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Quantitative Systematic Review of the effects of Non-pharmacological Interventions on  
Reducing Apathy in Persons with Dementia

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#### **Abstract**

**Aim.** To review the quantitative evidence concerning the effects of non-pharmacological interventions on reducing apathy in persons with dementia. **Background.** Apathy, a prevalent behavioral symptom among persons with Alzheimer Disease, is defined as a disorder of motivation with deficits in behavioral, emotional and cognitive domains and is associated with serious social and physical obstacles. Non-pharmacological interventions show promise as symptom control modalities among persons with dementia. **Design.** Quantitative systematic review. **Data sources.** CINAHL, PubMed, PSYCHinfo and Cochrane Trials databases were

searched for published English-language research inclusive through December 2014, with no early year limiters set. **Review methods.** Comprehensive searches yielded sixteen international randomized controlled trials or quasi-experimental studies based on inclusion criteria and a rigorous quality appraisal process. **Results.** A narrative summary analysis revealed that non-pharmacological interventions for apathy varied substantially and lacked specificity, conceptual clarity and were methodologically heterogeneous. Select interventions demonstrated effectiveness, but lacked systematic long-term follow-up. Limitations include publication bias and lack of a meta-analytic approach due to the methodological heterogeneity of included studies. **Conclusion.** Study results demonstrate promise for the use of non-pharmacological interventions, particularly music-based interventions, in reducing apathy levels in individuals with dementia. Intervening to reduce apathy may have a positive clinical impact and health care providers should be encouraged to incorporate positive sources of interest and intellectual stimulation into care. However, future research is needed to examine the etiologic mechanism and predictors of apathy, to improve evidence-based interventions and specificity and to optimize dosage and timing of non-pharmacological interventions across the disease trajectory. **Keywords:** Literature review, systematic review, dementia, Alzheimer's disease, gerontology, apathy, passivity, non-pharmacological, nursing

## SUMMARY STATEMENT

### **Why is this research or review needed?**

- Apathy in persons with dementia and systematic interventions to reduce the behavioral symptom among the population, are poorly understood.
- Non-pharmacological interventions for apathy among persons with dementia have shown promise as symptom control modalities, but have not been comprehensively and systematically reviewed to date.

### **What are the key findings?**

- The results of multiple, high-quality studies suggest that selected non-pharmacological interventions, particularly music-based interventions, are effective in reducing apathy among persons with Alzheimer Disease.
- Non-pharmacological interventions for reducing apathy among persons with dementia vary widely in participant selection, measurement of apathy, intervention delivery, approach, duration and dosage.
- Rigorous intervention studies, with the inclusion of adequate follow-up, focused on non-pharmacological interventions for reducing apathy in persons with dementia are lacking in the published literature.

### **How should the findings be used to influence policy/practice/research/education?**

- Health care providers should be encouraged to introduce positive sources of interest and intellectual stimulation to persons with dementia who are experiencing apathy.
- Future research is needed to examine the etiologic mechanism and predictors of apathy, as well as to optimize specificity, dosage and timing of non-pharmacological interventions across the disease trajectory.

## INTRODUCTION

Dementia is a widely used term encompassing various age-related neurodegenerative disorders characterized by the individuals' progressive loss of cognitive and functional ability. Alzheimer disease (AD) is a highly prevalent, age-related neurodegenerative disorder and subtype of dementia. AD currently affects 35.6 million persons worldwide and the prevalence is expected to rapidly rise (Prince *et al.* 2013). The World Health Organization estimates that 81.1 million people will be living with dementia by 2040, with the increased prevalence primarily attributed to the global aging population (Imtiaz *et al.* 2014). Furthermore, the projected increased prevalence will have a worldwide economic impact, as costs of care for individuals with dementia are expected to rise dramatically beyond the total 2010 worldwide costs of dementia estimated at \$604 billion US dollars (Wimo *et al.* 2013).

AD is initially characterized by subtle and often poorly recognized memory failure, but becomes increasingly severe, progressively destroying neurons in the cortex and limbic structures of the brain and impacting areas responsible for learning, memory, behavior, emotion and reasoning (Aderinwale *et al.* 2010, Bird 2010). There is currently no cure for this devastating disease (National Institute on Aging [NIA] 2015). Current dementia research has moved beyond identification of potential risk factors toward developing both pharmacological and non-pharmacological interventions to prevent or delay the onset of dementia and to manage associated behavioral symptoms (Imtiaz *et al.* 2014). Individuals with increasing care needs or disturbing behavioral symptoms such as sleeplessness, agitation, wandering, anxiety, apathy, anger, or depression (Lyketsos *et al.* 2002, Mega *et al.* 1996, NIA 2015) are often placed in facilities that provide a safe and supportive environment as they become increasingly dependent throughout the course of the disease (NIA 2015).

## Background

Apathy, a disorder of motivation with deficits in behavioral, emotional and cognitive domains, is a prevalent behavioral symptom among persons with AD, reportedly occurring with varying severity in over 90% of persons with AD across the disease trajectory (Benoit *et al.* 2008, Mega *et al.* 1996). Conservative estimates suggest apathy occurrence at closer to 30% (Lyketsos *et al.* 2002). Among a sample of individuals with AD, prevalence of apathy ranged from 53.0% (n=35) as measured by the Neuropsychiatric Inventory-Nursing Home version (NPI-NH) Apathy subscale to 71.4% (n=15) as measured by the Apathy Inventory (IA) in a subset of the 66 participants (Goris 2013). Additionally, the literature supports a distinction among apathy

and other neuropsychiatric symptoms experienced by individuals with dementia (Selbaek & Engedal 2012).

