

SOCIAL ISOLATION AND ANXIETY IN INDIVIDUALS WITH COGNITIVE  
IMPAIRMENT: SECONDARY ANALYSIS OF A NATIONALLY REPRESENTATIVE  
SAMPLE OF COMMUNITY RESIDING OLDER ADULTS

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To all people who believed in me

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## ABSTRACT

### SOCIAL ISOLATION AND ANXIETY IN INDIVIDUALS WITH COGNITIVE IMPAIRMENT: SECONDARY ANALYSIS OF A NATIONALLY REPRESENTATIVE SAMPLE OF COMMUNITY RESIDING OLDER ADULTS

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Anxiety is a common and distressing neuropsychiatric symptom in people with cognitive impairment (CI) such as mild cognitive impairment (MCI) or dementia, and up to 71% of individuals with CI experience anxiety. Anxiety in persons with CI is one of the most burdensome symptoms that family caregivers report. Although persons with CI are at risk of social isolation, there is limited information on social isolation among people who have already developed CI and how it contributes to their anxiety. Therefore, this dissertation focused on factors associated with anxiety, especially focusing on how social factors contributes to anxiety in persons with CI. In paper 1, we conducted an integrative review in order to examine factors related to anxiety in persons with CI. The integrative review was conducted using seven databases. Factors associated with anxiety in persons with CI included physical functioning, embarrassment about memory problems, social rejection, and social isolation. For Paper 2 and paper 3, secondary data analyses were conducted using the National Social Life, Health, and Aging Project (NSHAP) Wave 2 (2010-2011) and Wave 3 (2015-2016) datasets. Paper 2 aimed to determine whether social isolation is associated with anxiety in people with CI (n=1,343). We found that greater social isolation increased anxiety in people with CI. Paper 3 aimed (1) to compare social isolation and anxiety among people who develop CI and those who do not over a five-year period and (2) to determine whether CI moderates the relationship between changes in social isolation and changes in anxiety (n=1,119). The two groups who developed MCI and dementia tended to have increased social isolation compared to people who maintained intact

cognition. Feeling of increased social isolation over five years was related to increased anxiety over five years regardless of cognitive groups. As older adults still have social needs even when their cognition is impaired, healthcare professionals need to evaluate one's social needs when they make clinical assessments. It is also imperative to educate family members of persons with CI on the importance of meeting the social needs of their loved ones.

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## CHAPTER 1: INTRODUCTION TO THE DISSERTATION

Anxiety is a common and distressing neuropsychiatric symptom in people with cognitive impairment (CI) such as mild cognitive impairment (MCI) or dementia,<sup>1,2</sup> and it is reported that up to 71% experience anxiety.<sup>3</sup> For the purpose of this dissertation, anxiety refers to both the presence of symptoms of anxiety disorder (e.g., excessive worry, restlessness, irritability, or muscle tension) and/or the formal diagnosis of anxiety related disorder. Theoretically, there are two types of anxiety: state anxiety (how one feels at the moment) and trait anxiety (how one generally feels over a long period of time).<sup>4</sup> In this dissertation, anxiety is defined as trait anxiety. Anxiety in people with CI is a major contributor to caregiver distress<sup>5</sup> and caregiver burden.<sup>6</sup> Consequently, anxiety increases the risk of institutionalization.<sup>7</sup> Anxiety is also a strong predictor of poor quality of life in people with CI.<sup>6,8</sup>

Despite its high prevalence, little is known about factors associated with anxiety. In order for caregivers and clinicians to prevent or minimize anxiety, it is essential to examine underlying factors associated with anxiety in people with CI. Specifically, while previous studies on anxiety in CI have identified various physical or psychological factors associated with anxiety, such as poor physical health,<sup>9</sup> pain,<sup>10</sup> and depression,<sup>10,11</sup> much less is known about how social factors, such as social isolation, are associated with anxiety in this population.<sup>12</sup> In people without CI, social isolation leads to numerous negative physical, psychological, and behavioral outcomes, including anxiety.<sup>13,14</sup> What remains unknown is if social isolation among people with CI leads to poor psychological outcomes such as anxiety.<sup>12</sup> As fulfillment of social needs is an important part of successful aging,<sup>15,16</sup> exploring social needs of older adults with CI is essential.

People with CI are at risk of social isolation due to their impaired cognition. Individuals with CI lose their ability to maintain social roles and their social circles become smaller.<sup>17,18</sup> Indeed,

when people are diagnosed with dementia, they experience less frequent contact with family and friends because of their CI and feelings of stigma.<sup>19,20</sup> Social isolation is a well-known risk factor for the development of CI.<sup>21-24</sup> Yet, there is limited information on social isolation among people who have already developed CI and the associated outcomes, despite the fact that persons with CI are at risk for social isolation.<sup>19,20,25</sup> Moreover, it is unknown whether social isolation among people with CI is more severe compared to people with normal cognition. Therefore, the overall purpose of this three-paper dissertation is to examine factors associated with anxiety in people with CI, especially how social isolation is related to anxiety in persons with CI.

## **BACKGROUND AND SIGNIFICANCE**

### **Characteristics of people with cognitive impairment (CI)**

In this dissertation, people with cognitive impairment (CI) is used to refer to both people with mild cognitive impairment (MCI) and those with dementia. MCI is defined as symptomatic predementia stage with symptoms of impaired cognition beyond normal aging.<sup>26</sup> Dementia is defined as a chronic, progressive loss of multiple cognitive abilities leading to many functional disabilities.<sup>27</sup> Dementia is considered to be a disease continuum from asymptomatic preclinical stage, to symptomatic predementia stage, called MCI, with symptoms of impaired cognition beyond normal aging, and finally a diagnose with a type of dementia.<sup>26,28-30</sup> The number of people living with dementia is increasing worldwide and this number is expected to triple by 2050.<sup>31</sup> The most common cause of dementia is Alzheimer's disease followed by vascular dementia, Lewy body dementia, and frontotemporal dementia.<sup>32</sup> Since symptoms of cognitive impairment occur in both people with dementia and MCI, both diagnostic groups have a high risk of being socially isolated.<sup>19,20,25</sup> In addition, considering that up to 39% percent of people with MCI eventually develop dementia,<sup>33</sup> it is important to understand how cognitive changes influence perception of

social isolation and how their experience evolves as their CI worsens. Therefore, in this dissertation study, both individuals who have probable MCI or dementia measured by a screening tool, Montreal Cognitive Assessment (MoCA), were included.

One of the common characteristics of people with CI includes behavioral and psychological symptoms (BPSDs). As cognitive impairment worsens, BPSDs such as anxiety, aggression, depression, or wandering, occur more frequently. These symptoms may be due to unmet needs.<sup>34,35</sup> The presence of behavioral and psychological symptoms is not only difficult for people with CI but also it can lead to physical or emotional burdens for the caregivers.<sup>36,37</sup> Thus, it is important to prevent or minimize behavioral and psychological symptoms in people with CI.

### **Anxiety in people with CI**

Anxiety in people with CI is defined as symptoms of worry that is difficult to control as well as presenting with at least three additional symptoms including restlessness, irritability, muscle tension, excessive fears, and respiratory symptoms.<sup>2</sup> Among behavioral and psychological symptoms of people with CI described above, anxiety is the most common symptom.<sup>1</sup> The rate of anxiety among people with CI is significantly higher compared to those without CI.<sup>1</sup> There are a number of negative consequences when people with CI feel anxious. Anxiety is one of the most distressing behavioral and psychological symptoms in persons with CI that family caregivers report.<sup>5,6</sup> Family caregivers experience a high level of burden when a person whom they are caring for has anxiety, and both high frequency and severity of anxiety are known to increase caregiver burden.<sup>5</sup> This may be because family caregivers find it extremely difficult to manage their loved one's mood or problematic behavior.<sup>38</sup>

Nursing home placement is another negative outcome of anxiety in people with CI.<sup>7</sup> In general, older adults are concerned about being placed in nursing home because of poor quality of care,<sup>39</sup> challenges of leaving a known environment and adjusting to a different environment,<sup>40</sup> or

fear of becoming disconnected from society.<sup>41</sup> However, nursing home placement can be inevitable for older adults with CI when family caregivers experience high levels of care burden due to greater cognitive impairment or psychiatric symptoms such as anxiety.<sup>7</sup>

Anxiety is also associated with poor quality of life in people with CI.<sup>6,8</sup> This association was present in both self-reported quality of life measures and proxy-reported quality of life measures.<sup>6,8</sup> In a 12-month longitudinal study, presence of anxiety was associated with poor quality of life over.<sup>8</sup> Quality of life is considered as an indicator of an overall wellbeing of people with CI.<sup>42</sup> Thus, it is important to manage underlying factors such as anxiety that influence poor quality of life in people with CI.

As anxiety contributes to negative outcomes, attempts have been made to reduce anxiety in CI, including both pharmacological and nonpharmacological interventions. Although pharmacological treatments such as antipsychotics, anxiolytics, or antidepressants are widely used to relieve anxiety in people with CI, many side effects are reported from using the medications such as confusion, excessive sedation, falls, and fractures.<sup>43,44</sup> Therefore, non-pharmacological interventions are preferred, but they are limited to interventions such as music therapies<sup>45-49</sup> or cognitive behavioral therapies.<sup>50,51</sup> Even these interventions have conflicting results in terms of effectiveness. While some of the studies reduced anxiety,<sup>46-49,51</sup> others did not.<sup>45,50</sup> Examining modifiable factors associated with anxiety in people with CI is needed to develop effective non-pharmacological interventions.

### **Social isolation and anxiety**

Social isolation is defined as the “*subjective experience of a shortfall in one’s social resources such as companionship and support.*”<sup>52</sup> Previous literature described social isolation in two ways: (1) size of social network and (2) perceived social isolation such as loneliness or

perceived lack of support from close family or friends.<sup>52</sup> In this dissertation, the latter meaning was used as an operational definition because quality of the social networks rather than size becomes important in late life.<sup>53,54</sup> Indeed, a previous study reported that older adults or people who have limited time in their lives tend to seek for smaller but emotionally meaningful social networks.<sup>54</sup> According to the literature, perceived social isolation has two dimensions of feeling loneliness and lack of social support.<sup>52,55</sup> When there is a discrepancy between actual desired and actual interpersonal relationships, people tend to perceive that they are lonely and isolated.<sup>55,56</sup>

Social isolation is a well-known risk factor for the development of CI.<sup>21,22,24</sup> However, there is lack of research attention to social isolation among people who have already developed CI. In people with normal cognition, social isolation increases the risk of developing anxiety.<sup>14</sup> The lack of social connections or companionship can feel isolating.<sup>55</sup> In older adults, maintaining social relationships and a social support system is an important part of successful aging,<sup>15,16</sup> and people with CI are not exception. When individuals are formally diagnosed with dementia, they experience less contact with their family and friends.<sup>19,20</sup> This may be due to inappropriate social behaviors that accompany CI,<sup>57</sup> social stigma about cognitive impairment,<sup>58</sup> or intolerance to people with CI.<sup>24</sup> Inability to maintain a social support system may increase anxiety in people with CI. In fact, little social engagement and poor perceived social support are related to anxiety in people in nursing homes with and without CI.<sup>59</sup> While people with CI are vulnerable to social isolation, limited findings are available regarding the psychological effects of social isolation among people with CI.<sup>12</sup> In order to address the gaps described above, it is important to study how social factors, such as social isolation, are related to anxiety in people with CI. In addition, it is essential to investigate how people who develop CI experience social isolation and anxiety compared to those who do not develop CI.

## CHAPTER AIMS

This dissertation is a three-paper dissertation. The first paper was an integrative review to examine factors associated with anxiety in people with CI, and the second paper and the third paper were data-driven papers examining how social isolation is related to anxiety. Table 1.1 summarizes the chapter aims, hypotheses, main analysis plan, and data source of this three-paper dissertation.

**Table 1. 1. Chapter aims of the dissertation**

<b>Specific Aim</b>	<b>Hypothesis</b>	<b>Statistical Analysis</b>	<b>Data Source</b>	<b>Paper</b>
<b>Aim 1.</b> To conduct an integrative review to examine factors related to the <u>presence of anxiety</u> in persons with CI and to identify potentially modifiable factors among them	N/A	N/A	PsycINFO, CINAHL, AgeLine, PubMed, Embase, Web of Science, and Scopus.	Paper 1
<b>Aim 2.</b> To determine if social isolation is associated with <u>anxiety</u> in people with CI	More social isolation is associated with increased <u>anxiety</u> in people with CI.	Weighted linear regression analysis	NSHAP Wave 2	Paper 2
<b>Aim 3a.</b> To compare <u>social isolation and anxiety</u> among people who develop CI and those who do not over a 5-year period	People who develop cognitive impairment over a 5-year period will experience more <u>social isolation and anxiety</u> compared to people who do not develop cognitive impairment.	Weighted independent t-tests	NSHAP Wave 2 and Wave 3	Paper 3
<b>Aim 3b.</b> To determine if cognitive impairment moderates the relationship between changes in social isolation and	Compared to people who do not develop cognitive impairment, people who develop cognitive impairment will present a stronger positive association	Weighted linear regression analysis with a group interaction	NSHAP Wave 2 and Wave 3	Paper 3



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<u>changes in anxiety</u>	between changes in social isolation and <u>changes in anxiety.</u>
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Notes: Dependent variables are underlined.

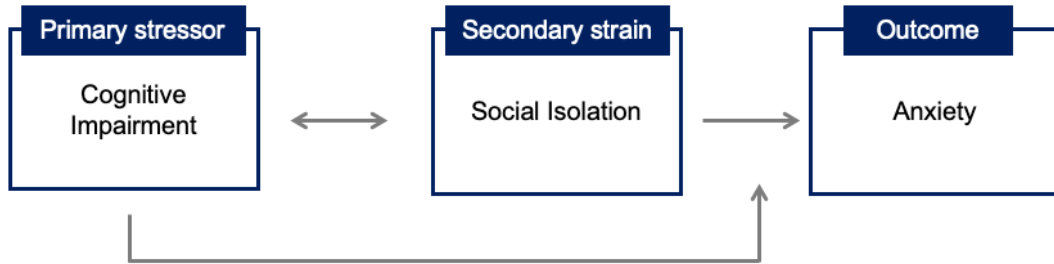
## CONCEPTUAL UNDERPINNINGS FOR THE STUDY

The proposed conceptual framework is adapted from the Stress Process Model for the Individuals with Dementia,<sup>60</sup> which explained that there are various levels of stressors that impact the wellbeing of individuals with CI. Figure 1.1 illustrates the conceptual framework of Paper 2 (Aim 2) and Paper 3 (Aim 3) of this dissertation. The Stress Process Model for the Individuals with Dementia explains that there are primary stressors such as cognitive status or functional status, which affect secondary strains such as family role strain, job role strain, or social role strain.<sup>60</sup> The Stress Process Model for the Individuals with Dementia suggested that primary stressors and secondary strains affect outcomes such as anxiety or depression.<sup>60</sup> In this study, cognitive impairment is considered as a primary stressor; social isolation is considered as a secondary strain; and anxiety is considered as an outcome.

Although social isolation is a well-known risk factor for the development of CI,<sup>21-24</sup> there is limited information available on the literature about social isolation among people who have already developed CI. Based on the Stress Process Model for the Individuals with Dementia, cognitive impairment is considered as an objective stressor. As a direct result of cognitive impairment, people may experience changes in their social roles as well as their relationships to others. These changes can lead to perceived social isolation which may result in one's psychological and emotional distress such as anxiety. Since the severity of cognitive impairment may impact the relationship between social isolation and anxiety, this dissertation also tried to

examine if there is a moderating effect of cognitive impairment on the relationship between social isolation and anxiety.

**Figure 1. 1. Conceptual framework of the relationship between social isolation and anxiety in people with cognitive impairment**



Notes: This conceptual framework is adapted from Judge et al. (2010) <sup>60</sup>

## **PARENT STUDY DATASET FOR SECONDARY ANALYSIS**

Paper 2 and Paper 3 of this dissertation analyzed data collected from parent studies called the National Social Life, Health, and Aging Project (NSHAP) Wave 2 (2010-2011) and Wave 3 (2015-2016). The NSHAP was funded by the National Institutes of Health/National Institute on Aging (R01AG033903, R01AG043538, R01AG048511, R37AG030481) and was conducted by the National Opinion Research Center (NORC) and principal investigators at the University of Chicago. The NSHAP studied general health and social factors to understand the wellbeing of a nationally representative sample of American older adults living in community. The data were collected via interviews and questionnaires from the participants. At the time of the interview, if interviewers felt that the respondent had inadequate cognitive ability to complete the questionnaire, those people were not enrolled. Only de-identified data are available, and the data are publicly

available for research if a formal request is made through the National Archive of Computerized Data on Aging located within the Inter-University Consortium for Political and Social Research.

In this dissertation, the NSHAP Wave 2 and Wave 3 were used because Wave 1 did not measure cognition which is a critical variable for the dissertation. The data for NSHAP Wave 2 were collected from August 2010 through May 2011, and the data for NSHAP Wave 3 were collected from September 2015 through November 2016. Each wave is a cross sectional data with one data time point. The NSHAP Wave 2 (2010-2011) included returning participants from the NSHAP Wave 1 (2005-2006) and a new cohort. The returning participants from the NSHAP Wave 1 were a nationally representative sample of adults whose ages were between 57 and 85 at the time of the Wave 1 interview. The new cohort was recruited from eligible, but non-interviewed respondents from the Wave 1, and cohabiting spouses or partners of the Wave 1 respondents or the Wave 1 non-interviewed respondents. In Wave 2, a total of 3,377 respondents participated in the study. The NSHAP Wave 3 (2015-2016) included returning participants from the NSHAP Wave 2 (2010-2011) and a new cohort. In this dissertation, for research objectives that need to investigate changes from Wave 2 to Wave 3, only the returning cohort (i.e., people who both participated in Wave 2 and Wave 3) were analyzed. Therefore, the returning cohort had two time points: Wave 2 as a baseline and Wave 3 as a 5-year follow up.

## **INNOVATION**

Paper 1 of this dissertation was an integrative review on modifiable factors associated with anxiety in people with CI. Examining modifiable factors associated with anxiety in people with CI is helpful for designing non-pharmacological interventions to prevent or minimize anxiety in people with CI. This paper is innovative due to the scarcity of knowledge available on underlying

factors associated with anxiety. Although there are several review studies in the literature that have focused on anxiety in people with CI, previous reviews are outdated,<sup>3</sup> lack a systematic process,<sup>61</sup> or only included quantitative studies focusing on people with CI living in residential facilities.<sup>62</sup> Thus, a review with updated information on factors precipitating anxiety is needed to include both people living with CI residing in nursing homes and living in the community. Paper 1 of this dissertation can provide rich knowledge on factors associated with anxiety in people with CI, addressing limitations in previous review studies.

Paper 2 and Paper 3 of this dissertation focused on the relationship between social isolation and anxiety in people with CI. Paper 2 and Paper 3 are particularly innovative as limited information is available on the relationship between social isolation and anxiety among people with CI, and no studies have compared the perception of social isolation and severity of anxiety between people with CI and people without CI. In the literature, social isolation and its relationships to psychological outcomes among people who have already developed CI are understudied. Because people with CI are at risk for social isolation,<sup>19,20,25</sup> it is important to examine social isolation in this population, especially its relationship to psychological outcomes such as anxiety. In addition, Paper 3 used 5-year longitudinal data to examine changes in social isolation and anxiety while previous studies have been cross-sectional in nature. The results of these two studies can provide knowledge on how people who develop CI experience social isolation and anxiety. As social isolation is potentially modifiable, results of Paper 2 and Paper 3 can contribute to improving anxiety in people with CI.

## **SUMMARY**

Anxiety is very common and distressing symptoms in people with CI and their caregivers, but only a few non-pharmacological interventions are available for the prevention and minimization of anxiety. Accordingly, this dissertation focuses on examining the underlying mechanism of anxiety so that new effective nursing interventions can be developed. This dissertation specifically focuses on the relationship between social isolation and anxiety since people with CI are at increased risk for social isolation. The findings of this dissertation can provide rich knowledge on the relationships between cognitive impairment, social isolation, and anxiety among people with CI.

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## CHAPTER 2: PAPER 1

### MODIFIABLE FACTORS ASSOCIATED WITH ANXIETY IN PERSONS WITH DEMENTIA: AN INTEGRATIVE REVIEW

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#### ABSTRACT

**Objectives:** The purpose of this integrative review was to examine factors related to the presence of anxiety in person with dementia (PWD) and to identify potentially modifiable factors among them.

**Methods:** An integrative review was conducted using PsycINFO, CINAHL, AgeLine, PubMed, Embase, Web of Science, and Scopus. Among 1,856 studies identified, 27 studies were included.

**Results:** A number of modifiable factors associated with anxiety were identified. Individual level factors included pain, physical health, physical functioning, fatigue, sleep disturbance, disclosure of diagnosis, embarrassment about memory problems, separation from caregivers, views about oneself and others, social rejection, social isolation, and interactions with others. Caregiver factors associated with anxiety in PWD included caregiver stress, caregiver's negative reactions towards the behavioral problems of PWD, and competence about caregiving.

**Conclusion:** The results of this review can be used to identify potential targets for interventions to reduce for anxiety in persons with dementia.

**Keywords:** Anxiety, anxiety symptoms, behavioral and psychological symptoms of dementia (BPSD), cognitive impairment, dementia, older adults, unmet needs

## INTRODUCTION

Anxiety, is one of the most common behavioral and psychological symptoms (BPSD) in persons with dementia (PWD).<sup>1,2</sup> 5% to 21% of PWD have anxiety disorders, and up to 71% experience anxiety symptoms.<sup>3</sup> In this paper, the term anxiety will be used referring to both symptoms of anxiety and a diagnosis of anxiety disorder. Anxiety in PWD has been associated with adverse outcomes, such as functional impairment,<sup>4</sup> poor quality of life,<sup>5</sup> and caregiver distress,<sup>6</sup> and increased the risk of institutionalization.<sup>7</sup> Anxiety is an emotional status characterized by apprehension and somatic symptoms of tension.<sup>8</sup> Symptoms of anxiety commonly include worried thoughts, restlessness, fast breathing, increased heart rate, and muscle tension.<sup>8,9</sup> However, detecting anxiety in PWD is more difficult than in persons without dementia.<sup>3,10</sup> While persons without dementia or persons with mild cognitive impairment (MCI) can express their concerns or nervousness and complete questionnaires to screen for anxiety, persons with moderate or severe dementia may have difficulty doing so due to their impaired cognition. While anxiety is common and distressing in PWD, it is yet under-identified and under-treated by clinicians. Therefore, it is important to identify factors associated with anxiety in PWD to enhance identification and inform interventions.

