CURRICULUM VITAE

Victoria Ann Nalls, GNP-BC, CWS, ACHPN

Contact information: vyckinalls@gmail.com

Doctoral Program in Nursing, July 2020

University of Maryland, School of Nursing

EDUCATION

July 2020	PhD Candidate, Nursing University of Maryland, School of Nursing
2008	Master of Science University of Maryland, School of Nursing
2005	Bachelor of Nursing Johns Hopkins School of Nursing
2004	Bachelor of Science, Minor in Spanish Elon University

PROFESSIONAL EXPERIENCE

2019 – 2020	Director of Education Capital Caring Health
2012 – 2019	Nurse Practitioner, Regional Educator, Clinical Services Manager Optum
2011 – 2012	Geriatric Nurse Practitioner Genesis Physician Services
2009 – 2011	Geriatric Nurse Practitioner Bravohealth

TEACHING EXPERIENCE

2016	Guest Lecturer University of Delaware Cognitive and Psychosocial Changes of Aging
2012 – 2014	Clinical instructor for NURS 687 University of Maryland, School of Nursing

PROFESSIONAL SERVICE

Academic Service

2019 – Present	Ad-Hoc Reviewer Journal of the American Medical Directors Association
2017	APRN Faculty for Education Pathway Hospice and Palliative Nurses Association (HPNA)

Community Service

2020 elect	Nominating Committee for Board of Directors Gerontological Advanced Practice Nurses Association (GAPNA)
2019 – Present	Board Member Mid-Atlantic Medical Directors Association (MMDA)
2019 – Present	Conference Planning Committee Member Hospice & Palliative Care Network of Maryland
2018 – Present	NP/PA Advisory Council American Medical Directors Association: Society for Post-Acute and Long-Term Care (AMDA)
2018 – Present	Conference Planning Committee Member AMDA
2015 – Present	Conference Planning Committee Member Education Co-Chair 2020 MMDA
2016 – 2018	Conference Planning Committee Member GAPNA
2013 – 2016	Mentor Johns Hopkins School of Nursing Alumni-Student Mentorship Program

PROFESSIONAL MEMBERSHIPS

2019 – Present	American Academy of Home Care Medicine (AAHCM)
2017 – Present	Association for the Advancement of Wound Care (AAWC)
2016 – Present	Sigma Theta Tau
2015 – Present	Hospice and Palliative Nurses Association (HPNA)
2015 – Present	American Geriatrics Society
2011 – Present	American Medical Directors Association: Society for Post-Acute and Long-Term Care (AMDA)
2011 – Present	Mid-Atlantic Medical Directors Association (MMDA)
2010 – Present	Gerontological Advanced Practice Nurses Association (GAPNA)

HONORS AND AWARDS

2018	Emerging Leaders Program United Healthcare
2018	Resnick-Sollins Gerontological Nursing Scholarship University of Maryland, School of Nursing
2017	SuperHero Nominee Optum
2017	Dr. Mary Susan Jamison Scholarship University of Maryland, School of Nursing
2017	Resnick-Sollins Gerontological Nursing Scholarship University of Maryland, School of Nursing
2016	Marriott Scholars Scholarship University of Maryland, School of Nursing
2015	Marriot Scholars Scholarship University of Maryland, School of Nursing
2013	Futures Program AMDA Foundation
2008	Sigma Theta Tau Induction into Honor Society
2004	Cum Laude Elon University

PUBLICATIONS

McClean, M., & Nalls, V. (2020). Palliative Care and the Pandemic: Resources for PALTC Providers and Families. *Caring for the Ages*, in press.

Ashraf, M., Gaur, S., Bushen, O., Chopra, Chung, P., Clifford, K., Hames, E., Hertogh, C., Krishna, A., Mahajan, D., Merh, D., Nalls, V., Rowe, T., Schweon, S., Sloane, P., Trivedi, K., van Buul, L., & Jump, R. (2020). Diagnosis, Treatment, and Prevention of Urinary Tract Infections in Post-Acute and Long-Term Care Settings: A Consensus Statement from AMDA's Infection Advisory Subcommittee. *Journal of the American Medical Directors Association*, *21*(1), 12.

Nalls, V. (2019, October 16). *Tag! You're It!* AAWC Wound Blog. https://aawconline.memberclicks.net/index.php?option=com_dailyplanetblog&view=entry&year=2019&month=10&day=16&id=79:tag-you-re-it-

Kolanowski, A., Boltz, M., Galik, e., Giltlin, L., Kales, H., Resnick, B., Van Haitsma, K., Knehans, A., Sutterlin, J., Sefcik, J., Liu, W., Petrovsky, D., Massimo, L., Gilmore-Bykovskyi, A., MacAndrew, M., Brewster, G., Nalls, V., Jao, Y-L, Duffort, N., & Scerpella, D. (2017). Determinants of behavioral and psychological symptoms of dementia: A scoping review of the evidence. *Nursing Outlook*, *65*(5), 515-529.

Galik, E., Resnick, B., Vigne, E., Holmes, S., & Nalls, V. (2017). Reliability and validity of the resistiveness to care scale among cognitive impaired older adults. *Journal of the American Medical Directors Association*, *18*(1), 59-64.

PRESENTATIONS

Bray, M., Nalls, V. & Scarborough, P. (2019). Wound care 101: Achieving excellence through best practice. Group presentation for Florida Medical Directors Association (FMDA) Annual Conference.

Nalls, V., Galik, E., & Resnick, B. (2019). Predictors of depressive symptoms in nursing home residents with severe cognitive impairment. Poster presented at Aging Research Symposium, University of Maryland, Baltimore.

Nalls, V. Not all things heal: Palliative wound care. (2019). Capital Caring Health (CCH) monthly CME lecture series.

Levine, J., Byrd, S., Bolhaek, S., Nalls,V., Brandeis, G., Litchford, M., Steinberg, K., Stone, A., Takahashi, P. (2019). Wound care boot camp: The basics and beyond. Group presentation for AMDA: Society for PA/LTC Annual Conference.

Nalls, V., Lapham, T., Verma, K. (2018) Foot and Ankle Wounds. Group presentation for GAPNA Annual Conference.

Nalls, V. (2017). Wound care in long term care: Looking at the whole patient. Virtual live presentation for continuing education (CE) for Optum Grand Rounds.

Maguire, M., & Nalls, V. (2016). Workshop on skin conditions and new technologies for wound care. Presentation for MMDA Annual Conference

Nalls, V. (2016). Presented for Dr. Barbara Resnick. - Immunization Update: Pneumonia Vaccines. MMDA Annual Conference

ABSTRACT

Title: Evaluating Antidepressant Use in Nursing Home Residents with Moderate to Severe Cognitive Impairment

Victoria Nalls, Doctor of Philosophy, 2020

Dissertation Directed by:

Elizabeth Galik, PhD, CRNP, FAAN, FAANP, Professor, School of Nursing

Barbara Resnick, PhD, CRNP, FAAN, FAANP, Professor, School of Nursing

Background: Antidepressants are commonly prescribed medications among nursing home residents and used to treat symptoms of dementia. Concerns have been raised, however, about disparities and potential inappropriate use of these medications within this population.

Purpose: The purpose of this dissertation was to: (1) Describe factors associated with antidepressant use in nursing home residents with moderate to severe cognitive impairment; (2) Describe differences in antidepressant use between white and black nursing home residents with moderate to severe cognitive impairment; (3) Evaluate trends in antidepressants and antipsychotics prescribing among nursing home residents with moderate to severe cognitive impairment.

Methods: This secondary data analysis used data from the Function and Behavior Focused Care (FBFC) for Nursing Home Residents with Dementia randomized control trial. A total of 336 residents were included in the study, who were mostly white, female, severely cognitively impaired (MMSE=7.8, SD=5.1) and the average age was 82. Data collection was done at baseline and 12 months and based on chart reviews, input from staff, and observation of residents. Descriptive statistics and logistic regression were

used to address aims 1 and 2. Generalized linear mixed modeling with a binary distribution and logit link function was used for aim 3.

Results: At baseline, 59% of the sample was taking an antidepressant. Race was significantly associated with antidepressant use (β=0.51; p=0.01). Black residents were half as likely to be on antidepressants compared to white residents (OR=0.499 CI=0.305-0.817) and received lower dosages of sertraline (t=2.68; p=0.01). There was no significant change in antidepressant or antipsychotic use at 12 months.

Conclusions: Black nursing home residents with moderate to severe cognitive impairment were significantly less likely to be on antidepressants and when treated, were likely to be on lower dosages of some antidepressants. It is unknown if this is due to misdiagnoses and disparities in treatment or lack of need for antidepressants or differences in responses to specific drug classes. Further research is needed to explore these differences and evaluate the influence of resident, prescriber, and facility factors on the use of antidepressants among nursing home residents with moderate to severe dementia.

Evaluating Antidepressant Use in Nursing Home Residents with Moderate to Severe Cognitive Impairment

by
Victoria Nalls

Dissertation submitted to the Faculty of the Graduate School of the
University of Maryland, Baltimore in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy
2020

DEDICATION

This work is dedicated to my Dad, LtCol Rodney McKitrick.

“A dream does not become reality through magic; it takes sweat, determination, and hard work.” -Colin Powell

ACKNOWLEDGEMENTS

I want to recognize and thank several key individuals, who without them, I would not have been able to pursue and complete my doctoral degree. First, to my co-chairs and mentors, Dr. Elizabeth Galik and Dr. Barbara Resnick. Thank you for over a decade of support, guidance, and mentorship. You set a path of excellence for others to follow, yet you do not let anyone travel that path alone. You selflessly impart your knowledge, share your time, encourage growth, and inspire myself and others. I am forever grateful.

I also want to thank my committee members, Dr. N. Jennifer Klinedinst, Dr. Nicole Brandt, and Dr. Nancy Lerner. Thank you for sharing your perspective and time to help me expand my thinking and support my growth on this academic journey.

To my MSMS girls, I am grateful for over 20 years of friendship. You have been there for so many crucial moments of my life, with nothing but love, hugs, and laughter. No matter hour many miles are between us, we come together and stay connected. To my best friend, Emily, thank you for always being there. I still say you are the smarter friend.

Saving the best for last, a huge thank you to my family, though words do not capture the gratitude I feel. Thank you, Mom, for teaching me the importance of empathy and compassion. Thank you, Dad, for instilling in me the value of knowledge and hard work. To my husband, thank you for your patience and love. We survived! To my in-laws, Bill and Michele, thank you for all your help and love. Lastly, my children, Tucker and Madeleine, thank you for accepting when mommy could not play and still giving me hugs. I love you both more than anything and hope you one day follow your dream.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

Abbreviation	Terms
BI	Barthel Index
BPSD	Behavioral and Psychological Symptoms of Dementia
CDC	Centers for Disease Control and Prevention
CMAI	Cohen-Mansfield Agitation Index
CMS	Centers for Medicare and Medicaid Services
CSDD	Cornell Scale for Depression in Dementia
FBFC	Function and Behavior Focused Care
FDA	Food and Drug Administration
MMSE	Mini-Mental Status Examination
NPS	Neuropsychiatric Symptoms
RCT	Randomized control trial
SEM	Social Ecological Model
SNRI	Serotonin and norepinephrine reuptake inhibitors
SSRI	Serotonin selective reuptake inhibitors
TCA	Tricyclic antidepressants

CHAPTER 1: Introduction and Background

Over the last few decades, antidepressants have become one of the most commonly prescribed medications in the United States, with prescriptions increasing the most among individuals 65 and older (Hanlon, Handler, & Castle, 2010; Mojtabai & Olfson, 2014; Maust, et al., 2017). The use of antidepressants is much higher among nursing home residents compared to community dwelling older adults, and antidepressant use ranges from 30% to 60% among nursing home residents with dementia (Iden, et al., 2014; Giebel, et al., 2015; Hiltunen, et al., 2016; Resnick, et al., 2019). Serotonin selective reuptake inhibitors (SSRIs) are the most commonly prescribed antidepressant drug class in long term care and approximately half of nursing home residents on an antidepressant are taking a SSRI (Hanlon, et al., 2011; Midlov, et al., 2014; Gadzhanova, Roughead, & Pont, 2018). Other antidepressant drug classes used in long term care include serotonin and norepinephrine reuptake inhibitors (SNRIs), tetracyclics (mirtazapine), serotonin modulators (trazodone), aminoketones (bupropion), and tricyclics (TCAs).

Antidepressants have Food and Drug Administration (FDA) approval for indications of depression and anxiety, but 30% to 40% of their use in long term care has also been for management of agitation, aggression, mood congruent psychosis, poor appetite, inappropriate vocalizations, resistance to care, and insomnia (Shah, et al., 2012; Echt, et al., 2013; Midlov, et al., 2014; Wei, et al., 2014; Iaboni, et al., 2016; Viscogliosi, Chiriac & Ettorre, 2017). These symptoms are known collectively as behavioral and psychological symptoms of dementia (BPSD) and occur in up to 90% of individuals with dementia (Lyketsos, et al., 2011; Kales, Gitlin, & Lyketsos, 2014). Ideally,

nonpharmacological interventions are recommended as the first-line treatment for BPSD (AGS, 2010; AMDA, 2018). Consistently and effectively managing BPSD can be challenging, and nursing home caregivers may lack confidence in their ability to utilize nonpharmacological strategies; consequently, it is not uncommon for a pharmacologic intervention to be preferred (Ervin, et al., 2014; Basnet, Acton, & Requejio, 2020).

Antipsychotics have also been commonly prescribed for pharmacologic management of BPSD, but professional organizations along with state and federal agencies discourage the use of these medications due to potential serious adverse events like extrapyramidal symptoms, cardiovascular events, falls, and increased mortality (Young, Taylor, & Lawrie, et al., 2015; McMaster, et al., 2018; Smeets, et al., 2018; Schwertner, et al., 2019; Fick, et al., 2019; Rubino, et al., 2020).

In 2012, the Centers for Medicare and Medicaid Services (CMS) implemented the National Partnership to Improve Dementia Care, which focused on reducing antipsychotic use in nursing home residents by requiring public reporting of their use and monetary penalties for their inappropriate use of these medications (CMS, 2014). National data trends demonstrated an overall reduction in the use of antipsychotics since 2012; however, use of other psychotropic medications, particularly antidepressants, may be increasing (Lucas & Bowblis, 2017; Olivieri-Mui, et al., 2018; Maust, et al., 2018; CMS, 2019). Longitudinal studies found antidepressants had a persistent prevalence of use above 50% among all nursing home residents (Ruths, et al., 2013; Vasudev, et al., 2015; Helvik, et al., 2017; Maust, et al., 2018). Some studies (Helvik, et al., 2017; Maust, et al., 2018) noted that use of antidepressants among residents in nursing homes remained stable over time while others found antidepressant use significantly increased

over time (Ruths, et al., 2013; Vasudev, et al., 2015). Ongoing use of antidepressants among older adults is not benign as there are potential adverse effects like sedation, gastrointestinal upset, hyponatremia, serotonin syndrome, increased falls and fractures, serious cardiovascular events and increased mortality risk (Draper & Berma, 2008; Andrade, et al., 2010; Huybrechts, et al., 2011; Sterke, et al., 2012; Wei, et al., 2016; Hiance-Delahaye, et al., 2018; Sobieraj, et al., 2019).

Effectiveness of Antidepressants

The assessment of depressive symptoms in dementia can be difficult as symptoms such as appetite changes, sleep disturbances, psychomotor changes, and irritability are also symptoms that may indicate dementia progression (Olin, et al., 2002; Sepehry, et al., 2017). The efficacy and safety of antidepressant use among individuals with dementia remains inconclusive (Leong, 2014). Two community-based randomized controlled trials evaluating sertraline, a SSRI, for depression in Alzheimer's dementia patients found no benefit of sertraline over placebo (Banerjee, et al., 2011; Dyer, et al., 2011). A recent Cochrane review of outpatient individuals with mild to moderate dementia also concluded that there was high-quality evidence of little or no difference in scores on validated depression scales between antidepressants and placebo (Dudas, et al., 2018).

As noted above, antidepressants have been used to treat symptoms of dementia such as agitation, insomnia, and loss of appetite. The effectiveness of antidepressants for treatment of these symptoms has also not been well substantiated, and/or there have been concerns about drug side effects outweighing the benefits of treatment. A large, community-based randomized controlled trial found citalopram, a SSRI, to be effective

for agitation in dementia; however, potential serious cardiac events are associated with citalopram, and further research is needed to assess whether citalopram would be effective in a nursing home residents with dementia (Porsteinsson, et al., 2014; Farina, Morrell, & Banerjee, 2017). A Cochrane review that included both community and long-term care individuals with dementia and no depression noted that antidepressants used to manage agitation and psychosis may be beneficial, but these studies were small or had methodological issues (Seitz, et al., 2011). Other non-SSRI antidepressants like mirtazapine and trazodone have also been evaluated for BPSD, but studies were small and exploratory, or their effectiveness did not outweigh adverse events in this population (Watt, et al., 2018; Zuidersma, et al., 2019). Lastly, a recent narrative review summarized randomized control trials that evaluated antidepressants for management of depression, agitation, psychosis, and apathy in dementia and found the evidence to support antidepressant use in persons with dementia weak (Farina, Morrell, & Banerjee, 2017).

Factors Associated with Antidepressant Use in Older Adults

There are numerous factors associated with the use of antidepressants among older adults. Specifically, these include age, gender, race, number of co-morbidities, functional status, and level of agitation (Karkare, et al., 2011; Gustafsson, et al., 2013; Smeets, et al., 2018; Bhattacharjee, et al., 2019; Bobo, et al., 2019; Resnick, et al., 2019). Individuals younger than 75 are more likely to be prescribed an antidepressant compared to those 75 or older (Karkare, et al., 2011; Bhattacharjee, et al., 2019; Bobo, et al., 2019). Females and older adults with a higher number of co-morbidities are also more likely to be prescribed an antidepressant (Gustafsson, et al., 2013; Dutcher, et al., 2014; Bobo, et

al., 2019). White older adults receive antidepressants significantly more often than other minorities (Karkare, et al., 2011; Wei, et al., 2016; Bobo, et al., 2019). Older adults who are more functionally independent are more likely to be on an antidepressant (Karkare, et al., 2011; Helvik, et al., 2017). Lastly, individuals who demonstrate more severe agitated behaviors are more likely to be on an antidepressant compared to those without agitation (Smeets, et al., 2018; Resnick, et al., 2019).

Research looking at antidepressant use among nursing home residents tends to include residents who are cognitively intact or with mild to moderate cognitive impairment and predominantly white (van Asch, et al., 2013; Iden et al., 2014; Midlov, et al., 2014; Hiltunen, et al., 2016; Brimelow, et al., 2018). Racial differences have been noted, however, such that black nursing home residents with depression were significantly less likely to be prescribed antidepressants compared to white residents with depression (Hanlon, et al., 2009; Gaboda, et al., 2011). The samples in those studies also included residents who were cognitively intact or only mildly impaired. It is unknown whether this disparity extends to residents with moderate to severe cognitive impairment. Often residents with moderate to severe dementia are excluded from antidepressant research in long term care due to the lack of ability to self-consent. Further research is needed to describe the use of antidepressants in persons with moderate to severe dementia and explore possible racial disparities among this vulnerable population. Given the previously described minimal efficacy, potential serious adverse events, and concerns that antidepressants may be increasing since implementation of the National Partnership to Improve Dementia, further research is also needed to describe the longitudinal use of

antidepressant among nursing home residents with moderate to severe cognitive impairment.

Conceptual Framework

The social ecological model (SEM) is a framework used to evaluate interrelations between people and their physical and social environments through four levels: intrapersonal, interpersonal, environment, and policy (Sallis, et al., 2006). This model addresses the comprehensive approach needed to evaluate antidepressant use among nursing home residents with moderate to severe cognitive impairment. As previously stated, age, gender, race, level of agitation, and functional status are associated with antidepressant use, which are intrapersonal examples (Gustafsson, et al., 2013; Smeets, et al., 2018; Bhattacharjee, et al., 2019; Bobo, et al., 2019; Resnick, et al., 2019). Interpersonal factors include nursing home staff's stress and workload, which if perceived as burdensome, can influence the prescription of an antidepressant (Zuidema, et al., 2011; Basnet, Acton, & Requijo, 2020). Having multiple providers treating the patient is also associated with antidepressant use (Bobo, et al., 2019). Environmental and policy factors that are associated with antidepressant use include low staff to patient ratios, insurance type, total number of facility beds, facility ownership, utilization of consulting psychiatric services, CMS requirements, and the National Partnership (Hanlon, Handler, & Castle, 2010; Karkare, et al., 2011; Bourgeois, et al., 2012; Smeets, et al., 2014; Smeets, et al., 2018; Resnick, et al., 2019). This study focuses on factors at the intrapersonal level of the SEM to evaluate antidepressant use in nursing home residents with moderate to severe cognitive impairment.

Purpose and Overview of Manuscripts

The primary aims of this dissertation were to: (Aim 1) Determine factors that influence antidepressant use in nursing home residents with moderate to severe cognitive impairment; (Hypothesis 1) Age, gender, race, number of co-morbidities, functional status, and level of agitation would be associated with antidepressant use in nursing home residents with moderate to severe dementia; (Aim 2) Describe differences in antidepressant use between white and black nursing home residents with moderate to severe cognitive impairment; (Hypothesis 2) There would be a greater use of all antidepressants in white versus black nursing home residents with moderate to severe cognitive impairment when controlling for depression, age, gender, functional status, level of agitation, and number of co-morbidities; (Aim 3) Evaluate trends in antidepressants and antipsychotics prescribing among nursing home residents with moderate to severe cognitive impairment; (Hypothesis 3) There would be an increase in the use of antidepressants and decrease in the use of antipsychotics between baseline and 12 months among nursing home residents with moderate to severe cognitive impairment when controlling for age, gender, race, functional status, number of co-morbidities, and treatment effects from the parent study.

Data for this dissertation comes from the Function and Behavior Focused Care (FBFC) for Nursing Home Residents with Dementia randomized, control trial (RCT) with repeated measures design. The parent study occurred from 2013 to 2018 and focused on evaluating the effectiveness of the FBFC intervention on optimizing function and physical activity while minimizing behavioral symptoms among nursing home residents with moderate to severe cognitive impairment.