While common, apathy is an under-recognized neuropsychiatric behavior in persons with AD (Landes *et al.* 2001, Lerner *et al.* 2007, Mega *et al.* 1996, Monastero *et al.* 2006, Robert *et al.* 2010) and a significant predictor of accelerated emotional and cognitive decline (Starkstein *et al.* 2006). Apathy negatively impacts several functional health outcomes among individuals diagnosed with AD (Lam *et al.* 2008). Specific consequences of apathy for persons with dementia include physical deconditioning, failure of rehabilitation, decreased performance of activities of daily living, uncooperativeness with care, combativeness and social isolation (Politis *et al.* 2004). Apathy also presents caregiving challenges (Kaufer *et al.* 2000, Sanders *et al.* 2008), as persons with AD may be depressed, disengaged, or indifferent (Marin 1996, Strauss & Sperry 2002). Caregiver burden may lead family members to more quickly institutionalize persons with AD, creating increased global health care costs and use (Alzheimer's Association 2015, Bakker *et al.* 2013).

Emerging evidence supports apathy as a nursing-sensitive outcome and non-pharmacological interventions show promise as symptom control modalities among persons with AD (Brodaty & Burns 2011, Chung *et al.* 2002, Lerner *et al.* 2007, Politis *et al.* 2004, Verkaik *et al.* 2005, Wells & Dawson 2000, Wood *et al.* 2009). Non-pharmacological interventions for behavioral symptoms in dementia may also help improve caregiver reactions to negative neuropsychiatric symptoms (Brodaty & Arasaratnam 2012). These interventions often build upon retained capacities including selected self-care, social, interactional and interpretive abilities (Wells & Dawson 2000, Wood *et al.* 2009). However, persons with dementia often become dependent on others to fully express these retained capacities (Landes *et al.* 2001, Wood *et al.* 2009). Individually tailored non-pharmacological interventions may then effectively improve quality of life and reduce social isolation among persons with AD (Lerner *et al.* 2007).

While health care providers should be encouraged to introduce sources of pleasure and intellectual stimulation to persons with apathy (Ishii *et al.* 2009), a better understanding of the etiology, measurement and risk factors for apathy is needed to inform the development and tailoring of pertinent non-pharmacological interventions. Systematic reviews focusing on specific non-pharmacological interventions for apathy, such as *Snoezlen*-based care (Chung *et al.* 2002) or the effects of non-pharmacologic methods on depressed, aggressive and apathetic

behaviors of persons with dementia (Verkaik *et al.* 2005) have been published. A meta-analysis focused on non-pharmacologic interventions to reduce several neuropsychiatric symptoms in people with dementia, delivered specifically by family caregivers, is also available in the literature (Brodaty & Arasaratnam 2012). Brodaty and Burns (2011) performed a systematic review of 56 non-pharmacologic intervention studies related to the management of apathy in dementia. However, apathy was not a primary outcome of the majority of interventions (Brodaty & Burns 2011).

This review expands upon previous work to include current research and a focus on studies with apathy as a primary outcome, as well as to provide an examination of dementia classification of participants, apathy measurement tools and intervention dosage. A rigorous quality appraisal process was also used to minimize bias at the individual study level. An improved understanding of the strengths and limitations of the evidence underlying current non-pharmacological interventions to reduce apathy among persons with dementia has the opportunity to inform future research, with potential for a positive impact at the international level.

## THE REVIEW

### Aim

The purpose of this quantitative systematic review was to evaluate the evidence concerning the effects of non-pharmacological interventions on reducing apathy in persons with dementia. The following specific research questions were addressed: What non-pharmacological interventions exist to reduce apathy in persons with dementia? What non-pharmacological interventions are effective in reducing apathy in this population? How does apathy measurement vary in studies of the effects of non-pharmacological interventions on apathy in persons with dementia?

### Design

Review questions were pursued in the context of published methods for use in evaluating quantitative data. Criteria were developed for study inclusion and studies were selected after a comprehensive data search (O'Connor *et al.* 2011). Studies with both randomized and non-randomized control groups were included in the review (Effective Practice and Organisation of Care Group [EPOC], 2013). Data were analyzed for quality and minimization of bias (Effective Practice and Organisation of Care Group [EPOC], 2015) and findings were summarized in text

and tables (Schunemann *et al.* 2011). Data interpretation and the drawing of conclusions were guided by recommendations from the Cochrane Collaboration (Schunemann *et al.* 2011), with data reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher *et al.* 2009).

#### Search Methods

A thorough search of the CINAHL, Pubmed, PSYCHinfo and Cochrane Trials databases was conducted to identify original research published through December 2014, with no early year limiters set. To ensure a comprehensive search, the authors consulted with a masters-prepared, university-based librarian. Keyword and controlled vocabulary searching of Medical Subject Headings (MeSH) search strategies were used. Hand searches using reference lists were conducted to ensure an exhaustive representation of relevant studies but did not yield additional studies meeting inclusion criteria. Previously published systematic reviews on related content (Brodaty *et al.* 2011, Chung *et al.* 2002, Verkaik *et al.* 2005) were examined for additional references. In each case, the reference did not meet inclusion criteria or was already included as part of the review. Please see online supplemental files for additional information.