Although pharmacological interventions are frequently used to lessen BPSD, critical side effects such as confusion or sedation have been reported.<sup>11,12</sup> However, non-pharmacological interventions have been found to safely improve BPSD, including anxiety.<sup>13,14</sup> Although several intervention studies have been conducted specifically to reduce anxiety in PWD, most of the interventions have been limited to music therapies<sup>15-19</sup> or cognitive behavioral therapies.<sup>20,21</sup> Even in these interventions, there appears to be a heterogenous response; while some reduced anxiety,<sup>16-19</sup> others did not.<sup>15,20</sup> The heterogenous response in music interventions may be due to various reasons including different types of musical interventions applied, different levels of musical experience among the participants, or varied inclusion criteria for severity of cognitive

impairment. Moreover, people might have had different reasons for anxiety that could not be improved by musical interventions. Similarly, the heterogenous response in cognitive behavioral therapies may be due to the fact that cognitive behavioral therapies are effective in individuals with more insight. Thus, exploring the factors that influence anxiety in PWD is important for developing and tailoring non-pharmacological interventions.

Several review studies have focused on anxiety in PWD.<sup>3, 9, 22</sup> Although these studies were designed to better understand the nature of anxiety in PWD and its correlates, they were either published a decade ago,<sup>3</sup> lacked a systematic process,<sup>9</sup> or only focused on PWD living in residential facilities with quantitative studies.<sup>22</sup> Thus, a review with updated knowledge on factors precipitating anxiety is needed to include both PWD residing in nursing homes and individuals living in the community.

Accordingly, the aims of this review are to examine the factors related to anxiety in PWD and identify modifiable factors among them. This study is an integrative review of quantitative and qualitative descriptive studies to better identify factors associated with anxiety in PWD. Two theoretical frameworks were used this review: the Socio-Ecological Model for Developing and Implementing Comprehensive Dementia Care<sup>23</sup> and the Need-driven Dementia-compromised Behavior.<sup>24</sup> The following research questions guided this review: (1) What factors are related to anxiety in PWD, and (2) Among those factors, which ones are modifiable?

### **Theoretical Frameworks**

The Socio-Ecological Model for Developing and Implementing Comprehensive Dementia Care<sup>23</sup> was developed from classic social-ecological framework and personhood in dementia.<sup>25</sup> This model provides six domains that influence dementia care: individuals with dementia, caregivers, living environments, neighborhood/ community, health and human services systems, and national policies.<sup>23</sup> This model emphasizes that it is important to consider all the



domains that potentially influence the well-being of PWD when caring for PWD.<sup>23</sup> This model can be applied to care for PWD with anxiety. Assessing comprehensive domains would provide a better understanding of why PWD experience anxiety and it would provide clues for developing more effective, non-pharmacological interventions to alleviate anxiety in PWD. The Need-driven Dementia-compromised Behavior model describes that BPSD such as wandering, vocalization, and aggression are caused by one's unmet needs.<sup>24</sup> According to the model, background factors such as physical or psychological health and proximal factors such as physical and social environments influence one's unmet needs thereby contributing to BPSD.<sup>24</sup> In other words, this model suggests that BPSD can be prevented when one's needs are met.

Figure 2.1 describes the conceptual framework of the present study, inspired by the two theoretical frameworks above.<sup>23, 24</sup> We adopted the six domains of the Socio-Ecological Model for Developing and Implementing Comprehensive Dementia Care on the left side to categorize factors related to anxiety in PWD.<sup>23</sup> The concept of unmet needs was adopted from the Need-driven Dementia-compromised Behavior model and it was inserted in the middle.<sup>24</sup> We hypothesized that individual's unmet needs may present in the form of anxiety. Since the concept of unmet needs is an implicit concept, the middle box was presented with dotted line. We chose to use the Socio-Ecological Model for Developing and Implementing Comprehensive Dementia Care<sup>23</sup> to categorize factors instead of using the original Need-driven Dementia-compromised Behavior model<sup>24</sup> in order to specify factors beyond individual level factors.

## **METHODS**

An integrative review of quantitative and qualitative descriptive research on the factors related to anxiety in PWD was conducted. An integrative review is a type of review that allows for the combination of different methodologies.<sup>26</sup> This type of review can provide a more comprehensive understanding of a phenomenon than reviews of only one type of research.<sup>27</sup> This

term has been interchangeably used with the terms “mixed studies review”<sup>27</sup> or “mixed research synthesis”.<sup>28</sup>

### **Data Sources**

A literature search was conducted across seven databases: PsycINFO, CINAHL, AgeLine, PubMed, Embase, Web of Science, and Scopus. These databases were utilized for the following reasons. PsycINFO was included because anxiety is a psychological concept; the CINAHL was included to capture nursing literature; AgeLine was included because dementia frequently occurs in the older population; and PubMed, Embase, Web of Science, and Scopus were used to include comprehensive biomedical literature. The search terms “dementia,” “senile dementia,” and “Alzheimer’s disease” in combination with “anxiety,” “anxiety disorders,” and “generalized anxiety disorder” were selected. These search terms were chosen to address not only anxiety but also anxiety as a mental disorder in PWD. In this review, MCI was not used as a search term because the nature of anxiety in PWD and MCI can differ. Similarly, search terms such as frontotemporal dementia, Lewy Body dementia, or vascular dementia were not used due to the different nature of the diseases. The searches were limited to literature published between January 1, 2009 and July 5, 2019 to address gaps in the literature since the most recent systematic review.<sup>3</sup> Only studies written in English were selected.

### **Study Selection**

The literature search and extraction flow chart in Figure 2.2 describes the study selection process. A total of 1,856 studies were found in the literature search of the seven databases. The study selection was completed using EndNote X8 software. With 771 duplicates removed, the titles of 1,085 studies were screened for relevance. 797 records were removed from the title screening because of irrelevant content. Next, 288 abstracts were screened for eligibility

for a full-text review. The inclusion criteria for this review were studies that had: (1) a population of PWD, (2) an original research design, (3) a primary outcome variable of anxiety in PWD, and (4) studies published in an academic journal. The exclusion criteria were as follows: (1) study participants exclusively with frontotemporal dementia, Lewy Body dementia, or vascular dementia, (2) study participants with MCI or subjective cognitive decline, (3) study participants containing people with and without dementia, (4) studies with anxiety as an independent variable, (5) instrument development or instrument validity testing studies, (6) case studies, (7) pharmacological studies, (8) review studies, (9) protocol development studies, and (10) experimental or intervention studies. We tried to exclude studies conducted exclusively with frontotemporal dementia, Lewy Body dementia, or vascular dementia due to their different nature of the diseases. However, it was inevitable to include studies that had sampled a mix of different types of dementia, as many studies did not specify the types of dementia of their study participants. Experimental or intervention studies were not included in this review because one of the aims of this review was to explore novel modifiable factors related to anxiety in PWD so that effective, non-pharmacological interventions can be developed.

Based on these criteria, 241 irrelevant studies were excluded from the abstract screening; the reasons for exclusion are described in Figure 2.2. A total of 47 studies were eligible for a full-text review. Based on the criteria above, 20 studies were excluded, resulting in the inclusion of 27 studies in this review (Figure 2.2).

### **Quality Assessment**

For the selected studies, quality assessments were conducted using the Joanna Briggs Institute (JBI) critical appraisal tools.<sup>29,30</sup> We chose the JBI critical appraisal tools because JBI provides tools for different types of studies. The JBI critical appraisal tools for analytical cross-sectional studies, cohort studies, and qualitative research were used. Due to the varying numbers

of items for each critical appraisal tool, it was difficult to compare the results of the critical appraisal. Thus, we used percentage scores so that each quality assessment score could be easily compared. The results of the quality assessments can be found in the supplementary materials (see Table S1 and S2 in supplementary material).

## **Data Analysis**

A narrative analysis was used for this integrative review as suggested by Whitemore et al. (2014).<sup>31</sup> It was difficult to use a statistical approach for this review because this review included both quantitative studies and qualitative studies. One reviewer (Y.H.) conducted data synthesis, and it was guided by the data analysis method from Whitemore and Knafl (2005).<sup>26</sup> The factors associated with anxiety in PWD were first categorized according to their characteristics. In this review, the Socio-Ecological Model for Developing and Implementing Comprehensive Dementia Care was used to classify factors in six domains: individuals living with dementia, their caregivers, their living environments, their neighborhoods or communities, health and human services systems, and national policies.<sup>23</sup> Then, a data comparison was conducted to determine whether there were any specific patterns or discrepancies. Each factor was assessed to determine whether it was a modifiable factor.

## **RESULTS**

Among the 27 studies included, 24 were quantitative studies and three were qualitative studies. The studies were conducted in various countries, including Belgium, Brazil, Greece, Japan, the Netherlands, Norway, Poland, Portugal, the United Kingdom, and the United States. In the studies examined in this review, eight instruments were used to measure anxiety in PWD: the Neuropsychiatric Inventory (NPI),<sup>32</sup> the Rating Anxiety in Dementia scale,<sup>33</sup> the Hospital Anxiety and Depression Scale,<sup>34</sup> the Hamilton Anxiety Scale,<sup>35</sup> the Self-Rating Anxiety Scale,<sup>36</sup> the

Philadelphia Geriatric Center Apparent Affect Rating Scale,<sup>37</sup> the Behavioral Pathology in Alzheimer's Disease Rating Scale,<sup>38</sup> and the Pain Anxiety Symptom Scale.<sup>39</sup> The most frequently used scale was the NPI (n=12).<sup>32</sup> Details about the study participants, settings, study designs, measurement scales, and results are available in the table of evidence (see Table S1 and S2 in supplementary material).

The factors associated with anxiety in PWD were categorized based on the Socio-Ecological Model for Developing and Implementing Comprehensive Dementia Care,<sup>23</sup> and three domains out of six were found: the individual level, the caregiver level, and the living environment level. Tables 1 through 3 describe the factors related to anxiety in PWD. The “+” symbol indicates a positive association with anxiety in PWD, and the “-” symbol indicates a negative association with anxiety in PWD. In cases where there were inconsistent results (positive and negative associations mixed), the “+/-” symbol was used. When describing factors in this review, the exact terms from the original study were used. For example, although “delusion” is a type of “psychosis”, they were used separately in Table 2.1 because the original study used the term “delusion” instead of “psychosis.”

### **Factors associated with anxiety in dementia at the individual level**

Table 2.1 describes the factors associated with anxiety in PWD at the individual level. Factors at the individual level were grouped again into four subcategories<sup>23</sup>: neuro-biological, health, behavioral and psychological, and social.

**Neuro-biological subcategory.** In the neuro-biological subcategory, the greater anxiety in PWD was related to a reduction in gray matter volume in the right precuneus and inferior parietal lobule and hyper perfusion in the bilateral anterior cingulate cortices on neuroimaging.<sup>40</sup> While one study reported that early onset of Alzheimer's disease at age younger than 65 was also related to

higher chances of having anxiety in PWD,<sup>41</sup> another study reported that early onset Alzheimer's disease was associated with less anxiety compared to late onset Alzheimer's disease.<sup>42</sup> An important factor in the neuro-biological subcategory was cognition. There were inconsistent associations between cognition scores measured by the Clinical Dementia Rating or Mini-Mental State Examination and anxiety in PWD. While some studies reported that either good or poor cognition was related to either increased anxiety or increased probability of having anxiety in PWD,<sup>43-46</sup> one study reported that poor cognition was related to less worsening anxiety over 12 months.<sup>47</sup> Other cognitive assessment tools, such as the California Verbal Learning Test II, the Trail Making Test, awareness of deficits, autobiographical memory, and self-knowledge about one's personality, were not significantly related to anxiety in PWD. Disease duration of dementia was not also related to anxiety in PWD. As dementia is a neurodegenerative disorder, no modifiable factors were found in the neuro-biological subcategory.

**Health subcategory.** In the health subcategory, having more pain, more vascular factors, poor physical health, and poor performance of activities of daily living were related to increased anxiety in PWD (Table 2.1). In terms of medications, the use of anxiolytics was related to more anxiety,<sup>43, 48</sup> but the use of anxiolytics was related to less increase in anxiety over time.<sup>47</sup> Greater use of antipsychotics, antidepressants, or psychotropic drugs was related to higher anxiety. Instrumental activities of daily living, difficulty breathing, lifetime alcohol load, caffeine intake, use of cognitive enhancers or use of hypnotics and sedatives were not related to anxiety in PWD. The modifiable factors in this health subcategory were pain, physical health, and activities of daily living.

**Behavioral and psychological subcategory.** Many factors related to anxiety in PWD fell into the behavioral and psychological subcategory (Table 2.1). Increased anxiety was related to

depression, arousal, worry, feelings of losing control, fatigue, less apathy, poor quality of life, self-concept, embarrassment about memory problems, personality traits, muscle tension, aberrant motor behavior, irritability, behavioral problems, and sleep disturbances. In terms of delusion, there were inconsistent results, with one study reporting a negative relationship between delusion and anxiety<sup>49</sup> and another reporting a positive relationship between the two concepts.<sup>41</sup> There were also inconsistent results about the relationship between psychosis and anxiety depending on the study design. For example, while one cross-sectional study reported that psychosis was related to increased anxiety in PWD,<sup>43</sup> a longitudinal study reported that greater psychosis at the baseline predicted a smaller increase in anxiety after 12 months.<sup>47</sup> Similarly, higher scores of affective symptoms predicted greater anxiety in a cross-sectional study,<sup>43</sup> while higher scores of affective symptoms predicted a smaller increase in anxiety in a longitudinal study.<sup>47</sup> Inconsistencies were also found regarding the relationship between agitation and anxiety. While there was a positive association between agitation and anxiety in one study,<sup>43</sup> another found that greater agitation at the baseline was related to a smaller increase in anxiety after 12 months.<sup>47</sup>

Additionally, there were also inconsistent results in terms of disclosure of diagnosis of Alzheimer's disease. Although a diagnosis of dementia contributed to increased anxiety in PWD,<sup>50</sup> the disclosure of a diagnosis of dementia eventually reduced the anxiety of PWD after three months.<sup>51</sup> Feeling keyed up or on edge, restlessness, and self-efficacy were not significantly related to anxiety in PWD. Many of the factors in the behavioral and psychological subcategory were modifiable. For example, adjusting other co-occurring behavioral problems, such as depression, or addressing anxiety-related symptoms, such as fatigue, worry, or sleep disturbances, may decrease anxiety.

**Social subcategory.** In the social subcategory, separation from caregivers, negative views about oneself and others, social rejection, less internalized shame, the patronizing attitudes of others,

social isolation, and social interactions at the within-person level were related to increased anxiety in PWD (Table 2.1). Apart from age of onset of dementia that was discussed earlier, younger age in general was also related to the presence of anxiety in PWD. There were inconsistent results regarding the relationship between gender and anxiety in PWD. For example, two studies reported that being male was related to the presence of anxiety in PWD<sup>41, 52</sup> and one study reported that being female was related to the presence of anxiety in PWD.<sup>48</sup> Other factors, including marriage status, race or ethnicity, education, social interaction at the between-person level, or relationship strains, were not related to anxiety in PWD. Many factors in the social subcategory were modifiable including separation from caregivers, views about oneself and others, social rejection, social isolation, and interactions with others.

#### **Factors associated with anxiety in dementia at the caregiver level**

Caregiver factors also influenced anxiety in PWD, as shown in Table 2.2. Under this category, staff members at nursing home facilities were also included as caregivers. At the caregiver level, higher caregiver stress, more staff reactions to behavior problems associated with dementia, and low competence of staff members were related to greater anxiety in PWD. All these factors are modifiable. Other factors, including caregiver–patient relationships, the age of staff members, caregivers’ views about themselves and others, the qualifications of the staff, the job satisfaction of the staff, and nursing home staff’s time spent on direct patient care, were not associated with anxiety in PWD.

#### **Factors associated with anxiety in dementia at the living environment level**

At the living environment level, specific time of day and length of stay in residential care were related to anxiety in PWD (Table 2.3). PWD expressed more anxiety in the afternoon than in the morning, and a longer duration of institutionalization was related to either less anxiety



or less probability of having anxiety in PWD who lived in nursing homes. Neither factor is easily modifiable. Other factors in this subcategory, such as type of assistive living, dementia special care units, number of patients per unit in nursing homes, or the presence of a walking circuit, were not associated with anxiety in PWD.

## **DISCUSSION**

The purpose of this integrative review was to examine the factors related to anxiety in PWD and to identify modifiable factors among them. Here in the discussion section, three major points are discussed: inconsistent results, important findings from quantitative studies and qualitative studies, and measuring anxiety in PWD.

### **Inconsistent Results**

As shown in Table 2.1, some of the results were inconsistent across studies. While two studies reported that poor cognition measured by the Clinical Dementia Rating scale was related to the presence of anxiety in PWD,<sup>43,44</sup> one study reported that poor cognition was related to less worsening anxiety over 12 months.<sup>47</sup> This difference may be due to the different study designs used (i.e. cross-sectional design or longitudinal design). This inconsistency may also be related to level of insight or awareness in PWD.<sup>53</sup> Staff members who worked with PWD described anxiety as occurring more frequently in early-stage dementia, as these individuals typically have greater insight.<sup>50</sup> As their cognitive ability declines, their worry and anxiety about the future may decrease. However, studies also failed to show a significant relationship between cognition and anxiety in PWD.<sup>49, 52, 54-57</sup> This inconsistency may be due to the different types of instruments used to measure cognition and anxiety. Further research is needed to examine how cognition levels influence anxiety in PWD.

Onset of dementia was another factor which showed inconsistent results; while one study reported that people with early onset Alzheimer's disease were more likely to have anxiety,<sup>41</sup> another study reported that early onset Alzheimer's disease was associated with less anxiety compared to late onset Alzheimer's disease.<sup>42</sup> Regarding the use of anxiolytics, while two studies indicated that the use of anxiolytics was related to increased anxiety,<sup>43, 48</sup> anxiolytics were associated with less increase in anxiety over time.<sup>47</sup> Inconsistent results were also found regarding the relationship between delusions and anxiety. While one study reported a negative relationship between delusions and anxiety,<sup>49</sup> another study reported a positive relationship between the two.<sup>41</sup> Neither study explained the mechanism of these relationships, but it may be assumed that this inconsistent result is due to limitations associated with the proxy-measured scale. The results regarding psychosis, affective symptoms, and agitation<sup>43, 47</sup> were inconsistent in regard to their relationship with anxiety (details are described in Table 2.1). This inconsistency may be explained by differences in study designs, as one used a cross-sectional design<sup>47</sup> and the other used a longitudinal design.<sup>43</sup> It is also possible that one's level of insight or awareness of the disease might have influenced the inconsistent results.

There were also inconsistent results regarding the disclosure of diagnosis of Alzheimer's disease. While diagnosis of dementia was a cause of anxiety in PWD in one study,<sup>50</sup> in a longitudinal study,<sup>51</sup> the disclosure of diagnosis of Alzheimer's disease reduced the anxiety of PWD after three months. Interestingly, the results regarding the association of gender with anxiety in PWD also varied. While two studies reported that being male was associated with anxiety in PWD,<sup>41, 52</sup> one study reported that being female was related to anxiety in PWD.<sup>48</sup> Calleo et al. (2011) explained that higher percentage of anxiety among men may be due to inclusion of military veterans; however, no further explanations could be found in the literature. Thus, future research is necessary to address these inconsistencies.

## **Important Findings from Quantitative Studies and Qualitative Studies**

To gain comprehensive information on factors that are related to anxiety in PWD, quantitative and qualitative studies were included. Often times in the literature, the voice of PWD is precluded when studying BPSD such as anxiety because of communication difficulties or lack of coherency. In this review, there were three qualitative studies included.<sup>50, 58, 59</sup> In their qualitative studies, several important themes related to anxiety in PWD were found: anxiety about diagnosis, anxiety about loss of skills or losing control, anxiety about relationships with others, anxiety about physical and environmental factors, and relationship between anxiety and depression. The findings from the qualitative studies were helpful in understanding the findings from quantitative studies.

**Anxiety due to diagnosis.** Qazi et al. (2010) reported in their qualitative study that PWD become anxious when they are diagnosed with dementia.<sup>50</sup> They explained that this type of anxiety is related to worry about the disease or uncertainty about their illness.<sup>50</sup> The concept of uncertainty and its relatedness to anxiety also appeared in another qualitative study.<sup>58</sup> Upon diagnosis of dementia, their life start to change in many ways. Since people in early stage dementia have relatively more insight, this may cause them to worry about their future. In addition, everyone needs time to accept their illness, especially if it is a serious illness such as dementia. While two qualitative studies in this review reported that disclosing the diagnosis can cause anxiety in PWD, a longitudinal quantitative study found that the disclosure of diagnosis reduced the anxiety of PWD after three months.<sup>51</sup> This may be because uncertainty about the disease may have diminished for a certain amount over a period of three months or PWD were able to accept their illness after three months. Future studies are needed to improve illness uncertainty and to ultimately reduce anxiety in early stage dementia.

