UNIVERSITY OF CALGARY | FACULTY OF MEDICINE

Best practices in the management of behavioural and psychological symptoms of dementia in residents of long-term care facilities in Alberta

A Health Technology Reassessment

The Health Technology Assessment Unit, University of Calgary

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ABBREVIATIONS

ABC	Aberrant Behavior Checklist
ABMI	Agitation Behaviour Mapping Instrument
AD	Alzheimer's Disease
ADL	Active Daily Living
ADL	Activities Of Daily Living
AD-RD	Alzheimer's Disease And Related Disorders Mood Scale
AGECAT	Automatic Geriatric Examination For Computer-Assisted Taxonomy
AMTS	Abbreviated Mental Test Scale
ASI	Anxiety Status Inventory
AUA	Appropriate Use of Antipsychotics
BARS	Brief Agitation Rating Scale,
BEHAVE-AD	Behavioural Pathology In Alzheimer's Disease Rating Scale
BIA	Budget Impact Analysis
BIP	Behavioural Observation Scale For Intramural Psychogeriatry
BOP	Beoordelingsschaal Voor Oudere Patienten
BPRS	Brief Psychiatric Rating Scale
BPSD	Behavioural And Psychological Symptoms Of Dementia
BSMT	Behavioural And Symptom Mapping Tool
CAM	Complementary and Alternative Medicine
CAPE-BRS	Clifton Assessment Procedures For The Elderly – Behavioral Rating Scale
CDR	Clinical Dementia Rating
CDS	Cornell Scale For Depression In Dementia
CMAI	Cohen-Mansfield Agitation Inventory
CPS	Cognitive Performance Scale
CVD	Alzheimer's Disease With Cerebrovascular Disease
DAT	Diagnosis Dementia Of The Alzheimer Type
DBS	Disruptive Behavioural Scale
DCM	Dementia-Care Mapping
DLB	Dementia With Lewy Bodies
DMAS	Dementia Mood Assessment Scale
DSM	Diagnostic And Statistical Manual Of Mental Disorders
GDS	Global Deterioration Scale
GDS	Global Deterioration Scale
GIP	Gedragsobservatieschaal Voor De Intramurale Psychogeriatrie
HD	Huntington's Disease
ICD	International Classification Of Diseases
LTC	Long-Term Care
MDS	Minimum Dataset
MIBM	Modified Interaction Behaviour Measure
MMSE	Mini-Mental State Examination
NINCDS ADRDA	National Institute Of Neurological And Communicative Disorders And Stroke-Alzheimer's Disease And Related Disorders Association

NPI	Neuropsychiatric Inventory
OAS	Observed Affect Scale
PAG	Physically Aggressive Behaviour
PAP	Psychomotor Activation Programme
PAS	Pittsburgh Agitation Scale
PCC	Person-Centered Care
PD	Parkinson's Disease
PNB	Physically Non-Aggressive Behaviour
RAI	Resident Assessment Instrument
RCT	Randomized Controlled Trials
SCN	Strategic Clinical Network
SCU	Special Care Unit
VA	Verbal Agitation
VD	Vascular Dementia

Glossary of Terms

Antipsychotic Medications: A class of drugs developed to treat psychotic conditions such as schizophrenia, bipolar disorder and psychotic depression. In older adults, antipsychotics are commonly used for delirium, psychotic and mood disorders, as well as for the managing behavioural and psychological symptoms of dementia. There are three major classes of antipsychotic medications based on their mechanism of action: typical, atypical and third generation.

Antidepressant Medications: A class of drugs developed to treat psychiatric conditions. These medications are effective in reducing distress and agitation when used to treat mood and anxiety disorders. Similar to antipsychotic medications, antidepressants are frequently indicated for neuropsychiatric symptoms in older adults with dementia. There are several classes of antidepressant medications that act by modulating the function of neurotransmitters in the brain, such serotonin and norepinephrine.

Agitation: A term used to describe excessive motor activity, commonly characterized by symptoms such as anxiety, irritability, motor restlessness and abnormal vocalization. Agitated individuals may also exhibit behaviours such as pacing, wandering, aggression, shouting and night time disturbance.

Aggression: A term used to describe the purposeful act of delivering a verbal or physical stimulus that is perceived to be noxious, to another person.

Behavioural and Psychological Symptoms of Dementia (BPSD): A broad term applied to non-cognitive symptoms of disturbed perception, thought content, mood or behaviour that frequently occur in persons with dementia. Such symptoms can include verbal and physical aggression, agitation, psychosis, delusions, hallucinations, anxiety, depression, sleep disturbances, repetitive motor activity and vocalization, hoarding and wandering.

Built Environment Intervention: An intervention involving direct manipulation of the physical structure of an individual's living environment. Such interventions can include a change or redesign of existing physical structures or spaces within a building, visual barriers or disguising of existing physical structures entry/exit ways, the addition of physical objects or spaces to the existing environment or the relocation of individuals to a novel living environment.

Clinical Practice Guidelines: A systematically developed body of statements that are based on the most current and best available evidence used to assist clinician and patient decision-making within specific practices of care. Implementation of clinical practice guidelines are thought to result in improved patient outcomes through the delivery of effective and appropriate healthcare.

Complementary and Alternative Medicines: Non-pharmacological interventions that are derived from non-synthetic origins and used to treat a variety of conditions, including behavioural and psychological symptoms of dementia. Herbal medicinal alternatives, acupuncture and acupressure are examples of complementary and alternative medicines.

Dementia: A chronic, progressive neurological disease that affects memory, orientation, comprehension, calculation, learning capacity, language, judgment and executive function. There are a variety of diseases grouped within dementia such as Alzheimer's disease, vascular dementia, dementia with Lewy bodies and fronto-temporal dementia.

Non-pharmacological Interventions: A broad term applied to any therapy that is not a synthetic drug. These constitute a variety of interventions such as aromatherapy, light and music therapy, recreational therapy, multisensory stimulation, use of herbal and vitamin supplements and even modifications to the structural or built environment. Non-pharmacological interventions are complementary to pharmacological interventions for the management of behavioural and psychological symptoms of dementia.

Person-Centered Care: An approach that that is centered on viewing a patient first as a person, instead of a collection of symptoms. Persons with a specific condition must be regarded individually with their own specific qualities and when providing person-centered care, their unique responses to a given condition or treatment must be taken into consideration.

Pharmacological Interventions: A broad term applied to any synthetically-derived drug therapy. In the management of behavioural and psychological symptoms of dementia, such interventions include antipsychotic and antidepressant medications.

1. BACKGROUND

Dementia is a chronic, progressive disease resulting in the loss of cognitive functions such as memory, orientation, comprehension, calculation, learning capacity, language, judgment, and executive function[1]. There are a variety of diseases grouped within dementia such as Alzheimer's disease, vascular dementia, dementia with Lewy bodies, and fronto-temporal dementia.

The burden of dementia is very high with approximately 40,000 people living with dementia in Alberta. By 2038, 100,000 Alberta residents are projected to be diagnosed with dementia[2]. Of the estimated 13,000 Albertans living in long-term care facilities (LTC), approximately 71% of them have a dementia diagnosis[3]. While the cognitive impairment of dementia is devastating, the accompanying symptoms, generally termed the behavioral and psychological symptoms of dementia (BPSD), are also quite challenging for patients, families and caregivers.

1.1. Behavioral and psychological symptoms of dementia

BPSD is the broad label applied to *non-cognitive* symptoms such as verbal and physical aggression, agitation, psychosis, delusions, hallucinations, anxiety, depression, sleep disturbances, repetitive motor activity, repetitive vocalization, hoarding and wandering[4]. An estimated 52% or 6600 of residents in Alberta's LTC display one or more types of BPSD[3]. The etiology of BPSD is multi-factorial; it is believed that symptoms can arise either due to chemical changes in the brain or due to external factors, particularly those related to communication. However, BPSD presents differently across patients and the triggers are highly individualized. It is, therefore, often difficult to attribute a particular behaviour to a single predisposing factor.

BPSD is extremely stressful to the person with dementia, as well as their caregivers and family members. Patients with BPSD can be at risk of harming themselves or their caregivers through aggression and agitation. Many other symptoms such as wandering, hoarding and sleep disturbance can be disruptive to normal everyday function, and can leave the patient in need of assistance[5]. In addition, patients with BPSD may find it difficult to participate in social activities with friends and family leading to further isolation.

1.2. Treatment for behavioral and psychological symptoms of dementia

Treatment options for BPSD are classified into pharmacological and non-pharmacological approaches. Pharmacological interventions for BPSD include antidepressants for anxiety or depression; trazodone for sleep disorders; trazodone or cholinesterase inhibitors for aggression or agitation; and antipsychotic medications for aggression, hallucinations, or delusions. Antipsychotic medications are a class of drugs developed to treat psychotic disorders such as schizophrenia, bipolar disorder and psychotic depression. These medications act via blocking the receptors for the neurotransmitters like dopamine and serotonin[6]. Typical or first generation

antipsychotics are known to be associated with motor side-effects such as tremors, rigidity and parkinsonism. Atypical or second generation antipsychotics, were adopted since they are better tolerated by patients[7]. A 2012 Cochrane review on the use of atypical antipsychotics for the treatment of BPSD concluded that while these drugs are moderately effective in reducing aggression and psychotic symptoms, they are associated with an increased risk of major side effects including cerebrovascular events (e.g., stroke), death, upper respiratory infections, and oedema[8]. In the presence of such major adverse events and moderate effectiveness, thoughtful consideration is required before prescribing antipsychotics. The majority of clinical guidelines, including the British Columbia guidelines on cognitive impairment in the elderly, recommend that antipsychotics should be used in the treatment of BPSD only when the patient is experiencing severe symptoms and after psychosocial and environmental interventions have been tried[1].

It is likely that antipsychotics are over-utilized in Alberta LTC facilities with a provincial average of 28% utilization in the absence of documented indications such as severe agitation, aggression and psychosis [1;9]. Therefore, the use of antipsychotic medications in BPSD patients, especially those living in LTC facilities, is a growing concern. The Appropriate Use of Antipsychotics (AUA) project is a health technology reassessment project intended to review current clinical practice and reduce the utilization of antipsychotic medications among LTC resident in Alberta. The development of evidence-based clinical practice guidelines outlining the utilization of antipsychotics in BPSD management is a major component of the AUA project.

As per the BC guideline, non-pharmacological interventions have been recommended as possible treatments for BPSD [1]. These interventions constitute a wide variety of therapies such as massage, acupressure, acupuncture, aromatherapy, light and music therapy, and use of herbal and vitamin supplements. In addition, modifications to the built environment have also been studied as possible measures for managing BPSD. These interventions can likely serve as alternatives for pharmacological treatment in some cases of BPSD. Therefore, a comprehensive review of the published evidence that informs the use of pharmacological or non-pharmacological alternatives to antipsychotics for the management of BPSD is required.

2. POLICY QUESTION

What is/are the best clinical practice(s) alternatives to antipsychotic use for the management of behavioural and psychological symptoms in dementia in long-term care facilities in Alberta?

3. RESEARCH OBJECTIVE

To summarize the clinical and cost-effectiveness evidence for pharmacological and non-pharmacological alternatives to antipsychotics to support the development of a clinical practice guideline and provincial policy development for the best clinical practice(s) alternatives to antipsychotics use for the management of behavioural and psychological symptoms of dementia in long-term care facilities in Alberta.

4. SOCIAL CONTEXT

4.1. Long-term care facilities in Alberta

As of January 2012, there were 425,000 seniors living in Alberta of which approximately 3% or 12,750 seniors were in LTC[10]. LTC facilities provide case management, rehabilitation therapy, palliative care, as well as assistance with personal care, meals, housekeeping/cleaning, exercise/health programs and planned recreation activities for its residents[11]. There are 174 LTC facilities in Alberta are located in each health zone in Alberta (**Table 1**) that offer 24 hour on-site care for seniors in need of support. LTC residential services may be recommended for patients with complex end of life care needs; complex medication management; complex nursing care; and inconsistent or unstable behavior that places them or their caregivers at risk.

Table 1: Number of LTC facilities by Alberta Health Designated Zone

ZONE	Number of LTC Facilitates
Calgary	41
Central	42
Edmonton	37
North	36
South	18
Grand Total	**174**

Approximately 66% of the LTC residents are female, the majority of whom are over 85 years of age (mean age 84.9), 59% are widowed and approximately 25% are married[3]. Patients in LTC have a high burden of disease with an average of 5.2 diseases per resident and an average of 7.9 regularly prescribed medications per resident. The most prevalent diseases are dementia, hypertension, arthritis and depression. Approximately 5% of LTC residents may be categorized as independent (i.e. able to complete personal hygiene tasks, toilet use, locomotion and eating on

their own) while 12% may be considered as totally dependent. The remaining 83% require varying degrees of assistance in their day to day functioning[3].

Typically, LTC facilities in Alberta are staffed by full-time personal care aides, licensed practical nurses and registered nurses. In addition, at least one physician is formally affiliated with each of the facilities. However, the exact composition of LTC staff varies across facilities[3].

4.2. Current care patterns for management of behavioural and physical symptoms of dementia in Alberta

4.2.1. Alberta Health Continuing Care Health Services Standards

The Alberta Health Seniors' Services and Continuing Care Division is responsible for overseeing the standards and service provision within continuing care in Alberta including LTC. Continuing Care Health Standards[12] were originally developed in May 2006 followed by revisions in 2007, 2008 and 2013. The most recent amendment of the Continuing Care Health Service Standards provides guidance for managing continuing care health service standards at the regional and operational levels. All LTC facilities in Alberta are required to comply with these standards[12]:

- *Individual care planning:* The needs of all LTC facilities clients shall be assessed using the RAI/2.0 assessment tool. Newer versions of the RAI tool may be used as it becomes available.
- *Medication management:* Safe medication management policies shall be established and put in place. An annual review shall be conducted on prescriptions, assessment of the order of prescriptions, implementation of the order, administration of medications, monitoring and disposal. Policies and processes shall include client specific information on medications, adherence to current best practice and monthly review of any medications used for chemical restraints to ensure appropriateness.
- *Provision of continuing care health services:* There shall be operational policies and processes in place for the provision of continuing care which reflect current evidence based best practices including policies on prevention and management of aggressive or violent behaviour; care of clients with dementia, cognitive impairment or mental health needs; and careful review of physical, chemical and environmental restraints to manage challenging behaviours.

4.2.2. Alberta Health Service Guidelines

In April 2009, Alberta Health Services adopted a guideline for management of antipsychotic medication in continuing care, of which LTC is one type of care setting. The purpose of this guideline was to optimize resident safety and to promote the adoption of judicious use of antipsychotic medications for the treatment of BPSD within Alberta Health Services operated facilities. Originally developed within the previous Calgary Health Zone, the guideline was adopted as a "legacy" guideline and the process for guideline development and consideration of evidence was not clearly documented. In addition, the uptake and roll-out of this guideline is

unclear. However, the main points of the guideline are summarized below (full guideline is provided in **Appendix A**):

- Non-pharmaceutical strategies for behavior management should the first consideration in the care of individuals living with dementia
- Antipsychotic medications should be considered if other strategies are either unavailable or limited in their effect
- The use of antipsychotic medications to manage behaviors associated with dementia should be guided by the philosophy of least restraint
- Considering the possible side effects of antipsychotic medications, antipsychotic use in patients should be carefully considered and regularly monitored
- The Behavior and Symptom Mapping Tool (BSMT) should be utilized to initiate and monitor response to antipsychotic treatment
- The benefits of antipsychotic therapy should be carefully weighed against the potential risks and the final decision should be shared with the family and staff
- Patients should be frequently reassessed for continued need for antipsychotics and progress should be documented

Despite the existence of these provincial guidelines, it is estimated that 28% of antipsychotic prescriptions in LTC residents are issued in the absence of a documented psychotic indication [9]. The "Appropriate Use of Antipsychotics (AUA)" was identified as a flagship health technology reassessment project by the Seniors Health Strategic Care Network (Seniors SCN). The AUA project is intended to reassess current practice and to develop strategies to reduce prescribing of antipsychotics among LTC resident in Alberta. One of the objectives of the AUA project is to identify existing *evidence-based* national or international guidelines that may be suitable for adaptation within the Alberta Context.

5. TECHNOLOGICAL EFFECTIVENESS

SUMMARY BOX

Overview of Approach: Systematic review and quality assessment utilizing the AGREE-II tool was completed to identify high-quality evidence based existing clinical practice guidelines for BPSD to adaption within Alberta. Once a suitable guideline was selected, 5 enhancement systematic reviews were undertaken to assess the evidence to support the effectiveness of non-pharmacological, antidepressants, complementary and alternative medications, the built environment and the cost-effectiveness of each intervention.

Key Findings:

Adaptable Guideline: *Best Practice Guideline for Accommodating and Managing Behavioural and Psychological Symptoms of Dementia in Residential Care: A Person-Centered Interdisciplinary Approach,* a recent evidence-based guideline from British Columbia, was identified as the most appropriate guideline; it is the most recent Canadian guideline and is comprehensive enough to be adapted to the Alberta context. Recommendations from the BC guidelines include: Adopting a person-centered approach; determining target behaviours in dementia; developing appropriate care plans; and considerations for non-pharmacological and pharmacological interventions.

Non-pharmacological interventions: From the 40 included Randomized Controlled Trials, 21 reported that the non-pharmacological intervention led to improvements in BPSD compared to a control; the remaining 19 studies reported no significant difference in BPSD between intervention and control groups. None of the studies reported adverse outcomes. All of the studies were small and of low to moderate quality. The use of non-pharmacological interventions is likely a viable first-line of treatment for managing BPSD in LTC residents as just over half of the studies reported improved outcomes, and none reported worsening.

Antidepressants as a substitute for antipsychotics: A high-quality recent systematic review of 6 RCTs reported no statistically significant differences in BPSD or drug tolerability between antidepressants (SSRIs) and antipsychotics (typical and atypical). One additional RCT also reported no significant differences in outcomes measures between SSRIs and antipsychotics. All studies included small sample sizes and were of low to moderate quality. None of the studies reported adverse outcomes.

Complementary and Alternative Medications: Four low to moderate quality studies reported on the utilization of CAM interventions to manage BPSD. All reported improvements indicating CAM may be a promising intervention. None of the studies reported adverse outcomes.

Built environment: Nine of the 12 included studies demonstrated improvements and 3 reported no difference in the frequency and/or severity of BPSD following the built environment intervention, compared to the control conditions. All of the studies were of low to moderate quality and reported varied outcome measures.

Cost-effectiveness: No literature was identified reporting the cost-effectiveness of any of the interventions.

5.1. Selection of guideline adaptable to the Alberta context

Summary of Findings:

Best Practice Guideline for Accommodating and Managing Behavioural and Psychological Symptoms of Dementia in Residential Care: A Person-Centered Interdisciplinary Approach, a recent evidence-based guideline from British Columbia, was identified as the most appropriate guideline to adapt to the Alberta context. It is the most recent Canadian guideline and incorporated many of the key components included in Alberta practice.

Key recommendations from the BC guidelines include: adopting a person-centered approach, determining target behaviours in dementia, developing appropriate care plans, and considerations for non-pharmacological and pharmacological interventions.

5.1.1. Research objective

To determine the best practice guideline(s) aimed at management of BPSD in LTC for the purpose of adaptation to the Alberta context.

5.1.2. Methods

Recognizing that much work has been completed in various jurisdictions, in order to leverage the available high-quality work of others, a systematic search for existing clinical practice guidelines on dementia was completed. Electronic databases (CINAHL, EMBASE, MEDLINE, PubMED and PsycINFO) and guidelines websites (including: CMA Infobase, National Guidelines Clearinghouse, TOP Guidelines Alberta and the TRIP database) were searched from 2003 to June 2013 to identify relevant English language clinical guidelines. The search terms included: dementia, Alzheimer's disease, antipsychotic drugs (both typical and atypical drugs prescribed in Canada and worldwide), practice guidelines, protocols and care pathways. A complete search strategy can be found in **Appendix B**.

The retrieved abstracts were reviewed and included for full-text review if the abstract was a guideline for dementia, included pharmaceutical or non-pharmaceutical management, was not a consensus letter/letter to the editor and was not exclusively in a clinical setting. Additionally, a Google hand-search was performed using the search terms "dementia guidelines". Full-text articles were also accepted from the Seniors SCN. Articles were excluded if they: did not include a BPSD component, were not in a guideline format, did not utilize a systematically identified evidence base, were primary care focused or were not specific to a LTC setting.

Quality of selected clinical practice guidelines regarding management of dementia was appraised by four independent reviewers using the standardized Appraisal of Guidelines, Research and

Evaluation II (AGREE II) tool. The AGREE II tool is a 23-item instrument used to assess the quality of clinical practice guidelines across 6 quality-related domains: scope and purpose, stakeholder involvement, rigour of development, clarity of presentation, applicability and editorial independence[13;14]. Each item in the AGREE II tool is scored using a 7-point response scale, to generate a possible total score of 161 that is recommended to be applied by 4 independent reviewers in order to assure reliability of guideline quality estimation[13;14].

To quantify the value of the guidelines, the categories for the AGREE II tool were classified as: high overall quality guideline (most domain scores >60%), moderate overall quality guideline (most domain scores between 30% and 60%), low overall quality guideline (most domain scores <30%), or a guideline with unclear results regarding its quality[15]. The full list of inclusion exclusion criteria is presented in **Table 2**.