Studies were included in the review if: (1) the design was preferably a RCT, but minimally included a separate control or comparison group or a randomized cross-over design; (2) a non-pharmacological intervention was tested; (3) focus was on apathy or passivity in dementia; (4) the population was limited to older adults; and (5) publication occurred in a peer-reviewed, English-language journal. Thus, descriptive or qualitative investigations, studies with a lack of focus on apathy/passivity in dementia, studies without a separate control or comparison group and lack of cross-over design, pharmacological or medical intervention studies and those involving only caregivers or physicians were excluded. Additionally, studies focusing on neurological disorders other than AD or unspecified dementia (e. g. Huntington's disease, Parkinson's disease) were excluded.

#### Search Outcome

The electronic database search resulted in 1,677 publications of which 1,648 did not meet specified inclusion criteria (Figure 1). As advised by the masters-prepared, university-based librarian, 'non-pharmacological' and related terms were not used in the search. This strategy was time intensive, but produced more comprehensive results. First and second authors independently reviewed all 1,677 titles and abstracts. Any discrepancies regarding inclusion or



exclusion, as related to the established criteria, were discussed and resolved. The authors agreed that 29 abstracts met inclusion criteria and 1,648 did not.

All 29 articles meeting inclusion criteria were obtained and read in their entirety. After the same two authors independently screened these papers, they met and compared results. Eleven additional studies were then excluded for various reasons (Figure 1). Specifically, a single study lacked a control group, which was only evident after the article was read in its entirety (Schneider & Camp 2003). Three papers were excluded based on study design (Fitzsimmons & Buettner 2002, Moyle *et al.* 2013, Orsulic-Jeras *et al.* 2000) and single study was excluded due to the use of a medical intervention (Suemoto *et al.* 2014). A lack of focus on apathy or passivity in dementia warranted the exclusion of seven additional studies (Baker *et al.* 2003, Brownell 2008, Holmes *et al.* 2006, Jarrott & Gigliotti 2010, Judge *et al.* 2000, Sakamoto *et al.* 2013, Serrani 2012). After these considerations, 18 studies were identified as appropriate and were evaluated for quality.

#### Risk of Bias Assessment

This review includes evidence from studies having a control or comparison group, increasing the ability to detect differences due to the intervention by reducing error and strengthening internal and conclusion validity (Burns & Grove 2009). Studies were assessed for quality and risk of bias according to the criteria suggested by the Cochrane Effective Practice and Organisation of Care Group (EPOC) (2015). Authors evaluated 18 studies for inclusion by responding to the following specific criteria, as guided by EPOC: generation of allocation sequence, concealment of allocation sequence, similarity of baseline outcome measurements, similarity of baseline characteristics, whether incomplete outcome data were adequately addressed, whether knowledge of allocated interventions was adequately prevented during the study, adequate protection against contamination, freedom from selective outcome reporting and other risks of bias. Upon quality appraisal, authors chose to exclude two studies from the review. Work by Maci and colleagues (2012) did not meet quality appraisal and risk of bias assessment standards due to limited consideration of confounding factors and an insufficiently described intervention. Tondi and colleagues (2007) failed to offer a detailed description of the study intervention and there was incomplete reporting. Please see online supplemental files for a quality appraisal and risk of bias assessment table (Table 2).

#### Data Abstraction

Data from the 16 studies included in the review were abstracted and examined. A special emphasis was placed on measurement tools used to assess apathy among study participants, as the literature demonstrates a lack of consensus in measuring apathy among persons with dementia. Please see online supplemental files for a comprehensive data table (Table 3).

#### Synthesis

A rigorous narrative summarization process was undertaken to acquire a thorough understanding of each intervention to identify commonalities and unique characteristics among the studies. This approach, as opposed to a statistical approach or meta-analysis, was conducted due to significant heterogeneity of the included studies. Authors reviewed each study independently, followed by a comparison of individual assessments to assure consistency. This effort was important in determining existing non-pharmacological interventions to reduce apathy among persons with dementia, how intervention strategies are best employed and the degree to which these approaches are effective in apathy reduction among the vulnerable population of older adults with AD.

### RESULTS

Results yielded a strong international sampling of studies, including 12 RCTs (Ferrero-Arias *et al.* 2011, Hsieh *et al.* 2010, Kolanowski *et al.* 2005, Kolanowski *et al.* 2011, Lam *et al.* 2010, Leone *et al.* 2013, Moyle *et al.* 2013, Niu *et al.* 2010, Politis *et al.* 2004, Raglio *et al.* 2010, Raglio *et al.* 2008, Staal *et al.* 2007) and four quasi-experimental studies (Fischer-Terworth & Probst 2011, Hattori *et al.* 2011, Tappen & Williams 2009, van Weert *et al.* 2005). All 16 studies targeted the reduction of apathy in persons with dementia as a main outcome variable, but also examined other outcomes. Specifically, half of the included studies examined activities of daily living (Ferrero-Arias *et al.* 2011, Hattori *et al.* 2011, Lam *et al.* 2010, Leone *et al.* 2013, Politis 2004, Raglio *et al.* 2010, Raglio *et al.* 2008, Staal *et al.* 2007) and the majority focused on reducing behavioral symptoms, such as agitation and depression, in addition to apathy (Ferrero-Arias *et al.* 2011, Fischer-Terworth & Probst 2011, Hattori *et al.* 2011, Hsieh *et al.* 2010, Kolanowski *et al.* 2005, Kolanowski *et al.* 2011, Lam *et al.* 2010, Leone *et al.* 2013, Moyle *et al.* 2013, Niu *et al.* 2010, Raglio *et al.* 2010, Raglio *et al.* 2008, Staal *et al.* 2007, Tappen & Williams 2009, van Weert *et al.* 2005).

