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Factors and Outcomes Associated With Potentially Inappropriate Medication Use in Rural Community-Dwelling Older Adults

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FACTORS AND OUTCOMES ASSOCIATED WITH POTENTIALLY INAPPROPRIATE

MEDICATION USE IN RURAL COMMUNITY-DWELLING OLDER ADULTS

By

Marcia Y Shade

A DISSERTATION

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For the Degree of Doctor of Philosophy

College of Nursing

Under the Supervision of Dr. Ann Berger

University of Nebraska Medical Center

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FACTORS AND OUTCOMES ASSOCIATED WITH POTENTIALLY INAPPROPRIATE MEDICATION USE IN RURAL COMMUNITY-DWELLING OLDER ADULTS

Marcia Y Shade, PhD (c), MSN, BS, RN

University of Nebraska, 2016

Advisor: Ann M. Berger, PhD

Potentially inappropriate medications (PIMs) use in older adults is a significant public health concern. The use of PIMs to avoid may lead to negative outcomes such as adverse drug events. Prior conceptual analysis of PIMs use and observation of health-related factors in rural adults led to the design of this dissertation study. A sample was recruited from a population of rural community-dwelling older adults to examine the following specific aims: 1) Describe the use of PIMs to avoid, 2) Explore individual demographic characteristics (age, gender, income, education, and rural home location), health experience (comorbidity, number of medications and health providers), and health status factors (physical and mental function, sleep disturbance, sleep quality, and 24 hours sleep-wake patterns) as predictors of use of PIMs to avoid, 3) Examine individual demographic characteristics, health experience, health status, and the use of PIMs to avoid as predictors of patient-reported adverse drug events (ADEs). One-on-one reviews of all prescribed and over-the-counter medications (OTC), vitamins, and supplements were performed on participants (N=138). The 2012 Beers Criteria were used to identify and record PIMs to avoid. Data were collected on: participant's demographics, subjective physical and mental health and sleep; objective sleep-wake patterns, and patient-reported ADEs. Almost half (49%) of the sample of rural community-dwelling older adults used both prescribed and OTC PIMs to avoid. The most frequently used PIMs to avoid taken by participants were prescribed and OTC non-steroidal anti-inflammatory drugs (33%), prescribed and OTC anticholinergic medications (28%), and

prescribed short-acting benzodiazepines (18%). The use of PIMs to avoid was associated with higher number of medications taken and medical providers (both $p<0.001$), and poor physical health ($p<0.05$). Higher number of medications was a significant predictor of an increased use of PIMs to avoid OR 1.8, 95% CI [1.19, 2.84]. One or more ADE was reported by 48% of participants; the most frequent being central nervous system (CNS) disturbances (16%), dry mouth (12%), hoarseness, gastrointestinal irritation, and decreased libido (8%). Higher patient-reported ADEs were associated with poor sleep and poor physical health ($p<0.05$). Younger age (65 to 78), poor physical health, and poor sleep quality were significant predictors of an increased probability of patient-reported ADEs ($p<0.05$). Implications for research include examining factors and outcomes associated with PIMs use in larger samples that compare both urban and rural primary care settings.

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CHAPTER I: INTRODUCTION

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BACKGROUND AND SIGNIFICANCE

An estimated 42% of community-dwelling older adults in the United States (U.S.) take medications that are potentially inappropriate (Davidoff et al., 2015). Potentially inappropriate medications (PIMs) are pharmaceutical products that have been determined to have risks that outweigh benefits according to the American Geriatrics Society Beers Criteria Expert Panel, (Radcliff et al., 2015). Prevalence estimates of the international use of PIMs in community-dwelling older adults are dependent on how they are measured, and reported to range anywhere from 22% to 56% (Moriarty, Bennett, Fahey, Kenny, & Cahir, 2015). PIMs use has vast implications for health safety and quality in older adults. Changes can occur in several body mechanisms that may increase the chances of harmful events as adults age. Polypharmacy, or the use of 5 or more medications, increases the risk of taking PIMs (Maher, Hanlon, & Hajjar, 2014). Older adults often have multiple chronic conditions and take numerous medications. An estimated 38% of older adults in the U.S. used at least 5 or more prescription drugs between 2007 and 2008 (Gu, Dillon, & Burt, 2010). Although the proper use of polypharmacy may be appropriate for maintaining stability of chronic conditions, health status, and symptom management, polypharmacy may lead to increased risk of drug-drug and disease-drug interactions (Cadogan, Ryan, & Hughes, 2015).

Many drug-related interactions may lead to an adverse drug event (ADE). An ADE is defined as an injury resulting from a drug medical intervention. An ADE can be a medical error, an adverse drug reaction, allergic reaction, and/or an overdose (Kohn, Corrigan, & Donaldson, 2000). The occurrence of ADEs is a persistent problem and has gained national attention. National data revealed that ADEs precipitated millions of physician office and emergency visits (Bourgeois, Shannon, Valim, & Mandl, 2010;

Budnitz, 2011) both studies confirm previous analyses by Gurwitz and colleagues who reported 27% of ADEs occurred among patients 65 and older (Gurwitz et al., 2003). Ensuring that older adults avoid inappropriate medications has implications for aging in place, maintaining health and preventing negative health outcomes, ADEs, and increased health costs (Dionne, Vasiliadis, Latimer, Berbiche, & Preville, 2013; Vasunilashorn, Steinman, Liebig, & Pynoos, 2012).

Health professionals need to understand predictors of older adults PIMs use in urban and rural community-dwelling settings. Rural-dwelling older adults have higher rates of chronic illness, poorer overall health, and less access to care than in urban areas (National Conference of State Legislatures, 2013; National Rural Health Association, 2014). Nearly 90% of adults over age 65 want to remain in their home for as long as possible (Keenan, 2010). A goal of Healthy People 2020 is to improve the health, home function, and quality of life (QOL) of older adults and baby boomers who have high expectations for QOL and maintaining cognitive, physical, and social functioning (Potkanowicz, Hartman-Stein, & Biermann, 2009). The prevention and appropriate management of chronic diseases may help older adults in both urban and rural settings remain independent.

<p align="center">**Concepts**</p>

A concept is an abstract phenomenon made up of one or two words that bear meaning, and are often placed into a theory and measured (Walker & Avant, 2011). The following paragraphs will provide explanation of the major concepts explored in this dissertation study; first with the major concept of PIMs use, followed by concepts that may predict PIMs use. These concepts were placed in a derivation of a nursing model to guide the dissertation study.

Potentially Inappropriate Medication Use

Chapter II provides an integrative review of PIMs use in community-dwelling older adults. The use of PIMs could lead to negative outcomes such as ADEs, increased hospitalizations, and health costs; all of which may impact the independence of an older adult (Finkle et al., 2011). The Beers Criteria was initially developed in the early 1990s for nursing home residents as a resource for health professionals, these criteria categorize high-risk medications in older adults based on their pharmacologic properties and the physiologic changes that occur in the older adult (American Geriatrics Society 2012 Beers Criteria Update Expert Panel, 2012). The updated Beers Criteria includes 13 drug combinations to avoid, a list of medications to avoid in older adults with poor renal function, three new medications and two medication classes to avoid in specific chronic diseases, and lastly several medications were removed or modified (Radcliff et al., 2015). Polypharmacy and PIMs use are under-recognized in their association with hospital readmissions (Finkle et al., 2011; Sehgal et al., 2013).

As discussed in chapter II, most studies have not examined the conceptual problem of PIMs use and only observe medication lists or prescribed medications. The independent community-dwelling adult can obtain PIMs over the counter (OTC) and without a prescription (Shade, Berger, & Chaperon, 2014). Older adults are independent individuals and this factor is often neglected in studies of PIMs use in the community setting. Adults may seek OTC drugs due to increased prescription costs, limited access to healthcare, suggestions from family and friends, and increased direct marketing to the public (Basu, Dodge, Stoehr, & Ganguli, 2003; Chui, Stone, Martin, Croes, & Thorpe, 2014). These factors differ from the institutionalized or hospitalized older adult whose medication regimens are routinely controlled and supervised.

Anticoagulants, antidiabetic, cardiovascular, analgesic, and central nervous system (CNS) agents have been reported as the most common drug classifications that

lead to ADEs (Salvi et al., 2012). The use of PIMs with anticholinergic effects may influence the CNS leading to altered balance and cognition (Koyama, Steinman, Ensrud, Hillier, & Yaffe, 2014). Community-dwelling older adults can acquire medications with CNS and or anticholinergic effects independently.

Rural Community-Dwelling Older Adults

Rurality is a complex concept and may be measured in terms of demographics and socioeconomics. According to the Census Bureau, urban-rural classification is fundamentally a delineation of geographical areas, identifying both individual urban and rural areas in the nation. The Census Bureau has a strict definition of what is considered urban. An urbanized area includes 50,000 or more people or an urban cluster of at least 2,500 and less than 50,000 people. Rural areas include populations, housing, and land not included within an urban area (U.S. Census Bureau, 2015).

About 13% of U.S. older adults live in rural areas (National Rural Health Association, 2014). Aging Americans that live in rural communities and are affected by health disparities, have issues with managing prescription costs, and poor coordination of services (Averill, 2012). Lower income and education have been associated with PIMs use in rural dwelling older adults (Blalock et al., 2005; Fu, Liu, & Christensen, 2004). A high proportion of older adults in rural communities are poor and have difficulty with access to health care; such as transportation and the ability to pay for services (National Conference of State Legislatures, 2013). As discussed in chapter III, obesity is common among adults living in rural areas, often leading to comorbid conditions (Befort, Nazir, & Perri, 2012). Less access and more out-of-pocket health costs may lead to poorer self-care behavior choices. Other self-care behaviors may include the use of over-the-counter medications, home remedies, contemporary supplements, and complementary

practices to manage chronic conditions (Basu et al., 2003; Eisenhauer, Hunter, & Pullen, 2010).

In rural settings, fragmented and limited access to health care may lead to inadequate management of chronic diseases. Nurses in rural settings are in a unique position to ensure continuity of patient care. Nearly 24% of Licensed Practical Nurses (LPNs), 16% of Registered Nurses (RNs), and 1% of Nurse Practitioners live in rural areas and can form partnerships with patients to improve medication use and safety (Health Resources and Services Administration Bureau of Health Professions, 2013). The nurse has the ability and professional responsibility to assess the use of all medications, the use of PIMs, and to monitor for patient-reported ADEs (Boltz, 2012). Person-centered approaches that focus on appropriateness of medications may impact PIMs use and health outcomes.

Health Status (Self-reported)

Health status is multi-dimensional and goes beyond objective measures of health. Health status includes physical health and behavior in addition to mental, emotional, and social functioning. Health status may have an important influence on the health decisions made by older adults.

Health Status. A patient's perceived physical and mental health are components of health related QOL; often measured as outcomes. Health related QOL is a concept that includes measures of patient-reported physical and mental health (CDC, 2013). A study by Fu and colleagues (2004) reported that U.S. older adults who used inappropriate prescription medications were more likely to report poorer health status as an outcome than those not using inappropriate prescription medications. In addition, the use of PIMs was common in a sample of community-dwelling older adults in New Zealand with perceived depressive symptoms (Lee et al., 2013). Common medications

classes to improve depressive symptoms such as serotonin–norepinephrine reuptake inhibitors, selective serotonin reuptake inhibitors, and tricyclic antidepressants are listed on the 2012 Beers Criteria (American Geriatrics Society 2012 Beers Criteria Update Expert Panel, 2012). Studies have not examined perceived physical and mental components of health status as predictors of PIMs use in rural community-dwelling older adults. Although they may be unaware of the risks, individuals with a poor perception of physical, emotional, or mental health may seek medications from health providers, the local pharmacy, or online websites to manage symptoms.

Sleep Quality and Sleep Disturbance. Sleep behavior is an important function of the human body. Sleep quality and sleep-wake disturbances are at times overlooked in association with health status in older adult populations. As seen in chapter III, there are significant relationships between poor self-reported sleep and high pain in obese mid-life and older rural women. These symptoms may not only impact health and chronic disease, but stimulate medication use. Some individuals seek sedative-hypnotics from primary care providers and others self-medicate with alcohol or over-the-counter sleep aids, with or without the knowledge of a health care provider (Basu et al., 2003). Sleep problems have been associated with the use of medications that promote sedation (Ancoli-Israel, Ayalon, & Salzman, 2008; Ancoli-Israel, 2009; Kryger, Monjan, Bliwise, & Ancoli-Israel, 2004). Medications with sedative properties have risks that outweigh patient benefits and are inappropriate for chronic use in the older adult (American Geriatrics Society 2012 Beers Criteria Update Expert Panel, 2012).

Adverse Drug Events

Adults 65 years or older are twice as likely as others to come to emergency departments for adverse drug events and nearly seven times more likely to be hospitalized after an emergency visit (CDC, 2012). Although Budnitz et al. (2007) did not

find an association between the 2003 Beers Criteria and ADE-related emergency department visits, ADEs are still a substantial problem. In older adults, a 13% increase in the odds of an ADE (OR 1.13) was associated with an increase in the prescribing of inappropriate medications (Lund, Carnahan, Egge, Chrischilles, & Kaboli, 2010). Community-dwelling older adults have reported falls when taking PIMs on a regular and occasional basis and PIMs use has been associated with lower physical function, geriatric syndromes, and reductions in cognitive status (Beer et al., 2011; Berdot et al., 2009).

Several medication categories (i.e. cardiovascular, non-opioid analgesics, hypoglycemic, and anticoagulants were associated with preventable ADEs in a sample of U.S. community-dwelling older adults (Gurwitz et al., 2003). U.S. older adults who had multiple comorbidities and took medications such as nonopioid analgesics and diuretics were at increased risk for ADEs in the ambulatory setting (Field et al., 2004). Other medications such as anticoagulants, opioids, and diabetic drugs have been targeted as part of an ADE Action Plan for the prevention of ADEs (Ducoffe et al., 2015). Although the prevalence of PIMs use in the community-dwelling older adult is evident, more studies are needed to address rural areas. In rural communities aging adults account for a larger share of the population and are becoming ethnically and culturally diverse (Rural Health Information Hub, 2016).

Studies of ADEs in community-dwelling older adults need to examine the patient-report of ADEs in addition to medical records. A patient-reported symptom such as dizziness could be an ADE that goes undetected and is managed by the use of over-the-counter medications or other self-care behaviors. More studies need to examine the relationship between PIMs use with the Beers Criteria; and patient-reported ADEs in

rural community-dwelling older adults in order to develop interventions to promote safe and quality health care.

Theoretical Foundations

This dissertation study will be the first to prospectively examine PIMs use and ADEs using a nursing theoretical model. As shown in Figure 1. Cox's Interaction Model of Client Health Behavior (IMCHB) is a middle range nursing theory developed in the early 1980s (Cox, 1982). The model represents the dynamic interactions that occur between the background and internal subconstructs of client singularity with elements of client professional interaction and health outcomes. The IMCHB has been adapted for this dissertation to include concepts that examine the relationships between the client singularity variables and health outcomes.

In the original model, client singularity was comprised of the background variables of demographic characteristics, social influence, health experience, and environmental resources. The internal variables included intrinsic motivation, cognitive appraisal, and affective response. Health outcome was comprised of five factors: utilization of health care services, health status indicators, severity of health care problem, adherence to treatment, and care satisfaction (Cox, 1982).