Antidepressant Use in Nursing Home Residents with Dementia (Manuscript 1)

Manuscript #1 focuses on describing antidepressant use and identifying the factors that influence antidepressant use among nursing home residents with moderate to severe cognitive impairment. As previously stated, age, gender, race, number of comorbidities, functional status, and level of agitation are associated with antidepressant use among older adults (Karkare, et al., 2011; Gustafsson, et al., 2013; Smeets, et al., 2018; Bhattacharjee, et al., 2019; Bobo, et al., 2019; Resnick, et al., 2019), but it is unknown if this association extends into persons with moderate to severe cognitive impairment. This manuscript used baseline data from the FBFC RCT and was a descriptive correlational analysis. It was hypothesized that age, race, gender number of co-morbidities, functional status, and level of agitation would be significantly associated with antidepressant use in nursing home residents with moderate to severe cognitive impairment and was tested using logistic regression. Findings from this work expand current knowledge around associations with antidepressant use in a population of nursing home residents with moderate to severe cognitive impairment.

Racial Differences in Antidepressant Use in Nursing Home Residents with Moderate to Severe Cognitive Impairment (Manuscript 2)

Manuscript #2 explored racial differences in antidepressant use among nursing home residents with moderate to severe cognitive impairment from a descriptive, exploratory design approach. Study populations evaluating antidepressant use among nursing home residents with dementia tend to have predominantly white participants, and residents with more severe cognitive impairment are generally excluded due to difficulty obtaining information as they cannot self-report (Banerjee, et al., 2011; Hanlon, et al.,

2011; Bali, et al., 2017; Mueller, et al., 2017; Wei, et al., 2016). Understanding the impact of race on antidepressant use among nursing home residents with dementia increases our awareness of potential health disparities occurring within this vulnerable population.

It was hypothesized that 1) controlling for depression, age, gender, functional status, level of agitation, and number of co-morbidities, there would be greater use of all antidepressants in white versus black nursing home residents with moderate to severe cognitive impairment; and 2) Black nursing home residents with moderate to severe cognitive impairment would receive lower dosages of the most commonly prescribed antidepressants compared to white nursing home residents with moderate to severe cognitive impairment. Baseline data from the FBFC RCT was used, where just under half of the sample was black. The first hypothesis was tested using logistic regression, and T-test or Mann-Whitney U Test was used to evaluate for significant differences in dosages. Findings from this study provide useful information about racial disparities with antidepressant use among nursing home residents with moderate to severe cognitive impairment. This information can be used by healthcare providers to focus on appropriate use or overuse of antidepressants by race in residents with moderate to severe cognitive impairment.

Patterns of Use of Antidepressants and Antipsychotics over One Year in Nursing Home Residents with Moderate to Severe Cognitive Impairment (Manuscript 3)

Using a longitudinal design, Manuscript #3 evaluated the use of antidepressants and antipsychotics between baseline and 12 months among nursing home residents with moderate to severe cognitive impairment, a year to 5 years after the implementation of

the National Partnership to Improve Dementia. Given previous concerns around possible unintended prescribing changes after the National Partnership implementation and limited evidence of antidepressant efficacy in this population (Lucas & Bowblis, 2017; Farina, Morrell, & Banerjee, 2017; Olivieri-Mui, et al., 2018; Maust, et al., 2018; CMS, 2019), it was hypothesized that there would be an increase in the use of antidepressants and a decrease in the use of antipsychotics between baseline and 12 months among nursing home residents with moderate to severe cognitive impairment, when controlling for age, gender, race, functional status, number of co-morbidities, and treatment effects of FBFC. Baseline and 12-month data were used from the FBFC RCT, and a generalized linear mixed model with a binary distribution and logit link function was used to evaluate the hypothesis. Findings from this work increase current knowledge regarding antidepressant and antipsychotic prescribing trends among nursing home residents with moderate to severe cognitive impairment following implementation of the National Partnership.

Definition of Terms

This study uses the following conceptual and operational definitions of terms:

1. Nursing home: Nursing homes are residential facilities that provide skilled nursing and related services to individuals who require medical or nursing care and/or rehabilitation services (Medicare, 2019). Only long-term care residents were recruited for the parent study.

2. Age: The length of time a person has been alive since birth; operationalized by using the date of birth from the chart to create a numerical value

3. Race: Refers to a person's physical characteristics such as bone structure, skin, hair or eye color; operationalized by matching the data collected to the identified race in the patient's chart, which included the following categories: 1)White, 2)Black/African American, 3)Asian, 4)Native Hawaiian/Pacific Islander, 5)Native American/Alaskan Native, 6)More than one race, 7)Don't know, or 8)Refused

4. Gender: A range of characteristics that may include biological sex, sex-based social structures, or gender identity; operationalized by matching the data collected to the identified gender in the patient's chart as either male or female

5. Co-morbidities: the presence of more than 1 distinct medical condition in an individual; operationalized by listing all co-morbid conditions and then counting them for a sum numerical total

6. Antidepressants: Medications which alter the availability of neurotransmitters known to impact mood such as serotonin, dopamine, and norepinephrine. Antidepressants include the following drug classes: serotonin selective reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclics (TCAs), serotonin modulators (trazodone), tetracyclics (mirtazapine), and unicyclic aminoketones (bupropion).

7. Antipsychotics: Medications that act on the brain by reducing dopaminergic neurotransmission; atypical antipsychotics also impact serotonin receptors. Antipsychotics include the following medications: chlorpromazine, prochlorperazine, fluphenazine, haloperidol, perphenazine, thiothixene, trifluoperazine, apripirazole, asenapine, brexpiprazole, cariprazine, clozapine, lurasidone, olanzapine, paliperdone, quetiapine, risperidone, ziprasidone

8.Functional Status: Functional status is conceptually defined as the individual's ability to participate with activities of daily living such as walking, bathing, dressing, grooming, feeding, and transfers. It is operationally defined as the total score on the Barthel Index, with 100 be completely independent (Mahoney & Barthel, 1965). This measure was completed by the nursing assistant providing care to the resident on the day of testing.

9. Cognition: Cognition is conceptually defined as the ability or lack of ability to recall, learn new things, concentrate, or make decisions that affect daily life (CDC, 2019a). It is operationally defined in this study by using the Mini-mental status examination (MMSE) (Folstein, Folstein, and McHugh, 1975). Individuals with a MMSE of 15 or less are considered to have moderate to severe cognitive impairment. Participants were initially screened, and those who had a MMSE greater than 15 were excluded from the study.

10. Level of Agitation: Level of agitation is conceptually defined as behavior that is socially inappropriate and manifested in 3 ways: 1) may be abuse or aggressive toward self or other; 2) an appropriate behavior performed with inappropriate frequency; or 3) inappropriate activity according to social standards for a specific situation (Cohen-Mansfield, 2014). It is operationally defined as a total score on the Cohen-Mansfield Agitation Inventory (CMAI) short form, where higher scores indicate more severe agitation.

11. Depressive Symptoms: mood disorder characterized by the presence of sadness, loss of pleasure, feelings of guilt and low self-esteem, altered sleep patterns and appetite, inattention, and/or fatigue, which can impact daily activities. Depressive symptoms were operationalized by using the Cornell Scale for Depression in Dementia (CSDD) (Alexopoulos, 1988), where a caregiver for the patient provides feedback on the

resident's mood and behavior over the past two weeks. A score greater than 8 implies probable depression, and a score higher than 18 is definitive for major depression (Alexopoulos, 2002).

Assumptions of the Study

1. The MMSE accurately screened individuals so that the sample consisted only of nursing home residents moderate to severe cognitive impairment as defined by a MMSE of 15 or less.
2. Age, gender, race, number of comorbidities, functional status, and level of agitation are associated with antidepressant use.
3. The feedback provided by proxy report or observation accurately reflected what was really occurring with the cognitively impaired participant who could not self-report

Summary

This first chapter provides background and justification for the purpose of this work. It also describes the aims and hypotheses to be addressed within this work. The conceptual framework was described and supported from empirical literature for its use within this work. Lastly, definition of terms and assumptions of the study were outlined.

CHAPTER 2: Antidepressant Use in Nursing Home Residents with Dementia

Abstract

Antidepressants are increasingly being prescribed in long term care for behavioral and psychological symptoms of dementia (BPSD). They have the highest prevalence and continuation rate but little evidence supporting their efficacy for BPSD. Antidepressants are associated with adverse events like falls and fractures. The purpose of this study was to describe antidepressant use in nursing home residents with moderate to severe dementia and test for factors that may influence their use. Using baseline data from the Function and Behavior Focused Care for Nursing Home Residents with Dementia randomized control trial, a secondary data analysis was performed. Logistic regression was used to assess for associations between age, gender, race, number of co-morbidities, functional status, and level of agitation and antidepressant use. Fifty-nine percent were on at least one antidepressant, and 39 individuals (12%) were taking two antidepressants. Race was significantly associated with antidepressant use, with black residents half as likely to receive an antidepressant when compared to white residents (OR=0.51; CI=0.32-0.83). Further research is needed to better understand the value of antidepressants in moderate to severe dementia.

Background

In 2016, the Centers for Disease Control and Prevention (CDC) reported that almost half of the 1,347,600 individuals residing in nursing homes have dementia (CDC, 2019b). The commonly seen behavioral disturbances associated with dementia are called behavioral and psychological symptoms of dementia (BPSD), or neuropsychiatric symptoms (NPS), and occur in up to 90% of nursing home residents with dementia (Halloran, 2014). BPSD include symptoms of depression, agitation, aggression, resistiveness to care, anxiety, apathy, and psychosis (Kales, Gitlin, & Lyketsos, 2015; Resnick, et al., 2017). Historically, antipsychotics were used to manage behavioral symptoms, such as agitation and aggression; however, antipsychotic medications increase risk of death and serious cardiovascular events with their use (Kleijer, et al., 2014; Masopust, et al., 2018). Due to concerns with overuse of antipsychotics, the Centers for Medicare and Medicaid Services (CMS) launched the National Partnership to Improve Dementia Care in 2012 with one of its goals focused on reducing antipsychotic use in nursing home residents with dementia (CMS, 2014). Since the initiation of the partnership, antipsychotic use has declined by 39% (CMS, 2019), but other psychotropic medications, particularly antidepressants, are increasingly being prescribed to older adults with dementia (Lucas & Bowblis, 2017; Olivieri-Mui, et al, 2017). Antidepressant use ranges from 30-60% among nursing home residents with dementia (Shah, et al., 2012; Iden, et al., 2014; Hiltunen, et al., 2016; Midlov, et al., 2014). In addition, antidepressants have the highest continuation rate compared to other psychotropic medications (Ozaki, Katsumata, & Arai, et al., 2019), and every third indication of an antidepressant is being used off label for managing BPSD (Iden, et al.,

2014). This is concerning because the use of antidepressants among older adults with dementia is associated with an increased risk of falls, fractures, and emergency room visits within 90 days of starting an antidepressant (Marci, et al., 2017; Sterke, et al., 2012; Gebara, et al., 2015; Wei, et al., 2016; Cameron, et al., 2018).

Antidepressants and Indications for Use

Antidepressants have been prescribed for management of depression, anxiety, agitation, appetite, aggression, and insomnia (Shah et al., 2012; Bobo, et al., 2019; Viscogliosi, et al., 2017; Iaboni, et al., 2016), though they only have Food and Drug Administration (FDA) approval for indications of depression and anxiety. Serotonin selective reuptake inhibitors (SSRIs) are the most common class of antidepressants prescribed in older adults (Bourgeois, et al., 2012; McMaster, et al., 2018; Bhattacharjee, et al., 2019; Bobo, et al., 2019). Research is mixed regarding the efficacy of SSRIs for depression in mild to moderate dementia in the community setting. For example, one randomized control trial found the SSRI, sertraline, to be effective for depression in Alzheimer's disease (Lyketsos, et al., 2000); however, more recent randomized control trials did not find sertraline or the tetracyclic drug, mirtazapine, efficacious for depression management in Alzheimer's disease (Rosenberg, et al., 2010; Banjeree, et al., 2011). A frequently referenced, randomized, placebo-controlled study looked at the SSRI, citalopram, for the management of agitation in dementia and did find that citalopram reduced agitation (Porsteinsson, et al.,2014). However, this study was in a community-based setting with patients who had mild to moderate dementia, was associated with potential cardiovascular events, and research is still needed to evaluate citalopram's efficacy in nursing home residents with more severe dementia (Farina, Morrel, &

Banerjee, 2017). Lastly, one Cochrane review looking at SSRIs for management of agitation and psychosis in dementia concluded few studies existed to support the use of antidepressants for agitation and psychosis in dementia (Seitz, et al., 2011).

Factors Associated with Antidepressant Use

Aside from a diagnosis of depression, research looking at mixed samples of community and nursing home patients found that antidepressant use was associated with age, gender, race, number of co-morbidities, severity of agitation, and functional status (Bobo, et al., 2019; Karkare, et al., 2011; Wei, et al., 2016; Smeets, et al., 2018; Gustafsson, et al., 2013). Individuals who were younger than 75 were more likely to be prescribed an antidepressant than those who were 75 or older (Bhattacharjee, et al., 2019; Bobo, et al., 2019; Karkare, et al., 2011). In addition, older adults with a higher number of comorbid conditions were more likely to receive an antidepressant (Bobo, et al., 2019). Women were more likely to be on an antidepressant compared to men (Gustafsson, et al., 2013; Dutcher, et al., 2014; Wei, et al., 2016; Bobo, et al., 2018). Regarding race, white older adults were more likely than individuals of color to receive an antidepressant (Karkare, et al., 2011; Wei, et al., 2016; Bobo, et al., 2019). Residents who exhibited more severe agitation were more likely to be on antidepressants (Smeets, et al., 2017; Resnick, et al., 2019). Lastly, those who were more functionally independent were more likely to be on an antidepressant (Karkare, et al., 2011; Gustafsson, et al., 2013; van Asch, et al., 2012).

It is important to evaluate antidepressant prescribing in patients with dementia and identify any trends of potential overuse of antidepressants to help reduce the risks of polypharmacy in residents with advanced cognitive impairment. Current research looking

at antidepressant use in nursing home residents often excludes those with more severe dementia due to measurement and consent issues and focuses mainly on white females (Karkare, et al., 2011; Hiltunen, et al., 2016; Bhattacharjee, et al., 2019; ; Bobo, et al., 2019). The primary aim of this study was to describe antidepressant use, following policy initiatives geared toward decreasing antipsychotics in nursing home settings, in residents with moderate to severe cognitive impairment. A secondary aim was to also test for factors that influence antidepressant use in a large sample of nursing home residents. It was hypothesized that, age, race, gender, number of co-morbidities, functional status, and level of agitation would be significantly associated with the use of antidepressants in nursing home residents with moderate to severe cognitive impairment.

Methods

Design

This was a secondary data analysis using baseline data from the Function and Behavior Focused Care for Nursing Home Residents with Dementia randomized control trial. The original study was a clustered, randomized controlled trial with a repeated measures design that took place from 2013 to 2018. Residents were recruited from 12 nursing homes in Maryland and could participate if they were 55 years or older, English-speaking, resided in long term care at time of recruitment, and scored a 15 or less on the Mini Mental Status Examination (MMSE) (Folstein, Folstein, & McHugh, 1975). Hospice or sub-acute rehabilitation residents were excluded from the study. Participants or their legally authorized representatives were asked to consent to participate in the study prior to determining eligibility. If the resident was not able to pass the evaluation to Sign Consent (Resnick, et al., 2007), he/she was asked to sign an assent form, and

consent was given by the legally authorized representative. This study was approved by a university institutional review board.

Sample

Initially, 1512 residents were screened for eligibility, and 498 residents were excluded due to being on hospice, receiving rehabilitation services, in the hospital, or younger than 55. Then 527 residents either refused or had proxy refusal for participation. The initial cognitive screening excluded another 146 residents due to their MMSE being greater than 15. Lastly, 2 individuals withdrew from the study, and 3 expired shortly after consent but before baseline measurement. This study examined the final 336 participants prior to randomization (see Figure 1).

Measures

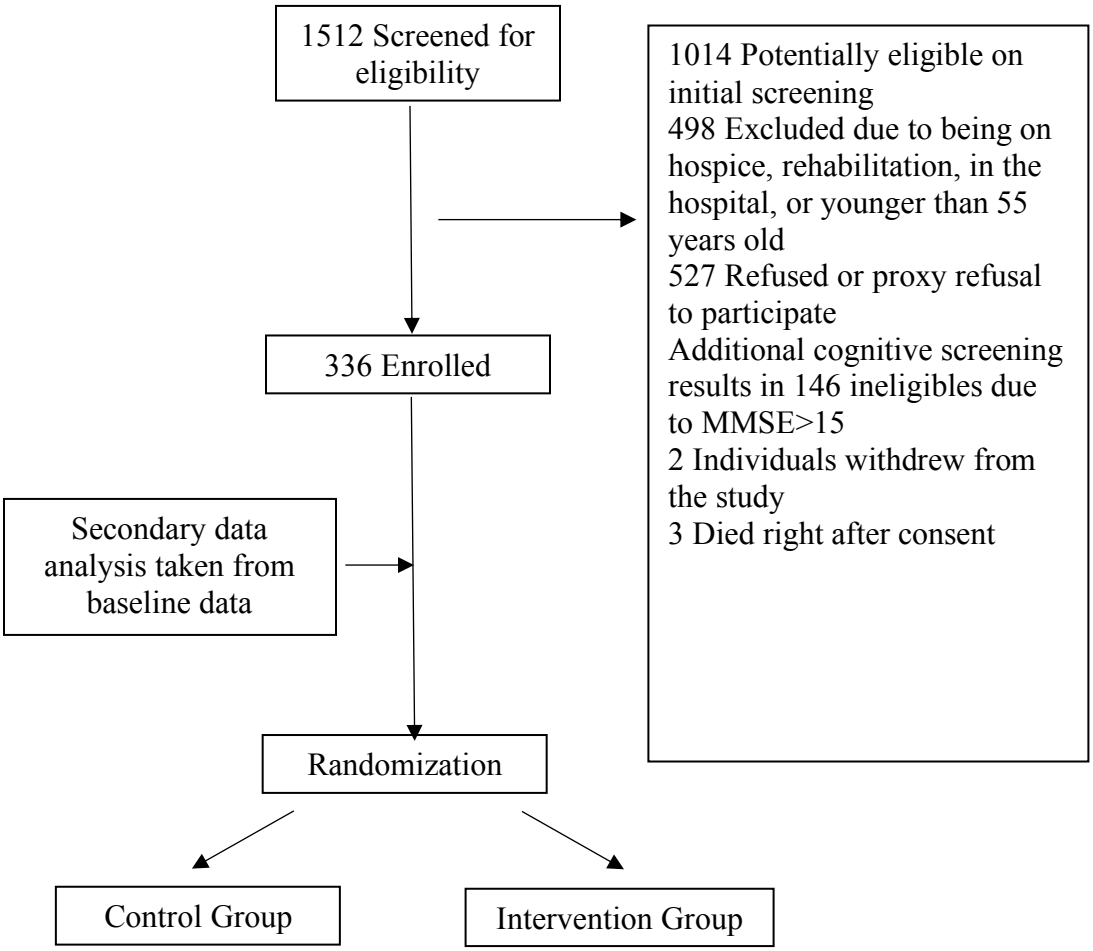
All residents were already determined to have moderate to severe cognitive impairment as determined by their initial MMSE screening. Measures were completed by a research evaluator through direct observation, proxy report from staff caring for the resident the day of testing, and chart abstraction. Descriptive information included age, marital status, gender, race, and number of comorbidities and were extracted from the medical chart. The MMSE was used to describe baseline cognitive status.

Depression

Depressive symptoms were measured using the Cornell Scale for Depression in Dementia (CSDD) (Alexopoulos, 1988). Prior use of this 19-item survey provided evidence of reliability based on Cronbach alpha values of .81 and 0.95 and validity compared to the SM-IV-TR (Barca, et al., 2015) to assess for depressive symptoms in residents with dementia. A score greater than 8 implies probable depression, and a score

higher than 18 is definitive for major depression (Alexopoulos, 2002). The CSDD was used to describe possible depressive symptoms in the sample at baseline.

Figure 1. Participant screening for eligibility for the Function and Behavior Focused Care for Nursing Home Residents with Dementia Randomized Control Trial



Functional Status

Functional status was operationalized by the Barthel Index (BI) (Mahoney & Barthel, 1965), which is a 14-item measure that assesses the resident's ability to perform activities of daily living like eating, dressing, and mobility. A sum score of 100 indicates

complete independence. This measure was completed by proxy report from the nursing assistant providing care to the resident on the day of assessment. The BI demonstrates high correlations (0.74-0.80) with other physical disability measures and has high inter-rater reliability (0.95) (Sainsbury, et al., 2005; O'Sullivan & Schmitz, 2007).

Agitation

Agitated behaviors were determined by the Cohen-Mansfield Agitation Inventory (CMAI) short version (Cohen-Mansfield, 2014). This short-form, 14-item CMAI uses a 5-point Likert scale to rate the frequency of behavioral symptoms in individuals with cognitive impairment. The factor structure is based on the original CMAI inventory and has several studies that confirm reliability and validity (Cohen-Mansfield, 2014).

Antidepressant Use

At baseline, antidepressant use was defined as any antidepressant being present on the medication record for routine use. These medications include serotonin selective reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), bupropion, trazodone, or mirtazapine.

Data Analysis

Descriptive statistics were done using SPSS 24 to describe the baseline sample characteristics, and data was assessed for outliers, missing items, and potentially skewed data (IBM Corp. Released 2016. IBM SPSS Statistics for Mac, Version 24.0. Armonk, NY: IBM Corp.). Marital status and race were dichotomized to married or not married, and white or black, respectively. The Chi-square test was used to evaluate differences between categorical predictors and the outcome, antidepressant use. Independent t-test was used to test for differences between continuous predictors and antidepressant use.