**Anxiety due to loss of skills or losing control.** Loss of skills or losing control due to dementia was a theme covered in all three qualitative studies in this review.<sup>50, 58, 59</sup> Anxiety in PWD was often caused from this feeling of losing control. Losing independence on their daily activities can lead them to worry about future and to trigger anxiety. While this concept of losing control and its relationship to anxiety was discussed in all qualitative studies in this review, it was not discussed in the quantitative studies. However, this concept of losing control can help to understand the findings on the relationship between functional abilities and anxiety. Interestingly, no significant relationships between anxiety and activities of daily living<sup>41, 43, 47</sup> or instrumental activities of daily living<sup>57</sup> were reported in the quantitative studies in this review. In contrast, the qualitative studies report that anxiety in PWD was associated with activities of daily living.<sup>50, 59</sup> When PWD could not perform everyday tasks<sup>50</sup> or when they spent more effort executing everyday tasks,<sup>59</sup> they tended to feel more anxious. These differences may be due to a sense of losing control rather than the limitations of the activities themselves.<sup>59</sup> For example, PWD may not feel anxious because of driving cessation due to dementia. Rather, they may become anxious because of losing one's independence by quit driving. Future quantitative studies should thus consider the sense of losing control as a mediator when examining the relationship between anxiety and activities of daily living in PWD.

**Anxiety due to change in relationships with others.** One of the important themes from a qualitative study was that PWD also showed anxiety because of their changes in relationship with others.<sup>50</sup> PWD reported that patronizing attitude from others trigger anxiety in PWD.<sup>50</sup> This can explain some findings from the quantitative studies. The reason why PWD are afraid of being separated from their caregivers<sup>41</sup> is probably because they do not want to be treated differently from others while being alone. This is also in line with the finding that social rejection causes anxiety in PWD.<sup>45</sup> The continued social rejection in relationships can gradually lead to social

isolation which can further worsen anxiety.<sup>45</sup> Clinicians experienced with PWD noted that it is important to create a secure and supportive environment for PWD to reduce anxiety.<sup>58</sup> As shown in Table 2.1, relatively small amount of literature existed on social subcategory compared to other subcategories. Future studies examining the relationship between social factors and anxiety are needed and appropriate interventions to create socially supportive environment may be helpful.

**Anxiety due to physical health factors.** In both quantitative and qualitative studies, poor physical health was related to anxiety in PWD.<sup>43,50</sup> For example, anxiety in PWD was related to increased pain,<sup>46</sup> poor sleep,<sup>60</sup> constipation, or infection.<sup>50</sup> Clinicians who had experience with PWD also described difficulty falling asleep as a symptom of anxiety.<sup>58</sup> It is difficult to examine the causality between health conditions and anxiety due to the limitations of cross-sectional study designs; however, the discomfort that PWD feel in relation to their health conditions may present in the form of anxiety, just as the unmet needs of PWD can cause BPSD.<sup>24</sup> Thus, identifying and addressing unmet physical health needs may decrease anxiety in PWD.

**Relationship between anxiety and depression.** One of the main findings in both quantitative and qualitative studies was the relationship between depression and anxiety in PWD.<sup>44, 46, 55, 57, 58</sup> Depressive symptoms were related to higher anxiety in PWD. Because depression and anxiety are highly correlated, it is desirable to control for depression when studying anxiety. However, only a few studies in this review controlled for depression when studying anxiety.<sup>44, 57</sup> Greater attention should be paid to controlling for depression when studying anxiety in future research to better understand the nature of anxiety. Due to the similarities between anxiety and depression in dementia, it is often difficult to distinguish one from the other.<sup>3</sup> Both anxiety and depression in PWD may carry similar symptoms of aggression, irritability, concentration problems, social isolation, or sleep disturbances.<sup>58</sup> In a qualitative study, Goyal and colleagues (2019) described

the differences between symptoms of anxiety and depression in PWD based on the experiences of clinicians. While depression was persistent at some level with past-oriented thoughts, anxiety was more situational with future-oriented thoughts.<sup>58</sup> They described PWD with anxiety as hyper-vigilant, alert, quick in motion, or restless, while PWD with depression were slower and displayed sad facial expressions.<sup>58</sup> This detailed description of anxiety and depression can be useful to caregivers, clinicians, and researchers in differentiating anxiety and depression in PWD.

### **Measuring Anxiety in PWD**

In the studies used in this review, a total of eight measurement scales were used to measure anxiety in PWD. The most frequently used scale was the NPI (n = 12), with which caregivers assess anxiety in PWD. Unlike people without cognitive impairment, PWD have difficulty expressing their feelings and thoughts in a logical way, rendering caregivers more responsible for detecting anxiety symptoms. Thus, many existing scales for anxiety associated with dementia are proxy-reported scales like NPI.<sup>32, 33, 38, 61</sup> Caution should be applied when using and interpreting proxy-measured scales because observations may not precisely determine the existence of anxiety in PWD. If a person with dementia can express their feelings with language, a self-reported scale should be considered first. When measuring anxiety in persons with mild dementia, it is desirable to use a self-rated scale or a scale that has both a proxy-reported and self-reported version. If both a proxy-reported and self-reported measures are used, the information from persons with dementia and their caregivers can be compared to better understand the anxiety state of the individual. When measuring anxiety in PWD with severe cognitive impairment, it is important to choose a valid measurement scale that addresses characteristics of anxiety in PWD.

### **Strengths and Limitations of the Study**

This current review has a number of strengths. We addressed limitations of previous reviews on anxiety in PWD.<sup>3, 9, 22</sup> By conducting the search and review in a systematic way, this review provided reliable and reproducible results. Additionally, we evaluated recent literature and included participants from nursing homes and those who are community dwelling. By choosing a methodology that includes both quantitative and qualitative studies, it was possible to comprehensively assess the factors related to anxiety in PWD. This review also identified many modifiable factors that can potentially reduce anxiety in PWD.

There are a few limitations of this review. First, the critical appraisal scores were not very strong. Although the guidelines of JBI critical appraisal tools do not provide a cut-off point for high-quality evidence,<sup>29, 30</sup> most of the studies scored between 70% and 80% (n = 13). Two studies scored less than 60%, six studies scored between 80% and 90%, and six studies scored 90% or greater. These scores may not be critical, considering the nature of the quantitative studies, but caution should be applied when interpreting the results of this study. Second, the studies included in this review contained different types of dementia; although studies conducted exclusively with frontotemporal dementia, Lewy Body dementia, or vascular dementia were excluded, it was inevitable to include different types of dementia, as many studies did not specify the types of dementia of their study participants. Third, the studies included in this review used various measurement scales, which made it difficult to synthesize the results. Fourth, compared to factors at the individual level, a limited number of factors were found at the caregiver level or at the living environment level. Finally, this review excluded studies that examined anxiety in people with MCI, frontotemporal dementia, Lewy Body dementia, or vascular dementia. Further research addressing these limitations would be helpful for broadening the knowledge of anxiety in PWD.

### **Implications for Future Research**

First, additional qualitative research will be helpful to understand the nature of anxiety in PWD. In this review, only three out of 27 studies were qualitative studies since there were limited number of qualitative literatures existed. Studies on improving illness uncertainty and anxiety in early stage dementia will be helpful because diagnosis of dementia itself can lead to anxiety in the early stage. It may also be helpful to investigate how the sense of losing control affects anxiety in PWD. This review also found that PWD are anxious about changes in social relationships with others. More studies are needed to determine how to support the person's social environment when cognitive abilities are diminished. More studies examining caregiver factors and environmental factors would be also useful in highlighting external factors related in anxiety in PWD. In addition, more studies are needed on examining how anxiety is different based on one's level of insight. As PWD gradually lose insight, they may be anxious of different factors, but there are limited and inconsistent knowledge on how those cognition stage influences anxiety.

The findings from this research can also be used to develop effective, non-pharmacological interventions. The conceptual framework of this study shows that investigating and meeting unmet needs can reduce anxiety in PWD (Figure 2.1). By addressing pain, promoting good physical health, and preserving one's ability to perform activities of daily living, anxiety in PWD may be improved. Interventions that help PWD retain independence of daily activities can give them a sense of control and may prevent them from developing anxiety symptoms. Since feelings of losing control or embarrassment about memory problems were related to anxiety in PWD, greater support from caregivers may lessen anxiety in PWD. In addition, improving the quality of life of PWD may also lessen anxiety, and disclosing a diagnosis of Alzheimer's disease can decrease anxiety in PWD over time. Encouraging PWD to have positive views about themselves and others and to maintain controllable social interactions may be helpful for lessening anxiety in PWD. Because many social factors, such as social



rejection or isolation, can make PWD more anxious, creating a safe environment for PWD where they do not feel detached may also be helpful for decreasing anxiety. Finally, by decreasing caregiver stress, regulating staff members' reactions to the behavior problems of PWD, and increasing the competence of staff members, anxiety in PWD may be reduced.

## **CONCLUSION**

This integrative review provided comprehensive assessments of the factors related to anxiety in PWD. Factors at the individual level, caregiver level, and living environment level were related to anxiety in PWD. The results of this study have the potential for use in future research and clinical practice. Many of the existing scales are completed by caregivers on behalf of the PWD<sup>32, 33, 38, 61</sup>; thus, the factors related to anxiety in PWD must be considered when caregivers assess anxiety in PWD based on observation. Finally, it was found that many factors related to anxiety in PWD were modifiable. Therefore, health professionals should consider these modifiable factors when developing a non-pharmacological intervention to decrease anxiety in PWD.

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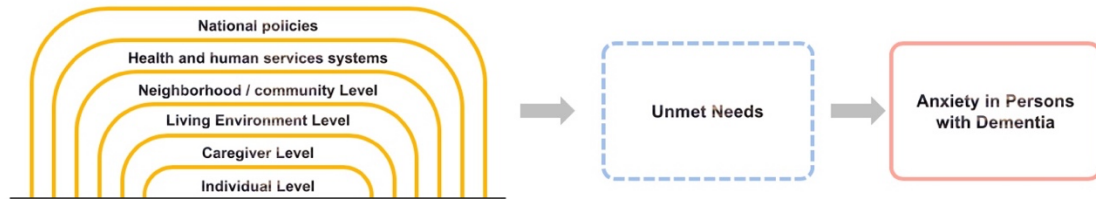
## **DECLARATION OF INTEREST**

None.

## **SUPPLEMENTARY MATERIALS**

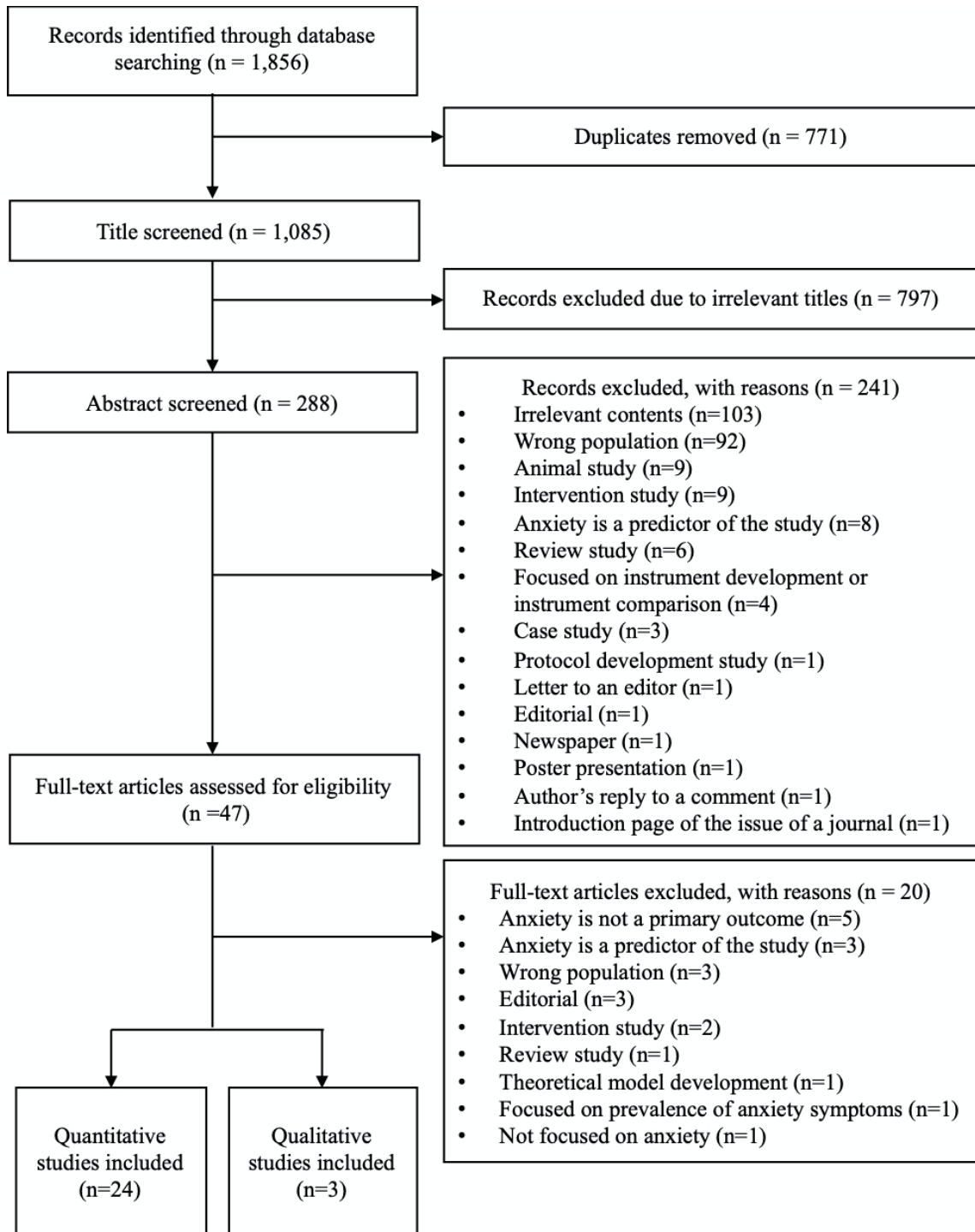
Supplementary material associated with this article can be found in Appendix.

**Figure 2. 1. Conceptual framework of factors associated with anxiety in PWD**



Notes: This conceptual framework was inspired by Gitlin and Hodgson (2018)<sup>23</sup> and Algase et al. (1996).<sup>24</sup> Since the concept of unmet needs is an implicit concept, the middle box was presented with dotted line.

**Figure 2. 2. Literature search and extraction flow chart**



**Table 2. 1. Factors associated with anxiety in dementia at the individual level**

Factors	Studies	Association with Anxiety (If any applicable)	Percentage of studies reporting association	Comments
<b>Neuro-Biological</b>				
Gray matter volume	40†	-	1/1 (100%)	Reduction in the gray matter volume in right precuneus and inferior parietal lobule were related to the greater anxiety in dementia.
Hyper perfusion in the bilateral anterior cingulate cortices	40†	+	1/1 (100%)	Hyper perfusion in the bilateral anterior cingulate cortices was related to the greater anxiety in dementia.
42 Clinical Dementia Rating	43†, 44†, 47†, 52	+/-	3/4 (75%)	While two studies reported that poor cognition was related to having anxiety in PWD, <sup>43, 44</sup> one study reported that poor cognition was related to less worsening in anxiety over 12 months. <sup>47</sup>
Early onset of Alzheimer's disease	41†, 42†, 62, 63	+/-	2/4 (50%)	While one study reported that early onset Alzheimer's disease was associated with higher chances of having anxiety in PWD, <sup>41</sup> another study reported that early onset Alzheimer's disease was associated with less anxiety compared to late onset Alzheimer's disease. <sup>42</sup>
Mini-Mental State Examination	41†, 44, 45†, 46†, 49, 54-57	+	3/9 (33%)	Higher cognitive ability was related to having anxiety. Kaiser et al. (2014) <sup>41</sup> found this relationship only

Factors	Studies	Association with Anxiety (If any applicable)	Percentage of studies reporting association	Comments
				in people with early onset Alzheimer's disease.
California Verbal Learning Test II	<sup>44</sup>	No association	0/1 (0%)	
Trail Making Test	<sup>44</sup>	No association	0/1 (0%)	
Awareness of deficits	<sup>62</sup>	No association	0/1 (0%)	
Autobiographical memory	<sup>64</sup>	No association	0/1 (0%)	
Self-knowledge about personality	<sup>64</sup>	No association	0/1 (0%)	
Length of dementia	<sup>41, 49</sup>	No association	0/2 (0%)	
<b><u>Health</u></b>				
Pain	<sup>46†</sup>	+	1/1 (100%)	More anxiety in PWD was related to having more pain.
Vascular factors	<sup>65†</sup>	+	1/1 (100%)	PWD who had severe vascular component reported more frequent and severe anxiety.
Anxiolytics	<sup>43†, 47†, 48†</sup>	+/-	3/3 (100%)	Two studies indicated that anxiolytics were more used in people with anxiety. <sup>43, 48</sup> More use of anxiolytics was related to less increase in anxiety over time. <sup>47</sup>
Antipsychotics	<sup>43†, 47†, 48†</sup>	+	3/3 (100%)	More use of antipsychotics was related to higher anxiety.
Psychotropic drugs	<sup>43†</sup>	+	1/1 (100%)	Use of psychotropic drugs was related to higher anxiety.
Antidepressants	<sup>43†, 47, 48†</sup>	+	2/3 (67%)	Use of more antidepressants was related to higher anxiety.
Physical health	<sup>43†, 47, 50†, 57</sup>	-	2/4 (50%)	Good physical health was related to less anxiety in PWD.

Factors	Studies	Association with Anxiety (If any applicable)	Percentage of studies reporting association	Comments
Activities of daily living	41, 43, 47, 50†, 59†	-	2/5 (40%)	Loss of skills on daily activities or more effort needed for daily activities made PWD feel anxious.
Instrumental activities of daily living	57	No association	0/1 (0%)	
Difficulty breathing	52	No association	0/1 (0%)	
Lifetime alcohol load	49	No association	0/1 (0%)	
Caffeine	66	No association	0/1 (0%)	
Cognitive enhancer	43, 47	No association	0/2 (0%)	
Hypnotics and sedatives	43, 47	No association	0/2 (0%)	
<b><u>Behavioral and Psychological</u></b>				
Depression	44†, 46†, 55†, 57†, 58†	+	5/5 (100%)	Depressive symptoms were related to higher anxiety in PWD.
Delusion	41†, 49†	+/-	2/2 (100%)	While one study reported negative relationship between delusion and anxiety, <sup>49</sup> the other study reported positive relationship between the two concepts. <sup>41</sup>
Psychosis	43†, 47†	+/-	2/2 (100%)	While one study reported that psychosis were related to more anxiety symptoms in PWD, <sup>43</sup> another study reported that higher psychosis at baseline predicted less increase in anxiety symptoms after 12 months. <sup>47</sup>
Affective symptoms	43†, 47†	+/-	2/2 (100%)	In a cross-sectional study, higher score of affective symptoms predicted higher anxiety. <sup>43</sup> However, in a longitudinal study, higher score of affective symptoms predicted less

Factors	Studies	Association with Anxiety (If any applicable)	Percentage of studies reporting association	Comments
Agitation	43†, 47†	+/-	2/2 (100%)	increase in anxiety symptoms at follow-up. <sup>47</sup> There was positive association between agitation and anxiety in one study. <sup>43</sup> However, it was reported that more agitation at baseline was related to less increase in anxiety after 12 months in another study. <sup>47</sup>
Arousal	43†, 47†	+	2/2 (100%)	Higher arousal was related to increased anxiety in PWD.
Disclosure of diagnosis of Alzheimer's disease	50†, 51†	+/-	2/2 (100%)	Diagnosis of dementia was a cause for anxiety in PWD in one study. <sup>50</sup> In a longitudinal study, <sup>51</sup> however, disclosure of diagnosis of Alzheimer's disease reduced the anxiety of PWD after three months.
Worry	52†, 58†	+	2/2 (100%)	More worry was related to more anxiety in PWD.
Feeling of losing control	59†	+	1/1 (100%)	Feeling of losing control was related to more anxiety in PWD.
Fatigue	52†	+	1/1 (100%)	People with generalized anxiety disorders had more moderate or severe fatigue symptoms than people without the disorder.
Apathy	49†	-	1/1 (100%)	Apathy was negatively related to higher anxiety in PWD.
Quality of life	57†	-	1/1 (100%)	Better quality of life was related to less anxiety in PWD.