The IMCHB has been used to effectively examine medication decision-making in individuals with psychiatric illness (Mahone, 2004). The model has been previously used to examine functional outcomes and health behaviors such as exercise and adherence specifically in samples of older adults (Cox, 1986; Douglas, 2012; Fields, 2002; Lee & Laffrey, 2006). Cox's IMCHB remains a popular model to evaluate patient behaviors and is useful for guiding research and developing person-centered interventions to achieve positive health outcomes (Chang et al., 2014). The target age of this study is 65 years

and older due to their increased risk of polypharmacy and PIMs use (Barnett et al., 2011;

Buck et al., 2009; Maher et al., 2014).
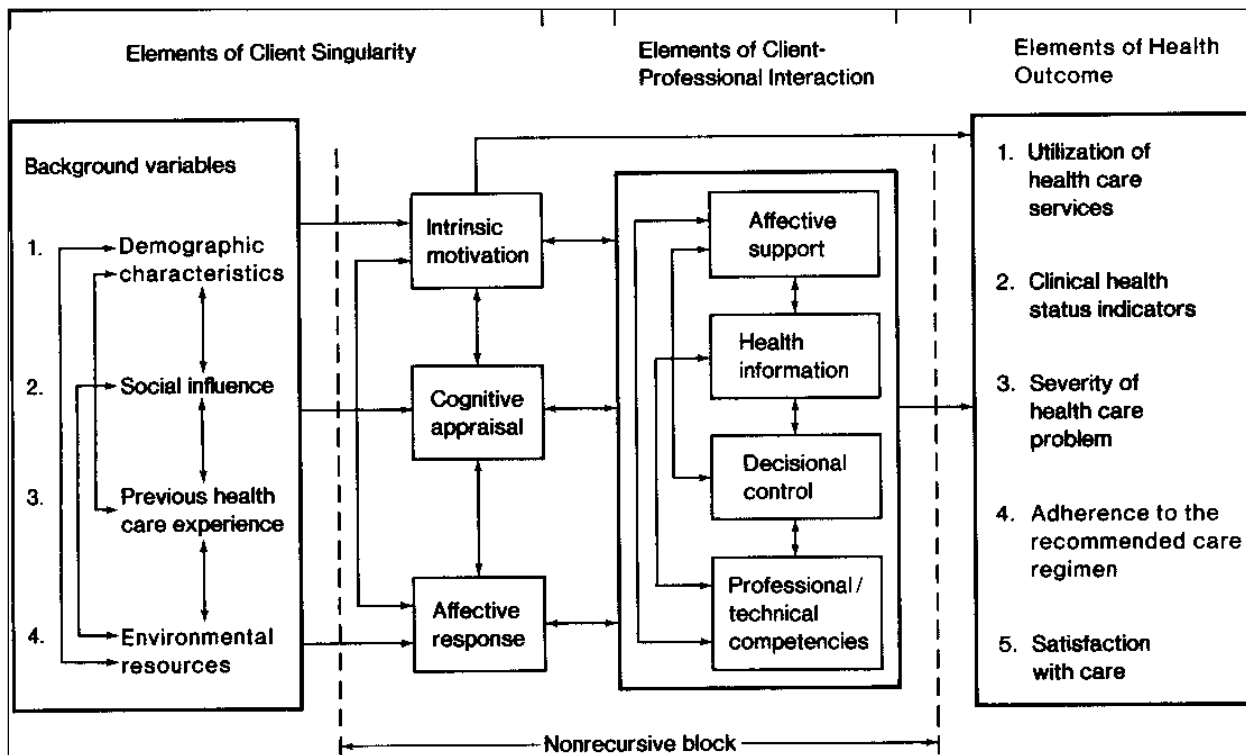
Figure 1. Cox's Interaction Model of Client Health Behavior (IMCHB).

The use of PIMs also has been associated with lower income and education in older adults (Blalock et al., 2005; Fu et al., 2004). Older adults living in rural communities receive care for multiple comorbidities and from general practitioners rather than geriatric specialists, a factor which has been associated with the use of PIMs (Blalock et al., 2005; Buck et al., 2009; Centers for Disease Control, 2013; Dall et al., 2013). The third predictor is health status and includes physical and mental health, sleep quality, sleep disturbance, and sleep-wake patterns. Sleep problems and depressive symptoms are associated with the use of several sedative and antidepressant medications that are listed on the 2012 Beers Criteria (Ancoli-Israel et al., 2008; Ancoli-Israel, 2009; Kryger et al., 2004)

As seen in the model derivation in Figure 2, the client singularity factors include demographics, health experience, and health- status. The use of PIMs and patient-reported ADEs will be explored as outcomes. Based on the findings of this dissertation study, the IMCHB can be used for intervention development.

SUMMARY

The purpose of this dissertation study was to explore the relationships and predictors of PIMs use. We used a derivation of the IMCHB to guide the study. Knowledge of PIMs use in rural community-dwelling older adults needs to be addressed to promote the safety of this population often challenged with health disparities. In general, research on PIMs use has been primarily led by pharmacists and physicians.

This dissertation has been prepared using the three manuscript format as approved by the supervisory committee. Chapter II provides an integrative review for the primary concept the use of potentially inappropriate medications (Shade et al., 2014). Chapter III explores the associations between self-reported sleep and pain, and objective sleep and health related factors in midlife and older rural women. The findings
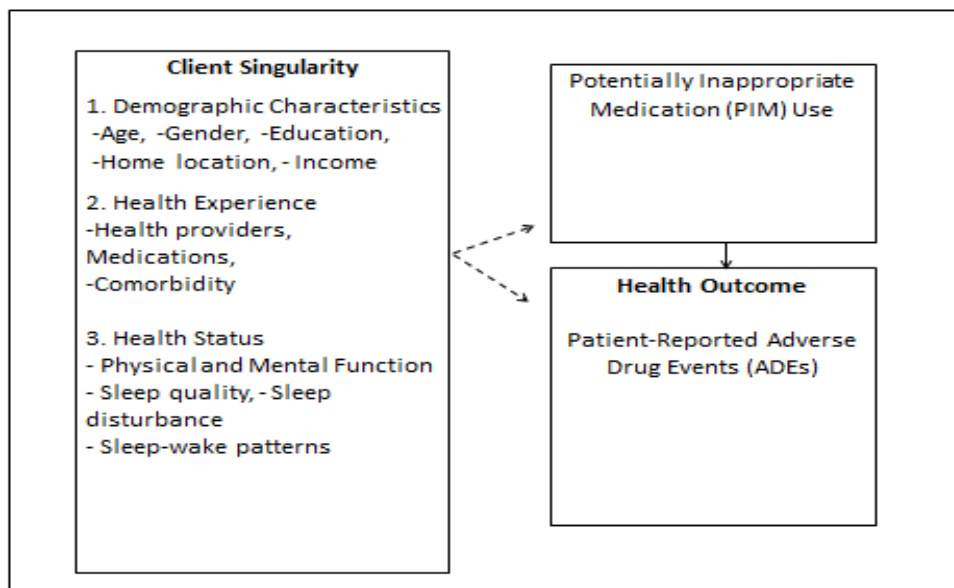
Figure 2. Research Model of Factors Associated with Potentially Inappropriate Medication Use in Community Dwelling Older Adults adapted from Cox's Interaction Model of Client Health Behavior

support significant relationships between poorer sleep and higher pain levels in mid-life and older rural women (Shade, Berger, Dizona, Pozehl, & Pullen, 2015). These factors may be predictors of increased odds of PIMs use and patient-reported ADEs. Chapter IV contains the manuscript of Aims 1 and 2 of the dissertation study and provides details of the methods, results, and discussion. Lastly, chapter V provides a summary and implications for future research and practice. Aim 3 of the dissertation study is included in Appendix A and will be submitted as a separate manuscript for publication.

Purpose and Specific Aims

The purpose of this study is to explore the use of, and the factors associated with, PIMs and patient-reported ADEs in rural community-dwelling older adults ≥ 65 years old. The specific aims were to:

1) Describe PIMs use in rural community-dwelling older adults ≥ 65 years old.

2) Investigate individual demographic characteristics, health experience and health status factors as predictors of PIMs use.

3) Examine demographic characteristics, health experience, health status, and PIMs use as predictors of patient-reported ADEs.

CHAPTER II: Manuscript #1

State of the Science on Potentially Inappropriate Medications in Community-Dwelling

Older Adults

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Abstract

Potentially inappropriate medications (PIMs) are a significant world-wide public health problem. Community-dwelling older adults are susceptible to the possibility of negative outcomes associated with the use of PIMs. A database search produced 19 prospective correlation and 10 intervention studies. The current state of the science reveals that the use of PIMs has been studied without clear analysis of the concept. The prevalence of the use of PIMs is well known from an abundance of descriptive studies. Researchers have not consistently examined their intervention's effects on health outcomes in community-dwelling older adults. Although independent older adults can acquire inappropriate medications outside of a provider; current interventions are aimed at changing the behavior of the prescribing physician and pharmacist. Nurses need to participate in PIMs research and collaborate in interventions to reduce the use of PIMs and examine the effects of interventions health outcomes.

Introduction

Potentially inappropriate medication (PIM) use is a problem related to safety in older adults. The prevalence of PIM use is approximately 50% in the older adult U.S. population, and many adults ≥ 65 years of age take at least one PIM (Beer et al., 2011). Commonly used PIMs are psychotropic drugs such as long-acting benzodiazepines, tricyclic antidepressants, and anticholinergic medications (Albert, Colombi, & Hanlon, 2010; Bao, Shao, Bishop, Schackman, & Bruce, 2012; Bierman et al., 2007; Howard, Dolovich, Kaczorowski, Sellers, & Sellors, 2004; Lau, Mercaldo, Shega, Rademaker, & Weintraub, 2011; Lechevallier-Michel et al., 2005; Lin, Liao, Cheng, Wang, & Hsueh, 2008; Maio, Yuen, Novielli, Smith, & Louis, 2006; Mort & Aparasu, 2000; Rochon et al., 2004; Zhan et al., 2001). These drugs have been documented for being high risk with negative effects and limited effectiveness.

According to the World Health Organization (WHO), an estimated 157 million Americans will be affected by at least one chronic condition requiring medication therapy by the year 2020 (Freudenberg & Olden, 2011). Older adults consume large numbers of medications, accounting for more than one-third of total outpatient spending on prescription medications in the US (National Institute on Drug Abuse, 2011). According to Gu, Dillon, & Burt (2010), 37% of adults age 60 and older use five or more prescription medications. Although the use of multiple medications (polypharmacy) may be necessary to manage chronic conditions long-term drug therapies can pose safety risks in the older adult.

Background

As the adult body ages, changes in pharmacodynamics and pharmacokinetics increase the hazards of medication use. Research has shown that the more medications are prescribed, the risk of PIMs increases (Blozik, Rapold, von Overbeck, & Reich, 2013). At times, side effects are mistaken for new onset illness or other comorbidities

that are treated with additional medications. This is sometimes referred to as the "prescribing cascade" and leads to additional PIMs (Knight & Avorn, 2001). PIMs can alter the central nervous system (CNS) and other mechanisms that increase the older adult's risk for injury and hospitalization (Finkle et al., 2011). Older adults are vulnerable to adverse drug reactions (ADRs) and adverse drug events (ADEs) that relate to poor health outcomes, mortality, and increased health costs (Pretorius, Gataric, Swedlund, & Miller, 2013). The use of PIMs by older adults has been studied in the nursing home and acute hospitalization settings where pharmaceutical management includes medication monitoring. Older adults living independently may seek multiple care providers and pharmacies that increase the risk of acquiring PIMs. Disease-drug and drug-drug interactions, falls, and functional decline are consequences that can lead to reduced independence, and reductions of quality of life (QOL) (American Geriatrics Society, 2012; Berdot et al. 2011).

Providing quality geriatric care and health management involves optimizing medication use. Fick & Semla (2012) emphasized the importance of decreasing problems related to PIM use as an attempt to improve the health of older adults. The World Health Organization (WHO) (2008) calls for awareness and assessment of the risks and benefits of medicines, and the National Institute on Aging has set a goal of disseminating evidence to decrease older adult's disease and disability and improve health and QOL (NIA, 2013).

Health care professionals who are aware of the science surrounding PIMs in the community-setting are prepared to prevent the consequences of their use. The purpose of this state of the science is to appraise the definitions, methods, models, measurements, and results of the literature addressing PIMs in community-dwelling older adults. This appraisal will also identify gaps in the knowledge and recommend directions for future research.

Methods

An electronic database search was conducted in June 2013 using CINAHL, MEDLINE, Biomedical Reference Collection, and PUBMED. The time frame of January 1991 through June 2013 was selected to identify specific articles based on the Beers criteria, which were first published in 1991. A keyword search included, but was not limited to: potentially, inappropriate medications, drugs, and prescriptions, polypharmacy, elderly, older adult, aged adult, community-dwelling, and home-dwelling.

Journal articles were included based on the following characteristics: (a) study sample of adults 65 and older who were community-dwelling and living independently; (b) primary goal was to reduce inappropriate medications; and (c) article was published in the English language. Studies were excluded if they were conducted in a nursing home/skilled facility, or acute hospital inpatient setting. Studies also were excluded that compared settings, examined specific disease states, explicit medications and tested instruments for measuring inappropriate medications, or if the a primary goal was not to reduce inappropriate medications.

Identifying older adults prior to, or in the midst of using PIMs is helpful in decreasing medication-related complications. The age of ≥65 years was chosen to align with societal norms, such as eligibility for Medicare. Community-dwelling older adults possess the independence to obtain medications from local pharmacies or retail establishments. Professional monitoring of medication use is not heavily regulated in these settings compared to environments such as nursing homes and acute care facilities.

Results

The search yielded 352 publications representing retrospective and prospective descriptive designs, intervention studies, and review articles. 285 Duplicates were removed leaving 67 articles for abstract review. 28 articles were limited to the exclusion

criteria. A manual search was performed on the identified articles to obtain additional studies 27 for review. After full-text examination the total of 38 retrospective, 19 prospective and 10 intervention studies were selected. Figure 1 provides a flow chart of the results of the literature search.

Definitions

Experts have yet to come to a consensus on the definition of PIMs. Several terms are used interchangeably with PIMs including: medication misuse, potentially inappropriate prescriptions and potentially inappropriate prescribing; the latter two have been represented by the same abbreviation (PIP). Defining the concept of PIMs is essential in studying the problem. Analysis of the concept of PIMs helps differentiate it from similar concepts. Dissection of each word and identification of attributes and antecedents allow for the conceptual definition to be derived (Walker & Avant, 2011). Conceptually PIMs are substances that may be unsuitable if taken for therapy. Attributes associated with the concept of PIMs in the independent community-dwelling older adult include: physician pharmacy, mis-communication, pharmacodynamics, pharmacotherapeutics, vulnerable, polypharmacy, and multiple chronic conditions. Antecedents of the concept of PIMs include recommending, advising, suggesting, advocating, proposing the use, and seeking of remedies that may be hazardous.

Experts have developed a variety of methods to identify PIMs operationally. The Beers criteria are considered the foundation for PIM use in older adults (≥65 years of age). Medications should be prescribed based on a risk-benefit definition of appropriateness. The risk benefit definition of appropriateness declares a drug as appropriate if its use and potential benefits outweigh the potential risks (Beers, 1997). The definition derived from Beers and his colleagues was chosen for use in this analysis. Studies presented in this analysis include combinations of PIM and PIP literature due to overlapping definitions. PIP also lacks conceptual definition, and has been described as

potentially prescribing medications in high frequency, for long durations, in the presence of multiple medications with interactions, and the underuse of beneficial medications (Gallagher, Barry, & O'Mahony, 2007; Page, Bryant, & Ruscin, 2010). A relationship exists between PIMs and PIP and studies regarding PIP are focused on the prescribing behaviors of the health care provider.

Experts have reported associations between PIMs, ADRs and ADEs. According to (Edwards & Aronson, 2000), the WHO has historically defined an ADE as "Any untoward occurrence that may be present during treatment with a pharmaceutical product, but does not necessarily have a causal relation to the treatment" (p. 1256). An ADR is a type of ADE that is defined as any harmful, unintended and undesired effect of a drug (WHO, 2008). Many reports use the terms interchangeably, do not define these concepts, or simply call them ADEs. Other reports use related but unique terms such as adverse drug effects.

<div align="center">**Models**</div>

The literature exemplifies underpinnings from a post positivist philosophical perspective. Studies were approached from the pharmaceutical models with minimal use of theoretical frameworks. Most models examining PIMS are pharmaceutical or medical in nature and lack conceptual definitions for what is being studied. The Andersen Newman Model is one sociological theoretic framework that has been used to explore PIMs in association with the societal and individual determinants of medical care utilization (Andersen & Newman, 2005). The model has been revised and has versions with the latest (phase 4) model involving the environment, population characteristics, health behavior, and outcomes. Feedback loops represent the circular effect of outcomes on predisposing factors (Andersen, 1995). Two teams have used this model, asserting better understanding of health care utilization and economical and humanistic outcomes resulting from the use of PIMs (Aparasu & Mort, 2004; Blalock et al., 2005).

The Andersen Newman model provides a theoretical approach on studying how PIM use can affect health service use. This model has the ability to predict and explain the use of health services (Andersen & Newman, 2005). The model is appropriate for use in the community dwelling older adult who is independent rather than the hospitalized or institutionalized adult. The model has been revised and has limited presence in current literature. A reason may be due to society's ever-changing health care system and health care needs. Andersen (1995) claims the variables of the model have been criticized as being conservative, and outcome measures being unrefined. The Andersen-Newman model has the ability to predict and explain the use of health services for translational research for community dwelling older adults.

<div align="center">**Measurement**</div>

The literature provides several criteria to operationalize or quantitatively measure the concept of PIMs. However, due to the lack of conceptually agreed definitions, studies have used measurements to quantify PIMs and potentially inappropriate prescribing (PIP) equally. Tools have been developed worldwide and will continue to be revised as older adults and health care change. Most strategies have involved the Delphi method to determine appropriate versus inappropriate medications (Brown, 1968). The following section is a description of the most popular measurements of PIMs in community-dwelling older adults.

Beers Criteria

In the US the Beers criteria were initially developed in 1991 in response to problems with medication use in nursing home residents. The list was revised in 1997, 2003, and 2012 for use in all care settings (American Geriatrics Society 2012 Beers Criteria Update Expert Panel, 2012; Beers et al., 1991; Beers, 1997; Fick et al., 2003) . PIMs are categorized into medications to avoid in older adults regardless of diseases or conditions, and medications that are considered potentially inappropriate when used in

older adults with specific diseases or syndromes. The updated American Geriatrics

Society (AGS) Beers criterion lists fifty-three medications or medication classes that are

divided into three categories. The current criteria can be viewed at

http://www.americangeriatrics.org/files/documents/beers/2012AGSBeersCriteriaCitations

.pdf.