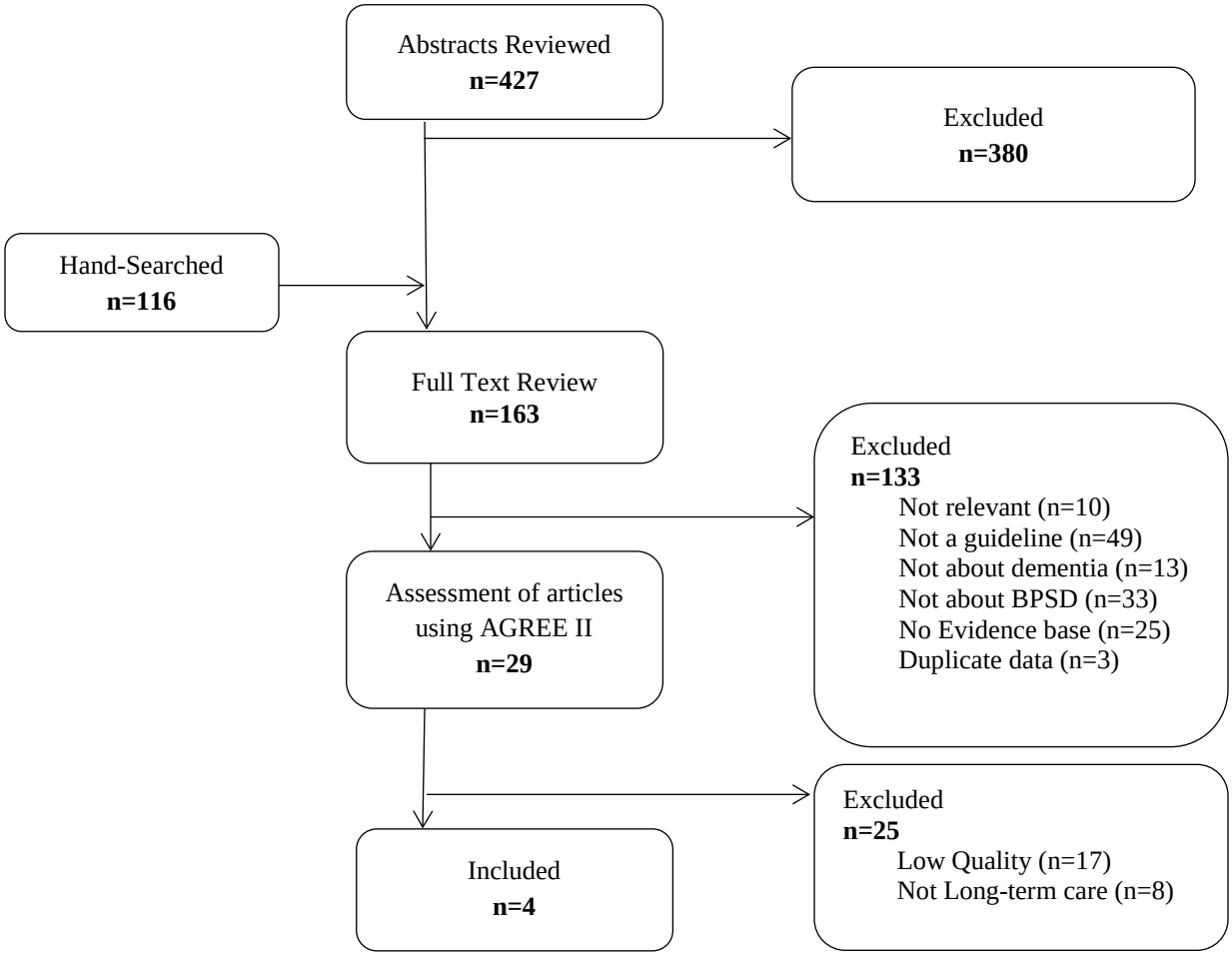
Table 2: Inclusion/Exclusion criteria for BPSD guidelines

Inclusion Criteria	**Exclusion Criteria**
• Seniors (≥ 65 years) with BPSD • LTC settings • Comparison of any intervention with standard of care • Effect on BPSD (efficacy) • Guideline Study Design	• Participants < 65 years • Primary endpoint not based on efficacy • Non-original data • RCT, Controlled trials, Commentaries, Letters, Editorials, Opinions, reviews (without systematic approach), Case Studies, or Biochemical Studies • Mouse/Non-human Studies • Only used pre-post comparisons of participants without a control group and also excluded studies that used a crossover study design • Preclinical or Animal Models

5.1.3. Results

Four hundred and twenty-seven abstracts were identified. An additional 116 full text documents were identified through hand searching websites and other sources. Twenty-nine guidelines were included in the quality assessment with four guidelines ranked as high quality and included for final consideration (**Figure 1**).

Figure 1: Flowchart for the assessment of existing dementia guidelines



5.1.4. Summary of Selected Guidelines

The four high quality guidelines identified from the AGREE II tool assessment included: the American Geriatrics Society and American Association for Geriatric Psychiatry *Consensus Statement on Improving the Quality of Mental Health Care in U.S. Nursing Homes: Management of Depression and Behavioral Symptoms Associated with Dementia*[16]; the National Institute for Health and Clinical Excellence *Guideline on Supporting People with Dementia and Their Carers in Health and Social Care* [17]; the Scottish Intercollegiate Guidelines Network's National Clinical Guideline *Management of Patients with Dementia*[18]; and the British Columbia *Best Practice Guideline for Accommodating and Managing Behavioural and Psychological Symptoms*[1]. All four guidelines were comprised of high levels of evidence and rated to be of high overall quality based on the AGREE II tool assessment. Guided by the clinical expert group, the British Columbia guideline was identified as the guideline that was most appropriate to adapt to the Alberta context as it was most recently published and developed within Canada.

5.1.4.1. Overview of the British Columbia Best Practice Guideline for Accommodating and Managing Behavioural and Psychological Symptoms

The British Columbia *Best Practice Guideline for Accommodating and Managing Behavioral and Psychological Symptoms of Dementia in Residential Care* (the BC guideline) was released in October 2012[1]. The main objectives of the BC guideline are to improve the quality of care of dementia patients in residential care, improve family member and caregiver engagement in the care spectrum, focus on the appropriate use of antipsychotics in BPSD patients in LTC facilities and build systemic capacity for better supporting assessment and care of patients with BPSD.

The recommendations included in the BC guideline were based on the *British Columbia (BC) Clinical Practice Guideline on Cognitive Impairment in the Elderly: Recognition, Diagnosis and Management* (2007, revised 2008)[19], as well as consensus with key stakeholders involved in the Canadian Coalition for Senior's Mental Health[20]. In communication with the BC guideline authors, it was confirmed that the clinical evidence base supporting the 2007 documents was current to 2005. The key recommendations of the BC guideline are highlighted below.

Determine target behaviours: Each of the behaviours under the umbrella of BPSD may have underlying factors and individuals frequently exhibit a specific pattern. BPSD symptoms are a manifestation of unmet needs of the patient that warrant a thorough, patient centered assessment. It is also necessary to distinguish dementia from delirium and depression utilizing the following tools: Cohen Mansfield Agitation Inventory (CMAI), Dementia Observation Scale and Behaviour Pattern Record.

Develop a care plan: Once a diagnosis of dementia has been established, the ABC model (Antecedent, Behaviour, and Consequences) can help in understanding triggers for BPSD. RAI

Clinical Assessment Protocols (CAPs) may be used for clinical assessment, decision-making and developing a care plan.

Non-pharmacological interventions should be considered as the first line of treatment: The decision to use a specific type of non-pharmacological intervention should be guided by the person-centered approach where individual background, preferences (e.g., cultural, linguistic, religious, and life experiences are taken into account. P.I.E.C.E.S., (**P**hysical, **I**ntellectual, **E**motional, **C**apabilities, **E**nvironment, and **S**ocial) which is a person-centered approach for assessment and care planning for BPSD, should be considered[21].

Pharmacological treatment may be considered as second line therapy: Antipsychotic medications should be considered when: alternative therapies are ineffective on their own, there is an identifiable risk of harm to the resident and others and the symptoms are severe enough to cause suffering and distress to the individual. The physician should rule out comorbidities like depression, infection, or metabolic disturbances before prescribing antipsychotics. An assessment using the ABC model should be conducted, along with inputs from caregivers and family members. A parallel non-pharmacological regimen may also be considered. While antipsychotics are indicated for aggression, agitation, or psychotic symptoms causing immediate risk of harm to the individual, there are many BPSD symptoms, such as wandering, hiding and hoarding, tugging at seatbelts, repetitive activity, inappropriate dressing/undressing and eating inedible objects, that *do not* benefit from antipsychotic treatment.

Upon the selection of appropriate medication, the guiding principle is to "start slow and go slow, and monitor frequently for clinical response and adverse effects." Antipsychotic drug therapy should be considered as a short term strategy aimed at the management of specific target symptoms. Healthcare providers should conduct regular reviews at least every three to six months with the goal to either reduce the medication or to wean completely. In the initial phase of antipsychotic therapy, reviews should be more frequent (weekly, every 2 weeks and then monthly).

5.1.4.2. Required adaptation to Alberta

Guided by the clinical experts, several required areas for enhancement were identified. The BC guideline included published evidence to 2005. Thus an update of the evidence base for non-pharmacological interventions is required to ensure that the Alberta guideline and policy is based on best-available current evidence. In addition, antidepressant medication, complementary and alternative medications, and the built environment as alternatives to antipsychotic medications for the management of BPSD as well as cost-effectiveness were not addressed within the BC guideline. In response to these identified needs, 5 specific systematic reviews were undertaken:

1) What is the current evidence to support effectiveness of non-pharmacological interventions for the management of BPSD among seniors residing in LTC facilities?

2) What is the current evidence to support the effectiveness of antidepressants as a substitute for antipsychotics for the management of BPSD among seniors residing in LTC facilities?
3) What is the current evidence to support the effectiveness of complementary and alternative medications for the management of BPSD among seniors residing in LTC facilities?
4) What is the current evidence to support the effectiveness of built environment for the management of BPSD among seniors residing in LTC facilities?
5) What is the current evidence to support the cost-effectiveness of non-pharmacological interventions, CAM and built environment for the management of BPSD among seniors residing in LTC facilities?

5.2. Non-pharmacological Interventions

Summary of Findings:

Forty RCTs in four categories of non-pharmacological interventions were identified: comprehensive assessments (n=3), social contact (n=15), structured activities (n=7) and sensory enhancement/ relaxation (n=15). All studies are small, of moderate to low quality and reported varied outcome measures. Improved outcomes were reported 21/40 studies with no adverse events reported.

5.2.1. Research Question

What is the effectiveness of non-pharmacological interventions for the management of BPSD among seniors residing in LTC facilities?

5.2.2. Methods

Non-pharmacological treatments were defined as any intervention for BPSD that is not orally delivered or injected and is not a prescribed pharmaceutical. A high-quality systematic review synthesizing the literature from 1980-2010 was identified and updated[22]. Electronic databases (MEDLINE, EMBASE, PSYCHINFO, Cochrane library, HTA Database, AMED, CINAHL, and AltHealth Watch) were searched from 2010 to 2013. The complete search strategy is in Appendix C. The full list of inclusion/exclusion criteria are presented in **Table 3**. Both abstract review and full-text review were completed in duplicate, and any disagreements were discussed among reviewers. Data on study characteristics and BPSD outcomes were extracted. Study quality was assessed using the Cochrane Risk of Bias Checklist[23]. This instrument uses a colour chart to identify risk of bias in six categories: sequence generator, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other bias[23]. Data from

included studies are presented numerically. No pooling was possibly due to the heterogeneity of the included studies.

Table 3: Inclusion/Exclusion criteria for non-pharmacological interventions on BPSD

Inclusion Criteria	**Exclusion Criteria**
• Seniors (≥ 65 years) with BPSD • LTC settings • Non-pharmaceutical interventions compared to standard of care • Reports effect on BPSD (efficacy) • RCT or controlled clinical trial	• Adults < 65 years • Pediatric population • Pharmacological interventions • Herbal medicines • Acupuncture • Acupressure • Primary endpoint not based on efficacy • Non-original data • No control group • Commentaries, Letters, Editorials, Opinions, Case Studies, or Biochemical Studies • Preclinical or Animal Studies • Chemistry or biological studies

5.2.3. Results

5.2.3.1. Study Selection

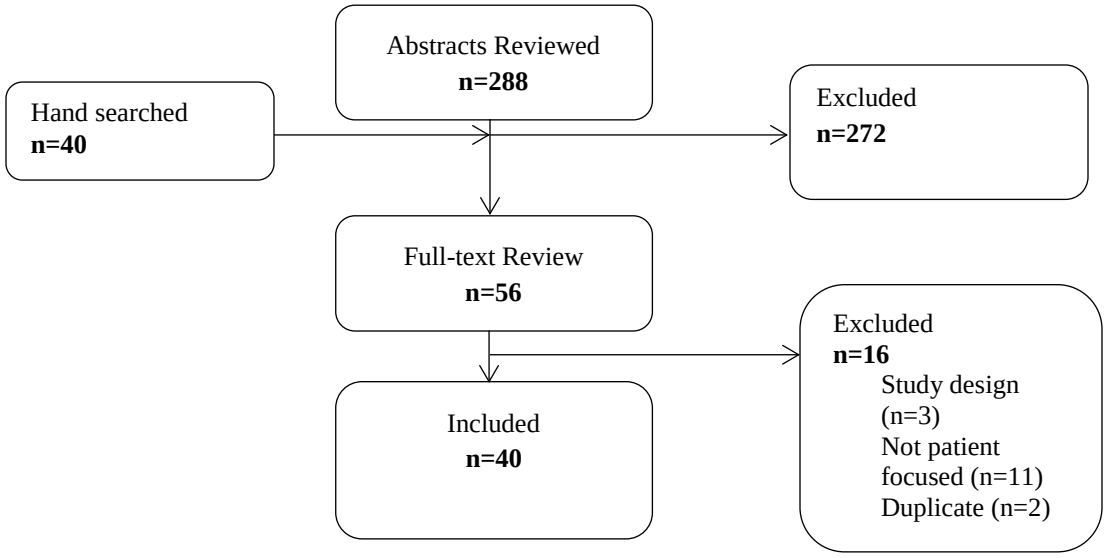
Two hundred and eighty-eight citations published from 2010-May 2013 were identified. Of those, 16 studies were assessed in full-text review; 11 of those were included in the final analysis. In addition, 40 studies published from 1980-2010 were identified from the previous systematic review. Of those, 29 were included, resulting in a total of 40 studies in the final analysis. **Figure 2** presents the flowchart of article selection for this abstract review.

5.2.3.2. Overview of Included studies

Four categories of interventions were identified: comprehensive assessments, social contact, structured activities and sensory enhancement/ relaxation. Of the 40 studies identified, 3 studies examined comprehensive assessments, 15 examined social contact, 7 evaluated structured activities and 15 examined sensory enhancement/relaxation. Sample size of studies ranged from 20 to 398 participants and all studies were designed as randomized controlled trials (RCT). A variety of outcomes were reported. The included studies in this review had low to moderate risk

of bias (**Appendix H**). Further details on study characteristics can be found in **Table 5**. In total, 21 of the 40 studies (53%) reported some benefit of the non-pharmacological intervention over the control intervention for a variety of behavioural symptoms, specifically aggression and agitation. The remaining 19 studies reported no statistically significant difference in BPSD outcomes between intervention and control groups; thus, none of the included studies reported worsening of outcomes with non-pharmacological intervention. All 40 included studies were RCTs published between 1996 and 2012. Of the 21 RCTs that reported improvements in BPSD, the majority (n=18) were published after 2002 (3 studies were published between 1996-1999) and were of low (n=12) to moderate (n=9 quality). All of the study participants were diagnosed with some type of dementia, living in a LTC setting (nursing and residential care included) and were assessed for BSPD using a variety tools.

Figure 2: Flowchart for the assessment of non-pharmacological interventions



5.2.3.3. Efficacy of Non-Pharmacological Interventions

5.2.3.3.1. Comprehensive assessment

Interventions within this category included are a variety of methods such as identifying specific triggers of BPSD through caregivers and family consultations, providing individualized non-pharmacological therapies to address unmet patient needs and patient engagement in group activities using a combination of interventions. Three studies were identified with 2 out of 3 studies showing an improvement in BPSD. Two studies were conducted in the USA[24;25] and one in Australia[26]. Studies were conducted between 1996 and 2007, had sample sizes ranging from

55 to 167 participants, and were of low to moderate quality. Based on the included studies, comprehensive assessment is likely to be clinical effective. With only three included studies, however, the evidence is quite limited.

5.2.3.3.2. Social contact interventions

Social contact interventions revolved around staff or care-givers providing additional personal attention to patients. Types of therapies in this category included validation therapy, family visit therapy, therapeutic conversation and reminiscence therapy. Fifteen studies were identified. Included studies reported the use of one or more validated scales for measuring BPSD such as the Aberrant Behavior Checklist, the Cohen-Mansfield Agitation Inventory, and the Clifton Assessment Procedures for the Elderly – Behavioral Rating Scale.

Nine studies were conducted in the USA[27-35]. Two studies were conducted in Australia[36;37], one from Italy[38], Taiwan[39], UK[40] and Netherlands[41]. Studies in this category were published between 1996 and 2012. Number of participants ranged in each study ranged from 20 to 398 dementia patients. The studies in this category had low to moderate risk of bias.

Eight of the included studies on social contact interventions showed no benefit of this non-pharmacological treatment on BPSD outcomes compared to the control treatment. The other six studies, however, reported improvements in a variety of BPSD symptoms (e.g., reduction in physical aggression, agitation, and verbal abuse). One study with two non-pharmacological interventions had discordant outcomes with validation therapy showing an improvement on BPSD and social contact showing no improvement on BPSD when compared to usual care[28]. The evidence on the clinical efficacy of the intervention is mixed, suggesting that social contact results in similar outcomes as control interventions. The evidence supporting improvements in BPSD with social contact interventions is also limited.

5.2.3.3.3. Structured activities

Structured activities involved therapies such as group exercise and walking. Seven studies were identified. Two studies in this category were conducted in the USA[42;43], the Netherlands[44;45], France[46;47] and one in Italy[48]. Studies in this category were published from 1999 to 2010. Number of participants in each study ranged from 29 to 160 dementia patients. Four studies reported an improvement in BPSD through an exercise or walking intervention while the other 3 studies showed no improvement. The evidence concerning clinical efficacy is mixed, suggesting that structured activities lead to similar outcomes as control interventions. Similarly, the evidence supporting improvements in BPSD following structured activities is also limited.

5.2.3.3.4. Sensory enhancement/relaxation

Sensory enhancement or relaxation of a patient involves the augmentation of their current surroundings though various stimulatory effects such as light, music, aromatherapy and touch in

order to reduce BPSD. Studies were conducted in Iceland[49], Italy[50], Japan[51] with two studies having been conducted in Canada[52;53],USA[54;55], UK[56;57], and three in Taiwan[58-60], Netherlands[61-63]. Studies were published between 1998 and 2012. Study sample sizes ranged from 19 to 145 participants. Six studies reported the use of music therapy, with five reporting positive outcomes on BPSD[49;50;54;59;60]. Two studies examined aromatherapy as an intervention to reduce agitation with contradicting results[51;56]. Three studies examined the impact of therapeutic touch, with one study demonstrating an improvement on BPSD and the other two showing no improvement [52;53;61]. Three studies investigated the effects of light on BPSD with one study demonstrating an improvement on BPSD and two demonstrating no improvement [55;57;63]. The evidence is mixed concerning the clinical efficacy of sensory enhancement/relaxation interventions. Similarly, the there is only limited evidence to support improvements in BPSD following sensory enhancement/relaxation.

5.2.3.4. Safety

None of the included studies provided details on the safety of the intervention. Incidence of adverse events was not reported. There is no clear documentation regarding Health Canada approval for any non-pharmacological intervention.

5.2.4. Discussion

Forty RCTs of non-pharmacological interventions were identified with interventions falling into four categories: comprehensive assessments (n=3), social contact (n=15), structured activities (n=7) and sensory enhancement/ relaxation (n=15). The range and styles of each class of intervention varied greatly. A little over half (21/40) studies reported an improvement, while the remaining 19 studies reported no improvement in the intervention group as compared to control. None of the included studies reported worsening of outcomes. All studies are small, of moderate to low quality and reported varied outcome measures. Among studies that reported improved outcomes in BPSD, no adverse events were reported.

Given the diversity of the interventions, continued thorough assessment of the patient's symptoms is required. Response to interventions is likely to be highly individualized with the degree of response to therapy based on the patient's background and the complexity of their symptoms. System-wide implementation of non-pharmacological interventions for management of BPSD in LTC facilities may prove challenging due to the individual nature of the therapies, significant investment in resources, and extensive staff training.

Several evidence gaps were identified. None of the studies compared non-pharmacological interventions with pharmacological interventions. Without direct comparisons between non-pharmacological with pharmacological interventions, decision-making on replacing a prescription drug with a specific non-pharmacological intervention is difficult. No study

reviewed the impact of transitioning a dementia patient from pharmacological intervention to a non-pharmacological intervention. None of the studies discussed the impact of increased staff workload on reduction of BPSD. One study did note that the majority of the interventions were carried out by staff external to the LTC setting which may limit the generalizability of study findings. Given that the studies only looked at a small number of dementia patients, it may be difficult to predict the implementation of the interventions at the health system level. Further, none of the studies reviewed cost, resources required, or feasibility and implementation barriers.

There are limitations to this review. Most of the included studies were short-term and their results may not be generalizable to long-term outcomes associated with the intervention. In addition, significant geographical variations exist across studies which make it difficult to generalize the findings to the local context.

5.2.5. Conclusion

The evidence synthesized in this review is consistent with the recommendations provided in the BC guidelines. Overall, there are no modifications required to the BC guideline to ensure the guideline reflects the most current evidence. The use of non-pharmacological interventions is likely to be a viable first-line of treatment for managing BPSD in LTC residents as the majority of studies reported improvement in outcomes and no adverse events. However, there is not enough published evidence about the resources required for their broader application in the healthcare system.