#### Intervention Approach

*Use of Theory or Model as a Framework.* Nearly half of the included intervention studies were theory-based (Kolanowski *et al.* 2005, Kolanowski *et al.* 2011, Lam *et al.* 2010, Raglio *et al.* 2010, Raglio *et al.* 2008, Staal *et al.* 2007, Tappen & Williams 2009, van Weert *et al.* 2005), although there were few commonalities in theories or models selected to provide a study framework. Kolanowski and colleagues (2005, 2011) used the Need-Driven Dementia-Compromised Behavior Model (Algase *et al.* 1996). Others theories providing a foundation for non-pharmacological interventions to reduce apathy among persons with dementia included Cognitive Behavioral Theory (Lam *et al.* 2010), Peplau's Theory of Interpersonal Relations (Tappen & Williams 2009) and discipline-specific philosophies such as Music Therapy Philosophy and Intersubjective Psychology (Raglio *et al.* 2010, Raglio *et al.* 2008). Van Weert and colleagues (2005) mentioned 'patient centeredness' as the underlying framework in their intervention study, while Staal and colleagues (2007) designed an intervention based on the theoretical framework of multi-sensory behavior therapy.

*Participant Selection based on Dementia Classification.* Studies included in this review varied widely in participant selection based on classification of dementia. Several studies enrolled participants using standard diagnostic criteria such as the tenth revision of the International Classification of Disease and Related Health Problems (ICD-10) diagnostic criteria (Fischer-Terworth & Probst 2011), the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) (van Weert *et al.* 2005), the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (Hsieh *et al.* 2010, Kolanowski *et al.* 2011, Lam *et al.* 2010, Moyle *et al.* 2013, Politis *et al.* 2004, Raglio *et al.* 2010, Raglio *et al.* 2008), or the National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and related Disorders Association (NINCDS/ADRDA) criteria (Niu *et al.* 2010, Tappen & Williams 2009). Other studies supplemented the use of standard diagnostic criteria with chart review of past medical history, current health status, or recent cognitive screening (Hsieh *et al.* 2010, Ferrero-Arias *et al.* 2011, Staal *et al.* 2007, Leone *et al.* 2013, Kolanowski *et al.* 2005). Hattori and colleagues (2011) included only participants exhibiting findings of AD on neuroimaging tests.

#### Quantitative Measurement of the Presence and Severity of Apathy

The methods by which the presence and/or severity of apathy were measured varied across the 16 studies and more than one measure of apathy was often used. The Neuropsychiatric

Inventory (NPI) was most commonly used among the studies included in this review (Ferrero-Arias *et al.* 2011, Fischer-Terworth & Probst 2011, Hsieh *et al.* 2010, Lam *et al.* 2010, Leone *et al.* 2013, Niu *et al.* 2010, Politis *et al.* 2004, Raglio *et al.* 2010, Raglio *et al.* 2008), though Leone and colleagues (2013) used a version of the NPI adapted for use in the nursing home (NPI-NH). Other English language measures of apathy included the Alzheimer's Disease and Related Disorders (ADRD) Mood Scale (Tappen & Williams 2009), the Apathy Evaluation Scale (AES) (Hsieh *et al.* 2010, Moyle *et al.* 2013), the Apathy Inventory – Clinician Version (AI-C) (Leone *et al.* 2013), the Assessment of Negative Symptoms in Alzheimer's Disease (SANS-AD) (Staal *et al.* 2007), the Dementia Apathy Interview and Rating (DAIR) scale (Ferrero-Arias *et al.* 2011), the Inventory to Assess Communication, Emotional Expression and Activity in Dementia (ICEA-D) (Fischer-Terworth & Probst 2011) and the Passivity in Dementia Scale (PDS) (Kolanowski *et al.* 2005, Kolanowski *et al.* 2011). Japanese (Hattori *et al.* 2011) and Dutch (van Weert *et al.* 2005) apathy measurement tools were also used.

Many included studies also used observational measures such as apathy ratings based on video recordings (Kolanowski *et al.* 2005, Kolanowski *et al.* 2011, Raglio *et al.* 2010, Raglio *et al.* 2008, Tappen & Williams 2009, van Weert *et al.* 2005). Kolanowski and colleagues (2005, 2011) video recorded each intervention session and recordings were reviewed to measure agitation, passivity and participant affect. In work by Raglio and colleagues (2008, 2010), music therapy sessions were videotaped and participants' behaviors were categorized using items from the Music Therapy Coding Scheme. Van Weert and colleagues (2005) obtained video recordings to make detailed observations regarding the effects of *Snoezelen*-based care, a form of multi-sensory stimulation (Chung *et al.* 2002, Pinkney 1997), on mood and behaviors.

#### Intervention Delivery and Dosage

*Intervention Delivery Setting.* While care settings for older adults vary internationally, the majority of reviewed studies were institution-based. Delivery settings included residential care or nursing home facilities (Ferrero-Arias *et al.* 2011, Hsieh *et al.* 2010, Kolanowski *et al.* 2005, Lam *et al.* 2010, Leone *et al.* 2013, Moyle *et al.* 2013, Politis *et al.* 2004, Raglio *et al.* 2010, Raglio *et al.* 2008, Tappen & Williams 2009), specialized dementia care units (Fischer-Terworth & Probst 2011, Kolanowski *et al.* 2011, van Weert *et al.* 2005), or adult day care (Ferrero-Arias *et al.* 2011, Hattori *et al.* 2011, Lam *et al.* 2010). Acute care intervention delivery settings such

as inpatient geriatric psychiatric units (Staal *et al.* 2007) or military sanatoriums (Niu *et al.* 2010) were also used.

