grisso & Appelbaum, 1998; Prusaczyk et al., 2017). If a person living with dementia is deemed to be incapable of making specific decisions related to the assessment or management of BPSD, informed consent should be obtained from their substitute decision maker. These discussions with the substitute decision maker should continue to engage the person living with dementia in decision-making discussions even if the person living with

dementia is incapable. This good practice statement endorses periodically reevaluating capacity and ability of the person living with dementia to provide informed consent, based on the clinical judgement of the health care provider.

Good Practice Statement #3

Incorporate information about the values, goals of care, and advance wishes of the person living with dementia in assessing and managing BPSD.

Understanding the values, preferences, goals of care, and advance wishes concerning the assessment and management of BPSD is critical to the coordination of care for the person living with dementia. Health care providers should offer opportunities to develop advanced care statements reflecting the person living with dementia's beliefs and preferences for current goals and future care (NICE, 2018). Health care providers can support the person living with dementia in identifying family members or other people who are aware of the goals and preferences of the person living with dementia as decision makers in advance care planning. Advanced care planning includes incorporating information such as how and where the person living with dementia would like to receive care if they are unable to remain at home, as well as details about their desires related to transfer to inpatient or other acute care settings.

Health care providers should ensure that values and goals for care are discussed when dementia is diagnosed and support people living with dementia and caregivers understand that their roles in decision making may change over time due to progressive changes related to dementia. These changes result in caregivers often having to assume an increasing role in decision making for the person living with dementia (Callahan, 2017; Edvardsson, 2015). Health care providers may need to alter clinical appointments to facilitate these discussions, including setting aside adequate time for the discussions, incorporating caregivers in clinical appointments, and communicating with other health care providers who will be involved in ongoing care and support (Callahan, 2017; Edvardsson, 2015; NICE, 2018). Providing information about dementia-friendly organizations and initiatives will help to provide support for people living with dementia in alignment with their values (Ismail, 2020). Health care providers should create opportunities for open and sensitive communication to understand the personal beliefs, goals for treatment, and advanced care plans for the person living with dementia to ensure they receive the care they prefer even when they may no longer be able to express values and preferences themselves (Callahan, 2017; Edvardsson, 2015; Jeon, 2013; NICE, 2023).

Dementia care also needs to address the palliative care needs for people living with dementia and incorporate the wishes related to palliative care outlined in advanced care plans and goals of care (Timmons, 2022). The palliative approach to care aims to improve the quality of life of people living with dementia, by prevention and relief of suffering through the early identification, assessment and treatment of physical, psychosocial and spiritual needs. Behavioural changes such as agitation are common among people with advanced dementia who are nearing end-of-life along with other distressing symptoms such as pain and dyspnea. The goals of managing BPSD for people at the end of life may differ from the management of these symptoms at less advanced stages of dementia. Providing timely and comprehensive palliative care services is an integral part of caring for people with dementia, particularly those with advanced dementia who may be nearing the end of life.

The Alzheimer Society of Canada (Alzheimer Society of Canada, 2024a) and Advanced Care Planning Canada (Advance Care Planning Canada, 2024) have developed resources to assist with advance care planning, including resources specific to different Canadian provinces.

Good Practice Statement #4

Review the underlying etiology of dementia, stage of dementia (mild, moderate, advanced), and the specific BPSD of concern, including the frequency, duration, severity and any associated risks when assessing BPSD.

The underlying etiology and stage of dementia along with BPSD severity is critical to the assessment of BPSD. When assessing people living with dementia experiencing BPSD, it is important to confirm the etiology of dementia through interviews with the person living with dementia, caregiver and health care provider informants, and include a review of prior health records and evaluations completed to date (e.g., cognitive testing, neuroimaging). If the etiology of dementia is unclear, current providers should obtain further history and investigations as needed to clarify the etiology.

Understanding the etiology, or likely causes of dementia, in an individual is important. Different BPSD may be more or less common in different types of dementia (Mukherjee, et al., 2017; Schwertner et al., 2022). Some treatments for BPSD vary in safety and effectiveness with different underlying causes of dementia. Different types of dementia can also influence prognosis and inform future planning for the person living with dementia (Liang et al., 2021). The majority of people living with dementia will have underlying Alzheimer's disease, vascular cognitive impairment, or mixed dementias which are often approached similarly in terms of assessing and managing BPSD. Particular attention should be given to distinguishing these types of dementia from other causes such as frontotemporal dementia, dementia with Lewy bodies or Parkinson's disease dementia, which have management strategies that differ from the strategies used for Alzheimer's disease and related dementias.

Understanding the stage or severity of dementia is important when identifying potential contributors to BPSD. Knowing the stage of dementia, and thus the person's abilities and limitations, will also inform the identification of effective psychosocial strategies. Similarly, some pharmacological treatments may vary in effectiveness depending on the stage of dementia. The severity of dementia can be assessed using validated brief cognitive evaluations combined with assessments of function (Tang-Wai et al., 2020).

Acknowledging the heterogeneity of specific BPSD along with the variation in the severity of BPSD within specific symptoms or syndromes, BPSD assessment should also incorporate assessments of BPSD severity. A suggested approach to categorizing BPSD severity follows:

- **Mild BPSD:** 1) BPSD cause minimal to no disruption in the environment; 2) BPSD are associated with minimal distress to the person living with dementia; and, 3) symptoms are intermittent or easily modified by psychosocial approaches.
- **Moderate BPSD:** 1) BPSD cause some disruption to the environment; 2) BPSD are associated with moderate distress for the person living with dementia; or, 3) symptoms are difficult to modify with psychosocial approaches.
- **Severe BPSD:** 1) BPSD are associated with a risk of harm to the person living with dementia or others; 2) BPSD are associated with severe and frequent disruption to the environment; 3) BPSD are associated with severe distress to the person living with dementia; and, 4) minimal or no modification with psychosocial approaches alone.

The guideline panel acknowledges that often assessments of the severity of BPSD in routine clinical practice are subjective, and therefore suggested an approach to categorizing BPSD severity that is intended to guide discussions regarding the potential risks and benefits related to specific management decisions. When assessing people living with dementia for overall BPSD, symptoms tools such as the Behavioural Supports Ontario–Dementia Observation System (BSO-DOS©) (Behavioural Supports Ontario, 2019a) or Neuropsychiatric Inventory (NPI) could be used. For specific BPSD and BPSD syndromes included in this CPG, assessment tools are discussed in the relevant guideline sections.

Good Practice Statement #5

Conduct a thorough evaluation of potential biological contributors to BPSD, including an assessment for delirium, a general medical and mental health history, pain, medication review, substance use, hearing and vision assessment, and other contributors.

Several factors often contribute to the development of BPSD in a person living with dementia. It can be helpful to categorize factors contributing to BPSD to facilitate a comprehensive and holistic review of contributors to BPSD. Some ways of categorizing contributors or causes of BPSD include reviewing contributors that may be related to the person living with dementia, caregivers, and the environment (Kales et al., 2015) or factors that may be predisposing, perpetuating, and protective (Watt, 2022). The guideline panel recommends that the assessment of BPSD include an evaluation of ***biological*** contributors, understanding the ***personhood*** of the person living with dementia, and identification of ***psychosocial or environmental*** factors contributing to BPSD. Structured approaches to investigating potential contributors to BPSD include the PIECES approach™ (PIECES Canada, 2020), The DICE Approach™ (Kales et al., 2014; Kales et al., 2015), or the IPA Approach (Investigate, Plan and Assess) proposed in the International Psychogeriatrics Association agitation treatment algorithm (Cummings et al., 2023).

A detailed medical history should be conducted to understand potential contributors to BPSD and identify possible medical causes of behavioural changes such as delirium. A first step in BPSD evaluation should include assessment and investigations if needed to rule out delirium as a cause of behavioural or psychological changes that could be mistakenly diagnosed as BPSD. People living with dementia are at higher risk than the general population for developing delirium (Fong, 2022). Delirium and BPSD may at times be mistaken for each other as delirium may present as a change in behaviour such as acute onset of psychotic symptoms or changes in mood (Canadian Coalition for Seniors Mental Health, 2014; Scottish Intercollegiate Guidelines Network, 2019). Investigations such as blood work or neuroimaging may be indicated in the evaluation of delirium, with the selection of investigations being determined by presenting symptoms and history (Laver, 2016; Scottish Intercollegiate Guidelines Network, 2019). A review of sleep patterns including potential sleep deprivation and sleep disorders should be completed as part of the general medical review. A detailed mental health history of the person living with dementia is important in determining whether psychiatric symptoms may be attributed to dementia or any other psychiatric disorder (Calsolaro, 2019).

After assessing and optimizing management of general medical and mental health conditions, clinical evaluations should be undertaken to identify and remove potential causes of pain or discomfort, which may be identified as unmet needs contributing to BPSD. This should include a review of potential painful health conditions (e.g., arthritis or acute injury) and optimizing pain management for these conditions (Achterberg, 2020). Addressing pain can help decrease some BPSD such as agitation (Husebo, 2014). Assessment of pain in dementia should incorporate tools which are validated for assessing pain in people living with dementia (Hadjistavropoulos, 2014) and other contributors such as thirst and hunger, and a review of bowel and bladder function, including how functional status or severity of dementia may affect these factors (Kales, 2014). A review of medications should be undertaken with a focus on identifying potentially inappropriate medications, those that may impair cognition or without a clear indication (American Geriatrics Society, 2019;

O'Mahony et al., 2020). In addition to prescribed medications, a review of over-the-counter medications, natural health products, and substance use such as alcohol, nicotine or cannabis should be completed. A review of sensory changes such as visual and hearing impairment, along with ensuring the use of eyeglasses or hearing aids, should be undertaken (Kales, 2014), as sensory impairment can contribute to the development of BPSD (e.g., auditory or visual hallucinations) and also provide barriers to providing psychosocial interventions to manage BPSD.

Good Practice Statement #6

Conduct a thorough review of the personhood of the person living with dementia, including sex, gender, sexual orientation, language, race, ethnicity, cultural background, trauma history, religious or spiritual beliefs, and other factors when attempting to understand contributors to BPSD, and to inform assessment and management.

The concept of personhood recognizes that every person possesses a distinct identity and acknowledges the inherent value, dignity, and humanity for all people living with dementia (Frank et al., 2020; Kim et al., 2021). It is important to understand that current responses to the environment are influenced by personal history and background of the person living with dementia (Cloak & Al Khalili, 2022). BPSD are influenced by broader intergenerational and social differences including trauma associated with experiences of poverty, war, racism, and sexual or gender discrimination (Ward, 2016; Morais, 2021). The experiences a person living with dementia may have related to equity, diversity, and inclusion are important to providing context to potential factors contributing to the development of BPSD (Morais, 2021; Ward, 2016). A thorough review of these factors will help to inform a person-centred and culturally appropriate treatment plan (Vila-Castelar, 2022).

Sex, gender, language, and cultural background are known to influence the experiences of people living with dementia including BPSD (Alzheimer Society of Canada, 2024b). Women living with dementia may experience significantly higher rates of symptoms of anxiety and depression as compared to men (Lee, et al., 2017; Lövheim et al., 2009), while men may exhibit irritability and agitation (Lee, et al., 2017; Tatsuru, 2012; Lövheim et al., 2009). Health care providers should seek to understand the potential impact of gender and nonbinary gender identities of people living with dementia related to care (Hunter, 2016). For example, people living with dementia from sexual minorities may be more socially isolated or estranged from their families of origin (Fredriksen-Goldsen, 2018). Many people who self-identify as lesbian, gay, trans, bisexual, queer, two-spirit, intersex or asexual (also referred to as 2SLGBTQI+) may have experienced traumatic early life events, which need to be considered during BPSD assessments.

Language can impact both the expression of BPSD and the strategies used to assess and manage them. When language differences between the person living with dementia and health care providers present a barrier to communication, professional medical translators should be engaged where available to support communication (Brijnath, 2023; Dilworth-Anderson, 2011; Hughson et al., 2016; Stone, 2008). Cultural background comprises a set of beliefs, values, traditions and styles of living shared by specific groups of individuals and is key to knowing the personhood of the person living with dementia (Vila-Castelar, 2022). Culture can play an important role in how BPSD are perceived, and sometimes stigma associated with dementia or mental health disorders can contribute to delays in seeking health care (Vila-Castelar, 2022). Other factors to consider when assessing personhood include early life experiences, family relationships, education, religion and spirituality, and preferred hobbies and activities.

The *"All About Me"* resource created by the Alzheimer Society of Canada can help people living with dementia share information about their personhood and guide discussions about personhood that will help guide BPSD assessment and management with their health care providers (Alzheimer Society of Canada, 2024c).

Good Practice Statement #7

Conduct a thorough review of psychosocial and environmental contributors to BPSD.

Psychosocial and environmental factors can play an important role in the development of BPSD (Kales, 2014; Watt, 2022; Jao, 2015). A thorough review of these contributors is essential for identifying possible interventions, such as education or training for caregivers or health care providers who are supporting the person living with dementia, or to identify potential changes to the physical environment to address BPSD (Wan et al., 2021).

Responsibility for most of the care needs of people living with dementia rests with family caregivers. This can contribute to caregiver stress and result in interpersonal relationship strain, particularly when the person living with dementia also has significant BPSD (Kim et al., 2021). Caregiving can be increasingly challenging when dementia is at a more advanced stage and caregivers are required to increase their supports for activities of daily living, and where language abilities become more impaired in the person living with dementia (Brodaty, 2009; Jao, 2015; Kim et al., 2017; Kim, 2012; Kwon, 2013; Song, 2013; Wan et al., 2021). Supporting caregivers to incorporate communication strategies with the person living with dementia using positive emotions, reframing BPSD so that caregivers do not take them personally, and providing direction to not directly confront or challenge the person living with dementia who is experiencing BPSD may help foster more positive communication and reduce psychosocial contributors to BPSD (Wan et al., 2021). Assessing the extent to which caregivers

are experiencing stress in their role is also important to supporting caregivers and the person living with dementia. If significant caregiver stress or emotional distress is identified in caregivers, they should be offered both psychoeducation about dementia and psychological psychotherapy to address their distress (Cheng et al., 2020). A home environment that offers privacy, social interactions, and appropriate levels of cognitive and sensory stimulation also may help to minimize BPSD (Cho, 2021; Wan et al., 2021). Providing caregivers with guidance on how to best support the person living with dementia at different stages of dementia, including aligning caregiver expectations with the functional abilities and strengths of the person living with dementia, can also help reduce BPSD (Kales, 2014; Kales, 2015). Similar principles around communication and attitudes related to BPSD apply to supporting health care providers involved in the care of people living with dementia.