Logistic regression was done with predictors of age, gender (female/male), race (black/white), number of comorbidities, functional status (BI total score), and level of agitation (CMAI total score) entered into the model, with the outcome variable of antidepressant use (yes/no). Predictors were accepted with a p-value of .05 or less. The Hosmer-Lemeshow Goodness of Fit Index was used to evaluate model fit, where lower values indicate better model fit (Hosmer & Lemeshow, 1980).

Results

As shown in Table 1, the sample was predominantly female (72%), an average age of 82.6 (Standard deviation (SD) = 10.1) years old, mostly unmarried (65.2%), and slightly more white residents (59.2%) than black residents (39.6%). The mean MMSE score was 7.8 (SD = 5.1) and mean CSDD was 4.5 (SD = 4.2), with 53 (15.8%) individuals meeting criteria for possible depressive symptoms. The mean CMAI score was 19.8 (SD = 6.1), indicating that the mean agitation was low. Addressing aim 1, over half of the sample was on at least one antidepressant (59.0%), and 39 individuals (12.0%) were taking two antidepressants. One individual from the sample was receiving three different antidepressants. SSRIs were the most commonly prescribed drug class (35%), and mirtazapine (19%) was the most commonly used antidepressant medication (see Table 2). Of the 281 individuals without probable depressive symptoms, 158 (56%) of them were taking an antidepressant. Lastly, 15 (28%) of the individuals with possible depressive symptoms were not taking an antidepressant (see Table 3).

In regard to aim 2, results of the logistic regression are provided in Table 4. The model was significant (χ^2=17.780, p=0.007) and explained 7.1% of the variance in antidepressant use and correctly classified 63.7% of the cases. Race was significantly

associated with antidepressant use, with black residents half as likely to receive an antidepressant when compared to white residents with moderate to severe cognitive impairment (Odds Ratio=0.51, Confidence Interval (CI)= 0.32-0.83)**.**

Table 1. Sample Characteristics: Demographics and Predictor Variables (N=336)

	Minimum	Maximum	Mean (SD)	N (%)
Age	57	105	82.6 (10.1)	
Number of Co-morbidities	0	9	2.9 (1.6)	
Barthel Index total score	0	99	45.2 (27.8)	
MMSE* total score	0	15	7.8 (5.1)	
CMAI* total score	14	47	19.8 (6.1)	
CSDD* total	0	23	4.5 (4.2)	
Depressed				53 (15.8)
Not Depressed				281 (83.6)
Missing				2 (0.6)
Gender				
Male				94 (28.0)
Female				242 (72.0)
Race				
White				199 (59.2)
Black				133 (39.6)
Missing				4 (1.2)
Marital Status				
Married				92 (27.4)
Unmarried				219 (65.2)
Missing				25 (7.4)
Taking an Antidepressant				
No				138 (41.0)
Yes				198 (59.0)
Taking 2+ AD*				39 (12.0)

*CSDD: Cornell Screening for Depression in Dementia; MMSE: Mini-mental status exam; CMAI: Cohen-Mansfield Agitation Index; AD: Antidepressants

Table 2.Prevalence of Antidepressants within Total Sample

	N(%)
SSRIs*	117 (34.8)
Citalopram	39 (11.6)
Sertraline	40 (11.9)
Escitalopram	30 (8.9)
Paroxetine	3 (0.9)
Fluoxetine	5 (1.5)
SNRIs*	18 (5.4)
Duloxetine	7 (2.1)
Venlafaxine	11 (3.3)
Trazodone	35 (10.4)
Mirtazapine	64 (19.0)
Bupropion	1 (0.3)

*SSRIs: serotonin selective reuptake inhibitors; SNRIs: serotonin and norepinephrine reuptake inhibitors

Table 3. Bivariate Analyses of Each Predictor and Antidepressant Use

	On Antidepressants		No Antidepressants		χ^2	t-test
	Mean (SD)	N (%)	Mean (SD)	N (%)	(p)	(p)
Depressive* Symptoms		38 (72)		15 (28)	3.787	
Yes		158 (56)		123 (44)	(0.052)	
No						
Gender						
Male		49 (52)		45 (48)	2.119	
Female		149 (62)		93 (38)	(0.145)	
Race						
Black*		**66 (50)**		**67 (50)**	**6.985**	
White		**129 (65)**		**70 (35)**	**(0.008)**	
Age	85.5 (9.95)		85.8 (10.30)			0.811
Functional Status*	48.4 (28.10)		42.9 (26.38)			0.070
Total Comorbidities	2.43 (2.03)		2.7 (2.04)			0.170
Agitation*	20.6 (6.58)		19.1 (5.87)			0.032

*Depressive symptoms: total Cornell Scale for Depression in Dementia; Functional status: total Barthel index; Agitation: total Cohen-Mansfield Agitation Index

Table 4. Logistic Regression Analysis for Factors Associated with Antidepressant Use

Final Model	β	S.E.*	p-value	Odds Ratio (95% CI*)	Hosmer & Lemeshow Test (p-value)
Functional Status*	0.01	0.01	0.26	1.01 (0.99-1.01)	16.433 (0.037)
Age	-0.01	0.01	0.25	0.99 (0.96-1.01)	
Black	**-0.67**	**0.25**	**0.01**	**0.51 (0.32-0.83)**	
Level of Agitation*	0.03	0.02	0.16	1.0 (0.99-1.07)	
Female	0.44	0.27	0.10	1.55 (0.92-2.62)	
Comorbidities	-0.08	0.06	0.19	0.93 (0.83-1.04)	

*Functional status = total Barthel index; Agitation = total Cohen-Mansfield Agitation Index; S.E. = Standard Error; CI= Confidence Interval

Discussion

This study described the prevalence of antidepressants within a vulnerable population of nursing home residents as well as identified potential factors that influence the use of antidepressants within nursing home residents with moderate to severe cognitive impairment. Fifty-nine percent of this population was taking at least one antidepressant, which is consistent with previous literature (Shah, et al., 2012, Iden, et al., 2014, Hiltunen, et al., 2016, Midlov, et al., 2014). SSRIs were the most commonly prescribed drug class, which also aligns with previous research (Bourgeois, et al., 2012; McMaster, et al., 2018; Bhattacharjee, et al., 2019; Bobo, et al., 2019).

Fifty-six percent of individuals on an antidepressant did not meet CSDD criteria for possible depressive symptoms, which is slightly higher than current research (Gaboda, et al., 2011; Hanlon, et al., 2011; Midlov, et al., 2014; Hiltunen, et al., 2016). Mirtazapine had the highest prevalence at 19%, which is consistent with previous research showing mirtazapine use between 12-19% (Bathena, et al., 2017; Bhattacharjee, et al., 2019; Bobo, et al., 2019). Unfortunately, the primary study did not look at indications for antidepressants, so one cannot conclude whether individuals in this study on antidepressants were being treated effectively for depression or were prescribed an antidepressant for an alternate reason. Some alternative reasons for treatment should still be considered. For example, it is known that mirtazapine is often used as an appetite stimulant (Simonson, 2019) and to help facilitate sleep (Chung et al., 2015). A part of the disease progression of dementia is weight loss and alterations in sleep, so it is possible that this more cognitively impaired group had mirtazapine prescribed for appetite and/or sleep rather than depression. Similarly, citalopram has been used for management of

agitation in dementia (Porsteinsson, et al., 2014). In addition, escitalopram and sertraline have also been tried for management of agitation in dementia (Aga, 2019). Participants in this sample that were on an antidepressant had a slightly higher CMAI total score, so it may be possible that these SSRIs were being used to manage agitation.

Serotonin and norepinephrine reuptake inhibitors (SNRIs) were used in 18% of this sample, with duloxetine being the most common SNRI. Duloxetine has FDA approval for both diabetic peripheral neuropathic pain and chronic musculoskeletal pain (Abou-Raya, Abou-Raya, & Helmii, 2012), which may be reasons for its use in this sample. Lastly, trazodone is often used off-label for insomnia, though it has also been prescribed for BPSD (Seitz, et al., 2011).

The logistic regression model suggested that black residents were less likely to be on antidepressant compared to white residents, which is consistent with prior research looking at persons with less severe cognitive impairment (Gaboda, et al., 2011; Karkare, et al., 2011; Vinson, et al., 2014). Typically, research looking at community-dwelling populations has shown that black older adults are less likely than non-Hispanic whites to receive antidepressants as well as less likely to receive adequate treatment for depressive symptoms (Gaboda, et al., 2011; Akincigil, et al., 2012; Vinson, et al., 2014). Further research is needed to understand if there are disparities in antidepressant use for black nursing home residents compared to white nursing home residents with moderate to severe cognitive impairment.

Strengths and Limitations

Major strengths of this study were that it included study participants that had moderate to severe cognitive impairment and there was a high percentage of black

residents, a typically understudied population of nursing home residents. The major limitation of this study was that it is a secondary data analysis and there was no data available to consider the indications for antidepressant use. Further research is needed to evaluate indications for use of antidepressants in residents with moderate to severe cognitive impairment. Another limitation of this secondary data analysis is the inability to include other known associations for antidepressant use into the model. For example, relationships between resident and professional caregiver, staffing ratios, facility ownership, consulting psychiatric services, and bed capacity have been shown to be associated with antidepressant use (Hanlon, Handler, & Castle, 2010; Karkare, et al., 2011; Smeets, et al., 2014; Bhattacharjee, et al., 2019). Another limitation is that the study only included facilities from a single state.

Despite some limitations, the findings from this study can be used to expand the current understanding of what factors influence antidepressant use in nursing home residents with more severe cognitive impairment. Future studies should consider other known associations for antidepressant use in residents with moderate to severe cognitive impairment. Additional reasons for antidepressant prescribing such as appetite stimulant, sleep, or agitation should also be explored.

Conclusion

This study found that more than half of these residents with moderate to severe cognitive impairment were receiving an antidepressant. Indications for use were unknown. Mirtazapine was the most commonly used antidepressant in this sample of moderate to severe cognitive impairment. Black residents were less likely to be on an antidepressant compared to white residents with moderate to severe cognitive

impairment. Research should continue to evaluate the benefits versus burdens of using these medications both on and off-label as well as evaluate for any potential racial disparities in the long-term care setting.

CHAPTER 3: Racial Differences in Antidepressant Use in Nursing Home Residents with Moderate to Severe Cognitive Impairment

Abstract

Racial disparities exist regarding symptom management of dementia between black and white older adults. Little is known about antidepressant use in black nursing home residents with moderate to severe cognitive impairment. The purpose of this secondary data analysis was to describe and compare the use of antidepressants between white and black nursing home residents with moderate to severe cognitive impairment. Data originated from the Function and Behavior Focused Care for Nursing Home Residents with Dementia randomized control trial. Chi-square and T-test were used to look for differences in antidepressant drug class use and dose by race. Controlling for depression, age, gender, functional status, level of agitation, and number of co-morbidities, logistic regression was used to assess for differences in antidepressant use by race. In adjusted models, race was significantly associated with antidepressant use, with black residents less likely to be prescribed antidepressants compared to white residents. A significant difference in the dose of sertraline was also noted, with black residents receiving, on average, 47.2mg (SD:40.4mg) and white residents receiving 86.6mg (38.1mg). Further research is needed to understand racial disparities as well as the benefits versus harms of this disparity with antidepressant use in nursing home residents with dementia.

Background

The prevalence rate of dementia is 64% higher for black compared to non-Hispanic whites (Steenland, et al., 2015). Despite having higher rates of dementia, differences exist with regard to management of dementia and dementia associated symptoms. (Zuckerman, et al., 2008; Barnes & Bennet, 2014). Behavioral and psychological symptoms of dementia (BPSD) occur in up to 90% of persons with dementia and include symptoms of aggression, agitation, depression, hallucinations, delusions, apathy, and anxiety (Halloran, 2014; Kales, Gitlin, and Lyketsos, 2015; Resnick, et al., 2017). Few studies look at BPSD symptoms by race, but those that have found that black individuals with dementia may have more hallucinations and psychosis compared to non-Hispanic whites, and non-Hispanic whites with dementia may present with higher levels of apathy compared to other minorities (Bassony, et al., 2000; Nagata, et al., 2017). In addition, although community research is consistent that white older adults are more likely to be appropriately assessed and diagnosed with depression than black older adults, few studies look at persons with moderate to severe dementia (Akincigil, et al., 2012; Burnett-Zeigler, et al., 2012; Grace, et al., 2018).

Antidepressants are commonly used psychotropic medications for treating depression, anxiety, disturbed sleep cycles, agitation, aggression, and appetite in persons with dementia (Banerjee, et al., 2011; Bourgeois, et al., 2012; Shah, et al., 2012; Iaboni, et al., 2016; Viscogliosi, et al., 2017; Bobo, et al., 2019). It is estimated that about 30-40% of antidepressants are being prescribed off-label (Shah, et al., 2012; Gustafsson, et al., 2013; van Asch, et al., 2013; Aga, 2019). Evidenced is limited and mixed regarding race and the off-label use of antidepressants (Lim & Jung, 2017; Maust, Sirey, & Kales,

2017). While one study looking at Medicare claims data (average patient age 67) found prescriptions for antidepressants without depressive symptoms greater among black older adults compared to white older adults (Lim & Jung, 2017), another study using a convenience sample from a randomized control trial (average patient age 69) found that being white was significantly associated with antidepressant prescribing without a major depression diagnosis (Maust, Sirey, & Kales, 2017).

Racial disparities exist in prescribing antidepressants for depression and anxiety, their Food and Drug Administrations (FDA) intended use. In community settings, black older adults without dementia are substantially less likely to be prescribed an antidepressant for depression compared to white older adults even with equal access to treatment (Strothers, et al., 2005; Weissman, et al., 2011; Akincigil, et al., 2012; Rhee, et al., 2018). Yet response to antidepressants may be similar between black and white older adults (Lesser, et al., 2010; Lesser, et al., 2011). Black nursing home residents with depressive symptoms and no or mild cognitive impairment were significantly less likely to be prescribed an antidepressant when compared to white residents with depressive symptoms (Hanlon, et al., 2009; Gaboda, et al. 2011). Race was significantly associated with antidepressant use in persons with dementia; however, it is unknown if there are racial differences in the use of antidepressants among nursing home residents specifically with moderate to severe cognitive impairment. (Karkare, et al., 2011; Wei, et al., 2016; Grace, et al., 2018).

Factors Associated with Antidepressant Use

Age, gender, number of co-morbidities, functional status, and level of agitation are associated with antidepressant use in older adults in addition to race and FDA

indications of depression and anxiety (Bobo, et al., 2019; Karkare, et al., 2011; Wei, et al., 2016; Smeets, et al., 2017; Gustafsson, et al., 2013). Individuals older than 75 were less likely to be prescribed an antidepressant compared to those who were 75 or younger (Bhattacharjee, et al., 2019; Bobo, et al., 2019; Karkare, et al., 2011). Females and individuals with a higher number of comorbidities are more likely to be taking an antidepressant (Gustafsson, et al., 2013; Dutcher, et al., 2014; Bobo, et al., 2019). In addition, older adults who are more functionally independent are more likely to be on an antidepressant (Karkare, et al., 2011; van Asch, et al., 2013; Gustafsson, et al., 2013). Lastly, persons who demonstrate more severe agitated behaviors are more likely to be on an antidepressant compared to those without agitation (Smeets, et al., 2018; Resnick, et al., 2019).

White nursing home residents tend to comprise over 75% of the study populations evaluating antidepressant use in dementia in long-term care settings. (Banerjee, et al., 2011; Hanlon, et al., 2011; Bali, et al., 2017; Mueller, et al., 2017; Wei, et al., 2016). In addition, residents with more severe cognitive impairment are generally excluded from these studies due to consent issues. Understanding the impact of antidepressants in nursing home residents with cognitive impairment by race, especially those with more severe cognitive impairment who cannot self-report their symptoms, can help provide guidance for patient-centered care and deprescribing. Given the importance of deprescribing, which is defined as the process of rational, supervised withdrawal of medication for which the risk currently outweighs the benefit, examining psychotropic medication use in those with moderate to severe cognitive impairment by race/ethnicity is a priority (Grace, et al., 2018; Harrison, et al., 2019). As a result, the purpose of this

study was to describe any potential differences in antidepressant use between white and black nursing home residents with moderate to severe cognitive impairment. It was hypothesized that 1) Controlling for depression, age, gender, functional status, level of agitation, and number of co-morbidities, there would be a greater use of all antidepressants in white versus black nursing home residents with moderate to severe cognitive impairment; and 2) Black nursing home residents with moderate to severe cognitive impairment would receive lower dosages of the most commonly prescribed antidepressants compared to white nursing home residents with moderate to severe cognitive impairment.

Methods

Design

This was a secondary data analysis using baseline data from the Function and Behavior Focused Care for Nursing Home Residents with Dementia randomized control trial. The original study occurred from 2012 to 2018 and was a cluster randomized controlled trial with a repeated measures design. Residents were recruited from 12 nursing homes in Maryland. To be included, the resident had to be 55 years or older, English-speaking, reside in long term care at time of recruitment, and score a 15 or less on the Mini Mental Status Examination (MMSE) (Folstein, Folstein, and McHugh, 1975). Hospice or sub-acute rehabilitation residents were excluded from the study. Participants or their legally authorized representatives were asked to consent to participate in the study prior to determining eligibility. If the resident was not able to pass the evaluation to Sign Consent (Resnick, et al., 2007), he/she was asked to sign an

assent form, and consent was given by the legally authorized representative. This study was approved by a university review board.

Sample

Initially, 1512 residents were screened for eligibility, and 498 residents were excluded due to being younger than 55, on hospice, receiving rehabilitation services, or in the hospital. An additional 527 residents either refused or had proxy refusal for participation. The initial cognitive screening excluded another 146 residents due to their MMSE being greater than 15. Lastly, 2 individuals withdrew from the study, and 3 expired shortly after consent but before baseline measurement. This study included the final 336 participants recruited.

Measures

As per the recruitment criteria, all residents had moderate to severe cognitive impairment based on their initial MMSE screening. Measures were completed by a research evaluator through observation, proxy report from staff caring for the resident the day of testing, and chart abstraction. Descriptive information included age, marital status, gender, race, level of education, and number of comorbidities were extracted from the medical chart.

Antidepressant Use

At baseline, antidepressant use was defined as any antidepressant being present on the medication administration record for routine use. Antidepressants include the following drug classes and medications: serotonin selective reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants

(TCAs), bupropion, trazodone, and mirtazapine. Medication name, dose, and frequency were collected.

Depressive Symptoms

Depressive symptoms were measured using the Cornell Scale for Depression in Dementia (CSDD) (Alexopoulos, 1988). Prior use of this 19-item survey provided evidence of reliability based on Cronbach alpha values of 0.81 and 0.95 and validity compared to the SM-IV-TR (Barca, et al., 2015) to assess for depressive symptoms in residents with dementia. A score greater than 8 implies probable depression, and a score higher than 18 is definitive for major depression (Alexopoulos, 2002).

Functional Status

The Barthel Index (BI) (Mahoney & Barthel, 1965) was used to assess functional status. The BI is a 14-item measure that assesses the resident's ability to perform activities of daily living like eating, dressing, and mobility. A sum score of 100 indicates complete independence. This measure was completed by proxy report from the nursing assistant providing care to the resident on the day of assessment. The BI demonstrates high correlations (0.74-0.80) with other physical disability measures and has high inter-rater reliability (0.95) (O'Sullivan & Schmitz, 2007; Sainsbury, et al., 2005).

Agitation

Agitation was measured by the Cohen-Mansfield Agitation Inventory (CMAI) short version (Cohen-Mansfield, 2014). This short-form, 14-item CMAI uses a 5-point Likert scale to rate the frequency of behavioral symptoms in individuals with cognitive impairment. The factor structure is based on the original CMAI inventory and has

several studies that confirm reliability and validity (Cohen-Mansfield, 2014). Higher total CMAI scores indicate higher levels of agitation.

Data Analysis

Descriptive statistics were done using SPSS 24 to describe the baseline sample characteristics, and data was assessed for outliers, missing items, and potentially skewed data (IBM Corp. Released 2016. IBM SPSS Statistics for Mac, Version 24.0. Armonk, NY: IBM Corp.). Marital status and race were converted to dichotomous variables of married or not married, and white or black, respectively. CSDD was also changed to a dichotomous variable. Those who had a CSDD total score greater than 8 (Alexopoulos, 2002) were scored as possible depression and those with a score of 8 or less were scored as no depression. Chi-square was used to evaluate for significant differences between categorical variables. Binary logistic regression was done to evaluate hypothesis one. Age, gender, depression, level of agitation, number of comorbidities, and functional status were entered into the logistic regression model to examine the association between race and antidepressant use. For hypothesis two, T-test or Mann-Whitney U Test was used to evaluate for significant differences in dosages of the top 5 most prescribed antidepressants independently within this sample. An alpha level of 0.05 was chosen to determine statistical significance for all analyses.

Results

As shown in Table 5, the mean age of the participants was 82.6 (SD=10.1), and they were predominantly female (72.0%), unmarried (65.2%), and not depressed (83.6%). The sample was almost evenly distributed by race, with 59.2% being white and 39.6% being black. In the adjusted model (Table 6), black residents were significantly less

likely to be on an antidepressant compared to white residents when controlling for depression, age, gender, number of co-morbidities, functional status, and level of agitation (Odds Ratio= 0.499, p=0.006).