The Health Plan Employer Data and Information Set (HEDIS) criteria were

recently updated (July 3, 2013) according to the 2012 AGS Beers criteria (NCQA, 2013).

The consensus panel of the National Committee on Quality Assurance originally

developed this quality measure to identify rates of inappropriate prescribing in the

elderly. A past criticism of the Beers criteria claimed the list contained medications no

longer commercially available or being used in clinical practice in the US. In the past the

Beers criteria have also been criticized for not including over the counter (OTC)

medications and not providing a list of alternative medications.

Physicians and pharmacists in several countries have used these criteria but

have not had optimal success due to different medication formularies. Fortunately,

countries such as Germany and Norway have developed lists such as the PRISCUS and

NORGEP to address PIMs in older adults based on their country's commonly used

medications (Holt, Schmiedl, & Thurmann, 2010; Rognstad et al., 2009).

Medication Appropriateness Index (MAI)

The MAI was developed in the early 1990s to assess the appropriateness of

medications. The 10 criteria include: indication, effectiveness, dosage, directions,

practicality, drug-drug interactions, drug-disease interactions, unnecessary duplications,

duration, and cost (Hanlon et al., 1992). The MAI has use for determining if medications

are proper to prescribe, but the MAI does not list specific inappropriate medications for

clinical guidance (Kaur, Mitchell, Vitetta, & Roberts, 2009).

Other criteria

The McLeod criteria were developed in Canada in 1997 as an attempt to expand the Beers criteria. Thirty-eight medications were placed into three categories: drugs generally contraindicated for elderly people, drug–disease interactions, and drug–drug interactions (McLeod, Huang, Tamblyn, & Gayton, 1997). The Zhan criteria also were developed in 2001 in response to an awareness of the limitations of the Beers criteria. Thirty-three drugs were placed in three categories: medications that should always be avoided, rarely appropriate, and medications that have some indication but are often misused (Zhan et al., 2001). There has been minimal application of the McLeod and Zhan criteria as a measure of PIMs in the current literature.

The screening tool of older person's potentially inappropriate prescriptions (STOPP) was developed in 2008 by Gallagher and colleagues. STOPP contains commonly occurring PIMs in older people including drug–drug and drug–disease interactions, drugs that negatively affect older patients at risk of falls, and duplicate drug class prescriptions. This tool was intended to be used along with a screening tool to alert doctors to the right treatment (START), also developed by Gallagher (Gallagher et al., 2008). The STOPP criteria are not used as widely as the Beers criteria in the community setting. The effectiveness of the STOPP criteria has been compared with the Beers criteria (Gallagher & O'Mahony, 2008).

 Assessing care of vulnerable elders (ACOVE) was developed by the RAND Corporation (Santa Monica, CA) and Pfizer Corporation (New York, NY) to establish indicators that measure quality of care. A set of quality indicators was released that focuses on pharmacological care provided to community-dwelling vulnerable adults (Shrank, Polinski, & Avorn, 2007). Although promising, there are limited prospective interventions using this tool to study PIMs in community-dwelling older adults.

Literature on PIMS in Community-Dwelling Older Adults

The goal of the state of the science is to synthesize the results of the literature, identify areas of strength and weakness, and designate gaps in the science for future study. The current literature regarding PIMs in community-dwelling older adults consist of reviews relating to PIMs use in all settings, descriptive correlation studies, and prospective intervention studies. To our knowledge, this is the first review of the evidence related to PIMs in independent community dwelling older adults.

Reviews

Most reviews analyzed literature that included all settings in the community, nursing home, and hospital health care settings rather than focusing exclusively on community-dwelling older adults. (Gallagher et al., 2007) focused on the prevalence of inappropriate prescribing in older adults and Kaur and team (2009) provided a synthesis of evidence for interventions for reducing inappropriate prescribing in various settings. (Opondo et al., 2012) published the only review focusing on extent of inappropriate medication "prescriptions" given to older adults in the primary care setting. These reviews examined inappropriate medication use as a function of prescribing behavior, missing the opportunities that independent older adults have to acquire PIMs by means other than a provider's prescription. A Cochrane review analyzed intervention studies to improve the use of appropriate medications in older adults (Patterson, Hughes, Kerse, Cardwell, & Bradley, 2012). The review reported poor methodology, design, and small samples in the studies. A Jano & Aparasu (2007) review examined health outcomes associated with inappropriate medication use as defined by Beers' criteria. The review concluded there is little existing evidence associating the use of PIMs in the community setting with mortality and health care utilization; however an association was noted with PIMs and increased hospitalization.

Descriptive Correlational Studies

   Retrospective Studies

Retrospective cohort study designs are the primary type of literature describing PIMs in community-dwelling older adults. This design uses large databases of past patient information to describe the prevalence, frequency, risk factors, and outcomes of PIMs (Bierman et al., 2007; Buck M. D. et al., 2009; Cannon, Choi, & Zuniga, 2006; Chen et al., 2009; Fialová et al., 2005; Fick, Mion, Beers, & L. Waller, 2008; French et al., 2007; Hanlon, 2002; Klarin, Wimo, & Fastbom, 2005; Lin et al., 2008).

Retrospective analyses have shown inconsistent results between PIM use and health outcomes. Some studies report an association between PIM use and adverse drug events, while others report no relationship (Budnitz, 2011; Chen et al., 2009; Fick et al., 2008; Hanlon, 2002; Lau et al., 2011). Studies varied in results describing the association between the use of PIMs and functional status. One study reported the use of PIMs in association with a decline in basic self-care but another did not report an association (Hanlon, 2002; Lau et al., 2011). Retrospective designs are useful for analysis but have limitations that may lead to an under representation of PIMs. Studies are limited to the records included in the database, and influential data may be absent that lead to inaccurate results.

Prospective Studies

The authors identified 19 published prospective studies examining PIM use in community-dwelling older adults. The primary investigator was a pharmacist or physician. The studies examined the prevalence of PIMs solely or the association of PIMs with falls, ADEs, ADRs, and functional status. The prevalence of PIP was addressed specifically in community outpatient, ambulatory clinic, and pharmacy settings. Four studies conducted in different countries reported varying prevalence rates when examining PIMs within the home (Ay, Akici, & Harmanc, 2005; Fiss et al., 2011; Pitkala, Strandberg, & Tilvis, 2002). Additionally the prevalence of PIP in Portuguese

community pharmacies differs when compared to the home setting (de, Soares, Foppe van Mil, & Cabrita, 2006).

Several factors influence PIM use in community-dwelling older adults also vary. Multiple medication use, comorbidities, female gender, and depression have been reported to increase the risk for PIM use (Blalock et al., 2005; Saab, Hachem, Sinno, & El-Moalem, 2006; Stuck, 1994). An adapted version of the Andersen Newman model was used to report that the risk of PIMs was higher in those with greater medication needs (Blalock et al., 2005).

In Lebanon, Saab et al. (2006) was one of three studies that specifically addressed the use of OTC medications. The additional factors of alcohol and OTC drug use were associated with an increased likelihood of PIM use in older adults visiting a community outpatient clinic. The study reported an 18% missed dose frequency and 13% incorrect frequency of medications used. The study reported PIM use prevalence higher than that reported by studies conducted in outpatient and ambulatory clinics in India and the US (Woelfel, Patel, Walberg, & Amaral, 2011; Zaveri, Mansuri, & Patel, 2010). Literature related to the use of PIMs in the rural community is limited.

A Nigerian study by Fadare, Agboola, Opeke, & Alabi (2013) investigated the prevalence of PIP for older adult patients being seen in a rural outpatient department. The prevalence was 25% higher than the study conducted by Ryan and team (2009) in an Irish primary care clinic. Ryan's study compared urban and rural community-dwelling adults in addition to comparing two criteria of PIM measurements. Overall PIP prevalence was found to be 18% with the Beers criteria and 21% with the STOPP tool.

Prospective evidence is limited linking the relationship between PIMs and ADEs in community-dwelling older adults. Chrischilles, VanGilder, Wright, Kelly, & Wallace (2009) used surveys and self-report to determine a relationship between PIM use and adverse drug effects. The study did not examine ADEs but specifically looked at "side-

effects" of PIMs. ADEs are commonly manifested as falls, orthostatic hypotension, heart failure, and delirium (Pretorius et al., 2013). In Taiwan Chang et al. (2005) found a positive association between potentially inappropriately prescriptions and possible ADRs (RR 15.3). In France, Berdot et al. (2009) examined the differences in regular and occasional users of PIMs, and reported an increase risk of falling. The odds ratios of falling were between 1.4 and 1.7 in regular users of psychotropic and anticholinergic medications and in occasional and regular users of long-acting benzodiazepines. An Australian study by Beer et al. (2011) reported 18.2% of community-dwelling older men ages 70 and 88 reported a fall that was associated with PIMs.

A relationship exists between cognitive status and PIM use over time in community-dwelling women with dementia (Koyama, Steinman, Ensrud, Hillier, & Yaffe, 2013). In Italy, Landi et al. (2007) reported that those using more than one PIM had significantly worse physical functioning. An older study in Chicago by Chin et al. (1999) reported that older adults presented to the emergency department with PIMs and were discharged with PIMs and these patients reported lower levels of quality of life. Lukazewski, Mikula, Servi, & Martin (2012) reported PIM use is associated with increased geriatric syndromes, including memory and cognitive problems that place older adults at risk for adverse events.

Interventions

The authors found ten published interventions aimed at ultimately reducing PIM use in community-dwelling older adults **(Table 1)**. Six of these studies were conducted in the US, and six lasted at least one year. The principle investigator was usually a pharmacist and one study was led by a nurse scientist. Interventions were geared toward changing the behavior of the prescribing physician and the monitoring of the pharmacist. Multifactorial approaches included medication review and screening, computerized, behavioral, and educational strategies.

Medication review and screening have been performed by teams or a pharmacist. Allard, Hébert, Rioux, Asselin, & Voyer (2001) longitudinal study used a multidisciplinary approach to conduct medication reviews in community-dwelling older adults at risk of losing autonomy in Canada. The intervention used a non-validated measurement tool and did not significantly decrease the number potentially inappropriate prescriptions. Pharmacists Dunn, Harrison, & Ripley (2011) used the Beers criteria as a screening intervention to alert physicians of PIMs. A reduction in the mean number of PIMs was found as patients were being seen in a US outpatient clinic. A pharmacist review intervention Taylor, Byrd, & Krueger (2003) reduced PIP, hospital and emergency room visits; and improved clinical levels of blood pressure, cholesterol, hemoglobin A1C, and coagulation values in older rural dwelling adults in Alabama. A similar study by Hanlon et al. (1996) involved a clinical pharmacist and nurse who used the MAI to identify PIMs during medication reviews to reduce PIP in an outpatient Veteran's Affairs clinic. The study provided evidence supporting the implementation of dual nurse and pharmacist medication reviews to decrease PIP and potentially reduce ADE.

Computerized approaches were used to alert pharmacists when patients' ≥ 65 years were newly prescribed PIMs (Raebel et al., 2007; Simon et al., 2006; Tamblyn et al., 2003). Although the studies significantly impacted PIP, computerized support for prescribing may not give a complete depiction of the medication use of the patient. Prescriptions for PIMs could be obtained from other providers and taken to other pharmacies not connected with the intervention alert. Additionally, PIMs can be purchased OTC without the pharmacist being aware. These circumstances could increase the older adult's risk of ADE's.

Three studies used educational and behavioral approaches to limit PIM use in older community-dwelling adults. The use of a multicomponent educational intervention

resulted in reductions in PIM use and exposure in Italian primary and outpatient clinics (Keith, Maio, Dudash, Templin, & Del Canale, 2013). In Denmark Bregnhoj, Thirstrup, Kristensen, Bjerrum, & Sonne (2009) used combined education and feedback to improve mean MAI scores. The only nurse-led study by Fick et al. (2004) used a strategy for behavior change in physicians to decrease PIM use of members continuously enrolled in a southeastern managed care organization.

Discussion

This review includes an appraisal of the research specifically exploring the definition, models, measurement, and results of studies addressing the use of PIMs in community-dwelling older adult. A strength of the literature is that scientists descriptively studied PIM use and its association with negative health outcomes. Researchers also have studied the effects of specific PIMs associated with specific diseases. Descriptive studies provide varying findings regarding prevalence, influencing factors, and outcomes associated with PIMs. Studies relating PIMs to ADE's, falls, and cognitive function are limited in the community-dwelling older adult. Also minimal research has been published focusing on interventions to reduce the use of PIMs and the resultant effects on health outcomes.

PIM research is limited by the lack of concrete and conceptual definitions. This state of the science clarifies the vague conceptualization of PIMs to promote shared understanding of the problem among colleagues that will assist in the development of evidence based practice. The literature represents blurred concepts that do not share the same meaning. Potentially inappropriate prescriptions are instructions given by health care providers and PIMs can involve any substance for treating a disease with or without a prescription. Assessing the prescribing behavior of the provider only examines one part of PIMs. Defined concepts should be placed into a research model and

measured operationally by tools that have established reliability and validity for that concept.

In several studies, pertinent prior health history such as cognitive status was not addressed prior to data collection by self-report, interview or survey. Responses given on self-report measurements of ADEs or falls may be inaccurate if older adults experience decline in cognitive status. Other conditions may be considered as confounders in data analysis of the research. Interventions focused on physician behavior without considering patient behavior or involvement. Studies would benefit if they described participant's medication seeking behaviors or beliefs about medications. This could provide additional insight on the use of PIMs from the perspective of the community-dwelling older adult for intervention development.

The Beers criteria were most commonly used; however some medications on this list are not available in certain countries. Few researchers reported specifically including OTC medications in their studies. PIMs can be acquired OTC and without a prescription. Studies on PIMs would have access to all medications by including OTC medications in addition to prescription drugs. The reliability of secondary outcome measures often were not reported. Of the published interventions a few were complex and/or multicomponent. It is difficult to determine to what extent the intervention was effective because one component may be more effective than the other. Based on the review of the literature, it is difficult to draw conclusions in this area of research.

This analysis examined the state of the science's knowledge on the use of PIMs in community-dwelling older adults and is not without limitations. Journal articles may have been missed that represent the population of interest. Studies conducted in the outpatient, ambulatory, or clinic settings may not provide complete information regarding the residential living conditions of the participants. Older adults who live in the nursing home can be seen in these settings and several articles did not identify the specific living

arrangements of their participants. The rationale for including these studies was an attempt to provide an analysis of any older adult living in community settings.

Implications for Nursing Research

The increased number of older adults and the prevalence of chronic conditions are implications for enhanced nursing oversight of pharmacologic interventions in older adults (Edlund, 2010). Prospective studies are needed using conceptual models and rigorous methods with appropriate sample size, power, and reliable and valid measures. Nurse-led studies with interprofessional colleagues are needed addressing PIM use with health status and independence in community-dwelling older adults. Interprofessional teamwork can increase the translation of science to improve patient care

Nursing professionals have not been engaged in studies addressing the prevention and use of PIMs in the community dwelling older adult. The nurse is an important member of the health care team; one who is trusted and in frequent contact with patients. The nurse frequently applies the skills of communication, monitoring and assessment of medication ADEs and ADRs. Teams of doctoral prepared nurses, advanced practice registered nurses (APRNs), pharmacists, and physicians can lead and evaluate interventions to reduce the use of PIMs. Studies with a PhD-prepared nurse as primary investigator can incorporate additional theoretical models into the study design for a different perspective.

Randomized controlled trials with large sample sizes are needed when pilot studies demonstrate positive effects. Randomized studies are needed that compare an intervention group with a control group other than usual care. Qualitative or mixed methods approaches could provide further strength in analysis and interventions for reducing PIM use. The use of quality indicators such as ACOVE in studies as well as incorporating the current version of the Beers criteria (2012) would provide current

evidence to the science (Shrank, Polinski, & Avorn, 2007; American Geriatrics Society, 2012).