A review of environmental contributors should include aspects related to the physical environment such as the presence of environmental cues or supports that may help reduce frustration for the person living with dementia and promote independent function. Environmental temperature should be reviewed as part of potential source of discomfort as well as lighting which may influence sleep-wake cycles. An environmental review should seek to identify and address potentially unmet needs and modifiable environmental factors. Overall levels of noise and environmental stimulation should be reviewed as both under- and over-stimulating environments may contribute to BPSD (Kales, 2015). Behavioural charting that includes the environmental and psychosocial context using tools such as the BSO-DOS© (Behavioural Supports Ontario, 2024) can help identify patterns of BPSD that are related to these contextual factors and help identify environmental or interpersonal strategies to address BPSD.

Good Practice Statement #8

Use person-centred language and incorporate specific descriptions of the BPSD using language appropriate for the intended audiences when communicating with people living with dementia, caregivers, or health care providers.

The guideline panel acknowledges there are many different terms used to describe changes in behaviour in the person living with dementia other than BPSD, such as: 'challenging behaviour', 'responsive behaviours', 'behaviours of concern', 'reactive behaviours', or 'personal expressions', among others. No single term has been agreed upon by all groups. Some people with dementia may view some of these terms as stigmatizing and harmful. To support a person-centred approach, where possible, ask the person living with dementia (or their caregiver), how they would prefer their experiences be described.

Incorporating person-centred language in communicating about BPSD can help reduce stigma and enable respectful and supportive approaches to the person living with dementia and their caregivers. Health care providers should collaboratively assess and develop management plans for BPSD with the person living with dementia, caregivers, and interdisciplinary health care providers. Using person-centred language in these management plans, and intentionally selecting language that appropriately and respectfully describes BPSD, should be tailored to the background of the individual receiving the information. Health care providers should seek to use language appropriate for the cultural identity or person living with dementia and strive to select terms that will not be offensive or insensitive to the person living with dementia (Alzheimer Society of Canada, 2017). Choice of language when describing BPSD can contribute to stigma, which impedes a person living with dementia and their caregivers from seeking out support. In contrast, thoughtful communication incorporating supportive and culturally appropriate language can help develop trust and improve outcomes for people living with dementia and caregivers (Brijnath, 2022). Health care providers should offer information to the person living with dementia and their caregivers relevant to the stage of dementia and use diverse methods of communicating such as appropriate language, providing information in plain language, or using visual aids (NICE, 2018).

Providing clear descriptions of BPSD can help prevent stigma and encourage reflection on the potential meaning behind behaviours (Regional Geriatric Program of Ontario, 2017). Maintaining awareness and avoidance of negative labelling of behaviours in dementia by health care providers may have several benefits, including: 1) rejecting a culture of blaming the person living with dementia for their behaviours; 2) supporting the recognition that the person living with dementia still retains personhood; and, 3) reducing the possibility of creating a medical power hierarchy (Edvardsson, 2015; Regional Geriatric Program of Ontario, 2017; Spring, et al., 2024). The Alzheimer Society of Canada and other organizations have developed resources to support person-centred language for use with people living with dementia (Alzheimer Society of Canada, 2017; Behavioural Supports Ontario, 2021; Regional Geriatric Program of Ontario, 2017).

Good Practice Statement #9

Psychosocial interventions are recommended for all BPSD, either alone or in combination with pharmacological treatments.

Health care providers should implement psychosocial interventions for all BPSD, with specific interventions being guided by a comprehensive assessment of the person living with dementia and factors contributing to BPSD. Psychosocial approaches have a strong evidence base for many BPSD as outlined in other sections of this CPG (Brodaty, 2012, Kales, 2015; Watt, 2020; Watt, 2021). The selection of specific

psychosocial approaches for a person living with dementia should take into account the specific BPSD, the background of the person living with dementia, the context of the BPSD as determined through a holistic person-centred BPSD assessment, and the availability of psychosocial interventions (Montgomery et al., 2017; Dyer, 2016).

Examples of evidence-based psychosocial interventions include training and approaches to care involving health care providers or caregivers, psychotherapies adapted for the person living with dementia, exercise, sensory-based approaches (e.g., aromatherapy, massage), and other interventions like music or animal-assisted therapy (see subsequent sections of the guideline). Prioritizing the psychosocial approaches to BPSD that are best suited to the background and strengths of the person living with dementia is more likely to be effective and supports the personhood of the person living with dementia. Implementation of multiple psychosocial interventions may be the most effective strategy to reduce BPSD. The psychosocial interventions used to support each person living with dementia may differ over time due to changes to the interests, abilities and availability of resources in the environment of the person living with dementia. While there are few direct comparisons between psychosocial interventions and pharmacological interventions, evidence suggests that psychosocial interventions are generally safe and have efficacy similar to or greater than the effects observed with pharmacological treatments for BPSD (Watt; 2019; Watt, 2021). People living with dementia and caregivers prioritize psychosocial approaches to dementia care when identifying their preferences for supports related to dementia (Wammes, 2021; Wehrmann, 2021).

Good Practice Statement #10

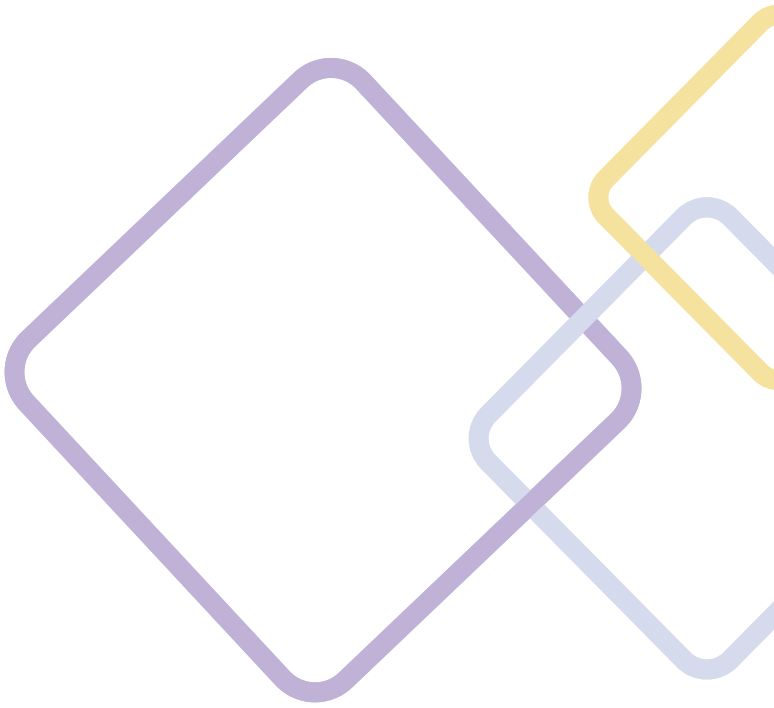
Select and tailor interventions that are likely to be safe and effective for the specific BPSD and avoid treatments that are neither safe nor effective.

Interventions have the potential to cause harm or to be ineffective. Careful consideration of both the possible benefits and the potential harms in managing BPSD is therefore required (NICE, 2023). The risks and benefits of implementing or not implementing a specific intervention depends on the level of severity and risks associated with each specific BPSD. Health care providers should identify the severity and risks associated with BPSD as the effectiveness of interventions may vary by degree of severity. The guideline panel recommends ensuring the careful selection and tailoring of interventions that are based on the assessment of biological, personhood and environmental factors to provide individualized, safe and effective care plans for specific BPSD. Sections of this CPG outline the safety and efficacy of interventions for specific BPSD to guide clinicians in the selection of interventions.

Good Practice Statement #11

Routinely assess the effectiveness of the BPSD management plan and evaluate the plan to consider adjusting, changing or discontinuing strategies as appropriate.

The effectiveness of management plans for BPSD should be routinely assessed at regular intervals. BPSD may change over time due to the progressive nature of dementia; the risks of treatments may be altered by changes to medical status; and changes in the care environment may influence the risks and benefits of ongoing treatment. Routine assessments should include a thorough review of current symptoms and any changes in BPSD, as well as the person with dementia's response to management strategies, to inform possible changes to the care plan (Laver, 2016, Brecher, 2016; Frederiksen, 2020; Tavassoli, 2013, Lee et al., 2022). Employing the same tools used in initial assessments in follow-up assessments can be helpful to monitor changes in BPSD more reliably over time. Management plans may be updated after each assessment based on new findings and the changing care needs of the person living with dementia.



5. Recommendations for Assessing and Managing Agitation in Dementia

Agitation is one of the most common BPSD and can be among the most challenging to assess and manage (Anatchkova, 2019). This section presents recommendations related to the diagnosis, assessment and management of agitation in dementia with a focus on Alzheimer's disease and related dementias. Clinical considerations for other types of dementia such as dementia with Lewy bodies, Parkinson's disease dementia and frontotemporal dementia are beyond the scope of this CPG and require different clinical considerations related to assessment and management.

Recommendation #1

We recommend the International Psychogeriatrics Association (IPA) consensus criteria for agitation in cognitive disorders to diagnose agitation in dementia. (Strong recommendation, moderate-quality evidence)

Efforts have been made to clarify and standardize the definition of agitation as a BPSD syndrome to facilitate research and clinical management of BPSD. This attempts to distinguish between behaviours that are BPSD, which may require specific assessment and management, and other behaviours that may be normal or adaptive behaviours for a person living with dementia.

The IPA created provisional criteria for agitation in neurocognitive disorders (Cummings et al., 2015) that are now accepted as the IPA consensus clinical and research definition for agitation in cognitive disorders (Sano et al., 2023). These criteria define agitation in cognitive disorders as having the following characteristics: A) an individual meets diagnostic criteria for cognitive impairment or a dementia syndrome; B) the individual expresses behaviours that are associated with observed or inferred distress, present for a minimum of two weeks or that are a significant change from their usual behaviour, which includes one or more of excessive motor activity, verbal aggression or physical aggression; C) the behaviours cause excess distress and disability beyond what would be anticipated for the cognitive disorder, including impacts on relationships, social functioning or ability to perform independent activities; and, D) symptoms are not due to other psychiatric, general medical conditions, delirium, the care environment or substances.

These criteria were developed by a consensus process with BPSD clinical and research experts and have been incorporated into recent clinical trials for the treatment of agitation. The guideline panel anticipates that these criteria will be used widely in the future for research and clinical care of individuals experiencing agitation. Given the relatively recent development of the IPA agitation criteria, however, much of the research evidence related to agitation in the CCSMH BPSD guideline has not used these clinical criteria.

The guideline panel acknowledges that while there are potential benefits associated with adopting these criteria, there are also concerns regarding potential harms associated with adopting this definition. A dissenting opinion from the guideline panel (D.H.C.) raised concerns about the implications of adopting this definition, and in general to the diagnosis of behaviours as "agitation" which was also raised by an external reviewer that was a person with lived experience (see full dissenting statement in the ***Appendix***).

Recommendation #2

We suggest the Neurobehavioral Rating Scale (NBRS), Empirical Behavioral Rating Scale (E-BEHAVE-AD), Neuropsychiatric Inventory-Agitation (NPI-Agitation), Spanish NPI-Agitation, French version of the Rating Scale for Aggressive Behaviour in the Elderly (F-RAGE) or Psychogeriatric Assessment Scale (PAS) for detecting agitation in dementia in specialty clinics. (Conditional recommendation, low-quality evidence)

and

We suggest the Neurobehavioral Rating Scale (NBRS), Empirical Behavioral Rating Scale (E-BEHAVE-AD), Neuropsychiatric Inventory-Agitation (NPI-Agitation), Spanish NPI-Agitation, French version of the Rating Scale for Aggressive Behaviour in the Elderly (F-RAGE), Cohen Mansfield Agitation Inventory (CMAI), or Psychogeriatric Assessment Scale (PAS) for detecting agitation in dementia in primary care or long-term care. (Conditional recommendation, very low-quality evidence)

and

We suggest the Cohen Mansfield Agitation Inventory (CMAI) for detecting agitation in dementia in primary care, specialty clinics, and long-term care. (Conditional recommendation, very low-quality evidence)

The guideline panel completed a systematic review of tools to detect symptoms of agitation or aggression, as per IPA criteria. Studies that compared these tools to reference standards, such as clinician assessment or other tools, which

included people living with dementia, and reported measures of accuracy such as sensitivity, specificity, or correlation coefficients were included. A total of 6,056 articles were identified, 266 were reviewed for full text and a total of 32 were included: 5 compared to a reference standard, and 27 looked at correlation between tools.

Seven tools were compared to a reference standard including the Neurobehavioral Rating Scale (NBRS) (Ismail et al., 2013; Rosen et al., 1999), Empirical Behavioral Rating Scale (E-BEHAVE-AD) (Ismail et al., 2013), Neuropsychiatric Inventory-Agitation (NPI-Agitation) (Ismail et al., 2013), Spanish NPI-Agitation (Vilalta-Franch et al., 1999), French version of the Rating Scale for Aggressive Behaviour in the Elderly (F-RAGE) (Adama et al., 2013), Cohen Mansfield Agitation Inventory (CMAI), or Pittsburgh Assessment Scale (PAS) (Rosen et al., 1999). Most studies reported sensitivities >80% and specificities >70% for these tools.

One study that evaluated the CMAI and the NPI clinician version reported minimal clinically important differences (De Mauleon et al., 2021). The quality of the evidence was judged to be low given single-study evidence for most tools, risk of bias in the individual studies (e.g., unclear blinding between assessments), and range in accuracy across tools.

Recommendation #3

We recommend interdisciplinary approaches to dementia care incorporating health care provider education on BPSD, structured approaches to assessment, individualized care plans, and personalized meaningful activities for the management of agitation in dementia. (Strong recommendation, moderate-level evidence)

A thorough evaluation of contributors to BPSD and understanding of the personhood of the person living with dementia is important for both the assessment and management of agitation. While available resources might vary across settings, ideally an interdisciplinary approach incorporating expertise from nursing, allied health, non-registered staff, physicians, pharmacists and other health care providers is recommended. Existing evidence from randomized controlled trials demonstrates interdisciplinary approaches to dementia care incorporating elements such as education on contributors to BPSD, structured approaches to assessment, individualized care plans and incorporation of personalized meaningful activities are associated with reductions in symptoms of agitation (SMD: -0.5, -0.99 to -0.01, N=4, n=552) (Watt et al., 2019). Examples of training programs that incorporate these approaches in Canada include the PIECES approach™ (PIECES Canada, 2020), U-first!® (Alzheimer Society of Ontario, 2024) and Gentle Persuasive Approaches® (Advanced Gerontological Education, 2024) as described in the general principles section of the CCSMH BPSD guideline.

Recommendation #4

We suggest robotic pets for the management of agitation in dementia (Conditional recommendation, moderate-quality evidence)

Robotic pets are effective for reducing symptoms of agitation in a person living with dementia. A meta-analysis of robotic pets for agitation in long-term care residents identified significant reductions in symptoms of agitation with robotic pet therapy (SMD: -0.37, -0.64 to -0.09, N=3, n=216) (Leng et al., 2019). Interventions included sessions with robotic pets two to three times per week with each session lasting 20 to 30 minutes.