Table 5. Characteristics of the Sample

	Minimum	Maximum	Mean (SD*)	N (%)
Age	54	102	82.6 (10.1)	
MMSE* total score	0	15	7.8 (5.1)	
Number of co-morbidities	0	8	2.9 (1.6)	
BI* total score	0	99	45.2 (27.8)	
CMAI* total score	14	47	19.8 (6.1)	
CSDD* total	0	23	4.5 (4.2)	
Possible Depressive Symptoms				53 (15.8)
Not Depressed				281 (83.6)
Missing				2 (0.6)
Gender				
Male				94 (28.0)
Female				242 (72.0)
Race				
White				199 (59.2)
Black				133 (39.6)
Missing				4 (1.2)
Marital Status				
Married				92 (27.4)
Unmarried				219 (65.2)
Missing				25 (7.4)
Level of Education				
Grades 1-8				67 (19.9)
Grades 9-11				43 (12.8)
High School Graduate				113 (33.6)
Trade School				7 (2.1)
Some College				33 (9.8)
College Graduate				22 (6.5)
Post-College Work				6 (1.8)
Unknown				39 (11.6)

*SD: Standard deviation; MMSE: Mini-mental status exam; CSDD: Cornell Screening for Depression in Dementia; BI: Barthel Index; CMAI: Cohen-Mansfield Agitation Index

Table 6. Evaluating Antidepressant Use by Race with Logistic Regression

	β	S.E.*	P-value	Odds Ratio (CI*)
Black	**-0.696**	**0.252**	**0.006**	**0.499 (0.305-0.817)**
Female	0.443	0.273	0.105	1.558 (0.912-2.662)
Level of Agitation*	0.015	0.022	0.485	1.015 (0.973-1.059)
Age	-0.018	0.013	0.165	0.982 (0.958-1.007)
Functional Status*	0.005	0.004	0.257	1.005 (0.996-1.014)
Total Comorbidities	-0.074	0.058	0.202	0.928 (0.828-1.041)
Possible Depressive Symptoms*	0.540	0.367	0.142	1.716 (0.835-3.525)

*S.E.: Standard Error; CI: Confidence Interval; Agitation: total Cohen-Mansfield Agitation Index; Functional Status: total Barthel Index; Depressive Symptoms: total Cornell Scale for Depression in Dementia

As noted in Table 7, there was a significant difference in antidepressant use by race with 129 (64.8%) of white residents and 66 (49.6%) of black residents being on an antidepressant (χ^2=7.06, p=0.006). There was no significant difference by race when looking at serotonin selective reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), trazodone, and mirtazapine (Table 7). The 5 most commonly prescribed antidepressants were mirtazapine, sertraline, citalopram, trazodone, and escitalopram (Table 8). Among the 5 drugs evaluated, the only differences by race were with regard to dosages of sertraline (t=2.68, p=0.01). Black residents, on average, received 47.2mg (SD=40.4mg) of sertraline while white residents, on average, received 86.6mg (SD=38.1mg).

Table 7. Racial Differences in Antidepressant Use by Drug Class or Medication

	White	Black	
	N (%)	N (%)	Chi-Square (p-value)
On Antidepressant	**129 (64.8)**	**66 (49.6)**	**7.60 (0.006)**
Not on Antidepressant	**70 (35.2)**	**67 (50.4)**	
On 2 Antidepressants	26 (13.1)	12 (9.0)	1.29 (0.257)
Not on 2 Antidepressants	173 (86.9)	121 (91.0)	
On SSRI*	78 (39.2)	39 (29.4)	3.41 (0.065)
Not on SSRI	121 (60.8)	94 (70.6)	
On SNRI*	13 (6.5)	5 (3.8)	1.20 (0.274)
Not on SNRI	186 (93.5)	128 (96.2)	
On Trazodone	21 (10.5)	13 (9.7)	0.05 (0.819)
No Trazodone	178 (89.5)	120 (90.3)	
Remeron	41 (20.6)	22 (16.5)	0.86 (0.355)
No Remeron	158 (79.4)	111 (83.5)	
Bupropion	1 (0.5)	0 (0.0)	
No Bupropion	197 (99.5)	0 (0.0)	

*SSRI: serotonin selective reuptake inhibitors; SNRI: serotonin and norepinephrine reuptake

Table 8. Dosing of Top 5 Antidepressants Prescribed by Race

	White		Black		T-test (p)
	Mean (SD)	Range	Mean (SD)	Range	
Escitalopram	12.4mg (6.0)	2.5-20mg	11.4mg (5.0)	5-20mg	0.46 (0.65)
Citalopram	15.6mg (6.0)	5-30mg	16.3mg (5.7)	5-20mg	-0.24 (0.82)
Sertraline	**86.6mg (38.1)**	**25-200mg**	**47.2mg (40.4)**	**25-150mg**	**2.68 (0.01)**
Mirtazapine	16.5mg (10.5)	7.5-45mg	17.7mg (10.0)	7.5-45mg	-0.45 (0.66)
Trazodone	52.4mg (20.8)	25-100mg	58.3mg (34.3)	25-150mg	n/a (0.93)*

*Trazodone dosing positively skewed, so Mann-Whitney U nonparametric test used

Discussion

The results of this study provided support for the first hypothesis demonstrating that black nursing home residents with moderate to severe cognitive impairment were significantly less likely than white nursing home residents with moderate to severe cognitive impairment to be prescribed an antidepressant. These findings are consistent with prior research showing that cognitively intact as well as mild cognitively impaired black nursing home residents were significantly less likely than white residents to be prescribed antidepressants (Hanlon, et al., 2009). Racial differences may be due to preferences of black individuals to avoid the use of antidepressant medication (Cooper, et al., 2003; Givens, et al., 2007). Black individuals may also believe that dementia and associated symptoms such as depression are a natural part of aging so families may not feel that pharmacologic management for these problems is necessary (Hipps, et al., 2003; Connell, Scott Roberts, & McLaughlin, 2007).

Unfortunately, the indications for use of antidepressants was not obtained during the parent study. As with all psychotropic medications there is appropriate and inappropriate use. Further research is needed to establish if the disparities in this study reflect inadequate management of potentially depressed or anxious black nursing home residents with dementia or if this disparity shows adequate management of a population that potentially does not require pharmacological intervention. In addition, it may reflect an overuse of antidepressants in white nursing home residents with dementia. Current evidence finds the use of antidepressants in residents with more severe dementia with limited benefit for treating depression (Farina, Morrell, & Banerjee, 2017; Orgeta, et al., 2017). Given that antidepressant use in persons with dementia is associated with serious

adverse events like falls and fractures (Hung, et al., 2017; Marci, et al., 2017; Wei, et al., 2016), it is particularly important to be cautious with regard to the prescribing of antidepressants and ascertain if the pharmacologic treatment is appropriate for each individual.

The second hypothesis was also partially supported. There was a significant difference in the dosage of sertraline prescribed by race. White residents (M:86.6mg, SD: 38.1mg), on average, took almost double the dose of sertraline compared to black residents (M:47.2mg, SD:40.4mg). One older small, randomized controlled trial looking at sertraline versus placebo for depression in dementia did find that white persons with dementia had a nonsignificant poorer response to sertraline compared to black persons with dementia; however, authors asserted that there was no known research to support why race may predict treatment response, so they felt it may be a chance finding due to a small sample size (Steinberg, et al., 2004). One possibility may be the dosing range for sertraline, which offers a wider range of dose adjustments (12.5mg to 200mg) compared to other antidepressants. Genetic research has discovered that black individuals tend to have a higher frequency of alleles that improve response rates to SSRIs, so that may also explain the differences in dose (Lotrich, Pollock, & Ferrell; 2003; O'Connell, et al., 2018). As noted above, the indication for use of sertraline was not noted in this study nor was there information about the effectiveness of the drug at the current dose. In addition, initiation of antidepressant use was also not known from the parent study, so it cannot be determined with this cross-sectional analysis whether participants were at therapeutic dose or still receiving medication adjustments with their antidepressant. Future research should focus on evaluating indications for use as well as appropriate

dosing of individual antidepressant medications in black nursing home residents with moderate to severe cognitive impairment.

Strengths and Limitations

A strength of this study was the inclusion of a high percentage of black residents with moderate to severe cognitive impairment. Another strength was individual evaluation of commonly used antidepressants in the long-term care setting. A major limitation of the study was that it was a secondary data analysis and included a relatively small sample from only 12 nursing homes in a single state that consented to participate in a study focused on optimizing function and physical activity. Lastly, there may have been other confounding factors that contribute to antidepressant use like professional caregiver stress, health care providers prescribing practices or environment that were not controlled for (Karkare, et al., 2011; Extavour & Perri III, 2018; Bhattacharjee, et al., 2019). Despite some limitations, the findings from this study provide descriptive information on potential disparities between white and black nursing home residents with moderate to severe dementia in terms of the use of antidepressant medications.

Conclusion

The study found racial significant differences with antidepressant use in nursing home residents with moderate to severe cognitive impairment. The likelihood of receiving antidepressants for black nursing home residents with moderate to severe cognitive impairment was about half that of white nursing home residents with moderate to severe cognitive impairment. In addition, there was a significant difference in sertraline dosing between black and white nursing home residents with moderate to severe cognitive impairment. Further research is needed to gain a better understanding of

the indications for use as well as appropriate prescribing of antidepressants in nursing home residents with dementia across all racial groups. A greater understanding of antidepressant treatment between black and white nursing home residents with moderate to severe cognitive impairment will help guide optimal patient-centered interventions for both appropriate prescribing and deprescribing of these psychotropic medications.

CHAPTER 4: Patterns of Use of Antidepressants and Antipsychotics in Nursing Home Residents with Moderate to Severe Cognitive Impairment

Abstract

Antidepressants and antipsychotics are commonly used psychotropic medication in nursing home residents with dementia despite limited efficacy and risk of serious adverse events. The purpose of this secondary data analysis was to describe the use of antidepressants and antipsychotics and evaluate trends in their prescribing among nursing home residents with moderate to severe cognitive impairment. It was hypothesized that there would be an increase in the use of antidepressants and a decrease in the use of antipsychotics at 12 months among nursing home residents with moderate to severe cognitive impairment, when controlling for age, gender, race, number of comorbidities, functional status, and treatment effect from the parent study. Baseline and 12-month data were used from the Function and Behavior Focused Care (FBFC) for Nursing Home Residents with Dementia randomized control trial. Descriptive statistics were used to describe the sample and individual medication daily dose changes from baseline to 12 months. Generalized linear mixed models with a binary distribution and logit link function was used to explore both antidepressant and antipsychotic use over time. At baseline, 58.9% were on at least one antidepressant and 17.3% were on at least one antipsychotic. At 12 months, 53.2% were on an antidepressant and 14.1% were on an antipsychotic. There was no significant change in antidepressant or antipsychotic use at 12 months. These results are promising that not only has there been a decrease in antipsychotic use but also no increase in antidepressant use in this vulnerable population.

Background

Psychotropic medications are commonly used in the long-term care setting, with an average of two thirds of all nursing home residents being on at least one psychotropic medication (Simoni-Wastila, et al., 2014; Bathena, et al., 2017; Helvik, et al., 2017; Smeets, et al., 2018; Resnick, et al., 2019). Often these medications are used in the management of behavioral and psychological symptoms of dementia (BPSD), also called neuropsychiatric symptoms (NPS), which include symptoms such as depression, apathy, euphoria, agitation, aggression, psychosis, sleep problems, and wandering (Lyketsos, et al., 2011; Kales, Gitlin, & Lyketsos, 2014). Management of BPSD is complex, and though nonpharmacological interventions are first-line recommendations, barriers like staff burnout and preference for pharmacologic interventions over nonpharmacological interventions, appropriate patient to staff ratios, and lack of reimbursement limit their implementation in long term care (AGS, 2010; Ervin, Cross, & Koschel, 2014; Kales, Gitlin, & Lyketsos, 2014; AMDA, 2018). As a result, prescribers often utilize antipsychotics and antidepressants for managing BPSD.

Antipsychotic Use Among Nursing Home Residents with Dementia

Antipsychotic use ranges from 28% to 43% in nursing home residents with dementia despite known serious adverse effects such as extrapyramidal symptoms, falls, stroke, and increased risk of death (Young, Taylor, & Lawrie, et al., 2015; McMaster, et al., 2018; Smeets, et al., 2018; Resnick, et al., 2019; Schwertner, et al., 2019; Rubino, et al., 2020). Though being prescribed off-label, their use may be appropriate in some instances when a person with dementia is at risk of physically harming themselves or others or is having severe psychotic symptoms (Jennings, & Grossberg, 2013; Reus, et

al., 2016). Given risks associated with their use, antipsychotics should be prescribed at the lowest effective dose, their efficacy and duration of use periodically evaluated, and they should not be prescribed indefinitely (Simoni-Wastila, et al., 2014; Reus, et al., 2016).

Several factors influence the use of antipsychotics in persons with dementia. Individuals who are younger than 85 years old and more functionally independent are more likely to be prescribed antipsychotics (Foebel, et al., 2013; Helvik, et al., 2017; Bakouni, Berbiche, & Vasiliadis, 2019; Lornstad, 2019). Males are more often on antipsychotics compared to females (Helvik, et al., 2017; Smeets, et al., 2018). Research is limited and mixed regarding race and antipsychotic use within nursing homes, where the most recent study found black residents less likely to be on an antidepressant compared to white residents (Miller, et al., 2006; Fashaw, et al., 2020). This research compared antipsychotic use at the facility level and looked at proportions of all black nursing home residents to antipsychotic use and did not specify the cognition status of the residents (Miller, et al., 2006; Fashaw, et al., 2020). Lastly, individuals with a higher number of co-morbid conditions were less likely to be prescribed an antipsychotic (Foebel, et al., 2013).

Given the concern for serious cardiovascular events and increased mortality associated with antipsychotics, and the widespread use of antipsychotics among nursing home residents with dementia, the Centers for Medicare and Medicaid Services (CMS) developed the National Partnership to Improve Dementia Care in 2012 (CMS, 2014). Under this initiative, nursing homes were mandated to publicly report their antipsychotic use and potentially receive monetary penalties for overuse of antipsychotics (CMS,

2014). Since the initiation of the partnership, there has been an overall national decrease in the use of antipsychotics by 40.1%, with some states reporting antipsychotic use under 10% among nursing home residents (CMS, 2019). Unfortunately, with this decrease in the use of antipsychotics, studies find that use of other psychotropic medications, particularly antidepressants, as well as anxiolytics and mood stabilizers has increased (Lucas & Bowblis, 2017; Olivieri-Mui, et al., 2018; Maust, et al., 2018; Early, et al., 2020).

Antidepressant Use Among Nursing Home Residents with Dementia

Prescriptions of antidepressants increase significantly following admission to a nursing home, and antidepressants have the highest continuation rate among all prescribed psychotropic medications for long term care residents (Iden et al., 2014; Atramount, et al., 2018; Ozaki, Katsumata, & Arai, 2019). Antidepressant use ranges from 30%-60% for nursing home residents with dementia (van Asch, et al., 2012; Dutcher, et al., 2014; Giebel, et al., 2015; Hiltunen, et al., 2016; Brimelow, et al., 2018). In addition, 30-40% of antidepressants prescribed for long-term care residents are prescribed off-label and not for Food and Drug Administration (FDA) indications of depression or anxiety (Midlov, et al., 2014; Wei, et al., 2014). Examples of off-label indications of use include agitation, aggression, mood congruent psychosis, lack of appetite, inappropriate vocalizations, resistance to care, and insomnia (Shah, et al., 2012; Echt, et al., 2013; Iaboni, et al., 2016; Viscogliosi, Chiriac & Ettorre, 2017).

Serotonin selective reuptake inhibitors (SSRIs) are the most commonly prescribed antidepressant drug class in long term care and approximately half of the residents on an antidepressant are taking a SSRI (Hanlon, et al., 2011; Midlov, et al., 2014; Gadzhanova,

Roughead, & Pont, 2018). Other antidepressant drug classes used in long term care include serotonin and norepinephrine reuptake inhibitors (SNRIs), tetracyclics (mirtazapine), serotonin modulators (trazodone), unicyclic aminoketones (bupropion), and tricyclics (TCAs).

Antidepressants are commonly prescribed for management of BPSD because they are considered to have a more favorable side effect profile compared to antipsychotics (Viscogliosi, Chiriac, & Ettorre, 2017; Bessey & Walaszek, 2019). Side effects do occur and range from sedation, gastrointestinal upset, hyponatremia, serotonin syndrome, increased falls and fractures, serious cardiovascular events and increased mortality risk (Draper & Berma, 2008; Andrade, et al., 2010; Huybrechts, et al., 2011; Sterke, et al., 2012; Wei, et al., 2016; Hiance-Delahaye, et al., 2018; Sobieraj, et al., 2019).

While antidepressant use is prevalent among individuals with dementia, evidence is limited regarding their efficacy in this population (Seitz, et al., 2011; Dudas, et al., 2018; Watt, et al., 2018; Zuidersma, et al., 2019). Two Cochrane reviews evaluating antidepressants (predominantly SSRIs) for depression and agitation in dementia concluded there was low-quality evidence to support clinical efficacy of their use in this population and further high-quality research was needed (Seitz, et al., 2011; Dudas, et al., 2018). Other non-SSRI antidepressants like mirtazapine and trazodone have also been evaluated, but studies were small and exploratory, or their effectiveness did not outweigh adverse events in this population (Watt, et al., 2018; Zuidersma, et al., 2019).

There are several factors associated with antidepressant use in older adults including age, gender, race, number of co-morbidities, and functional status. Those who are older than 75 are less likely to be placed on an antidepressant compared to those

younger than 75 years old (Karkare, et al., 2011; Bhattacharjee, et al., 2019), whereas females are more likely to be prescribed an antidepressant (Karkare, et al.,2011; van Asch, et al., 2012; Gustafsson, et al., 2013). The odds of receiving an antidepressant are greater for white compared to black older adults (Karkare, et al., 2011; Wei, et al., 2016). Older adults with a higher number of comorbid conditions are more likely to receive an antidepressant (Bobo, et al., 2019). Lastly, those individuals who are more functionally independent are more likely to be taking an antidepressant (van Asch, et al., 2012; Gustafsson, et al., 2013; Helvik, et al., 2017).

Longitudinal Use of Antipsychotics and Antidepressants

The continued use of antidepressants and antipsychotics over time in nursing home residents with dementia is variable. Some studies found antidepressant and antipsychotic use in nursing home residents with dementia high, with a prevalence above 50%, but their use remained stable and did not increase over time (Helvik, et al., 2017; Maust, et al., 2018). Other studies, while also confirming high prevalence, found antipsychotic use relatively stable or decreased over time, but antidepressant use significantly increased over time (Ruths, et al., 2013; Vasudev, et al., 2015; Ozaki, Katsumata, & Arai, 2019). Overall, antidepressants have been noted to be the most commonly prescribed psychotropic medication, and their continued use is significantly higher among residents with dementia compared to those without dementia (Ruths, et al., 2013; Helvik, et al., 2017; Brimelow, et al., 2018; Maust, et al., 2018; Ozaki, et al., 2018). These longitudinal studies had samples of nursing home residents with varying levels of cognition, and those with samples of residents with dementia did not specify the severity of dementia. Nursing home residents with more severe dementia are at greatest

risk for ongoing use as they cannot self-report symptoms while receiving an antidepressant or antipsychotic to determine efficacy, nor can they self-report feeling side effects from these medications. Consequently, the frequency and intensity of BPSD can increase as dementia progresses, and residents with advanced dementia often remain on these psychotropics potentially for life (Helvik, et al., 2017; Basnet, Acton, & Requijo, 2020; Ito, et al., 2020). Continued research is needed to focus specifically on antidepressant and antipsychotic use in persons with more severe cognitive impairment.

The purpose of this study was to describe the use of antidepressants and antipsychotics and evaluate trends between baseline and 12 months in antidepressant and antipsychotic prescribing among nursing home residents with moderate to severe cognitive impairment. Data was used from the Function and Behavior Focused Care (FBFC) for Nursing Home Residents with Dementia randomized control trial, which had a primary intervention focus of optimizing function and physical activity while minimizing behavioral symptoms among nursing home residents with moderate to severe cognitive impairment. For this secondary data analysis, it was hypothesized that there would be an increase in the use of antidepressants and a decrease in the use of antipsychotics at 12 months among nursing home residents with moderate to severe dementia, when controlling for age, gender, race, functional status, number of co-morbidities, and treatment effects of FBFC.