Table 4: Characteristics of included studies for non-pharmacological interventions/ effects of non-pharmacological interventions on BPSD

Author, Year, Country	Dementia Diagnosis	Group Allocation	# of Patients	% female	Mean Age	Outcome	Baseline Mean (SD)	Primary Endpoint Post Treatment	Difference	Outcome*
Comprehensive Assessment										
Rovner, 1996, USA[24]	DSM-III-R, "dementia"	Activity program, psychotropic drug management, educational rounds	42	86	82.0 (8.0)	Behaviour present	42/42 (100%)	12/42 (28.6)	71.4%	I > C p=.037
		Usual Care	39	67	81.2 (7.2)		39/39 (100%)	20/39 (51.3)	48.7%	
		Case management	28		82.9 (8.09)				26% reduction in NPI 19.4% reduction in BEHAVE-AD score	
Brodaty, 2003, Australia[26]	AMTS, DMS-IV, "dementia"	Consultation with specialist	27	72	82.9 (8.09)	NPI, BEHAVE-AD			5.1% reduction in NPI 6.9% reduction in BEHAVE-AD score	I = C
		Standard care	31		82.9 (8.09)				5.6% reduction in NPI 2.9% reduction in BEHAVE-AD score	
Cohen-Mansfield, 2007, USA[25]	AD, vascular, Parkinsons disease Dementia	Systematic non-pharmacological therapy	89	84.3	88.0 (6.4)	ABMI	5.17 (3.75)	3.23 (3.16)	- 1.94	I > C
		Usual care/educational sessions	78	75.6	85.0 (8.6)		5.05 (3.36)	4.10 (3.47)	- 0.95	F=10.22, p=.002

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		Consultation with specialist	27	72	82.9 (8.09)				5.1% reduction in NPI 6.9% reduction in BEHAVE-AD score	
		Standard care	31		82.9 (8.09)				5.6% reduction in NPI 2.9% reduction in BEHAVE-AD score	
Social Contact										
Mitchell, 1996, USA[27]	NINCDS-ADRDA, AD, multi-infarct dementia, Organic Brain	Individualized special instruction, 30 mins/day, + 5 days	15	60	78.6	ABC	48	52	Both groups deteriorated	I = C
		Waiting list	15	- -	78.6		40	48		

	Syndrome, "dementia"									
		Validation therapy, 4 x 30 min sessions/week	31	86	87.79 (5.95)				Reduction in physical aggressive behaviour at 3 months,	I > C p=.001
Toseland, 1997, USA[28]	MDS, "dementia"	Social contact, 4 30 min sessions/week	29	69	87.29 (6.12)	CMAI			aggressive or verbal	
		Usual care	28	68	87.78 (7.56)				At 1 year no difference in non-	I = C
McCallion, 1999, USA[29]	MDS and chart, "dementia"	Family visit communication program, 8 weeks then follow up, 4 1½ hr group sessions and 3 1 hr family conferences	32	93.8	86.4 (6.6)	CMAI total	37.4	36.2	"Only physically non-aggressive behaviours improved with treatment"	I = C
		Usual care	34	64.8	85.5 (6.7)		32.8	33.7		
		ADL with nursing staff, 45-60 mins/day	28	78.6	82.29 (8.9)		172.51 (191.47)	164.56 (154.95)		
		Psychosocial activity (25 standardized modules), 15-30 mins daily	29	82.1	82.18 (7.64)		348.02 (467.50)	383.24 (367.54)		
Beck, 2002, USA[30]	Unclear, "dementia"	Combined ADL and psychosocial activity, 90 mins/day	22	81.8	82.82 (9.81)	DBS	287.66 (373.73)	286.21 (365.78)	No significant difference between groups	I = C
		Usual Care	19	89.5	86.47 (6.37)		408.71 (427.24)	281.97 (410.85)		
		One-on-one interaction with nursing staff, 30 mins/day	29	75.9	86.45 (6.92)		325.96 (337.14)	336.80 (366.55)		

		Early intervention group	48	73	84.4 (6.9)				No change in counts of behaviour between groups during intervention	I = C
Opie, 2002, Australia[36]		Late intervention group (usual care)	51	73	83.7 (7.2)	CMAI BAGS			Restlessness and all behaviour decreased treatment group at 4 week follow-up No significant difference between groups over time	
Politis, 2004, USA[31]	DSM-IV, AD	Geriatric network kit, 30 mins, 3x/week	18	83.3	84.4 (4.5)	NPI	16.2 (21.2)	10.0 (10.3)	- 6.2	I = C
		Spend time together talk, patient decides	18	83.3	83.5 (4.9)		21.2 (16.4)	9.8 (11.5)	- 0.2	
Lichtenberg, 2005, USA[32]	AD (60%)	One-on-one pleasant event 3x/week, 20-30 mins, 3 months	9	90	84.8 (4.9)	BEHAVE-AD	15.5 (9.8)	8.0 (3.8)	- 7.5	I > C F=8.4, p=.01
Deponte, 2007, Italy[38]	"Dementia"	Usual care	11	90	85.0 (5.1)	NPI	12.4 (7.2)	7.0 (4.1)	- 5.4	?
		Validation Therapy	30	- -	86.8		18.9 (14.9)	14.9 (13.3)	- 4	
		Sensorial Reminiscence	- -	- -	- -		17.6 (15.4)	9.9 (9.1)	- 7.7	
		No treatment	- -	- -	- -		10.6 (10.3)	10.8 (9.0)	+ 0.2	
Tappen , 2009, USA[33]	NINCDS-ADRDA, AD	Therapeutic conversation (3x/week)	15	93	83.8 (7.45)	AD-RD (hostile) DMAS	AD-RD (hostile) 14.86 (4.2) DMAS 23.66 (14.73)	AD-RD (hostile) 15.7 (5.8) DMAS 21.26 (12.80)	DMAS - 2.4	I = C F=0.37, p=.5 F=3.59, p=.06
		Usual care	15	87	90.26		AD-RD (hostile)	AD-RD (hostile)	DMAS + 6.8	

					(5.95)		15.5 (7.9) DMAS 21.33 (15.67)	17.0 (3.7) DMAS 28.13 (12.21)		
Wang, 2009, Taiwan[39]	Mild-moderate dementia	Reminiscence Therapy	38	47.4	79.32 (6.35)	CAPE-BRS	13.97 (4.48)	12.87 (5.96)	- 1.1	I = C
		Usual care	39	48.7	78.76 (7.60)		13.90 (5.18)	14.37 (5.69)	+0.47	
Cohen-Mansfield, 2012, USA[34]	No subtype listed	Treatment Routes for Exploring Agitation (TREA)	89	--	85.9±8.6	ABMI	8.8±5.6	2.1±2.9		I > C
		Control group (placebo procedure)	36	--	85.3±9.6		7.2±7.6	7.9±9.1		
Kolanowski, 2011, USA[35]	Any except PD, HD,	Need-Driven Dementia-Compromised Behavior (NDB) model	32	--	85.3±6.1	CMAI	1.62±0.8	1.2±0.8		I > C
		Functional level (FL) Personality Style of Interest (PSI)	33	--	87.2±5.9		2.5±0.7	1.7±0.8		
		FL+PSI	31	--	86.0±7.1		1.9±0.7	1.5±0.8		
		Active control	32	--	85.9±4.9		1.9±0.7	1.1±0.8		
Low, 2012, Australia[37]	No subtype listed	LaughterBosses and ElderClowns (SMILE)- Humour Therapy	189	--	84.5±7.5	CMAI, NPI	CMAI 45.3±20.0 NPI 89.4±15.5	CMAI 42.0±18.3 NPI 23.2±22.0		I > C
		Usual care	209	--	84.5±8.7		CMAI 38.9±11.0 NPI 18.7±16.9	CMAI 39.0±11.7 NPI 23.2±22.0		
Spector, 2003, UK[40]	No subtype listed	Cognitive Stimulation Therapy Programme	115	--	85.7±6.2	RAID	8.4±8.0	Change from baseline -0.5±10.2		I = C
		Usual care	86	--	84.7±7.9		10.1±8.5	Change from baseline -0.7±10.3		
Bakker,	No subtype	Integrative	81	--	79.8±6.1	NPI	5.9±2.4	Time 2		I > C

2011, Netherlands[41]	listed	Reactivation and Rehabilitation (IRR)						4.0±2.2 Time 3 3.5±2.2 Time 2		
		Usual care	87	--	81.5±7.1		5.2±2.2	4.6±2.4 Time 3 3.8±2.1		
Structured Activities										
Alessi, 1999, USA[42]	all with dementia	Day time physical activity and nighttime intervention	15	86.7	88.6 (10.4)	# observations	9.4 (15.4)	7.3 (14.0)		I > C F=7.86, p=.009
		Nighttime intervention alone	14	92.9	88.3 (5.7)		5.9 (9.7)	14.7 (19.7)		
Hopman-Rock, 1999, Netherlands[44]	"dementia"	PAP, exercise group, 2x/week	45	91	83.8 (5.8)	BIP - restlessness	4.1 (2.8)	4.2 (2.7)		I = C F=1.38, p=.88
		Control usual care (usual activities)	47	98	84.2 (5.6)		5.0 (3.1)	4.6 (3.3)		
Landi, 2004, Italy[48]	AD – CPS score unclear	Exercise/physical activity	15	53	80.9 (8.5)	Physical Abuse	4/15 - 26% 5/15 - 32%	2/15 - 13% 5/15 - 32%	Significant reduction in behaviour problems	I > C
						Verbal Abuse	7/15 - 43%	3/15 - 22%		
	AD – "medium cognitive impairment"	Usual care	15	47	80.9 (8.5)		6/15 - 39%	5/15 - 32%	Not reported	?
Rolland, 2007, France[46]	Diagnosis of dementia on MMSE <25, NINDA-ADRDA, AD	Exercise program (1 hr, 2x/week)	67	71.7	82.8 (7.8)	BPSD multi-level scale [NPI]	10.7 (6.9)	8.3 (8.9)	- 2.5	I = C p=.78
		Routine care	67	79.1	83.1(7.0)		11.4 (7.7)	8.9 (10.4)	- 2.2	
Williams, 2007, USA[43]	AD, NINCDS-ADRDA	Comprehensive exercise, individually 5days/week	30	85	88 (6.32)	Anxiety Scale [Lawton OAS 2	+ 11.11 - 3.38 + 9.65	+ 11.11 - 3.38 + 9.65		I > C P=.006

						week positive]				
		Supervised walking	31	- -	- -	Anxiety Scale [Lawton OAS 2 week negative]	- 4.81 + 9.14	- 4.81 + 9.14		Comprehensive exercise group better than other groups at 2 weeks on negative affect
		Social conversation	29	- -	- -		- 5.65	- 5.65		
		Tai chi exercises	51	--	83±8.6		18.8±19.0	Mean difference 6 months -1.4 (-8.2 to 5.4) 12 months -3.9 (-9.4 to 1.5)	18.8±19.0	
Dechamps, 2010, France[47]	No subtype listed	Cognition-action group	49	--	83.2±8.3	NPI	25.9±23.1	Mean difference 6 months -4.8 (-11.6 to 2.0) 12 months -6.6 (-11.4 to 1.8)	25.9±23.1	I > C
		Control group (usual care)	60	--	80.9±10.1		27.9±11.8	Mean difference 6 months 9.9 (2.0-17.6) 12 months 14.2 (5.4 to 23.0)	27.9±11.8	
Eggermont, 2010, Netherlands[45]	AD, VD, FTD, other	Walking group	41	--					Walking program did not show a beneficial effect on night-time restlessness	I = C
		Control group (patient visits)	38	--	84.3±10	Actigraphy				
Sensory Enhancement/Relaxation										

Sung, 2006, Taiwan[58]	DSM-IV, "dementia"	Group music with movement, 30 mins, 2x/week	18	38.9	76.8 (9.1)	Modified CMAI, measured during the intervention	5.11 (2.45)	3.44 (1.29)	+ 1.67	I > C
		Usual care	18	27.8	78.4 (7.9)		4.72 (1.81)	4.50 (1.65)	- 0.22	
Svansdottir, 2006, Iceland[49]	ICD-10 AD	Music therapy, 30 min, 3x/week, 6 weeks	20	- -	71-87	Total BEHAVE-AD	5.5	4.4	- 1.1	I = C
		Routine care	18	- -	71-87		5.4	4.7	- 0.7	p=0.3
Raglio 2008, Italy[50]	AD, vascular, mixed	Music therapy	30	--	84.4 +/- 5.5	NPI	27	14.64	- 12.36	I > C
		Educational support	29	--	85.8 +/- 5.4		29.5	25.05	- 4.46	
Janata, 2012, USA[54]	No subtype listed	Widespread and Frequent Personalized Music Programming	19	--	80.9±9.6	CMAI, NPI			"Symptom severity were observed in both groups"	I > C
		Usual care	19	--	81.7±7.5					
Lin, 2010 Taiwan[59]	No subtype listed	Music intervention	49	--	81.5±7.3	CMAI	43.1±16.3	6th Session 35.89±8.53 12th Session 36.37±10.64 One Month 35.63±9.99		I > C
		Control group (usual daily activities)	51	--	82.2±6.3		37.8±11.04	6th Session 38.25±10.85 12th Session 38.55±10.27		

Sung, 2011, Taiwan[60]	No subtype listed	Group music intervention using percussion instruments with familiar music	27	--	81.4±9.1	RAID, CMAI	RAID 10.0±10.5 CMAI 36.3±13.3	One Month 37.75±9.70 RAID 10.0±10.5 CMAI 36.3±13.3		RAID I > C CMAI I = C
		Control group (usual care)	28	--	79.5±8.8		RAID 10.0±10.5 CMAI 36.3±13.3	RAID 10.0±10.5 CMAI 36.3±13.3		
Scherder, 1998, Netherlands[61]	NINCDS, CDS	Tactile stimulation massage (30 mins/day, 5 days/week)	16	- -	85.7	BOP	1.25	0.63	- 0.62	I = C
		Sham electrical stimulation	- -	- -	- -	Behaviour inventory	2.38	1.88	-0.5	F = 1.64, p = .22
Ballard, 2002, UK[56]	Severe dementia, CDR Stage 3	Aromatherapy with Melissa oil	36	56	77.2 (7.6)	CMAI total score	68.3 (15.3)	45.2 (10.4)		I > C Z=2.7, p=.005
		Placebo sunflower oil					60.6 (16.6)	53.3 (17.6)		$\chi 2$=16.3, p<.001
		Aromatherapy with Melissa oil	36	64	79.6 (8.5)	Response rate 30% improvement		21/36 (60%)		
		Placebo sunflower oil						5/36 (14%)		
Ancoli-Israel, 2003, USA[55]	NINCDS	2500 lux x 10 days (white light)	92	68.5)	82.3 (7.6)				"No significant change with any treatment in mean 24-hour total Physical Agitation ratings"	I = C
		Dim red light 300 lux	- -	- -	- -					

Van Weert, 2005, Netherlands[63]	DSM-III-R	Snoezelen	62	79	84.0 (8.6)	CMAI	14.51 (SE)	12.12 (SE)	- 2.39	I > C
		Usual Care	63	82.5	82.6 (8.2)		12.34 (SE)	13.83 (SE)	+ 1.49	
Woods, 2005, Canada[52]	DSM-IV, AD, vascular, mixed	Therapeutic touch, 5-7 mins, 2x/day	19	79	78.9 (3.78)	ABRS	1.55 (1.03)	1.03 (0.67)	- 0.52	I > C
		Routine care	19	84	81.16 (5.32)		1.53 (0.99)	1.48 (1.12)	- 0.05	
		"Minimized therapeutic touch" (placebo), 5-7 mins, 2x/day	19	79	82.37 (5.93)					
Scherder, 2006, Netherlands[62]	NINCDS-ADRDA, Probable AD	Cranial electrostimulation, 30m/day, 5 days/week	11	100	83.73	BOP Behaviour inventory	1.25	0.63	- 0.62	I = C F = 1.64, p = .22
		Control, "no current applied"	10	80	84.50		2.38	1.88	-0.5	
Hawranik, 2008, Canada[53]	AD	Therapeutic touch, once/day, 5 days	17	58.8	83.3 (8.32)	CMAI # behaviours			No significant difference across the three groups in the incidence of physically aggressive and verbally agitated behaviours	I = C
		Usual care	18	66.7	80.9 (7.41)					
		Placebo-stimulated therapeutic touch, once/day, 5 days	16	87.5	84.2 (6.20)				Less physically non- aggressive behaviours in TT vs. UC	I > C

Sakamoto, 2012, Japan[51]	No subtype listed	Lavender group	73	--	84.2±7.8	CMAI	24.3±5.2	22.9±2.3	- 12.5	I = C
		Control group (placebo)	72	--	84.1±7.7		24.6±6.9	24.0±3.7	- 8	
Burns, 2009, UK[57]	AD, vascular, DLB, mixed	Bright light for 2 weeks	22	73	84.5 (1.7)	CMAI	62.0 (18.4)	49.5 (13.8)		I = C
		Standard light	26	62	82.5 (1.5)		57.5 (13.8)	49.5 (10.4)		

PD=Parkinson's disease, Huntington's disease;AD=Alzheimer's disease; VD=vascular dementia; DLB=Dementia with Lewy bodies; CVD=Alzheimer's disease with cerebrovascular; ADL = activities of daily living; AGECAT = Automatic Geriatric Examination for Computer-Assisted Taxonomy; AMTS = Abbreviated Mental Test Scale; BIP = Behavioural Observation Scale for Intramural Psychogeriatry; CDR = Clinical Dementia Rating; CPS = cognitive performance scale; DAT = Diagnosis Dementia of the Alzheimer Type; DLB = dementia with Lewy bodies; DSM = Diagnostic and Statistical Manual of Mental Disorders; GDS = Global Deterioration Scale; ICD = international classification of diseases; LTC = long-term care; MDS = minimum dataset; MMSE = Mini-Mental State Examination; NINCDS –ADRDA = National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association; PAP = Psychomotor Activation Programme; SCU - Special Care Unit; SD = standard deviation.

5.3. Antidepressants as a Substitute for Antipsychotics

Summary of Findings:
A high-quality recent systematic review of 6 RCTs (2011) reported no statistically significant differences in BPSD or drug tolerability between SSRIs and antipsychotics (typical and atypical). One additional RCT also reported no significant differences in outcomes measures between SSRI and antipsychotics. All studies included small sample sizes and were of low to moderate quality. Based on the included studies, antidepressants appear to have similar outcomes to antipsychotics in terms of BPSD management and tolerability. Most of the included studies were short-term and may not be generalizable to long-term outcomes associated with the intervention.

5.3.1. Research Question

What is the effectiveness of antidepressants as a substitute for antipsychotics for the management BPSD among seniors residing in LTC facilities?

5.3.2. Methods

It was suggested by the EAG that current practice may involve the use of antidepressants as a substitute for antipsychotics for the management BPSD among seniors residing in LTC facilities and that the evidence surrounding this practice should be systematically reviewed. Previous published guidelines do not include recommendations for the use of anti-depressants as a pharmacological alternative for the management of BPSD. For this purpose, a previous high-quality systematic review published in 2011 was identified and updated. MEDLINE, CENTRAL Register of Controlled Trials, EMBASE, PsycINFO, Cochrane Database of Systematic Reviews, HTA Database, and NHSEED were searched from 2010-May 23rd, 2013. The search strategy for this review focused on combining terms for dementia, antidepressant medications, and antipsychotic medications. Details of this search strategy can be found in **Appendix D**. Results were filtered to exclude non-human studies and languages other than English or French. No other limits were used.

The abstracts retrieved were screened in duplicate using the inclusion/exclusion criteria outlined in **Table 5**. Abstracts were included for full-text review if they reported original data, included patients or residents with dementia diagnosed with behavioural and psychological symptoms in dementia (BPSD), involved the use of antidepressant medication as the intervention and antipsychotic medication as the comparator and reported on the clinical efficacy in the management of BPSD. All abstracts selected for inclusion by either reviewer proceeded to full-

text review. This initial screen was conducted using broad criteria to ensure that all relevant literature was captured. Studies included after the first screen proceeded to full-text review by two reviewers. Any disagreement between reviewers was resolved through discussion and consensus.

Table 5: Inclusion/Exclusion Criteria for Antidepressants as a Substitute for Antipsychotics for reduction of BPSD

Inclusion Criteria	Exclusion Criteria
• Measurement of BPSD or responsive behaviours in dementia in patients age 65 or older • Comparison of Anti-depressant medication and Anti-psychotic medication • Report change in frequency and/or severity in BPSD (frequency and/or severity) • Original Data • RCT Study design	• Not BPSD, no dementia • Pediatric population • Not anti-depressant medication intervention • Not anti-psychotic medication comparator • Primary endpoint not based on efficacy in treating BPSD • Chemistry or biological studies • Preclinical or Animal Models • Non-original data • Commentaries, Letters, Editorials, Opinions • Controlled clinical trial • Prospective Cohort Comparison • Observational Studies • Systematic Reviews • Case Studies

5.3.3. Results

5.3.3.1. Study Selection

Five hundred and forty-four citations were identified. Of those, 28 were included for full-text analysis. In full-text review, 27 were excluded and one article, not captured in the Seitz et al.[64] systematic review was identified. Given that one additional small study was identified, we summarized the findings from the previous systematic review and narratively synthesize the additional article.

5.3.3.2. Efficacy of Antidepressants: Summary of the Previous Systematic Review of Antidepressants

The systematic review, published in 2011, synthesized all randomized controlled trials (RCT) published between 1997 and 2007. Sample size across studies varied from 15 to 148 and included older individuals with a diagnosis or probable diagnosis of dementia[65-70]. For all included studies, the clinical efficacy of an antidepressant medication, or class of antidepressant

medication (e.g., selective serotonin reuptake inhibitors [SSRIs]), compared to an antipsychotic medication for the treatment of agitation and psychosis was examined[64]. Specifically, three studies evaluated the effects of SSRIs to typical antipsychotic medications[65;66;68]; two studies evaluated the effects of a specific antidepressant to typical antipsychotic medication [69;70]; and one study examined the effect of a specific antidepressant to atypical antipsychotic medication[67]. The findings for each category are summarized below.

Antidepressants Compared to Typical Antipsychotic Medications: Based on five low-quality small sample size RCTs, no statistically significant difference was found in BSPD-related outcomes or adverse events.

Antidepressants Compared to Atypical Antipsychotic Medications: Based on one low-quality small sample size RCTs, no statistically significant difference was found in BSPD-related or adverse events outcomes.

5.3.3.3. Efficacy of Antidepressants: Narrative Summary of Additional Study

One additional study was identified. In this double-blind RCT, the efficacy of a SSRI (Escitalopram) compared to an atypical antipsychotic (risperidone) for reducing BPSD was assessed. Conducted in Israel with twenty-seven patients with dementia who had a history of symptoms including psychosis, and agitation, patients were randomized into Escitalopram and risperidone groups using computer software and both assessors and patients were blind to their allocation. The Neuropsychiatric Inventory (NPI) was used to assess patients at baseline and again at six weeks.

During the six-week follow-up, no adverse events were reported from the Escitalopram group, while six patients of the risperidone group suffered adverse events; including extrapyramidal symptoms, myocardial infarction, pneumonia, and urosepsis. Both groups experienced statistically significant improvements from baseline to the last outcome measurement. This study found that although risperidone resulted in a greater improvement than Escitalopram as measured by NPI, the difference was non-significant[71].

5.3.3.4. Safety

Results are mixed on the safety of using antipsychotics compared to anti-depressants to address BPSD. Barak et al. found fewer adverse events associated with antidepressants[71], however, the review conducted by Seitz et al. reported no difference in adverse events between antidepressants and antipsychotics[64]. No consensus has been achieved in the current literature on the relative safety of antidepressants compared to antipsychotics for reducing BPSD.

5.3.4. Discussion

A recent high quality systematic review including 6 RCTs reported no difference in outcomes measured following the use antidepressants compared to antipsychotics for the treatment of BPSD. One additional published after the systematic review was identified and also reported no statistically significant difference in outcomes. All studies are of low-moderate quality, include small sample sizes and are short-term follow-up.

There are limitations to this review. Most of the included studies were short-term and their results may not be generalizable to long-term outcomes associated with the intervention. In addition, different drugs were assessed in the studies which may contribute to study heterogeneity.

5.3.5. Conclusion

Based on low to moderate quality evidence, antidepressants appear to have a similar outcome profile as antipsychotics (typical and atypical) in terms of BPSD management and tolerability.

5.4. Effectiveness of substituting antipsychotics with other drug classes

Summary of Findings: 3 small, high to moderate quality randomized control trials were identified comparing antipsychotic to non-antipsychotic medications. None of the studies reported statistically significant improvements in BPSD using a non-antipsychotic compared to an antipsychotic. The safety profiles, reported in two of the studies, were similar between antipsychotic to non-antipsychotic medications. The evidence suggests that there is no difference in BPSD following non-antipsychotic medication use, specifically cholinesterase inhibitors and/or anxiolytic medications, and antipsychotic use.

5.4.1. Research Question

What is the effectiveness of substituting antipsychotics for cholinesterase inhibitors, mood stabilizers, anti-epileptics, benzodiazepines, or sedatives for dementia patients suffering from neuropsychiatric symptoms (NPS) / behavioural or psychological symptoms of dementia (BPSD) in long term care (LTC) settings?

5.4.2. Methods

The EAG noted that due to the harm profile of antipsychotics, clinicians are experimenting with a variety of other drug classes before considering treatment with antipsychotics. Currently, the evidence associated with other drug classes has not been systematically reviewed and the current published guidelines do not include recommendations for the use of other drug classes as a pharmacological alternative for the management of BPSD. For this systematic review, MEDLINE, PsycINFO, PubMED, HTA Database, the Cochrane CENTRAL Registry of

Controlled Trials, and the Cochrane Database of Systematic Reviews were searched from 1950-July, 2013. Terms such as “dementia”, and “Alzheimer*” were combined using the Boolean operator “and” with terms for antipsychotics, cholinesterase inhibitors, benzodiazepines and melatonin. Results were limited to English or French language, and excluded comments, editorials and letters. No other limitations were used.