Recommendation #5

We suggest animal-assisted therapy for the management of agitation in dementia (Conditional recommendation, very low-quality evidence)

Animal-assisted therapy, typically involving dogs or other companion animals, may be effective for reducing symptoms of agitation in people living with dementia. A meta-analysis of three randomized trials, all involving animal-assisted therapy using dogs in a long-term care home, found that animal assisted-therapy was associated with a reduction in symptoms of agitation when compared to usual care, to a degree that approached statistical significance (SMD: -0.28, -0.58 to 0.02, p=0.06). Sessions were delivered twice weekly for 20 to 30 minutes and some studies included both individualized and group interventions.

Recommendation #6

We suggest physical exercise for the management of agitation in dementia. (Conditional recommendation, very low-quality evidence)

Several health benefits are associated with physical exercise including the potential for excercise to slow the rate of decline in cognition and function for people living with dementia. In addition to the potential benefits of physical exercise on cognitive symptoms of dementia, there is some evidence that exercise may be helpful for managing agitation among people living with dementia (Kouloutbani et al., 2023). A systematic review and meta-analysis demonstrated that physical exercise, primarily involving aerobic exercise or multicomponent exercise interventions, was associated with a reduction in overall neuropsychiatric symptoms as measured on the NPI (N=9, n=1,168, MD: =-5.28, 95% CI: -9.46 to -1.11, p=0.01). One study reported separately on the effects of exercise on symptoms of agitation as measured by the Agitated Behaviours Scale, as part of an aerobic exercise program involving walking, with significant reductions in symptoms of agitation reported when compared to usual care or cognitive activities (Venturelli et al., 2016).

Recommendation #7

We recommend music-based interventions using preferred music for the management of agitation in dementia. (Strong recommendation, moderate-quality evidence)

Music-based interventions have been studied extensively as potential approaches to help improve general BPSD including agitation (Abraha et al., 2017; Ueda et al., 2013) (N=11; n=397; SMD: -0.49 (95% CI -0.82 to -0.17, p=0.0003). Several individual studies identified that music-based interventions were effective in reducing agitation in people living with dementia (Gaviola et al., 2020; Ueda et al., 2013). A systematic review of receptive or passive music therapy was associated with a reduction in agitation as measured on the Cohen-Mansfield Agitation Inventory when compared to usual care (N=7, mean difference: -7.99, 95% CI: -15.11 to -0.87) (Pedersen et al., 2017; Tsoi et al., 2018). A second meta-analysis identified that music-based interventions were associated with a reduction in agitation (SMD: -0.61, 95% CI: -0.38 to -0.84). Music-based interventions can include a variety of approaches incorporating listening to music, either alone or in combination with other activities such as movement, singing, or playing musical instruments (Abraha et al., 2017). Most interventions involve music sessions delivered 2 to 3 times per week for approximately 30 minutes during each session (Abraha et al., 2017).

Recommendation #8

We suggest massage for the management of agitation in dementia. (Conditional recommendation, moderate-quality evidence)

Massage involves the relief of pain, tension or distress through manipulation or kneading of muscles and soft tissues. A systematic review of randomized controlled trials identified that massage was associated with a reduction in agitation as measured by the Cohen-Mansfield Agitation Inventory (N=6, n=365, SMD: -0.56, 95% CI: -0.95 to -0.17, p=0.005) (Margenfeld et al., 2019). These studies included a range of interventions including massage alone, aroma massage, and acupressure, and could involve different parts of the body including hands, feet, shoulders and back. Daily massages delivered five times per week with each massage lasting 10 to 30 minutes was the most frequent modality (Margenfeld et al., 2019).

Recommendation #9

We suggest aromatherapy for the management of agitation in dementia. (Conditional recommendation, low-quality evidence)

Aromatherapy is a therapeutic modality involving exposure to essential oils for therapeutic purposes. Aromatherapy has been demonstrated to be associated with a reduction in agitation (N=10, n=631; SMD: -0.45, 95% CI: -0.73 to -0.16, p=0.003) (Xiao et al., 2021). Studies included a variety of aromatherapy applications including topical administration (smearing), massage and inhalation. Among different aromatherapy applications, those involving lavender-based preparations were more effective than lemon oil. The frequency of aromatherapy varied from once a week to three times a week, with the duration of individual sessions lasting up to 120 minutes.

Recommendation #10

We suggest that cholinesterase inhibitors and memantine should be optimized for the pharmacological treatment of Alzheimer's disease and related dementia. (Conditional recommendation, very low-quality evidence)

In Canada, three cholinesterase inhibitors (donepezil, galantamine, and rivastigmine) and the NMDA receptor antagonist memantine are approved for the treatment of Alzheimer's disease. Both cholinesterase inhibitors and memantine have been demonstrated to be associated with modest improvements in cognitive and functional outcomes for individuals diagnosed with Alzheimer's disease (Birks & Evans, 2015; Birks & Harvey, 2018; Loy & Schneider, 2006; McShane et al., 2019; Tan et al., 2014). For this reason, it is recommended that these medications be discussed with patients and caregivers for the symptomatic treatment of Alzheimer's disease to help delay the progression of cognitive and functional impairment (Herrmann, Lanctôt, et al., 2013). Several of the studies undertaken with cholinesterase inhibitors and memantine primarily to assess cognitive endpoints also included measures of BPSD as secondary endpoints. It should be noted that these studies typically enrolled individuals with relatively mild BPSD at baseline and the studies were not intended to evaluate the efficacy of these medications among individuals with moderate-to-severe agitation or other BPSD. A meta-analysis of memantine that did not enrol individuals who had significant baseline agitation identified that treatment with memantine was associated with a decreased risk of agitation emerging as an adverse event during the trials when compared to placebo (N=15, n=3,904; RR: 0.76, 95% CI: 0.6 to 0.96) (McShane et al., 2019). A systematic review of cholinesterase inhibitors for psychosis in Alzheimer's disease demonstrated small benefits on psychotic symptoms when compared to placebo

(d'Angremont et al., 2023), and that donepezil, galantamine and memantine were associated with modest benefits on overall BPSD as measured by the Neuropsychiatric Inventory Scale (Jin & Liu, 2019; Tan et al., 2014).

Recommendation #11

We suggest against initiating cholinesterase inhibitors specifically for the treatment of moderate-to-severe agitation in Alzheimer's disease and related dementias. (Conditional recommendation, low-quality evidence)

and

Recommendation #12

We suggest against initiating memantine specifically for the treatment of moderate-to-severe agitation in Alzheimer's disease and related dementias. (Conditional recommendation, moderate-quality evidence)

In randomized controlled trials evaluating agitation as measured by the CMAI, no significant differences were noted between donepezil and placebo on symptoms of agitation (Jin & Liu, 2019). A large RCT of donepezil compared to placebo to treat significant symptoms of agitation in dementia (n=272 individuals) found no significant differences in symptoms of agitation for individuals treated with donepezil when compared to placebo (mean difference on CMAI: -0.06, 95% CI: -4.35 to 4.22) (Howard et al., 2007). Similarly, two randomized controlled trials focussed on treating agitation among people with dementia found no benefit for memantine when compared to placebo (Fox et al., 2012; Herrmann, Gauthier, et al., 2013).

Recommendation #13

We recommend citalopram for the treatment of moderate severity agitation in Alzheimer's disease and related dementias. (Strong recommendation, low-quality evidence)

Citalopram is a selective serotonin reuptake inhibitor frequently used for the treatment of depression and anxiety disorders in younger and older adults. Citalopram has been evaluated as a treatment for agitation in dementia, including in a large randomized controlled trial demonstrating efficacy of citalopram for treating agitation in dementia when compared to placebo (Porsteinsson et al., 2014). A network meta-analysis of antidepressants for agitation in dementia also demonstrated that citalopram was more effective than placebo for reducing agitation (SMD: -0.44, 95% CI: -0.72 to -0.16) and that citalopram was not associated with increased risk of adverse events when compared to placebo (OR: 1.01, 95% CI: 0.51 to 1.98) (Chen et al., 2023). It should be noted that the targeted dosage of citalopram used in most studies was 30 mg daily based on tolerability and response. However, dosages above 30 mg daily in older adults are not recommended due to concerns related to prolongation of the corrected QT interval (Health Canada, 2012). As such, the efficacy of citalopram at the maximum recommended dose of 20 mg is unclear, particularly since most trial participants (78%) received 30 mg indicating that some may not have adequately responded to lower doses. Pharmacological evaluations identified that serum concentrations of the S-enantiomer of citalopram, available as escitalopram, were associated with clinical benefits for individuals treated with citalopram (Ho et al., 2016) and a large clinical trial of escitalopram for agitation in dementia is currently underway (NCT: 03108846).

Recommendation #14

We suggest citalopram for severe agitation in circumstances where the risks and benefits of other pharmacological treatments for severe agitation (e.g., antipsychotics) preclude the use of alternative medications in Alzheimer's disease and related dementias. (Conditional recommendation, very low-quality evidence)

The largest RCT of citalopram for the treatment of agitation in dementia demonstrated that while citalopram was effective overall for agitation (Porsteinsson et al., 2014), there was heterogeneity in the pattern of response with certain patient populations more or less likely to respond to citalopram compared to placebo. Among the predictors of response, individuals with less advanced dementia (as defined by higher cognitive test scores) and those with less severe agitation at baseline were most likely to respond to citalopram, in contrast to individuals with more advanced dementia or severe symptoms (Schneider et al., 2016). In addition, the time to onset of clinical benefit with citalopram may be delayed with the majority of individuals needing up to nine weeks of treatment in order to observe clinical improvement in symptoms (Weintraub et al., 2015). Together, these findings may indicate that citalopram may not be an effective option for severe agitation. However, there are circumstances where the risks of antipsychotics may preclude their use in severe agitation. In situations where the risks of side-effects may potentially outweigh the benefits or where a patient or substitute decision maker may decide against antipsychotic treatment, treatment with citalopram may be acceptable as a treatment for severe agitation.

Recommendation #15

We suggest against using trazodone, sertraline, mirtazapine, and fluoxetine in the management of agitation in Alzheimer's disease and related dementias. (Conditional recommendation, low-quality evidence)

and

We suggest against using paroxetine, fluvoxamine, and tricyclic antidepressants in the management of agitation in Alzheimer's disease and related dementias. (Conditional recommendation, very-low quality evidence)

While antidepressants are frequently used for the management of agitation in dementia, there is very limited evidence that any antidepressant other than citalopram is safe and effective for the treatment of agitation. A network meta-analysis of antidepressants for agitation in dementia did not observe benefits for other antidepressants when compared to placebo. This included no benefits on symptoms of agitation for sertraline (SMD: -0.08, -0.43 to 0.27), trazodone (SMD: 0.03, -0.49 to 0.43), fluoxetine (SMD: 0.31, 1.49 to -0.87), and mirtazapine (SMD: -0.07, -0.68 to 0.55) (Chen et al., 2023). The meta-analysis with trazodone included one small study that included a small positive trial of trazodone for the treatment of frontotemporal dementia (Lebert et al., 2004), although the other trials of trazodone for agitation in dementia have also not demonstrated benefit when compared to placebo (Seitz et al., 2011; Teri et al., 2000). The network meta-analysis also demonstrated an increased risk of adverse events for trazodone as compared to placebo (OR: 4.58, 1.12 to 18.69) (Chen et al., 2023). Antidepressants such as paroxetine, fluvoxamine, or tricyclic antidepressants also are not recommended due to potential adverse events such as anticholinergic side-effects or their propensity to cause drug-drug interactions.

Recommendation #16

We suggest aripiprazole, brexpiprazole or risperidone for the treatment of severe agitation in Alzheimer's disease and related dementia. (Conditional recommendation, moderate-quality evidence)

The atypical antipsychotics aripiprazole, brexpiprazole, and risperidone all have been demonstrated to be more effective than placebo in short-term RCTs that evaluated agitation as a primary outcome in Alzheimer's disease. A network meta-analysis of RCTs demonstrated reductions in agitation on the Cohen Mansfield Agitation Inventory for both aripiprazole (N=3 SMD: -0.30, 95% CI: -0.55 to -0.05) and risperidone (N=7; SMD: -0.26, 95% CI: -0.37 to -0.15) (Yunusa et al., 2019). Information on brexpiprazole was not included in this network analysis although subsequent to this review information on three RCTs of brexpiprazole for agitation in Alzheimer's disease was published demonstrating effectiveness of brexpiprazole at 2 mg or 3 mg daily (Grossberg et al., 2020; Lee et al., 2023) and the U.S. Food and Drug Administration approved brexpiprazole for the treatment of agitation in dementia (U.S. Food & Drug Administration, 2023) followed by a similar recommendation by Health Canada (Otsuka Canada, 2024). Therefore, aripiprazole, brexpiprazole or risperidone could be considered initial treatments for severe agitation in Alzheimer's disease. In situations where one of these medications is either ineffective or not tolerated, it is suggested that a switch between risperidone and either aripiprazole or brexpiprazole be considered (or vice versa if aripiprazole or brexpiprazole were the initial medications of choice). Given the similarities between aripiprazole and brexpiprazole, the guideline panel did not recommend switching between these medications if either medication is ineffective or not initially tolerated.

Although some atypical antipsychotics may be associated with improvement in symptoms of agitation, evidence from RCTs and observational data have identified the risk of severe adverse events, such as cerebrovascular accidents and death with atypical antipsychotics, when compared to placebo. Meta-analyses have identified an elevated risk of mortality associated with atypical antipsychotics as a class (OR:1.54, 95% CI: 1.06 to 2.23) (Schneider et al., 2005) as well as increased risk of cerebrovascular adverse events (OR: 2.13, 95% CI: 1.20 - 3.75) (Schneider et al., 2006), along with elevated rates of other adverse events such as somnolence, gait changes, and worsening of cognition (Schneider et al., 2006). The previously referenced network meta-analysis identified that, of the three recommended medications, risperidone may have the greatest relative risk of cerebrovascular events compared to placebo with aripiprazole not having an increased risk of these adverse events when compared to placebo (Yunusa et al., 2019). Similarly, the risk of extrapyramidal symptoms with risperidone was greater than placebo, while aripiprazole was not associated with a significantly increased risk of adverse events (Yunusa et al., 2019). All atypical antipsychotics were associated with an increased risk of somnolence (Yunusa et al., 2019). Given these safety concerns, the use of any antipsychotics for the treatment of agitation in Alzheimer's disease should be limited to situations where individuals have severe symptoms of agitation that have not responded to non-pharmacological treatments or other appropriate pharmacological interventions (Watt, 2019).