Future studies need to examine the use and prevention of PIMs in relation to the older adult's family members, quality of life, health beliefs and behavior. Studies are needed that show the effects of medication optimization and tele-health strategies on PIMs and health outcomes. Collaborative and integrated models are best suited to respond to the chronic multi-morbidities of older adults and improve the pharmacological management of their conditions (Topinková, Baeyens, Michel, & Lang, 2012). A cooperative partnership between the nurse, pharmacist, provider, and patient may be the key.
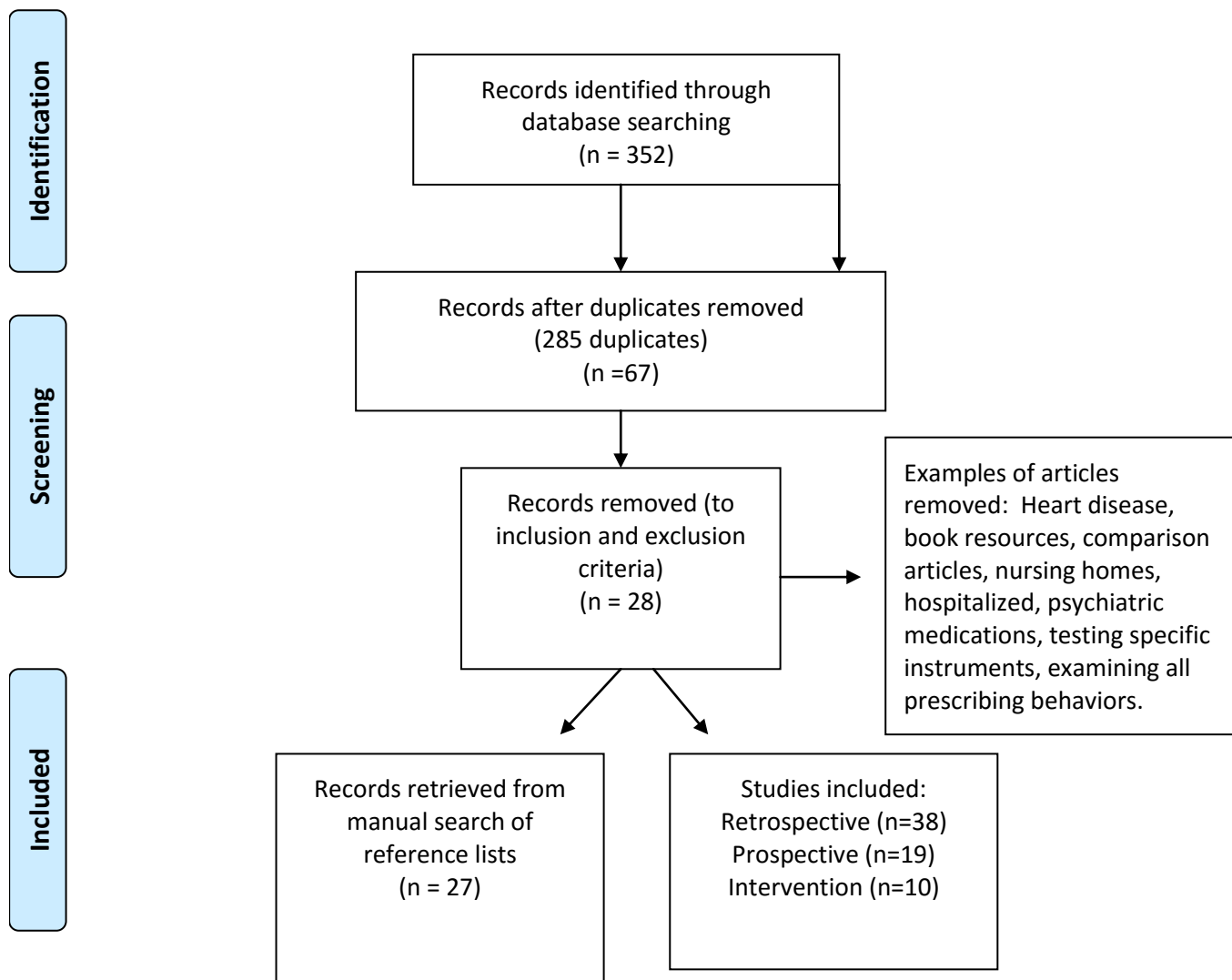
Figure 1. Flow chart of search results.

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Table 1. Interventions Potentially Inappropriate Medication Use In Community-Dwelling Older Adults

Author Design and Purpose	Intervention	Sampling and Setting	Measures and Analysis
Allard, Hébert, Rioux, Asselin, & Voyer, 2001 RCT 2 groups This was a 1-year longitudinal study. This is an intervention aimed at physicians to reduce potentially inappropriate prescriptions given to older adults.	1. The team consists of 2 physicians, 1 pharmacist, and 1 nurse reviewing the medications and diagnoses of the experimental group. 2. The team's suggestions were mailed to the primary care physicians justifying the changes. 3. The nurse followed up monthly with the patient.	N=266 patients Intervention: N=127 Control: N= 130 Age: ≥75 years Characteristics: Community- dwelling, at risk of losing autonomy, and taking >3 medications. Quebec, Canada	Potentially inappropriate prescriptions: Quebec Committee on Drug use list. Measures were completed before and after the intervention. Primary outcome: Number of potentially inappropriate prescriptions. Independent T tests Paired T test Analysis of covariance
		Results	**Limitations and Comments**
	Control group: The control group received normal health service	The intervention group had a larger decline in the mean number of potentially inappropriate prescriptions than the control, but this was not statistically significant.	There were 38% of the participants in the intervention group that did not receive the intervention. A possible interaction occurred between the primary investigator and the physicians and patients. Attrition

Author Design and Purpose	Intervention	Sampling and Setting	Measures and Analysis
Bregnhoj, Thirstrup, Kristensen, Bjerrum, & Sonne, 2009 RCT 3 groups This was a 3-month study. This intervention was a combined or single educational intervention aimed at to increase the prescribing of appropriate medications among general practitioners (GPs).	1. A combined interactive educational meeting plus feedback on patients' medications. or 2. A single interactive educational meeting or 3. A control group (no intervention)	N= 41 GPs N= 166 patients. Age: ≥65 years Characteristics: taking >5 scheduled medications over a 3-month period prior to recruitment Denmark	PIMs: Medication appropriateness index (MAI) MAI and number of medications in the intervention groups. Chi square test Wilcoxon signed rank test

		Results	Limitations and Comments
		The MAI mean scores improved in the combined intervention groups by 5-points. The change in number of medications in the combined intervention group had a significant decrease of −1.03 (95% CI −1.7 to −0.30).	The level of appropriateness of the medication may be overestimated due to the collection method (GPs and medical records). The Hawthorne effect could have occurred. The GP served as gatekeeper for medications

Author Design and Purpose	Intervention	Sampling and Setting	Measures and Analysis
Dunn, Harrison, & Ripley, 2011 Non-randomized prospective pre/post pilot study This intervention is aimed at decreasing the use of PIMS by conducting outpatient screening.	1. The medication profiles of the participants were screened using the Beers criteria before a patient's scheduled appointment. 2. The doctors were informed of PIMs and given options to discontinue, continue, or change the medications.	6 individual medicine and medicine specialty clinics. N= 120 charts of patients Age: ≥65 years USA	PIMs: Beers criteria 2003 Dependent measures t-test

		Results	Limitations and Comments
	3. The medication profiles were followed-up after the appointment.	37.5% of the subjects were taking PIMs. There was a statistically significant decrease in the mean number of Beers criteria medications p=.032.	The accuracy of the medication profiles was unknown. The knowledge of the Beers list among health care team was unknown.

Author Design and Purpose	Intervention	Sampling and Setting	Measures and Analysis
Fick et al., 2004 Randomized block design 2 groups This was an 18-month study. This intervention was designed to change physician behavior and decrease potentially inappropriate prescribing (PIP) in older patients.	1. The physician received a detailed brochure listing PIMs, suggested PIM alternatives, and a personally addressed letter from managed care organization (MCO) describing the patients taking 1 or more PIMs. 2. The physicians were invited to comment on PIM changes by using a fax-back form. Control group: usual care	N = 355 Medicare and choice product line of southeastern MCO physicians Intervention group: N=170 physicians Control group: N=185 physicians Age:≥65 USA	PIMs: Beers criteria 1997 Descriptive investigation of physician response to the PIMs responded to, and the action taken. Chi square tests
		Results	**Limitations and Comments**
		69.4% providers prescribed at least 1 PIM. 71% physicians responded back with the fax. 12.5% physicians discontinued the medication, 1.7% modified dosage, and 1.2% used alternative medication. The # of continuously enrolled members with at least 1 PIM declined from 19.4%-17.9% (p<.001).	The fax was not an efficient form of communication. The initial education brochure that was given 3 months prior to the study may have had an effect on the actual reality of the prescribing practices.
Author, Design, and Purpose	**Intervention**	**Sampling and Setting**	**Measures and Analysis**
Hanlon et al., 1996 RCT 2 groups This was a 1-year study This was an intervention to decrease PIP in outpatients.	Intervention group: Received usual and clinical pharmacist care. Usual care: a nurse reviewing current medications before and after their visit Clinical Pharmacist care: 1. Prior to the visit the clinical pharmacist monitors drug therapy, identifies drug related problems and meets with patient and caregivers. 2. Suggestions from the pharmacist are given to the physicians. 3. The pharmacist provided patient education following the physician visit. 4. The pharmacist provided compliance strategies to the patient. Control group: usual care	General Medicine Clinic, N=208 Intervention group: N=105 Control group: N=103 Age: ≥ 65 years, taking ≥5 medications from a Veterans Affairs Medical Center. USA	PIMs: MAI criteria Student T-tests Chi square or Fisher's exact test ANCOVA and MANCOVA on other outcomes. Baseline, 3 –month, and 12-month measures.
		Results	**Limitations and Comments**
		At 3 months the intervention group had a decline in PIP when compared to the control group (p=.0006) and was consistent at 12 months (p=.0006). Fewer patients experienced ADEs but this was not statistically significant.	There was patient randomization without physician randomization. This study focused on regularly scheduled medications only and did not include as needed or over-the-counter (OTC) medications.
Author Design and Purpose	**Intervention**	**Sampling and Setting**	**Measures and Analysis**
Keith, Maio, Dudash, Templin, & Del Canale, 2013	1. The physicians received a list of PIMs to always be avoided with alternatives,	Stratified by location N= 303 General Practitioners (GP) in the	PIMs: modified Beers criteria

		Parma Local Health Authority (LHA) N= 325 GPs in Reggio Emilia LHA.	Outcomes:
Prospective study 2 group design This was a 3-year study This was a multicomponent intervention designed to decrease potentially inappropriate prescribing (PIP) to older patients in primary care.	annual reviews of PIM incidence data. 2. Educational sessions on PIMs via academic information and case study reviews were done with the physicians. Reggio Emilia LHA was the comparator and received usual care.	Age: ≥65 Parma LHA N= 78482 patients at baseline Reggio Emilia LHA N= 81,597 at baseline Italy	1) The percentage of change in PIMs from baseline 2007 4th quarter to the end of the study post intervention 2009 4th quarter. 2) The significance of change in incidence rates over time within each LHA Chi square and estimated percentage of change
		Results	**Limitations and Comments**
		Both LHAs experienced reductions in PIM exposure rates.	The patient diagnosis data was not in the database The inpatient prescriptions and OTC medications were not available. There were possible confounding variables.

Author Design and Purpose	Intervention	Sampling and Setting	Measures and Analysis
Raebel et al., 2007 RCT using a 2-arm parallel-design This was a 1-year study. This intervention was designed to reduce newly prescribed PIMs in older adults.	1. The pharmacist was alerted when a patient ≥65 was prescribed one of 11 medications. 2. The pharmacist alerted the provider and made notes in the computer system. Control group: wait-listed for 6 months with usual care during that time period.	At Kaiser Permanente (KP) Colorado, a group model US Health maintenance organization (HMO), Age: ≥ 65 N=59,680 (29,840 each group). Physicians, patients, and pharmacists blinded to group assignment. USA	PIMs: physicians and pharmacists collaboration using Beers criteria, Zhan criteria and KP list of medications to avoid in older adults. Chi square and Wilcoxon rank and Fisher exact tests
		Results	**Limitations and Comments**
		There was a higher percentage of PIMs prescribed in the usual care group 2.2% than in the intervention group 1.8%. The most common prescriptions reduced were amitriptyline (p<.001), and diazepam (p=.02).	The use of health plan prescription data to assess drug dispensing does not ensure that patients did not go other places for prescriptions. This study did not consider the refilled prescriptions as PIMs for alerts.
Author Design and Purpose	**Intervention**	**Sampling and Setting**	**Measures and Analysis**
Simon et al., 2006 Cluster RCT Interrupted Time Series Analysis 2 groups Study conducted over 3- years. This intervention was designed to reduce newly prescribed PIMs in older adults.	1. The computer system gave age-specific alerts when older adults were prescribed specific PIMs. 2. The physician also received academic detail which is evidence-based education. Group 1: Alerts and academic detail intervention Group 2: Alerts only	Clinic sites total N=15 Group1: N=113 with 7 sites Patients=24,119 Group 2: N=91with 8 sites Patients: N=26,805 Age: ≥65 USA	PIMs: Investigator developed instrument PIMs dispensed per 10,000 patients per quarter T-tests Chi square Segmented regression models
		Results	**Limitations and Comments**
		There was a downward trend occurred in alerts for targeted medications being dispensed. The academic detailing did not statistically change the number of PIMs dispensed.	Generalizability

Author Design and Purpose	Intervention	Sampling and Setting	Measures and Analysis
Tamblyn et al., 2003 Clustered RCT 2 group design This was an intervention to reduce inappropriate prescriptions given to older adults.	1. The physicians were given computerized decision making support (CDS) consisting of a computer, health record software, and internet capabilities. 2. The physicians were given downloaded updates on prescriptions that were dispensed to their patients from the Regie de l'assurance maladie du Quebec (RAMQ) drug insurance program. 3. Alerts were generated describing the problem with the medication, consequences, and alternative therapies. Control group: usual care	N=107 primary care physicians N=12560 patients (aged ≥66, community-dwelling, and been seen on at least 2 occasions by their physician) Intervention group N=54 Control group N=53 Quebec, Canada	Primary Outcomes: Initiation and discontinuation rates of those given at least one inappropriate prescription. Prescribing problems Descriptive statistics Pearson correlation Poisson regression with generalized estimating equation

Results	Limitations and Comments
The number of newly prescribed inappropriate medications per 1000 visits was lower in the CDS group by 18% when compared to the control group [RR 0.82]. A non-statistically significant discontinuation (14%) of preexisting inappropriate prescriptions occurred in the CDS group. There was a significant difference in the discontinuation of prescriptions for drug-interactions among 68.6 per 1000 visits in the CDS group versus 51.5 per 1000 visits in the control group. Drug disease, drug-age, and excessive duration were common prescribing problems.	The previous computer experience of the physician was unknown. The patients received care from at least 3 other physicians prescribing medications.

Author Design and Purpose	Intervention	Sampling and Setting	Measures and Analysis
Taylor et al., 2003 RCT 2 group This was a 1 year study. Prevention and monitoring of PIP and drug-related problems in older rural dwelling adults.	1. The patient met with one of 4 pharmacists for 20 minutes before seeing the physician. 2. The pharmacist used published algorithms and guidelines to make recommendations to the provider. 3. Written and oral education was provided to the patient. The intervention group received usual care plus pharmaceutical care. The control group received usual care.	3 community family medicine clinics in rural Alabama Intervention N= 33 Control N= 36 USA	PIP: MAI Clinical endpoints: Blood pressure, hemoglobin A1C, Low density lipoproteins, and International Normalized Ratio. Number of hospitalizations and emergency department visits and quality of life. RMANOVA T-tests Chi square

		Results	Limitations and Comments
		The number of hospitalizations and emergency room visits decreased in the intervention group p=0.003. The intervention group was closer to or meeting the goal blood pressure, Hemoglobin A1C, cholesterol, and INR levels. Quality of life changes were not significant The percentage of PIP decreased in the intervention when compared with the control group.	Small sample Short follow-up period Physicians were not randomized, only the patients

CHAPTER III: Manuscript #2

Sleep and Health-Related Factors in Overweight and Obese Rural Women

In a Randomized Controlled Trial

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Abstract

This secondary analysis describes sleep and health-related factors in healthy overweight and obese mid-life and older rural women enrolled in the "Women Weigh-In for Wellness" randomized clinical trial. The aim of the trial was to promote healthy behaviors and weight-loss. We analyzed demographic, anthropometric, and biomarker variables, self-reported measurements of sleep disturbance and pain interference, and objective 24-hour sleep/wake patterns at baseline, 6 months, and the change over time. Although self-reported sleep disturbance reflected normal sleep, pain interference was slightly higher than normal. There were associations between higher self-reported sleep disturbance, pain interference and several other variables. Women who achieved 5% or more weight loss exhibited positive associations between sleep, pain, and health-related factors. Weight loss and lower pain predicted lower self-reported sleep disturbance. Our results suggest that overweight and obese rural women who adopt healthy behaviors and achieve weight loss also may experience improved sleep and other health benefits.

Introduction

The worldwide prevalence of obesity has increased dramatically. Over two-thirds of adults in the United States (US) are considered overweight and one-third are considered obese (Centers for Disease Control, 2014; Ogden, Carroll, Kit, & Flegal, 2014). The US has reported higher rates of obesity than other countries, in rural areas, and in women (Befort, Nazir, & Perri, 2012; Hartz et al., 2007; Organization for economic cooperation and development, 2012). Higher obesity trends have been paralleled by reports of short sleep duration and are likely to contribute to poor health outcomes of Americans (Centers for Disease Control and Prevention (CDC), 2011; Patel et al., 2008; Singh, Drake, Roehrs, Hudgel, & Roth, 2005; Vgontas et al., 2014).