Abstracts were screened in duplicate. Abstracts were only included for full-text review if they: were randomized controlled trials, controlled clinical trials or comparative observational cohorts which compared antipsychotics to another pharmacological intervention excluding antidepressants, involved patients who were living in long term care and displaying BPSD, reported clinical effectiveness, presented primary data, and were available in English or French. Abstracts selected for inclusion by either reviewer proceeded to full-text review. This initial screen was intentionally broad to ensure that all relevant literature was captured.

Studies meeting these inclusion criteria proceeded to duplicate full-text review. Studies were included in the review if they met the inclusion criteria presented in **Table 6**. Any disagreement between reviewers was resolved through discussion and consensus.

Data from the included studies were extracted in duplicate using a standardized data extraction form. General data including author, year, and country were extracted from each, in addition to method of description of intervention, patient characteristics, age, sex, dementia diagnosis, and outcomes measures such as MMSE scores and change in NPS. Each included study was assessed for quality using Cochrane collaboration risk of bias assessment tool.

Table 6: Inclusion/Exclusion Criteria for other classes of drugs as a substitute for antipsychotics for reduction of BPSD

Inclusion Criteria	Exclusion Criteria
• Full-text available in English or French • Original data • Relevant outcome data (clinical effectiveness) • Randomized controlled trial, controlled clinical trial, comparative cohort design • Residents of long-term care with dementia exhibiting BPSD • Comparison of antipsychotics to at least one of : cholinesterase inhibitors, mood stabilizers, anti-epileptics, benzodiazepines, or sedatives	• Full-text not available in English or French • Non-original, or duplicate data • No relevant outcome data • Non-comparative study design • Patients not residing in long term care • Comparison not between antipsychotics to at least one of : cholinesterase inhibitors, mood stabilizers, anti-epileptics, benzodiazepines, or sedatives

5.4.3. Results

5.4.4. Study Selection

Seven hundred and twelve citations were identified. Two articles were included through hand searching relevant systematic reviews. After screening, 15 were included for full-text review and three articles met the inclusion criteria for final analysis. The flowchart for article selection is presented in **Figure 3**.

5.4.5. Overview of Included studies

Table 7 presents an overview of the 3 included studies[72-74]. All three studies were randomized control trials (RCTs) published between 1996 and 2007 comparing an antipsychotic drug to a non-antipsychotics drug. Sample size ranged from 26 to 93 participants. The studies had high to moderate study quality. Two studies were performed in the United Kingdom (UK) and one in the United States of America (USA).

5.4.6. Efficacy of substituting antipsychotics for cholinesterase inhibitors, mood stabilizers, anti-epileptics, benzodiazepines, or sedatives

One study compared an antipsychotic (quetiapine), a cholinesterase inhibitor (rivastigmine) and placebo[75]. In this high-quality RCT, 31 patients were randomly allocated to each treatment arm. Included patients had a diagnosis of probable or possible Alzheimer's disease; age > 60; clinically significant agitation for at least six weeks and scores ≥ 4 on the irritability or aberrant motor behaviour scales of the neuropsychiatric inventory; and no use of antipsychotics or cholinesterase inhibitors for four weeks before entry into the study. Exclusion criteria were: patients known to be sensitive to cholinesterase inhibitors or antipsychotics and those with advanced, severe, progressive, or unstable disease that might interfere with efficacy or put the patient at special risk; disability that might prevent them from completing study procedures; those with severe, unstable, or poorly controlled medical conditions; bradycardia (< 50), sick sinus syndrome, or conduction defects; current diagnosis of active uncontrolled peptic ulceration within the past three months; and clinically significant urinary obstruction. Patients were followed for 26 weeks with the primary outcome of change in agitation measured by the Cohen-Mansfield agitation inventory assessed at both six weeks and 26 weeks. Of the 93 total participants enrolled in the trial, only 80 started treatment (26 quetiapine, 25 rivastigmine, and 29 placebo). There was no significant difference in agitation scores between treatment groups at baseline. Compared to placebo, those treated with an antipsychotic experienced a 3.5 change in agitation score at 6 weeks whereas those treated with a cholinesterase inhibitor experienced a 4.1 change in agitation score at 6 weeks. There was no statistically significant difference in the change in agitation scores between treatment groups at 6 or 26 weeks, suggesting that when compared to placebo, neither quetiapine nor rivastigmine is effective in the treatment of agitation.

In another RCT of medium quality, an antipsychotic (risperidone) was compared to a cholinesterase inhibitor (rivastigmine)[76]. Four of the twelve subjects (33%) enrolled in the risperidone arm experienced adverse events (one case of chest infection, one case of persistent agitation, one transient ischemic attack and one cellulitis). In the rivastigmine arm, nine of the fifteen participants experienced side effects (three cases of nausea and vomiting, three cases of persistent agitation, one case of constipation, one case of chest infection and one case of skin rash). The difference in the rate of adverse events was not statistically significant ($p > 0.1$). Study recruitment was stopped early, following the guidance provided by the Committee on Safety of Medicines. As a result, the power of the study was reduced from 80% to 74%. Therefore, it is likely that the study was not adequately powered to detect significant differences between the two groups. Patients were followed for 6 weeks with agitation measured using the Cohen-Mansfield agitation inventory. A statistically significant difference was reported in the mean agitation score change with those treated with an antipsychotic reporting larger decreases in agitation than those treated with a cholinesterase inhibitor (antipsychotic: -24.8 mean change in agitation score, cholinesterase inhibitor: -1.9 mean change in agitation score).

In the last RCT, an antipsychotic (haloperidol) was compared to an anxiolytic (buspirone)[73]. Twenty-eight patients were randomized in this medium quality study. The inclusion and exclusion criteria are not clearly stated, however, included patients had probable dementia and high levels of psychomotor activity, intrusive physical and verbal aggression. The primary outcome was the change in Brief Psychiatric Rating Scale at 10 weeks. As compared to haloperidol, the buspirone group experienced greater decreases in anxiety (11.1% vs. 2.1%) and tension (10.9% vs. 1.6%).

Figure 3: Flowchart for the assessment other classes of drugs as a substitute for antipsychotics

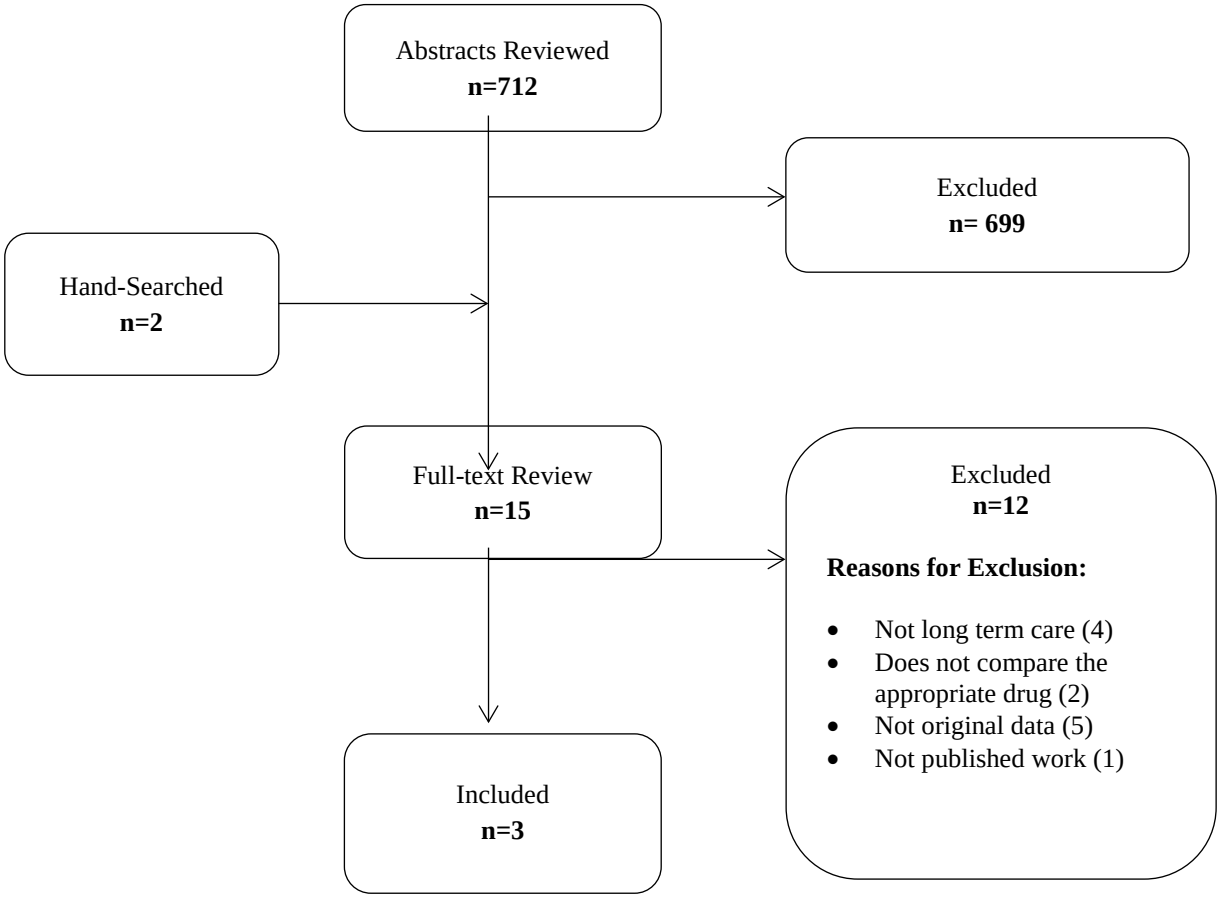


Table 7: Characteristics and outcomes of included studies in review other classes of drugs as a substitute for antipsychotics for reduction of BPSD

Author Year Country	**Intervention**	**Number of Participants**	**Age, Mean (SD)**	**Female Sex, N (%)**	**Dementia Diagnosis, Average MMSE Scores**	**Outcome Measure**	**Change in outcome**	**Outcome**	**Study Quality** Cochrane Risk of Bias
Ballard et al.[75] (2005) UK	Cholinesterase inhibitor (Rivastigmine 6–12 mg/day) Antipsychotic (Quetiapine 50–100 mg) Placebo	31 31 31	84.3 (7.8) 84.2 (8.6) 83.0 (6.8)	23 (74) 27 (87) 24 (77)	AD, dementia SIB: 58.8–69.0	CMAI at 6 weeks	− 5.1 − 4.0 − 6.2	Neither quetiapine nor rivastigmine are effective in the treatment of agitation	HIGH
Holmes et al.[76] (2007) UK	Cholinesterase inhibitor (Rivastigmine 3–6 mg/day) Antipsychotic (Risperidone 0.5–1 mg/day)	15 12	87.0 (6.5) 85.3 (5.0)	12 (80) 8 (67)	NINCDS–ADRDA, probable AD 6.3–9.0	CMAI ay 6 weeks	− 1.9 − 24.8*	Risperidone more effective than rivastigmine.	MODERATE

Cantillon et al.[73] (1996) USA	Anxiolytic (Buspirone 5 mg TID) Antipsychotic (Haloperidol 0.5 mg TID)	14 14	78.8 (5.1) 79.6 (4.9)	8 (66.7) 9 (64.3)	NINCDS-ADRDA, probable AD 2.5-2.6	BPRS total	ASI: -11.1% BPRS tension subscale: -10.9% ASI: -2.1% BPRS tension subscale: -1.6%	Buspirone more effective than Haloperidiol in the treatment of anxiety and tension	MODERATE

∗p < 0.05 when compared with placebo or other comparator medication in the study; – = not reported. NPS=Neuropsychiatric symptoms; AD = Alzheimer's disease; ASI: Anxiety Status Inventory; BPRS = Brief Psychiatric Rating Scale; CMAI = Cohen-Mansfield Agitation Inventory; MMSE = Mini-Mental State Examination; NINCDS–ADRDA = National Institutes of Neurological and Communicative Disorders and Stroke – Alzheimer's Disease and Related Disorders Association; SIB: Severe Impact Battery

5.4.7. Safety

Two studies reported adverse events. Both studies reported no statistically significant difference in adverse event rates; one study observed no clinically significant side effects between an antipsychotic (haloperidol) and an anxiolytic (buspirone) [73]while the other reported 12 events in the antipsychotic arm (risperidone) and 15 in the cholinesterase inhibitor (rivastigmine) arm[76] . These adverse events include chest infection, constipation, cellulitis, nausea, skin rash and transient ischemic attack.

5.4.8. Conclusion

This review identified only a small number of RCTs which reported on a comparison of non-antipsychotics to antipsychotics to treat BPSD in LTC settings. All studies were small, of moderate to high quality and reported on changes in symptoms like agitation and anxiety. Overall, none of the studies reported statistically significant improvements in BPSD using a non-antipsychotic compared to an antipsychotic.

5.5. Discontinuation of antipsychotic treatment

Key Findings: A recent Cochrane systematic review published in 2013 was used as a platform. An updated search of the literature and no additional articles were identified. Nine randomized control trials in long term care of medium to high quality were included in the Cochrane review. Incomplete and selective reporting among the RCTs limits the strength of the conclusions of this review. Five studies reported successful completion of the study (the primary outcome); four of the studies concluded was there no significant difference while one concluded a higher success rate in the control group than in the discontinuation group suggesting that there may be no difference between antipsychotic discontinuation and continued use.

5.5.1. Research question

What is the effectiveness of withdrawal of antipsychotics for dementia patients suffering from neuropsychiatric symptoms (NPS) / behavioural or psychological symptoms of dementia (BPSD) in long term care (LTC) settings?

5.5.2. Methods

The EAG noted due to the current overuse of antipsychotics, the use of antipsychotics in some patients is likely to be discontinued. However, little is known about the effectiveness, clinical impact and outcomes associated with discontinuation of antipsychotics. To leverage previous high-quality research, a Cochrane systematic review was used as a platform[77]. The Cochrane review addressed the effectiveness of withdrawal of antipsychotics in older people with dementia in both the community and long-term care. The search was completed in November 2012. As

such, the current systematic review was completed from January 2012 to July 2013. MEDLINE, PsycINFO, PubMED, CINAHL, LILACS, HTA Database, the Cochrane CENTRAL Registry of Controlled Trials, and the Cochrane Database of Systematic Reviews were searched from January 2012- July, 2013. The same search terms were used as the Cochrane review; terms such as "dementia", and "Alzheimer*" were combined using the Boolean operator "and" with terms for antipsychotic, withdrawal, discontinuation, cessation, reduction, taper and stop. Results were limited to English or French language, and excluded comments, editorials and letters. No other limitations were used.

Abstracts were screened in duplicate. The same inclusion and exclusion criteria were used as the Cochrane review. Abstracts were only included for full-text review if they: were randomized controlled trials, involved patients who were living in long term care and displaying BPSD, reported clinical effectiveness, presented primary data, and were available in English or French. Abstracts selected for inclusion by either reviewer proceeded to full-text review. This initial screen was intentionally broad to ensure that all relevant literature was captured.

Studies meeting these inclusion criteria proceeded to duplicate full-text review. Studies were included in the review if they met the inclusion criteria presented in **Table 8**. Any disagreement between reviewers was resolved through discussion and consensus.

Data from the included studies were extracted in duplicate using a standardized data extraction form. General data including author, year, and country were extracted from each, in addition to method of description of intervention, patient characteristics, age, sex, dementia diagnosis, MMSE scores, outcome measure, change in NPS and outcome. Each included study was assessed for quality using Cochrane collaboration risk of bias assessment tool.

Table 8: Inclusion/Exclusion criteria for discontinuation of antipsychotic medications

Inclusion Criteria	Exclusion Criteria
• Full-text available in English or French • Original data • Relevant outcome data (success of withdrawal) • Randomized controlled trial • Residents of long-term care with dementia exhibiting BPSD • Comparison of antipsychotic withdrawal to continuation	• Full-text not available in English or French • Non-original, or duplicate data • No relevant outcome data • Non-comparative study design • Patients not residing in long term care • Not comparison of antipsychotic withdrawal to continuation

5.5.3. Results

5.5.4. Study selection

One hundred and twelve citations were identified. After screening, one article was included for full-text review; however, no additional articles met the inclusion criteria for final analysis. The flowchart for article selection is presented in **Figure 4**.

5.5.5. Summary of Cochrane review

The systematic review, published in 2013, synthesized all relevant randomized control trials (RCT) from the published literature, clinical trials registries and grey literature sources[77]. Nine studies were included in the final analysis: seven were conducted in long-term care (LTC) settings, one was conducted in an out-patient setting, and the last included participants from both LTC and out-patient settings. Sample size across studies varied from 34 to 165 and included older individuals with a diagnosis or probable diagnosis of dementia, who were taking antipsychotic medication for BPSD (between at least 1-3 months prior) at the time of enrollment. For all included studies, the clinical efficacy of withdrawing the patient from an antipsychotic medication(s), either by tapering the medication dosage or abrupt discontinuation, compared to continued use of antipsychotic medication(s) (control) for the treatment of BPSD was examined. Specifically, three studies evaluated the effects of an abrupt withdrawal schedule[78-81]; two studies abruptly withdrew most participants off the medication and tapered dosage for the remainder[82;83]; and the remaining studies examined the effects of a tapering schedule[84-87]. All of the studies were generally found to be of medium to high quality, as assessed by the Cochrane Risk of Bias Tool. Only the findings for the studies conducted in LTC and the mixed setting (i.e. both LTC and out-patient care) are summarized below.

5.5.6. Success of Withdrawal from Antipsychotics

The success rate, defined as the ability to complete the study (no withdrawal from study due to behavioural deterioration) or relapse to antipsychotic medication, was the reported as a primary outcome measure in the majority of included studies. In 4 of the studies, there were no significant differences in the success rate between the discontinuation and the control groups[78-80;82;86]. One study reported an increased risk of relapse of behavioural problems in the discontinuation group compared to the control group[83]. For the remaining 3 studies, reporting of study withdrawal or relapse of BPSD was unclear or not provided[81;86;87]. Due to the heterogeneity in the manner that success rates were reported, the authors had difficulty in comparing outcomes across studies and pooling the data was not possible.

5.5.7. Severity of Behavioural and Psychological Symptoms of Dementia

The severity of BPSD was also assessed in most studies using a number of different instruments, including the Neuropsychiatric Inventory (NPI) scale, the NPI-Questionnaire (NPI-Q), the Cohen-Mansfield Agitation Inventory (CMAI), the physical aggressive behaviour (PAB) scale,

the Brief Psychiatric Rating Scale (BPRS) and the Behavioural Pathology in Alzheimer's disease Rating Scale (BEHAVE-AD). Four studies assessed BPSD using either the NPI scale or the NPI-Q [78-81;83] and reported no significance in score between treatment groups. Analysis of the pooled results from the two studies were pooling was possible[78-80] similarly revealed in no significant pooled difference in NPI scores between the discontinuation and control group (mean difference -1.49, 95% CI -5.39 to 2.40). Similarly for the remaining studies that measured severity of BPSD using either the PAB, CMAI, BPRS or BEHAVE-AD, there were no significant differences between withdrawn and continued use of antipsychotics reported[82;84;87].

5.5.8. Secondary Outcome Measures

Secondary outcomes measures related to change in cognition[78;80;83;84;86;87], quality of life[79] and use of physical restraint[82] were also reported in a subset of studies. In all cases, there were no significant differences in secondary outcome measures observed between treatment groups.

5.5.9. Safety

Adverse events were reported in only 5 of the included studies. No significant differences in the incidence of adverse events between treatment groups were reported[78;80;83;84;86;87]. Similarly, only two studies reported mortality rates[78;80;83] and did not significantly differ between control and discontinuation groups.

5.5.10. Limitations

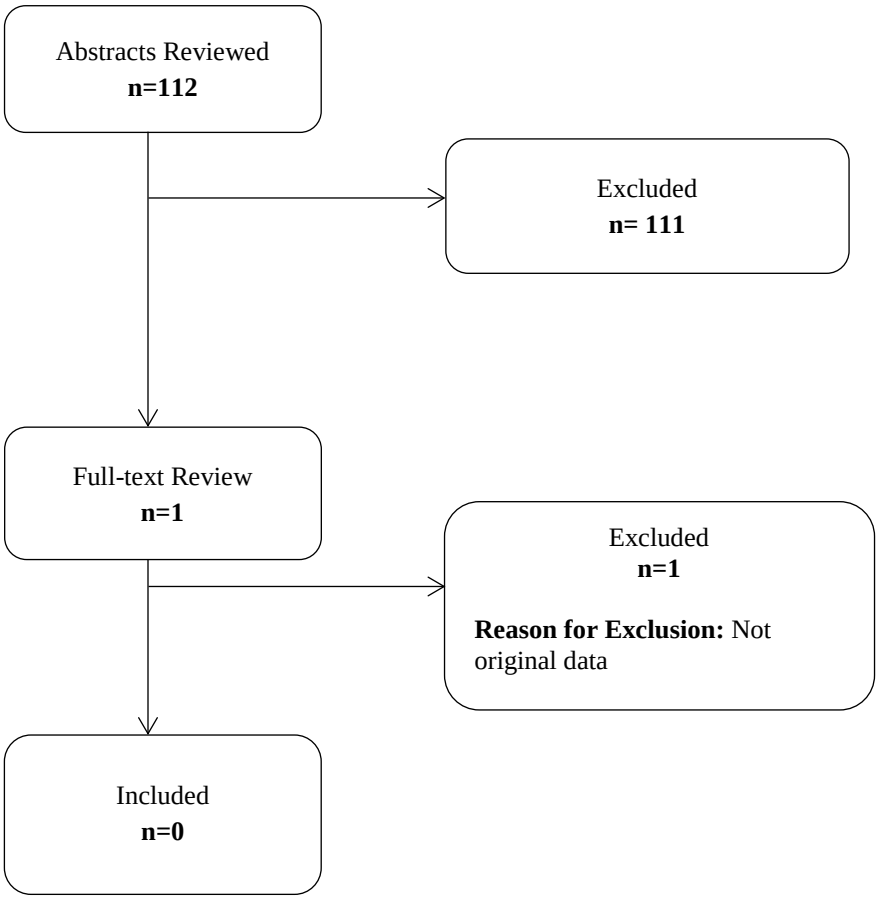
There were also a number of limitations amongst the included studies. Of note, there were several instances of incomplete outcome data amongst studies[78-80;82-84;87], as well as frequent selective reporting of outcome data. Specifically, many outcomes were not reported in numbers (narrative only provided)[86;87], outcomes initially listed were not subsequently reported on[87] and primary outcomes, nor occurrence of their selection, were not described[86]. It was also unclear if randomization of participants was successful, to ensure similarity of baseline characteristic between groups, for several studies[81;83;86].

5.5.11. Conclusions

Building upon a recent high quality Cochrane systematic review, an updated literature search did not identify any additional studies. The Cochrane review included 9 randomized control trials for medium to high quality; 7 of these were in long term care settings. The outcome measures used to measure BPSD were heterogeneous thus generalizability across studies is limited. Of the 5 studies that reported the primary outcome measure of the Cochrane review (successful completion rate of the study), 4 of the studies concluded was there no significant difference while 1 concluded a higher success rate in the control group than in the discontinuation group. Adverse events were not systematically assessed. However, among the 5 studies that did report adverse events, there was no statistically significant difference between groups. Incomplete and selective reporting among the trials limits the strength of the conclusions of this work.

However, the limited evidence available suggests no difference in BPSD between those that discontinue or continue antipsychotics.