Recommendation #17

We suggest quetiapine for the treatment of severe agitation for Alzheimer's disease and related dementias if symptoms are refractory to other pharmacological treatments, or in cases where other treatments are not tolerated due to extrapyramidal side-effects. (Conditional recommendation, low-quality evidence)

Quetiapine remains one of the most prescribed antipsychotics among older adults with dementia (Maust et al., 2021) and is frequently used in clinical practice to manage BPSD. The network meta-analysis of quetiapine for agitation in dementia did not demonstrate that quetiapine was more effective than placebo for reducing symptoms of agitation as measured by the Cohen-Mansfield Agitation Inventory (SMD: -0.25; -0.51 to 0.11) (Yunusa et al., 2019), although there were relatively few studies of quetiapine undertaken. The risk of stroke was not statistically higher than placebo for quetiapine (OR: 1.36, 95% CI: 0.45 – 4.25), and the risk of death (RR: 1.64, 0.74 – 3.63) associated with quetiapine was similar to that of other antipsychotics. Quetiapine was identified as having a relatively low propensity to cause extrapyramidal symptoms (OR: 0.59; 95% CI: 0.27 – 1.33) (Yunusa et al., 2019) and as such may be considered in the treatment of severe agitation when other treatments such as risperidone, aripiprazole or brexpiprazole are ineffective or are not tolerated due to extrapyramidal adverse events.

Recommendation #18

We recommend against using olanzapine for the treatment of agitation except for potential use as short-term emergency treatment of severe agitation in Alzheimer's disease and related dementias. (Strong recommendation, low-quality evidence)

In the network meta-analysis reviewed in the preceding recommendations, olanzapine was not more effective than placebo for reducing symptoms of agitation (SMD: -0.18; 95% CI: -0.37 to 0.02). Olanzapine was associated with the greatest relative increased risk of mortality (OR: 1.74; 95% CI: 0.74 to 4.07) and cerebrovascular adverse events (OR: 4.28; 95% CI: 1.26 to 14.56) (Yunusa et al., 2019). Although the differences between antipsychotic efficacy and safety outcomes were not statistically significant between different antipsychotic medications, the estimates of olanzapine compared to other atypical antipsychotics indicate that it may be less effective and less safe than other antipsychotic medications for treatment of agitation and is not recommended for ongoing treatment of agitation. Additional recommendations in subsequent sections of this guideline address the potential role of olanzapine in the short-term management of acute agitation, as it is one of few short-acting antipsychotic medications available in an intramuscular formulation.

Recommendation #19

We suggest typical antipsychotics could be considered for the treatment of agitation in dementia if symptoms are refractory to other pharmacological treatments including aripiprazole, brexpiprazole and risperidone. (Conditional recommendation, very low-quality evidence)

Typical antipsychotics, including medications such as haloperidol, can be effective for reducing symptoms of agitation in dementia. A meta-analysis of RCTs demonstrated that typical antipsychotics were associated with a significant reduction in symptoms of agitation when compared to placebo (N=4, n=361; SMD: -0.36; 95%: -0.57 to -0.15) (Mühlbauer et al., 2021). Three of the four studies evaluated haloperidol (doses of 1 to 6 mg daily) and haloperidol was also associated with a reduction in symptoms of agitation (SMD: -0.29; 95% CI: -0.51 to -0.07). (Mühlbauer et al., 2021). However, these medications were also associated with an increased risk of somnolence (OR: 2.62; 95% CI: 1.51 to 4.56) and extrapyramidal symptoms (OR: 2.26; 95% CI: 1.58 to 3.23) when compared to placebo (Mühlbauer et al., 2021).

Observational studies have demonstrated that the risk of death (Gill et al., 2007) and stroke (Gill et al., 2005) with typical antipsychotics is similar to, or greater than, the risks observed with atypical antipsychotics. Low doses of high-potency typical antipsychotics such as haloperidol could be considered for the management of severe agitation in Alzheimer's disease in situations where individuals have not responded to risperidone and one of either aripiprazole or brexpiprazole, provided that extrapyramidal side-effects were not experienced with these other medications. Informed consent related to the use of haloperidol or similar high-potency typical antipsychotics should include discussions about the potential risks of stroke, death, and other side-effects associated with atypical antipsychotics.

Recommendation #20

We suggest synthetic cannabinoids for the treatment of severe agitation in Alzheimer's disease and related dementias if symptoms are refractory to other pharmacological treatments. (Conditional recommendation, low-quality evidence)

Relatively few classes of medications have been evaluated as potential treatments for agitation in dementia other than those reviewed in the preceding recommendations such as cognitive enhancers, antidepressants, and antipsychotics. There are several studies of cannabinoids for the treatment of agitation and other BPSD, including studies evaluating natural cannabinoids or synthetic cannabinoids (e.g., dronabinol or nabilone). A meta-analysis of 7 randomized controlled

trials (n=251) did not find that cannabinoids were associated with a significant reduction in agitation (SMD: -0.69, -1.50 to 0.13) (Ruthirakuhan et al., 2019). There was heterogeneity identified related to the type of cannabinoids, with natural cannabinoids having no benefit on symptoms of agitation (N=3, SMD: 0.11, 95% CI: -0.23 to 0.46) when compared to synthetic cannabinoids (N=4, SMD: -1.67, 95% CI: -3.65 to 0.30) (Ruthirakuhan et al., 2019). A significantly increased risk of somnolence or sedation was reported with cannabinoids (RR: 1.73, 95% CI: 1.02 – 2.93) (Ruthirakuhan et al., 2019). Of the synthetic cannabinoids evaluated and available in Canada, one crossover RCT demonstrated a significant reduction in agitation with nabilone at a mean dose of 1.6 mg (SD: 0.5 mg) during a 6-week trial, along with greater rates of sedation when compared to placebo (45% vs. 16%) (Herrmann et al., 2019). A large placebo-controlled RCT of nabilone compared to placebo is underway (NCTNCT04516057). Given the relatively few studies on use of synthetic cannabinoids for agitation in Alzheimer's disease, these are currently recommended for severe agitation in circumstances where the medications identified in preceding recommendations have been trialed, and found to be ineffective.

Recommendation #21

We suggest carbamazepine for the treatment of severe agitation in Alzheimer's disease and related dementias if symptoms are refractory to other pharmacological treatments. (Conditional recommendation, very low-quality evidence)

The anticonvulsant medication carbamazepine has been studied in four small RCTs as a treatment for BPSD. The largest RCT involving a total of 51 individuals with dementia, demonstrated that carbamazepine at doses of approximately 300 mg daily was associated with significant reductions in BPSD as measured by the Brief Psychiatric Rating Scale (SMD: 1.13, 95% CI: 0.54 to 1.73), with improvements noted in agitation (Tariot et al., 1998). An unpublished systematic review identified that carbamazepine was associated with an increased rate of adverse effects when compared to placebo (74% vs 21%, p=0.03) (personal communication, Benjamin, 2023). A small negative trial of oxcarbazepine for agitation in dementia also has been published (Sommer et al., 2009). Given the relatively small number of studies involving carbamazepine, its known side-effect profile, and high liability to cause drug-drug interactions via induction of metabolism potentially decreasing the efficacy of other medications, the use of carbamazepine as a treatment for agitation in dementia should be restricted to individuals who have refractory agitation and who have not responded to antidepressant or antipsychotic treatment.

Recommendation #22

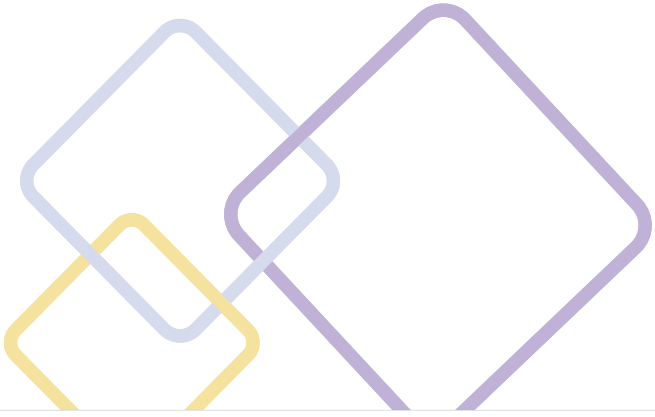
We suggest neither for nor against prazosin to treat agitation in dementia. (Conditional recommendation, low-quality evidence)

Prazosin, an alpha-1 adrenergic antagonist most commonly used to treat hypertension, has been used as a treatment for symptoms of post-traumatic stress disorder among people without dementia (Reist et al., 2021). A small RCT including 22 individuals with Alzheimer's disease and agitation noted a significant reduction in BPSD over eight weeks as measured by the Neuropsychiatric Inventory and Brief Psychiatric Rating Scale (mean dose: 5.9 mg, SD: 0.9 mg) (Wang et al., 2009). There were no significant differences in adverse events reported in the study. A large follow-up RCT of prazosin as a treatment for agitation initially planned to enrol 186 participants with 35 participants eventually randomized to either prazosin or placebo (NCT: 03710642). The full results from this study have not been published at the time of this guideline's writing in February 2024. Given the uncertainty, the guideline panel suggested neither for nor against the use of prazosin as a treatment for severe agitation in dementia.

Recommendation #23

We recommend against valproic acid or sodium divalproex for the treatment of agitation in dementia. (Strong recommendation, moderate-quality evidence)

Valproic acid and sodium divalproex are closely related anticonvulsant medications which have been investigated as a treatment for agitation and BPSD. Overall, in RCTs evaluating valproic acid for agitation, there was no difference noted between valproic acid and placebo on the CMAI (N=5, n=563; MD: -1.67, -6.49 to 3.14, p=0.5) and a non-significant increased risk of adverse events (RR: 1.27, 95% CI: 0.97 to 1.66) (Liu & Wang, 2020). A separate RCT evaluating divalproex sodium to prevent the development of agitation in Alzheimer's disease did not find that divalproex delayed the onset of psychotic symptoms or agitation and was associated with greater risk of somnolence, gait changes, tremor, other adverse events and accelerated brain atrophy (Tariot et al., 2011).



Recommendation #24

We suggest neither for nor against the use of electroconvulsive therapy in the management of severe agitation in dementia. (Conditional recommendation, very low-quality evidence)

Electroconvulsive therapy (ECT) can be highly effective for the treatment of some psychiatric disorders such as major depression, and there is increasing interest in its potential as a treatment for refractory agitation in dementia. Preliminary evidence from observational studies has indicated that ECT may be effective for some individuals with agitation that is refractory to pharmacological treatments, with the majority of participants included in studies being reported as having some benefit from ECT (van den Berg et al., 2018). Adverse events associated with ECT were not reported frequently, although several studies had incomplete reporting of adverse events. Some BPSD treatment algorithms have also recommended ECT as a potential treatment for severe agitation that is refractory to pharmacological treatments (Davies et al., 2018; Sano et al., 2023). ECT may be a potential treatment for severe agitation, although given the potential for adverse events, significant resource implications and lack of RCT evidence, at this time the guideline panel recommends neither for nor against the use of ECT as a treatment for agitation.

Recommendation #25

We recommend against using seclusion and physical restraint for the management of agitation in dementia. (Strong recommendation, moderate-quality evidence)

Despite the known risks of restraints and seclusion for people living with dementia, there continues to be relatively high use of restraints in clinical care settings. Estimates of restraint use among people living with dementia in residential care settings worldwide has been reported to be as high 30% to 60% (Pu & Moyle, 2022) and up to 8% of all older adults in acute care settings in Canada may be physically restrained during hospitalization (Jones et al., 2022). Among hospitalized individuals with dementia, those who were restrained had longer and more costly hospitalizations (Singh et al., 2023). Efforts to reduce restraint use in Canadian LTC settings has led to decreased use to approximately 2.5% of residents in Ontario being restrained (Health Quality Ontario, 2022). Although restraints are often implemented to prevent injury, evidence indicates that the risk of injury, falls and death is increased by restraints (Evans et al., 2003). The guideline panel therefore strongly recommends against use of restraints to manage agitation or to reduce the risk of an individual becoming lost or leaving an area. Restraints may be considered as a last resort for short-term use in specialized dementia inpatient settings employing staff trained in the appropriate emergency use of restraints, their application, and monitoring, and where there is imminent risk of severe physical harm to the person living with dementia or those around them.

Recommendation #26

We suggest short-acting antipsychotics that are available in both oral and intramuscular formulations for the emergency treatment of severe agitation that is associated with imminent risk of physical harm towards self or others on a short-term basis in Alzheimer's disease and related dementias. (Conditional, very low-quality evidence)

and

Recommendation #27

We suggest short-acting benzodiazepines that are available in both oral and intramuscular formulations for the emergency treatment of severe agitation that is associated with imminent risk of physical harm towards self or others on a short-term basis in Alzheimer's disease and related dementias if other medications are unavailable or contraindicated. (Conditional, very low-quality evidence)

At times, a person living with dementia may have severe agitation that places them or others at imminent risk of harm. In these circumstances, immediate treatment with antipsychotics may be required to attempt to reduce agitation to safely facilitate a more thorough evaluation of the contributors to agitation and to formulate a comprehensive management plan (Kales et al., 2015). These situations may require short-term emergency treatment using medications that can be administered intramuscularly, as individuals with severe agitation may refuse oral medications. There are relatively few studies evaluating the acute treatment of agitation in dementia. One RCT evaluated the effects of intramuscular olanzapine (5 mg or 2.5 mg) compared to intramuscular lorazepam (1 mg) or placebo among acutely agitated patients with dementia (Meehan et al., 2002). There was a significant reduction in agitation noted with olanzapine 5 mg and lorazepam 1 mg on symptoms of agitation measured two hours after injection. Both olanzapine dosage groups had significantly reduced agitation 24 hours after injection, while lorazepam did not.

While olanzapine is not recommended as a long-term treatment for agitation in Alzheimer's disease, it is the only atypical antipsychotic currently available in Canada in short-term intramuscular formulation and may be appropriate for short-term treatment of severe acute agitation. In situations where short-acting intramuscular antipsychotics are either unavailable or contraindicated due to potential extrapyramidal symptoms or allergies, the use of low-dose intramuscular lorazepam (0.5 - 1 mg) could be considered as an alternative treatment.

Recommendation #28

We suggest that if a pharmacological intervention for agitation in dementia is ineffective after 8 weeks of treatment, including at least two weeks at a therapeutic dose, then the treatment should be discontinued. (Conditional recommendation, low-quality evidence)

For all pharmacological treatments, the lowest effective dose of medication should be used to minimize the risk of potential adverse effects. If medications are prescribed, they should be started at a low dose. If BPSD persist and the medication is tolerated, the medication could be increased gradually over time until a minimum effective dose is reached. Dose increases should not occur more frequently than every 1 to 2 weeks and attempts should be made to reach a minimum therapeutic dose within 4 to 6 weeks of initiating treatment. Most treatment trials of antipsychotics, antidepressants and other medications used in the treatment of agitation in dementia have had a total treatment duration of between 6 to 12 weeks (Chen et al., 2023; Yunusa et al., 2019). Studies of the onset of action of citalopram have indicated that among individuals who responded to treatment at the end of nine weeks of treatment, the majority who responded had not achieved response within the initial three weeks of treatment (Weintraub et al., 2015). With antipsychotic medications, a lack of any response within the first two weeks of treatment was a predictor of eventual response to treatment at week eight (Yoshida et al., 2017). It is important to ensure that pharmacological treatments are trialed for an appropriate duration of time and at an appropriate dose, while also avoiding unnecessary treatment with medications that are ineffective.