Sleep duration of 7-9 hours each night is recommended for optimal health (Hirshkowitz et al., 2015; Watson et al., 2015). Prior evidence has suggested that short self-reported sleep duration and poor sleep quality are risk factors for the development of obesity; but trends have been most consistent in children (Beccuti & Pannain, 2011; Grandner, 2012; Hung et al., 2013; Nielsen et al., 2010). In adults, short self-reported sleep duration has been associated with several factors such as female gender, older age, higher BMI, waist circumference, and hypertension (Befort et al., 2012; Di Milia, Vandelanotte, & Duncan, 2013; Hartz et al., 2007; St-Onge et al., 2010; Theorell-Haglow, Berglund, Janson, & Lindberg, 2012). Regardless of previous sleep patterns, American women who reported sleeping 7 hours or less duration per night were more likely to be obese (Anic, Titus-Ernstoff, Newcomb, Trentham-Dietz, & Egan, 2010).

Among those living in rural America, short self-reported sleep disturbance was associated with obesity-related risk factors such as less physical activity, low intake of healthy foods, and high fat and fast food consumption (Stamatakis et al., 2008). In addition, short self-reported sleep duration of 6 hours or less was found to be

significantly associated with higher body mass index (BMI) in men and women living in rural Iowa (Kohatsu et al., 2006). The risk of insomnia symptoms has been reported to be increased among individuals in rural areas with poor health, older age, female gender, low income and education (Hartz et al., 2007). Rural health disparities, behavior patterns, culture, socioeconomic, and environmental factors may be associated with shorter sleep duration and obesity trends (Bennett, Probst, & Pumkam, 2011; Crosby, Wendel, Vanderpool, & Casey, 2012; Jones, Parker, Ahearn, & Jayachandran, 2009;Whinnery et al. 2014). Additional examination of sleep in overweight and obese mid-life and older rural women is warranted as this population is underrepresented.

In addition to obesity, self-reported short sleep duration and sleep disturbances have been associated with inflammation, cardiometabolic disease risk, and hypertension (Bansil, Kuklina, Merritt, & Yoon, 2011; Grandner, Sands-Lincoln, Pak, & Garland, 2013; Grandner, Jackson, Pak, & Gehrman, 2012). The relationship of sleep with increased risk of cardiometabolic disease is particularly important in women due to high mortality rates from heart disease (Go et al., 2014). Women who self-reported short sleep duration of 6 hours or less per night had a greater risk of hypertension; obesity may potentiate this relationship (Gangwisch, Feskanich, Malaspina, Shen, & Forman, 2013; Guo et al., 2013). Pain also may have a significant relationship with sleep and weight status. A recent survey reported that adults who experienced pain slept less and had poorer sleep quality than those without pain (Knutson, 2015). In obese individuals, pain has been associated with chemical mediators and difficulty sleeping (Okifuji & Hare, 2015). We are only aware of one study that found an association between self-reported sleep disturbance and pain in overweight and obese women (Wachholtz, Binks, Suzuki, & Eisenson, 2009). Closer observation may show that sleep could be associated with pain and health among rural women who are overweight or obese.

Objectively measured short sleep duration was found to be associated with higher BMI and greater waist circumference in adults, but other studies reported these relationships were not maintained over time (Appelhans et al., 2013; Evans et al., 2011; Lauderdale et al. 2009; Mezick, Wing, & McCaffery, 2014; Moraes et al. 2013). The relationship between objectively measured sleep and weight status remains unclear. Further examination of the longitudinal relationship between sleep and obesity is needed.

Sleep behavior has been reported to influence quality of life, body function and performance (Czeisler, 2015; Lee et al., 2009). Likewise, improving healthy behaviors may influence sleep and overall health. Alfaris et al. (2015) reported significantly higher self-reported sleep duration and sleep quality in obese men and women with 5% or more weight loss while enrolled in a behavioral weight loss intervention. A slightly different relationship was reported by Thomson et al. (2012); they found that higher self-reported sleep quality and quantity increased the likelihood of weight loss by 33% in overweight and obese women enrolled in a weight loss program. In contrast, moderate-intensity exercise, stretching, and behavioral weight loss programs have reduced BMI but did not significantly change sleep quality in adults (O'Brien et al., 2012; Tworoger et al., 2003). Weak associations were found between self-reported shorter time to fall asleep and weight loss (O'Brien et al., 2012). Additional evidence is needed to clarify the relationships between weight loss, sleep quality, duration and other health factors. The purpose of this paper is to describe self-reported and objective measurements of sleep and the relationships between sleep, pain, and demographic and health-related factors in overweight and obese mid-life and older rural women enrolled in a randomized controlled trial.

The specific aims were to:

1) Characterize self-reported sleep disturbance, pain interference, and health-related factors.

2) Describe objective indirect measurements of sleep.

3) Observe relationships between sleep, pain, and health-related factors (total sample and in non-achievers and achievers of weight loss).

4) Identify the predictors of change in self-reported sleep disturbance.

Methods

The "Women Weigh-In for Wellness" trial was designed to promote healthy eating, physical activity, and weight loss. The detailed protocol for the study has been published (Hageman, Pullen, Hertzog, Boeckner, & Walker, 2011). The randomized clinical trial was investigator-initiated and community-based and approved by the Institutional Review Board at a Midwestern US University. All participants provided written informed consent prior to study enrollment. The clinical trial evaluated the effectiveness of theory-based web-delivered interventions for promoting healthy eating and activity among mid-life and older rural women with the goal of achieving 5-10% weight loss and weight maintenance over a 30-month period. There were three arms of the intervention: interactive web site, interactive web site plus a peer -led discussion board, and interactive web site plus email counseling. An interactive web site was available to all women that provided weekly messages, opportunities to monitor and post goals, calories, fat grams, weight in pounds, and physical activity behaviors. Individualized feedback of the results of the assessment visits were posted online. At baseline and 6 months, actigraphy measurements were obtained as well as other behavioral, biomarker and anthropometric measurements. This secondary analysis

examined data at baseline, 6 months and the change over time. These times represent Phase 1, called the Weight Loss phase, of the 30 month study.

Sample and Setting

A total of 301 overweight and obese mid-life and older rural women enrolled. Eligible individuals resided in large, small, or isolated rural areas as defined by Rural Urban Commuting Area (RUCA) codes (Hart & Casey, 2012). The women resided in one of 16 rural counties in a Midwestern state in the US (Hageman, Pullen, Hertzog, Boeckner, & Walker, 2011).

Inclusion and Exclusion Criteria

Women were included in the study if they: a) were 40-69 years of age; b) overweight or Class I & II obese (BMI 28 to 39.9) or BMI 40 to 45 with physician clearance; c) able to speak and read English; d) able to communicate over the telephone, e) made a commitment to lose weight through changing eating and physical activity behaviors; f) able to use a computer with minimal assistance to access the internet and complete electronic forms; g) made a commitment to access the website as required by the research intervention; h) had or were willing to obtain an email account; i) had access to a DVD player; j) able to walk without assistance (including cane, crutches, walker, oxygen); k) answered 'no' to all questions on the Physical Activity Readiness Questionnaire (PAR-Q) or obtained clearance from their physician to become more active and participate in the assessment of physical activity biomarkers (Cardinal, 1997); and l) resided within approximately 60-mile radius of the research site in a Midwestern state.

Women were excluded from participating if: a) diagnosed with Type 1 diabetes, b) diagnosed with Type 2 diabetes and required insulin, c) had a ≥10% weight loss in last 6 months; d) were currently enrolled in a weight loss management program; e)

taking medications that affect weight loss or weight gain; f) enrolled in or undergoing a formal program of cardiac rehabilitation; and g) other physical or medical restrictions that would preclude following the minimum recommendations for moderate physical activity and healthy eating.

Measurements

Demographic/Anthropometric/Biomarkers. Assessments were gathered using reliable and valid measures. Demographic and health history data were obtained via an investigator developed questionnaire. Age and menopausal status were measured by self-report items on the health history questionnaire. Participants were asked "Have you gone through menopause?" and "If yes, at what age did you go through menopause?" We also collected anthropometric measurements. Height and weight were collected using The Tanita Model Composition Analyzer, Scale, Printer & Height Rod [TBF-215, Tanita Corporation of America, Inc.]. Prior to assessment, women fasted, refrained from exercise, alcohol use, and voided. BMI was calculated as weight in kilograms divided by height in meters-squared. A weight loss of 5% or more represents a significant change of weight (Wing, Lang, Wadden, Safford, 2011). Participants who did not achieve weight loss of at least 5% or more were considered non-achievers, and those who did were achievers. Waist circumference was measured in inches by placing a snug tape in a horizontal plane around the abdomen at the level of the iliac crest at the end of expiration; the average of two measurements was recorded (US Department of Health and Human Services, 1998).

Blood pressure was collected using the e-sphyg 2 [9002] Automatic Sphygmanometer [American Diagnostic Corporation, Hauppauge, NY]. The women did not consume caffeine or participate in exercise or smoking prior to blood pressure assessment. Blood pressure was assessed using standard technique after 5 minutes of

quiet sitting (Perloff et al., 1993). A minimum of two blood pressure measurements separated by at least 30 seconds were obtained. Systolic and diastolic blood pressures were recorded as the mean of the two measurements within 5 mmHg (Perloff et al., 1993).

Self-reported Sleep Disturbance and Pain Interference. Self-reported sleep disturbance and pain interference were each measured from the respective four item subscale of the Patient Reported Outcomes Measurement System (PROMIS-29v1.0) and interpreted from participants' T-scores based on general population norms. A T-score of 50 represents the mean score in the general population and a higher PROMIS T-score represents poorer sleep or more pain interference (Gershon, Rothrock, Hanrahan, Bass, & Cella, 2010). Sleep disturbance items assessed the participant's self-reported perceptions of sleep quality, depth, and restoration over 7 days. The measurement included five-point Likert-style choices (ranging from very poor to very good) in response to the participant's sleep quality, if sleep was refreshing, difficulty falling asleep, as well as problems with sleep (Gershon, Rothrock, Hanrahan, Bass, & Cella, 2010). The PROMIS sleep disturbance subscale demonstrated an alpha reliability of 0.87 at baseline and 6 months.

Four self-reported pain interference subscale items measured self-reported consequences of pain and the extent of how pain hinders engagement in all activities over 7 days. The measurement included five-point Likert-style choices (ranging from not at all to very much) in response to the participant's pain interference with activities (Gershon et al., 2010). The PROMIS pain interference subscale demonstrated an alpha reliability of 0.93 at baseline and 0.97 at 6 months.

Objective Indirect Sleep. The ActiGraph wGT3X [ActiGraph, Pensacola, FL] was used to collect indirect measurements of 24-hour sleep/wake patterns. Women

were instructed on proper wear of the ActiGraph and wore it for 24-hours a day. Women completed a sleep diary that was used to identify bedtime and out-of-bed times during analysis. Most studies measure objective sleep parameters by wrist-worn actigraphy; this study used hip-worn placement.

An addendum study was implemented on a sub-sample of 26 participants who were recruited to compare sleep parameter measurements using wrist and hip actigraphy. Results indicated mostly reliable and correlated measures between the sites. High correlations were found for three variables (TST, WASO, and percent awake) between wrist and hip measures (r= 0.93, 0.85, and 0.87 respectively); but not for number of awakenings (r= .39, p=.083). As illustrated in Figure 1, the actigraph monitor was worn on the dominant hip. We examined four objective sleep parameters: total sleep time (TST), number of awakenings, wake after sleep onset (WASO), and percent sleep. The TST is the number of minutes of actual sleep while in bed and the number of awakenings is the number of wake counts after the onset of sleep. The WASO minutes are the amount of time spent awake after sleep has begun. Percent sleep is the ratio of TST to the amount of time spent in bed. Normal values are considered 7-9 hours for TST, less than 6 number of awakenings, less than 30 minutes for WASO, and a percent sleep of 85% or higher. Values not within normal limits may indicate sleep disturbance (Berger et al., 2005).

Data Analysis

As shown in the consort diagram, we were unable to use data from 32 participants due to attrition and 48 participants due to lack of actigraphy data. A minimum number of 4 nights of wear were required for analyzing sleep/wake data. We compared the baseline data of the 80 women without actigraphy data with the 221 women in the analysis and found no significant differences between study variables. We

analyzed n=221 participants who had 4 nights of actigraphy measurements, complete sleep diaries and PROMIS questionnaires at baseline and 6 months.

Descriptive statistics were used for aims 1 and 2 to determine the mean, range, percent, and standard deviations of demographic, anthropometric, and biomarker variables at baseline and 6 months. The change variable from baseline to 6 months was calculated for weight, BMI, waist circumference, and blood pressures such that an increase in those variables is represented positively and a decrease is represented negatively. Pearson correlations were used for aims 3 and 4 to examine the associations between study variables. Weight loss was treated as a single dichotomous variable with non-achievers being labeled 0 and achievers labelled as 1. A two-tailed level of significance of p= .01 was used to examine the relationships between non-achievers and achievers of weight loss. Due to the exploratory nature of this study, the use of a stringent p value may conceal potential relationships that merit further study. Multiple linear regression modeling was used in aim 4 on the change scores to determine if specific factors contributed to a meaningful amount of influence on self-reported sleep disturbance. Our primary predictors were weight change and pain interference; and we controlled for age and arthritis because they were potential confounders. This was done to determine if weight change had a meaningful influence on self-reported sleep disturbance. A two-tailed level of significance was designated at p= .05. SPSS v22 statistical software package was used.

Results

Baseline Characteristics

Baseline characteristics are shown in Table 1. Of the participants 97% were Caucasian and 84% married; 43% had completed some college; 68% were employed full-time, and over 90% had health insurance. The mean age was 54.5 years and most

women were post-menopausal. The self-reported sleep disturbance score and actigraphy measurements reflected normal sleep characteristics. Pain interference scores were slightly higher than normal.

Characteristics: Overall and in Non-Achievers and Achievers

Characteristics at 6 months and the change over time of the 221 women are displayed in Table 2. The self-reported sleep disturbance scores, pain interference scores, and actigraphy variables did not change considerably, but the anthropometric and biomarker variables decreased from baseline to 6 months. Table 2 also shows characteristics and significant changes in women who were non-achievers (53%) and achievers (47%) of 5% or more weight loss.

Overall Relationships at Baseline, 6-Months, and Change Scores in the Total Sample

Significant relationships were found at baseline. Higher self-reported sleep disturbance scores were associated only with higher pain interference scores (r= .252, p<.05). We also found associations between the higher pain interference score and higher weight (r= .214, p<.05) and BMI (r= .218, p<.05). Objectively measured sleep was not associated with any other study variables.

Table 3 shows the relationships of the variables at 6 months. Weak associations were found between higher self-reported sleep disturbance scores and higher blood pressures. Higher sleep disturbance was moderately associated with higher pain interference scores. Pain interference scores were associated with most of the anthropometric and biomarker variables. Higher pain interference scores had weak to moderate associations with older age, higher weight, BMI, waist circumference, and systolic, but not diastolic blood pressure. Relationships also were found between objective sleep variables. Weak associations were observed between higher objective

WASO minutes and higher pain interference scores. Higher WASO minutes and number of awakenings were associated with higher BMI and blood pressure. Lower percent sleep had weak associations with higher weight, BMI, and pain interference scores.

We observed relationships between change scores in self-reported sleep disturbance and pain interference and the change in anthropometric and biomarker measures. There were weak positive associations between the change in self-reported sleep disturbance score and change in weight (r=.202, p<.05), BMI (r=.211, p<.05), waist circumference (r= .169, p<.05), and diastolic blood pressure (r= .137, p<.05). Positive associations also were found between the change in pain interference scores and several of the same variables including change in weight (r= .185, p<.05), BMI (r= .205, p<.05), waist circumference (r =.153, p<.05), and systolic blood pressure (r=.152, p<.05).

Next, we evaluated the relationships between the change scores in objective sleep measurements and the change in anthropometric and biomarker measures. Change in total sleep time was not associated with either the change in BMI or weight. Weak positive associations were found between the number of awakenings per actigraphy and changes in weight (r= .167, p<.05), BMI (r= .171, p<.05), waist circumference (r= .173, p<.05), and both systolic (r= .175, p<.05) and diastolic (r= .208, p<.05) blood pressures.

Relationships among Non-Achievers and Achievers of 5% Weight Loss

Table 4 shows the relationships in non-achievers and achievers at 6 months. In non-achievers, higher self-reported sleep disturbance and self-reported sleep quality scores were moderately positively associated with higher pain scores. We also found that higher pain interference scores had a weak association with higher WASO minutes.