Figure 4: Flowchart for the discontinuation of antipsychotic medications



5.6. Complementary and Alternative Medication (CAM)

Summary of Findings:

Four studies reported on the utilization of CAM interventions in LTC settings to manage BPSD. All reported improvements indicating CAM is a promising intervention to manage BPSD. The overall quality of the included studies was low to moderate. Implementation of certain CAM interventions, such as Yi-Gan Sa, may not necessarily be generalizable to a Canadian context. Given the diversity of the intervention types, a thorough appraisal of the patients' symptoms, as well as the healthcare system's ability to provide these interventions is necessary.

5.6.1. Research Question

What is the effectiveness of complementary and alternative medications for the management BPSD among seniors residing in LTC facilities?

5.6.2. Methods

A systematic review was conducted to gather evidence on the clinical effectiveness of complementary and alternative medications (CAM) for the management of BPSD. Included in this were herbal medicinal alternatives, acupuncture and acupressure. MEDLINE, Cochrane CENTRAL Register of Controlled Trials, EMBASE, PsycINFO, AMED, CINAHL, AltHealth Watch were searched from 1995 to 2013. The search strategy can be found in Appendix E. The full list of inclusion/exclusion criteria is presented in **Table 9**. Abstract and full-text review was performed in duplicate by two authors and any disagreements in article inclusion discussed. Quality of the studies based on randomized controlled trials was assessed Cochrane's Risk of Bias tool[23] and Down's and Black Assessment Tool[88]. This checklist includes 27 criteria, widely covering areas reporting quality, external and internal validity, and power. Studies are assigned a value of "1" if they meet the question criteria, and "0" if they do not or if it is not possible to determine; with one exception where a study may be given "2" points for completely listing possible confounders (Question 5). Studies are then assigned a total value out of a possible 28 points.

Table 9: Inclusion/Exclusion Criteria for CAMs for reduction of BPSD

Inclusion Criteria	Exclusion Criteria
• Seniors (≥ 65 years) with BPSD • Long term care or related setting • Herbal, acupuncture, or acupressure intervention compared to standard of care • Report effect on BPSD (efficacy) • RCT, controlled clinical trial, prospective cohort comparison or observational study	• Participants < 65 years • Pharmacological intervention • Non-pharmacological interventions • Primary endpoint not based on efficacy • Non-original data • Commentaries, Letters, Editorials, Opinions, Case Studies • Chemistry or biological studies • Preclinical or Animal Models

5.6.3. Results

5.6.3.1. Study Selection

Five hundred and eight citations were identified. After screening, 34 were included for full-text review and 4 articles met the inclusion criteria for final analysis. The flowchart for article selection is presented in **Figure 5**.

5.6.3.2. Overview of Included studies

Of the 4 studies identified, 3 were RCTs and 1 was an observational comparative cohort study. Each study assessed a different intervention. The quality of studies was assessed by the Cochrane Risk of Bias checklist for all RCTs and the Downs and Black checklist for the comparative cohort study are provided in **Appendix I** and **J**, respectively. Overall, the included studies were of low to moderate quality. An overview of each study is provided below (**Table 10**). A synopsis of the effectiveness of various CAM strategies is provided in **Table 11**. Included studies were published between 2005 and 2009. Sample size ranged from 20 to 133 participants. All studies were conducted in LTC facilities with patients with dementia exhibiting some degree of BPSD.

5.6.3.3. Efficacy of CAM

In 2005, Iwasaki et al.[89] performed a 4 week RCT which reported that Yi-Gan Sa (YGS) improved BPSD. YGS is a traditional Asian herbal medicine. Patients with mild-to-severe dementia in a long term care facility in Japan were randomized to 2.5g of YGS powder (1.5 g of extract) 3 times a day before meals for 4 weeks (n=27) or no intervention (n=25). Improvements were seen in the NPI scores of those in the YGS group (37.9±16.1 to 19.5±15.6) but no significant change was observed for those in the control group (33.6±20.1 to 31.0±20.8). This study was of moderate quality with a high risk of bias due to a lack of blinding and allocation concealment.

Lin et al.[90] performed a double-blind RCT crossover study. Three interventions were assessed: acupressure, presence and Montessori methods. Acupressure is an alternative medicine used to treat a variety of conditions through applying pressure using hands, elbows or other devices to specific points on the patient. The presence treatment involved simply engaging the patient in conversation, and attempting to maintain their attention. Montessori methods involved a series of activity program for persons with dementia grouped into five major categories of activities associated with daily living: scooping, pouring, squeezing, fine motor skills, environmental care, and personal care. Each patient received each intervention but was randomized into one of three sequences: acupressure-presence-Montessori methods, Montessori methods-acupressure-presence and presence-Montessori methods-acupressure. All treatments were done once a day, 6 days per week, for a 4-week period. The primary outcome was agitation measured using the validated, standardized CMAI tool. Pre- and post-test assessments were performed after each treatment type in each treatment arm session. Substantial improvement in agitated behaviors, aggressive behaviors and physically nonaggressive behaviors was observed in the treatment session, relative to the control session. This study was of moderate quality with a high risk of bias due to unclear sequence allocation and concealment.

Kudoh et al.[91] performed a RCT including patients with BPSD from a LTC facility in Japan who were randomly selected to receive either foot care with green tea paste (n=10) or usual care without foot care treatment (n=12). Foot care was performed by care workers every evening twice a week for four weeks. Foot care involved massaging the feet of the patients for five minutes with the green tea paste. Green tea paste has no medicinal properties in terms of BPSD but was used because it is a common tool in Japan for the treatment of tinea manuun. The primary outcome was changes in BPSD measured by the NPI. Foot care treated patients showed an improved NPI score after 4 weeks (32±10 to 16±19) while the control, no treatment group showed no significant improvement (33±13 to 27±14). This study was of moderate quality with a high risk of bias due to a lack of blinding and allocation concealment.

Yang et al.[92] used a cross-over study where each patient served as his or her own control. Twenty patients received 4 weeks of acupressure treatment (treatment period) followed by a treatment-free week and then an additional 4 weeks of visiting and conversation (control period). The primary outcome was agitation measured using the validated, standardized CMAI tool. Pre- and post-treatment assessment periods were performed before each treatment and control periods for each patient. Results indicated a significant decline in CMAI scores between pre- and post-treatment assessment for the acupressure period but an increase in CMAI at the end of the control period. This study was of low quality receiving 16 points of 25 on the Downs and Black scale.

5.6.3.4. Safety

There is no clear documentation for Health Canada approval for any CAM intervention.

Figure 5: Flowchart for the assessment of complementary alternative medicine

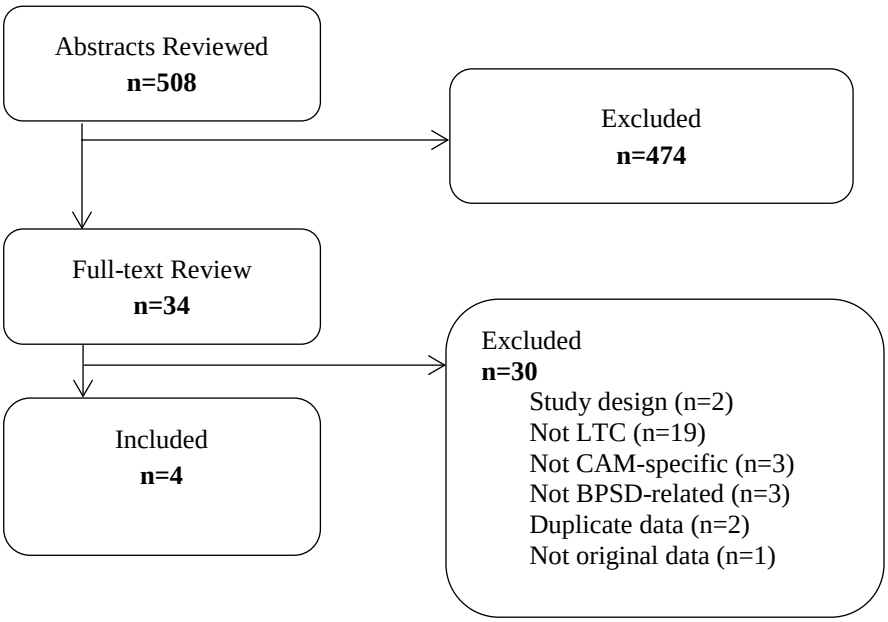


Table 10: Characteristics of included studies for CAM

Author, Year	Intervention	Country	Dementia Type	Study Type	Group Allocation	Number of Participants	Sex (male:female)	Age (Mean±SD) (Years)
Iwasaki, 2005[89]	Yi-Gan Sa (YGS)	Japan	AD, VD, DLB, CVD	Randomized, observer blind, controlled trial	YGS Group	27	13:14	77.0±9.6
					Control Group (No Treatment)	25	11:14	84.0±6.7
Lin, 2009[90]	Acupressure and Montessori-Based Activities	Taiwan	No subtypes listed	Randomized, double-blind experimental cross-over design	Sequence I	42	27:15	80.9±7.8
					Sequence II	39	33:6	78.2±9.4
					Sequence III	52	38:14	80.9±7.1
Kudoh, 2009[91]	Foot care using green tea paste	Japan	No subtypes listed	Randomized controlled trial	Foot Massage	10	4:6	79±11
					Control Group (No Treatment)	12	4:8	80±12
Yang, 2007[92]	Acupressure	Taiwan	No subtypes listed	Longitudinal cohort study	None	20	13:7	74.2±6.7

YGS= Yi-Gan Sa, LTC=Long Term Care, AD=Alzheimer's disease, VD=vascular dementia, DLB=Dementia with Lewy bodies, CVD=Alzheimer's disease with cerebrovascular disease

Table 11: Effects of CAM intervention on BPSD

Author, Year	Intervention	Scale	Group Allocation	Number of Participants	Baseline Score (Mean±SD)	Endpoint Score (Mean±SD)	Significance
Iwasaki, 2005[89]	Yi-Gan Sa (YGS)	NPI	YGS Group	27	37.9±16.1	19.5±15.6	I > C
			Control Group (No Treatment)	25	33.6±20.1	31.0±20.8	
Lin, 2009[90]	Acupressure and Montessori-Based Activities	CMAI	Sequence I	42	41.0±6.9	The intervention groups saw a significant decrease in agitated behaviors, aggressive behaviors, and physically nonaggressive behaviors than the presence group.	I > C
			Sequence II	39	39.7±6.7		
			Sequence III	52	39.3±6.2		
Kudoh, 2009[91]	Foot care using green tea paste	NPI	Foot Massage	10	32±10	16±19	I > C
			Control Group (No Treatment)	12	33±13	27±14	
Yang, 2007[92]	Acupressure	CMAI	None	20	19.45±11.4[a]	-2.15±7.3[b]	I > C

YGS=Yi-Gan Sa, NPI=Neuropsychiatric Inventory, CMAI=Cohen-Mansfield Agitation Inventory, NS=Not significant
[a]Difference between pre- and post-treatment results for acupressure group [b]Difference between pre- and post-treatment results for control group

5.6.4. Discussion

Four articles reported on the use of CAM to manage BPSD in LTC: 3 RCTs and 1 observational cohort. The interventions in the included studies were diverse, ranging from YGS, acupressure to foot massage with green tea paste. All studies reported improvements in symptoms like agitation and aggression. All studies are of moderate to low quality.

Interventions like Yi Gan Sa may not be easy to implement in a Canadian context. Other interventions like massage or acupressure may be resource intensive and may require careful consideration before implementation at a large scale.

Several gaps in the evidence base supporting the use of CAM were identified. Variations in therapies including dosing, timing and length make it challenging to comment on the appropriate approach. None of the included studies provided details on the safety of the intervention. In addition, studies did not comment on the simultaneous use of antipsychotics or other drugs thus the true impact of CAM remains unknown.

Limitations of this review include study quality, small sample size, and short follow-up periods.

5.6.5. Conclusion

Based on four studies reporting improvements, CAM interventions are promising to manage BPSD. The studies were, however, of low to moderate quality. Given the diversity of the interventions, a thorough appraisal of the patient's symptoms is necessary to determine applicability of the CAM interventions. Further investigation of the healthcare system's ability to fund and provide these interventions, as well as the generalizability of the interventions to a Canadian context, are required before recommendations can be for adaptation of the care guidelines for Alberta.

5.7. Built Environment

Summary of Findings:

Twelve articles were identified examining 4 broad categories of interventions: change or redesign of existing physical space, use of visual barriers or disguises, addition of physical objects to existing environment, and type of living environment. The overall quality of included studies was low to moderate and a variety of outcome measures were reported across studies. However, the majority of studies reported some improvement in outcomes related to quality of life and BPSD for dementia patients following the intervention.

5.7.1. Research Question

What is the effectiveness of built environment for the management BPSD among seniors residing in LTC facilities?

5.7.2. Methods

A previously published high-quality systematic review of the literature published from 1970 to 2002[93] was updated. MEDLINE, CENTRAL Register of Controlled Trials, EMBASE, PsycINFO, Cochrane Database of Systematic Reviews, HTA Database, NHSEED, Environment Complete, Social Work Abstracts, SocINDEX, CINAHL, Urban Studies Sociological abstracts, and Social Services Abstracts were searched from 2000-May 2013. An overlap of dates was selected to ensure what all relevant articles were captured. The search strategy focused on combining terms for dementia and built environment. The first set of terms such as “dementia”, “Alzheimer’s disease”, and “Alzheimer’s” were searched. This first set of terms was combined using the Boolean operator “or”. A second set of terms focused on interventions related to the built environment and combined words such as “environment design”, “facility design and construction”, “hospital design and construction”, and “health facility environment” with the Boolean operator “or”. To obtain the final results, the two sets of terms were combined using the Boolean operator “and.” Details of this search can be found in Appendix F. Results were filtered to exclude non-human studies and languages other than English or French. No other limits were used.

The abstracts retrieved were screened in duplicate. Abstracts were included for full-text review if they reported original data, were set in a long-term care or specialized dementia care facility, included patients or residents with dementia diagnosed with behavioural and psychological symptoms in dementia (BPSD), involved an environment intervention specific to the physical or built structure of the living environment (e.g. architectural design, building reconstruction, interaction/use of the physical environment by staff or patients, etc.) and reported on the clinical efficacy of built environment interventions on BPSD. All abstracts selected for inclusion by

either reviewer proceeded to full-text review. This initial screen was conducted using broad criteria to ensure that all relevant literature is captured.

Studies included after the first screen proceeded to full-text review by two reviewers. Studies were included if they met the inclusion criteria presented in **Table 12**. Any disagreement between reviewers was resolved through discussion and consensus. A kappa statistic for reviewer agreement was also calculated, which measures agreement above and beyond that expected by chance alone.

Table 12: Inclusion/Exclusion Criteria for Built Environment for reduction of BPSD

Inclusion Criteria	Exclusion Criteria
• BPSD or responsive behaviours in dementia • Long-term care (LTC) • Environmental interventions (architectural design, interactions/use of the physical environment by staff or patients, etc.) • Outcome measure related to BPSD (change in frequency and/or severity) • Original Data • Randomized Controlled Trials • Prospective Comparative Cohort Studies • In English or French	• No BPSD, no dementia • Pediatric population • Not focused on built environment • Not in LTC special dementia care facility • Non-pharmacological treatments • Preclinical/Animal studies • Non-original data • Grey Literature • Not RCTs or Comparative Cohort Studies • Not English or French

Data from the included studies was extracted in duplicate using a standard data extraction form. Any discrepancy was resolved through consensus and discussion. Participant information, study design details, procedure information, and relevant outcome measures were extracted from each included study. Specifically, outcomes assessed in this report included the efficacy of built environment interventions in the management of BPSD or responsive behaviours in dementia. This data was also extracted from each study after inclusion.

Each included study was assessed for quality using the Downs and Black Checklist[88]. This checklist includes 27 criteria, widely covering areas reporting quality, external and internal validity, and power. Studies are assigned a value of "1" if they meet the question criteria, and "0" if they do not or if it is not possible to determine; with one exception where a study may be given "2" points for completely listing possible confounders (Question 5). Studies are then assigned a

total value out of a possible 28 points. All studies were assessed in duplicate with discrepancies resolved through discussion and consensus.

5.7.3. Results

5.7.3.1. Study Selection

The update search (containing literature from 2000-2013) identified 258 unique abstracts. Of those, 216 were excluded based on abstract review and forty-two proceeded to full-text review. Combined with the fifty-one articles from Gitlin et al.[93], ninety-three articles proceeded to full-text review. Based on full-text review, 81 of these articles were excluded. Ultimately, 12 studies were included in the final analysis (Kappa = 0.521, 95% CI 0.212-0.830) (**Figure 6**).

5.7.3.2. Overview of Included studies

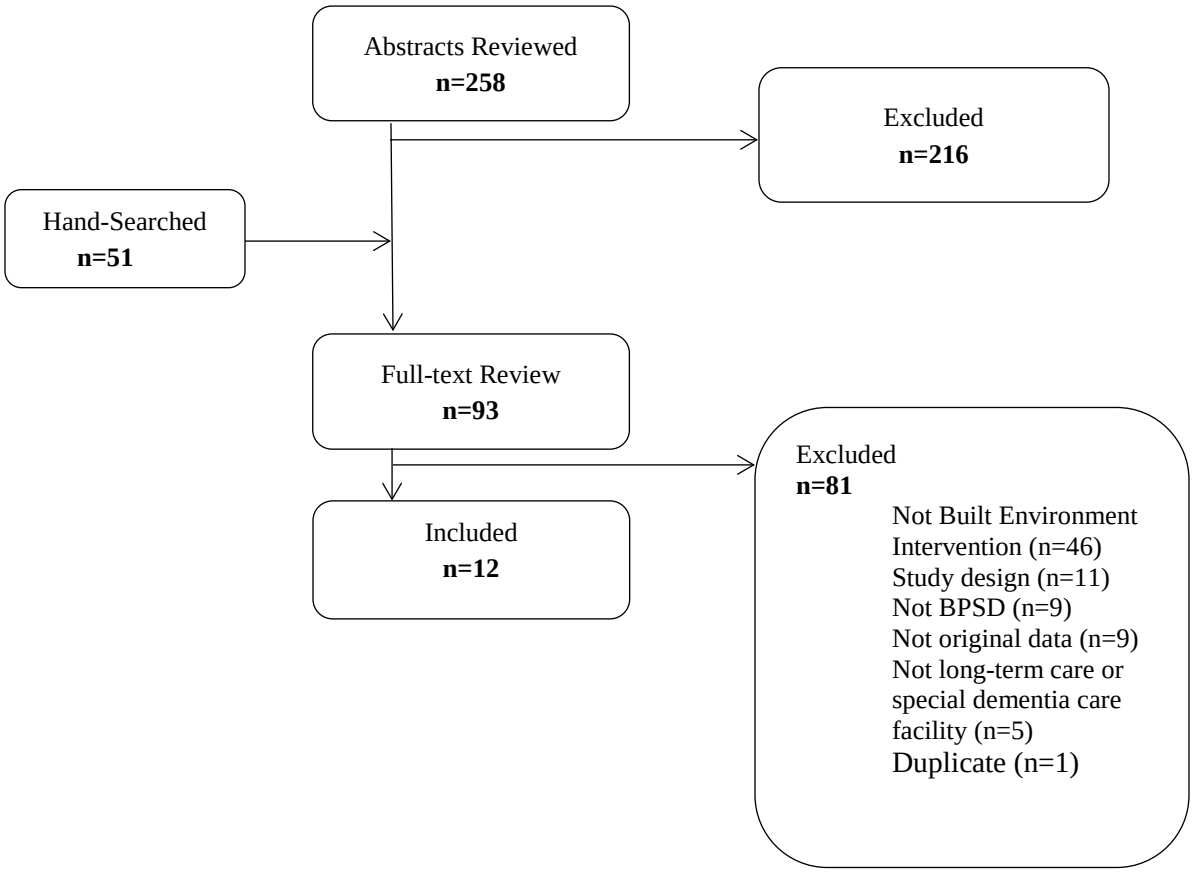
All 12 included studies were non-randomized comparative cohort studies published between 1987 and 2010. Characteristics from each of these studies were summarized in Table 3. Eight studies were conducted in the United States[94-101]; two were conducted in Australia[102;103]; and the remaining two studies were conducted in Canada[104] and Scotland[105]. All of the studies were conducted on senior patients with dementia, who were residing in LTC facilities or specialized dementia care facilities. Half of the included studies were conducted in long-term care (LTC) facilities[94;96;97;102-104]. The sample size varied across studies, between 8 and 185 participants per study. The studies included in this systematic review are of low to moderate quality. Using the Downs and Black Checklist, the included studies scored between 13[95] and 18[96;103] points for quality, out of a possible 28 points (**Table 13**). Blinding, randomization, and sample representativeness were the areas of lowest quality, while compliance and clear intervention descriptions were some of the areas that were consistently assessed as being high quality.

In general, study participants were identified as patients of the specified healthcare settings, with known diagnoses of BPSD. Eleven of the studies utilized a pre- and post-intervention design where the population exposed to the intervention served as their own historical control group. The control group for the remaining study (not exposed to the intervention) was sampled from two separate LTC facilities compared to those in the intervention group[104].

With the operational definition of a built environment intervention pertaining to any manipulation in the physical structure of the living environment of study participants, the types of intervention examined included: a change or redesign of existing physical structures or spaces within the environment[94;98-100;105]; visual barriers or disguising of existing physical structures[95-97]; the addition of physical objects or spaces to the existing environment[101;102]; the relocation of the study population to a novel living environment[103;104]. Given the range in responsive behaviours or forms of BPSD targeted by the various built environment interventions, there were no standard outcomes measures reported across all studies and due to this heterogeneity the results

could not be pooled. The results from each study, organized according to the general type of built environment intervention, are discussed below and summarized in **Table 14**.

Figure 6: Flowchart for the assessment of built environment



5.7.3.3. Efficacy of Built Environment Interventions

5.7.3.3.1. Change or Redesign of Existing Physical Structures or Spaces

Five of the included studies examined the impact of changing or redesigning the existing physical structures or spaces within the living environment on the BPSD of study participants[94;98-100;105].

Two of the pre- and post-test studies implemented a single change to the built environment of their study participants. In the study conducted by Namazi et al.[98], the efficacy of visual signs and arrows to indicate the washroom location, on washroom utilization by patients with dementia, was examined in two specialized care facilities. Over the 2-week study period the authors found that the visual cues, particularly use of a "TOILET" sign led to increased

washroom utilization[98]. A second study conducted by Namazi et al.[99] found that unlocking the doors to the common courtyard of a specialized care facility led to decreased agitation amongst patients with dementia compared to the control conditions when the doors were locked[99].

Three studies examined the impact of larger manipulations or redesigns of the existing environment[94;100;105]. One study aimed at increasing the level of dressing independence for patients with dementia in a specialized care facility, found that modification to the patients' individual closets (i.e. clothes arranged in the order they will be worn by the patient for a given week) led to an increase in dressing independence relative prior to the closet redesign[100]. In the study conducted by Brush et al.[94], the redesign of the dining room area in a specialized dementia care facility, which included elevated light levels in the room and changes to the colour and contrast of dining table settings, similarly led to in an increase in both the food intake and communication of patients with dementia following the intervention[94]. Lastly, one study that examined a large-scale redesign of an existing main corridor or a large psychiatric hospital found there was no difference in the measured patient behaviours before and 3-months after the built environment intervention[105].