Recommendation #29

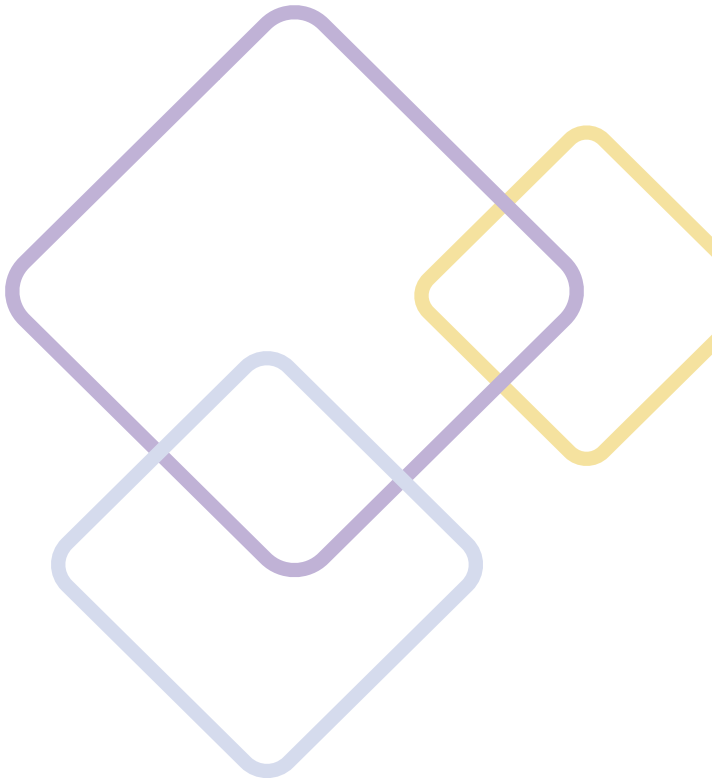
We recommend against using polypharmacy to treat agitation in dementia. (Strong recommendation, low-quality evidence)

There is no RCT evidence to support the use of combinations of medications, or polypharmacy, to treat agitation in dementia, and the risks of polypharmacy in older adults, particularly older adults with cognitive impairment, is significant and can include falls, functional and cognitive decline, and increased risk of death (Fried et al., 2014). As such, polypharmacy should be avoided in the treatment of agitation in dementia, although some agitation treatment algorithms suggest that polypharmacy may be considered in limited circumstances such as a severe refractory agitation that has not responded to other pharmacological and non-pharmacological treatments (Cummings et al., 2023; Davies et al., 2018).

Recommendations #30

We recommend against using long-acting injectable antipsychotics for the treatment of behavioural and psychological symptoms of dementia unless there is a co-occurring chronic psychotic illness that requires treatment with a long-acting injectable antipsychotic. (Strong recommendation, low-quality evidence)

Intramuscularly administered long-acting injectable antipsychotics are antipsychotics that may only require administration every two weeks to three months, depending on the medication and formulation. These medications can be effective for managing symptoms of chronic serious mental illnesses, such as schizophrenia or bipolar disorder, particularly when medication adherence has contributed to worsening of symptoms. However, in the absence of a co-occurring chronic psychotic illness pre-dating the diagnosis of dementia, these medications should be avoided in people living with dementia. There are no RCTs evaluating the safety and efficacy of long-acting antipsychotics for the treatment of agitation in dementia. The available doses and prolonged half-lives of these medications may place people living with dementia at elevated risk for serious antipsychotic-related adverse events which may persist for long periods of time due to the long half-lives of these medications.



6. Recommendations for Assessing and Managing Psychosis in Dementia

Recommendation #31

We recommend the International Psychogeriatric Association criteria for psychosis in major neurocognitive disorders for the diagnosis of psychosis in dementia. (Strong recommendation, moderate-quality evidence)

Psychosis is a relatively common BPSD in Alzheimer's disease and more frequently observed in other types of dementia, such as dementia with Lewy bodies or Parkinson's disease dementia. Criteria for diagnosing psychosis in dementia were initially proposed in 2000 (Jeste & Finkel, 2000) to describe the unique aspects of psychosis in the context of dementia and to distinguish features of psychosis in neurodegenerative conditions from symptoms of psychosis observed with other conditions.

These criteria were subsequently updated through an international consensus process and finalized as the International Psychogeriatric Association criteria for psychosis in mild or major neurocognitive disorders (Cummings et al., 2020). These criteria include: A) the presence of either hallucinations or delusions; B) a diagnosis of major neurocognitive disorder due to Alzheimer's disease or another etiology; C) the psychotic symptoms have not been continuously present prior to the onset of the major neurocognitive disorder; D) symptoms of psychosis present for at least one month; E) symptoms cause disruption or impairment in daily functioning or a safety concern for the patient or others; and, F) the symptoms are not accounted for by a pre-existing psychotic disorder such as schizophrenia, occurring only during a delirium, are due to effects of a substance or medical condition; the symptoms are not culturally appropriate, or are due to the effects of sensory impairment. Psychosis in major neurocognitive disorder also can include additional specifiers to identify if these symptoms also occur with symptoms of agitation or depression.

Recommendation #32

We suggest the psychosis subscale of the Neuropsychiatric Inventory be considered for detecting symptoms of psychosis in dementia in primary care, specialty clinics and long-term care. (Conditional recommendation, very low-quality evidence)

A systematic review of studies evaluating tools to detect symptoms of psychosis in dementia (i.e., hallucinations and delusions) as compared to a reference standard (e.g., clinical assessment) was undertaken. A total of 5,155 abstracts and 471 full texts were screened and only one full text was included (Rapoport et al., 2001). This study examined the Neuropsychiatric Inventory (NPI) and the Columbia University Scale for Psychopathology in Alzheimer's Disease (CUSPAD) as compared to a clinical interview. The NPI psychosis subscale using the delusions and hallucinations NPI items had a sensitivity of 82.6%, and a specificity of 92.3% and the CUSPAD had a sensitivity of 90.0% and a specificity of 89.7% for detecting psychosis (Rapoport et al., 2001). The risk of bias was related to unclear reporting of blinding, and the time interval between tools and reference standard. Given the paucity of evidence, the quality of evidence was very low.

Recommendation #33

We suggest that psychosocial interventions found to be effective for other BPSD (e.g., interdisciplinary approaches to care, music) be considered in the management of symptoms of psychosis in dementia. (Conditional recommendation, very low-quality evidence)

There are very few studies evaluating non-pharmacological management strategies for psychosis in Alzheimer's disease and related dementias. There is evidence, however, that some non-pharmacological approaches such as interdisciplinary approaches to care incorporating health care provider training, communication strategies, personalized pleasant activities, and psychosocial interventions (e.g., music) are helpful for several different types of BPSD. Clinical experience suggests that these approaches can be effective for reducing symptoms of psychosis. Additionally, many studies of non-pharmacological interventions for BPSD reported improvements in global measures of BPSD, which may have included changes in psychosis, although psychotic symptoms were not reported separately in these trials.

The guideline panel did not identify any RCTs of non-pharmacological treatments for psychosis in dementia and only one prospective cohort study was identified (Chen et al., 2014). This cohort study evaluated the effects of a non-pharmacological interdisciplinary program on BPSD including symptoms of psychosis among 104 men in two long-term care homes for veterans in Taiwan (Chen et al., 2014). The intervention included twice weekly sessions of music and art-based activities, and exercise. LTC home staff received dementia education training over 12 weeks in one of the intervention homes. The control group involved staff education in dementia care only. Participants in the intervention home had a significant reduction in overall BPSD as measured by the NPI as well as reductions in subscale scores for delusions, hallucinations, and agitation (Chen et al., 2014).

Recommendation #34

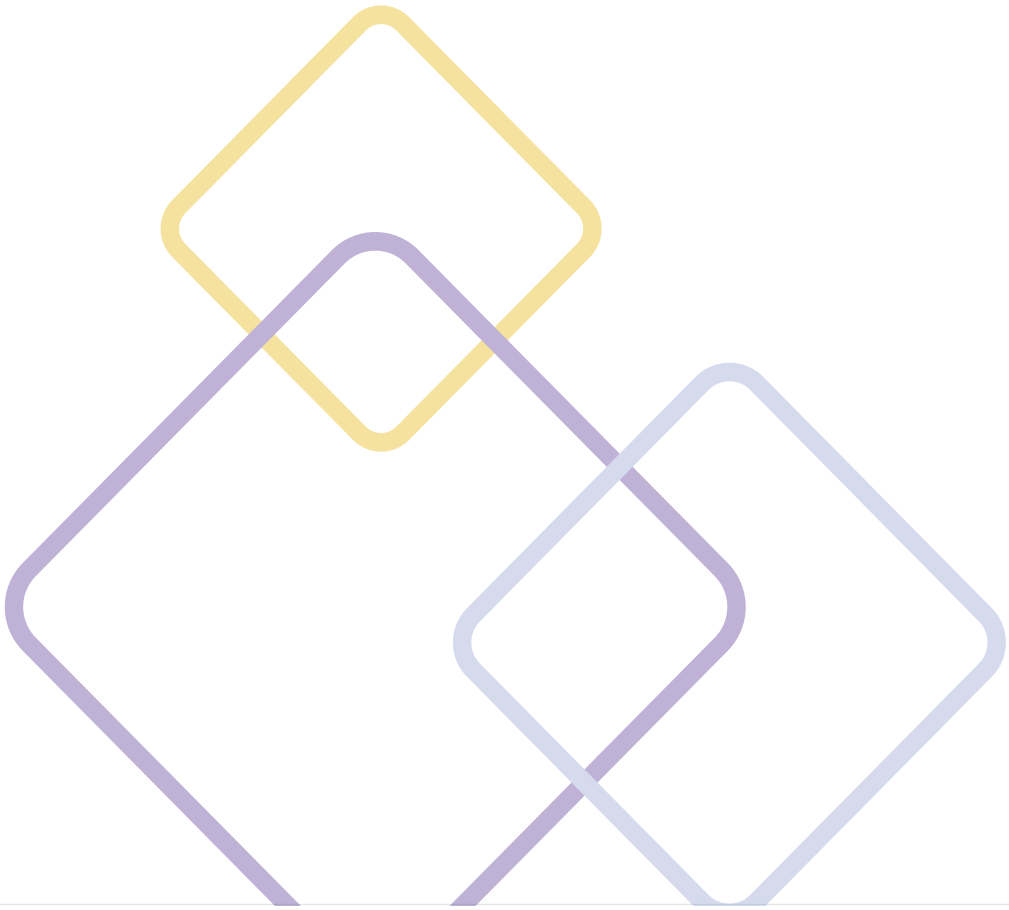
We suggest citalopram for the treatment of psychotic symptoms of moderate severity for individuals with Alzheimer's disease and related dementias. (Conditional recommendation, low-quality evidence)

A large RCT of citalopram for the treatment of agitation in Alzheimer's disease evaluated changes in symptoms of psychosis during treatment (Leonpacher et al., 2016). This nine-week study compared citalopram, up to 30 mg daily, to placebo and reported that individuals in the citalopram arm of the trial were less likely to report delusions than those in the placebo group as measured by the Neuropsychiatric Inventory (OR: 0.4, 95% CI: 0.18 to 0.91). There was also a reduction in the median hallucination subscore (Leonpacher et al., 2016). Studies comparing citalopram to the typical antipsychotic perphenazine (Pollock et al., 2002) and atypical antipsychotic risperidone (Pollock et al., 2007) indicated that the changes in symptoms of psychosis were comparable for citalopram when compared to antipsychotics. The mean doses of citalopram used in all these studies were above 20 mg daily, which is greater than the maximum daily recommended doses of citalopram in older adults (due to the safety concerns related to QTc prolongation). Additional information about the safety of citalopram is outlined in the agitation section of this guideline.

Recommendation #35

We suggest aripiprazole or risperidone for the treatment of symptoms of psychosis associated with Alzheimer's disease and related dementias if symptoms are severe or have not responded to other treatments. (Conditional recommendation, low-quality evidence)

Similar to the recommendation for treatments of severe agitation (see Section 5, Recommendation 16), there is evidence to support the use of risperidone and aripiprazole as a treatment for psychosis if previous treatment approaches have been ineffective. A network meta-analysis identified reductions in symptoms of psychosis in studies using a placebo comparator for both risperidone (N=5, SMD: -0.16, -0.28 to -0.05) and aripiprazole (N=4, SMD: -0.17, -0.32 to -0.02) (Huang et al., 2022). The agitation section of this guideline (Section 5) provides additional information related to the potential adverse effects associated with the use of all antipsychotics, as well as specific considerations related to the use of risperidone and aripiprazole. The guideline panel acknowledges the limited evidence related to pharmacological treatments of psychosis in dementia and that at times other pharmacological treatments may need to be considered depending on the effectiveness and tolerability of the medications recommended in this CPG.



7. Recommendations for Assessing and Managing Depressive Symptoms and Depression in Dementia

Recommendation #36

We recommend the National Institutes of Mental Health - depression in Alzheimer's disease criteria to diagnose depression in dementia. (Strong recommendation, low-quality evidence)

Diagnostic criteria for depression in dementia were first proposed to address the unique manifestations of depression among individuals with Alzheimer's disease (Olin et al., 2002). These criteria were modified from DSM-5 criteria for depression. The major clinical changes to the criteria were to change the original criteria for depression so that a diminished positive affect or enjoyment due to social contacts or usual activities could be used in place of anhedonia in the DSM-5-TR. The original depression symptom criteria related to a reduction in concentration was removed from the depression in Alzheimer's disease criteria and two additional symptoms of irritability and social isolation or withdrawal were added. The total number of depressive criteria required for a diagnosis of depression was reduced from five to three symptoms with at least one of the three symptoms having to include either sadness or diminished pleasure in activities, and must have lasted two weeks (Olin et al., 2002). Symptoms of depression only need to be present at some point in the two-week period, in contrast to DSM-5 criteria which requires symptoms to be present for the majority of the two-week period. The criteria also require a diagnosis of dementia and exclude mood changes that occur as part of delirium, or mood changes better accounted for by a medical condition, substance use, or another mental health condition. Subsequent validation studies of these depression in dementia criteria have been conducted, which retained the original diagnostic criteria (Teng et al., 2008) and demonstrated that the prevalence of depression using these criteria were higher than estimates provided with the DSM-5-TR criteria for major depression (44% vs 13%) (Teng et al., 2008).