In achievers, we found weak associations between lower self-reported sleep quality and disturbance scores and lower pain interference scores. Several weak to moderate associations were observed between lower pain interference scores and weight loss, and smaller waist circumference. Objectively measured lower WASO minutes, number of awakenings, and higher sleep percent had weak associations with lower BMI. Achievers also demonstrated weak relationships between higher objectively measured percent sleep and weight loss.

A regression model was fit to predict lower self-reported sleep disturbance scores. Table 5 shows higher weight loss and lower pain interference as significant predictors of lower self-reported sleep disturbance at 6 months. Approximately 6% of the variance in the change in self-reported sleep disturbance was accounted for by the change in pain interference, weight, age, and arthritis. Age and arthritis were non-significant predictors of change in self-reported sleep disturbance when holding constant change in weight and pain interference. Both change in weight and change in pain interference had similar importance to the model. For every pound lost, a corresponding drop of 0.163 was seen in the self-reported sleep disturbance score when holding constant age, arthritis, and change in pain. In addition, for every one unit drop in pain interference, a corresponding drop of 0.142 was seen in the self-reported sleep disturbance score when holding constant age, arthritis, and change in weight.

Discussion

This secondary analysis describes self-reported and objective sleep and their relationships with health-related factors in 221 mid-life, overweight and obese rural women who participated in the "Women Weigh-In for Wellness" clinical trial. This is the first known report of concurrent self-reported and objective measurement of sleep parameters in healthy, mid-life, overweight and obese rural women. We will now discuss

these findings in relationship to each specific aim and provide implications for research and practice.

Women self-reported sleep disturbance similar to norms and self-reported higher pain interference. While the women did not have high sleep disturbance, our findings were complementary to previous reports of overweight or obese women exhibiting pain (Wachholtz et al., 2009). Overall, women were not hypertensive according to the current JNC-8 guidelines (James et al., 2014). Aside from being overweight and obese, women had fairly normal self-reported sleep, pain, and biomarker characteristics. "The Women Weigh-in for Wellness" trial may have had a positive influence on health-related characteristics by lowering weight, BMI, waist circumference, and blood pressures in some women.

We were surprised to find that the objective indirect measurements of sleep reflected very good sleep at baseline and 6 months. There was not much room for improvement of sleep duration; actigraphy results revealed that over 7 days, women were sleeping a mean duration of over 7 ½ hours. The sleep duration was in accordance with current recommendations. Women in our sample were mid-life and older, with the majority employed. These women may have had scheduled day activities and maintained regular sleep habits. Also, a ceiling effect could have occurred in the indirect measurement of sleep. Prior studies collected longitudinal data over years whereas this study included data at baseline and 6 months. Considering data from 30 months was not yet available, we are unable to project if the women will maintain good sleep duration.

Overall, we found consistent relationships among higher self-reported sleep disturbance with higher pain interference. Pain interference was revealed to be a noteworthy variable as it also was associated with multiple anthropometric, biomarker and ultimately objective indirect sleep variables. Pain could be associated with sleep

because these centers may have reciprocal relationships within the brain (Moldofsky, 2001). Women who suffer from disturbed sleep may report pain, and those who have pain may report disturbed sleep (Finan, Goodin, & Smith, 2013).

Previous studies also reported associations between self-reported sleep duration and BMI or weight (Di Milia et al., 2013; Kohatsu et al., 2006; St-Onge et al., 2010; Theorell-Haglow et al., 2012). Although we did not measure self-reported sleep duration, we found higher self-reported sleep disturbance was associated with higher blood pressures (Bansil, Kuklina, Merritt, & Yoon, 2011;Fang et al., 2012; Grandner, Jackson, Pak, & Gehrman, 2012; Guo et al., 2013). Our findings are consistent with several studies that did not support the immediate or longitudinal relationship between objectively measured short sleep duration and higher BMI or weight (Appelhans et al., 2013; Evans et al. 2011; Lauderdale et al., 2009; Mezick et al., 2014; Moraes et al., 2013). Over the 6 months, change scores reflected improved sleep and pain that were associated with lower weight, BMI, waist circumference, and blood pressure.

Women who achieved 5% or more weight loss had improved sleep, pain interference, and blood pressure. Our analysis adds to the evidence supporting the association of better self-reported sleep quality and duration with weight loss (Alfaris et al., 2015; O'Brien et al., 2012; Thomson et al. 2012). Weight loss and lower pain interference were predictors of lower self-reported sleep disturbance. Weight loss could lower pain and contribute to less disruption in sleep. Women with less sleep disruption may sequentially show lower blood pressure. These results support the relationship between sleep and weight change; sleep may be a factor in achieving weight loss, or vice versa. Thus, it is important for obese or overweight women to adopt healthy sleep, diet, and physical activity to improve or maintain health status.

There were strengths of this secondary analysis. This was the first study to examine self-reported sleep and objective indirect measurement of sleep duration and its association with health factors in healthy obese and overweight mid-life and older rural women. The parent study used reliable and valid instruments. Our secondary analysis assessed both self-reported sleep disturbance with the PROMIS and an objective indirect measurement of sleep**.**

Our analysis is not without limitations. Even though this analysis included data from 73% of the original sample; selection bias could have occurred. The main limitation of this study was the positioning of the actigraph on the hip. Zinkhan et al. (2014) recently reported differences in agreement between hip-worn actigraph, polysomnogram, and the wrist-worn device. This limitation affects validity of the results using number of awakenings and comparison to other studies using wrist actigraphy. Women were not screened for diagnoses of sleep apnea or other sleep disorders. Obesity is a risk-factor for obstructive sleep apnea and can result in sleep disturbance (Knutson, Zhao, Mattingly, Galli, & Cizza, 2012). Weight loss may not improve sleep if a sleep disorder is present. Medications were not recorded; however women were excluded if they took medications that influenced weight. This study did not collect a medication history to confirm the use of medications that influence sleep.

Conclusion

Sleep quantity and quality influence health. This secondary analysis was performed to provide a description of sleep and its association with health factors in a sample of rural overweight and obese mid-life and older women. The results are promising support for interventions aimed at communities to improve health and sleep behaviors.

Grandner (2012) suggests that the science of sleep could benefit from interventions that are clearly conceptualized and performed at the community level. Other research implications include the need for consistent use of reliable and valid self-reported and objective measures of sleep quality and duration. Studies need to confirm the norms for sleep variables per actigraphy in mid-life and older women. Self-reported sleep is often over or under-estimated and data collected in epidemiological studies may not correspond to objective indirect measures of sleep using actigraphy (Girschik, Fritschi, Heyworth, & Waters, 2012). Self-reported sleep duration has shown negative agreement with objectively measured sleep/wake parameters (Girschik et al., 2012). We observed that self-reported sleep disturbance was not significantly correlated with objectively measured sleep. Self-report quality measures complement, but are not equivalent to quantify actigraphy parameters such as sleep duration (total sleep time), WASO, and number of awakenings. Thus, examining sleep quantity, quality, and disturbance using self-reported and objective measures is recommended (Grandner, 2012; Madsen, Huang, & Gogenur, 2015). Measuring sleep by both methods provides a well-rounded depiction of sleep's association with being overweight or obese and with weight loss or gain. Science could benefit from more studies of mid-life and older women living in rural and small communities and specifically target ethnicities other than Caucasian in which obesity/overweight and hypertension are prevalent. Intervention studies are needed that specifically focus on the impact of weight loss on sleep and pain.

Health professionals need to translate research evidence on sleep into practice. Implications for practice include screening, assessment, and management of sleep disorders and disturbances, pain, and blood pressure in overweight and obese women. Health professionals need to educate and encourage non-pharmacologic and/or

pharmacologic management of sleep disturbances and pain as indicated. Clinicians

need to encourage and monitor healthy lifestyle behaviors, paying particular attention to

evidence based strategies appropriate for rural women to promote weight loss through

healthy eating, physical activity, and sleep.

All procedures followed were in accordance with the ethical standards of the responsible

committee on human experimentation (institutional and national) and with the Helsinki

Declaration of 1975, as revised in 2000. Informed consent was obtained from all patients

for being included in the study.

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Figure 1. Hip-worn actigraphy

Figure 2.   Consort Diagram

Table 1
Sleep, Pain, and Anthropometric, Biomarker, Characteristics as Measured by Self-report (PROMIS) and Actigraphy at Baseline
(N=301)

Variable	N	Baseline Data Secondary Analysis N = 221 M (SD)	N	Baseline Data Not in Secondary Analysis N= 80 M(SD)
Sleep Disturbance Score (S)	221	49.0 (7.2)	80	48.9 (6.8)
Pain Interference Score (S)	220	51.6 (7.2)	80	54.1 (7.3)
Total Sleep Time (A)	221	455.1 (42.8)	80	458.9 (44.5)
Wake After Sleep Onset (A)	221	17.5 (10.2)	80	22.6 (12.8)
Number of Awakenings (A)	221	4.8 (2.2)	80	5.9 (2.8)
% Sleep (A)	221	96.3% (2.1)	80	94.9% (2.4)
Age (years)	221	54.5 (7.0)	80	52.3 (6.2)
Weight (lbs)	221	205.4 (28.7)	80	210.4 (28.8)
Body Mass Index	221	34.6 (4.2)	80	35.4 (4.2)
Waist Circumference (inches)	221	42.8 (4.3)	80	42.9 (4.3)
Arthritis	221	27.6%	80	23.8%
Systolic BP	221	123.1 (11.8)	80	123.0 (12.5)
Diastolic BP	221	76.9 (7.8)	80	76.4 (8.2)

Note: A= Actigraph, S= Self-report
Note: no significant differences were found between groups
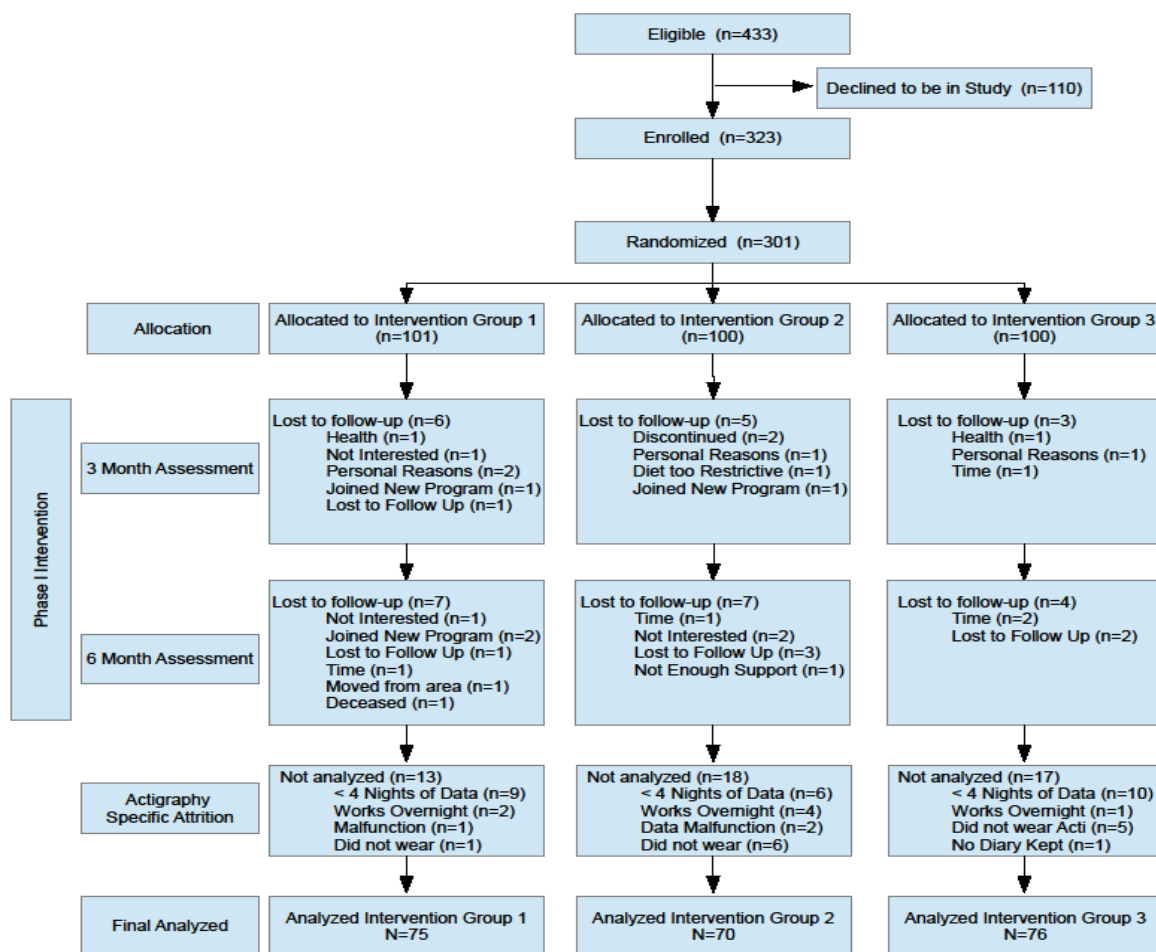
Table 2 Sleep, Pain, and Anthropometric, Biomarker Characteristics as Measured by Self-report (PROMIS) and Actigraphy at 6 Months, and Change Over Time (N=221)

Note: A= Actigraph, S= Self-report

Variable	6-months			Base to 6 Months Change			Base to 6 Month Change in Non-Achievers			Base to 6 Month Change in Achievers	
	N	M(SD)	N	M(SD)	N	M (SD)	N	M (SD)			
Sleep Disturbance Score (S)[a]	220	48.8 (6.9)	220	-0.2 (6.3)	117	1.3 (6.4)	103	-1.9 (5.8)			
Pain Interference Score (S)[a]	220	51.7 (8.5)	219	0.1 (7.4)	116[*]	1.4 (7.2)	103	-1.3 (7.3)			
Total Sleep Time (A)	221	457.3 (43.6)	221	2.2 (38.2)	118	4.0 (37.8)	103	0.4 (38.9)			
Wake After Sleep Onset (A)	221	17.1 (10.1)	221	-0.4 (11.4)	118	0.4 (12.3)	103	-1.2 (10.2)			
Number of Awakenings (A)	221	4.5 (2.3)	221	-0.3 (2.1)	118	0.1 (2.3)	103	-0.8 (1.9)			
% Sleep (A)	221	96.4% (2.0)	221	0.7% (2.3)	118	0.0 (2.5)	103	0.2 (2.1)			
Weight (lbs)[a]	221	193.7 (31.5)	221	-11.7 (13.3)	118	-1.9 (5.6)	103	-22.95 (10.3)			
Body Mass Index[a]	221	32.6 (4.8)	221	-2.0 (2.2)	118	-0.3 (0.9)	103	-3.8 (1.6)			
Waist Circumference (inches)[a]	221	40.4 (4.7)	221	-2.4 (2.9)	118	-0.8 (2.3)	103	-4.2 (2.3)			
Systolic BP[a]	221	120.4 (13.6)	221	-2.7 (11.2)	118	0.9 (9.6)	103	-6.9 (11.2)			
Diastolic BP[a]	221	75.6 (4.8)	221	-1.2 (6.4)	118	1.3 (5.4)	103	-4.0 (6.3)			

[a] Denotes significant changes between Non-achievers and Achievers from baseline to 6 months; *Denotes that participant did not answer a pain item.