Factors	Studies	Association with Anxiety (If any applicable)	Percentage of studies reporting association	Comments
Self-concept	64†	+	1/1 (100%)	Self-concept regarding family was in positive relationship with anxiety.
Embarrassment about memory problems	57†	+	1/1 (100%)	Embarrassment about memory problems predicted more anxiety in PWD.
Cluster A personality traits	67†	+	1/1 (100%)	People with Cluster A personality traits had higher score of anxiety symptoms.
Muscle tension	52†	+	1/1 (100%)	High muscle tension predicted generalized anxiety disorder in PWD.
Aberrant Motor Behavior	41†	+	1/1 (100%)	Aberrant motor behavior was positively related to more anxiety in PWD.
Irritability	41†, 52	+	1/2 (50%)	There was positive association between irritability and anxiety in PWD.
Behavioral problems	55†, 57	+	1/2 (50%)	High frequency of behavioral problems was related to more anxiety of PWD.
Sleep disturbance	52, 60†	+	1/2 (50%)	In the group of CDR 0.5, people with sleep disturbances had higher percentage of having anxiety.
Keyed up or on edge	52	No association	0/1 (0%)	
Restlessness	52	No association	0/1 (0%)	
Self-efficacy	57	No association	0/1 (0%)	
<b>Social</b>				
Separation from caregivers	41†	+	1/1 (100%)	There was positive association between separation from caregivers



Factors	Studies	Association with Anxiety (If any applicable)	Percentage of studies reporting association	Comments
Views about self in attachment	<sup>56†</sup>	-	1/1 (100%)	and anxiety in early onset Alzheimer's disease. Positive views about self in attachment predicted less anxiety in PWD.
Views about others in attachment	<sup>56†</sup>	-	1/1 (100%)	Positive views about others in attachment predicted less anxiety in PWD.
Social rejection	<sup>45†</sup>	+	1/1 (100%)	More social rejection was related to higher anxiety in female PWD.
Internalized shame	<sup>45†</sup>	-	1/1 (100%)	More internalized shame was related to less anxiety in PWD.
People's patronizing attitude	<sup>50†</sup>	+	1/1 (100%)	People's patronizing attitude caused feelings of anxiety in PWD.
Social isolation	<sup>45†</sup>	+	1/1 (100%)	More social isolation was related to more anxiety in dementia.
Social interaction (within-person)	<sup>54†</sup>	+	1/1 (100%)	Greater social interaction with people predicted more anxiety in PWD in within-person level.
Gender	<sup>41†, 43, 45, 47, 48†, 52†, 55-57</sup>	+/-	3/9 (33%)	While two studies reported that male was in association with the presence of anxiety in PWD, <sup>41, 52</sup> one study reported female was related to the presence of anxiety in PWD. <sup>48</sup>
Age	<sup>41, 43, 47, 48†, 52, 55, 56</sup>	-	1/7 (14%)	People who were younger tend to have more anxiety in dementia.
Marriage	<sup>43</sup>	No association	0/1 (0%)	
Race/Ethnicity	<sup>41, 52, 57</sup>	No association	0/3 (0%)	
Education	<sup>41, 43, 49, 52, 57</sup>	No association	0/5 (0%)	

<b>Factors</b>	<b>Studies</b>	<b>Association with Anxiety (If any applicable)</b>	<b>Percentage of studies reporting association</b>	<b>Comments</b>
Social interaction (between-person)	<sup>54</sup>	No association	0/1(0%)	
Relationship strain	<sup>57</sup>	No association	0/1 (0%)	

<sup>†</sup> Study which showed association with anxiety in PWD

+ Positive association

- Negative association

+/- Inconsistent association (positive and negative associations mixed)

**Table 2. 2. Factors associated with anxiety in dementia at the caregiver level**

Factors	Studies	Association with Anxiety (If any applicable)	Percentage of studies reporting association	Comments
Caregiver stress	44†	+	1/1 (100%)	Higher caregiver stress was related to higher anxiety of PWD.
Staff's reaction to behavior problems of dementia	55†	+	1/1 (100%)	More staff's reaction to resident behaviors was related to higher anxiety in PWD.
Competence of the staff	55†	-	1/1 (100%)	Higher competence predicted lower anxiety in PWD.
Caregiver and care-receiver relationship	57	No association	0/1 (0%)	
Age of the staff	55	No association	0/1 (0%)	
Views about self in attachment (among caregivers)	56	No association	0/1 (0%)	
Views about others in attachment (among caregivers)	56	No association	0/1 (0%)	
Qualification of staff (Nurse's aid or others)	55	No association	0/1 (0%)	
Job satisfaction of the staff	55	No association	0/1 (0%)	
Nursing home staff's time spent on direct patient care in hours each day	48	No association	0/1 (0%)	

† Study which showed association with anxiety in PWD

+ Positive association

- Negative association

**Table 2. 3. Factors associated with anxiety in dementia at the living environment level**

<b>Factors</b>	<b>Studies</b>	<b>Association with Anxiety (If any applicable)</b>	<b>Percentage of studies reporting association</b>	<b>Comments</b>
Time of day (afternoon)	54 <sup>†</sup>	+	1/1 (100%)	PWD showed more anxiety in the afternoon than in the morning.
Length of stay in residential care	43, 47 <sup>†</sup> , 48 <sup>†</sup>	-	2/3 (66%)	Shorter duration of institutionalization was related to anxiety in PWD who lived in nursing homes.
Type of assistive living	68	No association	0/1 (0%)	
Dementia Special Care Unit	48	No association	0/1 (0%)	
Patients per unit in nursing home	48	No association	0/1 (0%)	
Walking circuit present	48	No association	0/1 (0%)	

<sup>†</sup> Study which showed association with anxiety in PWD

+ Positive association

- Negative association

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## CHAPTER 3: PAPER 2

### THE RELATIONSHIP BETWEEN SOCIAL ISOLATION AND ANXIETY IN PEOPLE LIVING WITH DEMENTIA IN THE UNITED STATES

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#### ABSTRACT

**Objectives:** While social isolation is a well-known risk factor for the development of dementia, social isolation among older adults with dementia is understudied. The purpose of this study is to examine the relationship between social isolation and anxiety in people living with dementia (PLWD) in the United States.

**Methods/Design:** Secondary data analyses were conducted using the National Social Life, Health, and Aging Project Wave 2 (2010-2011) dataset which includes a nationally representative sample of American older adults living at home. A total of 1,343 people who had probable dementia measured by a Montreal Cognitive Assessment score of 22 or less were selected. Anxiety was measured using the anxiety measure of Hospital Anxiety and Depression Scale (HADS-A) and social isolation was measured using Perceived Social Isolation Scale. A weighted multivariable linear regression analysis and weighted F tests were used to examine the relationship between social isolation and anxiety.

**Results:** We observed that greater social isolation was related to increased anxiety in PLWD (Coefficients=0.7242,  $t=2.51$ ,  $p=0.015$ ), adjusting for cognitive function, race, pain, depression, activities of daily living, and instrumental activities of daily living. Weighted F tests showed that persons with clinically significant anxiety ( $HADS-A \geq 8$ ) had higher levels of loneliness, including

feeling a lack of companionship, feeling left out, and greater social isolation.

**Conclusions:** The results of our study suggest that PLWD can feel social isolation and it may contribute to their anxiety. An effective non-pharmacological intervention program which can lessen social isolation is needed for the wellbeing of PLWD.

**Key words:** Social needs, loneliness, dementia, behavioral and psychological symptoms of dementia (BPSD), neuropsychological symptoms

### **Key points**

- 24.9% of the participants with dementia who lived at home presented with clinically significant anxiety (HADS-A $\geq$ 8).
- Greater social isolation was related to increased anxiety in people living with dementia.
- The group with clinically significant anxiety (HADS-A $\geq$ 8) had greater loneliness compared to the group without anxiety.

## INTRODUCTION

In 2021, there are 6.2 million people over the age of 65 living with dementia in the United States, which means 1 out of 9 Americans aged 65 and older has dementia.<sup>1</sup> The number of new cases of dementia is estimated to double by 2050 as Baby Boomers age.<sup>1</sup> Dementia is characterized by a chronic, progressive loss in multiple cognitive abilities, leading to many functional disabilities.<sup>2</sup> Many people living with dementia (PLWD) quit their jobs upon diagnoses and withdraw from their hobbies, sports, or social activities.<sup>1</sup> Gradual functional decline that people living with dementia (PLWD) experience can also hinder active participation in social activities. For example, difficulty with driving a car or using a telephone may make it difficult for PLWD to engage in social activities.<sup>3,4</sup> In fact, PLWD report less frequent contact with their family and friends.<sup>5,6</sup> These indicate that PLWD are at increased risk for social isolation.<sup>7,8</sup>

Social isolation is defined as the “subjective experience of a shortfall in one’s social resources such as companionship and support.”<sup>9</sup> Previous studies have demonstrated socially and mentally active lifestyles may be protective against the development of dementia and that individuals who are socially isolated are more likely to develop dementia.<sup>10-12</sup> Yet, there is lack of research attention to social isolation among people who are experiencing cognitive impairment. In a qualitative study which examined older adults' perspectives on the components of healthy or successful aging, older adults reported that social engagement, sense of connections, or maintaining social relationships are key components for successful aging.<sup>13</sup> It is therefore likely that social engagement remains important for PLWD regardless of their impaired cognition.

Feeling socially isolated from society is known to be related to anxiety in older adults without dementia.<sup>14-16</sup> Indeed, low social engagement and poor perceived social support are known to be related to anxiety in older adults living in nursing homes and other residential facilities.<sup>14</sup> Poor social support<sup>15</sup> or participating in fewer leisure activities<sup>16</sup> are also related to

increased anxiety in cognitively intact older adults. However, there is lack of information available in the literature how social isolation is related to psychological wellbeing of PLWD.

Assessing the needs of PLWD and meeting the needs of PLWD are important in dementia care.<sup>17,18</sup> According to literature, unmet needs of PLWD can lead to behavioral and psychological symptoms such as anxiety, and it is possible that unmet social needs can lead to psychological symptoms such as anxiety.<sup>17,18</sup> However, there is a lack of empirical studies that tested this relationship. Because PLWD are at risk for social isolation,<sup>5,6,19</sup> it is important to examine social isolation in this population, especially as it relates to psychological outcomes such as anxiety. Therefore, this study aims to examine the influence of social isolation on anxiety in PLWD.

### **Theoretical Framework**

The Stress Process Model for the Individuals with Dementia<sup>20</sup> guided this study. There are stressors that lead to anxiety, depression, or poor quality of life in PLWD.<sup>20</sup> Primary stressors such as cognitive status or functional status affect secondary strains including family role strain, job role strain, or social role strain.<sup>20</sup> According to the Stress Process Model for the Individuals with Dementia, the primary stressors and secondary strains overall can influence wellbeing of PLWD.<sup>20</sup> In our study, we conceptualized level of cognitive function as a primary stressor; social isolation as a secondary strain; and anxiety as an outcome (Figure 3.1). Our hypothesis is that greater social isolation results in increased anxiety in PLWD.

## **METHODS**

### **Participants**

We analyzed secondary data collected from, the National Social Life, Health, and Aging Project (NSHAP) Wave 2 to examine the relationship between social isolation and anxiety in



PLWD.<sup>21</sup> The NSHAP studied general health and social factors to understand the wellbeing of nationally representative American older adults living at home, and the data was collected from August 2010 through May 2011 using interviews and questionnaires.<sup>22</sup> More information about the design of Wave 2 can be found here.<sup>23</sup> Participants who were not able to complete the interview because of physical or cognitive limitations were not included in the study. A total of 3,377 respondents originally participated in Wave 2. In this study, we included 1,343 persons who were 65 years and older and probable dementia measured by a Montreal Cognitive Assessment (MoCA) score of 22 or less. The data was obtained with permission from the National Opinion Research Center and Principal Investigators at the University of Chicago via National Archive of Computerized Data on Aging. This study was approved by the Institutional Review Board at the University of Pennsylvania (IRB protocol number: 842535).

## **Measures**

**Cognitive function.** We used the Montreal Cognitive Assessment (MoCA) as an inclusion criterion for this study. The MoCA was developed to screen mild cognitive impairment and dementia in older adults.<sup>24</sup> The MoCA has good reliability with Cronbach's  $\alpha$  of 0.83.<sup>24</sup> In the NSHAP Wave 2, a survey adaptation of the Montreal Cognitive Assessment (MoCA-SA) was used.<sup>25</sup> The MoCA-SA was developed specifically for NSHAP to help non-medically trained personnel to administer surveys in a home setting.<sup>25</sup> The 18-item MoCA-SA is highly correlated with the original MoCA and demonstrates good internal reliability with Cronbach's  $\alpha$  of 0.76.<sup>26</sup> The MoCA-SA score range from 0-20 but the following equation was used to convert MoCA-SA to the original MoCA scale:  $MoCA = 6.83 + (1.14 \times MoCA-SA)$ .<sup>25,26</sup> Lower scores indicate poor cognitive function. A cutoff score of 22 or less was used to indicate PLWD.<sup>27</sup> In the literature, cutoff scores for cognitive impairment are controversial ranging from 22 to 26.<sup>24,27-29</sup> We utilized

the cutoff score of 22 or less based on the studies which used community sample,<sup>27,28</sup> and this cutoff score is also consistent with previous studies which used NSHAP data.<sup>7,30</sup>

**Social Isolation.** Social isolation was measured by Perceived Social Isolation Scale.<sup>9,31</sup> This scale consists of two dimensions including loneliness and perceived lack of social support from family, friends, and spouse or current partner. The nine self-reported items were measured with 3-point Likert scale. Each item was standardized and the average of nine items was used to indicate social isolation.<sup>9,31</sup> Higher scores indicated greater social isolation. The scale has acceptable level of reliability with Cronbach's  $\alpha$  of 0.70.<sup>31</sup>

**Anxiety.** Anxiety was measured with the Hospital Anxiety Depression Scale (HADS).<sup>32</sup> There are fourteen items in the HADS, with seven items measuring anxiety symptoms and the seven remaining items measuring depressive symptoms. In the current study, only the anxiety measure (HADS-A) was used, and all items were self-reported. A 4-point Likert scale from 0 to 3 was used with possible scores range from 0 to 21, and higher scores indicated more anxiety. The HADS-A has high reliability with Cronbach's  $\alpha$  of 0.82<sup>33</sup> and is widely used with PLWD.<sup>34-36</sup>

**Covariates.** Known confounders of anxiety were included in the analysis.<sup>37-42</sup> Severity of cognitive impairment, race, pain, depression, activities of daily living, and instrumental activities of daily living were included as covariates. Cognitive function was measured by the MoCA by the interviewer of the NSHAP study. Race was self-reported. Pain was measured by the question, "In the past four weeks, have you had any pain?" and the answer was either "yes" or "no." Depression was measured with the 11-item Center for Epidemiologic Studies Depression Scale with higher scores indicating more severe depression. 7-item Activities of Daily Living and 8-

item Instrumental Activities of Daily Living were used, and higher scores indicated better physical function.

### **Data analysis**

A person-level weight was provided by NSHAP Wave 2 which adjusted for differential probabilities of selection and non-response. This weight was applied to all statistical analysis in this study except descriptive data analyses.

Descriptive data analyses including the means, standard deviations, and percentages were obtained to describe the characteristics of the participants (see Table 3.1). To examine the associations between the covariates and anxiety, we obtained bivariate correlation coefficients and conducted multivariable weighted F tests. We first calculated a weighted correlation coefficient to examine the relationship between social isolation and anxiety. Next, we performed a weighted regression analysis for anxiety controlling for covariates. All analyses were performed using the Stata BE 17. The level of statistical significance was set at  $\alpha = 0.05$ . Bonferroni approach was used to adjust for multiple comparison when evaluating items of the social isolation scale.

## **RESULTS**

Table 3.1 shows the characteristics of the participants in this study. The unweighted mean age was  $76.3 \pm 7.0$  (Min-Max: 65-93). Most of the study participants were female (51.8%), white (64.8%), and not employed (87.9%). All of the study participants had a MoCA score of less than 22 with the unweighted mean of  $17.9 \pm 3.4$  (Min-Max: 6.8-21.65). The unweighted mean of anxiety score by HADS-A was  $5.1 \pm 3.7$  (Min-Max: 0-19), and 24.9% of the participants had clinically significant anxiety ( $\text{HADS-A} \geq 8$ ).<sup>43</sup>

We evaluated the relationships between the covariates and anxiety using weighted F tests and Z-test for correlation coefficients. The weighted F tests for the categorical variables showed that the weighted means of anxiety scores differed significantly by race ( $F=3.13, p=0.03$ ) and pain ( $F=26.55, p<0.001$ ). Weighted Z-test for correlation coefficients for continuous variables showed that poor cognitive function ( $r=-0.0684, p=0.025$ ), greater depressive symptoms ( $r=0.3437, p<0.001$ ), difficulty with activities of daily living ( $r=-0.1414, p<0.001$ ), and instrumental activities of daily living ( $r=-0.1514, p<0.001$ ) were significantly related to increased anxiety. Greater social isolation was related to increased anxiety in PLWD ( $r=0.1745, p<0.001$ ).

Table 3.2 describes the results of weighted multivariable linear regression analyses on anxiety in PLWD. The model showed that greater social isolation (Estimate=0.7242,  $t=2.51, p=0.015$ ) was related to increased anxiety in PLWD after adjusting for the covariates (i.e., cognitive function, race, pain, depression, activities of daily living, and instrumental activities of daily living) ( $R^2 = 0.15, F = 20.35, p < 0.001$ ). Multicollinearity was checked with variance inflation factors, and no multicollinearity was detected (Table 3.3).

We conducted additional analyses to assess which aspects of the social isolation scale was related to anxiety. Using the cutoff score of 8 for HADS-A,<sup>43</sup> we dichotomized study participants into two groups: the presence of clinically significant anxiety and no clinically significant anxiety. We then compared the two groups using weighted F tests for each item of the social isolation scale (Table 3.4). Compared to the group without anxiety, the group with clinically significant anxiety showed higher scores on feeling a lack of companionship ( $F=10.86, p=0.002$ ), feeling left out ( $F=13.25, p<0.001$ ), and feeling social isolation from others ( $F=19.28, p<0.001$ ). As shown in Table 3.4, all these items were from the loneliness dimension of the social isolation scale.

## DISCUSSION

While social isolation among PLWD and its psychological impact are understudied, the result of this study suggests that social isolation is closely related to anxiety in PLWD. According to an integrative review of factors associated with anxiety in PLWD, while there are numerous physical and psychological factors associated with anxiety, such as pain or depression, only limited information is available on social factors.<sup>44</sup> This study fills that gap in the literature by examining the relationship between social isolation and anxiety in PLWD using a nationally representative sample.

As hypothesized, when PLWD felt socially isolated, they were more likely to experience increased anxiety. The results are in line with previous studies on older adults with normal cognition. Older adults felt more anxiety when they received lower levels of social support,<sup>15</sup> and older adults who had fewer leisure activities were more likely to experience increased anxiety.<sup>16</sup> Our study showed that social isolation and unmet social needs contribute to anxiety even in those with cognitive impairment.

Social stigma and perceived social rejection among PLWD can contribute to social isolation and anxiety.<sup>38</sup> PLWD are known to experience less frequent contact with their family and friends because of their impaired cognition.<sup>5,6</sup> In a qualitative study, PLWD reported social embarrassment and emotional difficulties when others treated them differently because they had dementia.<sup>5</sup> PLWD also reported that they felt anxious when they experienced patronizing attitudes from other people around them.<sup>40</sup> Social stigma about dementia among the public can provoke social isolation and anxiety among PLWD. Therefore, it is essential to educate the public to reduce social stigma on PLWD.

Previous works suggest that in later life, the quality of the social relationship is more important than the size of the social network.<sup>45,46</sup> As the size of social networks tends to shrink in PLWD,<sup>7,8</sup> it is especially important for those individuals to maintain a meaningful relationship

within the social network. Indeed, a perceived positive relationship between PLWD and family caregiver is also known to be protective against anxiety in PLWD.<sup>36</sup> We suggest that health care professionals, family, and friends of PLWD pay greater attention to spending good quality of time with PLWD and to maintaining positive relationships with PLWD.

Importantly, it may be inappropriate to merely increase social interaction in PLWD without taking personality preferences or the quality of these interactions into account. Prior work has shown that high levels of social interaction may cause more anxiety in some PLWD.<sup>47</sup> Indeed, one's comfort level for social interaction may differ by one's personality. Therefore, approaches to meet a PLWD's social needs should be personalized. For example, if a person has an outgoing personality and accustomed to many social activities prior to cognitive decline, fostering an environment where the person can continuously enjoy a number of social activities may help to reduce the person's social isolation and anxiety. On the other hand, if a person tends to prefer a smaller social network, building an environment where the person can spend good quality time with close friends and family would help them to improve perceived social isolation and anxiety level.

There are a few limitations for this study. As this study used a secondary data, we were unable to determine duration of cognitive impairment of an individual or history of formal diagnoses of dementia which may be important covariates for anxiety. Although we were unable to include this information in the current study, we tried to control for severity of cognitive impairment when examining the relationship between social isolation and anxiety. Future studies addressing the duration of cognitive impairment or whether a formal diagnosis has been made may be helpful to understand the relationship between social isolation and anxiety. Because this study is a cross-sectionally designed study, it is difficult to determine causal relationships between social isolation and anxiety; therefore, a longitudinal study is needed in the future to further examine how cognitive impairment, social isolation, and anxiety are related over time.

Anxiety is not only associated with poor quality of life in PLWD,<sup>48,49</sup> but also it is associated with increased caregiver burden among family members.<sup>48,50</sup> In this study, we observed that increased social isolation was related to increased anxiety among PLWD. When we conducted additional analyses to assess which aspect of the social isolation scale was better related to anxiety, people with anxiety had significantly higher scores on loneliness dimension of the social isolation scale. This may indicate that perception of loneliness is highly associated with anxiety. As non-pharmacological interventions such as group activities or shared activities are effective to improve loneliness in older adults,<sup>51</sup> similar non-pharmacological interventions to reduce loneliness should be developed and applied to PLWD.

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## **DATA AVAILABILITY STATEMENT**

The data that support the findings of this study are available from the National Archive of Computerized Data on Aging located within the Inter-University Consortium for Political and Social Research upon request.

## **CONFLICT OF INTEREST**

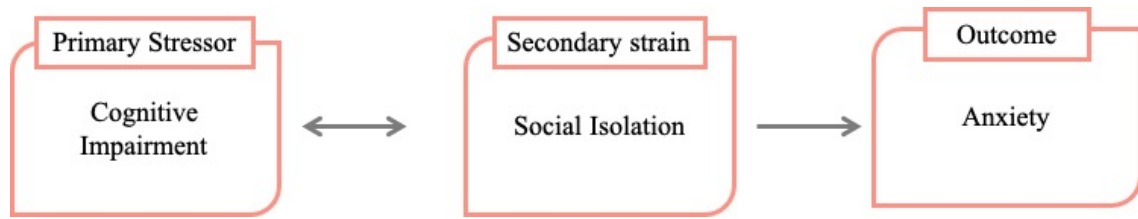
The authors declare they have no conflict of interest.

## **ETHICS APPROVAL STATEMENT**

This study was approved by the Institutional Review Board at the University of Pennsylvania (IRB protocol number: 842535).