*Intervention Focus.* The majority of interventions to decrease apathy among persons with dementia were delivered by specialized therapists (Ferrero-Arias *et al.* 2011, Lam *et al.* 2010, Niu *et al.* 2010, Moyle *et al.* 2013, Raglio *et al.* 2008, Raglio *et al.* 2010), trained students (Kolanowski *et al.* 2005, Tappen & Williams 2009) or research assistants (Hattori *et al.* 2011, Hsieh *et al.* 2010, Kolanowski *et al.* 2011, Staal *et al.* 2007, Tappen & Williams 2009). However the specific non-pharmacological interventions tested to reduce apathy among persons with dementia were heterogeneous in nature. Select studies used music therapies including music alone (Raglio *et al.* 2008), music therapy in addition to standard care (Raglio *et al.* 2010), or music therapy in combination with Treatment and Education of Autistic and related Communication Handicapped Children (TEACCH) based cognitive-behavioral and environmental interactions (Fischer-Terworth & Probst 2011). Ferrero-Arias and colleagues (2011) intervened using a combination music, art, psychomotor activity and mime intervention. Niu and colleagues (2010) used cognitive stimulation therapy, while Hattori and colleagues (2011) used art therapy as a form of intervention to reduce apathy. Multisensory stimulation techniques were also employed in an attempt to reduce apathy among persons with dementia in the form of Multi-sensory Behavior Therapy (Staal *et al.* 2007) or *Snoezelen*-based care (van Weert *et al.* 2005). Hsieh and colleagues (2010) implemented reminiscence group therapy (RGT), where participants were encouraged to discuss friendship, work and significant life experiences.

Other studies focused less on the type of intervention and more on tailoring interventions to each participant's skill level or interest (Kolanowski *et al.* 2005, Kolanowski *et al.* 2011, Lam *et al.* 2010, Politis *et al.* 2004) as a means to decrease apathy among persons with dementia. For example, the standard kit-based activities used by Politis and colleagues (2004) provided mental stimulation based on participants' interests in things like geography, foods, farm animals, or musical instruments. Tappen and Williams (2009) intervened with therapeutic conversation and participants interacted with companion robots (PARO) in work by Moyle and colleagues (2013). Finally, Leone and colleagues (2013) targeted some interventions toward staff members. Staff received training sessions which included teaching the 'do's' and 'dont's' of caring for persons

with apathy and techniques to engage individuals and promote autonomy in persons with apathy, depression and deficits in activities of daily living (Leone *et al.* 2013).

*Intervention Duration and Dosage.* The duration of the interventions conducted in each of the 16 studies varied widely from three weeks (Kolanowski *et al.* 2011) to 18 months (van Weert *et al.* 2005). Intervention dosage in minutes for each of the 16 studies was calculated by multiplying the length of the intervention interaction by the number of interactions. Intervention dosage varied immensely across studies, ranging from 180 minutes to 725,760 minutes, although the substantial intervention duration for the van Weert (2005) study was considered an outlier. The median intervention dosage for included studies was 900 minutes (Table 3).

#### Effectiveness of Interventions

Fourteen of the 16 studies included in the review noted a statistically significant reduction in apathy or passivity outcomes. A variety of interventions, specifically including music-based interventions targeting older adults with dementia, demonstrated effectiveness in reducing apathy (Raglio *et al.* 2010, Raglio *et al.* 2008). Regular one-on-one personal contact tailored to the individual's skill level or interest also led to improvements in apathy and other neuropsychiatric disturbances in people with dementia (Kolanowski *et al.* 2005, Kolanowski *et al.* 2011, Lam *et al.* 2010, Politis *et al.* 2004).

Additional interventions demonstrating significant reductions in apathy levels in persons with dementia included the use of cognitive stimulation therapy (Niu *et al.* 2010), multi-sensory behavior therapy (Staal *et al.* 2007), TEACCH-based behavioral and environmental interventions (Fischer-Terworth & Probst 2011), group art therapy (Hattori *et al.* 2011), the use of therapeutic conversation (Tappen & Williams 2009), reminiscence group therapy (Hsieh *et al.* 2010) or *Snoezelen*-based care (van Weert *et al.* 2005). A combination of music, art, psychomotor activity and mime also reduced apathy in a sample of persons with dementia based on apathy measurement using the DAIR scale (Ferrero-Arias *et al.* 2011). However, no significant difference was noted when evaluating apathy using the NPI-Q measure (Ferrero-Arias *et al.* 2011).

#### Sustainability of Intervention Effect

The majority of studies (n=12) did not continue with systematic post-intervention follow-up to assess the long-term effectiveness of interventions to reduce apathy among persons with dementia. Among the studies that continued to monitor outcome measures post-intervention,

follow-up was conducted at one week post-intervention (Kolanowski *et al.* 2011), four weeks post-intervention (Raglio *et al.* 2008), one month after the last wash-out period between music therapy cycles (Raglio *et al.* 2010), or more long-term (Lam *et al.* 2010). In work by Lam and colleagues (2010), 1-month and 4-month post-intervention follow-up was conducted following an eight-week individually tailored occupational therapy intervention.

Two studies including systematic long-term follow-up found that interventions effective in reducing apathy, initially, did not demonstrate sustained significant effects (Kolanowski *et al.* 2011, Lam *et al.* 2010). During the intervention phase, passivity decreased among participants assigned to the prescribed activity intervention groups with interventions individualized by functional level and ‘personality style of interest’ in work by Kolanowski and colleagues (2011). However, passivity levels returned to baseline one week after the conclusion of the intervention (Kolanowski *et al.* 2011). Lam and colleagues (2010) found that the intervention group had significantly reduced apathy levels one month post-intervention. However, apathy levels increased in participants four months post-intervention.