Methods

Design

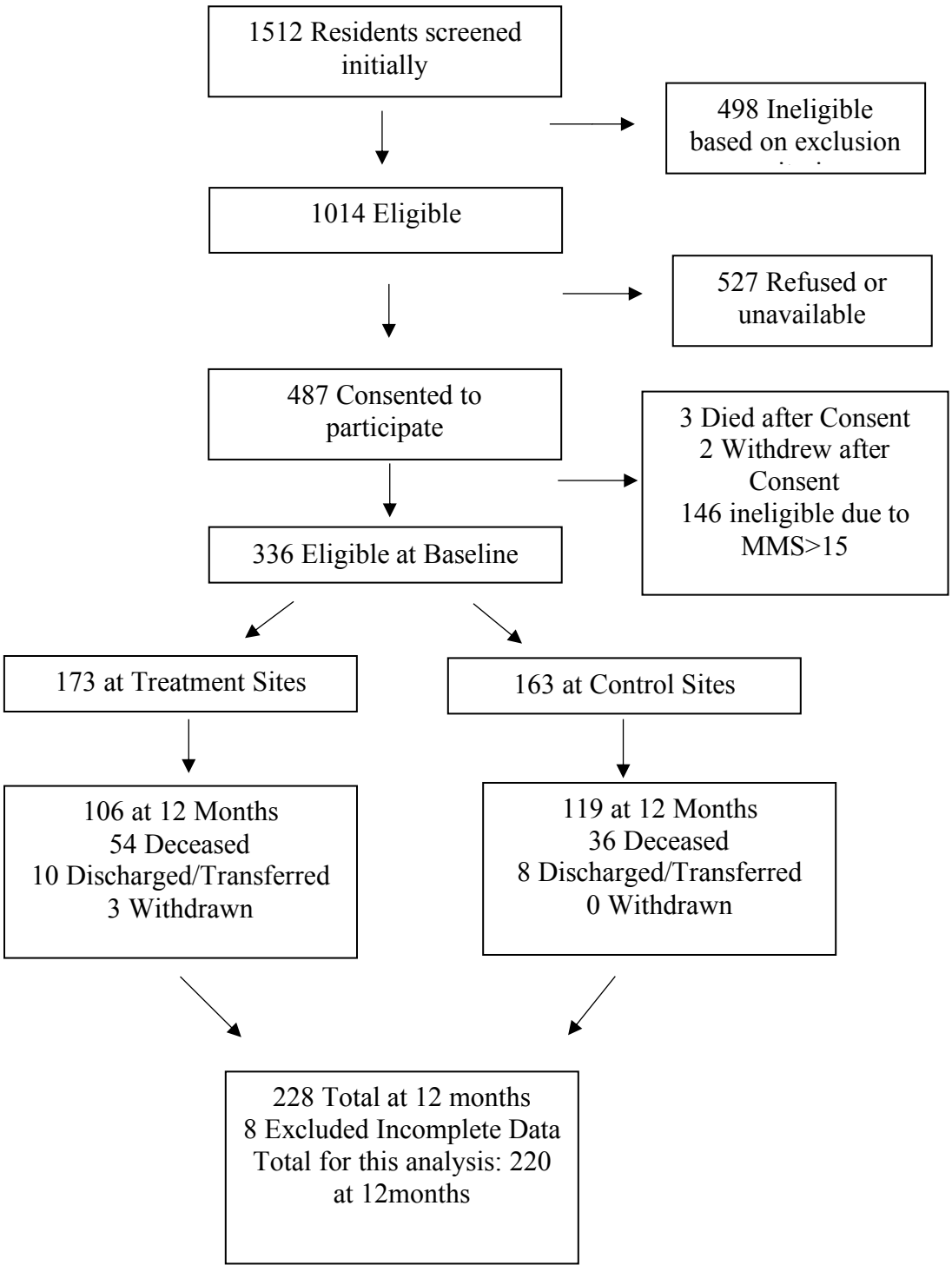
This was a secondary data analysis using data from the Function and Behavior Focused Care (FBFC) for Nursing Home Residents with Dementia randomized control

trial, which took place from 2013 to 2018. The original study was a clustered, randomized controlled trial with a repeated measures design. Residents were recruited from 12 Maryland nursing homes and could participate if they were 55 years or older, English-speaking, resided in long term care at time of recruitment, and scored a 15 or less on the Mini Mental Status Examination (MMSE) (Folstein, Folstein, and McHugh, 1975). Hospice or sub-acute rehabilitation residents were excluded from the study. Prior to determining eligibility, potential participants were approached about their participation in the study. If the resident was not able to pass the Evaluation to Sign Consent (Resnick, et al., 2007), he/she was asked to provide assent to participate and consent was given by the resident's legally authorized representative. This study was approved by a university review board.

Sample

There were 1512 residents screened for eligibility. There were 498 residents excluded due to being on hospice, receiving rehabilitation services, admitted to the hospital, or younger than 55. There were 527 residents who either refused or had proxy refusal for participation. The initial cognitive screening excluded another 146 residents due to their MMSE being greater than 15. Lastly, 2 individuals withdrew from the study, and 3 expired shortly after consent but before baseline measurement. The final baseline sample included 336 individuals. Figure 2 explains the loss of individuals between baseline and 12 months. For this study, the total sample of 228 at 12 months was used, with 8 individuals having incomplete data. Therefore, the final sample for this secondary data analysis at 12 months was 220 participants.

Figure 2. Participant Loss During FBFC Trial and This Study



Intervention

Nursing homes were randomized to either the intervention or educational control group. Those in the intervention group received a Function and Behavior Focused Care (FBFC) Research Nurse, who worked with a facility based champion and the nursing home staff for 10 hours a week for 14 months to implement the 3 parts of the intervention: 1) Environmental and Policy Assessments; 2) Education and Training of Nursing Home Staff; and 3) Mentoring and motivating of nursing staff. Further details about the intervention are to be published elsewhere (under review). The nursing homes in the control group received the educational component of the intervention, but no FBFC research nurse nor the other 2 parts of the intervention.

Measures

Measures were completed by a research evaluator through observation, proxy report from staff caring for the resident the day of testing, and/or chart abstraction. Age, marital status, gender, race, and number of comorbidities and were extracted from the medical chart. All residents were already known to have moderate to severe cognitive impairment as determined by their initial MMSE screening. The MMSE was used to describe baseline cognitive status.

Functional Status

Functional status was determined by the Barthel Index (Mahoney and Barthel, 1965), which is a 14-item measure that assesses the resident's ability to perform activities of daily living like eating, dressing, and locomotion. A sum score of 100 indicates complete independence. The Barthel index demonstrates high inter-rater reliability (0.95) as well as high correlations (0.74-0.80) with other physical disability measures

(O'Sullivan and Schmitz, 2007; Sainsbury, et al., 2005). This measure was completed by the nursing assistant providing care to the resident on the day of testing.

Medications

The resident's medication list was recorded at baseline and 12 months. It included the medication name, the dose, and the frequency given. Indications for use and duration of use of antidepressants and antipsychotics were not collected during the primary study. As needed (PRN) medications were not included in this study. Antidepressants included any medications that fell into the following drug classes or names: serotonin selective reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), trazodone, bupropion, or mirtazapine. Antipsychotics included chlorpromazine, clozapine, compazine, droperidol, haloperidol, loxapine, mellaril, novane, olanzapine, fluphenazine, quetiapine, risperidone, stelazine, perphenazine, aripiprazole, or ziprasidone.

Medication Changes Over Time

Comparing antidepressant and antipsychotic use over time was done in two ways. First a dichotomous variable of yes/no was created, where the presence of any routine antidepressant on the medication list was scored as "yes". Any participant without an antidepressant listed on the medication list was scored as "no." The same approach was used for antipsychotics. The presence of any routine antipsychotic on the medication list was a "yes," and the absence was a "no."

Given that individual daily dose changes could occur and not be captured in this dichotomized approach, a dose change variable of 3 levels was also created (decrease, no change, and increase), where the total daily dose amount at baseline was compared to the

total daily dose amount at 12 months. Reductions of an antidepressant medication dose (ex: citalopram 20mg to 10mg) or the removal of an antidepressant (no longer listed on the medication list) qualified as a decrease. Any antidepressant that stayed the same (same individual drug and dose) between time intervals or any individual remaining off an antidepressant between time intervals was considered no change. Increases of an antidepressant medication dose (ex: citalopram 10mg to 20mg) or a new antidepressant noted on the medication list was considered to be an increase. Individuals that switched from one antidepressant to another antidepressant, whether within the same drug class (citalopram to sertraline) or switched to a different drug class (SNRI to SSRI), were excluded from the dose change descriptive analysis. As previously stated, the baseline sample was 336 participants, and the sample at 12 months was 220 participants. For the antidepressant dose change calculation, and 15 individuals were excluded due to switching antidepressant drug classes or having a PRN prescription. A total of 205 individuals were used in this descriptive analysis. For the antipsychotic dose change calculation, 7 individuals were excluded due to switching antipsychotic drug classes or having a PRN prescription. A total of 213 individuals were included in this descriptive analysis. The sample sizes differ for these descriptive analyses due to individuals not necessarily being on antidepressant and antipsychotic (i.e. one or the other), based on which drug class had data missing, or the fact that more individuals switched types of antidepressants compared to antipsychotics.

Data Analysis

Descriptive statistics were done using SPSS 24 to describe the sample characteristics, and data was assessed for outliers, missing items, and potentially skewed

data (IBM Corp. Released 2016. IBM SPSS Statistics for Mac, Version 24.0. Armonk, NY: IBM Corp.). Marital status and race were converted to dichotomous variables of married or not married, and black or white, respectively. Treatment group assignment (treatment/control) was also dichotomized. Generalized linear mixed models with a binary distribution and logit link function was used to explore antidepressant use over time, with fixed effects of age, gender, race, treatment vs. control, functional status (total BI score), and number of comorbidities entered into the model. The outcome was the dichotomous variable (yes/no) of either receiving or not receiving any routine antidepressant. The random intercept for residents was included to adjust for multiple measurements on each resident. A p-value of less than or equal to 0.05 level of significance was used for all analyses. The same modeling, fixed effects, and random intercept were also done to explore antipsychotic use over time. The dichotomous outcome of either receiving or not receiving any routine antipsychotic was used. Descriptive statistics were utilized to evaluate dose changes from baseline to 12 months.

Results

As shown in Table 9, the average age of residents was 82.6 (SD: 10.08) years old, and they were predominantly female (72.0%), white (59.2%) and unmarried (65.2%). On average, the mean Barthel Index was 45.2 (SD:27.8) and mean comorbidities was 2.9 (SD:1.6). At baseline, 58.9% of the sample was on at least one antidepressant and 17.3% was on at least one antipsychotic (Table 10). SSRIs (34.8%) were the most common antidepressant drug class, and mirtazapine (19.3%) was the most prevalent individual antidepressant medication at baseline. Most of the sample receiving an antipsychotic were taking atypical antipsychotics (16.4%), with risperidone (5.4%) being the most

prevalent individual antipsychotic medication at baseline. Lastly, at baseline 39 (11.6%) individuals were prescribed both a routine antidepressant and antipsychotic.

Table 9. Sample Characteristics

	Mean (SD*)	Range	Frequency (%)
Age	82.6 (10.1)	57-105	
Total BI*	45.2 (27.8)	0-99	
Total Comorbidities	2.9 (1.6)	0-9	
Total MMSE*	7.8 (5.1)	0-15	
Gender			
Female			242 (72.0)
Male			94 (28.0)
Missing			0
Race			
Black			133 (39.6)
White			199 (59.2)
Missing			4 (1.2)
Marital Status			
Married			92 (27.4)
Not Married			219 (65.2)
Missing			24 (7.4)

*SD: Standard deviation; BI: Barthel Index; MMSE: Mini-mental status examination

Table 10. Describing Antidepressant and Antipsychotic Use at Baseline & 12 months

	Baseline (N=336) N(%)	12 months (N=220) N(%)
Total Antidepressants (AD)		
Yes	198 (58.9)	117 (53.2)
No	138 (41.1)	103 (46.8)
SSRIs*	117 (34.8)	63 (28.6)
SNRIs*	18 (5.4)	11 (5.0)
Trazodone	33 (9.8)	25 (11.4)
Mirtazapine	65 (19.3)	45 (20.5)
Bupropion	1 (0.2)	0 (0.0)
Taking 2 or more AD	39 (11.6)	25 (11.4)
Antipsychotics (AP)**		
Yes	58 (17.3)	31 (14.1)
No	278 (82.7)	189 (85.9)
Typical antipsychotics	5 (1.5)	3 (1.4)
Haloperidol	3 (0.9)	1 (0.5)
Perphenazine	0 (0.0)	1 (0.5)
Compazine	2 (0.6)	0 (0.0)
Atypical antipsychotics	55 (16.4)	28 (12.7)
Olanzapine	15 (4.5)	7 (3.2)
Risperidone	18 (5.4)	10 (4.5)
Quetiapine	16 (4.8)	9 (4.1)
Aripiprazole	4 (1.2)	2 (0.9)
Clozapine	1 (0.3)	0 (0.0)
AP + AD Use Concurrently	41 (12.2)	19 (8.6)

*SSRIs: serotonin selective reuptake inhibitors; SNRIs: serotonin and norepinephrine reuptake inhibitors.
**One person received 2 antipsychotics at baseline; no one was on 2 antipsychotics at 12 months

At 12 months, 53.2% of the sample was on at least one antidepressant and 14.1% was on an antipsychotic. SSRIs (28.6%) were the most common antidepressant drug class, and mirtazapine (20.5%) the most common individual antidepressant medication at 12 months. Atypical antipsychotics (12.7%) were most prevalent in those with antipsychotic prescriptions, risperidone (4.5%) was the most common individual antipsychotic medication, and 19 (8.6%) individuals were taking both a routine antidepressant and antipsychotic at 12 months. When new psychotropic medications

appeared on the medication administration record (not listed at baseline but then listed at 12 months), mirtazapine and trazodone were the most common antidepressants, and risperidone and quetiapine the most common antipsychotics to be added to the drug regimens (not shown in tables).

Table 11 provides dose changes at baseline and 12 months of both antidepressants and antipsychotics. A total of 38 (11.3%) participants had an individual dose increase or a new antidepressant started, and 42 individuals (12.5%) had either a total daily dose reduction or an antidepressant discontinued. Twenty (6.0%) antipsychotic users had either a total daily dose decreased or antipsychotic discontinued compared to 12 (3.6%) antipsychotic users that had a total daily dose increase or antipsychotic started.

Table 11. Dose Changes of Antidepressants and Antipsychotics from 0 to 12 Months

	Antidepressants N(%)	Antipsychotics N (%)
Dose Increase	38 (11.3)	12 (3.6)
Dose Decrease	42 (12.5)	20 (6.0)
No Changes	132 (39.3)	187 (55.7)
Drug Data Missing	124 (36.9)	117 (34.8)

As shown in Table 12, the adjusted model comparing changes in antidepressant use between baseline and 12 months (yes or no receiving any antidepressant) found no significant change among participants (β=-0.20; p=0.369). Regardless of time, black race (β=-0.72, p=0.011) and individuals with more co-morbidities (β=-0.14, p=0.028) were significantly less likely to be on an antidepressant. The adjusted model for comparing antipsychotic changes from baseline to 12 months (yes or no receiving any antipsychotic) also found no significant change among participants (β=-0.25; p=0.306) (Table 13). Regardless of time, individuals who were older (β=0.04, p=0.028) were significantly less likely to be on an antipsychotic.

Table 12. Adjusted Model for Antidepressant from Baseline to 12 months

Variable	β Coefficient (S.E.*)	95% CI*	P-value
Age	-0.02 (0.02)	-0.05 - 0.01	0.151
Female	0.49 (0.31)	-0.12 - 1.10	0.117
Black	**-0.72 (0.28)**	**-1.27- -0.17**	**0.011**
BI* total	0.01 (0.01)	-0.01 - 0.01	0.150
FBFC* Treatment	0.08 (0.27)	-0.45 - 0.62	0.760
Co-morbidities	**-0.14 (0.07)**	**-0.27- -0.01**	**0.031**
At 12 Months	-0.20 (0.22)	-0.62 - 0.23	0.369

*BI: Barthel Index; FBFC: Function and Behavior Focused; S.E.: Standard Error; CI: Confidence Interval

Table 13. Adjusted Model for Antipsychotic Use from Baseline to 12 Months

Variable	β Coefficient (S.E.*)	95% CI*	P-value
Age	**-0.04 (0.02)**	**-0.08- -0.01**	**0.028**
Female	0.47 (0.39)	-0.30-1.23	0.229
Black	-0.61 (-0.40)	-1.30-0.08	0.077
BI* total	0.01 (0.01)	-0.01-0.02	0.249
FBFC* Treatment	0.55 (0.33)	-0.09-1.19	0.091
Co-morbidities	-0.11 (-.08)	-0.28-0.05	0.184
At 12 Months	-0.25 (0.29)	-0.81-0.31	0.374

*BI: Barthel Index; FBFC: Function and Behavior Focused; S.E: Standard Error; CI: Confidence Interval

Discussion

The purpose of this study was to describe the use of antidepressants and antipsychotics and evaluate trends between baseline and 12 months in antidepressant and antipsychotic prescribing among nursing home residents with moderate to severe cognitive impairment. The hypothesis that there would be an increase in the use of antidepressants and a decrease in the use of antipsychotics at 12 months among nursing home residents with moderate to severe cognitive impairment, when controlling for age, gender, race, functional status, number of co-morbidities, and treatment effects of FBFC was not supported. The dose change comparison from baseline to 12 months showed

more medication adjustments made to reduce or remove the use of antipsychotics and antidepressants compared to increasing or starting them. These results suggest a positive rather than a negative trend in psychotropic medication use overall following the implementation of the National Partnership at least among residents with moderate to severe cognitive impairment. Further, the prevalence of antipsychotics within this sample was below the national average at baseline and continued to decline, which aligns with the goals of the National Partnership (CMS, 2020).

These results may also reflect prescribers incorporating an increased focused on deprescribing. Deprescribing is a strategy endorsed by CMS and used by providers to address polypharmacy in older adults (Harrison, et al., 2019). Outcomes of deprescribing include reduced all-cause mortality, reduced number of falls, and decreased hospitalizations (Thiruchelvam, K., et al., 2017; Kua, et al., 2019). Healthcare providers within these Maryland nursing homes may have implemented describing practices that guided the reduction of both antidepressants and antipsychotics in this sample.

In contrast to deprescribing, prescribers within these Maryland facilities may have been utilizing other psychotropics not captured in this study. Though evidence supports antidepressants being the most prevalent psychotropic medication, other drug classes like anxiolytics and mood stabilizers are also becoming more common in long term care for management of BPSD (Gustafsson, et al., 2013; Masopust, et al., 2018; Maust, et al., 2018; Early, et al., 2020). Like antidepressants, anxiolytics and mood stabilizers are not required for public reporting and quality measures. Common drug combinations include antidepressants with anxiolytics, antidepressants with mood stabilizers, and antipsychotics with anxiolytics (Gulla, et al., 2016; Bathena, et al., 2017; Westbury, et al.,

2020). Anti-dementia drugs are also being used for management of BPSD (Dyer, et al., 2018). The use of multiple psychotropics, even at minimal doses, still puts residents with dementia at risk of drug interactions, serious adverse events, and perpetuates polypharmacy. Future research should continue to evaluate the appropriate or inappropriate use of drug combinations to manage BPSD.

Although there was no evidence of an increase in antidepressant use, similar to prior research, the prevalence and persistent use of antidepressants was above 50% at both time points, and over half the participants at both time points taking an antidepressant were on SSRIs (Hanlon, et al., 2011; van Asch, et al., 2012; Ruths, et al., 2013; Midlov, et al., 2014; Hiltunen, et al., 2016; Helvik, et al., 2017; Brimelow, et al., 2018). One consideration is the influence of family members on psychotropic use in nursing home residents with dementia. Prescribers felt less comfortable recommending gradual dose reductions with antidepressants and other psychotropic medications if family members felt the need to continue them (Djatche, et al., 2018; Aerts, et al., 2019). This is concerning since evidence exists that antidepressants have limited effectiveness in persons with dementia and monitored discontinuation of antidepressants in nursing home residents with dementia has been successful with minimal adverse events (Seitz, et al., 2011; Bergh, Selbaek, & Engedal, 2012; Dudas, et al., 2018). The Beers Criteria is a list of potentially inappropriate medications to be avoided in older adults (Fick et al., 2019). SSRIs were added to this list in 2012 due to associations with falls and fractures in persons with dementia (AGS, 2012). In 2019, the Beers Criteria added SNRIs as they are also associated with falls and fractures in persons with dementia (Fick, et al., 2019). Research should continue to assess antidepressant use over time in nursing home

residents with moderate to severe cognitive impairment as these guidelines become more common knowledge and evaluate psychotropic trends when using these guidelines to educate families.

Strengths and Limitations

A strength of this study was that it looked at antidepressant use and compared it to antipsychotic use at baseline and 12 months in a large sample of nursing home residents with more severe cognitive impairment. In addition, there was a large group of black individuals within this sample, which is uncommon in nursing home-focused research. The major limitation of this study was the design of being a secondary data analysis. The parent study did not collect indications for use of either psychotropic drug class, so this study was unable to evaluate whether the antidepressants and antipsychotics were prescribed appropriately. The parent study also did not collect data regarding timing of the initiation of either psychotropic medication, so one cannot evaluate whether an antidepressant was started when an antipsychotic was discontinued or vice versa. In addition, data was collected from nursing homes within the same state. Lastly, attrition was 116 individuals over the year, which may have affected the results of this study. Despite these limitations, this study expands the current knowledge around antidepressants and antipsychotics longitudinally and coincidentally a year after the initiation of the National Partnership in this vulnerable nursing home population.

Conclusion

This study found no significant change in antidepressant and antipsychotic use between baseline and 12 months when controlling for age, gender, race, number of comorbidities, functional status, and treatment effect from the parent study. Though

results did not support the original hypothesis, this study did describe patterns of use of antidepressants and antipsychotics in a population with more severe cognitive impairment. A nonsignificant decrease of both psychotropic medications was observed. Individual medication doses were reduced more often than increased for both antidepressants and antipsychotics. These results support a positive trend in antidepressant and antipsychotic use since implementation of a national initiative to reducing their use in persons with moderate to severe dementia.

CHAPTER 5: Discussion, Implications, and Recommendations

Introduction

The purpose of this dissertation was to: (Aim 1) Determine factors that influence antidepressant use among nursing home residents with moderate to severe cognitive impairment; (Hypothesis 1) Age, gender, race, number of co-morbidities, functional status, and level of agitation would be associated with antidepressant use in nursing home residents with moderate to severe cognitive impairment; (Aim 2) Describe any potential differences in antidepressant use between white and black nursing home residents with moderate to severe cognitive impairment; (Hypothesis 2) There would be a greater use of all antidepressants in white versus black nursing home residents with moderate to severe cognitive impairment when controlling for depression, age, gender, functional status, level of agitation, and number of co-morbidities; (Aim 3) Evaluate trends in antidepressants and antipsychotics prescribing among nursing home residents with moderate to severe cognitive impairment; (Hypothesis 3) There would be an increase in the use of antidepressants and decrease in the use of antipsychotics between baseline and 12 months among nursing home residents with moderate to severe cognitive impairment when controlling for age, gender, race, functional status, number of co-morbidities, and treatment effects from the parent study.

The three manuscripts are provided in Chapters 2, 3,and 4. Chapter 2 addresses hypothesis 1, chapter 3 addresses hypothesis 2, and chapter 4 addresses hypothesis 3. Data for this work came from the Function and Behavior Focused Care (FBFC) for Nursing Home Residents with Dementia randomized control trial, which was a repeated measures design and took place from 2013 to 2018. This chapter details the major

findings from each manuscript, describes practice implications and recommendations for future research, and discusses the strengths and limitations of this dissertation.