**Figure 3. 1. Conceptual framework of the study**



Note: This conceptual framework was adapted from Judge et al. (2010).<sup>20</sup>

**Table 3. 1. Characteristics of the Participants (n=1,343)<sup>†</sup>**

<b>Characteristics</b>	<b>Mean±SD or n (%)</b>	<b>Min-Max</b>
Age	76.3±7.0	65-93
Sex		
Male	647 (48.2)	
Female	696 (51.8)	
Education		
Less than High School	487 (36.3)	
High School Diploma/Equivalency	374 (27.9)	
Vocational Certificate or Some College	351 (26.1)	
Bachelors or More	131 (9.8)	
Race		
White / Caucasian	865 (64.8)	
Black / African American	327 (24.5)	
American Indian / Alaskan Native / Asian / Pacific Islander	28 (2.1)	
Other	116 (8.7)	
Employment Status		
Employed	159 (11.8)	
Not Employed	1,180 (87.9)	
Pain		
Pain in Past 4 Weeks	596 (44.4)	
No Pain in Past 4 Weeks	306 (22.8)	
Depression	5.2±4.7	0-25
Activities of Daily Living	5.8±1.8	0-7
Instrumental Activities of Daily Living	6.2±2.0	0-8
Cognitive Function (MoCA)	17.9±3.4	6.8-21.65
Social Isolation	0.003±0.6	-1.3-2.2
Anxiety	5.1±3.7	0-19
Anxiety (HADS-A ≥8)	260 (24.9)	
No Anxiety (HADS-A <8)	783 (75.1)	

<sup>†</sup>The unweighted total number of participants were 1,343. Data in this table are unweighted. HADS-A=Hospital Anxiety and Depression Scale-Anxiety; MoCA= Montreal Cognitive Assessment

**Table 3. 2. Weighted Multivariable Linear Regression on Anxiety in People with Cognitive Impairment (n=856)**

		<b>Coefficients</b>	<b>SE</b>	<b>t</b>	<b>p</b>
<i>Independent variable</i>	Social Isolation	0.7242	0.2886	2.51	<b>0.015</b>
<i>Covariates</i>	Cognitive Function	0.0083	0.0418	0.20	0.843
	Race	-0.2531	0.1805	-1.40	0.167
	Pain	0.9729	0.3067	3.17	0.003
	Depression	0.2411	0.0433	5.56	<0.001
	Activities of Daily Living	0.0014	0.0860	0.02	0.987
	Instrumental Activities of Daily Living	-0.0472	0.1087	-0.43	0.666
	Constant	3.7030	1.2073	3.07	0.003
$R^2 = 0.15, F = 20.35, p < 0.001$					

**Table 3. 3. Assessment of Multicollinearity using Variance Inflation Factor (VIF)**

	Variance Inflation Factor
Social Isolation	1.12
Cognitive Function	1.19
Race	1.07
Pain	1.07
Activities of Daily Living	1.81
Instrumental Activities of Daily Living	1.89
Depression	1.26
Mean VIF	1.34

**Table 3. 4. Weighted Means of Social Isolation Scale by Anxiety Group**

<b>Perceived Social Isolation</b>	<b>Anxiety (n=260)</b>	<b>No anxiety (n=783)</b>	<b>F</b>	<b>p</b>
<b>Loneliness</b> (1=hardly ever or never, 2=some of the time, 3=often)				
1. How often do you feel that you lack companionship?	1.71	1.50	10.86	<b>0.002</b>
2. How often do you feel left out?	1.56	1.36	13.25	<b>&lt;0.001</b>
3. How often do you feel socially isolated from others?	1.54	1.31	19.28	<b>&lt;0.001</b>
<b>Perceived Social Support</b> (1=often, 2=some of the time, 3=hardly ever or never)				
4. How often can you open up to members of your family?	1.70	1.64	0.88	0.352
5. How often can you rely on members of your family?	1.47	1.42	0.66	0.419
6. How often can you open up to your friends?	2.03	2.12	1.92	0.173
7. How often can you rely on your friends?	1.82	1.88	0.94	0.337
8. How often can you open up to your spouse or partner?	1.32	1.29	0.30	0.587
9. How often can you rely on your spouse or partner?	1.18	1.19	-.11	0.741

Note: Anxiety group was defined with Hospital Anxiety and Depression Scale-Anxiety cut-off scores of 8. Adjusted Wald tests were conducted.

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## CHAPTER 4: PAPER 3

### COGNITIVE IMPAIRMENT, SOCIAL ISOLATION, AND ANXIETY IN OLDER ADULTS: A 5-YEAR LONGITUDINAL STUDY

Prepared according to guidelines for submission to *International Psychogeriatrics*.

#### ABSTRACT

**Objectives:** (1) To compare the level of social isolation and anxiety among older adults who developed dementia and mild cognitive impairment (MCI) and those who maintained normal cognitive function over 5 years; and (2) to determine if cognitive impairment moderates the relationship between changes in social isolation and changes in anxiety over 5 years.

**Design:** A secondary data analysis using a 5-year longitudinal data (National Social Life, Health, and Aging Project (NSHAP): Wave 2 (2010-2011) and Wave 3 (2015-2016)).

**Setting:** Older adults living at home in the United States.

**Participants:** Using Wave 2 and 3, the participants were categorized into three groups: participants who developed dementia over 5 years ( $n=56$ ), developed MCI ( $n=226$ ), and maintained normal cognitive function ( $n=837$ ).

**Measurements:** Montreal Cognitive Assessment, Hospital Anxiety and Depression Scale, and Perceived Social Isolation Scale were used. We performed adjusted Wald tests and weighted linear regression analyses with a group interaction.

**Results:** At the 5-year follow up, there were statistically significant differences in social isolation between the three groups ( $F=3.37$ ,  $p=0.043$ ). Persons who developed dementia and MCI tended to endorse more social isolation. Our regression analyses showed that increased social isolation over

time was related to increased anxiety over 5 years regardless of cognitive status after controlling for depression and activities of daily living (Estimate=0.725,  $p=0.017$ ).

**Conclusions:** The relationship between increased social isolation and increased anxiety was a universal phenomenon regardless of cognitive status. Non-pharmacological interventions targeting both people with or without cognitive impairment are needed to lessen social isolation and anxiety.

**Keywords:** Social isolation, loneliness, anxiety, cognitive impairment, dementia

**Words limit:** 250 / 250 words

## INTRODUCTION

Anxiety, which presents with worry, nervousness, muscle tension, irritability, restlessness, or difficulty concentrating,<sup>1</sup> is extremely common in older adults around the world.<sup>2</sup> It is reported that up to 52.3% of older adults living at home experience anxiety.<sup>3</sup> Anxiety in older adults is related to poor health outcomes such as poor quality of life,<sup>4</sup> increased depression,<sup>5</sup> decreased executive function,<sup>6</sup> and higher mortality rates.<sup>7</sup> A leading factor associated with anxiety in older adults is loneliness or social isolation.<sup>8</sup> Because emotionally meaningful social relationships becomes important as people age,<sup>9</sup> unmet social needs may lead to anxiety in older adults. Indeed, previous literature suggests that negative partner relationships,<sup>10</sup> poor social support,<sup>11</sup> and fewer social activities<sup>12</sup> contribute to anxiety in older adults.

What remains unknown is the relationship between social isolation and anxiety in older adults with cognitive impairment- such as dementia or mild cognitive impairment (MCI). Anxiety is common and distressing in older adults with cognitive impairment.<sup>13</sup> Up to 71% of older adults with cognitive impairment experience anxiety.<sup>14</sup> Not only do people with cognitive impairment experience poor quality of life when anxiety is present,<sup>15</sup> their family caregivers also experience more stress.<sup>15,16</sup> In addition, anxiety increases the risk of nursing home placement in people with cognitive impairment.<sup>17</sup>

It can be difficult to identify underlying causes of anxiety in older adults with cognitive impairment due to memory impairment and difficulties in logically explaining their feelings.<sup>14</sup> According to an integrative review on factors associated with anxiety in older adults with cognitive impairment,<sup>18</sup> while there were many physical and psychological factors associated with anxiety, there was limited information on the relationship between social factors and anxiety. Older adults with cognitive impairment are at increased risk for social isolation, as they progressively lose their ability to maintain social roles.<sup>19</sup> However, only a few existing studies have examined the relationship between social factors and anxiety among people with cognitive

impairment.<sup>20,21</sup> Similar to older adults with normal cognition, it is possible that older adults with cognitive impairment can experience anxiety when socially isolated. It is also possible that change in cognition over time can influence one's social isolation and anxiety.

The aims of this study are: (1) To compare social isolation and anxiety among people who develop dementia and MCI and those who maintained normal cognition over a 5-year period; and (2) to determine if cognitive impairment moderates the relationship between changes in social isolation and changes in anxiety. We hypothesized that people who developed dementia or MCI would experience increased social isolation and anxiety at the 5-year follow up compared to those who maintained with normal cognitive function. It was also hypothesized that there would be differences in the groups in terms of the strength of the relationship between changes in social isolation and changes in anxiety.

### **Conceptual framework**

The conceptual framework of this study is shown in Figure 4.1. The proposed conceptual framework is adapted from Stress Process Model for the Individuals with Dementia,<sup>22</sup> which suggests that there are various levels of stressors that impact wellbeing. Primary stressors included cognitive status or functional status and secondary strains included family role strain, job role strain, or social role strain. The primary stressors and secondary strains overall are known to influence wellbeing of an individual.<sup>22</sup> In this study, cognitive change was used as a primary stressor; social isolation was used as a secondary strain; and anxiety was used as an outcome. Based on the Stress Process Model for the Individuals with Dementia, cognitive impairment is considered as an objective stressor. As a direct result of cognitive impairment, people may experience changes in their social roles as well as their relationships to others. These changes can lead to perceived social isolation which may result in one's psychological and emotional distress such as anxiety. Since the severity of cognitive impairment may impact the relationship between

social isolation and anxiety, this study also examined if there is a moderating effect of cognitive impairment on the relationship between social isolation and anxiety.

## **METHODS**

### **Participants**

This study analyzed data collected from national studies called the National Social Life, Health, and Aging Project (NSHAP): Wave 2 (2010-2011) and Wave 3 (2015-2016). The NSHAP studied general health and social factors to understand the wellbeing of nationally representative American older adults living at home.<sup>23</sup> The data for NSHAP Wave 2 were collected from August 2010 through May 2011, and the data for NSHAP Wave 3 were collected from September 2015 through November 2016. The data were collected using interviews and questionnaires and each wave had one data time point.

The NSHAP Wave 3 (2015-2016) included returning participants from the NSHAP Wave 2 (2010-2011) and a new cohort. Since this study aimed to investigate cognitive changes from Wave 2 to Wave 3, only the returning cohort (i.e., people who both participated in Wave 2 and Wave 3) was used. The returning cohort had two time points: baseline (Wave 2) and 5 years after baseline (Wave 3). Figure 4.2 indicates the flowchart of the study participants selection. Among 4,777 participants who participated in Wave 3, we intentionally selected 1,119 individuals who were at the age of 65 years old and older and had normal cognition at baseline in order to examine how cognitive decline over time influence social isolation and anxiety. This study was approved from the Institutional Review Board at the University of Pennsylvania (IRB protocol number: 842535).

### **Measurements**

**Cognition.** The Montreal Cognitive Assessment (MoCA)<sup>24</sup> was used to measure cognition in older adults to detect cognitive impairment. The NSHAP Wave 2 and Wave 3 used the Montreal Cognitive Assessment-Survey Adaptation (MoCA-SA) which was designed for administration by non-medical personnel.<sup>25</sup> The MoCA-SA consists of eighteen items, and it is highly correlated to the original MoCA scale and had good internal consistency (Cronbach's  $\alpha=0.76$ ).<sup>26</sup> As previously described, the MoCA-SA has a different number of items and total score, therefore the following equation was used to convert MoCA-SA to original MoCA ( $\text{MoCA} = 6.83 + (1.14 \times \text{MoCA-SA})$ ).<sup>25,26</sup> Suggested cutoff scores of MoCA for cognitive impairment range between 22 and 26.<sup>24,27-29</sup> As community samples tend to have lower cutoff scores<sup>28,29</sup> compared to a clinic-based sample,<sup>24,27</sup> the current study utilized the cutoff score that was based on community sample. Therefore, a MoCA score greater than 22 points was considered normal cognition and a MoCA score of 22 or below was considered cognitive impairment.<sup>29,30</sup> For the purpose of this current study, normal cognition was defined as  $\text{MoCA} > 22$ ; MCI was defined as MoCA score between 18 and 22 inclusive; and dementia was defined as a  $\text{MoCA} < 18$ .

In this study, the participants whose cognitive function was normal in Wave 2 were categorized into three groups depending on their MoCA score at Wave 3 follow up visit which occurred 5 years after their baseline visit: (1) participants who developed dementia ( $n=56$ ), (2) participants who developed MCI ( $n=226$ ), and (3) participants who maintained normal cognitive function ( $n=837$ ). In order to classify these three groups, changes in cognition score were used. For example, if a person with normal cognition in Wave 2 showed normal cognition again in Wave 3, this person was considered to remain cognitively normal over 5 years. If a person with normal cognition ( $\text{MoCA} > 22$ ) in Wave 2 showed MCI ( $\text{MoCA}$  between 18-22) in Wave 3, this person was considered to develop MCI over 5 years. If a person with normal cognition ( $\text{MoCA} > 22$ ) in Wave 2 showed dementia ( $\text{MoCA} < 18$ ) in Wave 3, this person was considered to developed dementia over 5 years.



**Anxiety.** The Hospital Anxiety and Depression Scale (HADS) was used to measure anxiety symptoms.<sup>31</sup> The HADS has fourteen items, seven items measuring anxiety symptoms and the other seven items measuring depression. The anxiety measure (HADS-A) was only used in this study. Each item has a 4-point Likert scale, and the possible total scores range from 0 to 21. The higher score of the HADS-A indicated severe anxiety. The HADS-A has established a high reliability with a Cronbach's  $\alpha$  value of 0.82 in older adults.<sup>32</sup> This scale has been frequently used in people with cognitive impairment.<sup>33-35</sup>

In order to measure the changes of anxiety between Wave 2 and Wave 3, the anxiety score of Wave 2 was subtracted from the anxiety score of Wave 3 (Wave 3 – Wave 2). A positive value indicated that the person had a worsening anxiety over 5-years.

**Social Isolation.** Perceived Social Isolation Scale was used to measure social isolation.<sup>36,37</sup> There are nine items examining loneliness and perceived lack of social support from family, friends, and spouse or current partner. Each item is scored using 3-point Likert scale. Each item was standardized, and the mean of the nine items were used to indicate social isolation.<sup>36,37</sup> A higher score indicated more social isolation. Internal consistency of the scale was acceptable when it was developed (Cronbach's  $\alpha=0.70$ ).<sup>37</sup>

To measure the change in social isolation between Wave 2 and Wave 3, the score of Wave 2 was subtracted from the score of Wave 3 (Perceived social isolation score of Wave 3 – Perceived social isolation score Wave 2). A positive value indicated that the person had a worsening in perceived social isolation over 5-years.

**Covariates.** Covariates included depression and activities of daily living. Covariates were selected based on their known relationships to anxiety.<sup>38-41</sup> Depression was measured with Center

for Epidemiologic Studies Depression Scale. This 11-item scale has 4-point Likert scale, and the total score ranges from 0 to 33, with the higher score indicating severe depression.<sup>42</sup> Activities of daily living was measured with 7-item scale with the higher scores demonstrating better functional independence.

### **Data Analysis**

Both NSHAP Wave 2 and Wave 3 have provided person-level weight which adjusts for differential probabilities of selection and non-response. In order to ensure representativeness, this study used the weights to all statistical analysis except descriptive analyses.

A descriptive data analysis was conducted by calculating the means, standard deviations, and frequency distributions to illustrate the characteristics of the participants. Adjusted Wald tests were used to compare the level of social isolation and anxiety among people who developed dementia or MCI and those who did not (defined by MoCA cutoffs described above) between the initial assessment in Wave 2 and 5-years later in Wave 3. To examine the moderating effect of cognitive impairment on the relationship between changes in social isolation and anxiety at a 5-year interval, this study used a weighted linear regression analysis with a interaction term between cognitive group and social isolation in the model.

Before performing linear regression analysis, we calculated correlation coefficients between the independent variable, covariates, and the dependent variable. Only variables with statistically significant correlation among them were included in the final regression model. Multicollinearity between the independent variables and covariates were checked. All analysis was performed using the Stata BE 17. The level of statistical significance was set at  $p < 0.05$ .

## RESULTS

Table 4.1 describes the characteristics of the study participants. The mean age of the participants was  $72.4 \pm 5.8$ . Most participants were female ( $n=614$ , 54.9%), white or Caucasian ( $n=989$ , 88.6%), and not employed ( $n=842$ , 75.3%). Among 1,119 participants who were cognitively intact in Wave 2, 74.8% of the participant remained cognitively intact in Wave 3 ( $n=837$ ), 20.2% of the participants were categorized as MCI ( $n=226$ ), and 5.0% of the participants were categorized as dementia ( $n=56$ ) (Table 4.2).

The weighted means of social isolation and anxiety were compared among three cognitive groups: (1) people who developed dementia; (2) people who developed MCI; and (3) people who maintained normal cognition over 5 years. At the 5-year follow up, there were statistically significant differences in social isolation in between the three groups ( $F=3.37$ ,  $p=0.043$ ); whereby people who developed dementia and MCI tended to have higher ratings of social isolation. However, there were no differences between the anxiety scores of the three groups ( $F=1.67$ ,  $p=0.199$ ) (Table 4.3).

The second aim of the study was to determine if cognitive function moderates the relationship between changes in social isolation and changes in anxiety. We first conducted a weighted univariate regression analysis to determine if increased social isolation over a 5-year period was related to increased anxiety over the 5-year period. However, changes in social isolation were not related to changes in anxiety (Coefficient=0.463, SE=0.340,  $t=1.36$ ,  $p=0.179$ ). Because the Perceived Social Isolation Scale uses the mean of nine standardized items, the changes in mean may not represent the overall trend of change of the nine items. Therefore, we evaluated the change score for each item to examine if the mean value represents the overall trend of the nine items. As shown in Table 4.4, while the scores for item 1 and item 4 of the social isolation scale decreased over the 5-year period, the scores of the remaining items increased over the 5-year period. Therefore, when averaging the nine items of the social isolation scale, it is

likely that the mean value does not represent the overall trend of the nine items in the Perceived Social Isolation Scale. Therefore, we decided to analyze each item separately to examine which aspects of changes in social isolation was related to changes in anxiety.

Weighted univariate regression analyses on changes in anxiety were conducted using changes of individual items of the Perceived Social Isolation Scale. Among the nine items, increased feeling of being left out was marginally related to increased anxiety over five years (Coefficient= 0.613, SE=0.310,  $t=1.98$ ,  $p=0.053$ ), and increased feeling of social isolation was significantly related to increased anxiety over five years (Coefficient= 0.750, SE=0.262,  $t=2.86$ ,  $p=0.006$ ). Based on these results, we decided to separately use changes of these two items as changes in social isolation as they were related to the dependent variable, changes in anxiety.

Before we conducted the final regression analysis, we examined whether baseline characteristics were related to changes in anxiety using correlation coefficients test. Baseline depression was related to decreased anxiety over five years ( $r=-0.110$ ,  $p=0.041$ ), and greater independence in activities of daily living at baseline was related to decreased anxiety over five years ( $r=-0.091$ ,  $p=0.037$ ). We therefore included depression and activities of daily living in the final regression analysis as covariates.

Table 4.5 shows the results of the weighted multivariable linear regression analysis on changes in anxiety. Increased feeling of social isolation over five years was related to increased feeling of anxiety over five years after controlling for covariates (Coefficient=0.725, SE=0.293,  $t=2.47$ ,  $p=0.017$ ). There were no statistically significant interactions for the cognitive groups. Multicollinearity was assessed using variance inflation factor, but all values were under 10, indicating no multicollinearity (Table 4.6).

## DISCUSSION

In this study, we examined the relationship between cognitive impairment, social isolation, and anxiety. First, we compared social isolation and anxiety among people who developed dementia, who developed MCI, and those who maintained normal cognition over a 5-year period. As hypothesized, our study showed that people who developed cognitive decline experienced greater social isolation compared to people who maintained normal cognition. This result aligns with a previous study which found that people living with dementia experience more social isolation and loneliness compared to older adults with normal cognition.<sup>43</sup> Loss of cognitive function can make it difficult for people to engage in social activities and this can exclude them from society. However, there was no difference in anxiety between people who developed dementia or MCI and people who maintained normal cognition over 5 years. This might have been due to individual personality or different coping strategies that this study was unable to capture. We were also unable to know how long they experienced cognitive impairment, which may be an important covariate to anxiety. Future studies should consider these potentially important covariates.

From the regression analyses, we found that changes in social isolation was related to increased anxiety. There were no differences observed between cognitive groups, indicating that people with cognitive impairment can feel loneliness and anxiety in the same manner that people without cognitive impairment perceive. This finding is similar to a recent study which was conducted during the coronavirus-2019 (COVID-19) pandemic.<sup>44</sup> During COVID-19, when social isolation was a universal phenomenon around the world, people living with dementia also reported social isolation and increased anxiety.<sup>44</sup>

When we examined changes in the Perceived Social Isolation scale items to evaluate their relationships to changes in anxiety, we found that perceived loneliness was related to increased anxiety rather than perceived social support. According to a large study which examined 1,445

people with mild to moderate dementia, perception of loneliness was very common; around 35.5% of the participants felt loneliness and the loneliness was related to poor quality of life.<sup>45</sup> Yet, there is lack of research attention paid to perception of people with cognitive impairment and whether one's perception can be changed regardless of cognitive status. Only a few studies applied cognitive behavioral therapy to improve anxiety in people with cognitive impairment.<sup>46-48</sup> Evidence-based tailored interventions that can support people with cognitive impairment to feel less isolation may be helpful.

One solution to meet social needs of people with cognitive impairment can be made through effective communication. Difficulties in communication can magnify social isolation and anxiety in people with cognitive impairment.<sup>49</sup> Meaningful communication between their family and friends where people with cognitive impairment can feel engaged in can improve social isolation and anxiety. When people with cognitive impairment were asked what made meaningful communication, they reported that communication was promoted when people around them empowered their ability to communicate and maintain social interaction.<sup>49</sup> People with cognitive impairment valued sharing moments and feeling emotionally connected.<sup>49</sup> However, when people with cognitive impairment felt inferior or pressured to provide correct answers, it hindered their communications.<sup>49</sup> Therefore, educating family caregivers as well as the public about how to communicate with people with cognitive impairment can help them to spend meaningful time with their loved ones and make people with cognitive impairment feel involved in their community.