Recommendation #37

We recommend the Cornell Scale for Depression in Dementia (CSDD) for detecting depressive symptoms in dementia in specialty clinics. (Strong recommendation, moderate-quality evidence)

and

We suggest the CSDD for detecting depressive symptoms in dementia in long-term care homes. (Conditional recommendation, moderate-quality evidence)

and

We suggest the CSDD for detecting depressive symptoms in dementia in primary care. (Conditional recommendation, low-quality evidence).

A systemic review completed in 2015 (Goodarzi et al., 2017) and updated in 2023 by our guideline panel examined the diagnostic test accuracy of tools for detecting depressive symptoms in dementia compared to a reference standard. Nine different tools were examined in the included studies which were conducted in specialty clinics and LTC homes.

Twelve studies examined the CSDD. Five studies reported specific cut-offs for which the pooled estimates were as follows; cut-off of ≥6 (sensitivity =0.90 [95% CI 0.82-0.95]; specificity =0.74 [95% CI 0.50-0.89]) and ≥8 (sensitivity=0.79 [95% CI 0.69-0.87]; specificity=0.81 [95% CI 0.60-0.93]). The CSDD was developed specifically to assess symptoms of depression in people living with dementia. A cut-off score of 6 on the CSDD had the highest sensitivity, with no significant heterogeneity. The GDS and MADRS in pooled estimates had low sensitivity across cut-off scores.

Although our CPG did not address apathy as a BPSD, it is also important that clinical assessments and assessment tools used in depression are able to distinguish depression from apathy (Lanctôt et al., 2023).

Management of Depressive Symptoms in Dementia

Recommendation #38

We recommend interdisciplinary approaches to dementia care incorporating health care provider education, structured approaches to assessment, individualized care plans and personalized meaningful activities for the treatment of depressive symptoms in dementia in community settings. (Strong recommendation, moderate-quality evidence)

and

We suggest interdisciplinary approaches to dementia care incorporating health care provider education, structured approaches to assessment, individualized care plans and personalized meaningful activities for the treatment of depressive symptoms in dementia in LTC settings. (Conditional recommendation, low-quality evidence)

A systematic review and network meta-analysis of 256 studies (28,483 people living with dementia) compared the efficacy of pharmacologic and non-pharmacologic interventions for reducing symptoms of depression in people living with dementia with or without a concurrent diagnosis of depression (Watt et al., 2021). Interdisciplinary care was defined as an assessment and care plan developed and implemented by more than one health care provider in a collaborative fashion (e.g., doctor, nurse, occupational therapist). Structured assessments involve consideration of the contributors to behaviours and approaches to support the interdisciplinary team in developing and evaluating the effectiveness of individualized care plans, which may incorporate non-pharmacologic or pharmacologic interventions. This review found that interdisciplinary approaches were more efficacious than usual care for reducing depressive symptoms in people living with dementia without a concurrent diagnosis of depression (mean difference on the CSDD -1.98, 95% CI -3.80 to -0.16) (Watt et al., 2021). The probability of meeting the minimum clinically important difference (i.e., the threshold above which people living with dementia and clinicians would perceive an improvement in symptoms) on the CSDD was 49.1% based on this review and network meta-analysis (Watt et al., 2021).

A network meta-analysis of randomized trials conducted in a clinic or community setting found that interdisciplinary care reduced depressive symptoms in people with dementia when compared to usual care (mean difference on CSDD -3.99, 95% CI -6.92 to -1.18); whereas, a similar subgroup meta-analysis of randomized trials conducted in LTC did not find that multidisciplinary care reduced depressive symptoms when compared to usual care (Watt et al., 2021). Implementing interdisciplinary approaches could lessen reliance on psychoactive medications for treating depressive symptoms in people living with dementia, which is important given the potential risk of harm from psychoactive medications in people living with dementia (Watt et al., 2018).

Recommendation #39

We suggest animal therapy for the management of depressive symptoms in dementia in long-term care (Conditional recommendation, low-quality evidence) or community settings. (Conditional recommendation, very low-quality evidence)

An overview of systematic reviews found animal therapy (e.g., interactions with dogs, cats or birds in individual or group settings) was more efficacious than usual care for reducing depressive symptoms in people living with dementia without a concurrent diagnosis of depression in a meta-analysis (mean difference on the CSDD -4.82,95% CI -8.97 to -0.8]). These treatment effects were both clinically and statistically significant (Watt et al., 2021). The probability of meeting the minimum clinically important difference on the CSDD was 90.9% based on this systematic review and meta-analysis (Watt et al., 2021). People living with dementia who participated in animal therapy met with a dog twice weekly in a small group for 30 minutes each time (Olsen et al., 2016).

Recommendation #40

We suggest robotic pets for the management of depressive symptoms in dementia. (Conditional recommendation, moderate-quality evidence)

The overview of systematic reviews identified four systematic reviews, including studies comparing the efficacy or effectiveness of robotic pets to usual care or another non-pharmacologic intervention in people living with dementia experiencing depressive symptoms (Aarskog et al., 2019; Ardelean & Redolat, 2023; Hirt et al., 2021; Yu et al., 2022). A meta-analysis of data from three RCTs comparing the efficacy of robotic pets to usual care in people living with dementia did not detect a statistically significant improvement in depressive symptoms; however, data were heterogeneous with regards to length of follow-up and co-morbid clinical conditions (Yu et al., 2022). Individual studies narratively synthesized in each systematic review supported the efficacy or effectiveness of robotic pet therapy for reducing depressive symptoms in people living with dementia.

Recommendation #41

We recommend cognitive stimulation therapy for the management of depressive symptoms in mild-to-moderate dementia in community and long-term care settings. (Strong recommendation, moderate-quality evidence)

A systematic review and network meta-analysis found that cognitive stimulation therapy, – defined as structured cognitive stimulation therapy (e.g., one or two sessions per week, for a defined number of hours) with sessions intended to promote cognitive function – was more efficacious than usual care for reducing depressive symptoms in people living with dementia without a concurrent diagnosis of depression (mean difference on the CSDD -2.93, 95% CI -4.35 to -1.52). These treatment effects were both clinically and statistically significant (Watt et al., 2021). The probability of meeting the minimum clinically important difference on the CSDD was 90.4% based on this systematic review and network meta-analysis (Watt et al., 2021).

Recommendation #42

We recommend massage and touch therapy for management of depressive symptoms in mild-to-moderate dementia in community and long-term care settings (Strong recommendation, moderate-quality evidence)

and

We suggest massage and touch therapy for the management of depressive symptoms in severe dementia in community and long-term care settings. (Conditional recommendation, low-quality evidence)

A systematic review found that massage and touch therapy was more efficacious than usual care for reducing depressive symptoms in people living with dementia without a concurrent diagnosis of depression (mean difference on CSDD -9.03 95% CI -12.28 to -5.88) (Watt et al., 2021). This benefit was both statistically and clinically significant. The probability of meeting the minimum clinically important difference on the CSDD was 100% based on this systematic review and network meta-analysis (Watt et al., 2021). Massage and touch therapy was defined by massage, acupressure, or therapeutic touch.

Recommendation #43

We recommend physical exercise for the treatment of depressive symptoms in dementia in community and long-term care settings. (Strong recommendation, moderate-quality evidence)

A systematic review and network meta-analysis found that physical exercise, defined as active engagement in aerobic, resistance or balance training, was more efficacious than usual care for reducing depressive symptoms in people living with dementia without a concurrent diagnosis of depression (mean difference on the CSDD -2.42, 95% CI -4.55 to -0.34) (Watt et al., 2021). This benefit was both statistically and clinically significant and the probability of meeting the minimum clinically important difference on the CSDD was 63.9% based on this systematic review and meta-analysis (Watt et al., 2021).

Recommendation #44

We recommend reminiscence therapy for the management of depressive symptoms in dementia in long-term care settings. (Strong recommendation, moderate-quality evidence)

and

We suggest reminiscence therapy for the management of depressive symptoms in dementia in community settings. (Conditional recommendation, low-quality evidence)

Reminiscence therapy comprises interventions that provide people living with dementia with reminders of their past or their family members. A systematic review and network meta-analysis found that reminiscence therapy was more efficacious than usual care for reducing depressive symptoms in people living with dementia without a concurrent diagnosis of major depression (mean difference on the CSDD -2.30, 95% CI -3.68 to -0.93) (Watt et al., 2021). This benefit was both statistically and clinically significant. Reminiscence therapy was defined as any intervention to give people living with dementia reminders of their past or family members. A meta-analysis of nine randomized trials conducted in a long-term care or assisted living setting found that reminiscence therapy reduced depressive symptoms in people living with dementia as compared to usual care (mean difference on the CSDD -3.01, 95% CI -4.61 to -1.35). A similar subgroup analysis of randomized trials conducted in a community or clinic setting did not find that reminiscence therapy reduced depressive symptoms when compared to usual care (Watt et al., 2021).

Recommendation #45

We suggest occupational therapy for the treatment of depressive symptoms in dementia in community and long-term care settings. (Conditional recommendation, low-quality evidence)

Occupational therapy was defined as case management or activities to enhance functional independence performed by an occupational therapist. A systematic review and network meta-analysis found that occupational therapy was more efficacious than usual care for reducing depressive symptoms in people living with dementia without a concurrent diagnosis of depression (mean difference on the CSDD -2.59, 95% CI -4.70 to -0.40) (Watt et al., 2021). This benefit was both statistically and clinically significant. From an implementation perspective, occupational therapy assessments may be available in some community and LTC settings, although they may be infrequently involved in implementing strategies specifically aimed at reducing symptoms of depression in dementia.

Recommendation #46

We recommend against using pharmacologic interventions for the treatment of depressive symptoms in dementia who do not have a concurrent diagnosis of depression. (Strong recommendation, low-quality evidence)

A systematic review and network meta-analysis identified in our overview of systematic reviews found direct evidence from randomized trials comparing the efficacy of antidepressants (n=9 studies), antipsychotics (n=8), mood stabilizers (n=2), stimulants (n=1), cholinesterase inhibitors (n=5), NMDA receptor antagonists (n=2), and hormonal therapies (n=9) to placebo that did not demonstrate that pharmacologic interventions were more efficacious than placebo for reducing depressive symptoms in people living with dementia without a concurrent diagnosis of major depression; neither did evidence from mixed treatment comparisons (Watt et al., 2021). The quality of evidence was judged to be low because of concerns of risk of bias in included randomized trials and methodological and clinical differences across included randomized trials. However, because of the potential risk of harm associated with using certain pharmacologic interventions in people living with dementia, the guideline panel made a strong recommendation against prescribing antidepressants and other psychotropic medications for the treatment of depressive symptoms in people with dementia.

Management of Depression in Dementia

Recommendation #47

We suggest home-based problem-based therapy and behaviour therapy for the management of depression in dementia in community settings. (Conditional recommendation, low-quality evidence)

A systematic review and network meta-analysis identified that home-based problem adaptation therapy and behaviour therapy were efficacious for reducing depression in community dwelling people living with dementia in one identified randomized trial for each therapeutic approach (Kiosses et al., 2015; Teri et al., 1997). Problem adaptation therapy is an active non-pharmacologic intervention that tries to improve emotional regulation through an individualized approach that considers each person's cognitive, functional, and physical limitations, involving the person living with dementia, and their caregiver as needed (Kiosses et al., 2015). In a randomized trial where one session was administered each week for 12 weeks, problem adaptation therapy involved problem-solving approaches, compensatory strategies, and environmental adaptation tools such as calendars and notebooks (Kiosses et al., 2015). Behaviour therapy involved pleasant events or problem-solving in the randomized trial focused on this approach (Teri et al., 1997). Caregivers were taught how to increase pleasant events and implement problem-solving strategies to help improve behaviours associated with depression in the person living with dementia over nine one-hour sessions each week (Teri et al., 1997). Additional research is needed to understand the efficacy of non-pharmacologic interventions for reducing depression in people living with dementia living in LTC settings.

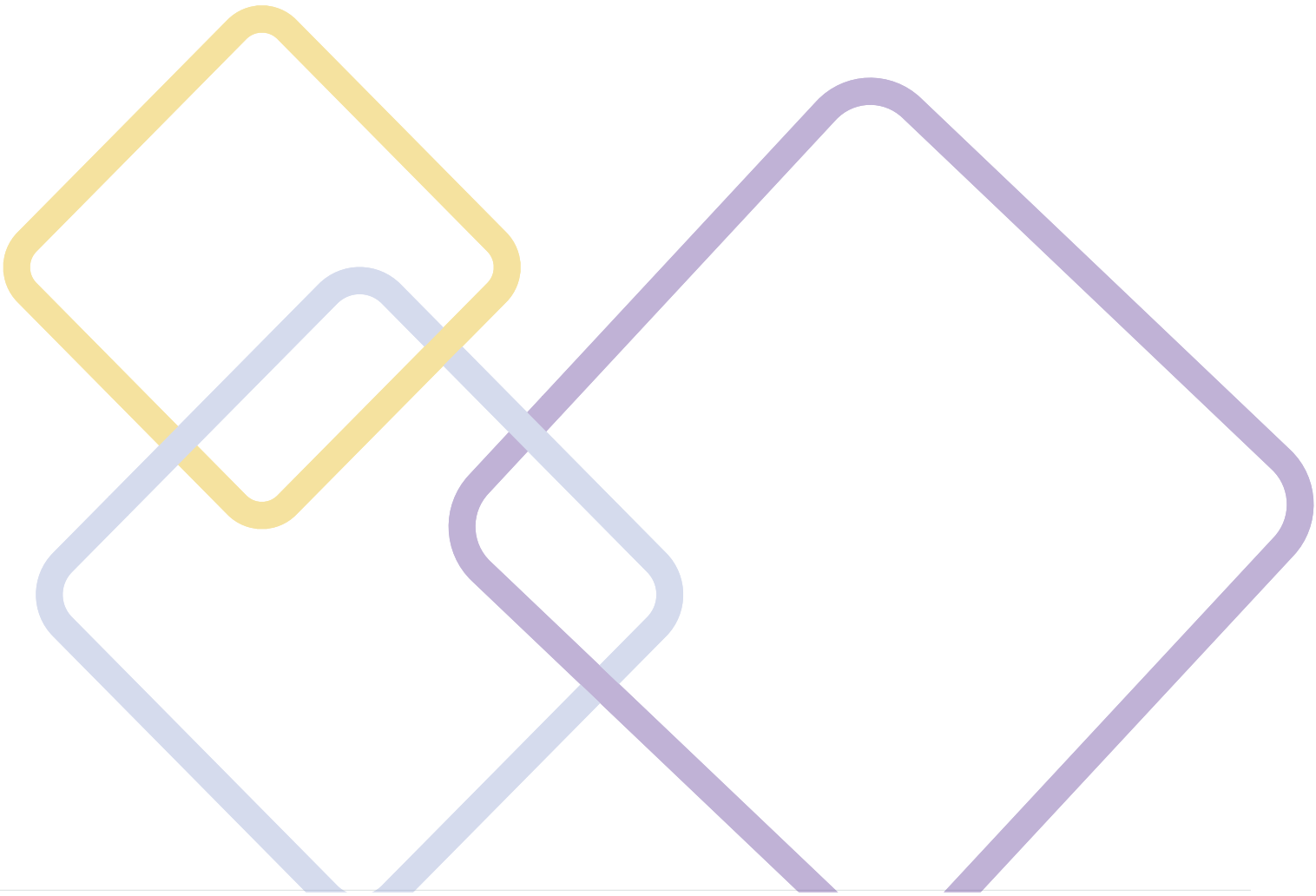
Recommendation #48

We suggest antidepressants for the treatment of moderate-to-severe depression in dementia that has not responded to psychosocial interventions. (Conditional recommendation, low-quality evidence)

Data to guide treatment of depression in people with dementia is limited and studies demonstrating the comparative efficacy and safety of pharmacologic interventions for treating depression in people living with dementia are urgently needed. A rapid overview of systematic reviews identified a network meta-analysis (Watt et al., 2021) which found mixed evidence concerning the efficacy of sertraline in people with depression and dementia (Lyketsos et al., 2003; Magai et al., 2000; Rosenberg et al., 2010). One randomized trial (Lyketsos et al., 2003) demonstrated that sertraline, with doses up to 150 mg daily, was efficacious compared to placebo for reducing depression in community-

dwelling older adults living with Alzheimer's disease (Lyketsos et al., 2003). This systematic review also identified one RCT demonstrating the efficacy of clomipramine relative to placebo in people living with depression and dementia (Petracca et al., 1996). However, given the substantive anticholinergic side-effects and potential to worsen cognitive impairment associated with clomipramine use, this was not viewed as an acceptable treatment for people living with depression and dementia by the guideline panel (Petracca et al., 1996).