Summary of Study Findings

Evaluating Factors that Influence Antidepressant Use in Nursing Home Residents with Moderate to Severe Cognitive Impairment

This study described the prevalence of antidepressant use and evaluated factors associated with antidepressant use among nursing home residents with moderate to severe cognitive impairment. It was hypothesized that age, race, gender, number of co-morbidities, and level of agitation would be significantly associated with the use of antidepressants among nursing home residents with moderate to severe cognitive impairment. Using baseline data from the FBFC randomized control trial, descriptive statistics were used to identify the prevalence of overall antidepressants and then prevalence by drug class within this sample. Consistent with prior research, serotonin selective reuptake inhibitors (SSRIs) were the most common drug class (Karkare, et al., 2011; Harris, et al., 2012; Bobo, et al., 2019). Mirtazapine was the most common antidepressant, though its prevalence in this study was higher than prior research (Karkare, et al., 2011; Bourgeois, et al., 2012; Shah, et al., 2012; Bobo, et al., 2019). Participants within this study may have been more cognitively impaired than prior research, and weight loss and insomnia are commonly seen and expected in persons with more severe dementia. Although indications for use were not available from the parent study, mirtazapine is commonly prescribed off label for appetite or insomnia in addition to its Food and Drug Administration (FDA) indication of depression or anxiety (Alam, Voronovich, & Carley, 2013; Bobo, et al., 2019).

Logistic regression was used to address the hypothesis, and the model was significant (χ^2=17.780, p=0.007) and explained 7.1% of the variance of antidepressant use among these nursing home residents with moderate to severe cognitive impairment. Race (β=-0.67; p=0.01) was the only variable significantly associated with antidepressant use among nursing home residents with moderate to severe dementia, with black residents half as likely to be on an antidepressant compared to white residents. This was consistent with prior research supporting differences in antidepressant use among nursing home residents who are cognitively intact or with mild cognitive impairment (Hanlon, et al., 2009; Gaboda, et al., 2011).

In this study, age, gender, number of co-morbidities, functional status, and level of agitation were not found to be significantly associated with antidepressant use among nursing home residents with dementia. This may be due to the homogeneity of the sample as the participants had little to no agitation (M=19.8; SD=6.1), a low number of co-morbidities (M=2.9; SD=1.6), severe cognitive impairment (M=7.8; SD=5.1), and functional disability (M=46.1; SD=27.5). Regarding age and gender, prior research (Karkare, et al., 2011; Gustafsson, et al., 2013; Bhattacharjee, et al., 2019; Bobo, et al., 2019) found an association with antidepressant use among mixed samples of older adults from the community and nursing homes that included participants with and without dementia.

The final model in this study explained very little (7%) of the variance in antidepressant use among nursing home residents with moderate to severe cognitive impairment. This study utilized the intrapersonal factors associated with antidepressant use. Consistent with a SEM, there may also be interpersonal factors that contribute to

antidepressant use such as staff's attitude towards residents with dementia, their skill and stress level, and low patient to staff ratios (Zuidema, et al., 2011; Anderson, et al., 2016; Røen, et al., 2018). Environmental and policy factors that are associated with antidepressant use include the facility's profit status, bed capacity, the involvement of the medical director, the utilization of external psychiatric consulting services, and overall facility adaptation of state and federal regulations (Hanlon, Handler, & Castle, 2010; Karkare, et al., 2011; Bourgeois, et al., 2012; Smeets, et al., 2014; Smeets, et al., 2018; Resnick, et al., 2019).

In summary, this secondary data analysis provides evidence that antidepressant use is prevalent in nursing home residents with moderate to severe cognitive impairment and expands current knowledge of factors associated with antidepressant use in this specific population. Future research should include the intrapersonal factors with staffing and facility factors described above to better understand what influences the use of antidepressants among nursing home residents with moderate to severe cognitive impairment.

Racial Differences in Antidepressant Use in Nursing Home Residents with Moderate to Severe Cognitive Impairment

This study focused on describing potential differences between race and antidepressant use among nursing home residents with moderate to severe cognitive impairment. Two hypotheses were addressed: 1) Controlling for depression, age, gender, functional status, level of agitation, and number of comorbidities, there would be greater use of all antidepressants in white versus black nursing home residents with moderate to severe cognitive impairment, and 2) Black nursing home residents with moderate to

severe cognitive impairment would receive lower dosages of the most commonly prescribed antidepressants compared to white nursing home residents with moderate to severe cognitive impairment. Using baseline data from the FBFC randomized control trial, binary logistic regression was used for the first hypothesis. When controlling for depression, age, gender, number of co-morbidities, functional status, and level of agitation, black residents were significantly less likely to be on an antidepressant compared to white nursing home residents with moderate to severe cognitive impairment (Odds Ratio=0.499, p=0.006), which is consistent with prior research among nursing home residents who were less cognitively impaired (Hanlon, et al., 2009; Gaboda, et al., 2011).

There was, however, no significant difference found by race when looking at specific antidepressant drug classes. Of the five most commonly prescribed antidepressants found in this study, there was a significant difference by race in dosages of sertraline (T=2.68,p=0.01). Black residents (M:47.2mg, SD: 40.4mg) were on half the average dose of sertraline compared to white (M:86.6mg, SD: 38.1mg) residents with moderate to severe cognitive impairment.

There are a few possibilities to consider from these results. Black individuals tend to choose nursing homes based on proximity to the family, racial composition of the facility, and their financial situation (Rahman & Foster, 2015). Unfortunately, these factors have contributed to segregation across long-term care facilities, where many of the facilities with large minority groups are predominantly subsidized by Medicaid (Konetzka, et al., 2015; Rahnam & Foster, 2015; Mack, et al., 2020). Some studies have found that there is a relationship between facilities mostly funded by Medicaid and

poorer quality of care, with limited in-house access to mental health services but higher rates of psychiatric hospitalizations (Sengupta, et al., 2012; Mack, et al., 2020).

In the nursing home, black and Hispanic residents have been shown to report fewer depressive symptoms; however, there are concerns that staff may not be as sensitive to the symptoms of residents of color and that appropriate mental health services may not be available (Grabowski, et al., 2010; Li, et al., 2018). Significant racial disparities exist in the diagnosis and treatment of depression among community-dwelling older adults with and without dementia, with blacks significantly less likely to be diagnosed and treated for depression compared to whites even with equal access to healthcare (Akincigil, et al., 2012; Pickett, et al., 2014; Bhattacharjee, et al., 2017). Experiences of societal discrimination have led some minorities to be skeptical of mental health services, and the effectiveness of mental health treatment may be questioned (Gaston, et al., 2016; Alang, 2019). There is some research that suggests that racial differences may be due to the preferences of black individuals to avoid the use of antidepressant medication when possible (Cooper, et al., 2003; Givens, et al., 2007). Some studies indicate that black individuals may believe that dementia and associated neuropsychiatric symptoms such as depression are associated with the aging process, so families may not fully support the use of these medications (Hipps, et al., 2003; Connell, Scott Roberts, & McLaughlin, 2007) and believe that the potential benefits may not be worth the risk of possible adverse events associated with pharmacological intervention.

In addition, some research has supported that black individuals have expressed concern of misdiagnosis and inappropriate treatment by white providers who may exhibit bias (unconscious or conscious) towards individuals of color (Parker & Satkoske, 2012).

Research focused on the impact of implicit bias in health care has demonstrated that health care professionals across various levels of training and specialties may possess negative associations and implicit bias (evaluation that may reside outside of conscious control or awareness) against individuals of color (Hall, et al., 2015; Maina, et al., 2018). The impact of implicit bias by healthcare providers on patient outcomes is unknown, but there is evidence that this bias negatively impacts patient-provider interactions and may lead to under diagnosis and lack treatment of health conditions among individuals of color (Hall, et al., 2015; Maina, et al., 2018).

In addition to considering the impact of bias, another possible explanation for the racial difference seen in antidepressant use among nursing home residents with moderate to severe cognitive impairment may be influenced by genomics. The tolerance and success or response failure to antidepressants has been correlated to the CYP2D6 gene, which has 77 different alleles (Krauter & Cook, 2011). Pharmacodynamic components of SSRI response have shown differences in allele frequencies among racial groups (McMahon, et al., 2006; Ruhé, et al., 2009). Black individuals tend to have higher alleles that improve response rates to SSRIs, so that may explain the difference in dose of sertraline within this study (Lotrich, Pollock, & Ferrell, 2003; O'Connell, et al., 2018). Newer research looking at genetic African ancestry as opposed to self-reported race also found response differences to antidepressants between blacks and whites (Murphy, et al., 2013).

In summary, this study expands our current knowledge of antidepressant use by race among nursing home residents with moderate to severe cognitive impairment. This study also provides more detail about specific drug classes and dosages by race among

nursing home residents with moderate to severe cognitive impairment. Given that the parent study did not collect indications for use or duration of use of antidepressants in this sample, it cannot be determined whether participants were receiving antidepressants for FDA approved indications of depression or anxiety or if being used off-label for other symptoms. It also cannot be determined with this cross-sectional approach whether the participants were at therapeutic doses or were still receiving medication adjustments. Further research is needed with larger, nationally diverse samples to explore the possible impact of racial disparities from prescriber, societal, and policy factors in addition to addressing possible genomic factors with nursing home residents with dementia.

Patterns of Use of Antidepressants and Antipsychotics in Nursing Home Residents with Moderate to Severe Cognitive Impairment

In 2012, the Centers for Medicare and Medicaid Services (CMS) launched the National Partnership to Improve Dementia Care in Nursing Homes, which focused on improving the quality of life for residents with dementia through patient-centered care and reduction of inappropriate antipsychotic use (CMS, 2014). The larger mission of this Partnership was to promote the use of nonpharmacologic approaches and other person-centered dementia care practices and reduce overall inappropriate psychotropic medication use (CMS, 2014). CMS partnered with multiple state and federal agencies as well as professional organizations and public advocacy groups to disseminate the National Partnership. The FBFC for Nursing Home Residents with Dementia randomized control trial took place from 2013 to 2018, thus followed the initiation of the National Partnership. This timing allowed for evaluation of the potential impact of the National Partnership within nursing homes participating in the parent study. In

evaluation of the study outcomes, it is critical to consider the impact of history and the initiation of the National Partnership. The focus of this secondary data analysis was to describe the use of antidepressants and antipsychotics and evaluate trends between baseline and 12 months in antidepressant and antipsychotic prescribing among nursing home residents with moderate to severe cognitive impairment. The hypothesis stated that when controlling for age, gender, race, number of co-morbidities, functional status, and treatment effects from the parent study, there would be an increase in the use of antidepressants and decrease in the use of antipsychotics between baseline and 12 months among nursing home residents with moderate to severe cognitive impairment. The hypothesis was not supported, and the adjusted models for both antidepressant (β=-0.20; p=0.369) and antipsychotic (β=-0.25; p=0.306) use between baseline and 12 months found no significant change among participants. When evaluating doses changes from baseline to 12 months, both antipsychotics and antidepressants had more medication adjustments to reduce or remove the use of these medications compared to increasing or starting a new medication. These results are inconsistent with prior research, where antidepressants either remained stable or increased over time (Ruths, et al., 2013; Vasudev, et al., 2015; Helvik, et al., 2017; Maust, et al., 2018; Ozaki, Katsumata, & Arai, 2019). One explanation may be the fact 116 participants were lost mostly to death between baseline and 12 months, which may have affected the results of this study. Another possibility may be prescribers responding and acting on recommendations provided by the National Partnership. The antipsychotic trend seen within this study is consistent with prior research and national data that antipsychotic use has decreased since the implementation of the National Partnership to Improve Dementia (Maust, et al. 2018;

Roitto, et al., 2019; CMS, 2019). Overall, these results are positive and align with the goals of the National Partnership.

Unfortunately, these results may not capture an increase in the use of other psychotropic medications not evaluated with this study. There is some evidence to show that the prescribing of anxiolytics and mood stabilizers for nursing home residents with dementia is also increasing (Maust, et al., 2018; Ozaki, Katsumata, & Arai, 2019; Early, et al., 2020). An accelerated growth with the use of mood stabilizers was noted since implementation of the National Partnership, though their prevalence was not as high as antidepressants (Maust, et al., 2018). Further research is needed to explore whether the National Partnership has inadvertently shifted prescribing practices to the use of other psychotropic medications as antipsychotic use declines among nursing home residents with dementia.

In summary, this study supports a positive trend in antidepressant and antipsychotic use among nursing home residents with moderate to severe cognitive impairment since implementation of the National Partnership to Improve Dementia. This study adds to current knowledge by expanding upon antipsychotic and antidepressant use over time through evaluation of total daily dose changes between two time points in a specific population of residents with more severe cognitive impairment.

Implications

Improving the quality of care, particularly appropriate medication use, for nursing home residents has been a national focus since the implementation of the Nursing Home Reform Act in 1987. The National Partnership to Improve Dementia Care not only focused on reducing antipsychotics but also advocated for improved goal-directed,

individualized care for nursing home residents with dementia (CMS, 2014). Nonpharmacological interventions avoid the risks associated with psychotropics and typically incorporate the person's specific needs, preferences, and functional abilities, which aligns with the concept of person-centered care (Fitzsimmons, et al., 2014). Furthermore, inappropriate medication use is associated with hospitalizations, increased mortality, and increased healthcare costs (Harrison, et al., 2018). Reducing polypharmacy has never been more important. With the current pandemic, removal of inappropriate medications reduces the risk of transmission of coronavirus by minimizing the number of medication administrations needed, and therefore potential exposures between resident and staff (Peter Lamy Center, 2020). Careful monitoring of gradual dose reductions and then the discontinuation of antidepressants has been successful in a small group of residents with dementia (Bergh, Selbæk, & Engedal, 2012). Given the prevalence and persistent use of antidepressants and potential serious adverse events (Ruths, et al., 2013; Vasudev, et al., 2015; Helvik, et al., 2017; Hiance-Delahaye, et al., 2018; Sobieraj, et al., 2019), it is important to evaluate the ongoing need for antidepressant use among nursing home residents with moderate to severe cognitive impairment.

The findings from this dissertation provide guidance on antidepressant use among nursing home residents with moderate to severe cognitive impairment in a few ways. Although the prevalence of antidepressants was above 50%, the decline in overall antidepressant use between baseline and 12 months is promising. This may be from fewer antidepressants being initiated or from deprescribing, both of which can significantly reduce the use of potentially inappropriate medications (Kua, Mak, & Lee,

2019). Deprescribing is defined as "the systematic process of identifying and discontinuing drugs in instances which existing or potential harms outweigh existing or potential benefits within the context of an individual's care goals, current level of functioning, life expectancy, values, and preferences" (Scott, et al., 2015). Long term care prescribers should continue to assess the need for initiation and ongoing use of antidepressants among nursing home residents with moderate to severe cognitive impairment. This assessment can be difficult in this population due to their lack of ability to self-report. Furthermore, screening assessments like the Patient Health Questionnaire (PHQ-9) that are embedded in the Minimum Data Set (MDS) 3.0 are not specifically designed for residents with more severe cognitive impairment. Therefore, when starting or deprescribing antidepressants, it is important to observe behaviors consist with depression and other behavioral symptoms such as tearfulness, anxiety, social withdrawal, changes in sleep and appetite, irritability, and agitation that cannot be explained by a medical cause. It is also critical that providers engage nursing staff and families for feedback about these residents when assessing medication changes.

In addition, all three studies found race significantly associated with antidepressant use among nursing home residents with moderate to severe cognitive impairment. Furthermore, there was a significant difference in dosing of sertraline between black and white nursing home residents with moderate to severe cognitive impairment as noted in manuscript 2.

Interactions of historical, cultural, and social factors influence black individuals' perceptions of seeking and utilizing mental health treatment (Parker & Stakoske, 2012). Historically, there have been cases of racial mistreatment in healthcare that resonate with

older adults (Parker & Satkoske, 2012). Hence, there may be mistrust, especially when the healthcare prescriber is not of the same race or culture (Parker & Satkoske, 2012; Gaston, et al., 2016). It has also been found that healthcare providers may have implicit bias towards minorities that impact the quality of interactions between patient and provider (Hall, et al., 2015; Maina, et al., 2018). Furthermore, a disproportionate number of individuals of color have been found to still have active symptoms with limited follow up after starting antidepressant medication (Pickett, et al., 2014). Given the fact that the number of individuals of color residing in long term care is increasing (Feng, et al., 2011; Spetz, et al., 2015), healthcare prescribers should be cognizant of these factors to ensure appropriate, quality care is provided to nursing home residents of color.

Looking from a cultural and social perspective, black individuals may be less likely to report behavioral symptoms and may be concerned about stigma associated with the use of psychiatric medications and mental health treatment (Gitlin, et al., 2012; Li, et al., 2018). There may be greater reliance on prayer and the social support of family to deal with symptoms and may believe medications are ineffective for mental health (Cooper, et al., 2003). Furthermore, the progression of dementia and associated symptoms may be viewed as a normal part of the aging process, and black individuals may not believe that pharmacological intervention is warranted (Hipps, et al., 2003; Connell, Scott Roberts, & McLaughlin, 2007). Healthcare providers need to be more aware of culture related differences in symptom reporting and family concerns about treatment with psychoactive medications and elicit discussions to increase understanding of family concerns.

Recommendations for Future Research

The findings from this dissertation provide ground work for future research regarding antidepressant use among nursing home residents with moderate to severe cognitive impairment. This study included the intrapersonal factors associated with antidepressant use from the SEM framework. Additional factors from the intrapersonal, environmental, and policy levels should be added for improved model analysis. Examples of relevant additional factors include staff's attitude towards and knowledge of persons with dementia, staff's distress level, staff to patient ratios, insurance type, total number of facility beds, number of providers involved in the care of the patient, facility ownership, and the facility's adaptation of state and federal regulations (Hanlon, Handler, & Castle, 2010; Karkare, et al., 2011; Zuidema, et al., 2011; Bourgeois, et al., 2012; Smeets, et al., 2014; Smeets, et al., 2018; Resnick, et al., 2019). Next steps include establishing associations with antidepressant use among this population and then evaluating their influence on appropriate versus inappropriate use of antidepressants among nursing home residents with moderate to severe cognitive impairment.

The findings from this study also suggested that antidepressant use was significantly associated with race among nursing home residents with moderate to severe cognitive impairment. It is unknown if racial differences reflect appropriate prescribing practices or if there is an inappropriate disparity between different races. As previously mentioned, there are concerns around the impact of racial disparities, decreased access to behavioral health care, and implicit bias that may contribute to the prescribing decisions made by healthcare providers (Hall, et al., 2015; Maina, et al., 2018). Among community older adults in their 80s, racial disparities are found with a disproportionate number of

black and Hispanic patients undertreated with antidepressants (Pickett, et al., 2014). Further research is needed to understand how race impacts the appropriate use of antidepressants as well as influences the treatment approach of healthcare prescribers in long term care.

The lack of participation of black individuals in dementia research is impacted by mistrust towards healthcare professionals given historical disregard for the protection of participants in research, lack of engagement of research staff with the community, and the lack of diversity and cultural sensitivity of the research team (Jones & Jablonski, 2014; Epps, Skemp, & Specht, 2015). Future research should be mindful of these barriers and employ strategies to overcome them to engage blacks and other minorities in research. Some examples include research staff resembling the population of interest, participation coming at no cost to the individual, utilizing the word "study" as opposed to research, and being knowledgeable of colloquial expressions (Jones & Jablonski, 2014; Alang, 2019).

Strengths and Limitations

One strength of this dissertation was that the parent study took place one to five years after the implementation of the National Partnership and evaluated antidepressant use in a nursing home population that is difficult to access due to challenges around consent and difficult to evaluate longitudinally due to loss to follow up. Another strength is the large number of black individuals with dementia that participated in the study given the known difficulties of recruiting blacks for research. The main limitation of this work is the fact that all studies were secondary data analyses. As outlined in Chapter 1, antidepressant use is associated with intrapersonal, interpersonal, environmental, and

policy factors. Variables were limited to data collected by the parent study, which only included intrapersonal factors associated with antidepressant use. Indications for use were also not collected, so it is unknown if antidepressants were being used appropriately or inappropriately. Generalizability of results are limited given that the data was collected from nursing homes within the same state. Despite these limitations, this research expands current knowledge around factors associated with antidepressant use and trends of antidepressant use in nursing home residents with moderate to severe cognitive impairment.

Summary

This chapter summarized key findings from this research, reviewed clinical implications, and suggested modifications for future research. Strengths and weaknesses were reviewed based on the secondary data analysis design. This dissertation contributes to current research by expanding on associations and trends with antidepressant use among a specific population that is typically excluded from research due to measure or consent issues, which are nursing home residents with moderate to severe cognitive impairment.

References

Abou-Raya, S., Abou-Raya, A., & Helmii, M. (2012). Duloxetine for the management of pain in older adults with knee osteoarthritis: randomized placebo-controlled trial. *Age and Ageing, 41*, 646-652.

Aerts, L., Cations, M., Harrison, F., Jessop, T., Shell, A., Chenoweth, L., & Brodaty, H. (2019). Why deprescribing antipsychotics in older people with dementia in long-term care is not always successful: Insights from the HALT study. *International Journal of Geriatric Psychiatry*, *34,* 1572-1581.

Aga, V. (2019). When and how to treat agitation in Alzheimer's disease dementia with citalopram and escitalopram. *American Journal of Geriatric Psychiatry*, *27*(10), 1099-1107.

AGS: American Geriatrics Society. (2010). *A guide to dementia diagnosis and treatment.* Retrieved from http://unmfm.pbworks.com/f/American+Geriatric+Society+Dementia+Diagnosis+03-09-11.pdf

AGS: American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. (2012). *Journal of the American Geriatrics Society, 60*(4), 616-631.

Akincigil, A., Olfson, M., Siegel, M., Zurlo, K., Walkup, J., & Crystal, S. (2012). Racial and ethnic disparities in depression care in community-dwelling elderly in the United States. *American Journal of Public Health*, *102*(2), 319-328.

Alam, A., Voronivich, Z., & Carley, J. (2013). A review of therapeutic uses of mirtazapine in psychiatric and medical conditions. *The Primary Care Companion for CNS Disorders, 15*(5).

Alang, S. (2019). Mental health care among blacks in America: Confronting racism and constructing solutions. *Health Services Research*, *54*(2), 346–355.

Alexopoulos, G., Abrams, R., Young, R., & Shamoian, C. (1988). Cornell scale for depression in dementia. *Biological Psychiatry*, *23*(3), 271-284.