Another solution to make people with cognitive impairment less socially isolated can be made through public education on lessening social stigma on dementia. People with cognitive impairment are known to perceive social stigma regarding their dementia.<sup>50</sup> According to a national survey in Australia, 42% of the study participants with dementia felt that other people would avoid spending time with them because they were diagnosed with dementia.<sup>50</sup> 41% of the

survey participants answered that they wished to have more social contact with people in the community.<sup>50</sup> As such social stigma can lead to poor quality of life in people with cognitive impairment<sup>51</sup>, improving stigma among the public and creating a dementia friendly environment is desirable to meet social needs of people with cognitive impairment.<sup>50</sup>

The Perceived Social Isolation Scale that we used in this study was originally developed for general population and it measures loneliness as well as social support from partners, family, and friends comprehensively. However, for people with cognitive impairment, other characteristics such as frequency of social interactions, quality of the social interactions, or duration of the social interactions can be important factors to perception of social isolation. Therefore, a development of a new, inclusive social isolation scale for people with cognitive impairment is desirable. Moreover, more information on the contexts in which persons with cognitive impairment feel social isolation would be helpful to understand underlying mechanisms of perceived social isolation and anxiety. As a previous study suggested,<sup>43</sup> qualitative assessments for social isolation will also be helpful to understand the needs of people with cognitive impairment.

There are a few limitations of this study. First, only two timepoints for social isolation and anxiety were available: The baseline and a 5-year follow-up. If there were additional information available between the 5 years, it might have generated richer information on how changes in social isolation leads to changes in anxiety. It is also possible that people who experienced radically worsening changes in cognition and social isolation might have deceased between the 5 years. Another limitation is that the data were collected years ago. Moreover, since we used secondary data analyses, information on individual coping strategies or duration since cognitive decline was not available in the study which might have been important confounding variables to changes in anxiety over five years. Therefore, future longitudinal studies which

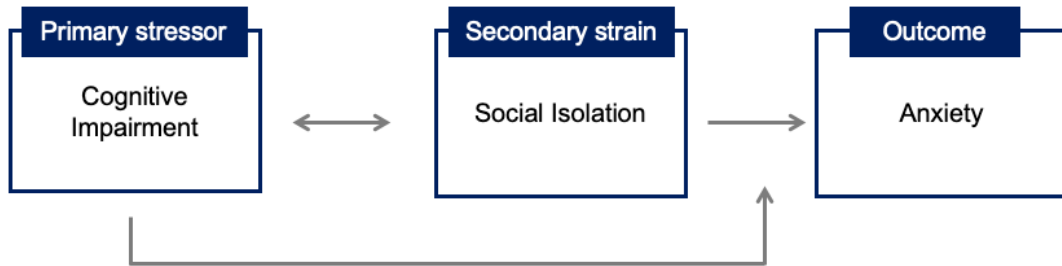
include additional information are needed to better understand the relationship between cognition impairment, social isolation, and psychological outcomes.

## **CONCLUSION**

This 5-year longitudinal study showed that people who developed cognitive impairment such as dementia or MCI experienced higher social isolation compared to people who maintained intact cognition, and increased social isolation was related to increased anxiety regardless of cognition status. Although there were no differences between the strength of the association between social isolation and anxiety by cognitive groups, even people who developed cognitive impairment could feel social isolation which led to anxiety. In the literature, there is only little information available on social isolation among people with cognitive impairment. Health care professionals should pay close attention in assessing social needs of people with cognitive impairment, and more research efforts are needed to improve social isolation among these people.

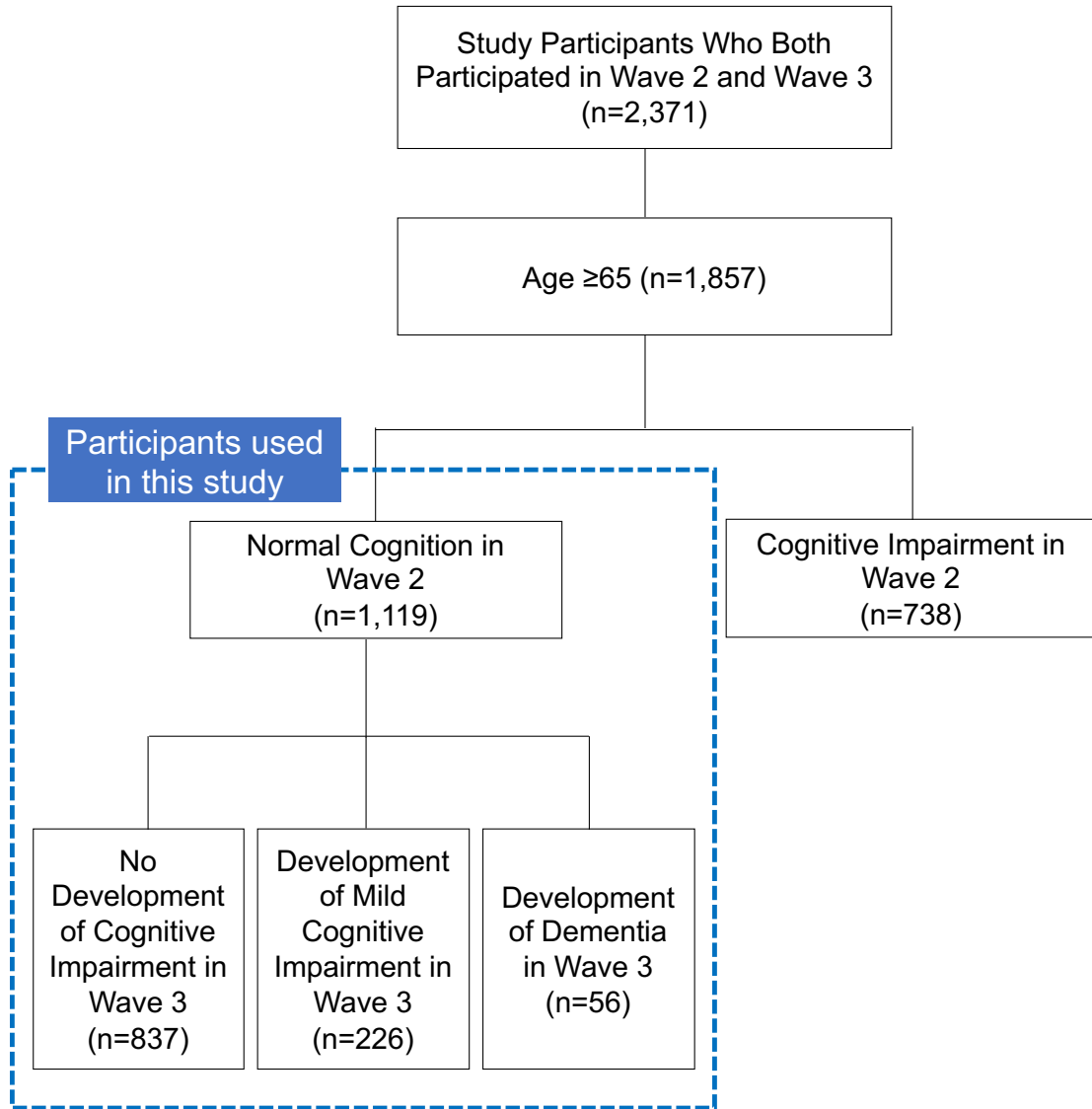


**Figure 4. 1. Conceptual framework of the relationship between social isolation and anxiety in persons with cognitive impairment**



Notes: This conceptual framework was adapted from Stress Process Model for Individuals with Dementia.<sup>22</sup>

**Figure 4. 2. Number of Study Participants Used in the Study**



**Table 4. 1. Characteristics of the Participants (n=1,119) \***

	<b>M±SD or n (%)</b>	<b>Min</b>	<b>Max</b>
<b>Dependent variable</b>			
Changes in Anxiety	-0.043±3.647	-18	16
<b>Independent variable</b>			
Changes in Social Isolation	0.004±0.508	-2.029	2.326
Changes in Lack of Companionship	-0.026±0.640	-2	2
Changes in Feeling Left Out	0.002±0.554	-2	2
Changes in Feeling Socially Isolated	0.009±0.512	-2	2
Changes in Opening Up to Family	-0.020±0.833	-2	2
Changes in Relying on Family	0.074±0.717	-2	2
Changes in Opening Up to Friends	0.073±0.775	-2	2
Changes in Relying on Friends	0.132±0.802	-2	2
Changes in Opening Up to Spouse	0.073±0.586	-2	2
Changes in Relying on Spouse	0.044±0.471	-2	2
Changes in Cognition	1.484±3.062	-5.700	14.820
Maintained Normal Cognition	837 (74.8)		
New Development of Mild Cognitive Impairment	226 (20.2)		
New Development of Dementia	56 (5.0)		
<b>Baseline Covariates</b>			
Age	72.389±5.810	65	90
<b>Sex</b>			
Male	505 (45.1)		
Female	614 (54.9)		
<b>Education</b>			
Less than High School	63 (5.6)		
High School Diploma/Equivalency	271 (24.2)		
Vocational Certificate or Some College	378 (33.8)		
College degree or higher	407 (36.4)		
<b>Race</b>			
White / Caucasian	989 (88.6)		
Black / African American	86 (7.7)		
American Indian / Alaskan Native /	21 (1.9)		
Asian / Pacific Islander			
Other	20 (1.8)		
<b>Employment Status</b>			
Employed	277 (24.8)		
Not Employed	842 (75.3)		
<b>Pain</b>			
Pain in Past 4 Weeks	634 (67.3)		
No Pain in Past 4 Weeks	308 (32.7)		
<b>Depression</b>			
Activities of Daily Living	6.466±1.145	0	7
Instrumental Activities of Daily Living	7.267±1.156	1	8

\*The unweighted total number of participants were 1,119. Data in this table are unweighted.

Note: Changes in Anxiety indicates anxiety scores in Wave 3 minus anxiety scores in Wave 2, and positive scores indicate increased anxiety over 5 years; Changes in Social Isolation Scales indicates social isolation scores in Wave 3 minus social isolation scores in Wave 2 and positive scores indicate increased social isolation; Changes in Cognition scores indicate cognition scores in Wave 2 minus cognition scores in Wave 3 and positive scores indicate increased cognition impairment.

**Table 4. 2. Table of Cognitive Function Classification using Montreal Cognitive Assessment (MoCA) Score Cut-off Scores (Age ≥65)**

Cognitive Function (Wave 2)	Cognition Function (Wave 3)				Statistic
	Normal	Mild Cognitive Impairment	Dementia	Total	
Normal	837	226	56	1,119	Frequency
	74.80	20.20	5.00	100.00	Row %

**Table 4. 3. Weighted Means of Social Isolation and Anxiety among People who Develop Cognitive Impairment and People who Remained Cognitively Intact**

Variables	Maintained Normal Cognition (n=837)	Developed Mild Cognitive Impairment (n=226)	Developed Dementia (n=56)	F	<i>p</i>
Social Isolation in Wave 3	-0.039	0.066	0.119	3.37	<b>0.043</b>
Anxiety in Wave 3	4.027	4.394	4.690	1.67	0.199

Note: Montreal Cognitive Assessment (MoCA) cutoff score of 22 were used for the cognitive group. People who were cognitively intact in Wave 2 were followed up in Wave 3 and categorized into three groups; a group who maintained normal cognition, a group who developed MCI, and a group who developed dementia.

**Table 4. 4. Changes in Social Isolation Scale from Wave 2 to Wave 3 (n=1,119)**

Perceived Social Isolation Score (Wave 3-Wave 2)	n	Mean	SD
Loneliness (1=hardly ever or never, 2=some of the time, 3=often)			
1. How often do you feel that you lack companionship?	938	-0.026	0.640
2. How often do you feel left out?	938	0.002	0.554
3. How often do you feel socially isolated from others?	933	0.009	0.512
Perceived Social Support (1=often, 2=some of the time, 3=hardly ever or never)			
4. How often can you open up to members of your family?	1004	-0.020	0.833
5. How often can you rely on members of your family?	1008	0.074	0.717
6. How often can you open up to your friends?	1022	0.073	0.775
7. How often can you rely on your friends?	1020	0.132	0.802
8. How often can you open up to your spouse or partner?	750	0.073	0.586
9. How often can you rely on your spouse or partner?	747	0.044	0.471

Note: Positive mean score indicates increased social isolation over 5 years.

**Table 4. 5. Weighted Multivariable Linear Regression on Changes in Anxiety (n=920)**

		<b>Coefficient</b>	<b>SE</b>	<b>t</b>	<b>p</b>
<i>Independent variable</i>	Changes in PSI: Loneliness	0.523	0.307	1.71	0.094
	Item 2: Feeling Left Out				
	Item 3: Feeling Socially Isolated	0.725	0.293	2.47	<b>0.017</b>
	Cognition				
	Maintained Normal Cognition	reference			
	New Development of MCI	-0.284	0.333	-0.85	0.397
	New Development of Dementia	-0.187	0.813	-0.23	0.819
	Interaction Terms (×)				
	Item #2 × New Development of MCI	-0.235	0.547	-0.43	0.669
	Item #2 × New Development of Dementia	0.327	0.953	-0.34	0.733
Item #3 × New Development of MCI	-1.26	0.862	-1.46	0.150	
Item #3 × New Development of Dementia	-1.04	2.16	-0.49	0.629	
<i>Covariates</i>	Activities of Daily Living	-0.388	0.163	-2.38	0.021
	Depression	-0.133	0.056	-2.38	0.021
	Constant	2.931	1.172	2.50	0.016
$R^2 = 0.05, F = 2.81, p=0.0094$					

Note: Montreal Cognitive Assessment (MoCA) cutoff score of 22 were used for the cognitive group. People who were cognitively intact in Wave 2 and developed cognitive impairment in Wave 3 were categorized as “New Development of Mild Cognitive Impairment (MCI) (n=226)” and “New Development of Dementia (n=56).” People who were cognitively intact in Wave 2 and again in Wave 3 were categorized as “Maintained Normal Cognition (n=837)”. ×=interaction; PSI = Perceived Social Isolation

**Table 4. 6. Assessment of Multicollinearity using Variance Inflation Factor (VIF)**

	Variance Inflation Factor
Changes in feeling left out (Item #2)	1.79
Changes in feeling Isolated (Item #3)	1.62
Changes in cognition	1.03
Activities of Daily Living	1.06
Depression	1.06
Mean VIF	1.31

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## CHAPTER 5: DISCUSSION AND CONCLUSION

Globally, there is an increasing number of people who live with cognitive impairment (CI), such as Mild Cognitive Impairment (MCI) or dementia.<sup>1</sup> As of 2021, 6.2 million people over the age of 65 are living with CI in the United States; one out of every nine older adults have CI.<sup>2</sup> As dementia progresses, behavioral psychological symptoms of dementia (BPSDs), such as anxiety, aggression, depression, wandering, or sleep disturbances, are frequently exhibited.<sup>2</sup> Such BPSDs can add physical and emotional burdens to family caregivers of people with CI, and anxiety is one of the most distressing and burdensome BPSDs that family caregivers report.<sup>3,4</sup> Because of the associated emotional distress and demands placed on family caregivers, anxiety in people with CI increases the risk for nursing home placement.<sup>5</sup> In order to prevent or reduce anxiety among people with CI, it is essential to assess the contributing factors so that appropriate intervention programs targeting risk factors can be developed.

In particular, unmet social needs can increase anxiety.<sup>6,7</sup> Unfortunately, there has been a lack of research focused on social isolation among people with CI and how, exactly, unmet social needs can contribute to anxiety.<sup>8-10</sup> It is important to note that people with CI are at increased risk for social isolation.<sup>11,12</sup> Because people with CI progressively lose their memory and become unable to maintain their occupation, they experience smaller social networks and relationships.<sup>11,12</sup> In fact, people with CI report less social contact with others as their cognition progressively decline.<sup>8,9</sup> In later life, people tend to pursue close and meaningful social relationships,<sup>13,14</sup> and older adults with CI need not be exceptions. As social isolation and loneliness can trigger anxiety in older adults,<sup>15</sup> this causal relationship may also hold in the case of older adults with CI.

Therefore, **Paper 1** of this three-paper dissertation was an integrative review which aimed to examine factors related to anxiety in persons with CI and to identify potentially modifiable factors among them. I conducted this literature review to identify gaps in this research

area; I found a relative lack of research focused on social factors, compared to research on physical or psychological factors. This led me to design **Paper 2**, which aimed to determine whether social isolation is associated with anxiety in people with CI. I hypothesized that more severe instances of social isolation would be associated with increased anxiety in people with CI. In **Paper 3**, I (1) compared social isolation and anxiety among people who develop CI and those who do not over a five-year period and (2) assessed whether CI moderates the relationship between changes in social isolation and changes in anxiety. I hypothesized that people who develop CI over a five-year period would experience more social isolation and anxiety compared to people who do not develop CI. Another hypothesis was that people who develop CI would present stronger positive associations between changes in social isolation and changes in anxiety compared to people who do not develop CI. For Paper 2 and Paper 3, I analyzed data from the National Social Life, Health, and Aging Project (NSHAP) Wave 2 (2010-2011) and Wave 3 (2015-2016), which examined general health and social factors of nationally representative American older adults living at home to understand their wellbeing. The original data were obtained from the National Archive of Computerized Data on Aging located within the Inter-University Consortium for Political and Social Research.

## **SUMMARY AND DISCUSSION OF PRINCIPAL FINDINGS**

### **Chapter 2: Paper 1**

In paper 1, I conducted an integrative review to examine underlying factors associated with anxiety in people with CI. In order to comprehensively evaluate the factors, the review included both quantitative and qualitative studies. Using PsycINFO, CINAHL, AgeLine, PubMed, Embase, Web of Science, and Scopus, a total of 1,856 studies were identified, from which I selected 27 based on the inclusion criteria. I used the Socio-Ecological Model of Developing and Implementing Comprehensive Dementia Care<sup>16</sup> to categorize the factors

associated with anxiety. The model describes six interrelated domains that impact the quality of life of people with CI and their families. The six domains were: individuals with CI, caregivers, living environments, neighborhood/community, health and human services systems, and national policies.<sup>16</sup> In this review, the factors found were categorized into three of the six domains: the individual level, the caregiver level, and the living environment level.

Most of the factors associated with anxiety in people with CI were at the individual level, which consisted of four subcategories: neuro-biological, health, behavioral and psychological, and social. Each of these subcategories, in turn, had several factors associated with anxiety. The neuro-biological subcategory included factors such as reduced gray matter volume and either high or low cognition level. Factors under the subcategory of health included pain, poor physical health, and decreased functional independence. Under the behavioral and psychological subcategory, factors such as anxiety, fatigue, and sleep disturbance were associated with anxiety. In the social subcategory, factors included social isolation and social rejection. As for the caregiver level, factors associated with anxiety included caregiver stress and low competence of staff. Finally, the environmental level included time of the day and length of stay in residential care as factors associated with anxiety.

In Paper 1, I indicated directionality of the association. If there was a positive association between the factor and anxiety, I indicated it with '+' mark, and if there was a negative association, I indicated it with '-' mark. For example, since greater depression was related to greater anxiety, I marked depression with a '+'. While many factors presented only one direction, several factors had mixed directions: The association with anxiety was positive in some instances but negative in others. This may be due to unidentified mechanisms or a lack of empirical studies. For those with mixed results, more studies are needed to evaluate the directionality of the relationships.

One example of this mixed association with anxiety was cognition. While some studies reported that anxiety was common in people with severe CI, other studies observed anxiety more commonly in people with relatively intact cognition. It is possible that severe CI makes it more difficult to understand the goings-on in one's surroundings, thus provoking anxiety. On the other hand, people with relatively intact cognition may easily become anxious as they are aware of their progressive cognitive decline and, as a result, worry about their future. Additional studies are needed to examine the precise relationships between cognition and anxiety in people with CI.

While there are several review studies which examined anxiety in persons with CI, they were either conducted 10 years ago, targeted on people who lived in nursing homes using quantitative studies, or lacked a systematic process.<sup>17-19</sup> This integrative review provided updated information on underlying factors related to anxiety in people with CI. As this study included both quantitative and qualitative studies, it was able to provide richer information on those underlying factors.

This integrative review found a number of modifiable factors at the individual level, the caregiver level, and the environmental level. Most of the factors belonged to the individual level, because anxiety is an emotion of the individual. Among the studies I reviewed, there was limited information on the relationship between social factors and anxiety compared to physical and psychological factors. Because people with CI are at risk for social isolation<sup>11,12</sup> and social support is essential for psychosocial wellbeing,<sup>20</sup> I decided to examine the relationship between social factors and anxiety in people with CI. The results of Paper 1 motivated and informed my designs for Paper 2 and Paper 3, which aimed to ascertain whether social isolation increases anxiety in people with CI and the extent to which this differs from the effects of social isolation on people with normal cognition.

### **Chapter 3: Paper 2**

Paper 2 aimed to examine whether social isolation increases anxiety in people with CI. This paper analyzed the NSHAP Wave 2 (2010-2011) dataset which includes a nationally representative sample of American older adults living at home. A total of 1,343 people who had probable CI were included for this study. The main regression analyses showed that greater social isolation increases anxiety in people with CI, controlling for cognitive function, race, pain, depression, activities of daily living, and instrumental activities of daily living. In addition to the regression analyses, I conducted adjusted Wald tests to identify the aspects of the social isolation scale which were related to anxiety in people with CI. I found that persons with clinically significant anxiety (Anxiety scale of the Hospital Anxiety Depression Scale, HADS-A $\geq$ 8) had higher levels of loneliness, including feeling a lack of companionship, feeling left out, and greater social isolation.

This study used a conceptual framework that was adapted from the Stress Process Model for Individuals with Dementia.<sup>21</sup> This model explains that primary and secondary stressors can impact the wellbeing of individuals with CI.<sup>21</sup> In this context, primary stressors are symptoms of dementia, such as cognitive status or functional status; secondary stressors include direct results from the disease, such as changes in social roles and self-perception or feeling.<sup>21</sup> The model explains that both primary and secondary stressors influence the overall wellbeing of individuals with CI.<sup>21</sup> In this study, I treated social isolation as a secondary strain because it resulted from cognitive decline and consequent changes in occupational or social roles. As hypothesized based on the conceptual framework of the study, when people with CI felt socially isolated, they were more likely to experience increased anxiety.