Information included in the *CCSMH Canadian Guidelines on Prevention, Assessment and Treatment of Depression Among Older Adults* was also considered (Canadian Coalition for Seniors Mental Health, 2021). This guideline recommends sertraline or duloxetine as first-line treatment for major depression in older adults without dementia. The recommendation to support duloxetine for older adults with depression was based on a systematic review and meta-analysis that identified three randomized trials comparing the efficacy of duloxetine to placebo in older adults with recurrent depression (Tham et al., 2016). Older adults without dementia who had recurrent depression had greater odds of acute response and remission, however duloxetine was associated with an increased rate of side-effects including dry mouth, diarrhoea, dizziness, and constipation compared to placebo (Tham et al., 2016).



8. Recommendations for Assessing and Managing Anxiety in Dementia

Recommendation #49

We suggest the Diagnostic and Statistical Manual of Mental Disorders –5-Text Revision (DSM-5-TR) criteria for anxiety disorders to diagnose anxiety in dementia. (Conditional recommendation, very low-quality evidence)

Unlike agitation, psychosis, and depression, the guideline panel was unable to identify any criteria specific to the diagnosis of anxiety in dementia. Most studies that evaluated rating scales for anxiety in people with dementia used Diagnostic and Statistical Manual of Mental Disorders (DSM) 5 criteria for generalized anxiety disorders as the reference standard for assessing anxiety. Until changes and criteria are established, the guideline panel recommends using DSM-5-TR criteria for anxiety disorders to diagnose anxiety in people with Alzheimer's disease and related dementias (American Psychiatric Association, 2022).

Recommendation #50

We recommend the Rating Anxiety in Dementia (RAID) scale for detecting anxiety symptoms in dementia in specialty clinics. (Strong recommendation, moderate-quality evidence)

and

We suggest the RAID for detecting anxiety symptoms in dementia in primary care and long-term care settings. (Conditional recommendation, low-quality evidence)

A systematic review of tools for anxiety symptoms or disorders in persons with dementia as compared to reference standards was first completed in 2017 (Goodarzi et al., 2019) and subsequently updated in 2023. The original review looked at 9,626 abstracts, 1,101 full text and included four studies and one new article was found in the 2023 update.

Five tools were found: Geriatric Anxiety Inventory (GAI), Penn State Worry Questionnaire (PSWQ), Neuropsychiatric Inventory (NPI-anxiety item), Hamilton Anxiety Rating Scale (HAM-A) and the Rating Anxiety in Dementia (RAID) scale.

Three studies examined the RAID scale. Meta-analysis found that at a cut-off ≥11, the RAID scale had a pooled sensitivity of 89% (95% CI: 78%-95%, I2=1.68%) and a pooled specificity of 73% (95% CI: 60%-82%, I2=7.58%) (Feghali et al., 2020; Goyal et al., 2017; Shankar et al., 1999). The Diagnostic and Statistical Manual - 5 criteria for Generalized Anxiety Disorder were the reference standard. The RAID scale was studied primarily in specialty clinic settings, leaving uncertainty regarding its accuracy in primary care or LTC. The RAID scale was specifically designed for people living with dementia, had the most evidence, highest sensitivity and in meta-analyses, minimal heterogeneity.

Recommendation #51

We suggest education and training programs for caregivers of people with dementia for the management of anxiety in dementia. (Conditional recommendation, low-quality evidence)

A systematic review of caregiver and person living with dementia interventions for BPSD identified two RCTs that evaluated the effects of caregiver interventions on symptoms of anxiety as measured on the RAID scale (Poon, 2022). Both interventions involved caregivers to assist people living with dementia in applying strategies to reduce symptoms of anxiety through learning anxiety-reducing skills with the person living with dementia and reinforcing cognitive behavioural strategies between treatment sessions (Spector et al., 2015; Stanley et al., 2013). Meta-analysis of these interventions demonstrated that there was a significant reduction in symptoms of anxiety as measured by the RAID scale (SMD: -0.66, -1.16 to -0.15) (Poon, 2022).

Recommendation #52

We suggest cognitive behavioral therapy, adapted for individuals with dementia, for the management of anxiety in mild-to-moderate dementia. (Conditional recommendation, low-quality evidence)

A small RCT compared cognitive behavioural therapy to usual care for symptoms of anxiety among people living with dementia (Stanley et al., 2013). The intervention included therapy adaptations for people living with dementia and was delivered weekly for 12 weeks for outpatients with dementia and anxiety. Participants in this study were restricted to those with mild-to-moderate severity of dementia as defined by a Clinical Dementia Rating scale sum-of-the-boxes score of 0.5 to 2. At the end of 12 weeks, a significant reduction in anxiety symptoms as measured by the RAID scale was noted for individuals in the cognitive behavioural therapy group when compared to usual care (effect size: 0.99) (Stanley et al., 2013).

Recommendation #53

We recommend music therapy with preferred music for the management of anxiety in dementia. (Strong recommendation, moderate-quality evidence)

Music therapy has been evaluated for several BPSD including symptoms of anxiety. A meta-analysis of music-based interventions for anxiety symptoms found that music was associated with a significant reduction in anxiety symptoms (N=8, n=258; SMD: -0.64, 95% CI: -1.05 to -0.24) (Abraha et al., 2017). Additional considerations related to music therapy are provided in the agitation section of this guideline (Section 5).

Recommendation #54

We suggest citalopram for the management of moderate-to-severe anxiety in Alzheimer's disease or related dementias. (Conditional recommendation, very low-quality evidence)

A large randomized controlled trial of citalopram for the treatment of agitation in Alzheimer's disease evaluated the effects of citalopram on symptoms of anxiety among trial participants, as measured on the anxiety item of the NPI (Leonpacher et al., 2016). Among participants with anxiety symptoms at baseline, 49% of individuals in the citalopram arm no longer had symptoms of anxiety by week 9. In contrast, only 12% of individuals in the placebo arm with anxiety symptoms at baseline no longer had these symptoms at week 9. Anxiety was also less likely to emerge during the study for individuals who received citalopram (36%) when compared to placebo (18%). Given the limited evidence available on the management of anxiety among people living with dementia, additional guidance related to management of anxiety in older adults is available in the CCSMH CPG on anxiety in older adults (Canadian Coalition for Seniors' Mental Health, 2024).

9. Recommendations for Assessing and Managing Sexual Expressions of Potential Risk in Dementia

Recommendation #55

We suggest that sexual expressions of potential risk be defined as a disruptive verbal or physical act of an explicit or perceived sexual nature, which is either intrusive or engaged in without the consent of those around the person living with dementia. (Conditional recommendation, very low-quality evidence)

There is no widely accepted definition or terminology for classifying sexually disinhibited behaviour in people living with dementia (Johnson et al., 2006). However, the definition of inappropriate sexual behaviour as "a verbal or physical act of an explicit, or perceived, sexual nature, which is unacceptable within the social context in which it is carried out" is highly cited in literature describing the assessment and management of sexually disinhibited behaviour in people with brain injury or dementia (Johnson et al., 2006). This definition encompasses measured domains of sexually disinhibited behaviour including hypersexuality, lewd/aberrant sexual behaviour, inappropriate sexual advances, inappropriate sexual comments, and socially disruptive sexually disinhibited behaviours (Chapman & Spitznagel, 2019). In attempts to avoid labelling behaviours as "appropriate" or "inappropriate", which can be highly subjective, the guideline panel emphasized focusing on identifying sexual behaviours that may pose a risk to the person or others.

The term "sexual expressions of risk" was adopted by Behavioural Supports Ontario (BSO) (Behavioural Supports Ontario, 2019b). This term incorporates both verbal sexual expressions of risk (e.g., explicit sexual comments, intrusive sexual questions, requests for sexual favours, sexualized language) and physical sexual expressions of risk (e.g., sexual gestures, intrusive physical contact, non-consensual initiation of sexual activity, masturbation in the presence of others without consent) (Behavioural Supports Ontario, 2019b). BSO recognizes that because not all sexual behaviours pose a risk, it is crucial to assess whether a person's sexual behaviour poses risks, whether there is a need for people around the person living with dementia to respond to these behaviours, and how to respond effectively. This terminology was acceptable to the guideline panel, with the modification to "sexual expression of potential risk", because it implies that sexual expressions that do not pose a potential risk to the person with dementia or others do not require intervention. Future research will be needed to understand the acceptability of this definition to health care providers, people living with dementia, and family and friend caregivers.

Recommendation #56

We suggest the St. Andrew's Sexual Behaviour Assessment Scale (SASBA Scale) for detecting sexual expressions of potential risk in dementia. (Conditional recommendation, very low-quality evidence)

The St. Andrew's Sexual Behaviour Assessment Scale (SASBA) identifies behaviours (e.g., verbal comment, touching others, exposure, non-contact), antecedent events contributing to the behaviour, and interventions delivered to reduce the behaviour after it has occurred in people with progressive or acquired neurological impairment (Knight et al., 2008). The SASBA has been assessed for content validity, face validity, and inter-rater reliability, but no study was found describing its diagnostic test accuracy (Knight et al., 2008). One systematic review of tools for measuring sexual expressions of potential risk in people living with dementia was found in the rapid overview of systematic reviews (Chapman & Spitznagel, 2019); however, none of the identified tools focused exclusively on detecting or measuring sexual expressions of potential risk in people living with dementia, which is why the SASBA is suggested as the preferred tool (Chapman & Spitznagel, 2019). The similarity of SASBA's three-component approach aligns with other behavioural assessment approaches such as the BSO-DOS©, which is familiar to many clinicians who care for people living with dementia, so it was felt that health care providers could implement this tool with appropriate education and training. Future research is needed to describe SASBA's measurement properties in people living with dementia in Canada, particularly among those living in LTC.

Recommendation #57

We suggest psychosocial approaches such as patient and caregiver education, removal of environmental triggers, changes in environment, and strategies to engage people living with dementia in other activities for reducing sexual expressions of potential risk in dementia. (Conditional recommendation, very low-quality evidence)

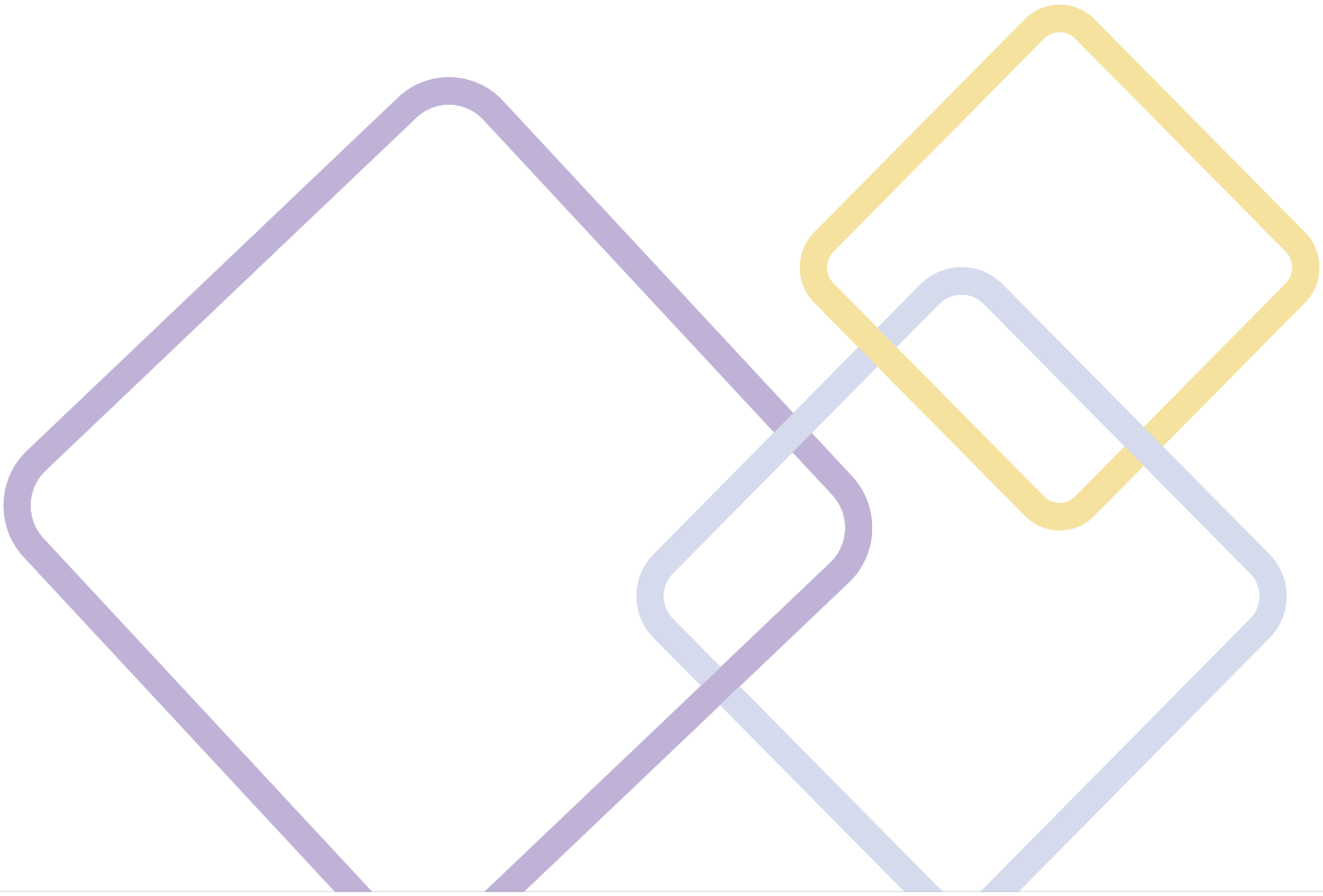
A rapid review of primary studies describing the effectiveness and safety of non-pharmacologic and pharmacologic interventions for reducing sexual expressions of potential risk in people living with dementia (PROSPERO 2023 CRD42023469625) was conducted. Patient and caregiver education, removal of environmental triggers, changing the

environment, strategies to engage the person living with dementia exhibiting sexual expressions of potential risk in another activity, and allowing the person living with dementia to express their sexuality in a manner that does not pose risks to others (e.g., expressing sexuality in a private location or alone) were identified as effective interventions (Lane et al., manuscript in preparation). However, this rapid review retrieved only case reports and case series, which is why this is a conditional recommendation.