Two studies including systematic long-term follow-up demonstrated sustained effects on apathy (Raglio *et al.* 2008, Raglio *et al.* 2010). Raglio and colleagues (2008) demonstrated a significant reduction in apathy among intervention group participants involved in a four-week music therapy intervention. The intervention group in later work by Raglio and colleagues (2010) demonstrated significantly lower apathy scores with the implementation of music therapy, including educational and entertainment activities and sustained this significant reduction four weeks, post-intervention.

## DISCUSSION

The results of multiple, high-quality studies suggest that selected non-pharmacological interventions are effective in reducing apathy among persons with AD. Specifically, music therapy, tailored personal contact, cognitive stimulation therapy, multi-sensory behavior therapy (including *Snoezelen*), group art therapy and therapeutic conversation show promise for reducing apathy without producing negative side effects. Overall, these interventions are heterogeneous in many ways, including their method of engaging a person with dementia, the apparent target of their therapeutic effect (behavioral, emotional, or cognitive domains of apathy) and the extent to which interventions were tailored to a specific individual. The interventions also share characteristics. For example, all interventions were delivered by trained health care providers.

And, importantly, the interventions were all complex in nature, meaning that they consisted of many interconnecting parts, which may contribute to challenges in generating reproducible and sustained effects (Campbell *et al.* 2000).

Based upon this review, the type of non-pharmacologic intervention with the strongest evidence for reducing apathy in persons with dementia is music therapy. In particular, four studies evaluating music therapy, alone or in combination with other components, produced a statistically significant reduction in apathy with small to large effect sizes in institutionalized persons with dementia (Ferrero-Arias *et al.* 2011, Fischer-Terworth & Probst 2011, Raglio *et al.* 2008, Raglio *et al.* 2010). In two of these studies (Raglio *et al.* 2008, Raglio *et al.* 2010), reductions were sustained up to four weeks post-intervention. While the interventions were not identical, the common element among them was the delivery of music, with most studies delivering at least 30-minute interventions for at least 10 sessions. The mechanism of action of music therapy in the reduction of apathy is not evident from a review of these studies and remains an important area of inquiry.

While apathy is considered a behavioral symptom distinct from other neuropsychiatric symptoms (Selbaek & Engedal 2012), characteristics of studies included in this review suggest a lack of focus on apathy as the specific intervention target. Each of the 16 studies examined apathy as a primary outcome variable but also included other behavioral symptom outcomes. In many cases, the intervention had a positive effect on more than one behavioral symptom (Fischer-Terworth & Probst 2011, Hsieh *et al.* 2010, Kolanowski *et al.* 2005, Kolanowski *et al.* 2011, Lam *et al.* 2010, Niu *et al.* 2010, Raglio *et al.* 2010, Raglio *et al.* 2008, Staal *et al.* 2007, Tappen & Williams 2009, van Weert *et al.* 2005). These observations may reflect overlapping etiologies across behavioral symptoms in dementia. Alternatively, the observations may reflect an incomplete understanding of the etiologies of specific behavioral symptoms in persons with dementia such that there is insufficient rationale for the development and/or selection of any particular complex intervention. Further research is needed to identify the personal and environmental factors that influence the occurrence and characteristics of behavioral symptoms such as apathy to develop and test interventions that target the underlying etiology.

The lack of focus on apathy as a specific intervention target may also suggest a lack of conceptual clarity around the phenomena of apathy in persons with dementia. First, not all studies identified a guiding conceptual framework and no single conceptual framework was used



by more than one research team. Second, there was little consensus for measurement of the presence and/or severity of apathy. Twelve different questionnaires, as well as various observational measures of apathy based on video recordings, were used. The NPI, which provided the main measure of apathy among studies included in this review, has been credited with excellent reliability and validity (Cummings *et al.* 1994, Kaufer *et al.* 2000). Several studies used more than one measure of apathy. These observations point to the complexity of this behavioral symptom and the need for additional effort to clarify the components that define apathy and that distinguish apathy from other behavioral symptoms. Conceptual and operational clarity will further facilitate meta-analyses and the comparative effectiveness of non-pharmacological interventions for reducing apathy in persons with dementia.

In addition to variability in the measurement of apathy, the studies included in this review exhibited considerable methodological heterogeneity in other areas. For example, participant selection strategies varied. All studies included, at a minimum, the use of at least one standard diagnostic criteria for dementia. Notably, the intervention delivery approach and duration differed substantially across studies, yielding wide variability in dosage and duration of effect. While the majority of studies demonstrated a significant reduction in apathy or passivity outcomes in the short-term, intervention effects were not sustained in all but two interventions. Significant dosage variability and a lack of long-term follow-up make drawing global conclusions about the sustainability of non-pharmacological apathy reduction interventions especially challenging.

This quantitative systematic review adds to the knowledge base concerning interventions for apathy by extending the timeframe for the inclusion of studies beyond those included in prior reviews and focusing on intervention studies with apathy as a primary outcome. Additionally, this review offers further examination of methodological detail, specifically including dementia classification of participants, apathy measurement tools and intervention dosage. Another strength of the review is the minimization of risk of bias at the individual study level through a rigorous quality appraisal process. Limitations, however, are acknowledged. First, while a comprehensive search strategy was conducted for published research, efforts were not made to locate unpublished work. Second, the methodological heterogeneity of the included studies prohibited the use of a meta-analytic approach to the review, which would allow a more quantitative estimate of the overall and relative effectiveness of the different interventions. While

all included studies are relatively recent and relevant to contemporary practice, the authors may have benefitted from specifying a less open timeframe for the literature search. Finally, the use of additional search terms and limits, specifically for the PubMed database, may have reduced the initial yield of unrelated studies.