5.7.3.3.2. Use of Visual Barriers or Disguising of Existing Physical Structures

Three pre- and post-test studies that investigated manipulations intended to disguise or act as visual barriers to exit/entrance doorways of the built environment. The study conducted by Hussian et al.[95], had a small sample of 8 patients and found that the use of horizontal and vertical grid patterns placed prior to a specific doorway threshold resulted in a reduced number of exit door contacts by participants compared to control conditions[95]. Similarly, Namazi et al.[97] found that the use of visual barriers (e.g., coloured tape, cloth covers) specifically on the doorknobs of exit doors led to a reduction door exiting by participants, particularly for those with visual agnosia[97]. Use of a larger wall mural painted over an entire locked exit/entrance doorway and adjacent walls also led to a significant reduction in door testing over the 6-week testing period[96]. The authors found that in particular, calm or passive door testing and door testing in teams of patients was reduced following the painting of the wall mural[96].

5.7.3.3.3. Addition of Physical Objects or Spaces to the Existing Environment

Two studies examined the impact of adding new physical objects or features. Specifically, Namazi et al.[101] found that implementation of two types of snacking refrigerators, throughout a specialized care facility, resulted in no change in the level of independent snacking for the 22 patients in the study. A second study measured time spent in the control living room setting compared in two multisensory environments added to the LTC facility – a Snoezelen room and a landscaped garden[102]. There were no differences observed in the various affect states before and

after time spent in any of the three environments; the only significant difference was the recording of more 'sadness' in the living room relative to either multisensory environment[102].

5.7.3.3.4. Relocation to a Novel Living Environment

Two studies examined the impact of several responsive or agitated behaviours for patients following a complete relocation in living environments. The relocation of a small sample of 16 patients from a traditional care unit to a specialized dementia care unit within a single LTC facility resulted in decreased agitation amongst participants, specifically in verbally aggressive behaviour, 6-months post-intervention[103]. In a larger study of 185 patients conducted by Reimer et al.[104], quality of life – which included measures of responsive behaviours such as agitation, socially appropriate behaviour, social withdrawal and interest in the environment, were compared between participants in traditional LTC facilities (control group) and in a purpose-built specialized dementia care facility[104]. One year post-intervention, the authors reported that the overall quality of life was similar or better for the intervention group compared to controls; however, there were no significant differences with regards to the levels of agitation, socially appropriate behaviour, and social withdrawal between study groups[104].

5.7.3.4. Safety

None of the included studies provided details on the safety of the intervention. Incidence of adverse events if any was also not reported. There is no clear documentation for Health Canada approval for any built environment intervention.

5.7.4. Discussion

Twelve relevant articles were identified. The included studies were all comparative cohort studies and no RCTs were identified. All of the studies were relatively small and, with the exception of 3 studies[94;98;104], the study participants were sampled from only 1 healthcare facility[95-97;99-103;105]. In all, 9 of the included studies demonstrated improvements and 3 reported no difference in the frequency and/or severity of BPSD following the built environment intervention, compared to the control conditions.

While four general categories of built environment interventions emerged from the literature in this review, there was still some degree of variability within categories with regards to the specific interventions. Only one intervention category, the relocation to a novel built environment, was a specific intervention examined in more than 1 of the included studies[103;104]. The variability in potential manipulations to the built environment may suggest that there are a number of innovations in this area of research, where potential interventions are tailored or created in response to specific behaviours exhibited by the dementia patient(s).

Several limitations were identified. The overall quality of the included studies, deemed to be of low to moderate quality by the Downs and Black Checklist, proved to be problematic for final analyses. In particular, many of the studies scored low in representativeness, sampling and disclosure of characteristics. Due to the nature of built environment intervention studies, it was also not possible to blind either the assessor or the subject or to randomize participants to intervention groups. In an attempt to remain focused on the interventions to the physical or built structure of the living environment for patients with dementia in LTC or specialized care facilities, other interventions applied to the built environments for temporary housing, adult daycares, or non-specialized acute care facilities were excluded from this review. Additionally, interventions that involved manipulations experienced by the patients within the environment, but without any physical or structural manipulation to the environment (e.g. aromatherapy, artificial bright light therapy, music therapy) were classified as general non-pharmacological interventions and were not included here. Studies with either a RCT or nonrandomized comparative cohort design were also exclusively selected for synthesis in this report, as these are the highest level of evidence. As such, other forms of observational studies, for example those without comparators were excluded from final analysis.

5.7.5. Conclusion

Based on the results of the included studies, built environment interventions result in improvement or no difference in the frequency and/or severity of BPSD. However, the range of built environment interventions is broad, with some requiring more resources than others. Thus, it is difficult to determine a single, most effective intervention that can be applied to all situations.

Table 13: Characteristics and Results of Included Studies for Built Environment

Author, year	Intervention	Country	Dementia Diagnosis	Health Care Setting	Type of Control Group	Number of Participants	Dose/Intensity	Outcome Measure(s)	Main Results
Change or Redesign of Existing Physical Structures or Spaces									
Brush, 2002[94]	Increased light levels and table setting contrast in dining room	USA	Unspecified "dementia"	One long-term care facility and one special care facility	Historical controls (pre-post-test design)	Intervention group: **25** Control group: **25**	Three meals per day for 4 weeks	Caloric intake for 3-day period Functional abilities Communication	Three-day caloric intake and communication increased following the intervention.
Edgerton, 2010[105]	Redesign of an existing corridor	Scotland	Unspecified "dementia"	Specialized long term care facility for psychiatric patients	Historical controls (pre-post-test design)	Intervention group: **47** Control group: **53**	Three months of living with redesigned corridor	Patient behaviour	No significant difference in overall patient behaviour while in corridor.
Namazi, 1991[98]	Visual signs and arrows indicating direction of washrooms	USA	Probable Alzheimer's disease	Two special care facilities	Historical controls (pre-post-test design)	Intervention group: **44** Control group: **44**	Visual signs and arrows in place for 2 weeks	Number of times resident looks at sign Number of times resident enters facility Evidence of use	Increased utilization of washrooms, particularly when word "toilet" was used as cue.
Namazi, 1992a[99]	Unlocked doors to courtyard	USA	Probable Alzheimer's disease	Special Care Facility	Historical controls (pre-post-test design)	Intervention group: **22** Control group: **22**	Five hours a day over 10 days – total of 50 hours per condition	Agitation and behaviour	Decreased agitation when doors were unlocked compared to when doors were locked.
Namazi, 1992b[100]	Closet Hanging clothes in closet in sequential order	USA	Probable Alzheimer's disease	Special Care Facility	Historical controls (pre-post-test design)	Intervention group: **8** Control group: **8**	One dressing station per participant	Dressing independently Dressing time Number of times staff member checked on participant	Level of dressing independence among residents increased due to closet modification.

Use of Visual Barriers of Disguising of Existing Physical Structures									
Hussian, 1987[95]	Horizontal and vertical grid patterns on floors by exit doors	USA	"Primary degenerative dementia"	Specialized long term care facility psychiatric patients	Historical controls (pre-post-test design)	Intervention group: **8** Control group: **8**	Grid patterns in place for 2 month period	Number of exit door contact	Reduction in number of contacts made with exit door.
Kincaid, 2003[96]	Painted wall mural to disguise entrance/exit doorway	USA	Unspecified "dementia"	One special Care Unit of Nursing home in Gastonia, North Carolina	Historical controls (pre-post-test design)	Intervention group: **12** Control group: **12**	Wall mural in place for 6 week period	Frequency of door testing behaviours	Significant reduction in door testing, particularly calm door testing and door testing in teams.
Namazi, 1989[97]	Visual barriers such as tape, cloth, and door knob covers	USA	Probable Alzheimer's disease	Dementia Unit of Long-term care facility	Historical controls (pre-post-test design)	Intervention group: **9** Control group: **9**	Visual barrier conditions in place for 2 weeks	Number of exits through doors	Visual barriers reduced exiting through doors, particularly door knob covering for those with visual agnosia.
Addition of Physical Objects or Spaces to the Existing Environment									
Cox, 2004[102]	Two multisensory environments - landscaped garden and Snoezelen room	Australia	Unspecified "dementia"	One Nursing Home in Victoria Australia	Historical controls (pre-post-test design)	Intervention group: **24** Control group: **24**	Three 16 minute sessions in control, Snoezelen room and garden –total of nine 16 minute sessions	Affect: Pleasure, Anger, Anxiety/fear, Sadness, Interest, Contentment	No significant differences in affect states before and after intervention, between the 3 environments. The only significant difference was that more sadness was recorded in the living room environment compared to the garden or Snoezelen room.

Namazi, 1992c[101]	Placement of two types of snacking refrigerators: Glass door and dorm-style in accessible areas	USA	Probable Alzheimer's disease	Special Care Facility	Historical controls (pre-post-test design)	Intervention group: **22** Control group: **22**	Refrigerators in place for 4 weeks	- Independent snacking behaviour: o Opening refrigerators o Taking snacks independently o Requesting snacks o Requesting and receiving help with snacks o Eating snack	No significant differences in frequency of snacking for before and after intervention, and between the two refrigerator types.
Relocation to a Novel Living Environment									
Reimer, 2004[104]	Move to purpose-built specialized care facilities	Canada	Unspecified "dementia"	Twenty four long-term care facilities with four designated assisted living environments in an urban center in Western Canada	Separate controls	Intervention group: **62** Control group: **123**	One year living in specialized care facility	- Quality of life, including: o Agitation o Activities of daily living o Interest in environment o Social withdrawal o Depression o Concentration o Memory	Quality of life in intervention group was similar or better compared to control group.
Wilkes, 2005[103]	Move to a Special Care Unit	Australia	Unspecified "dementia"	Long-term care facility in the west of Sydney Australia	Historical controls (pre-post-test design)	Intervention group: **16** Control group: **16**	Six months living in either specialized care unit or regular unit	- Agitation behaviour o Aggressive o Physically Non-aggressive o Verbal	Reduction of verbally agitated behaviour in intervention group compared to control group.

6. ECONOMIC EFFECTIVENSS (E)

Summary of Findings: No published studies were found evaluating the cost-effectiveness of non-pharmaceutical interventions, the use of anti-depressants, CAM, or the built environment to manage BPSD in LTC.

6.1. Review of the Literature

6.1.1. Research Question

What is the published evidence for the cost-effectiveness of non-pharmacological, antidepressants, CAM and built environment interventions for the management of BPSD in LTC facilities?

6.1.2. Methods

MEDLINE, Pubmed, Cochrane Database of Systematic Reviews, NHSEED, HTA Database, EMBASE, PsycINFO, and EconLit were searched from 1980 to 2013 utilizing economic search terms combined with clinical terms. In addition, all clinical searches described in the previous sections were screened for economic articles. Abstract and full-text review was completed in duplicate and any disagreements were discussed. The search strategy can be found in Appendix G. The full list of inclusion/exclusion criteria is presented in **Table 15**.

Table 15: Inclusion/Exclusion Criteria for Cost-effectiveness Studies for the Reduction of BPSD

Inclusion Criteria	Exclusion Criteria
• BPSD or responsive behaviours in dementia • Long-term care (LTC) or related • CAM, non-pharmacological or built environment intervention • Outcome measures related to clinical efficacy (change in frequency and/or severity of BPSD) and cost-effectiveness • Original Data	• No BPSD, no dementia • Pediatric population • Chemistry/biological studies • Preclinical/Animal studies • Non-original data • Commentaries, Letters, Editorials, Opinions • Case Studies

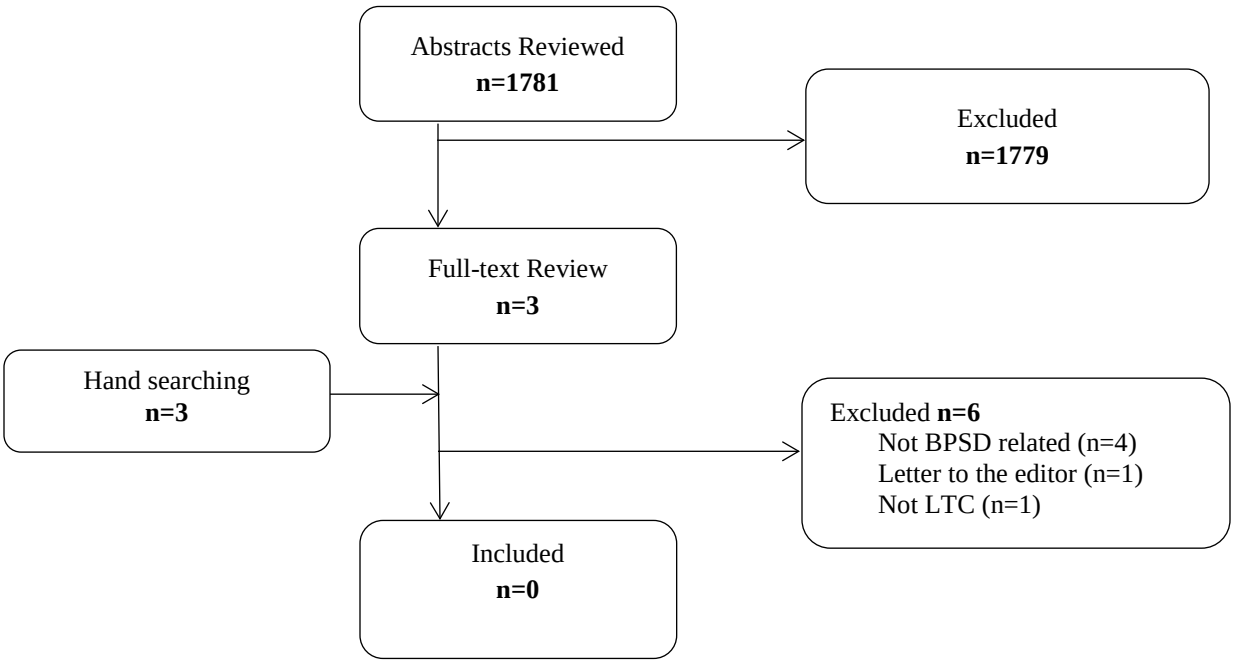
6.1.3. Results

In all, 1782 abstracts were identified. Three abstracts were selected for full-text review and 3 other studies were included from hand searching. None of the studies met all of the inclusion criteria for this review. Studies were excluded primarily due to: lack of inclusion of BPSD as an outcome, inappropriate study setting (not LTC), or inappropriate study design. **Figure 7** presents the flowchart for article selection for the update systematic review.

6.1.4. Conclusion

No published literature assessing the cost-effectiveness of non-pharmacological, anti-depressants, CAM and built environment interventions were identified. This is a critical gap in knowledge.

Figure 7: Flowchart for the assessment of economic evaluation and BPSD



6.2. Budget Impact Analysis (BIA)

6.2.1. Approach to BIA

In order to assess the annual budget impact of implementing non-pharmacological interventions in LTC facilities, the following key variables are needed:

- Size of the target population (seniors with BPSD, who are living in LTC facilities in Alberta)
- Current rate of antipsychotic use among the target population
- Average annual cost per patient on antipsychotics
- Average annual cost per patient for non-pharmaceutical interventions, CAM, and costs incurred in modifying the built environment
- Expected decrease in antipsychotic use (5%, 10%, 15%) and the corresponding increase in the use of non-pharmacological interventions so that the change intervention types can be adequately captured

While majority of the variables are available in the Alberta context, it may be difficult to quantify the average annual cost of non-pharmaceutical interventions, CAM, and costs incurred in modifying the built environment. In the absence of these estimates, a reliable budget impact analysis is not feasible.

7. CONCLUSIONS

BPSD is a heterogeneous set of complex symptoms that may require a multifaceted approach to their successful management. This evidence synthesis generally supports the recommendations within the BC guidelines. Non-pharmacological interventions are likely a viable first-line of treatment for managing BPSD with 21/40 RCTs reporting improved outcomes, and no studies reporting worsening behavior or adverse events. The evidence to support alternative pharmacological treatments such as antidepressants, cholinesterase inhibitors, mood stabilizers, anti-epileptics, benzodiazepines, and sedatives is limited. There are a small number of studies of low to moderate quality. However, these studies generally support that alternative pharmacological treatments have a similar impact on BPSD outcomes and similar short-term safety profiles. Evidence assessing modifications to the built environment to manage BPSD show small improvements or no difference in the frequency and/or severity of BPSD. The cost-effectiveness of the above mentioned alternatives to antipsychotics has not been formally assessed.

(1) Ministry of Health of British Colombia. Best practice guideline for accommodating and managing behavioural and psychological symptoms of dementia in residential care : a person-centered interdisciplinary approach. 2012.

(2) Dudgeon S. *Rising Tide: The Impact of Dementia on Canadian Society: a Study*. Alzheimer Society of Canada, 2010.

(3) Strain LA. Designated Assisted Living (DAL) and Long-term Care (LTC) in Alberta selected highlights from the Alberta Continuing Care Epidemiological Studies (ACCES). 2011; Available from: ACCES Research Group, University of Alberta.

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Appendix A: Guideline for Management of Antipsychotic Medication in Continuing Care

Alberta Health Services

Long Term Care Formulary E – 01

SECTION	SUBJECT	PAGE		
EDUCATION	Guidelines for Management of Antipsychotic Medication in Continuing Care	1 of 4		
		YY	MM	DD
	Original	02	06	25
	Revised	05	01	01
	Revised	09	08	27

Subject/Title:	No.	Page
GUIDELINE FOR MANAGEMENT OF ANTIPSYCHOTIC MEDICATION IN CONTINUING CARE		1 of 4
	Date Established: **April 2009**	
Approving Authority: Integrated Supportive & Facility Living/ Long Term Care Pharmacy and Therapeutics Committee	Date(s) Revised: **September, 2009**	

REASONS FOR GUIDELINE

1. To optimize resident safety while receiving antipsychotic medications.
2. To promote consistent adoption of least use of antipsychotic medications for treatment of the behavioural and psychological symptoms of dementia.
3. To ensure all persons involved in the care of the individual are informed and understand the implications of antipsychotic medication use including which behaviors may be responsive to antipsychotic therapy, the potential side effects that may occur, the expected therapeutic effects and the assessment monitoring.
4. To ensure judicious consideration of risks and benefits of initial and ongoing use of a antipsychotic medications as it pertains to the individual's choices and experiences.
5. To prevent ongoing use of antipsychotic therapy without review of continued necessity or effectiveness.
6. To comply with the Alberta Health and Wellness Continuing Care Health Service Standards.

THE FOLLOWING MEDICATIONS ARE DEFINED AS ANTIPSYCHOTIC AGENTS:

Tranquilizers (28:16.08)

- chlorpromazine (Largactil®)
- fluphenazine decanoate (Modecate®)
- loxapine (Loxapac®)
- pericyazine (Neuleptil®)
- risperidone (Risperdal®)
- zuclopenthixol (Clopixol Depot®/Accuphase)
- olanzapine (Zyprexa®; Zydis®) ***
- flupenthixol (Fluanxol®)
- haloperidol (Haldol®)
- methotrimeprazine (Nozinan®)
- perphenazine (Trilafon®)
- trifluoperazine (Stelazine®)
- clozapine (Clozaril®)***
- quetiapine (Seroquel®) ***
- other antipsychotic agents agreed upon as per Formulary processes as well as those approved as a special authorization

SECTION	SUBJECT	PAGE		
EDUCATION	Guidelines for Management of Antipsychotic Medication in Continuing Care	2 of 4		
		YY	MM	DD
	Original	02	06	25
	Revised	05	01	01
	Revised	09	08	27

GUIDELINE STATEMENT

1. Non-pharmaceutical strategies for behavior management are the first consideration in the care of individuals living with dementia.

2. The absence or limited effect of other strategies may trigger consideration of antipsychotic medications when the situation poses a risk to the individual or others. The use of antipsychotic medications to manage behaviors associated with dementia is guided by the philosophy of least restraint.

3. Antipsychotic medications can cause serious side effects and comprehensive evidence of antipsychotic efficacy is limited. Should the physician determine the need for antipsychotic medication given the individual circumstances, health professionals must provide comprehensive and accurate information about the situation, proceed with caution and closely monitor the individual on a scheduled basis.

4. The Behavior and Symptom Mapping Tool (BSMT) will be adopted by organizations to initiate and monitor response to antipsychotic treatment in accordance with the guidelines set down below. The completion of the BSMT (included in guideline) is required to initiate, change, maintain, or discontinue antipsychotic medications.

5. Assessment information collected will be reviewed by the resident's physician/prescriber, professional nurse and the pharmacist to determine therapeutic plan of care. Discussion of this review should be documented.

6. The decision to use antipsychotic medication must be shared with the family and staff and include a discussion of expected benefits, possible risks, and the fit of the treatment into the individual therapeutic plan of care and the processes for ongoing assessment and monitoring. Where disagreement occurs, an opportunity for further discussion and ethical review must be provided.

7. Physicians are required to review the continued need for and use of antipsychotic therapy for BPSD monthly, in keeping with the Alberta Health & Wellness Continuing Care Health Service Standards (2008).

8. For residents with other health concerns, assessment and monitoring of the use of antipsychotic medications is considered to be best practice. This form will assist you in supporting this practice, provides continuity of monitoring and will be familiar to your staff. As such use of the tool is recommended for all residents on antipsychotic medications therapy.

SECTION	SUBJECT	PAGE		
EDUCATION	Guidelines for Management of Antipsychotic Medication in Continuing Care	3 of 4		
		YY	MM	DD
	Original	02	06	25
	Revised	05	01	01
	Revised	09	08	27

ASSUMPTIONS

1. The limited definitive evidence for the use of antipsychotic medications in the treatment of behavioural and psychological symptoms of dementia (BPSD) requires individual physician judgment as to the appropriateness of the medication in each unique resident situation. Physician decision making requires accurate and comprehensive input from other health professionals, direct care providers, and significant others including where possible the resident.

2. Ongoing and structured monitoring of individual response directs continued treatment.

3. In keeping with the philosophy of least restraint, once the behavior has been managed, review and consideration of the need for continued antipsychotic therapy is required.

DEFINITIONS

Behavioral and Psychological Symptoms of Dementia (BPSD) – a spectrum of new and persistent "non-cognitive manifestations of dementia, that include verbal and physical aggression, agitation, psychotic symptoms (delusions and hallucinations), and wandering" (Lee, et al, 2004).

Antipsychotic Medications – are used to treat symptoms associated with psychiatric disease; in the presence of dementia, antipsychotic medications may manage behaviors such as hallucinations, delusions, aggression (to self or others), and anxiety (interfering with the person's ability to carry out daily activities).

Chemical Restraint: "any medication that is used to inhibit a particular behaviour or restrict movement and that is not the standard treatment for a resident's medical or psychiatric condition" (Alberta Health and Wellness. (2008). Continuing Care Health Services Standards).

APPLICABILITY

All Continuing Care facilities and contract providers will utilize this tool. Facility and contract provider policies will include the guideline elements in policy development.

GUIDELINES

1. A comprehensive assessment of the resident that must include:
   - Assessment of the clinical or environmental factors that may be affecting the behaviours.
   - Evidence that non-drug interventions have been trialed.
   - Evidence that behaviours have been described and identified as not responsive or may respond to antipsychotic medications.