Alexopoulos, G. (2002). The Cornell scale for depression in dementia: Administration and scoring guidelines. Retrieved from http://www.scalesandmeasures.net/files/files/The%20Cornell%20Scale%20for%20Depression%20in%20Dementia.pdf

AMDA: Society for Post-Acute and Long Term Care. (2018). Dementia Care. *Clinical Practice Guideline.*

Anderson, K., Bird, M., MacPherson, S., & Blair, A. (2016). How do staff influence the quality of long-term dementia care and the lives of residents? A systematic review of the evidence. *International Psychogeriatrics*, *28*(8), 1263–1281.

Andrade, C., Sandarsh, S., Chethan, K. & Nagesh, K. (2010). Serotonin reuptake inhibitor antidepressants and abnormal bleeding: a review for clinicians and a reconsideration of mechanisms. *Journal of Clinical Psychiatry*, *7*(12), 1565-1575.

van Asch, I., Numen, J., Veerbeek, M., Frijters, D., Achterberg, W., & Pot, A. (2013). The diagnosis of depression and use of antidepressants in nursing home residents with and without dementia. *International Journal of Geriatric Psychiatry*, *28,* 312-318.

Atramont, A., Bonnet-Zamponi, D., Bourdel-Marchasson, I., Tangre, I., Fagot-Campagna, A., & Tuppin, P. (2018). Health status and drug use 1 year before and 1 year after skilled nursing home admission during the first quarter of 2013 in France: A study based on the French National Health Insurance Information System. *European Journal of Clinical Pharmacology*, *74*(1), 109-118.

Bakouni, H., Vasiliadis, H, & Berbiche, D. (2019). Off-label use of antipsychotics and associated factors in community living older adults. *Aging & Mental Health*, *23*(2), 158-165.

Bali, V., Chatterjee, S., Johnson, M. L., Chen, H., Carnahan, R. M., & Aparasu, R. R. (2017). Risk of Mortality in Elderly Nursing Home Patients with Depression Using Paroxetine. *Pharmacotherapy*, *37*(3), 287–296.

Banerjee S, Hellier J, Dewey M, Romeo R, Ballard C, Baldwin R, Bentham P, Fox C, Holmes C, Katona C, Knapp M, Lawton C, Lindesay J, Livingston G, McCrae N, Moniz-Cook E, Murray J, Nurock S, Orrell M, & O'Brien J. (2011). Sertraline or mirtazapine for depression in dementia (HTA-SADD): a randomised, multicentre, double-blind, placebo-controlled trial. *Lancet*, *378*(9789), 403–411.

Barca, M., Engedal, K., Selbaek, G., Knapskog, A., Laks, J., Coutinho, E., & Benth, J. (2015). Confirmatory factor analysis of the Cornell scale for depression in dementia among patients with dementia of various degrees. *Journal of Affective Disorders*, *188*, 173-178.

Barnes, L., & Bennett, D. (2014). Alzheimer's disease in African Americans: Risk factors and challenges for the future. *Health Affairs*, *33*(4), 580-586.

Basnet, P., Acton, G., & Requijo, P. (2020). Psychotropic medication prescribing practice among residents with dementia in nursing homes: A person-centered care approach. *Journal of Gerontological Nursing*, *42*(2), 9-17.

Bassony, M., Steinberg, M., Rosenblatt, A., Baker, A., & Lyketsos, C. (2000). Delusions and hallucinations in Alzheimer's disease: prevalence and clinical correlates. *International Journal of Geriatric Psychiatry, 15,* 99-107.

Bathena, S., Leppik, I., Kanner, A., Birnbaum, A. (2017). Antiseizure, antidepressant, and antipsychotic medication prescribing in elderly nursing home residents. *Epilepsy & Behavior*, *69*, 116-120.

Bergh, S., Geir Selbæk, & Engedal, K. (2012). *Discontinuation of antidepressants in people with dementia and neuropsychiatric symptoms (DESEP study): Double blind, randomised, parallel group, placebo controlled trial* BMJ Publishing Group.

Bessey, L., & Walaszek. (2019). Management of behavioral and psychological symptoms of dementia. *Current Psychiatry Reports*, *21*(66), 1-11

Bhattacharjee, S., Lee, J., Patanwala, A., Malone, D., Vadiei, N., Knapp, S., Lo-Ciaganic, W., & Burke, W. (2019). Extent and predictors of potentially inappropriate antidepressant use among older adults with dementia and major depressive disorder. *American Journal of Geriatric Psychiatry*, 27(8), 794-805.

Bhattacharjee, S., Oh, Y. M., Reiman, E. M., & Burke, W. J. (2017). Prevalence, Patterns, and Predictors of Depression Treatment among Community-Dwelling Elderly Individuals with Dementia in the United States. *The American Journal of Geriatric Psychiatry*, *25*(7), 803–813.

Bobo, W., Grossardt, B., Lapid, M., Leung, J., Stoppel, C., Takahasi, P., Hoel, R., Chang, Z., Lachner, C., Chauhan, M., flowers, L., Brue, S., Fyre, M., Sauver, J., Rocca, W., & Sutor, B. (2019). Frequency and predictors of the potential overprescribing of antidepressants in elderly residents of a geographically defined US population. *Pharmacology Research & Perspectives, 1*, e00461.

Bourgeois, J., Elseviers, M., van Bortel, L., Petrovic, M., & Stichele, R. (2012). The use of antidepressants in Belgian nursing homes. *Drugs & Aging*, *29,* 759-769.

Brimelow, R., Wollin, J., Byrne, G., & Dissanayaka, N. (2018). Prescribing of psychotropic drugs and indicators for use in residential aged care and residents with dementia. *International Psychogeriatrics*, *31*(6), 837-847.

Burnett-Zeigler, I., Zivin, K., Igen, M., Szymanski, B., Blow, F., Kales, H. (2012). Depression treatment in older adult veterans. *The American Journal of Geriatric Psychiatry*, *20*(3), 228-238.

Cameron, E., Bowles, S., Marshall, E., & Andrew, M. (2018). Falls and long-term care: A report from the care by design observational cohort study. *BMC Family Practice*, *19*(1), 1-7.

CDC: Centers for Disease and Control and Prevention. (2019a). *Healthy Brain Initiative.* Retrieved from https://www.cdc.gov/aging/healthybrain/index.htm

CDC: Centers for Disease Control and Prevention. (2019b). *Vital and Health Statistics: Long-term Care Providers and Service Users in the United States, 2015-2016.* Retrieved from: https://www.cdc.gov/nchs/data/series/sr_03/sr03_43-508.pdf

Chung, S., Park, M., Choi, J., Yang, T., Park, M., Kim, N., & Moon, S. (2015). Is mirtazapine really effective in the treatment of Korean elderly depressed patients

with insomnia after previous antidepressant failure? An open-label multicenter study. *Sleep Medicine*, *16* (Supplement 1): S240.

CMS: Centers for Medicare and Medicaid Services. (2019). *National Partnership to Improve Dementia Care in Nursing Homes: Antipsychotic Medication Use Data Report.* Retrieved from: https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/SurveyCertificationGenInfo/Downloads/Antipsychotic-Medication-Use-Data-Report.pdf

CMS: Centers for Medicare and Medicaid Services. (2014). *National partnership to improve dementia care exceeds goal to reduce use of antipsychotic medications in nursing homes: CMS announces new goal.* Retrieved from: https://www.cms.gov/newsroom/press-releases/national-partnership-improve-dementia-care-exceeds-goal-reduce-use-antipsychotic-medications-nursing

Cohen-Mansfield, J. (2014). *Instructional manual for the Cohen-Mansfield Agitation Inventory*. Retrieved from https://www.pdx.edu/ioa/sites/www.pdx.edu.ioa/files/CMAI_Manual%20%281%29.pdf

Connell, C., Scott Roberts, J., & McLaughlin, S. (2007). Public opinion about Alzheimer disease among blacks, Hispanics, and whites: results from a national survey. *Alzheimer Disease and Associated Disorders*, *21*(3), 232-240.

Cooper, L. A., J. J. Gonzales, J. J. Gallo, K. M. Rost, L. S. Meredith, L. V. Rubenstein, N. Y. Wang, and D. E. Ford. (2003). The Acceptability of Treatment for Depression among African-American, Hispanic, and White Primary Care Patients. *Medical Care 41*(4), 479–489.

Djatche, L., Lee, S., Singer, D., Hegarty, S., Lombardi, M., & Mai, V. (2018). How confident are physicians in deprescribing for the elderly and what barriers prevent deprescribing? *Journal of Clinical Pharmacy and Therapeutics, 43,* 550-555.

Draper, B. & Berman, K. (2008). Tolerability of selective serotonin reuptake inhibitors: Issues relevant to the elderly. *Drugs & Aging*, *25*(6), 501-519.

Dudas, R., Malouf, R., McCleery, J., & Dening, T. (2018). Antidepressants for treating depression in dementia. *Cochrane Database of Systematic Reviews.* 8, CD003944.

Dutcher, S., Rattinger, G., Langenberg, P., Chhabra, P., Liu, X., Rosenberg, P., Leoutsakos, J., Simoni-Wastila, L., Walker, L., Franey, C., & Zuckerman, I. (2014). Effect of medications on physical function and cognition in nursing home residents with dementia. *Journal of the American Geriatrics Society, 62,* 1046-1055.

Dyer, L. T., Martin, B. K., Frangakis, C. E., Meinert, C. L., Mintzer, J. E., Munro, C. A., Porsteinsson, A. P., Rabins, P. V., Rosenberg, P. B., Schneider, L. S., Weintraub, D., & Lyketsos, C. G. (2011). Do treatment effects vary among differing baseline depression criteria in depression in Alzheimer's disease study ± 2 (DIADS-2)? *International Journal of Geriatric Psychiatry*, *26*(6), 573–583.

Early, N., Fairman, K., Ma, J., & Hong, K. (2020). Changes in psychotropic prescribing for patients with dementia, 2014-2016: Potential implications for pharmacists. *The Senior Care Pharmacist*, *35*(5), 207-219.

Echt, M., Samelson, E., Hannan, M., Dufour, A., & Berry, S. (2013). Psychotropic drug initiation or increased dosage and the acute risk of falls: a prospective cohort study of nursing home residents. *BMC Geriatrics*, *13*(19), 1-8.

Epps, F., Skemp, L., & Specht, J. (2015). Using culturally informed strategies to enhance recruitment of African Americans in dementia research: A nurse researcher's experience. *Journal of Research Practice, 11*(1), 1-19.

Ervin, K., Cross, M., & Koschel, A. (2014). Barriers to managing behavioural and psychological symptoms of dementia: Staff perceptions. *Collegian*, *21*, 201-207.

Farina, N., Morrell, L., & Banerjee. (2017). What is the therapeutic value of antidepressants in dementia? A narrative review. *International Journal of Geriatric Psychiatry*, *32*, 32-49.

Fashaw, S., Chisholm, L., Mor, V., Meyers, D., Liu, X., Gammonley, D., & Thomas, K. (2020). Inappropriate antipsychotic use: The impact of nursing home socioeconomic and racial composition. *Journal of the American Geriatrics Society*, *68,* 630-636.

Feng, Z., Fennell, M. L., Tyler, D. A., Clark, M., & Mor, V. (2011). The Care Span: Growth of racial and ethnic minorities in US nursing homes driven by demographics and possible disparities in options. *Health Affairs (Project Hope)*, *30*(7), 1358–1365.

Fick, D., Semla, T., Steinman, M., Beizer, J., Brandt, N., Dombrowski, R., DeBeau, C., Pezzullo, L., Epplin, J., Flanagan, N., Morden, E., Hanlon, J., Hollmann, P., Laird, R., Linnebur, S., & Sandhu, S. (2019). American Geriatrics Society 2019 Updated AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *Journal of the American Geriatrics Society, 67*(4), 674-694.

Fitzsimmons, S., Barba, B., Stump, M., & Bonner, A. (2014). Nonpharmacological Interventions in Long-Term Care. *Journal of Gerontological Nursing*, *40*(5), 10–14.

Foebel, A., Liperoti, R., Onder, G., Finne-Soveri, H., Henrard, J., Lukas, A., Denkinger, M., Gambassi, G., & Bernabei, R. (2013). Use of antipsychotic drugs among residents with dementia in European long-term care facilities: results from the SHELTER study. *Journal of the American Medical Directors Association*, *15*, 911-917.

Folstein, M., Folstein, S., & McHugh, P. (1975). Mini-mental state: A practice method for grading the cognitive state of patients for the clinician. *Journal of Psychiatry and Research, 2,* 189-198.

Gaboda, D., Lucas, J., Siegel, M., Kalay, E., & Crystal, S. (2011). No longer undertreated? Depression diagnosis and antidepressant therapy in elderly long-stay nursing home residents, 1999 to 2007. Journal of American Geriatrics Society, *59*, 673-680.

Gadzhanova, S., Roughead, E., & Pont, L. (2018). Antidepressant switch patterns in the elderly. *International Psychogeriatrics*, *30*(9), 1365-1374.

Gaston, G. B., Earl, T. R., Nisanci, A., & Glomb, B. (2016). Perception of mental health services among Black Americans. *Social Work in Mental Health*, *14*(6), 676–695.

Gebara, M., Lipsey, K., Karp, J., Nash, M., Iaboni, A., & Lenze, E. (2015). Cause or Effect? Selective serotonin reuptake inhibitors and falls in older adults: A systematic review. *American Journal of Geriatric Psychiatry*, *23*(10), 1016-1028.

Giebel, C., Sutcliffe, C., Renom-Guiteras, A., Arve, S., Hallberg, I., Soto, M., Zabalegui, A., Hamers, J., Saks, K., & Challis, D. (2015). Depressive symptomatology in severe dementia in a European sample: prevalence, associated factors, and prescription rate of antidepressants. *International Psychogeriatrics*, *27*(4), 657-667.

Gitlin, L. N., Chernett, N. L., Dennis, M. P., & Hauck, W. W. (2012). Identification of and beliefs about depressive symptoms and preferred treatment approaches among community-living older African Americans. *The American Journal of Geriatric Psychiatry*, *20*(11), 973–984.

Givens, J. L., I. R. Katz, S. Bellamy, and W. C. Holmes. (2007). Stigma and the Acceptability of Depression Treatments among African Americans and Whites. *Journal of General Internal Medicine* 22(9), 1292–1297.

Grabowski, D., Aschbrenner, K., Rome, V., & Bartels, S. (2010). Quality of mental health care for nursing home residents: A literature review. *Medical Care Research and Review : MCRR*, *67*(6), 627–656.

Grace, E., Allen, R., Ivey, K., Knapp, S., Burgio, L. (2018). Racial and ethnic differences in psychotropic medication use among community-dwelling persons with dementia in the United States. *Aging & Mental Health*, *22*(4), 458-467.

Gulla, C., Selbaek, G., Flor, E., Kjome, R., Kirkevold, O., & Husebo, B. (2016). Multi-psychotropic drug prescription and the association to neuropsychiatric symptoms in three Norwegian nursing home cohorts between 2004 and 2011. *BMC Geriatrics*, *16*(115), 1-9.

Gustafsson, M., Sandman, P., Karlsson, S., Gustafson, Y., & Lovheim, H. (2013). Association between behavioral and psychological symptoms and psychotropic drug use among old people with cognitive impairment living in geriatric care settings. *International Psychogeriatrics, 25*(9), 1415-1423.

Hall, W., Chapman, m., Lee, K., Merino, Y., Thomas, T., Payne, K., Eng, E., Day, S., & Coyne-Beasley, T. (2015). Implicit racial/ethnic bias among health care professionals and its influence on health care outcomes: A systematic review. *American Journal of Public Health, 105*(12), e60-e76.

Halloran, L. (2014). Behavioral and psychological symptoms of dementia. *Journal for Nurse Practitioners, 10*(8), 625-626.

Hanlon, J., Wang, X., Castle, N., Stone, R., Handler, S., Semla, T., Pugh, M., Berlowitz, D., & Dysken, M. (2011). Potential underuse, overuse, and inappropriate use of antidepressants in older veteran nursing home residents. *Journal of the American Geriatrics Society, 59,* 1412-1420.

Hanlon, J. T., Handler, S. M., & Castle, N. G. (2010). Antidepressant prescribing in US nursing homes between 1996 and 2006 and its relationship to staffing patterns and use of other psychotropic medications. *Journal of the American Medical Directors Association*, *11*(5), 320–324.

Hanlon, J., Wang, X., Good, B., Rossi, M., Stone, R., Semla, R., Cunningham, F., Handler, S. (2009). Racial differences in medication use among older, long-stay veteran affairs nursing home care unit patients. *The Consultant Pharmacist*, *24*(6), 439-446.

Harris, T., Carey, I., Shah, S., Dewilde, S., & Cook, D. (2012). Antidepressant prescribing in older primary care patients in community and care home settings in England and Wales. *Journal of the American Medical Directors Association, 13*, 41-47.

Harrison, S., O'Donnell, L., Milte, R., Dyer, S., Gnanamanickam, E., Bradley, C., Liu, E., Hilmer, S., & Crotty, M. (2018). Costs of potentially inappropriate medication use in residential aged care facilities. *BMC Geriatrics, 18*(9), 1-10.

Helvik, A., Benth, J., Wu, B., Engedal, K., & Selbaek, G. (2017). Persistent use of psychotropic drugs in nursing home residents in Norway. *BMC Geriatrics*, *17*(52), 1-13.

Hiance-Delahaye, A., de Schongor, F., Lechowski, K., Teillet, L., Arvieu, J., Robine, J., Ankri, J., & Herr, M. (2018). Potentially inappropriate prescription of antidepressants in old people: characteristics, associated factors, and impact on mortality. *International Psychogeriatrics*, *30*(5), 715-726,

Hiltunen, H., Tan, E., Ilomaki, J., Hilmer, S., Visvanathan, R., Emery, T., Robson, L., Jones, M., Hartikainen, S., & Bell. (2016). Factors associated with antidepressant use in residents with and without dementia in Australian aged care facilities. *Therapeutic Advances in Drug Safety*, *7*(3), 79-88.

Hipps, Y., Roberts, J., Farrer, L., & Green, R. (2003). Differences between African Americans and Whites in their attitudes toward genetic testing for Alzheimer's disease. *Genetic Tests, 7,* 39-44.

Hosmer, D. W., Jr., & S. Lemeshow. (1980). Goodness-of-fit tests for the multiple logistic regression model. Communications in Statistics—Theory and Methods 9: 1043–1069.

Hung, S., Lin, C., Hung, H., Lin, C., & Lai, S. (2017). Use of selective serotonin reuptake inhibitors and risk of hip fracture in the elderly: A case-control study in Taiwan. *Journal of the American Medical Directors Association*, *18,* 350-354.

Huybrechts, K., Rothman, K., Silliman, R., Brookhart, A., & Schneeweiss, S. (2011). Risk of death and hospital admission for major medical events after initiation of psychotropic medications in older adults admitted to nursing homes. *CMAJ: Canadian Medical Association Journal*, *183*(7), E411-E419.

Iaboni, A., Bronskill, S., Reynolds, K. Wang, X., Rochon, P., Herrmann, N., & Flint, A. (2016). Changing pattern of sedative use in older adults: A population-based cohort study. *Drugs & Aging*, *33,* 523-533.

Iden, K., Engedal, K., Hjorleifsson, S., Ruths, S. (2014). Prevalence of depression among recently admitted long-term care patients in Norwegian nursing homes: Associations with diagnostic work up and use of antidepressants. *Dementia and Geriatric Cognitive Disorders*, *37,* 154-162.

Ito, E., Berge, L., Husebo, B., Nouchi, R., & Sandvik, R. (2020). The negative impact of psychotropic drug use on quality of life in nursing home patients at different stages of dementia: Cross-section analyses from the COSMOS trial. *Journal of the American Medical Directors Association*.

Jennings, L., & Grossberg, G. (2013). Antipsychotics continue to have a place in the management of difficult behavior problems in patients with dementia. *Journal of the American Medical Directors Association*, *14*, 443-449.

Jones, C., & Jablonski, R. A. (2014). "I don't want to be a guinea pig": recruiting older African Americans. *Journal of Gerontological Nursing*, *40*(3), 3–4.

Kales, H., Gitlin, L., & Lyketsos, C. (2015). Assessment and management of behavioral and psychological symptoms of dementia. *BMJ: British Medical Journal*, 350, h369.

Kales, H., Gitlin, L., & Lyketsos, C. (2014). Assessment and management of behavioral and psychological symptoms of dementia. *BMJ: British Medical Journal*, *350,* h369.

Karkare, S., Bhattacharjee, S., Kamble, P., & Aparasu, R. (2011). Prevalence and predictors of antidepressant prescribing in nursing home residents in the United States. *The American Journal of Geriatric Pharmacotherapy, 9*(2), 109-119.

Kleijer, B., van Marum, R., Frijters, D., Jansen, P., Ribbe, M., Egberts, A., & Heerdink, E. (2014). Variability between nursing homes in prevalence of antipsychotic use in patients with dementia. *International Psychogeriatrics, 26*(3), 363-371.

Konetzka, R. T., Grabowski, D. C., Coca Perraillon, M., & Werner, R. M. (2015). Nursing Home 5-Star Rating System Exacerbates Disparities In Quality, By Payer Source. *Health Affairs*, *34*(5), 819–827.

Krauter, R. R., & Cook, S. S. (2011). Pharmacogenetics and the pharmacological management of depression. *The Nurse Practitioner*, *36*(10), 14–21.

Kua, C.-H., Mak, V. S. L., & Huey Lee, S. W. (2019). Health Outcomes of Deprescribing Interventions Among Older Residents in Nursing Homes: A Systematic Review

and Meta-analysis. *Journal of the American Medical Directors Association*, *20*(3), 362–372.

Leong, C. (2014). Antidepressants for depression in patients with dementia: a review of the literature. *The Consultant Pharmacist : The Journal of the American Society of Consultant Pharmacists*, *29*(4), 254–263.