## CONCLUSION

Findings from this quantitative systematic review hold several important implications for policy, practice, research and education. At the level of institutional policy and clinical practice, a continued need exists to support the appropriate assessment of the presence and severity of apathy among persons with dementia

to identify persons in need of intervention. While this review provides some evidence to support the use of several non-pharmacologic interventions to reduce apathy, multiple high-quality studies point to a role for music therapy for the purpose of apathy reduction in institutionalized persons with dementia. Findings suggest a need for appropriately trained staff to then support the implementation and evaluation of music therapy in this population.

In addition, the results of this review suggest numerous avenues for future research. Most urgent is the need to better understand the etiologic mechanisms and predictors of apathy based upon a refined conceptual definition of the phenomena, which may lead to stronger measurement tools that fully capture the phenomena of apathy and are sensitive to change over time. This work could also provide a basis for more sensitive and specific interventions by targeting non-pharmacologic interventions to the underlying etiologic mechanism. Additional research is needed to optimize the dosage and timing of interventions, particularly to determine if these interventions are specific to any particular stage of the dementia trajectory. Systematic long-term follow-up is also imperative to learn whether long-term reduction in apathy is possible among individuals with dementia and to examine the clinical impact this reduction may have. Trials to compare the effectiveness of non-pharmacological interventions to reduce apathy will also be an important area of inquiry to determine the relative clinical utility and cost-effectiveness of these interventions. Finally, the extension of apathy intervention research to persons with dementia living at home is needed.

The results of this review can also be integrated into curricula for nurses across educational programs to help ensure the delivery of evidence-based care of older adults with dementia. Intervening to reduce behavioral symptoms in persons with dementia, even in the later

stages of the disease, is an important nursing function. To that end, communicating the importance of assessing for behavioral symptoms, such as apathy, in persons with dementia is critical. In addition, communicating the potential utility of non-pharmacological interventions for apathy reduction among persons with dementia is essential, given the potentially serious side effects of pharmacological interventions.

Nurses play a critical role in the care of persons with dementia, whether in home or institutional settings. Nurses are in key positions in institutional settings, in particular, to facilitate the introduction of positive sources of interest and intellectual stimulation to persons with dementia who are experiencing apathy. While this quantitative systematic review demonstrates that several non-pharmacological interventions are effective in reducing apathy among institutionalized persons with dementia, additional research is needed to further refine and optimize intervention delivery to achieve stronger and more sustained results.

#### **Author Contributions:**

All authors have agreed on the final version and meet at least one of the following criteria (recommended by the ICMJE\*):

- 1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data;
- 2) drafting the article or revising it critically for important intellectual content.

\* <http://www.icmje.org/recommendations/>

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# Author Manuscript

**Table 1.** Summary of Included Studies (N=16)

<b>Author (Yr)</b>	<b>Setting</b>	<b>Intervention</b>	<b>Key Relevant Findings</b>
Ferrero-Arias et al. (2011)	Institution-based, including adult day care	Combination music, art, psychomotor activity and mime intervention	Significant difference in apathy, as measured using DAIR scale, between intervention and control periods (95% CI: 0.07 - 0.34, Z = -2.844, p= 0.004). No significant difference in apathy, as measured using the NPI-Q Apathy subscale, between intervention and control periods (Z= -1.840, p= 0.07).
Fischer-Terworth & Probst (2011)	Institution-based, dementia-specific and traditional care units	Structured teaching using Treatment and Education of Autistic and related Communication handicapped Children (TEACCH)-based behavioral and environmental interventions adapted for dementia plus music therapy	Significant decrease in apathy, as measured by the NPI – Apathy subscale, in the IG (F= 9.41, p< .01), despite a marked increase in apathy in the CG.
Hattori et al. (2011)	Institution-based, outpatient geriatric clinic	Small group art therapy accompanied by a family member	IG showed significant improvement in Apathy Scale scores (p= 0.0014). Pre-intervention Mean (SD)= 15.9 (7.1) Post-intervention Mean (SD)=12.7 (6.1)

Author (Yr)	Setting	Intervention	Key Relevant Findings
Hsieh et al. (2010)	Institution-based, nursing home	Participants were encouraged to share life experiences on topics such as friendship, work experience, and significant events, and were encouraged to bring meaningful items to sessions.	Significant improvement in the behavioral ( $Z = -3.10$ , $p = 0.002$ ) and cognitive ( $Z = -1.95$ , $p = 0.050$ ) domains of apathy, as measured by the AES-C, in the IG. Non-significant change in the emotional domain of apathy in the IG ( $Z = -0.69$ , $p = 0.490$ ). No significant improvement was noted as measured by NPI-Apathy subscale for the IG ( $Z = -1.74$ , $p = 0.082$ ).
Kolanowski et al. (2005)	Institution-based, traditional care unit	Prescribed activities matched to skill level only (treatment A), style of interest only (treatment B), and skill level and style of interest (treatment C)	Treatments A, B, and C significantly reduced passivity compared with baseline, ( $p = 0.026$ , $p = 0.002$ , and $p < 0.001$ , respectively) with the exception of the emotions subscale, where treatment A did not differ from baseline. Treatment comparisons indicated that for each subscale, treatment C resulted in significantly less passivity compared with treatment A ( $p = 0.033$ ), but not treatment B ( $p = 0.220$ ), and treatments A and B did not differ ( $p = 0.833$ ).