- Evidence that when the safety of staff or other residents is not compromised two weeks of behaviour mapping is completed to establish a baseline for ongoing assessments.
- Continued monitoring of behaviours as soon as any drug therapy has begun and continue until the behaviour is resolved or the drug therapy is deemed ineffective.

2. A process of planned physician review and documentation to meet Alberta Health and Wellness Continuing Care Health Service Standards (2008), for determination of ongoing need.

3. A process to educate families and residents about the organization's antipsychotic drug therapy philosophy, policy, procedures and accountabilities.

4. A process to educate staff and physicians about the organization's antipsychotic drug therapy philosophy, policy, procedures and accountabilities.

6 A process that provides evidence that decisions around drug therapy use involve the physician, staff, the resident and the family/decision maker in discussions around resident choice, lifestyle surrounding the benefits and risks of drug therapy.

7 Where disagreement occurs, an opportunity for further discussion and ethical review must be provided.

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Appendix B: Search Strategy for Guideline Review

Dementia Guidelines MEDLINE March 14 2013

1. exp Dementia/
2. (dementia or dementias or alzheimer*).tw.
3. 1 or 2
4. Clozapine/
5. Risperidone/
6. (aripiprazole or abilify or asenapine or saphris or clozapine or clozaril or lurasidone or latuda or olanzapine or zyprexa or paliperidone or invega or quetiapine or seroquel or risperidone or risperidal or ziprasidone or zeldox).tw.
7. (atypical adj3 antipsychotic*).tw.
8. 4 or 5 or 6 or 7
9. Haloperidol/
10. exp Loxapine/
11. (haloperidol or haldol or loxapine or loxapac or xylac).tw.
12. 9 or 10 or 11
13. antipsychotic agents/ or chlorpromazine/ or flupenthixol/ or fluphenazine/ or methotrimeprazine/ or perazine/ or perphenazine/ or pimozide/ or thiothixene/ or trifluoperazine/
14. (antipsychotic or antipsychotics or chlorpromazine or largactil or fluphenazine or modecate or moditen or methotrimeprazine or nozinan or pericyazine or trilafon or pipotiazine or piportil or thioperazine or stelazine or flupentixol or fluanxol or thiothixene or navane or zuclopenthixol or clopixol or pimozide or orap).tw.
15. 13 or 14
16. (amisulpride or solian or blonanserin or lonasen or carpipramine or prazinil or clocapramine or clofekton or clotiapine or entumine or iloperidone or fanapt or fanapta or zomaril or mosapramine or cremin or perospirone or lullan or remoxipride or roxiam or sertindole or serdolect or sulpiride or sulpirid or eglonyl or zotepine or nipolept).tw.
17. practice guideline/
18. Critical Pathways/
19. Clinical Protocols/
20. (clinical pathway* or consensus or directive or directives or guideline* or protocol*).tw.
21. ((standard or standards) adj3 (care or practice*)).tw.
22. 17 or 18 or 19 or 20 or 21
23. limit 22 to yr="2003 -Current"
24. limit 23 to animals
25. limit 23 to (animals and humans)
26. 24 not 25
27. 23 not 26
28. limit 27 to english language
29. 8 or 12 or 15 or 16
30. 3 and 28 and 29

Appendix C: Search Strategy for Non-Pharmacological Interventions

MEDLINE (OVID)
Cochrane CENTRAL Register of Controlled Trials (OVID)

1. exp *Dementia/
2. (dementia* or alzheimer*).tw.
3. 1 or 2
4. limit 3 to (english language and yr="2010 -Current")
5. Art Therapy/
6. Therapeutic Touch/
7. Recreation Therapy/
8. exp Aromatherapy/
9. acoustic stimulation/ or music therapy/ or exp psychotherapy/ or exp physical therapy modalities/ or counseling/ or occupational therapy/
10. exp Reality Therapy/
11. (art therap* or rhythm therap* or touch therap* or recreational activit* or aromatherapy* or (recording* adj5 family) or music or sound or exercise* or nonpharmacologic* or non-pharmacologic* or physical activit* or reality orientation therap* or reminiscence therap* or validation therap* or cognitive stimulation therap* or sensory stimulation or snoezelen or psychotherapy* or physical therap* or psychotherapeutic counsel* or recreation* therap* or occupational therap*).tw.
12. 5 or 6 or 7 or 8 or 9 or 10 or 11
13. 4 and 12
14. Long-Term Care/
15. exp Residential Facilities/
16. (nursing home* or long term care or residential care or residential facilit* or assisted living or homes for the aged or old age home*).tw.
17. ltc facilit*.tw.
18. 14 or 15 or 16 or 17
19. 13 and 18
20. limit 19 to (case reports or editorial or letter)
21. 19 not 20

EMBASE (OVID)

1. exp *dementia/
2. (dementia or dementias or alzheimer*).tw.
3. 1 or 2
4. limit 3 to (english language and yr="2010 -Current")
5. alternative medicine/ or aromatherapy/
6. exp recreation/ or exp exercise/ or exp physical activity/
7. exp cognitive therapy/
8. exp sensory stimulation/
9. (art therap* or rhythm therap* or touch therap* or recreational activit* or aromatherapy* or (recording* adj5 family) or music or sound or exercise* or nonpharmacologic* or non-pharmacologic* or physical activit* or reality orientation therap* or reminiscence therap* or

validation therap* or cognitive stimulation therap* or sensory stimulation or snoezelen or psychotherapy* or physical therap* or psychotherapeutic counsel* or recreation* therap* or occupational therap*).tw.
10. exp psychotherapy/
11. exp physiotherapy/
12. counseling/
13. recreational therapy/
14. occupational therapy/
15. art therapy/ or cognitive rehabilitation/ or cognitive therapy/ or dance therapy/ or music therapy/ or narrative therapy/ or reality therapy/ or sociotherapy/ or validation therapy/
16. 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15
17. 4 and 16
18. long term care/
19. assisted living facility/ or nursing home/
20. residential care/
21. residential home/
22. home for the aged/
23. (nursing home* or long term care or residential care or residential facilit* or assisted living or homes for the aged or old age home*).tw.
24. ltc facilit*.tw.
25. 18 or 19 or 20 or 21 or 22 or 23 or 24
26. 17 and 25
27. limit 26 to (conference abstract or editorial or letter)
28. 26 not 27
29. case report/
30. 28 and 29
31. 28 not 30

PsycINFO (OVID)
1. exp *dementia/ or *alzheimer's disease/
2. (dementia or alzheimer*).tw.
3. 1 or 2
4. limit 3 to (english language and yr="2010 -Current")
5. exp Art Therapy/
6. Rhythm/
7. physical contact/
8. Social Interaction/ or Recreation/
9. Aromatherapy/
10. exp Music Therapy/
11. auditory stimulation/
12. Interpersonal Interaction/
13. exp Exercise/
14. exp Physical Activity/
15. reality therapy/

16. reminiscence/
17. psychotherapeutic techniques/ or animal assisted therapy/
18. verbal stimuli/
19. exp Cognitive Therapy/
20. exp Auditory Stimulation/ or exp Perceptual Stimulation/ or exp Visual Stimulation/
21. stimulation/
22. (art therap* or rhythm therap* or touch therap* or recreational activit* or aromatherapy* or (recording* adj5 family) or music or sound or exercise* or nonpharmacologic* or non-pharmacologic* or physical activit* or reality orientation therap* or reminiscence therap* or validation therap* or cognitive stimulation therap* or sensory stimulation or snoezelen or psychotherapy* or physical therap* or psychotherapeutic counsel* or recreation* therap* or occupational therap*).tw.
23. exp Psychotherapy/
24. exp Physical Therapy/
25. exp Psychotherapeutic Counseling/
26. exp Recreation Therapy/
27. exp Occupational Therapy/
28. 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27
29. 4 and 28
30. long term care/
31. exp Nursing Homes/
32. exp Assisted Living/
33. residential care institutions/ or group homes/
34. (nursing home* or long term care or residential care or residential facilit* or assisted living or homes for the aged or old age home*).tw.
35. ltc facilit*.tw.
36. 30 or 31 or 32 or 33 or 34 or 35
37. 29 and 36
38. limit 37 to (editorial or letter)
39. 37 not 38

Appendix D: Search Strategy for Antidepressants as a Substitute for Antipsychotics

MEDLINE (OVID)
Cochrane CENTRAL Register of Controlled Trials (OVID)

1. exp Dementia/
2. (dementia or dementias or alzheimer*).tw.
3. 1 or 2
4. Clozapine/
5. Risperidone/
6. (aripiprazole or abilify or asenapine or saphris or clozapine or clozaril or lurasidone or latuda or olanzapine or zyprexa or paliperidone or invega or quetiapine or seroquel or risperidone or risperidal or ziprasidone or zeldox).tw.
7. (atypical adj3 antipsychotic*).tw.
8. Haloperidol/
9. exp Loxapine/
10. (haloperidol or haldol or loxapine or loxapac or xylac).tw.
11. antipsychotic agents/ or chlorpromazine/ or flupenthixol/ or fluphenazine/ or methotrimeprazine/ or perazine/ or perphenazine/ or pimozide/ or thiothixene/ or trifluoperazine/
12. (antipsychotic or antipsychotics or chlorpromazine or largactil or fluphenazine or modecate or moditen or methotrimeprazine or nozinan or pericyazine or trilafon or pipotiazine or piportil or thioperazine or stelazine or flupentixol or fluanxol or thiothixene or navane or zuclopenthixol or clopixol or pimozide or orap).tw.
13. (amisulpride or solian or blonanserin or lonasen or carpipramine or prazinil or clocapramine or clofekton or clotiapine or entumine or iloperidone or fanapt or fanapta or zomaril or mosapramine or cremin or perospirone or lullan or remoxipride or roxiam or sertindole or serdolect or sulpiride or sulpirid or eglonyl or zotepine or nipolept).tw.
14. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
15. antidepressive agents/ or benactyzine/ or clorgyline/ or deanol/ or iproniazid/ or isocarboxazid/ or lithium carbonate/ or lithium compounds/ or moclobemide/ or nialamide/ or phenelzine/ or pizotyline/ or rolipram/ or sertraline/ or tranylcypromine/ or antidepressive agents, second-generation/ or 5-hydroxytryptophan/ or amoxapine/ or bupropion/ or citalopram/ or fluoxetine/ or fluvoxamine/ or maprotiline/ or mianserin/ or paroxetine/ or quipazine/ or ritanserin/ or sulpiride/ or trazodone/ or tryptophan/ or viloxazine/ or antidepressive agents, tricyclic/ or amitriptyline/ or clomipramine/ or desipramine/ or dothiepin/ or doxepin/ or imipramine/ or iprindole/ or lofepramine/ or nortriptyline/ or opipramol/ or protriptyline/ or trimipramine/
16. (antidepressive or antidepressant* or benactyzine or clorgyline or deanol or iproniazid or isocarboxazid or lithium or moclobemide or nialamide or phenelzine or pizotyline or rolipram or sertraline or tranylcypromine or 5-hydroxytryptophan or amoxapine or bupropion or citalopram or fluoxetine or fluvoxamine or maprotiline or mianserin or paroxetine or quipazine or ritanserin or sulpiride or trazodone or tryptophan or viloxazine or amitriptyline or clomipramine or desipramine or dothiepin or doxepin or imipramine or iprindole or lofepramine or nortriptyline or opipramol or protriptyline or thymoanaleptic* or thymoleptic* trimipramine).tw.
17. exp Serotonin Uptake Inhibitors/
18. exp Adrenergic Uptake Inhibitors/
19. exp Monoamine Oxidase Inhibitors/

20. (selective serotonin reuptake inhibitor* or SSRI* or serotonin-norepinephrine reuptake inhibitor* or SNRI* or SARI* or norepinephrine reuptake inhibitor* or NRI* or monoamine oxidase inhibitor* or MAOI*).tw.
21. (amitriptyine or bupropion or citalopram or clomipramine or desipramine or doxepin or duloxetine or escitalopram or fluoxetine or fluvoxamine or imipramine or maprotiline or mirtazapine or moclobemide or nortriptyline or paroxetine or phenelzine or sertraline or tranylcypromine or trazodone or trimipramine or venlafaxine).tw.
22. (lithium or citalopram or mirtazepine or trazodone or escitalopram or lexapro or cipralex or paroxetine or paxil or seroxat or fluoxetine or prozac or fluvoxamine or luvox or sertraline or zoloft or lustral or desvenlafaxine or pristiq or duloxetine or cymbalta or milnacipran or ixel or savella or venlafaxine or effexor or etoperidone or axiomin or etonin or lubazodone or YM-992 or YM-35,995 or nefazodone or serzone or nefadar or trazodone or desyrel or atomoxetine or strattera or reboxetine or edronax or viloxazine or vivalan or bupropion or wellbutrin or zyban or dexmethylphenidate or focalin or methylphenidate or ritalin or concerta or amphetamine or adderall or dextroamphetamine or dexedrine or dextromethamphetamine or desoxyn or lisdexamfetamine or vyvanse or amitriptyline or elavil or endep or butriptyline or evadene or clomipramine or anafranil or desipramine or norpramin or pertofrane or dosulepin or dothiepin or prothiaden or doxepin or adapin or sinequan or imipramine or tofranil or iprindole or prondol or lofepramine or feprapax or gamanil or lomont or melitracen or adaptol or nortriptyline or pamelor or opipramol or insidon or protriptyline or vivactil or trimipramine or surmontil or amoxapine or asendin or maprotiline or ludiomil or mianserin or bolvidon or norval or tolvon or mirtazapine or remeron or isocarboxazid or marplan or moclobemide or aurorix or manerix or phenelzine or nardil or pirlindole or pirazidol or selegiline or deprenyl or eldepryl or zelapar or emsam or tranylcypromine or parnate).tw.
23. 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24. 3 and 14 and 23
25. limit 24 to animals
26. limit 24 to (animals and humans)
27. 25 not 26
28. 24 not 27
29. limit 28 to yr="2005 -Current"
30. limit 29 to (english or french)

EMBASE (OVID)
1. exp *dementia/
2. (dementia or dementias).tw.
3. 1 or 2
4. atypical antipsychotic agent/ or aripiprazole/ or asenapine/ or clozapine/ or lurasidone/ or olanzapine/ or paliperidone/ or quetiapine/ or risperidone/ or ziprasidone/
5. (aripiprazole or abilify or asenapine or saphris or clozapine or clozaril or lurasidone or latuda or olanzapine or zyprexa or paliperidone or invega or quetiapine or seroquel or risperidone or risperidal or ziprasidone or zeldox).tw.

6. (atypical adj3 antipsychotic*).tw.
7. haloperidol/
8. loxapine/
9. (haloperidol or haldol or loxapine or loxapac or xylac).tw.
10. neuroleptic agent/ or chlorpromazine/ or flupentixol/ or flupentixol decanoate/ or fluphenazine/ or fluphenazine decanoate/ or periciazine/ or perphenazine/ or pimozide/ or pipotiazine/ or thioproperazine/ or thioproperazine methanesulfonate/ or trifluoperazine/ or trifluoperazine derivative/ or zuclopenthixol/
11. (antipsychotic or antipsychotics or chlorpromazine or largactil or fluphenazine or modecate or moditen or methotrimeprazine or nozinan or pericyazine or trilafon or pipotiazine or piportil or thioperazine or stelazine or flupentixol or fluanxol or thiothixene or navane or zuclopenthixol or clopixol or pimozide or orap).tw.
12. amisulpride/ or iloperidone/ or perospirone/ or remoxipride/ or sertindole/ or sulpiride/ or zotepine/
13. exp atypical antipsychotic agent/
14. (amisulpride or solian or blonanserin or lonasen or carpipramine or prazinil or clocapramine or clofekton or clotiapine or entumine or iloperidone or fanapt or fanapta or zomaril or mosapramine or cremin or perospirone or lullan or remoxipride or roxiam or sertindole or serdolect or sulpiride or sulpirid or eglonyl or zotepine or nipolept).tw.
15. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
16. exp antidepressant agent/
17. (antidepressive or antidepressant* or benactyzine or clorgyline or deanol or iproniazid or isocarboxazid or lithium or moclobemide or nialamide or phenelzine or pizotyline or rolipram or sertraline or tranylcypromine or 5-hydroxytryptophan or amoxapine or bupropion or citalopram or fluoxetine or fluvoxamine or maprotiline or mianserin or paroxetine or quipazine or ritanserin or sulpiride or trazodone or tryptophan or viloxazine or amitriptyline or clomipramine or desipramine or dothiepin or doxepin or imipramine or iprindole or lofepramine or nortriptyline or opipramol or protriptyline or thymoanaleptic* or thymoleptic* trimipramine).tw.
18. adrenergic receptor affecting agent/
19. (selective serotonin reuptake inhibitor* or SSRI* or serotonin-norepinephrine reuptake inhibitor* or SNRI* or SARI* or norepinephrine reuptake inhibitor* or NRI* or monoamine oxidase inhibitor* or MAOI*).tw.
20. (amitriptyine or bupropion or citalopram or clomipramine or desipramine or doxepin or duloxetine or escitalopram or fluoxetine or fluvoxamine or imipramine or maprotiline or mirtazapine or moclobemide or nortriptyline or paroxetine or phenelzine or sertraline or tranylcypromine or trazodone or trimipramine or venlafaxine).tw.
21. (lithium or citalopram or mirtazepine or trazodone or escitalopram or lexapro or cipralex or paroxetine or paxil or seroxat or fluoxetine or prozac or fluvoxamine or luvox or sertraline or zoloft or lustral or desvenlafaxine or pristiq or duloxetine or cymbalta or milnacipran or ixel or savella or venlafaxine or effexor or etoperidone or axiomin or etonin or lubazodone or YM-992 or YM-35,995 or nefazodone or serzone or nefadar or trazodone or desyrel or atomoxetine or strattera or reboxetine or edronax or viloxazine or vivalan or bupropion or wellbutrin or zyban or dexmethylphenidate or focalin or methylphenidate or ritalin or concerta or amphetamine or adderall or dextroamphetamine or dexedrine or dextromethamphetamine or desoxyn or lisdexamfetamine or vyvanse or amitriptyline or elavil or endep or butriptyline or evadene or

clomipramine or anafranil or desipramine or norpramin or pertofrane or dosulepin or dothiepin or prothiaden or doxepin or adapin or sinequan or imipramine or tofranil or iprindole or prondol or lofepramine or feprapax or gamanil or lomont or melitracen or adaptol or nortriptyline or pamelor or opipramol or insidon or protriptyline or vivactil or trimipramine or surmontil or amoxapine or asendin or maprotiline or ludiomil or mianserin or bolvidon or norval or tolvon or mirtazapine or remeron or isocarboxazid or marplan or moclobemide or aurorix or manerix or phenelzine or nardil or pirlindole or pirazidol or selegiline or deprenyl or eldepryl or zelapar or emsam or tranylcypromine or parnate).tw.
22. 16 or 17 or 18 or 19 or 20 or 21
23. 3 and 15 and 22
24. limit 23 to yr="2005 -Current"
25. limit 24 to animal studies
26. 24 not 25
27. limit 26 to (english or french)
28. limit 27 to exclude medline journals
29. limit 28 to (book or book series or editorial or letter or trade journal)
30. 28 not 29

PsycINFO (OVID)
1. exp dementia/
2. (dementia or dementias).tw.
3. 1 or 2
4. aripiprazole/ or clozapine/ or olanzapine/ or quetiapine/ or risperidone/
5. (aripiprazole or abilify or asenapine or saphris or clozapine or clozaril or lurasidone or latuda or olanzapine or zyprexa or paliperidone or invega or quetiapine or seroquel or risperidone or risperidal or ziprasidone or zeldox).tw.
6. (atypical adj3 antipsychotic*).tw.
7. haloperidol/
8. loxapine/
9. (haloperidol or haldol or loxapine or loxapac or xylac).tw.
10. neuroleptic drugs/
11. chlorpromazine/
12. Fluphenazine/
13. Perphenazine/
14. Trifluoperazine/
15. Thiothixene/
16. pimozide/
17. (antipsychotic or antipsychotics or chlorpromazine or largactil or fluphenazine or modecate or moditen or methotrimeprazine or nozinan or pericyazine or trilafon or pipotiazine or piportil or thioperazine or stelazine or flupentixol or fluanxol or thiothixene or navane or zuclopenthixol or clopixol or pimozide or orap).tw.