Lesser, I. M., Myers, H. F., Lin, K., Bingham Mira, C., Joseph, N. T., Olmos, N. T., Schettino, J., & Poland, R. E. (2010). Ethnic differences in antidepressant response: a prospective multi-site clinical trial. *Depression & Anxiety (1091-4269)*, *27*(1), 56–62.

Lesser, I., Zisook, S., Gaynes, B., Wisniewski, S., Luther, J., Fava, M., Khan, A., McGrath, P., Warden, D., Rush, A., & Trivedi, M. (2011). Effects of race and ethnicity on depression treatment outcomes: The CO-MED trial. *Psychiatric Services*, *62*(10), 1167-1179.

Li, Y., Cai, X., Harrington, C., Hasselberg, M., Consell, Y., Cen, X., & Temkin-Greener, H. (2018). Racial and ethnic differences in the prevalence of depressive symptoms among U.S. nursing home residents. *Journal of Aging & Social Policy, 31*(1), 30-48.

Lim, D., & Jung, J. (2017). Racial-ethnic differences in off-label antidepressant use, by insurance type. *Psychiatric Services*, *68*(12), 1271-1279.

Lornstad, M., Aaroen, M., Bergh, S., Benth, J., & Helvik. A. (2019). Prevalence and persistent use of psychotropic drugs in older adults receiving domiciliary care at baseline. *BMC Geriatrics*, *19*(1), 1-13.

Lotrich, F., Pollock, B., & Ferrell, R. (2003). Serotonin transporter promoter polymorphism in African Americans: allele frequencies and implications for treatment. *American Journal of Pharmacogenomics: Genomic-Related Research in Drug Development and Clinical Practice*, *3*(2),145-147.

Lucas, J., & Bowblis, J. (2017). CMS strategies to reduce antipsychotic drug use in nursing home patients with dementia show some progress. *Health Affairs*, *36*(7), 1299-1308.

Lyketsos, C., Carrillo, M., Ryan, J., Khachaturian, A., Trzepacz, P., Amatniek, J., Cedarbaum, J., Brashear, R., & Miller, D. (2011). Neuropsychiatric symptoms in Alzheimer's disease. *Alzheimer's & Dementia*: *The Journal of the Alzheimer's Association*, *7*(5), 532-539.

Lyketsos, C. G., Sheppard, J. M., Steele, C. D., Kopunek, S., Steinberg, M., Baker, A. S., Brandt, J., & Rabins, P. V. (2000). Randomized, placebo-controlled, double-blind clinical trial of sertraline in the treatment of depression complicating Alzheimer's disease: initial results from the Depression in Alzheimer's Disease study. *The American Journal of Psychiatry, 157*(10), 1686–1689.

Mack, D. S., Jesdale, B. M., Ulbricht, C. M., Forrester, S. N., Michener, P. S., & Lapane, K. L. (2020). Racial Segregation Across U.S. Nursing Homes: A Systematic Review of Measurement and Outcomes. *Gerontologist*, *60*(3), e218–e231.

Mahoney, F., & Barthel, D. (1965). Functional evaluation: The Barthel index. *Maryland State Medical Journal*, *14*(2), 61-65.

Maina, I., Belton, T., Ginzberg, S., Singh, A., & Johnson, T. (2018). A decade of studying implicit racial/ethnic bias in healthcare providers using the implicit association test. *Social Science & Medicine, 199*, 219-229.

Marci, J., Iaboni, A., Kirkham, J., Maxwell, c., Gill, S., Vasudev, A., Whitehead, M., & Seitz, D. (2017). Association between antidepressants and fall-related injuries among long-term care residents. *American Journal of Geriatric Psychiatry*, *25*(12), 1326-1336.

Masopust, J., Protopopova, D., Valis, M., Pavelek, Z., & Klimova, B. (2018). Treatment of behavioral and psychological symptoms of dementias with psychopharmaceuticals: a review. *Neuropsychiatric Disease and Treatment, 14,* 1211-1220.

Maust, D., Kim, M., Chiang, C., & Kales, H. (2018). Association of the Centers for Medicare & Medicaid Services' national partnership to improve dementia care with the use of antipsychotic and other psychotropics in long-term care in the United States from 2009 to 2014. *Journal of the American Medical Association: Internal Medicine*, *178*(5), 640-647.

Maust, D., Blow, F., Wiechers, I., Kales, H., & Marcus, S. (2017). National trends in antidepressant, benzodiazepine, and other sedative-hypnotic treatment of older adults in psychiatric and primary care. *Journal of Clinical Psychiatry*, *78,* e363-e371.

Maust, D., Sirey, J., & Kales, H. (2017). Antidepressant prescribing in primary care to older adults without major depression. *Psychiatric Services, 68*(5), 449-455.

McMahon, F. J., Buervenich, S., Charney, D., Lipsky, R., Rush, A. J., Wilson, A. F., Sorant, A. J. M., Papanicolaou, G. J., Laje, G., Fava, M., Trivedi, M. H., Wisniewski, S. R., & Manji, H. (2006). Variation in the Gene Encoding the Serotonin 2A Receptor Is Associated with Outcome of Antidepressant Treatment. *The American Journal of Human Genetics*, *78*(5), 804–814.

McMaster, M., Fielding, E., Lim, D., Moyle, W., & Beattie, E. (2018). A cross-sectional examination of the prevalence of psychotropic medications for people living with dementia in Australian long-term care facilities: Issues of concern. *International Psychogeriatrics*, *30,* 7, 1019-1026.

Medicare. (2019). *Nursing Home Compare Glossary*. Retrieved from: https://www.medicare.gov/NursingHomeCompare/Resources/Glossary.html#:~:text=Nursing%20home%20is%20a%20term,nursing%20facilities%20and%20nursing%20facilities.&text=This%20nursing%20home%20participates%20in%20the%20Medicare%20program%20and%20can,Generally%20Medicare%20covers%20short%20stays.

Midlov, P., Andersson, M., Ostgren, C., & Molstad, S. (2014). Depression and use of antidepressants in Swedish nursing homes: a 12-month follow-up study. *International Psychogeriatrics*, *26*(4), 669-675.

Miller, S. C., Papandonatos, G., Fennell, M., & Mor, V. (2006). Facility and county effects on racial differences in nursing home quality indicators. *Social Science & Medicine*, *63*(12), 3046–3059.

Mojtabai, R., & Olfson, M. (2014). National trends in long-term use of antidepressant medications: results from the U.S. National Health and Nutrition Examination Survey. *Journal of Clinical Psychiatry, 75,* 169-177.

Mueller, C., Huntley, J., Stubbs, B., Sommerlad, A., Carvalho, A. F., Perera, G., Stewart, R., & Veronese, N. (2017). Associations of Neuropsychiatric Symptoms and Antidepressant Prescription with Survival in Alzheimer's Disease. *Journal of the American Medical Directors Association*, *18*(12), 1076–1081.Murphy, E., Hou, L., Maher, B. S., Woldehawariat, G., Kassem, L., Akula, N., Laje, G., & McMahon, F. J. (2013). Race, genetic ancestry and response to antidepressant treatment for major depression. *Neuropsychopharmacology*, *38*(13), 2598–2606.

Nagata, T., Nakajima, S., Shinagawa, S., Plitman, E., Graff-Guerrero, A., Mimura, M, et al. (2017). Psychosocial or clinico-demographic factors related to neuropsychiatric symptoms in patients with Alzheimer's disease needing interventional treatment: analysis of the CATIE-AD study. *International Journal of Geriatric Psychiatry, 32,* 1264-1271.

O'Connell, C., Goldstein-Piekarski, A., Nemeroff, C., Schatzberg, A., Debattista, C., Carrillo-Roa, T., Binder, E., Dunlop, B., Craighead, W., Mayberg, H., & Williams, L. (2018). Antidepressant Outcomes Predicted by Genetic Variation in Corticotropin-Releasing Hormone Binding Protein. *American Journal of Psychiatry*, *175*(3), 251–261.

Olin, J. T., Katz, I. R., Meyers, B. S., Schneider, L. S., & Lebowitz, B. D. (2002). Provisional Diagnostic Criteria for Depression of Alzheimer Disease: Rationale and Background. *The American Journal of Geriatric Psychiatry*, *10*(2), 129–141.

Olivieri-Mui, B., Devlin, J., Ochoa, A., Schenck, D. & Briesacher, B. (2018). Perception vs. evidence: therapeutic substitutes for antipsychotics in patients with dementia in long-term care. *Aging & Mental Health*, *22*(4), 544-549.

Orgeta, V., Tabet, N., Nilforooshan, R., & Howard, R. (2017). Efficacy of antidepressants for depression in Alzheimer's Disease: Systematic review and meta-analysis. *Journal of Alzheimer's disease, 58,* 725-733.

O'Sullivan, S., & Schmitz, T. (2007). Physical Rehabilitation, Fifth edition. F.A. Davis Company, Philadelphia, PA, 385.

Ozaki, T., Katsumata, Y., & Arai, A. (2019). Association between changes in the use of psychotropic drugs and behavioural and psychological symptoms of dementia over 1 year among long-term care facility residents. *Psychogeriatrics*, *19(*2), 126-134.

Parker, L., & Satkoske, V. (2012). Ethical dimensions of disparities in depression research and treatment in the pharmacogenomic era. *Journal of Law, Medicine, & Ethics, 40*(4), 886-903.

Peter Lamy Center on Drug Therapy and Aging. (2020). *Optimizing medication management during the COVID-19 pandemic: Implementation guide for post-acute and long-term care.* Retrieved from: https://www.pharmacy.umaryland.edu/media/SOP/wwwpharmacyumarylandedu/centers/lamy/covid19-med-mgmt/complete-implementation-guide_042420.pdf

Pickett, Y., Bazelais, K., Greenberg, R., & Bruce, M. (2014). Racial and ethnic variation in home healthcare nurse depression assessment of older minority patients. *International Journal of Geriatric Psychiatry, 29*, 1140-1144.

Porsteinsson, A., Drye, L., Pollock, B., Devanand, P., Frangakis, C., Ismail, Z., Marano, C., Meinert, C., Mintzer, J., Munro, C., Pelton, G., Rabins, P., Rosenberg, P., Schneider, L., Shade, D., Weintraub, D., Yesavage, J., & Lyketsos, C. (2014). Effect of citalopram on agitation in Alzheimer disease: The CitAD randomized clinical trial. *JAMA: Journal of the American Medical Association*, *311*(7), 682-691.

Rahman, Momotazur, and Andrew D. Foster. 2015. "Racial Segregation and Quality of Care Disparity in US Nursing Homes." *Journal of Health Economics* 39 (January): 1–16.

Resnick, B., Kolanowski, A., van Haitsma, K., Galik, E., Boltz, M., Ellis, J., Behren, L., Eshraghi, K., & Zhu, S. (2019). Current psychotropic medication use and contributing factors among nursing home residents with cognitive impairment. *Clinical Nursing Research*, 1-21.

Resnick, B., Kolanowski, A., van Haitsma, K., Galik, E., Boltz, M., Ellis, J., Behrens, L., Flanagan, N., Eshragi, K., & Zhu, S. (2017). Testing the evidence integration triangle for implementation of interventions to manage BPSD: Protocol for a pragmatic trial. *Research in Nursing Health, 41*, 228-242.

Resnick, B., Gruber-Baldini, A., Aboff-Petzer, I., Galik, B., Russ, K., & Zimmerman, S., (2007). Reliability and validity of the Evaluation to Sign Consent Measure. *The Gerontologist, 47*, 69-77.

Reus, V., Fochtmann, M, Eyler, A., Hilty, D., Horvitz-Lennon, M., Jibson, M., Lopez, O., Mahoney, J., Pasic, J., Tan, Z., Wils, C., Rhoads, R., & Yager, J. (2016). The American Psychiatric Association Practice Guideline on the use of antipsychotics

to treat agitation or psychosis in patients with dementia. *The American Journal of Psychiatry, 173*(5), 543-546.

Rhee, T., Schommer, J., Capistrant, B., Hadsall, R., & Uden, D. (2018). Potentially inappropriate antidepressant prescriptions among older adults in office-based outpatients settings: National trends from 2002 to 2012. *Administration and Policy in Mental Health*, *45*(2), 224-235.

Røen, I., Kirkevold, Ø., Testad, I., Selbæk, G., Engedal, K., & Bergh, S. (2018). Person-centered care in Norwegian nursing homes and its relation to organizational factors and staff characteristics: A cross-sectional survey. *International Psychogeriatrics*, *30*(9), 1279–1290.

Roitto, H.-M., Kautiainen, H., Aalto, U. L., Öhman, H., Laurila, J., & Pitkälä, K. H. (2019). Fourteen-year trends in the use of psychotropic medications, opioids, and other sedatives among institutionalized older people in Helsinki, Finland. *Journal of the American Medical Directors Association*, *20*(3), 305–311.

Rosenberg, P., Drye, L., Martin, B., Frangakis, C., Mintzer, J., Weintraub, D., Prosteinsson, A., Schneider, L., Rabins, P., Munro, C., Meinert, C., & Lyketsos, C. (2010). Sertraline for the treatment of depression in Alzheimer's disease. *American Journal of Geriatric Psychiatry*, *18*(2), 136-144.

Rubino, A., Sanon, M., Ganz, M., Simpson, A., Fenton, M., Verma, S., Hartry, A., Baker, R., Duffy, R., Gwin, K., & Fillit, H. (2020). Association of the US Food and Drug Administration Antipsychotic Drug Boxed Warning with Medication Use and Health Outcomes in Elderly Patients with Dementia. *JAMA Network Open*, *3*(4), e203630.

Ruhé, H. G., Ooteman, W., Booij, J., Michel, M. C., Moeton, M., Baas, F., & Schene, A. H. (2009). Serotonin transporter gene promoter polymorphisms modify the association between paroxetine serotonin transporter occupancy and clinical response in major depressive disorder. *Pharmacogenetics and Genomics*, *19*(1), 67–76.

Ruths, S., Sorensen, P., Kirkevold, O., Husebo, B., Kruger, K., Halvorsen, K., & Selbaek, G. (2013). Trends in psychotropic drug prescribing in Norwegian nursing homes from 1997 to 2009: a comparison of six cohorts. *International Journal of Geriatric Psychiatry*, *28*(8), 868-876.

Sainsbury, A., Seebass, G., Bansal, A., & Young, B. (2006). Reliability of the Barthel index when used with older people, *Age Ageing, 34*, 228-232.

Sallis, J. F., Cervero, R. B., Ascher, W., Henderson, K. A., Kraft, M. K., & Kerr, J. (2006). An ecological approach to creating active living communities. *Annual Review of Public Health*, *27*, 297–322.

Schwertner, E., Secnik, J., Garcia-Ptacek, S., Johansson, B., Nagga, K., Eriksdotter, M., Winblad, B., & Religa, D. (2019). Antipsychotic treatment associated with increased mortality risk in patients with dementia. A registry-based observational cohort study. *Journal of the American Medical Directors Association*, *20*(3), 323–329.

Scott, I. A., Hilmer, S. N., Reeve, E., Potter, K., Le Couteur, D., Rigby, D., Gnjidic, D., Del Mar, C. B., Roughead, E. E., Page, A., Jansen, J., & Martin, J. H. (2015). Reducing inappropriate polypharmacy: the process of deprescribing. *JAMA Internal Medicine*, *175*(5), 827–834.

Seitz, D., Adunuri, N., Gill, S., Gruneir, A., Herrmann, N., & Rohon, P. (2011). Antidepressants for agitation and psychosis in dementia. *Cochrane Database of Systematic Reviews*, 2, CD008191.

Sengupta, M., Decker, S. L., Harris-Kojetin, L., & Jones, A. (2012). Racial differences in dementia care among nursing home residents. *Journal of Aging and Health*, *24*(4), 711–731.

Sepehry, A. A., Lee, P. E., Hsiung, G.-Y. R., Beattie, B. L., Feldman, H. H., & Jacova, C. (2017). The 2002 NIMH provisional diagnostic criteria for depression of Alzheimer's disease (PDC-dAD): Gauging their validity over a decade later. *Journal of Alzheimer's Disease*, *58*(2), 449–462.

Shah, S., Schoenbachler, B., Streim, J., & Meeks, S. (2012). Antidepressant prescribing patterns in the nursing home: second-generation issues revisited. *Journal of the American Medical Directors Association*, *13*(4), 406e13-406e18.

Simoni-Wastila, L., Wei, Y., Luong, M., Franey, C., Huang, T., Rattinger., G…(2014). Quality of psychopharmacological medication use in nursing home residents. *Research in Social & Administrative Pharmacy*, *10*(3), 494-507.

Simonson, W. (2019). Should mirtazapine be used to improve appetite and reverse weight loss? *Geriatric Nursing (New York, N.Y.)*, *40*(5), 531–532.

Smeets, C., Gerritsen, D., Zuidema, S., Teerenstra, S., van der Spek, K., Smalbrugge, M., & Koopmans, R. (2018). Psychotropic drug prescription for nursing home residents with dementia: prevalence and associations with non-resident-related factors. *Aging & Mental Health*, *22(*9), 1244-1252.

Smeets, C. H. W., Smalbrugge, M., Zuidema, S. U., Derksen, E., de Vries, E., van der Spek, K., Koopmans, R. T. C. M., & Gerritsen, D. L. (2014). Factors related to psychotropic drug prescription for neuropsychiatric symptoms in nursing home residents with dementia. *Journal of the American Medical Directors Association*, *15*(11), 835–840.

Sobieraj, D., Martinez, B., Hernanadez, A., Coleman, C., Ross, J., Berg, K., Steffens, D., & Baker, W. (2019). Adverse effects of pharmacologic treatments of major depression in older adults. *Journal of the American Geriatrics Society, 67*(8), 1571-1581.

Spetz, J., Trupin, L., Bates, T., & Coffman, J. M. (2015). WORKFORCE. Future Demand for Long-Term Care Workers Will Be Influenced by Demographic and Utilization Changes. *Health Affairs*, *34*(6), 936–945.

Steenland, K., Goldstein, F., Levey A., & Wharton, W. (2015). A meta-analysis of Alzheimer's disease incidence and prevalence comparing African Americans and Caucasians. *Journal of Alzheimer's Disease*, *50,* 71-6.

Steinberg, M., Munro, C., Samus, Q., Rabin, P., Brandt, J., & Lyketsos. (2004). Patient predictors of response to treatment of depression in Alzheimer's disease: the DIADs study. *International Journal of Geriatric Psychiatry*, *19,* 144-150.

Sterke, C., Ziere, G., Beeck, E., Looman, C., & Cammen, T. (2012). Dose-response relationship between SSRI and injurious falls: a study in nursing home residents with dementia. *British Journal of Clinical Pharmacology*, *73*(5), 812-820.

Strothers, H., Rust, G., Minor, P., Fresh, E., Druss, B. & Satcher, D. (2005). Disparities in antidepressant treatment in Medicaid elderly diagnosed with depression. *Journal of the American Medical Directors Association*, *53,* 456-461.

Thiruchelvam, K., Hasan, S., Wong, P., & Kairuz, T. (2017). Residential aged care medication review to improve the quality of medication use: A systematic review. *Journal of the American Medical Directors Association*, *18*(87), 87.e1-87.e14.

Vasudev, A., Shariff, S., Liu, K., Burhan, A., Herrmann, N., Leonard, S., & Mamdani, M (2015). Trends in psychotropic dispensing among older adults with dementia living in long-term care facilities: 2004-2013. *American Journal of Geriatric Psychiatry, 23*(12), 1259-1269.

Vinson, L., Crowther, M., Austin, A., & Guin, S. (2014). African Americans, mental health, and aging. *Clinical Gerontologist*, *37*, 4-17.

Viscogliosi, G., Chiriac, I., & Ettorre, E. (2017). Efficacy and safety of citalopram compared to atypical antipsychotics on agitation in nursing home residents with Alzheimer Dementia. *Journal of the American Medical Directors Association*, *18,* 799-802.

Watt, J., Gomes, T., Bronskill,, S., Huang, A., Austin, P., Ho, J., & Straus, S. (2018). Comparative risk of harm associated with trazodone or atypical antipsychotic use in older adults with dementia: A retrospective cohort study. *CMAJ: Canadian Medical Association Journal*, *190*(47), E1376-E1383.

Wei, Y., Simoni-Wastila, Zuckerman, I., Huang, T., Brandt, N., Moyo, P., & Lucas, J. (2014). Quality of psychopharmacological medication prescribing and mortality

in Medicare beneficiaries in nursing homes. *Journal of the American Geriatric Society, 62,* 1490-1504.

Wei, Y., Simoni-Wastila, L., Lucas, J., & Brandt, N. (2016). Fall and fracture risk in nursing home residents with moderate-to-severe behavioral symptoms of Alzheimer's disease and related dementia initiating antidepressants or antipsychotics. *Journals of Gerontology: Medical Sciences*, *72*(5), 695-702.

Westbury, J., Gee, P., Ling, T., Kitsos, A., & Peterson, G. (2019). More action needed: Psychotropic prescribing in Australian residential aged care. *Australian & New Zealand Journal of Psychiatry, 53*(2), 136-147.

Young, S., Taylor, M., & Lawrie, S. (2015). "First do no harm." A systematic review of the prevalence and management of antipsychotic adverse effects. *Journal of Psychopharmacology*, *29*(4): 353-262.

Zuckerman, I., Ryder, P., Simoni-Wastila, L., Shaffer, T., Sato, M., Zhao, L., & Stuart, B. (2008). Racial and ethnic disparities in the treatment of dementia among Medicare beneficiaries. *Journal of Gerontology: Social Sciences*, *63B*(5), S328-S333.

Zuidema, S. U., de Jonghe, J. F. M., Verhey, F. R. J., & Koopmans, R. T. C. M. (2011). Psychotropic drug prescription in nursing home patients with dementia: influence of environmental correlates and staff distress on physicians' prescription behavior. *International Psychogeriatrics*, *23*(10), 1632–1639.

Zuidersma, M., Chua, K., Hellier, J., Voshaar, R., & Banerjee, S. (2019). Sertraline and Mirtazapine versus placebo in subgroups of depression in dementia: Findings from the HTA-SADD randomized controlled trial. *American Journal of Geriatric Psychiatry*, *27*(9), 920-931.