Table 3 Correlations between Sleep, Pain, Anthropometric, and Biomarker Variables at 6 Months (N=221)

Variable	Age	Weight	Body Mass Index	Waist Circumference	Systolic BP	Diastolic BP	Pain Interference
Sleep Quality (S)	.109	-.124	-.105	-.087	-.111	-.141*	-.347**
Sleep Disturbance Score (S)	-.050	.099	.080	.087	.136*	.139*	.434**
Pain Interference Score (S)	.147*	.260**	.228**	.258**	.166*	.054	-
Total Sleep Time (A)	.030	-.029	-.044	-.011	.050	.060	.062
Wake After Sleep Onset (A)	.033	.126	.168*	.095	.142*	.099	.146*
Number of Awakenings (A)	.073	.122	.177**	.110	.167*	.150*	.113
% Sleep (A)	-.029	-.135*	-.172*	-.106	-.125	-.075	-.140*
Age	-	-.098	-.070	.014	.069	-.147*	.147*
Weight (lbs.)	-.098	-	.871**	.846**	.334**	.288**	.260**
Body Mass Index	-.070	.871**	-	.814**	.339**	.317**	.228**
Systolic BP	.069	.334**	.339**	.257**	-	.689**	.166*
Diastolic BP	-.147*	.288**	.317**	.276**	.689**	-	.054

Note: A= Actigraph, S= Self-report; *p<.05 (2-tailed), **p<.01 (2-tailed)

Table 4 Correlations between Sleep, Pain, Anthropometric, and Biomarker Variables in Non-Achievers (n=118) and Achievers (n=103) at 6 Months

Variable	Age		Weight		Body Mass Index		Waist Circumference		Systolic BP		Diastolic BP		Pain Interference	
	Non-Achiever	Achiever	Non-Achiever	Achiever	Non-Achiever	Achiever	Non-Achiever	Achiever	Non-Achiever	Achiever	Non-Achiever	Achiever	Non-Achiever	Achiever
Sleep Quality (S)	0.073	0.168	-015	-.207	-.054	-.101	.041	-.173	-.103	-.082	-.193	-.032	-.340**	-.339**
Sleep Disturbance Score (S)	-0.027	-0.094	.016	.105	.029	.029	-.002	.089	.155	.057	.187	.019	.462**	.371**
Pain Interference Score (S)	.188	0.085	.184	.263**	.155	.212	.129	.315**	.173	.090	.042	-.011	-	-
Total Sleep Time (A)	0.04	0.014	-.010	-.120	-.111	-.051	.015	-.100	.078	-.009	.086	.004	.145	-.055
Wake After Sleep Onset (A)	0.104	-0.057	.020	.216	.071	.261**	.009	.140	.165	.091	.099	.071	.244**	.009
Number of Awakenings (A)	0.141	-0.018	.017	.150	.038	.258**	-.016	.145	.195	.081	.157	.085	.197	-.031
% Sleep (A)	-0.099	0.054	-.017	-.248**	-.078	-.270**	-.008	-.176	-.139	-.090	-.064	-.063	-.218	-.038
Age	-	-	-.096	-.166	-.096	-.104	-.005	-.009	.066	.054	-.206	-.110	.188	.085
Weight (lbs)	-0.096	-0.166	-	-	.811**	.863**	.736**	.880**	.339**	.168	.270**	.131	.184	.263**
Body Mass Index	-0.096	-0.104	.811**	.863**	-	-	.681**	.842**	.346**	.165	.325**	.129	.155	.212
Systolic BP	0.066	0.054	.339**	.168	.346**	.165	.217	.118	-	-	.650**	.695**	.173	.090
Diastolic BP	-.206	-0.11	.270**	.131	.325**	.129	.239**	.137	.650**	.695**	-	-	.042	-.011

Note: A= Actigraph, S= Self-report **p<.01 (2-tailed) due to potential collinearity (SP) between variables

Table 5 Ordinary Least Squares Regression Predicting Change from Baseline to 6 Months in Self-reported Sleep Disturbance (PROMIS) (N=221)

Predictor Variables	Unstandardized B	Standardized β Coefficient	t
Age (baseline)	-.045	-.051	- .719
Arthritis (baseline)	-1.068	-.078	-1.089
Weight Change	.163	.173	2.489*
Pain Interference Change	.142	.171	2.476*
Adjusted R^2 = .061, F(4, 214) = 4.316 p=0.002			

*p<.05 (2-tailed)

CHAPTER IV: Manuscript #3

Submitted to Research in Nursing and Health

Factors Associated with Potentially Inappropriate Medication Use

In Rural Community-Dwelling Older Adults

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Abstract

Taking potentially inappropriate medications (PIMs) is a serious public health problem in older adults. The use of PIMs may lead to adverse events and increased health costs. The purpose of this study was to explore the prevalence, characteristics, and factors associated with the use of PIMs in rural, community-dwelling older adults. Participants (N=138) underwent one-on-one reviews of all prescribed and over-the-counter medications, vitamins, and supplements. The 2012 Beers Criteria were used to record PIMs to avoid. Data were collected on participants' demographics, subjective physical and mental health, sleep, and objective sleep-wake patterns. Almost half (49%) of the sample used both prescribed and over-the-counter (OTC) PIMs in the past month. Prescribed and OTC non-steroidal anti-inflammatory drugs (33%) and medications with anticholinergic properties (28%) were the most frequently used PIMs taken by participants. The participants also took short-acting benzodiazepines. The use of PIMs was associated with higher number of medications (r=0.331, p<0.01), more medical providers (r=0.223, p<0.001) and poor physical health (r=-0.193, p<0.05). More medications was the only significant predictor of an increased probability of the use of PIMs, OR 1.8, 95% CI [1.19, 2.84]. Results highlight the importance of monitoring community-dwelling older adults taking multiple medications because they may be taking PIMs. As primary health provider shortages loom in rural areas, interventions need to include health care team collaboration to systematically reduce the prescribing and OTC use of PIMs.

Keywords: Rural, Older adults, Medications, Sleep, Actigraphy

Introduction

Older adults are at risk for using potentially inappropriate medications (PIMs) (Weng et al., 2013). A PIM is any pharmaceutical product, prescription or over-the-

counter (OTC) that has been determined to have risks that outweigh benefits (Beers, 1997). PIMs use has been studied over two decades in terms of health provider prescribing patterns. The use of PIMs has been associated with adverse drug events (ADEs), defined as any injury resulting from a pharmacological medical intervention. An ADE can be comprised of medical errors, adverse drug reactions, allergic reactions, and overdoses (Institute of Medicine, 2007; Kohn, Corrigan, & Donaldson, 2000).

An estimated 42.6% of community-dwelling older adults are prescribed PIMs, the most frequent being non-steroidal anti-inflammatory drugs (NSAIDS) and anticholinergic medications (Davidoff et al., 2015; Kachru, Carnahan, Johnson, & Aparasu, 2015). The use of 5 or more medications has been reported to increase the risk of taking PIMs and several PIMs can be purchased OTC without health care provider prescription or knowledge (Maher, Hanlon, & Hajjar, 2014).

The Beers Criteria is an example of a resource derived from scientific evidence associating PIMs use with the risk of negative health outcomes. The 2012 Beers Criteria lists 53 medications or medication classes that are divided into three categories: recommended medications and classes to avoid in older adults, medications and classes to avoid in older adults with certain diseases, and finally medications to be used with caution in older adults (American Geriatrics Society 2012 Beers Criteria Update Expert Panel, 2012).

Older age (65 and older), female gender, and the use of a higher number of medications have been associated with PIMs use (Guaraldo, Cano, Damasceno, & Rozenfeld, 2011). Among rural older adults, Blalock and colleagues, (2005) found that greater medication needs, lower social support, higher levels of disability, and being diagnosed with chronic conditions such as osteoarthritis were associated with greater PIMs use. The use of PIMs in rural communities (population less than 50,000) also was associated with a lack of geriatric care providers (Blalock et al., 2005; Dall et al., 2013;

National Conference of State Legislatures, 2013). In community-dwelling older adults, the likelihood of the use of potentially inappropriate anticholinergic medications was increased in females, those residing in southern states, and the presence of an anxiety disorder (Kachru et al., 2015). Health care providers may not be aware of their patients OTC drug use at home (Chui, Stone, Martin, Croes, & Thorpe, 2014; Torrible & Hogan, 1997). Factors such as these could lead to inappropriate management of medications and chronic diseases in rural settings.

In the U.S., older adults comprise 18% of residents in rural counties versus 12% in urban settings. The age distribution of counties has a tendency to get older along with rural (National Rural Health Association, 2014; NORC Walsh Center for Rural Health Analysis, 2014). Special attention should be given to the health of older adults living in rural areas. In Nebraska, one-third of residents live in rural counties and an estimated 34% of inhabitants of rural counties are 60 years and older (Department of Health and Human Services DHHS, 2015). In comparison to urban settings, older adults in rural settings have higher rates of chronic illness, poorer overall health, and less access to care (National Conference of State Legislatures, 2013; National Rural Health Association, 2014).

The health experience of rural dwelling older adults is manifested by multiple co-morbidities, managing symptoms of disease, and seeking health care from multiple providers (Arcury et al., 2012). Rural dwelling older adults rest, reduce activities, and take OTC medicine to manage co-morbidities and symptoms of disease (Arcury et al., 2012). Pain may promote the use of prescribed or OTC non-opioid medications. An Australian study reported the mean length of duration of prescribed treatment of pain with non-steroidal anti-inflammatory drugs (NSAIDs) was almost 5 years (Gnjidic et al., 2014). Long-term use of prescribed or OTC NSAIDs is potentially inappropriate and

needs to be carefully considered and monitored in older adults (Barkin et al., 2010; Findley & Bulloch, 2015; Gnjidic et al., 2014).

The use of PIMs in older adults may be associated with poorer physical and/or mental health status. U.S. older adults who used inappropriate prescription medications were more likely to report poorer health status than those not using PIMs (Fu, Liu, & Christensen, 2004). Use of PIMs also was common in a sample of community-dwelling older adults with perceived depressive symptoms in New Zealand (Lee et al., 2013).

Approximately 50% of older adults experience sleep-wake disturbances that are associated with factors such as pain or medication use for chronic illness (Ancoli-Israel, 2009; Foral, Knezevich, Dewan, & Malesker, 2011; Martin, Tamblyn, Ahmed, & Tannenbaum, 2013). Sleep quality and sleep-wake disturbances are often overlooked in association with health status and older adults do not routinely report sleep problems to their providers (Ancoli-Israel, 2009; McCall, 2004; Ohayon, 2002).

Some individuals seek sedative-hypnotics from primary care providers and others self-medicate with alcohol or OTC sleep aids with or without the knowledge of a health care provider (Basu, Dodge, Stoehr, & Ganguli, 2003). Sleep problems have been associated with the use of medications that promote sedation, have anticholinergic properties, and are potentially inappropriate for older adults (Ancoli-Israel, 2005; Ancoli-Israel, 2009; Lee et al., 2013; Radcliff et al., 2015; Steinman, Handler, Gurwitz, Schiff, & Covinsky, 2011). Medications for insomnia are more likely to be used by older adults with high income and who take other medications with sedative effects (Bertisch, Herzig, Winkelman, & Buettner, 2014). Self-reported physical and/or mental health and sleep have not been routinely explored as factors associated with the use of PIMs.

Therefore, the purpose of this study was to explore the use of, along with the factors associated with, the use of PIMs in rural community-dwelling older adults ≥ 65 years old. The specific aims were to 1) Describe the use of PIMs to avoid and 2) Explore

individual demographic characteristics (age, gender, income, education, and rural home location), health experience (comorbidity, number of medications and health providers), and health status factors (physical and mental function, sleep disturbance, sleep quality, and 24 hours sleep-wake patterns) as predictors of use of PIMs to avoid.

Methods

Design and Conceptual Framework

This study used an exploratory descriptive study design. A derivative of Cox's Interaction Model of Client Health Behavior (IMCHB) guided the study (Cox, 1982). Cox's IMCHB is a middle range nursing theory that characterizes interactions that occur between client singularity, client-professional interaction, and health outcomes. Figure 1 displays how the IMCHB was adapted for this study. The model included concepts that examined the relationships between client singularity variables and a single health outcome.

Sample/Setting

A convenience sample of older adults was recruited from a rural family practice clinic in the Midwest. The rural setting was determined according to rural urban commuting area (RUCA) codes 7 and 10. Participants were screened according to inclusion and exclusion criteria. Inclusion criteria: males and females ≥ 65 years of age; taking ≥ 3 prescribed medications, living independently in the community, responsible for personal medication regimen, able to physically complete questionnaires, read and speak English, not taking medications for cognitive impairment, and scoring ≥ 26 on the Montreal Cognitive Assessment (MOCA) (Nasreddine et al., 2005).

Measurements

Demographic Characteristics. Demographic data included age, gender, education, zip code, marital status, and household income.

Health Experience. Participants were asked about the number of medications taken as well as their current number of health providers. Medications taken in the last month included: prescribed, OTC, herbal, vitamin, and supplements. Names of drugs, dosage, frequency, and length of use were verified with patient records. Additional information such as routine for taking medications and pharmacies were recorded. Medical diagnoses were recorded from each participant's medical records. The Charlson Comorbidity Index was used to assess comorbidity (Charlson, Pompei, Ales, & MacKenzie, 1987). The index is weighted and takes into account the number and the seriousness of comorbid diseases and age. Comorbidities are associated with the risk of dying. Scores are assigned for each condition and the age of the individual, and then summed to predict mortality. In the original index 19 conditions were included that are scored from 1 through 6; additional points are added for age with 1 point for each decade over the age of 40. (Charlson, Szatrowski, Peterson, & Gold, 1994). Higher scores are indicative of higher severity of comorbidity. The index has established validity (Deyo, Cherkin, & Ciol, 1992).

Health Status. The 12-Item Medical Outcomes Survey (MOS) Short Form (SF-12) was developed to describe patient-reported physical and mental health status and to measure health related quality of life (QOL). The SF-12 is a comprehensive and shorter version of the SF-36 that measures physical and mental component scores (PCS and MCS). SF-12 summary scores (PCS and MCS) range from 0 to 100 and higher scores indicate better health. Age may influence norms and scores in those 65 and older have been reported as a PCS of 43.4 and MCS of 55.2 (Ware, Kosinski, & Keller, 1996). The tool has established reliability and validity in the older adult (Cernin, Cresci, Jankowski, & Lichtenberg, 2010; Jakobsson, 2007). The PCS and MCS demonstrated Cronbach alphas of 0.77 and 0.73 in this study.

Sleep was measured using both subjective and objective instruments. The Pittsburgh Sleep Quality Index (PSQI) measures perceived sleep quality. The tool contains 19 self-response items and five questions related to the bed partner that were not included in analysis. The PSQI responses are grouped into seven component scores; each weighted equally on a 0-3 scale, and summed to obtain a global score. The global score can range from 0 to 21 points with high scores indicating poor sleep quality. As recommended by developers, the global scale has a cut-off score $\geq$ 5 to indicate poor sleepers. The PSQI subjectively measures sleep quality, sleep duration, sleep latency, sleep disturbances, daytime dysfunction, habitual sleep dysfunction, and sleep medication use (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). This tool has demonstrated reliability and validity in the older adult (Spira et al., 2012) and Cronbach's alpha was 0.74 in this study.

The Patient Reported Outcomes Measurement Information System (PROMIS)-Sleep Disturbance SF-8A is a patient-reported sleep measure developed in partnership with the National Institutes of Health (Cella et al., 2010). The questionnaire contains 8 items for sleep disturbance and sleep-related impairment. A score of 50 is considered average for the U.S. general population and scores can be above or below the mean (standard deviation = 10). T-scores above 50 indicate poor sleep. The PROMIS short form was shown to have greater measurement precision than the PSQI (Yu et al., 2011). No published report of this measurement was found in studies in community-dwelling older adults. The Cronbach's alpha was 0.88 in this study.

Sleep-wake patterns were measured by wrist actigraphy. The wrist GT3X wrist actigraph by Actigraph ® (Pensacola, FL) is a non-invasive method of indirectly estimating sleep-wake and activity-rest patterns (Actigraph, 2016). The device is small and similar to a watch worn on the non-dominant wrist. It records a digitally-integrated measure of gross motor activity used to visualize activity-rest patterns and to quantify

physical activity or sleep (de Souza et al., 2003). Actigraph monitors have demonstrated reliability in the older adult (Rowe et al., 2008).

In this study, total sleep time (TST), wake after sleep onset (WASO), and wake percent were examined as sleep-wake parameters from the actigraph (Berger et al., 2008). TST is the number of minutes of actual sleep while in bed and WASO minutes are the amount of time spent awake after the initiation of sleep (Schutte-Rodin, Broch, Buysse, Dorsey, & Sateia, 2008). Wake percent is the ratio of TST to the amount of time spent in bed divided by 100. Normal values are considered 7-9 hours for TST, less than 30 minutes or 10% of time in bed for WASO, and a wake percent of 15% or less. Values not within normal limits may indicate sleep disturbance (Berger et al., 2005). Participants wore the actigraph for seven 24 hour cycles. Those participants with four or more nights of data were included in actigraphy analysis. Sleep data were analyzed using the Cole Kripke algorithm in the Actilife software by Actigraph ® (Pensacola, FL). The sleep diary in and out of bed times were used to assist with processing and analysis of the actigraph data.

Potentially Inappropriate Medications (PIMs). To identify the use of PIMs, prescribed and OTC medications were compared to the 2012 Beers Criteria. This study focused on medications and classes of medications to avoid in older adults. The criteria are based on a Delphi method of expert evidence base (American Geriatrics Society 2012 Beers Criteria Update Expert Panel, 2012). All prescribed, OTC home medications and supplements taken within the past month were reviewed and recorded by the first author. Medications to be used with caution were not included for analysis. Chronic medication use was defined as the weekly use of a medication for the past 3 months. Next, the first author categorized each medication as PIMS or non-PIMS on an investigator-derived PIMs log. The final step was to review each medication (PIMS vs.

non-PIMS) with a pharmacist with expertise in geropharmacology. The medications were discussed until consensus was achieved at 100% agreement.

Procedures

Approval of the study was obtained from the Institutional Review Board. After enrollment, each participant was taught how to complete the questionnaires, sleep diary, properly wear the wrist actigraph, and given instructions on what to bring to the clinic for the follow-up visit. Participants were reminded to bring all prescribed, OTC medications, vitamins, and herbal supplements taken in the last month from home in the red bag(s).