Author (Yr)	Setting	Intervention	Key Relevant Findings
Kolanowski et al. (2011)	Institution-based, dementia-specific care unit	Prescribed activities adjusted to functional level but opposite “personality style of interest” (FL Treatment), activities adjusted to “personality style of interest” and deliberately functionally challenging (PSI Treatment), activities adjusted for both functional level and “personality style of interest” (FL+PSI Treatment)	Participants randomized to PSI or FL+PSI activities demonstrated greater engagement, more alertness, and more attention than participants randomized to FL or CG activities (LSM= 18.42, 95% CI: 15.8 - 21.1 vs. LSM= 16.29, 95% CI: 12.9 - 19.6, p= 0.02). Passivity, specifically, did not differ according to IG, but was notably improved over baseline. One week post- intervention, significantly greater passivity was noted in the FL group (LSM = 11.82, 95% CI = 8.4-15.2 vs LSM = 16.68, 95% CI = 13.4-19.9, P<0.001).
Lam et al. (2010)	Institution-based, including adult day care and traditional care unit	Tailored functional and skills training group sessions with problem solving	Significant decrease in apathy prevalence, as measured by the NPI – Apathy subscale, at 1-month post-intervention in IG (Mean (SD)= 0.42 (0.94), p= 0.04). A decrease in apathy prevalence, as measured by the NPI- Apathy subscale, was not significant in the CG ((Mean (SD)= 0.55 (1.23), p= 0.06). From 1 to 4 months post-intervention, there was a rebound of apathy (paired t-test= 2.7, p= 0.01) in the IG.

Author (Yr)	Setting	Intervention	Key Relevant Findings
Leone et al. (2013)	Institution-based, traditional care unit	Staff instruction with “do’s” and “don’ts” of caring for patients with apathy or depression and recommended various broad non-pharmacological interventions	Emotional blunting, as measured by AI-C, significantly decreased between baseline and week 4 (difference of means (SD)= 0.32 (1.1), $p < 0.01$ ) and between baseline and week 17 (difference of means (SD)= -0.34 (1.16), $p < 0.01$ ) in the IG. Emotional blunting, as measured using the Group Observational Scale, significantly decreased between baseline and week 17 (difference of means (SD)= 1.01 (4.56), $p < 0.01$ ) in the IG. No significant decrease in apathy, as measured by NPI-NH, between IG and CG.
Moyle et al. (2013)	Institution-based, traditional care unit	Interaction with PARO, a therapeutic, robotic, companion seal. Activities encouraged discussion and interaction with PARO	No significant change in pre-intervention and post-intervention scores in apathy as measured by the AES.
Niu et al. (2010)	Institution-based, military sanatorium	Individual cognitive stimulation therapy (CST) sessions	Significant decrease in apathy, as measured by the NPI-Apathy subscale, in the IG ( $Z = -2.594$ , $p = 0.017$ ).
Politis et al. (2004)	Institution-based, dementia-specific care	Kit-based activities designed to provide mental stimulation based on participants’ interests	Significant decrease in apathy, as measured by the NPI, in both IG ( $Z = -1.919$ , $p = 0.055$ ) and CG ( $Z = -2.676$ , $p = 0.007$ ). Despite significant improvement

Author (Yr)	Setting	Intervention	Key Relevant Findings
	unit		in apathy scores, no clear advantage to IG over the CG experiencing one-on-one time and attention control.
Raglio et al. (2008)	Institution-based, traditional care unit	Music therapy sessions using rhythmical and melodic instruments	Apathy, as measured by the NPI – Apathy subscale, significantly decreased in the IG (Test di Friedmann (X <sup>2</sup> )= 8.10, p<0.05).
Raglio et al. (2010)	Institution-based, traditional care unit	Music therapy sessions in groups of 3 participants plus standard care (educational and entertainment activities)	Apathy, as measured by the NPI, - Apathy subscale, significantly decreased in the IG (MANOVA= 5.17, p< 0.01).
Staal et al. (2007)	Institution-based, inpatient geriatric psychiatric unit	Multi-sensory Behavior Therapy (MSBT) sessions and standard psychiatric inpatient care (pharmacological therapy, occupational therapy, structured hospital environment)	Significant decrease in apathy, as measured by SANS-AD, in IG (F(1,20)= 4.47, p= 0.04). Repeated measure analysis revealed that only the IG demonstrated improvements in apathy from baseline to session six (F(6,120)= 3.15, p= 0.01). Multiple regression analysis predicted that within the IG, activities of daily living (KI-ADL) increased as apathy and agitation decreased (R <sup>2</sup> = 0.42, p= 0.03).
Tappen & Williams (2009)	Institution-based, traditional care unit	Individual therapeutic conversation sessions	Significant decrease in apathy, as measured by the Apathetic subscale of the AD-RD Mood Scale, in IG (F= 4.21, p= 0.05), with no significant change in CG.



<b>Author (Yr)</b>	<b>Setting</b>	<b>Intervention</b>	<b>Key Relevant Findings</b>
van Weert et al. (2005)	Institution-based, dementia-specific inpatient geriatric psychiatric units	Individual 24-hour Snoezelen-based care program informed by family history and stimulus preference screening	Significant treatment effect with respect to apathetic behavior, as measured by the BIP, in IG ( $X^2= 5.16$ , $df=1$ , $p< 0.05$ ).

CI= Confidence Interval (included when reported), CG= Control Group, IG = Intervention Group, LSM= Least Squares Mean, RCT = Randomized Controlled Trial

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**Figure 1.** Flow Diagram of the Study Selection Process