People with CI are vulnerable to being socially isolated.<sup>2,8,22</sup> As cognition progressively declines, people with CI experience difficulties of completing familiar tasks in daily life including executing responsibilities at work.<sup>2</sup> This can lead them to withdraw from work and isolate themselves at home.<sup>2</sup> Moreover, confusion about time, place, or people, difficulties with driving,



or challenges in following up conversations with others can also make people with CI become or feel detached from social activities.<sup>2</sup> In addition, they may avoid being social because of the CI they experience and embarrassment about the associated changes.<sup>2,8</sup> Furthermore, social stigma about dementia can expedite social isolation.<sup>8,22</sup> Unmet social needs in people with CI can provoke BPSDs such as anxiety.<sup>6,7</sup> Efforts are needed to include people with CI in social activities to reduce or prevent social isolation.

### **Chapter 4: Paper 3**

The research aims of Paper 3 were twofold: (1) to examine social isolation and anxiety among people who develop MCI and dementia, compared to those who maintained intact cognition over a five-year period and (2) to determine whether CI moderates the relationship between changes in social isolation and changes in anxiety. Secondary data analyses were conducted using the NSHAP Wave 2 (2010-2011) and Wave 3 (2015-2016) datasets. Wave 2 was used as the baseline dataset and Wave 3 was used as a five-year follow up. Among people who participated in both Wave 2 and Wave 3, I selected individuals whose age was 65 or older and who had normal cognition at baseline. I followed up with those people with normal cognition at baseline to examine whether changes in social isolation and anxiety differed by severity of cognitive decline over time. For data analyses, adjusted Wald tests and weighted linear regression analyses with group interaction were used.

The participants were categorized into three groups: (1) those who kept their level of cognition intact over five years, (2) those who developed MCI over five years, and (3) those who developed dementia over five years. Of the 1,119 participants who were cognitively intact at baseline, 74.8% remained cognitively intact, 20.2% acquired MCI, and 5% developed dementia at the follow up. At the five-year follow up, the two groups who developed MCI and dementia tended to have increased social isolation. Feeling of increased social isolation over five years was

related to increased anxiety over five years. There were no statistically significant interactions found for the three cognitive groups.

This study found that it is a universal phenomenon regardless of one's cognitive status that increased social isolation is related to increased anxiety over a span of several years. As people age, they tend to seek emotionally meaningful relationships,<sup>14</sup> and fulfillment of social needs is an important part of successful aging.<sup>23,24</sup> As a result, it is likely that older adults feel anxiety when they experience a lack of social support or diminished social connection.<sup>18,25,26</sup> In line with a previous study,<sup>27</sup> this study found that people with CI still have social needs. This study also supports the results of a recent study during the coronavirus-2019 (COVID-19) pandemic that people with CI reported increases in social isolation and increased anxiety similar to people without CI.<sup>28</sup> Since people with CI feel isolation and emotional difficulties differently from people with intact cognition, the social needs of people with dementia should not be overlooked.

## **LIMITATIONS**

### **Chapter 2: Paper 1**

Paper 1 has several limitations. The literature included in this review did not always show high scores on critical appraisal scales. Because the Joanna Briggs Institute critical appraisal tool used in Paper 1 did not specify a cut-off score for high quality evidence, I did not exclude those studies with relatively low appraisal scores. Although most of the studies included in the review had high scores on critical appraisal scales, readers should be cautious when interpreting the results. Another limitation is that it was inevitable that the various types of dementia were all lumped together, since many studies did not provide specific information on the types of dementia of their study participants. Additionally, different measurement scales for anxiety were

used in the literature including both proxy-reported scales and self-reported scales, which made it difficult to synthesize the results.

### **Chapter 3: Paper 2**

In Paper 2, people with probable CI were defined by the Montreal Cognitive Assessment (MoCA). In addition to such screening measurements, MRI results or in-depth evaluations by clinicians are required for accurate diagnoses of CI such as MCI or dementia. However, as the MoCA has been validated as a very effective screening tool for CI,<sup>29</sup> the use of MoCA for CI was expected to identify probable CI. Facts as to whether subjects were formally diagnosed with dementia might have constituted an important covariate in terms of social isolation and anxiety, due to their perceived stigma on dementia.<sup>30</sup> Although I was unable to include this information as a covariate because of the nature of secondary data analyses, I tried to control for the severity of CI when examining the relationship between social isolation and anxiety.

Another limitation of Paper 2 was that the parent study did not recruit people with severe CI. Although a portion of the study participants were categorized as dementia based on MoCA, the NSHAP did not include people in the original study who were be incapable of completing the survey. Although interviewers of the NSHAP did not conduct a formal screening for CI at the beginning of the interview to exclude people with CI, the exclusion of people with severe CI might have reduced the number of people with severe CI in the NSHAP. Finally, because Paper 2 analyzed cross-sectional data using the NSHAP Wave 2, it was difficult to examine the causal relationship between social isolation and anxiety.

### **Chapter 4: Paper 3**

Similar to Paper 2, one limitation of Paper 3 is that only probable MCI or dementia measured by the MoCA was used to indicate people with CI, not formal diagnoses. Although

MoCA is a valid screening tool for CI,<sup>29</sup> caution should be applied when interpreting the results. Because formal diagnoses of dementia can influence one's perception of social isolation,<sup>27</sup> it might have been helpful to have more information on whether individuals had a history of formal diagnoses.

As this study used secondary data analyses of existing data, there were only two timepoints available for social isolation and anxiety: the baseline and a five-year follow-up. As social isolation and anxiety may change over time, additional timepoints between the five-year period might have provided richer information. Another limitation is that I was unable to include information on individual coping strategies for psychological stress or duration since cognitive decline. If available, this information might have provided important confounding variables when examining the relationship between changes in social isolation and changes in anxiety.

## **AREAS FOR FUTURE RESEARCH**

Paper 1 of this three-paper dissertation found a number of factors associated with anxiety that are modifiable. Compared to factors at the individual level, such as pain, physical health, or social isolation, not many factors were found at the caregiver level or environmental level. Additional studies are needed to examine the relationship between external factors and anxiety in persons with CI, as adjusting these factors may prevent or improve anxiety in persons with CI.

An important prospect for future research involves conducting qualitative studies on anxiety in persons with CI. Although it is possible that persons with CI experience anxiety for different reasons, there is lack of information on why or when persons with CI feel anxiety. Even focusing solely on persons with CI, the nature of anxiety may vary significantly based on the severity of CI. For example, when a person has relatively intact cognitive abilities, he or she may be anxious about the uncertainties regarding illness. On the other hand, when a person has diminished cognitive abilities, he or she may be anxious about events in his or her immediate

surroundings which he or she does not understand. However, quantitative studies to date have not found consistent results on the relationship between levels of cognition and anxiety. Therefore, qualitative studies exploring the nature of anxiety based on the severity of CI are needed.

This dissertation examined the relationship between social isolation and anxiety in persons with CI who live at home. However, there is a lack of information on persons with CI who live in nursing homes or long-term care facilities. Persons who live in nursing homes may have less opportunity to maintain social connections outside of the nursing homes and may experience less support from family or friends compared to those who live at home. In future studies, I suggest examining social isolation and its outcomes among persons with CI who live in nursing homes, so that appropriate interventions can be applied. It would be also meaningful to compare social isolation and its outcomes between people who live at home and those who live in nursing homes.

In addition, more information on perceived social isolation and the contexts in which persons with CI feel social isolation would be helpful, because it is essential to know the underlying mechanisms of perceived social isolation and anxiety. For example, it is possible that people with CI choose to be less social because of the changes they experience.<sup>2</sup> It is also possible that refraining from driving or the increased difficulties in using cellular phones may accelerate social isolation and anxiety. To assess more information on perceived social isolation and anxiety among people with CI, a qualitative approach is suggested.

In future research, replication studies are needed with important covariates such as whether the individual was formally diagnosed with dementia, how long they experienced dementia, or individuals' coping strategies for stress. For instance, diagnosis of dementia itself can trigger the perception of social stigma as well as the feeling of isolation, and the duration of cognitive decline may buffer the relationship between social isolation and anxiety in persons with

dementia. Individual coping strategies for stress may provide important information on the relationship between social isolation and anxiety.

Studies are also needed on whether perceptions of social isolation differ by personality in people with CI. For example, it is possible that extraverts may be at an increased risk for perceiving social isolation upon cognitive decline. In addition, comfort level for social connectedness may differ by personality or severity of cognition decline. According to Environmental Press Theory by M. Powell Lawton,<sup>31</sup> people's comfort levels are based on environmental press and competencies. It is possible that comfort level for social environment may vary by personality and cognitive functioning. Examining social comfort level for individuals for CI is an important area for future research as the information can be helpful in designing individualized interventions.

Another area for future research is to design non-pharmacological interventions to improve social isolation and anxiety in persons with CI. In the Perceived Social Isolation Scale used in this dissertation, there were two domains: loneliness and social support. This dissertation found that the loneliness domain was more related to anxiety in persons with CI. A systematic review on non-pharmacological interventions to improve loneliness in older adults with intact cognition found that group activities or shared activities were effective for mitigating loneliness.<sup>32</sup> Since there is lack of information available on non-pharmacological interventions for persons with CI, approaches similar to those taken on behalf of older adults with normal cognition should be tested on people with CI for effectiveness.

## **RESEARCH IMPLICATIONS**

The results of this dissertation found that perceived social isolation increased anxiety even when cognition is impaired. As older adults still have social needs even when their cognition is impaired, healthcare professionals need to evaluate one's social needs when they make clinical

assessments. As unmet social needs can lead to social isolation as well as anxiety, it is imperative to educate family members of persons with CI on the importance of meeting the social needs of their loved ones. The families of persons with CI can start with simple activities. For example, they can share house chores with the person with CI so that persons with CI can maintain a social role within the family and feel more of a sense of belonging. Family and friends of persons with CI can also try not to exclude their loved ones from social gatherings.

It is also important for healthcare professionals to educate the public on reducing the social stigma of dementia, because it can make people with CI feeling isolated from the society. A more educated public will be able to understand the nature of people living with dementia. Ultimately, dementia-friendly communities can be created where people with CI feel less isolated from society.

Because social isolation and loneliness can be alleviated by shared group activities, healthcare professionals should develop diverse and effective shared group activity programs for persons with CI at the community level, for example, through daycare centers. At the policy level, broadening Medicare coverage will be helpful so that more beneficiaries have access to the activities available at those daycare centers.

## **CONCLUSION**

Anxiety is not only associated with poor quality of life in persons with CI<sup>3,33</sup> but is also associated with increases in caregiver burdens among family members.<sup>3,4</sup> This dissertation focused on how social factors such as social isolation can influence anxiety in persons with CI. Using a national cohort study NSHAP, this dissertation found that people who developed CI experienced higher social isolation compared to people who maintained intact cognition, and that increased social isolation is associated with increased anxiety regardless of cognition status. Even people who developed CI could feel social isolation which led to anxiety. Health care

professionals should pay close attention in assessing the social needs of people with CI, and more research efforts are needed to mitigate social isolation among people with CI.



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**APPENDIX: SUPPLEMENTARY MATERIAL**

**Table S 1. Table of evidence: Quantitative studies**

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
123 Bidzan et al. (2014) 83.3% (Poland)	Cross-sectional design	To examine if vascular factors influence the frequency or intensification of neuropsychiatric symptoms in dementia	<ul style="list-style-type: none"> <li>• n=48</li> <li>• Mean age: 70.00±8.02 (Range: 52-85)</li> <li>• Mean MMSE: 15.96±4.91</li> <li>• Setting: Nursing home</li> </ul>	Diagnosis of Alzheimer's Disease	t-test	Severity of vascular components (Mild or severe)	Hachinski scale	t-value not specified, $p<0.05$	NPI-NH Anxiety Frequency
								t-value not specified, $p<0.05$	NPI-NH Anxiety Intensification
								t-value not specified, $p<0.05$	NPI-NH Anxiety Frequency × Intensification
Burgener et al.	Longitudinal design	To examine	<ul style="list-style-type: none"> <li>• n=50</li> <li>• Mean age:</li> </ul>	Diagnosis of dementia		Social rejection	SIS-subscale	$\beta=-0.004$ , $p=0.82$	RAID

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
(2015) 85.7% (United States)		the association between perceived stigma and QoL outcomes (depression, anxiety, behavioral symptoms, personal control, physical health, self-esteem, social support, and activity)	78.3±8.3 years (Age range is not specified) • Mean MMSE: 22.6±3.9 • Setting: Community or assisted living setting		Linear fixed model	Internalized shame	SIS-subscale	$\beta=-0.05$ , $p=0.01$	
						Social isolation	SIS-subscale	$\beta=0.03$ , $p=0.05$	
						Gender: female (1) vs. male (0)	Gender	$\beta=0.20$ , $p=0.19$	
						Cognitive function	MMSE	$\beta=0.04$ , $p<.001$	
						Social rejection × gender	SIS-subscale and gender	$\beta=0.07$ , $p=0.003$	

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
		participation)							
Caddell & Clare (2012)  75% (United Kingdom)	Cross-sectional design	To examine how different aspects of identity are associated with mood and quality of life	<ul style="list-style-type: none"> <li>n=50</li> <li>Mean age: 77.8±7.4 years (Range: 60-91)</li> <li>Mean MMSE: 23.7±2.7</li> <li>Setting: Unknown (Participants were recruited from memory clinics and patient research participation register)</li> </ul>	Diagnosis of dementia using ICD-10 Criteria	Multiple regression analysis	Physical identity  Personal identity  Family identity	TSCS-Physical domain  TSCS-Personal domain  TSCS-Family domain	$\beta=-0.286$ , $p=0.052$  $\beta=-0.162$ , $p=0.262$  $\beta=0.292$ , $p=0.039$	HADS
Calleo et al. (2011)  100%	Cross-sectional design	To examine characteristics of GAD in	<ul style="list-style-type: none"> <li>n=43</li> <li>Mean age: 78.9±9.3 years (An inclusion criteria is age 50</li> </ul>	Diagnosis of dementia	Logistic regression analysis	Female	Gender (Male/Female)	OR=0.10 [0.18-4.87], $p=0.02$	GAD

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
(United States)		people with dementia, identify associated anxiety symptoms in GAD, and to determine factors that predict GAD in people with dementia	or older but actual age range is not specified) • Mean CDR: 1.43 (SD not available) • Setting: Unknown (Participants were recruited from outpatient clinics and community day centers)			CDR	CDR	OR=0.95 [0.18-4.87], $p=0.77$	
						Low Muscle Tension	An item from RAID	OR=0.12 [0.02-0.90], $p=0.04$	
						Low Fatigue	An item from RAID	OR=0.42 [0.09-2.09], $p=0.29$	
Dawson et al. (2012) 75%	Cross-sectional design	To examine how illness experien	• n=131 • Mean age: 77.15±9.45 years (Range: 50-95)	Diagnosis of dementia or memory loss	Multiple regression analysis	Race	Race	$\beta=-0.11$ , $p>0.05$ (Exact p-value not specified)	Anxiety (Self Rating Anxiety Scale)



APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors		Anxiety	
						Factors	Measures	Statistical Significance	Anxiety measures
(United States)		ce from the perspective of the individuals of dementia influence well-being using the Stress Process Model for Individuals with Dementia	<ul style="list-style-type: none"> <li>• Mean MMSE: 22.48±5.84</li> <li>• Setting: Unknown (Participants were recruited from social service agencies)</li> </ul>			Education	Education	$\beta=0.02$ , $p>0.05$ (Exact p-value not specified)	
						Caregiver/Care receiver Relationship	Items retrieved from previous literature	$\beta=0.07$ , $p>0.05$ (Exact p-value not specified)	
						Gender	Gender	$\beta=0.12$ , $p>0.05$ (Exact p-value not specified)	
						Relationship strain: role capacity	Items retrieved from previous literature	$\beta=0.10$ , $p>0.05$ (Exact p-value not specified)	
						Difficulty with IADLs	Items retrieved from	$\beta=0.06$ , $p>0.05$ (Exact p-	

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors		Anxiety
						Factors	Measures	Statistical Significance
							previous literature	value not specified)
						Caregiver reported behavior	Items retrieved from previous literature	$\beta=-0.05$ , $p>0.05$ (Exact p-value not specified)
						MMSE	MMSE	$\beta=0.01$ , $p>0.05$ (Exact p-value not specified)
						Health strain: physical	Items retrieved from previous literature	$\beta=0.09$ , $p>0.05$ (Exact p-value not specified)
						Relationship strain: dyad	Items retrieved from previous literature	$\beta=0.14$ , $p>0.05$ (Exact p-value not specified)

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
						Embarrassment about memory problems	Items retrieved from previous literature	$\beta=0.22$ , $p=0.022$	
						Self-efficacy perception: inner strength/growth	Items retrieved from previous literature	$\beta=0.07$ , $p>0.05$ (Exact p-value not specified)	
						Depression	CES-D	$\beta=0.22$ , $p<0.05$ (Exact p-value not specified)	
						Quality of Life	QoL-AD	$\beta=-0.16$ , $p<0.05$ (Exact p-value not specified)	
De Oliveria et al. (2015)	Cross-sectional design	To examine the relations	• n=217 • Mean age: 73.19±6.8 years (Range: 52-88)	Diagnosis of Alzheimer's Disease using	Spearman -rho correlations, and	Apathy	NPI	$r=-0.0790$ , $p<0.05$ (Exact p-	NPI-Anxiety

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
75% (Brazil)		hip between cognition, behavior, and functional independence in PWD, and to examine impacts of education, APOE haplotypes, length of dementia, age, and alcohol use, and NPI	<ul style="list-style-type: none"> <li>• Mean MMSE: 15.64±5.8</li> <li>• Setting: Unknown (Participants were recruited from health care center)</li> </ul>	National Institute on Aging-Alzheimer's Association criteria	multiple linear regression analysis	Delusion	NPI	r=-0.0046, p<0.05 (Exact p-value not specified)	NPI-Anxiety

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
Ferreira et al. (2018) 100% (Portugal)	Cross-sectional design	To compare the frequency and severity of neuropsychiatric symptoms in EOAD and LOAD.	<ul style="list-style-type: none"> <li>• n=70 (n=35 with EOAD and n=35 with LOAD)</li> <li>• Mean age of EOAD: 64.5±6.5years</li> <li>• Mean age of LOAD: 76.0±3.5 (Age ranges are not specified)</li> <li>• Mean MMSE of EOAD: 16.2±8.1</li> <li>• Mean MMSE of LOAD: 16.8±6.0</li> <li>• Setting: Unknown (Participants were recruited from outpatient clinic)</li> </ul>	Diagnosis of Alzheimer's Disease	Chi-square test	EOAD, LOAD	Diagnosis of dementia before age of 65 was classified as EOAD.	p=0.748, (Chi-square value not specified)	NPI-Anxiety Frequency
								p=0.900, (Chi-square value not specified)	NPI-Anxiety Severity
Goyal et al. (2018a)	Longitudinal design	To examine	• n=298 (f/u n=205)	Diagnosis of dementia by	Multilevel	Age	Age	β=-0.027, p=0.729	Increase in RAID

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
85.7% (Norway)		the course of anxiety over 12 months and to identify factors that are related to increase in anxiety symptoms over 12 months	<ul style="list-style-type: none"> <li>• Mean age: 85.5±6.8 years (An inclusion criteria is age 65 or older but actual age range is not specified)</li> <li>• Mean CDR-sob: 12.8±3.5</li> <li>• Setting: Nursing homes</li> </ul>	either the International Statistical Classification of Diseases and Related Health Problems (ICD-10); the Diagnostic and Statistical Manual of Mental Disorders (DSM-V); or by the International Classification of Primary Care-2 (ICPC-2)	regression models	Male	Gender	$\beta=-0.006$ , $p=0.996$	over 12 months
						Length of stay in residential care	In days	$\beta=-0.001$ , $p=0.317$	
						Cognition	CDR-sob	$\beta=-0.200$ , $p=0.374$	
						Activities of Daily living	PSMS sum	$\beta=0.063$ , $p=0.682$	
						Physical health	GMHR-excellent/good	$\beta=-0.187$ , $p=0.872$	
						Psychosis (Delusions and hallucinations)	NPI-Q sub-syndrome-psychosis	$\beta=-0.741$ , $p=0.067$	
						Affective (Dysphoria, anxiety, apathy, and appetite)	NPI-Q sub-syndrome-affective	$\beta=-1.079$ , $p<0.001$	

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors		Anxiety	
						Factors	Measures	Statistical Significance	Anxiety measures
						Agitation (agitation, irritability, disinhibition, and aberrant motor)	NPI-Q sub-syndrome-agitation	$\beta=-0.396$ , $p=0.095$	
						Aroused (euphoria, nighttime disturbances)	NPI-Q sub-syndrome-aroused	$\beta=1.265$ , $p=0.027$	
						Anxiolytics	Medical records	$\beta=-3.227$ , $p=0.039$	
						Antidepressants	Medical records	$\beta=-0.212$ , $p=0.851$	
						Antipsychotics	Medical records	$\beta=3.928$ , $p=0.006$	
						Hypnotics and sedatives	Medical records	$\beta=0.060$ , $p=0.960$	
						Cognitive enhancers	Medical records	$\beta=-0.381$ , $p=0.747$	

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
Goyal et al. (2017)  75% (Norway)	Cross-sectional design	To examine the prevalence of anxiety symptoms in people with dementia living in nursing homes in Norway, and to identify correlations to anxiety symptoms.	<ul style="list-style-type: none"> <li>n=298</li> <li>Mean age: 85.5±6.8 years (An inclusion criteria is age 65 or older but actual age range is not specified)</li> <li>Mean CDR-sob: 12.8±3.5</li> <li>Setting: Nursing homes</li> </ul>	Diagnosis of dementia by either the International Statistical Classification of Diseases and Related Health Problems (ICD-10); the Diagnostic and Statistical Manual of Mental Disorders (DSM-V); or by the International Classification of Primary	Stepwise multivariate linear regression analysis	Cognition	CDR-sob	Not significant (Unstandardized B value and p values are not provided)	RAID
						Physical health	GMHR-excellent/good	B=-1.426, p=0.029	
						Psychosis (Delusions and hallucinations)	NPI-Q sub-syndrome-psychosis	B=0.907, p<0.001	
						Affective (Dysphoria, anxiety, apathy, and appetite)	NPI-Q sub-syndrome-affective	B=1.350, p<0.001	



APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
				Care-2 (ICPC-2)		Agitation (agitation, irritability, disinhibition, and aberrant motor)	NPI-Q sub-syndrome-agitation	B=0.294, p=0.019	
						Aroused (euphoria, nighttime disturbances)	NPI-Q sub-syndrome-aroused	B=0.812, p=0.009	
						Anxiolytics	Medical records	B=2.741, p=0.002	
						Antidepressants	Medical records	Not significant (Unstandardized B value and p values are not provided)	

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
						Antipsychotics	Medical records	Not significant (Unstandardized B value and p values are not provided)	
						1 $\geq$ psychotropic drugs	Medical records	Not significant (Unstandardized B value and p values are not provided)	
Hynninen et al. (2012) 100% (Norway)	Cross-sectional design	To investigate the prevalence of anxiety in mild dementia and to identify socio-	<ul style="list-style-type: none"> <li>n=169</li> <li>Mean age: 76.0<math>\pm</math>7.5 years (Range: 50-90)</li> <li>Mean MMSE: 23.8<math>\pm</math>2.3 (An inclusion criteria is having MMSE score 20 or more)</li> </ul>	Diagnosis of dementia by the Diagnostic and Statistical Manual of Mental Disorder (DSM-IV)	Binary logistic regression analysis	Dementia Severity	CDR	OR=3.8 [1.5, 9.6] (Exact p-value is not specified)	NPI
						Dementia Severity-Community affairs	CDR subscale	OR=2.8 [1.3, 6.0], (Exact p-value is not specified)	

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
		demographic and clinical variables .	<ul style="list-style-type: none"> <li>Setting: Unknown (Participants were recruited from outpatient clinic)</li> </ul>			Dementia Severity-Home and hobbies	CDR subscale	OR=2.8 [1.5, 5.0], (Exact p-value is not specified)	
						Caregiver stress	RSS	OR=1.1 [1.0, 1.1], (Exact p-value is not specified)	
Jao et al. (2018) 100% (United States)	Repeated measured study	To examine the relationship between social interactions and	<ul style="list-style-type: none"> <li>n=126</li> <li>Mean age: 86.1±6.0 years (Range: 65-99)</li> <li>Mean MMSE: 14.2±4.5 (An inclusion criteria is having MMSE</li> </ul>	Diagnosis of dementia by the Diagnostic and Statistical Manual of Mental	Linear mixed-effects models	Afternoon  Cognition	Afternoon observation / Morning observation  MMSE	β=0.16, p=0.02  β=-0.02, p=0.93	Philadelphia Geriatric Center Apparent Affect Rating Scale

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors		Anxiety	
						Factors	Measures	Statistical Significance	Anxiety measures
		affect (including anxiety) in PWD residing in nursing homes.	score between 7-24 • Setting: Nursing homes	Disorder (DSM-IV)		Social interaction, between person	Interaction with People (IP) subscale of the Passivity in Dementia Scale (PDS)	$\beta=-0.13$ , $p=0.22$	
						Social interaction, within-person	Interaction with People (IP) subscale of the Passivity in Dementia Scale (PDS)	$\beta=0.20$ , $p<0.001$	

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
Kabeshita et al. (2017)  75% (Japan)	Cross-sectional design	To examine the relationships between sleep disturbances and BPSD among PWD at different cognition stage.	<ul style="list-style-type: none"> <li>• n=684</li> <li>• Mean age of AD without sleep disturbances: 76.2±8.6 years</li> <li>• Mean age of AD with sleep disturbances: 76.8±9.2 (Age range is not specified)</li> <li>• Mean MMSE of AD without sleep disturbances: 19.2±5.2</li> <li>• Mean MMSE of AD with sleep disturbances: 17.4±5.6</li> <li>• Setting: Unknown (Participants were recruited</li> </ul>	Diagnosis of Alzheimer's Disease by DSM-III-R criteria	Chi-square test	AD with sleep disturbances group/ AD without sleep disturbances group	NPI-sleep (1 or more score on NPI sleep was categorized as sleep disturbance group)	$\chi^2=10.62$ , p=0.002	NPI-anxiety

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
			from health care center)						
Kaiser et al. (2014)  75% (United States)	Cross-sectional design	To examine prevalence of anxiety among EOAD and	<ul style="list-style-type: none"> <li>n=45 (EOAD n=23, LOAD n=22)</li> <li>Mean age of EOAD: 57.68±4.19 years</li> <li>Mean age of</li> </ul>	Diagnosis of Alzheimer's Disease	Spearman -rho correlation, Logistic regression analysis	Male	Gender (Male/Female)	OR=8.5 [1.58-45.8], p=0.013	NPI-Anxiety

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors		Anxiety	
						Factors	Measures	Statistical Significance	Anxiety measures
		LOAD and to explore factors that are related to anxiety in EOAD and LOAD	LOAD: 80.32±5.89 (Age ranges are not specified) • Mean MMSE of EOAD (Anxiety Present): 21.79 • Mean MMSE of EOAD (Anxiety Absent): 15.43 • Mean MMSE of LOAD (Anxiety Present): 19.33  • Mean MMSE of LOAD (Anxiety Absent): 21.75 (Standard deviations are not presented) • Setting: Unknown (Participants			EOAD	EOAD/LOAD	OR=9.68 [1.98-47.4], p=0.005	
						MMSE*EOAD	MMSE*EOAD	OR=1.18, p=0.050 (95% CI is not specified)	

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures

were recruited from health care center)

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Kang et al. (2010) 75% (United States)	Cross-sectional design	To describe and compare characteristics in people residing in DSAL or TAL	<ul style="list-style-type: none"> <li>n=46 (DSAL n=18, TAL n=28)</li> <li>Mean age: 83.89±7.23 years (Age range is not specified)</li> <li>Mean MMSE: 19.8±6.6</li> <li>Setting: Assistive living</li> </ul>	Meeting DSM-IV-TR criteria for dementia and National Institute of Disorders Association (NINCDS/A DRDA) criteria for probable or possible Alzheimer's disease (AD)	Kruskal-Wallis test	Type of assistive living	Dementia-specific assisted living (DSAL)/ Traditional assistive living (TAL)	p=0.42 (Specific statistics was not provided)	HARS
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APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
Kromhout et al. (2014) 50% (Netherlands)	Cross-sectional design (96 hours)	To explore the relationships between caffeine and behavioral symptoms in PWD.	<ul style="list-style-type: none"> <li>n=31</li> <li>Mean age: 84±6.6 years (Range: 69-96)</li> <li>Mean MMSE: Not specified</li> <li>Setting: Nursing home</li> </ul>	The article just used the word "dementia."	Kendall's tau correlation coefficient	Total caffeine consumption per day	Records of the number of cups of coffee, tea, and coke	r=-0.135, p=0.39	NPI-NH Anxiety
Mormont et al. (2014) 75% (Belgium)	Prospective study	To examine the modification of anxiety and depression after disclosure of the diagnosis of AD after	<ul style="list-style-type: none"> <li>n=100 (n=96 after three months)</li> <li>Mean age: 77±6.7 years (Range: 56-88)</li> <li>Mean MMSE: 22.7±3 (Range: 17-28)</li> <li>Setting: Unknown (Patients were recruited from after</li> </ul>	Diagnosis of probable AD according to the NINCDS-ADRDA criteria	Friedman test, Wilcoxon signed-rank test	Disclosure of the diagnosis of the AD	Disclosure of the diagnosis of the AD	p=0.001 (Friedman test) p=0.05 (Wilcoxon signed-rank test)	NPI-Anxiety

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
		three months.	outpatient memory clinic)						
Nelis et al. (2012) 75% (United Kingdom)	Cross-sectional design	* To examine the relationship between attachment in PWD and carers to the well-being of	* n=97 PWD & n=89 carers * Mean age of PWD: 77.98±7.68 (Range: 51-90) * Mean MMSE: 24.43±2.64 * Setting: Unknown (Participants were recruited from memory clinics)	Diagnosis of dementia by International Statistical Classification of Diseases and Related Health Problems (ICD-10)	Multiple regression analysis	Age  Gender	Age  Gender	Not significant (Standardized $\beta$ value and p values are not provided)  Not significant (Standardized $\beta$ value and p values are not provided)	HADS

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors		Anxiety
						Factors	Measures	Statistical Significance
		the two groups.				Cognition	MMSE	Not significant (Standardized $\beta$ value and p values are not provided)
						View of self in PWD regarding attachment	Relationship Questionnaire	$\beta=-0.230$ , $p=0.022$
						View of others in PWD regarding attachment	Relationship Questionnaire	$\beta=-0.283$ , $p=0.005$
						View of self in caregiver regarding attachment	Relationship Questionnaire	Not significant (Standardized $\beta$ value and p values are

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors		Anxiety	
						Factors	Measures	Anxiety measures	
								not provided)	
						View of others in caregiver regarding attachment	Relationship Questionnaire	Not significant (Standardized $\beta$ value and p values are not provided)	
Neville & Teri (2011)  87.5% (United States)	Cross-sectional design	To examine the prevalence of anxiety in PWD who live in	<ul style="list-style-type: none"> <li>n=148 (PWD)</li> <li>n=140 (staff)</li> <li>Mean age: 86.2±6.7 years (Range: 69-101)</li> <li>Mean MMSE: 15.52±5.21</li> <li>Setting: Assistive living</li> </ul>	Diagnosis of dementia by the Diagnostic and Statistical Manual of Mental Disorder	Multiple regression analysis	Age	Age	$\beta=-0.09$ , p=0.26	RAID
						Female	Gender	$\beta=-0.04$ , p=0.62	

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
		assisted living and to identify factors that are related to anxiety symptoms in PWD.		(DSM-IV-TR)		Frequency of Behavior Problems	Revised Memory Behavior Checklist	$\beta=0.34$ , $p=0.001$	
						Depression	GDS	$\beta=0.40$ , $p<0.001$	
						Cognition	MMSE	$\beta=-0.04$ , $p=0.07$	
						Age (Staff)		$\beta=-0.13$ , $p=0.18$	RAID
						Qualification (Staff)		$\beta=-0.03$ , $p=0.80$	
						Staff Reaction to Behavior Problems	Revised Memory Behavior Checklist	$\beta=0.57$ , $p<0.001$	

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
						Staff Competence	Short Sense of Competence Questionnaire	$\beta=-0.20$ , $p=0.04$	
						Job satisfaction	Short Sense of Competence Questionnaire	$\beta=-0.04$ , $p=0.70$	
Prior et al. (2016) 50% (United Kingdom)	Cross-sectional design	To examine the relationship between premorbid personality traits and BPSD	<ul style="list-style-type: none"> <li>n=217</li> <li>Mean age: Not specified (Range: 67-98)</li> <li>Average cognition status: Not specified</li> <li>Setting: Nursing homes or old-age psychiatric services</li> </ul>	Diagnosis of probable dementia (Did not specify exact criteria for "probable dementia")	Did not specify which statistical method was used. (Non-parametric comparison between	Cluster A traits (Solitary/paranoid)	Standard Assessment of Personality (SAP)	$p=0.038$ (Exact statistical value is not specified)	NPI-Anxiety

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
					two groups)				
Tagai et al. (2014) 100% (Japan)	Cross-sectional design	To explore the association between anxiety symptoms in AD and structural and functional	<ul style="list-style-type: none"> <li>• n=26</li> <li>• Mean age: 74.95±7.29 (Age range is not specified)</li> <li>• Mean MMSE: 23±5.23</li> <li>• Setting: Unknown (Participants were recruited from outpatient clinic)</li> </ul>	Diagnosis of probable AD according to the NINCDS-ADRDA criteria	General linear model	Right precuneus	Voxel-based Morphometry	p=0.026 (negative correlation, statistical value is not specified)	Behave-AD
						Right inferior parietal lobule (IPL)	Voxel-based Morphometry	p=0.018 (negative correlation, statistical value is not specified)	

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
		changes in brain				Anterior Cingulate Cortex (ACC)	Single Photon Emission Tomography (SPECT)	p=0.015 (positive correlation, statistical value is not specified)	
Tsatali et al. 2014 75% (Greece)	Cross-sectional design	To examine the effect of anxiety and depression on pain intensity and other psychological characteristics and to identify relationships between	<ul style="list-style-type: none"> <li>n=25 (Group 1: AD with comorbid depression and anxiety disorders), n=31 (Group 2: AD with no psychological disturbances)</li> <li>Mean age: 75.01±3.59 (Group 1), 71.04±7.44 (Group 2) (Range: 55-85)</li> <li>Mean MMSE: 21.67±0.70 (Group 1), 20.60±0.82 (Group 2)</li> </ul>	Diagnosis of Alzheimer's Disease by DSM-IV-TR criteria	Pearson correlation coefficient	Depressive symptoms	Patient Health Questionnaire	p<0.01	PASS (pain anxiety)
						Depression diagnosis	Depression diagnosis	p<0.01	



APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
		depressive symptoms and pain anxiety.	<ul style="list-style-type: none"> <li>Setting: Unknown (Participants were recruited from outpatient care center)</li> </ul>						
van Vliet et al. (2012) 71.4% (Netherlands)	Longitudinal design	To investigate the frequency of NPI in EOAD and to compare it with the results from LOAD.	<ul style="list-style-type: none"> <li>n=98 (EOAD), n=123 (LOAD)</li> <li>Mean age: 61.2±4.9 (EOAD), 78.8±5.9 (LOAD) (Age ranges are not specified)</li> <li>Mean MMSE: 18.5±06.4 (EOAD), 18.3±4.4 (LOAD)</li> <li>Setting: Day care facilities, university medical centers, and regional community mental health</li> </ul>	<ul style="list-style-type: none"> <li>EOAD: Diagnosis of dementia by DSM-IV-TR</li> <li>LOAD: Diagnosis of dementia</li> </ul>	Logistic regression analysis	EOAD	Diagnosis of dementia before age of 65 was classified as EOAD.	OR=0.4 [0.18-0.89], p=0.025	NPI-Anxiety

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
			services for EOAD, and memory clinic, and community health care team for LOAD.						
van Vliet et al. (2013) 85.7% (Netherlands)	Longitudinal design	To examine the relationships between awareness and affective	<ul style="list-style-type: none"> <li>n=142 (EOAD), n=126 (LOAD)</li> <li>Mean age: 61.6±4.8 (EOAD), 79.1±6.1 (LOAD) (Age ranges are not</li> </ul>	<ul style="list-style-type: none"> <li>EOAD: Diagnosis of dementia by DSM-IV-TR</li> <li>LOAD: Diagnosis of dementia by NINCDS-ADRDA</li> </ul>	Logistic regression analysis	LOAD	Diagnosis of dementia on 65 years or older was classified as LOAD.	OR=1.29 [0.67-2.52], p=0.446	NPI-Anxiety

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
		symptoms (anxiety and depression) in PWD.	specified) <ul style="list-style-type: none"> <li>• Average cognition status: Not specified.</li> <li>• Setting: Day care facilities, university medical centers, and regional community mental health services for EOAD, and memory clinic, and community health care team for LOAD.</li> </ul>			Level of awareness: moderately disturbed	Rating of Awareness Deficits (GRAD)	OR=1.38 [0.53-3.63], p=0.514	
						Level of awareness: mildly disturbed	Rating of Awareness Deficits (GRAD)	OR=1.54 [0.56-4.24], p=0.405	
						Intact	Rating of Awareness Deficits (GRAD)	OR=2.01 [0.65-6.20], p=0.226	
Zuidema et al. 2010  75% (Netherlands)	Cross-sectional design	To investigate the influence of environmental factors	<ul style="list-style-type: none"> <li>• n=1289</li> <li>• Mean age: 83±8 years (Age range is not specified)</li> <li>• Average cognition status: Not specified.</li> </ul>	Diagnosis of dementia by the Diagnostic and Statistical Manual of Mental	Logistic regression analysis	Female  Age	Gender  Age	OR=2.62 [1.82-3.79], p<0.05  OR=0.968 [0.951-0.985], p<0.05	NPI-NH Depression/Anxiety (based on factor analysis from a

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors			Anxiety
						Factors	Measures	Statistical Significance	Anxiety measures
		on neuropsychiatric symptoms in PWD who live in nursing homes.	• Setting: Nursing home	Disorder (DSM-IV)		Duration of institutionalization	Months	OR=0.989 [0.983-0.995], p<0.05	previous study)
						Antipsychotics	Prescribed medication	OR=1.38 [1.05-1.80], p<0.05	
						Anxiolytics	Prescribed medication	OR=1.54 [1.09-2.16], p<0.05	
						Antidepressants	Prescribed medication	OR=1.84 [1.40-2.43], p<0.05	
						Patients per unit	Number of patients per unit	OR=0.99 [0.97-1.02], p>0.05	
						Walking circuit present	Presence of an walking circuit	OR=0.96 [0.62-1.50], p>0.05	

APA Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Statistics	Predictors		Anxiety	
						Factors	Measures	Statistical Significance	Anxiety measures
						Dementia Special Care Unit for high symptom level	Dementia Special Care Unit designed for patients with high levels of neuropsychiatric symptoms compared to regular unit	OR=1.72 [0.73-4.05], p>0.05	
						Time spent on patient care	Time spend on direct patient care per patient (in hours each day)	OR=0.73 [0.42-1.26], p>0.05	

**Table S 2. Table of evidence: Qualitative studies**

Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Analyses	Results
Goyal et al. (2019) 90% (Norway)	Descriptive design	To describe clinicians' experience of anxiety in PWD.  <ul style="list-style-type: none"> <li>• Q1) What is clinicians' perception of the nature of anxiety in patients with dementia?</li> <li>• Q2) How do clinicians identify anxiety in patients with dementia?</li> <li>• Q3) How do clinicians differentiate anxiety from depression in patients with dementia?</li> </ul>	* Informants  <ul style="list-style-type: none"> <li>• n=7 (2 specialist psychologists, 2 geriatric psychiatrists, 1 psychiatric nurse, 2 consultant physicians)</li> <li>• Mean age: 50 years (Range: 40-71)</li> <li>• Clinical experience with older adults with mental illness ranges from 7 to 40 years.</li> </ul>	Just mentioned patients with any type and stage of dementia	<ul style="list-style-type: none"> <li>• Data collection method: semi-structured interview</li> <li>• Data analysis: qualitative content analysis</li> </ul>	There were three categories found from this study.  (1) A reaction to loss and worries - Anxiety in PWD are usually related to one's loss and worries. Anxiety is triggered by feeling insecurity, loss or uncertainty. Clinicians report that living alone is also related to feeling anxiety in PWD. (2) Symptoms of anxiety and depression interfere with each other - Compared to depression, anxiety symptoms are situational and not persistent. While depression is past-oriented concept, anxiety is future-oriented. While people with depression tend to be indecisive, apathetic, and slow, people with anxiety are often action-oriented, hyper vigilant, and alert. They are "quick in motions, restless, and express less despair as compared to depression." While people with depression get up early in the morning, people with anxiety have difficulty falling a sleep at night.

Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Analyses	Results
						<p>(3) Anxiety in dementia-a multidisciplinary task  - An assessment tool is needed for measuring anxiety in PWD. In addition, understanding patient's life story and explaining them what is happening is helpful in lessening anxiety in PWD. Observing patient's facial expressions and showing empathy is also important in managing anxiety in PWD.</p> <p>In mild dementia, anxiety symptoms often include "feeling insecure, being less social, refusing to go to the doctor for check-ups, and reducing activities of daily living." In moderate dementia, anxiety symptoms include "worries, irritability, paranoia, accusations about things being stolen, fear of being alone or being abandoned, and following the caregiver like a shadow."</p>

Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Analyses	Results
Johannessen et al. (2018) 80% (Norway)	Grounded theory	To examine how people with young-onset dementia describe the course of dementia, their needs, and their coping strategies.	<ul style="list-style-type: none"> <li>* Informants</li> <li>• n=10 (People with young-onset dementia (age at onset of dementia before 65))</li> <li>• Mean age: 60 years (Range: 49-67)</li> <li>• Informants include both genders, living alone, from the southern and western parts of Norway</li> <li>• Setting: Nursing home and home mixed</li> </ul>	Diagnosis of dementia	Grounded theory method (except formulating a theory)	PWD felt anxious about losing control and misunderstandings. PWD also had anxiety in that they spend more effort in everyday tasks.



Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Analyses	Results
Qazi et al. (2010)  70% (United Kingdom)	Narrative study	To investigate the view of PWD, staff, and family caregivers on the causes and management of anxiety in dementia.	<ul style="list-style-type: none"> <li>• n=81 (23 PWD, 32 staff, 26 family caregivers)</li> <li>• Mean age: 78 (PWD), 46 (staff), 26 (family caregivers)</li> <li>• Mean MMSE of PWD: 24</li> <li>• Mean working time with dementia for staff: 22 years</li> <li>• Types of family caregivers: 10 husbands, 13 wives, 2 daughters, 1 friend</li> <li>• Setting: Mixed</li> </ul>	Diagnosis of dementia	Focus group interviews	<p>* Causes of anxiety</p> <p>(1) Diagnosis of dementia: PWD become anxious when they are diagnosed with dementia. Staff felt that anxiety was more frequent in early stage dementia as they have more insight.</p> <p>(2) Loss of skills: When PWD cannot do everyday tasks (for example, writing down name, answering the phone, driving a car, remembering grand-children's name), PWD felt more anxious.</p> <p>(3) Physical and environmental factors: Health conditions such as infections, constipation, pain and poor sleep were some causes for anxiety. Noise, social isolation, and being in crowds were environmental factors that cause anxiety.</p> <p>(4) Relationships with others: Other people's patronizing attitude also causes anxiety in PWD.</p> <p>* Management of anxiety</p> <p>(1) Being with other peers when diagnosed with dementia</p> <p>(2) Person centered care</p>

Reference, JBI (Country)	Study Design	Purpose	Sample Characteristics at Baseline	How Dementia Was Defined	Analyses	Results
						(3) Memory aids such as diary and notes (4) Enjoyable and distracting activities such as playing the piano, listening to music, and going out for a walk, or drive in the car (5) Detecting and managing physical and environmental problems (6) Medication as a last remedy