18. (amisulpride or solian or blonanserin or lonasen or carpipramine or prazinil or clocapramine or clofekton or clotiapine or entumine or iloperidone or fanapt or fanapta or zomaril or mosapramine or cremin or perospirone or lullan or remoxipride or roxiam or sertindole or serdolect or sulpiride or sulpirid or eglonyl or zotepine or nipolept).tw.
19. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20. exp antidepressant drugs/
21. exp monoamine oxidase inhibitors/
22. lithium/
23. (antidepressive or antidepressant* or benactyzine or clorgyline or deanol or iproniazid or isocarboxazid or lithium or moclobemide or nialamide or phenelzine or pizotyline or rolipram or sertraline or tranylcypromine or 5-hydroxytryptophan or amoxapine or bupropion or citalopram or fluoxetine or fluvoxamine or maprotiline or mianserin or paroxetine or quipazine or ritanserin or sulpiride or trazodone or tryptophan or viloxazine or amitriptyline or clomipramine or desipramine or dothiepin or doxepin or imipramine or iprindole or lofepramine or nortriptyline or opipramol or protriptyline or thymoanaleptic* or thymoleptic* trimipramine).tw.
24. exp serotonin reuptake inhibitors/
25. (selective serotonin reuptake inhibitor* or SSRI* or serotonin-norepinephrine reuptake inhibitor* or SNRI* or SARI* or norepinephrine reuptake inhibitor* or NRI* or monoamine oxidase inhibitor* or MAOI*).tw.
26. (amitriptyine or bupropion or citalopram or clomipramine or desipramine or doxepin or duloxetine or escitalopram or fluoxetine or fluvoxamine or imipramine or maprotiline or mirtazapine or moclobemide or nortriptyline or paroxetine or phenelzine or sertraline or tranylcypromine or trazodone or trimipramine or venlafaxine).tw.
27. (lithium or citalopram or mirtazepine or trazodone or escitalopram or lexapro or cipralex or paroxetine or paxil or seroxat or fluoxetine or prozac or fluvoxamine or luvox or sertraline or zoloft or lustral or desvenlafaxine or pristiq or duloxetine or cymbalta or milnacipran or ixel or savella or venlafaxine or effexor or etoperidone or axiomin or etonin or lubazodone or YM-992 or YM-35,995 or nefazodone or serzone or nefadar or trazodone or desyrel or atomoxetine or strattera or reboxetine or edronax or viloxazine or vivalan or bupropion or wellbutrin or zyban or dexmethylphenidate or focalin or methylphenidate or ritalin or concerta or amphetamine or adderall or dextroamphetamine or dexedrine or dextromethamphetamine or desoxyn or lisdexamfetamine or vyvanse or amitriptyline or elavil or endep or butriptyline or evadene or clomipramine or anafranil or desipramine or norpramin or pertofrane or dosulepin or dothiepin or prothiaden or doxepin or adapin or sinequan or imipramine or tofranil or iprindole or prondol or lofepramine or feprapax or gamanil or lomont or melitracen or adaptol or nortriptyline or pamelor or opipramol or insidon or protriptyline or vivactil or trimipramine or surmontil or amoxapine or asendin or maprotiline or ludiomil or mianserin or bolvidon or norval or tolvon or mirtazapine or remeron or isocarboxazid or marplan or moclobemide or aurorix or manerix or phenelzine or nardil or pirlindole or pirazidol or selegiline or deprenyl or eldepryl or zelapar or emsam or tranylcypromine or parnate).tw.
28. 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27
29. 3 and 19 and 28
30. limit 29 to animal
31. limit 29 to (animal and human)
32. 30 not 31

33. 29 not 32
34. limit 33 to yr="2005 -Current"
35. limit 33 to (english or french)

Cochrane Database of Systematic Reviews (OVID)
HTA Database (OVID)
NHSEED Database (OVID)
1. (dementia or dementias).tw.
2. (aripiprazole or abilify or asenapine or saphris or clozapine or clozaril or lurasidone or latuda or olanzapine or zyprexa or paliperidone or invega or quetiapine or seroquel or risperidone or risperidal or ziprasidone or zeldox).tw.
3. (atypical adj3 antipsychotic*).tw.
4. (haloperidol or haldol or loxapine or loxapac or xylac).tw.
5. (antipsychotic or antipsychotics or chlorpromazine or largactil or fluphenazine or modecate or moditen or methotrimeprazine or nozinan or pericyazine or trilafon or pipotiazine or piportil or thioperazine or stelazine or flupentixol or fluanxol or thiothixene or navane or zuclopenthixol or clopixol or pimozide or orap).tw.
6. (amisulpride or solian or blonanserin or lonasen or carpipramine or prazinil or clocapramine or clofekton or clotiapine or entumine or iloperidone or fanapt or fanapta or zomaril or mosapramine or cremin or perospirone or lullan or remoxipride or roxiam or sertindole or serdolect or sulpiride or sulpirid or eglonyl or zotepine or nipolept).tw.
7. 2 or 3 or 4 or 5 or 6
8. (antidepressive or antidepressant* or benactyzine or clorgyline or deanol or iproniazid or isocarboxazid or lithium or moclobemide or nialamide or phenelzine or pizotyline or rolipram or sertraline or tranylcypromine or 5-hydroxytryptophan or amoxapine or bupropion or citalopram or fluoxetine or fluvoxamine or maprotiline or mianserin or paroxetine or quipazine or ritanserin or sulpiride or trazodone or tryptophan or viloxazine or amitriptyline or clomipramine or desipramine or dothiepin or doxepin or imipramine or iprindole or lofepramine or nortriptyline or opipramol or protriptyline or thymoanaleptic* or thymoleptic* trimipramine).tw.
9. (selective serotonin reuptake inhibitor* or SSRI* or serotonin-norepinephrine reuptake inhibitor* or SNRI* or SARI* or norepinephrine reuptake inhibitor* or NRI* or monoamine oxidase inhibitor* or MAOI*).tw.
10. (amitriptyine or bupropion or citalopram or clomipramine or desipramine or doxepin or duloxetine or escitalopram or fluoxetine or fluvoxamine or imipramine or maprotiline or mirtazapine or moclobemide or nortriptyline or paroxetine or phenelzine or sertraline or tranylcypromine or trazodone or trimipramine or venlafaxine).tw.
11. (lithium or citalopram or mirtazepine or trazodone or escitalopram or lexapro or cipralex or paroxetine or paxil or seroxat or fluoxetine or prozac or fluvoxamine or luvox or sertraline or zoloft or lustral or desvenlafaxine or pristiq or duloxetine or cymbalta or milnacipran or ixel or savella or venlafaxine or effexor or etoperidone or axiomin or etonin or lubazodone or YM-992 or YM-35,995 or nefazodone or serzone or nefadar or trazodone or desyrel or atomoxetine or strattera or reboxetine or edronax or viloxazine or vivalan or bupropion or wellbutrin or zyban or dexmethylphenidate or focalin or methylphenidate or ritalin or concerta or amphetamine or

adderall or dextroamphetamine or dexedrine or dextromethamphetamine or desoxyn or lisdexamfetamine or vyvanse or amitriptyline or elavil or endep or butriptyline or evadene or clomipramine or anafranil or desipramine or norpramin or pertofrane or dosulepin or dothiepin or prothiaden or doxepin or adapin or sinequan or imipramine or tofranil or iprindole or prondol or lofepramine or feprapax or gamanil or lomont or melitracen or adaptol or nortriptyline or pamelor or opipramol or insidon or protriptyline or vivactil or trimipramine or surmontil or amoxapine or asendin or maprotiline or ludiomil or mianserin or bolvidon or norval or tolvon or mirtazapine or remeron or isocarboxazid or marplan or moclobemide or aurorix or manerix or phenelzine or nardil or pirlindole or pirazidol or selegiline or deprenyl or eldepryl or zelapar or emsam or tranylcypromine or parnate).tw.
12. 8 or 9 or 10 or 11
13. 2 and 7 and 12
14. limit 13 to yr="2005 -Current"

Appendix E: Search Strategy for CAM Interventions

MEDLINE (OVID)
Cochrane CENTRAL Register of Controlled Trials (OVID)
1. exp *Dementia/
2. dementia.ti.
3. 1 or 2
4. exp Medicine, East Asian Traditional/ or exp Herbal Medicine/ or exp Medicine, Chinese Traditional/ or exp Plants, Medicinal/
5.(herbal medicine* or chinese medicine* or herbals or traditional medicine* or medicinal herb* or medicinal plant*).tw.
6. 4 or 5
7. 3 and 6
8. limit 7 to (yr="2000 -Current" and (english or french))
9. limit 8 to animals
10. limit 8 to (animals and humans)
11. 9 not 10
12. 8 not 11

EMBASE (OVID)
1. exp *dementia/
2. exp *Alzheimer disease/
3. dementia.ti.
4. 1 or 2 or 3
5. alternative medicine/ or exp medicinal plant/
6. exp traditional medicine/
7. (herbal medicine* or chinese medicine* or herbals or traditional medicine* or medicinal herb* or medicinal plant*).tw.
8. 5 or 6 or 7
9. 4 and 8
10. limit 9 to ((english or french) and yr="2000 -Current")
11. limit 10 to animals
12. limit 10 to (human and animals)
13. 11 not 12
14. 10 not 13
15. limit 14 to (conference abstract or conference paper or conference proceeding or "conference review" or editorial or letter or note or short survey or trade journal)
16. 14 not 15
17. limit 16 to exclude medline journals

PsycINFO (OVID)
1. exp *Dementia/
2. exp *Alzheimer's Disease/
3. (dementia or alzheimer*).ti.

4. 1 or 2 or 3
5. exp Alternative Medicine/ or exp "Medicinal Herbs and Plants"/ or exp Dietary Supplements/
6. (herbal medicine* or chinese medicine* or herbals or traditional medicine* or medicinal herb* or medicinal plant*).tw.
7. 5 or 6
8. 4 and 7
9. limit 8 to ((english or french) and yr="2000 -Current")
10. limit 9 to animal
11. limit 9 to (animal and human)
12. 10 not 11
13. 9 not 12
14. limit 13 to (abstract collection or bibliography or chapter or "column/opinion" or "comment/reply" or editorial or encyclopedia entry or letter or poetry or review-book or review-media or review-software & other)
15. 13 not 14

AMED (OVID)
1. exp Dementia/ or exp Alzheimers disease/
2. (dementia or alzheimer*).ti.
3. 1 or 2
4. limit 3 to ((english or french) and yr="2000 -Current")
5. limit 4 to (annotated bibliography or bibliography or brief communication or brief report or clinical note or commentary or conference or congress or congress proceedings or editorial or equipment note or "equipment review" or interview or lecture or letter or monograph or news or notes or proceedings or study guide or symposium or technical note or thesis or thesis summary)
6. 4 not 5
7. exp Plants medicinal/ or exp Drugs chinese herbal/ or exp Herbal drugs/
8. (herbal medicine* or chinese medicine* or herbals or traditional medicine* or medicinal herb* or medicinal plant*).tw.
9. 7 or 8
10. 6 and 9
11. limit 6 to ("herbalism or herbal drugs" or "homeopathy or homeopathic drugs" or medicinal plants)
12. 10 or 11

CINAHL (EBSCO)
1. (dementia or alzheimer*)[Title]
2. MM Dementia+
3. 1 or 2
4. limit 3 to ((english or french) and yr="2000 -Current")
5. MH (Medicine, Herbal or Medicine, Chinese Traditional or Medicine, Oriental Traditional or Plants, Medicinal)
6. (herbal medicine* or chinese medicine* or herbals or traditional medicine* or medicinal herb* or medicinal plant*)[Title/Abstract]

7. 5 or 6
8. 4 and 7

AltHealth Watch (EBSCO)
1. (dementia or alzheimer*)[Title]
2. limit 1 to ((english or french) and yr="2000 -Current")
3. (herbal medicine* or chinese medicine* or herbals or traditional medicine* or medicinal herb* or medicinal plant*)[All Fields]
4. 2 and 3

Appendix F: Search Strategy for Built Environment

MEDLINE (OVID)
Cochrane CENTRAL Register of Controlled Trials (OVID)
1. exp Dementia/
2. exp Alzheimer Disease/
3. (dementia or alzheimer*).tw.
4. 1 or 2 or 3
5. built environment*.tw.
6. Environment Design/
7. "facility design and construction"/ or "hospital design and construction"/
8. health facility environment/
9. 5 or 6 or 7 or 8
10. 4 and 9
11. limit 10 to (yr="1995 -Current" and (english or french))
12. limit 11 to animals
13. limit 11 to (animals and humans)
14. 12 not 13
15. 11 not 14

EMBASE (OVID)
1. exp *dementia/
2. exp *Alzheimer disease/
3. (dementia or alzheimer*).tw.
4. 1 or 2 or 3
5. environment/
6. hospital design/
7. built environment*.tw.
8. built environment.mp.
9. (built environment or built environment assessment or built environmental change or built environmental pattern or built infrastructure).sh.
10. 5 or 6 or 7 or 8 or 9
11. 4 and 10
12. limit 11 to ((english or french) and yr="1995 -Current")
13. limit 12 to animals
14. limit 12 to (human and animals)
15. 13 not 14
16. 12 not 15
17. limit 16 to (book or book series or editorial or letter)
18. 16 not 17
19. limit 18 to conference abstract
20. 7 and 19
21. 18 not 19
22. 20 or 21

PsycINFO (OVID)

1. exp Dementia/
2. exp Alzheimer's Disease/
3. (dementia or alzheimer*).tw.
4. 1 or 2 or 3
5. therapeutic environment/ or exp facility environment/
6. exp Built Environment/
7. built environment*.tw.
8. 5 or 6 or 7
9. 4 and 8
10. exp Environmental Planning/
11. 4 and 10
12. 9 or 11
13. limit 12 to ((english or french) and yr="1995 -Current")

Cochrane Database of Systematic Reviews
HTA Database (OVID)
NHSEED (OVID)
1. (environment* or design* or facility planning).tw.
2. (dementia or alzheimer*).tw.
3. 1 and 2
4. limit 3 to ((english or french) and yr="1995 -Current")

Environment Complete (EBSCO)
Social Work Abstracts (EBSCO)
SocINDEX (EBSCO)
CINAHL (EBSCO)
Urban Studies (EBSCO)
1. (environment* or design* or facility planning)[All Fields]
2. (dementia or alzheimer*)[All Fields]
3. 1 and 2
4. limit 3 to ((english or french) and yr="1995 -Current")

Sociological abstracts (ProQuest)
Social Services Abstracts (ProQuest)
1. (environment* or design* or facility planning)[Anywhere]
2. (dementia or alzheimer*)[Anywhere]
3. 1 and 2
4. limit 3 to ((english or french) and yr="1995 -Current")

Appendix G: Search Strategy for Cost Effectiveness

MEDLINE (OVID)
Cochrane CENTRAL Register of Controlled Trials
1. exp *Dementia/
2. (dementia* or alzheimer*).tw.
3. 1 or 2
4. Long-Term Care/
5. exp Residential Facilities/
6. (nursing home* or long term care or residential care or residential facilit* or assisted living or homes for the aged or old age home*).tw.
7. ltc facilit*.tw.
8. exp Home Care Services/
9. 4 or 5 or 6 or 7 or 8
10. 3 and 9
11. exp "Costs and Cost Analysis"/
12. (economic* or cost or costs).tw.
13. 11 or 12
14. 10 and 13
15. limit 14 to yr="2012 -Current"
16. limit 15 to english language
17. limit 16 to (editorial or letter)
18. 16 not 17

PubMED
1. Dementia[MeSH]
2. (dementia* or alzheimer*)[tiab]
3. 1 or 2
4. Long-Term Care[MeSH]
5.Residential Facilities[MeSH]
6. (nursing home* or long term care or residential care or residential facilit* or assisted living or homes for the aged or old age home*)[tiab]
7. ltc facilit*[tiab]
8. Home Care Services[MeSH]
9. 4 or 5 or 6 or 7 or 8
10. 3 and 9
11. "Costs and Cost Analysis"[MeSH]
12. (economic* or cost or costs)[tiab]
13. 11 or 12
14. 10 and 13
15. limit 14 to yr="2013 -Current"
16. limit 15 to english language

EMBASE (OVID)
1. exp *dementia/

2. (dementia or dementias or alzheimer*).tw.
3. 1 or 2
4. long term care/
5. assisted living facility/ or nursing home/
6. residential care/
7. residential home/
8. home for the aged/
9. (nursing home* or long term care or residential care or residential facilit* or assisted living or homes for the aged or old age home*).tw.
10. ltc facilit*.tw.
11. exp home care/
12. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13. 3 and 12
14. exp economic evaluation/
15. exp economic aspect/
16. (economic or cost or costs).tw.
17. 14 or 15 or 16
18. 13 and 17
19. limit 18 to english language
20. limit 19 to (book or book series or conference abstract or editorial or letter)
21. 19 not 20
22. limit 21 to yr="2005 -Current"

PsycINFO (OVID)
1. exp *dementia/ or *alzheimer's disease/
2. (dementia or alzheimer*).tw.
3. 1 or 2
4. long term care/
5. exp Nursing Homes/
6. exp Assisted Living/
7. residential care institutions/ or group homes/
8. (nursing home* or long term care or residential care or residential facilit* or assisted living or homes for the aged or old age home*).tw.
9. ltc facilit*.tw.
10. exp Home Care/
11. 4 or 5 or 6 or 7 or 8 or 9 or 10
12. 3 and 11
13. "costs and cost analysis"/ or health care costs/
14. (economic* or cost or costs).tw.
15. 13 or 14
16. 12 and 15
17. limit 16 to english language

18. limit 17 to (abstract collection or bibliography or chapter or "column/opinion" or "comment/reply" or editorial or letter or review-book or review-media or review-software & other)
19. 17 not 18
20. limit 19 to yr="2005 -Current"

Cochrane Database of Systematic Reviews (OVID)
1. (dementia* or alzheimer*).tw.
2. (nursing home* or long term care or residential care or residential facilit* or assisted living or homes for the aged or old age home* or ltc facilit*).tw.
3. (economic* or cost or costs).tw.
4. 1 and 2 and 3
5. limit 4 to yr="2012 -Current"

NHSEED (OVID)
1. (dementia* or alzheimer*).tw.
2. (nursing home* or long term care or residential care or residential facilit* or assisted living or homes for the aged or old age home* or ltc facilit*).tw.
3. 1 and 2
4. limit 3 to yr="2012 -Current"

HTA Database (OVID)
1. (dementia or alzheimer*).ti.
2. (nursing home* or long term care or residential care or residential facilit* or assisted living or homes for the aged or old age home* or ltc facilit*).tw.
3. 1 and 2
4. limit 3 to english language
5. "2013".di. or "2012".di. or "2011".di.
6. 4 and 5

EconLit (EBSCO)
1. (dementia* or alzheimer*)[Title/Abstract]
2. (nursing home* or long term care or residential care or residential facilit* or assisted living or homes for the aged or old age home* or ltc facilit*)[Title/Abstract]
3. 1 and 2
4. limit 3 to yr="2012 -Current"

Appendix H: Risk of bias assessment for non-pharmacological interventions on BPSD

Author, Year	Sequence Generator	Allocation Concealment	Blinding	Incomplete Outcome Data	Selective Outcome Reporting	Other Bias
Comprehensive Assessment						
Rovner, 1996[24]	🟢	🟡	🟢	🟢	🟢	🟢
Brodaty, 2003[26]	🟢	🟡	🟢	🟢	🟢	🟢
Cohen-Mansfield, 2007[25]	🔴	🔴	🟡	🟢	🟢	🟢
Social Contact						
Mitchell 1996[27]	🟡	🟡	🟢	🟢	🔴	🟢
Toseland 1997[28]	🟡	🟡	🟢	🔴	🟢	🟢
McCallion 1999[29]	🟡	🟡	🟢	🟢	🟢	🟢
Beck 2002[30]	🟡	🟡	🟡	🟢	🟢	🟢
Opie 2002[36]	🟡	🟡	🟡	🟢	🟢	🟢
Politis 2004[31]	🟢	🟡	🟢	🟢	🟢	🟢
Lichtenberg 2005[32]	🟡	🔴	🟢	🟢	🟢	🟢
Deponte 2007[38]	🟡	🟡	🟡	🟢	🟢	🟢
Tappen 2009[33]	🟡	🟡	🟢	🟢	🟢	🟢
Wang 2009[39]	🟢	🟢	🟢	🟢	🟢	🟢
Cohen-Mansfield, 2012[34]	🟢	🟢	🟢	🟢	🟢	🟢
Kolanowski, 2011[35]	🟢	🟢	🟢	🟢	🟢	🟢
Low, 2012[37]	🟢	🟡	🟢	🟢	🟢	🟢
Spector, 2003[40]	🟡	🟡	🟢	🟢	🟢	🟢

Bakker, 2011[41]	🟡	🟡	🟡	🟢	🟢	🟢
Structured Activities						
Alessi 1999[42]	🟡	🟡	🟡	🟢	🟢	🟢
Hopman-Rock 1999[44]	🟡	🟡	🟡	🟢	🟢	🟢
Landi 2004[48]	🟡	🟡	🟡	🟡	🟡	🟢
Rolland 2007[46]	🟢	🟡	🟢	🟢	🟢	🟢
Williams 2007[43]	🟡	🟡	🟢	🟢	🟢	🟢
Dechamps, 2010[47]	🟡	🟢	🟡	🟢	🟢	🟢
Eggermont, 2010[45]	🟡	🟡	🟡	🟢	🟢	🟢
Sensory Enhancement/ Relaxation						
Sung 2006[58]	🟢	🟡	🟡	🟢	🟢	🟢
Svansdottir 2006[49]	🟡	🟡	🟢	🟡	🟢	🟢
Raglio 2008[50]	🔴	🔴	🟢	🟡	🟢	🟢
Janata, 2012[54]	🟢	🟡	🔴	🟢	🟢	🟢
Lin, 2010[59]	🟢	🟡	🟡	🟢	🟢	🟢
Sung, 2011[60]	🟢	🟡	🟡	🟢	🟢	🟢
Scherder 1998[61]	🟡	🟡	🟢	🟢	🟢	🟢
Ballard 2002[56]	🟢	🟡	🟢	🟢	🟢	🟢
Ancoli-Israel 2003[55]	🟡	🟡	🔴	🟡	🟢	🟢
Van Weert 2005[63]	🟢	🔴	🔴	🔴	🟢	🟡
Woods 2005[52]	🟢	🟡	🟢	🟢	🟢	🟢

Scherder 2006[62]	🟢	🟡	🟢	🟢	🟢	🟢
Hawranik 2008[53]	🟡	🟡	🟡	🟢	🟢	🟢
Sakamoto, 2012[51]	🟢	🟡	🟡	🟢	🟢	🟢
Burns 2009[57]	🟢	🟡	🟢	🟢	🟢	🟢

🟢=low risk of bias; 🔴 =high risk of bias; 🟡=unclear risk of bias

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Appendix I: Risk of bias assessment CAM intervention on BPSD

Author, Year	Sequence Generator	Allocation Concealment	Blinding	Incomplete Outcome Data	Selective Outcome Reporting	Other Bias
Iwasaki, 2005[89]	🟢	🟡	🔴	🟢	🟢	🟢
Lin, 2009[90]	🟡	🟡	🟢	🟢	🟢	🟢
Kudoh, 2009[91]	🟢	🟡	🔴	🟢	🟢	🟢

🟢=low risk of bias; 🔴 =high risk of bias; 🟡=unclear risk of bias

Appendix J: Downs and Black Quality Assessment for CAM intervention on BPSD

Author, Year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15	Q16	Q17	Q18	Q19	Q20	Q21	Q22	Q23	Q24	Q25
Yang, 2007[92]	1	1	1	1	0	1	1	0	1	1	1	1	1	0	0	0	1	1	1	1	0	0	0	0	1

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Appendix K: Downs and Black Quality Assessment for Built Environment

	Reimer[104]	Wilkes[103]	Cox[102]	Kincaid[96]	Edgerton[105]	Brush[94]	Hussian[95]	Namazi[97]	Namazi[98]	Namazi[99]	Namazi[100]	Namazi[101]
Q1	1	1	1	1	1	1	0	1	1	1	1	1
Q2	1	1	1	1	1	1	0	1	1	1	1	1
Q3	1	1	0	1	1	1	1	1	1	1	1	1
Q4	1	1	1	1	1	1	1	1	1	1	1	1
Q5	2	0	0	0	0	0	0	0	0	0	0	0
Q6	1	1	1	1	1	1	1	1	1	1	1	1
Q7	0	1	0	1	0	0	0	0	0	0	0	0
Q8	1	0	0	1	0	0	1	0	0	1	0	0
Q9	1	0	0	0	0	0	1	1	0	0	1	1
Q10	1	1	0	1	0	0	0	0	0	0	0	0
Q11	UTD	UTD	UTD	UTD	UTD	UTD	UTD	UTD	UTD	UTD	UTD	UTD
Q12	UTD	UTD	UTD	UTD	UTD	UTD	UTD	UTD	UTD	UTD	UTD	UTD
Q13	1	1	1	1	1	1	1	1	1	1	1	1

Q14	0	0	0	0	0	0	0	0	0	0	0	0
Q15	0	0	0	0	0	0	0	0	0	0	0	0
Q16	1	1	1	1	1	1	1	1	1	1	1	1
Q17	0	1	1	1	1	1	1	1	1	1	1	1
Q18	1	1	1	1	1	1	0	0	0	0	0	0
Q19	1	1	1	1	1	1	1	1	1	1	1	1
Q20	1	1	1	1	1	1	1	1	1	1	1	1
Q21	0	1	1	1	1	1	1	1	1	1	1	1
Q22	UTD	1	1	1	1	1	1	1	1	1	1	1
Q23	0	0	0	0	0	0	0	0	0	0	0	0
Q24	0	0	0	0	0	0	0	0	0	0	0	0
Q25	0	1	1	1	0	1	1	1	1	1	1	1
Q26	1	1	UTD	UTD	UTD	UTD	UTD	1	UTD	UTD	1	1
Q27	1	1	1	1	1	1	0	1	1	1	0	1
Total	17	18	14	18	14	15	13	16	14	15	15	16