Recommendation #58

We suggest neither for nor against the use of pharmacologic interventions for reducing sexual expressions of potential risk in dementia. (Conditional recommendation, very low-quality evidence)

A rapid review of primary studies describing the effectiveness and safety of pharmacologic and non-pharmacologic interventions for reducing sexual expressions of potential risk in people living with dementia (CRD42023469625) was undertaken. This review identified only case reports and case series with no RCTs, which is why the guideline panel felt that it could not recommend for or against the use of any pharmacologic interventions for reducing sexual expressions of potential risk in people living with dementia (Lane et al., In Preparation). Retrieved studies described the effects of hormonal therapies, antipsychotics, antidepressants, benzodiazepines, anticonvulsants, lithium, memantine, cholinesterase inhibitors, synthetic cannabinoids, 5-alpha reductase inhibitors, and buspirone (Lane et al., In Preparation). Although certain drug classes were described as effective in one or more case reports or case series, there are concerns about potential risk of harm related to pharmacologic interventions, and the balance of risks and benefits remain unclear. Future research involving more rigorous study designs (i.e., randomized or nonrandomized comparative studies) is needed.



10. Recommendations for Deprescribing Medications in BPSD

Recommendation #59

We recommend deprescribing antipsychotics in people living with dementia who do not have a history of severe agitation or psychosis or another potentially appropriate indication for antipsychotics such as a history of serious mental illness. (Strong recommendation, low-quality evidence)

As outlined in the preceding sections of this guideline (Sections 5 and 6), the use of antipsychotics among people living with dementia should be limited to circumstances where there is an appropriate indication for their use (e.g., severe agitation or psychosis that has not responded to other management strategies). There is increasing interest in reducing the inappropriate use of antipsychotics and the rates of inappropriate antipsychotic use has declined significantly in Canada and other countries due to these efforts (Kirkham et al., 2017). As antipsychotic medications are associated with significant risks such as mortality and stroke, it is strongly recommended that antipsychotics be deprescribed in situations where there was no appropriate indication for their use, such as severe agitation or psychosis in dementia, or a history of serious mental illness (e.g., schizophrenia) for which treatment with antipsychotics is considered appropriate.

Recommendation #60

We suggest deprescribing antipsychotics in people living with dementia who initially had severe agitation or psychosis, after considering their current symptoms, the total duration of antipsychotic treatment, dosage of medication required to stabilize BPSD, and initial severity of symptoms. (Conditional recommendation, low-quality evidence)

Many people living with dementia who initially had appropriate indications for antipsychotic medications can have antipsychotic medications safely deprescribed. A systematic review of RCTs included 10 unique RCTs in 632 individuals. Most trials included individuals who had received antipsychotics for at least three months and the majority used a tapering schedule for antipsychotics when individuals were receiving relatively high doses of medication (van Leeuwen, 2022). In RCTs examining deprescribing of antipsychotics (often implemented as a substitution of placebo for active treatment) when compared to continuation of treatment, ~70% of individuals had antipsychotics successfully discontinued without a worsening of BPSD (Ballard, 2004; Van Leeuwen et al., 2018). Most trials reporting on changes in BPSD over time did not find a significant worsening of symptoms for participants who had discontinued treatment compared to those who continued treatment. One RCT identified an approximately 50% reduced risk of mortality over 12 months for individuals who had their antipsychotics discontinued, when compared to those who continued treatment (Ballard et al., 2009). Predictors of successful antipsychotic discontinuation include less severe BPSD at baseline (Ballard et al., 2009; Ballard, 2004) and lower doses of antipsychotics being required initially to stabilize BPSD symptoms (Ruths, et al., 2008). Therefore, while it is important to periodically review whether antipsychotics are required for each person living with dementia, individuals who have been prescribed medications for longer periods of time, those who had less severe symptoms at baseline or those who stabilized on lower doses could be most appropriate for a trial of deprescribing.

The guideline panel acknowledges that some people living with dementia may have BPSD such as agitation which has been successfully treated with medications that are not recommended in this CPG. Unless there are other reasons to deprescribe the medications that stabilized BPSD, such as side-effects or loss of effectiveness, these medications should not be deprescribed, or other medications substituted, unless there is an indication for deprescribing. Unnecessary deprescribing of effective medications, including substitution of other medications, may result in an unnecessary risk of worsening of BPSD.

Recommendation #61

We suggest deprescribing antipsychotics by decreasing the dose by 25-50% every 1-2 weeks until discontinued, and that dosage reduction be stopped at the lowest effective dose if BPSD worsen. (Conditional recommendation, low-quality evidence)

If a decision is made to try deprescribing antipsychotic medications, it is recommended that antipsychotics be tapered gradually over time. Of the studies evaluating antipsychotic discontinuation among people with dementia, the majority of trials (7 of 10) used a gradual dose reduction strategy (Van Leeuwen et al., 2018). Deprescribing organizations (*deprescribing.org*, 2024) and previous antipsychotic deprescribing guidelines (Bjerre et al., 2018) recommend gradual tapering of antipsychotic medications. Gradual dose reduction is recommended compared to abrupt withdrawal of antipsychotics for several reasons. Gradual dose reduction may enable monitoring for a recurrence of BPSD during the withdrawal process, which may allow for reintroduction of the previously effective dose of an antipsychotic or initiation of non-pharmacological interventions prior to emergence of more severe BPSD which may be more difficult to stabilize. Some individuals with BPSD who are unable to discontinue antipsychotics completely without recurrence of BPSD may be able to remain stabilized on a lower dose than they were initially prescribed, which may

be beneficial with respect to reducing the risk associated with dose-related adverse effects of antipsychotics even without complete cessation of treatment.

Recommendation #62

We suggest that other psychotropic medications be reviewed routinely for potential discontinuation in people with dementia including benzodiazepines and antidepressants. (Conditional recommendation, very low-quality evidence)

Medications such as benzodiazepines are not recommended for the treatment of BPSD due to the lack of evidence of efficacy, and known risks associated with the use of benzodiazepines among both older adults without dementia and people living with dementia (Ng et al., 2018). Similar to the evidence on successful discontinuation of antipsychotics, many older adults who are prescribed benzodiazepines can have these medications discontinued, although very gradual dose reduction strategies need to be employed to avoid withdrawal symptoms which can be severe, particularly with high doses and prolonged use (Ng et al., 2018; Pottie et al., 2018). Studies evaluating benzodiazepine discontinuation in older adults have found that 60% of individuals can have benzodiazepines reduced, most frequently through gradual dose reduction either alone or combined with cognitive behavioural therapy (Paquin et al., 2014). Similarly, benzodiazepine receptor agonists (i.e., "Z-drugs") also should be considered for deprescribing with tapering schedules consistent with those recommended for benzodiazepines (Pottie et al., 2018). One RCT comparing discontinuation of benzodiazepines or antipsychotics among people in residential care demonstrated a 21% relative reduction in benzodiazepines was observed over 6 months following a multicomponent intervention program although the proportion of individuals with dementia in the study was not reported (Westbury et al., 2018).

Less is known about the deprescribing of antidepressant medications among older adults with dementia. Depression guidelines for individuals who have a history of major depressive disorder, particularly with severe symptoms or recurrent episodes of depression may require indefinite treatment with antidepressants due to the high risk of relapse of symptoms (Canadian Coalition for Seniors' Mental Health, 2006). However, many individuals with dementia may have had treatment initiated for BPSD such as agitation or other indications, such as sleep changes, and there are very few long-term antidepressant treatment trials for BPSD or RCTs evaluating antidepressant discontinuation (Bergh et al., 2012). A RCT comparing discontinuation of antidepressants to continuation of antidepressants among older adults with dementia in LTC found that individuals who had antidepressants discontinued were more likely to experience a small but statistically significant worsening of depressive symptoms when compared to those who continued (Bergh et al., 2012). An increase in overall BPSD was also noted in the discontinuation group on the NPI, although this did not reach statistical significance (Bergh et al., 2012). The majority of individuals in the discontinuation group did not have meaningful worsening of depressive symptoms and the study's authors concluded that many people with dementia may be able to have antidepressants discontinued, although they need to be monitored for potential worsening of symptoms during the process. Members of the guideline panel led development of a guideline on the deprescribing of cognitive enhancers in dementia which includes considerations related to BPSD (Herrmann et al., 2022).

Recommendations #63

We suggest interdisciplinary education interventions, interdisciplinary medication reviews, educational interventions for family physicians, and pharmacist-led medication reviews to facilitate antipsychotic deprescribing in people with dementia at the organizational level in long-term care and other residential care settings. (Conditional recommendation, low-quality evidence)

Sustained reductions in the inappropriate use of antipsychotics among people living with dementia in long-term care are possible, as evidenced by the decline in their use in Canada, the U.S. and other countries (Kirkham et al., 2017). The preceding recommendations related to deprescribing of antipsychotics in this guideline are based on RCTs comparing individuals who continued antipsychotics to individuals who discontinued antipsychotics or who were randomized to placebo. Evidence related to which strategies are effective for reducing antipsychotic use at the organizational level typically evaluate the impact of interventions administered at the organizational level such as in individual LTC homes or other residential care environments. These studies also report outcomes at the organizational level, such as the proportion of LTC residents who are prescribed antipsychotics in intervention homes when compared to control homes.

A systematic review of RCTs evaluating optimal prescribing in LTC identified 25 studies reporting on a variety of prescribing outcome measures, including but not limited to the prescribing of antipsychotics in LTC (Almutairi et al., 2020). This review identified several organizational strategies that were associated with reductions in antipsychotic use, including: interdisciplinary staff education on BPSD assessment and management (N=5); interdisciplinary medication reviews (N=2); educational interventions for family physicians (N=2); and, pharmacist-led reviews to identify potential candidates for deprescribing (N=2). Many successful interventions included more than one component (Almutairi et al., 2020). Few studies examining interventions aimed at reducing antipsychotics at the LTC home level reported on BPSD outcomes, although there was no worsening of BPSD reported in the studies that did report this (Almutairi et al., 2020; Cosette et al., 2022).

11. Conclusions

The CCSMH Canadian Clinical Practice Guidelines for Assessing and Managing BPSD offer health care providers with current evidence and recommendations related to the management of BPSD in a Canadian context. This guideline provides advice and direction underlying the assessment and management of all BPSD, as well as specific guidance related to the management of BPSD syndromes including agitation, psychosis, depression, anxiety and sexual expressions of potential risks. The guideline also provides recommendations related to the deprescribing of antipsychotics and other medications frequently used in the management of BPSD.

There are limitations to these guidelines, including that for some topic areas there are relatively few high-quality studies from which to derive evidence-based recommendations notably for non-pharmacological interventions for specific BPSD other than agitation and depression, and pharmacological interventions for BPSD other than agitation. There is a pressing need for research in these areas, specifically, to enhance the current evidence base in these important areas, and a need for more research generally.

This guideline also does not address all BPSD syndrome areas, such as sleep changes and apathy, due to the priorities identified initially, and guideline time and resource limitations.

For similar reasons, this guideline addresses evidence related to Alzheimer's disease and related forms of dementia such as vascular or mixed dementia. Separate recommendations or guidelines may need to be developed to address other types of dementia, such as dementia with Lewy bodies, Parkinson's disease dementia, frontotemporal dementia and other less common types of dementia.

Implementation and evaluation of the guidelines will be an ongoing process following the publication of the CPG in March 2024. The CCSMH anticipates that these guidelines will stimulate improvements in clinical care and the guideline panel hopes that health care providers, organizations, and researchers will consider implementing and evaluating the impact of this BPSD guideline in their current and future work.

The CCSMH has developed a knowledge mobilization resource to collate evidence-informed resources related to BPSD at the Behaviours in Dementia Toolkit website (*www.behavioursindementia.ca*) to help people living with dementia, caregivers, and health care providers to identify resources that may assist in the practical implementation of the BPSD guideline recommendations.

Appendix

Dissenting Opinion Related to Recommendation #1

We recommend the International Psychogeriatrics Association (IPA) consensus criteria for agitation in cognitive disorders to diagnose agitation in dementia. (Strong recommendation, moderate-quality evidence)

I respectfully disagree with the majority decision provided by the guideline panel for this recommendation and generally disagree with diagnosing behaviours as 'agitation'. Although I appreciate the benefits to standardizing language, there are significant risks in adopting such language for behaviours that don't fit the IPA definition and for those that do. Many behaviours expressed by individuals living with dementia are distressing for them and those around them, but do not meet the IPA criteria (e.g., behaviour that has occurred for less than two weeks); and thus, fall outside of the recommendations of this guideline. This gap leaves care providers without guidance regarding how best to respond.

More concerning are behaviours that meet the IPA criteria leading to people living with dementia being diagnosed/labelled with 'agitation'. This language reflects a biomedical lens that pathologizes the behavioural responses expressed by people living with dementia. Instead of viewing behaviours as expressions of unmet needs or normal human reactions to situations (e.g., a stranger attempting to undress you and washing your genitals without you asking them to do so), the person gains a new diagnosis that needs to be 'treated'. Alternatively, an unmet need lens puts the responsibility on the care team to consider context and possible contributing factors to the specific behaviours, and to find individualized approaches to meet the need.

Debbie Hewitt Colborne, RN, MScN

- Registered Nurse, Project Advisor, Behavioral Supports Ontario Provincial Coordinating Office, North Bay Regional Health Centre

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Notes

Canadian Coalition for Seniors' Mental Health (CCSMH)

info@ccsmh.ca

1-888-214-7080 extension 102

www.ccsmh.ca

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