After 1 week, participants returned the binder of completed questionnaires, sleep diary, wrist actigraph, and red bag(s) of home medications, vitamins, and supplements. Private space in the medical clinic was used for the investigator to conduct in-person medication reviews and record medications in the red bag(s). Review questions included: how often the medication/vitamin/supplement was taken, how long taken, and for what diagnosis. Participants were specifically asked about the duration of use for pain medications and if they use substances such as caffeine or alcohol that may interfere with pharmacokinetics. Allergies and history of ADEs also were assessed. All medications, vitamins, and supplements were returned to the participant along with information about medication safety and a $25 gift card. Participants' primary care providers were updated on each person's home medications.

Statistical Analysis

An a priori conservative sample size and power analysis was performed based on aim 2 using the SF-12 PCS. Since PCS is a continuous predictor and the response variable (PIMS use: yes vs no) is categorical, determining power and sample sizes in this case would be equivalent to determining power and sample sizes for a two-sample

two-sided t-test, comparing 2 groups (PIMS use: yes vs no) with respect to the continuous variable PCS.

The following estimates were used for the PCS means and standard deviations of the two groups: Group 1 (Mean = 35, SD = 8); and Group 2 (Mean = 40, SD = 10). The null hypothesis (Ho) in this case is that the population means for both groups were equal to 35, against the alternative hypothesis (Ha) that one mean is 35 whereas the other is 40, with the respective standard deviations. The conclusion is that group sample sizes of n=53 (for a total of N=106) achieve 80% power to detect a difference of 5 between Mean=35 and Mean=40 with estimated group standard deviations of, respectively, 8 and 10, and with a significance level (alpha) of 0.05 using a two-sided two-sample t-test.

Statistical analyses were performed using the SPSS version 23 software package. For aim 1, PIMs were categorized according to the 2012 Beers Criteria and coded by dummy variables (yes=1, no=0). Descriptive statistics were conducted to determine the proportion of participants and category of PIMs in this sample. Independent samples t-tests were performed to compare variables in PIMs and non-PIMs users.

For aim 2, univariate descriptive statistics were performed to analyze variables of demographic characteristics, health experience, and health status factors. Demographic characteristics were coded as dummy variables (gender [male=1, female=2]; marital status [married or cohabitating=1, single or widowed=2]; highest education [high school graduate=1, college and above or trade school=2]; income [below poverty level=1, above poverty level=2]; home location [small rural town=7, rural=10]). The number of medications and health providers were counted and values were used from subjective questionnaires and actigraphy instruments. Chi square tests and point biserial

correlations were performed to explore relationships between variables. A less stringent p value of 0.20 was used to screen and explore potential relationships.

A binary logistic regression analysis was performed to determine which statistically significant variables predict the probability of the use of PIMs to avoid. The dependent variable was coded as PIMs use: yes=1 and no=0. The other numerical predictor variables were transformed into standardized form due to the variation of units. Overall model evaluation was performed. The Hosmer-Lemeshow test for logistic regression was performed to test the goodness of fit for the overall model. A p-value > 0.05 on the Hosmer-Lemeshow test indicates adequate model fit (Lemeshow & Hosmer, 1982). Due to the exploratory nature of the study, the threshold level of significance for individual predictors in the logistic regression was established at p<0.20. The results include relationships of significance and trend.

Results

Recruitment and Retention

During the recruitment period from January to October 2015, N= 141 older adults enrolled in the study. A total of 3 participants withdrew (2 for health reasons and 1 reconsidered their decision after completing the questionnaires). Missing data included: medical record (1), < 4 nights of complete actigraphy data (6), no data related to income (12), and highest education level (1).

Sample Characteristics

Sample characteristics are displayed in Table 1. Participants' mean age was 77 years old and they took a mean of 11.6 medications and supplements and had a moderately high mean comorbidity score of 4.6. Participants' mean body mass index was 30.5, indicative of obesity.

As seen in Table 2, the mean physical component score was 38.7 and mental component score was 53.2. These data indicate poorer self-reported physical and

mental health than expected for adults ages ≥65 years. The majority of participants (84%) reported moderate (27%) to extreme (28%) interference from pain in the past month that interfered with normal work. The PROMIS score of 46.9 reflected sleep disturbance no different than the norm but the mean PSQI score of 6.5 indicated poor sleep quality. Per actigraphy, TST, and wake percent were within normal limits; however mean WASO minutes per night (50.6) was slightly more than 10% of TST (456 minutes).

PIMs Use

The prevalence of the use of PIMs to avoid was 49%; 32% of the sample used at least one and 17% used 2 or more PIMs. Of the participants who took PIMs, 51% used prescribed PIMs; 24% used OTC PIMs; and 25% used both prescribed and OTC PIMs. Table 3 lists the frequency of the common classifications of PIMs taken by individuals in this sample. NSAIDS, medications with anticholinergic properties, short acting benzodiazepines, and non-benzodiazepine receptor agonists were the most frequently used PIMs. Of the anticholinergics, antihistamines were used most often and acquired OTC. Of the NSAIDs, the majority also were acquired OTC.

Independent-samples t-tests were conducted to compare variables in PIMs and non-PIMs users. PIMs users were more likely to have lower physical component scores [M=36.8, SD=8.9; t (136) =-2.2, p = 0.024; versus M=40.6, SD=10.3] indicating poor physical health, more health providers [M=2, SD=0.9; t (136) =2.6, p =0.009; versus M=1, SD=0.8], and higher number of medications [M=13, SD=5; t (136) =4.0, p =0.001; versus M=10, SD=4]. There was a trend toward significance for PIMs users to have higher PSQI scores [M=7.1, SD=3.7; t (136) =1.8, p=0.065; versus M=6, SD=3.2] indicating poorer sleep quality. The use of PIMs was no different based on gender, age, education, or income (p> 0.05).

As shown in Table 4, several significant relationships were found between PIMs and the client singularity variables. Higher use of PIMs was associated with higher

number of medications, seeing more providers, poor physical health, and poor sleep quality (p< 0.20). The use of PIMs was not associated with comorbidity, mental health, self-reported sleep disturbances, or objective sleep or wake parameters (p>0.05).

Predictors of PIMs Use

As seen in Table 5, a logistic regression analysis was conducted to predict the probability of use of PIMs. The number of medications, number of providers, physical component score, and PSQI were chosen as client singularity predictors. The overall model was examined for fit and 17% of the variance of the use of PIMs was explained by this model. Higher number of medications was the only significant predictor of the increased probability of the use of PIMs. Every increase in 1 count of medication increased the odds of the use of PIMs by 1.8 or 85%, 95% CI [1.19, 2.84].

Discussion

The main result was that the use of PIMs to avoid was prevalent among this sample of rural community-dwelling older adults. A rate of 49% of the participants took at least one PIM, which is higher than the national estimated prevalence of 42%. Consistent with national results, the participants frequently used NSAIDs and medications with anticholinergic properties (Davidoff et al., 2015; Kachru et al., 2015). The use of PIMs was associated with use of higher number of medications, higher number of health providers, and poor self-reported physical health. Higher number of medications was the single significant predictor of an increased probability of the use of PIMs. The following discussion will focus on results, implications for research, practice and conclusions.

Prior studies of the use of PIMs have focused on the prescribing patterns of health care providers. Half of the older adults in this study took prescribed PIMs. Prescriptions are written based on patient status and provider expertise. The benefit may outweigh the risk and the prescribing of PIMs may be the only viable treatment option.

The prevalence of prescription PIMs use may reflect the pharmaceutical management of chronic illness in rural areas that may be associated with obesity such as pain (National Conference of State Legislatures, 2013; National Rural Health Association, 2014). Community-dwelling older adults also contribute to the prevalence rates of the use of PIMs. PIMs users took both prescribed and OTC PIMs. Consistent with Arcury et al. (2012), independent participants seem to take OTC medicine to manage symptoms of disease.

Pain was a common symptom; it was not surprising to find participants frequently using PIMs with anti-inflammatory properties. Most NSAIDs were obtained OTC and this finding highlights the importance of provider pain assessment and prevention of long-term NSAID use. The long-term use of NSAIDs is discouraged because it may lead to gastrointestinal injury, fluid retention, renal failure, and increased bleeding time in older adults (Gnjidic et al., 2014). Recommendations may be necessary for anti-inflammatory medications similar to the new recommendations that warn of acetaminophen toxicity (Kennelty, Parmelee, & Wilson, 2015).

In this study, use of PIMs was associated with poorer physical health, but not mental health, similar to findings reported by Fu et al. (2004). Compared to urban settings, individuals in rural areas are less likely to report or have access to mental and behavioral health specialists (Thomas, Macdowell, & Glasser, 2012). Older adults may not be routinely prescribed PIMs for the treatment of mental or behavioral health. In addition, there are few OTC medications for behavioral health and older adults may be seeking supplements that are not included on the Beers Criteria.

The use of PIMs was associated with a higher number of medications and visiting or seeing or seeking treatment from more health providers. Unlike previous studies, no association was found between PIMs use and age, gender, income, or comorbidity (Blalock et al., 2005; Guaraldo et al., 2011; Kachru et al., 2015). The

majority of participants in this study had incomes above poverty level guidelines and comorbidity has not been measured routinely making it difficult to compare with published studies. When compared to Blalock and colleagues (2005), participants in this study had a higher mean severity of comorbidity and this may be one reason for the difference in the prevalence of the use of PIMs.

Objective measurement by actigraphy showed sleep quantity to be within normal limits. Similar to previous studies, older adults self-reported poor sleep quality and use of PIMs to help them relax or improve their sleep (Ancoli-Israel, 2005; Ancoli-Israel, 2009; Lee et al., 2013; Radcliff et al., 2015; Steinman et al., 2011). Consistent with Bertisch and team (2014) and Basu et al. (2003), medications with benzodiazepine properties were prescribed to promote sleep. In this study, participant use of OTC sleep aids with anticholinergic properties and prescribed benzodiazepines are of concern. Medications with sedative and anticholinergic properties cause falls, dry mouth, dry eyes, dizziness, confusion, constipation, and increase the risk of delirium and dementia. Sleep problems may be perceived as an inevitable result of aging by older adults or health care providers and patients may have ambivalent feelings towards taking medications to promote sleep. Nevertheless, OTC medications are filling the void. With NSAIDs and medications with anticholinergic properties readily available for use OTC, health care professionals need to partner with patients to ensure safe medication management.

Higher number of medications was the only significant predictor for an increased probability of PIMs use. Consistent with Maher and colleagues (2014), polypharmacy increased the chance of using PIMs. This relationship highlights the necessity for all health care professionals to closely monitor older adults taking multiple medications.

Strengths and Limitations

This study was the first to use Cox's nursing model to describe factors associated with the use of PIMs to avoid. The model was beneficial for demonstrating

the role of client singularity in the use of PIMs. An individual's health experience and

their health status (self-reported physical health and sleep quality) were associated with

the use of prescribed and OTC PIMs. The use of Cox's model may be helpful in the

development of nursing interventions to reduce the use of PIMs.

Most prior studies of PIMs have been conducted in acute or long-term care

settings with minimal information about rural community-settings. A modest sample of

rural older adults was obtained to explore the concepts. An additional strength is that

medications were recorded from the participants' actual medication and supplement

bottles, instead of the medical record or patient lists. PIMs were reviewed with a

pharmacist with expertise in geropharmacology. Indirect objective measures of sleep-

wake patterns were recorded in addition to self-reported sleep. Actigraph measures

were complete for analysis because 94% of participants wore the actigraph for the

duration of the study.

In addition to strengths, the study also had limitations. Generalizability is limited

because the convenience sample was small and mostly Caucasian. Participants were

from a Midwest farming community, from one clinic in one rural small town and selection

bias may have occurred. Although patients stated they brought in all medications and

supplements for review, it is possible that participants may not have brought all

medications taken in the last month.

Implications for Nursing Research and Practice

There are several implications for research on PIMs and optimized use of

medications in rural community-dwelling older adults. The use of PIMs needs to be

evaluated using a standard method such as the Beers Criteria. Prospective work could

explore PIMs in multiple outpatient settings and medical specialties. Studies need to be

conducted in more diverse samples of older adults (Colby & Ortman, 2015); particularly,

in rapidly growing rural populations such as the Hispanic Latino population.

Interventions not only need to be initiated by physicians or pharmacists but by multi-disciplinary teams including nurses. In the rural primary care setting, nurses can collaborate with the health care team to develop interventions to reduce and monitor the use of prescribed and OTC PIMs. Screening tools using updated versions of the Beers Criteria and patient-reported ADEs can be evaluated by health care staff in primary care clinics. Health researchers can test randomized controlled trials that promote a team intervention to reduce commonly used PIMs. Studies can compare non-pharmacological interventions to the use or tapering of a pharmacologic intervention.

All health care professionals need to consistently monitor medications. Initial nursing assessments can encourage alternative strategies for sleep problems and pain in older adults. Medication reconciliation has been encouraged, but medications need to be critically appraised. Medication appraisal needs to identify all PIMs in older adults engaged in polypharmacy and in poor physical health, paying close attention to current use and duration of NSAIDs use and medications with central nervous system and anticholinergic effects. A primary care protocol could promote:

- Regularly planned interactive medication reviews (nurse initiated with pharmacist available using Beers Criteria and evaluating all home prescribed and OTC medications, vitamins, and supplements).

- Assessment of patient pharmaceutical literacy; provision of patient education and resources (PIMs and ADEs).

- Mandatory follow-up phone calls to evaluate patients taking new medications or changes to regimen (blood pressure, blood sugar, hydration, CNS disturbances, falls, gastrointestinal disturbance).

Conclusion

PIMs use is a serious public health concern. This study confirmed that despite the evidence of risk, the use of prescribed and OTC PIMs to avoid is prevalent in rural

settings. The use of PIMs in rural community-dwelling older adults impacts the

patient/family and health care team. Health care professionals in rural primary care

settings need to collaborate with community-dwelling older adults to reduce the use of

PIMs.

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Figure 1. Research Model of Factors Associated with Potentially Inappropriate Medication Use in Community-Dwelling Older Adults adapted from Cox's Interaction Model of Client Health Behavior

Table 1. Sample Characteristics

Demographic Variables (N=139)				
Gender			Number of Participants	% of Participants
Male			78	56
Female			61	44
Home Location				
Small rural town			83	60
Rural area			56	40
	Mean/Median	SD		
BMI	30.5/29.3	6.3		
Age	77.7/78	7.3		
Young old (65-78)			51	37
Old old (79-99)			61	44
Race/Ethnicity				
Caucasian			137	98
Hispanic			1	1
Native American/Alaskan American			1	1
Marital Status				
Married/Cohabitating			101	74
Single/Widowed			36	26
Income (N=127)				
Under Poverty (10K and below)			4	3
Over Poverty			123	97
Refused Answer (12)				
Highest Education (N=137)				
12 Grade and Under			95	69
College or Trade School			43	31

Table 2. Sample Characteristics of Health Experience and Health Status Variables

Variable	Mean	SD
Health Experience		
Number of Medications	11.6	4.8
Charlson Comorbidity Index	4.6	1.5
Number of Providers	2.0	0.8
Health Status (N=139)*		
Physical Component Score (SF-12)	38.7	9.9
Mental Component Score (SF-12)	53.2	8.6
Subjective Sleep (N=139)*		
Sleep Disturbance (PROMIS SF8a)	46.9	7.8
Sleep Quality (PSQI Total)	6.5	3.5
Actigraphy (N=133)		
Total Sleep Time hours (TST)	7.2	0.9
Wake After Sleep Onset minutes (WASO)	50.6	27.8
Wake Percent	12.4	8.6

Normal Values of Physical Component Score: 43.4, Mental Component Score: 55.2 for those 65 and older, PROMIS Sleep Disturbance: 50, PSQI Total: less than 5, TST: 7-9 hours, WASO: less than 30 minutes or 10% of time in bed, Wake Percent: 15% or less

Note. * participants completed questionnaires only

Table 3. Characteristics of PIMs To Avoid (N=138)

	N	Number of Participants Using Medicines	% of Participants Using Medicine
One PIM	138	44	32
Two or More PIMs	138	23	17
Total PIMs use		67	49
Prescribed PIMs	67	34	51
Over the Counter PIMs	67	16	24
Taking Prescribed and Over the Counter PIMs	67	17	25
Classification of Most Common PIMS to Avoid*			
Anticholinergics	67	19	28
Antihistamines (84% of anticholinergics)	67	16	24
Prescribed (11% of antihistamines)	67	2	3
OTC (94% of antihistamines)	67	15	22
Skeletal Muscle Relaxants	67	2	3
Tricyclic Antidepressants	67	3	4
Alpha 1 Blockers	67	12	18
Short Acting Benzodiazepines	67	12	18
Non benzodiazepine Receptor Agonist	67	4	6
Estrogen	67	7	10
Non-Steroidal Anti-inflammatory Drugs (NSAID)	67	22	33
Prescribed (32% of NSAIDs)	67	7	11
OTC (68% of NSAIDs)	67	15	22
History of Falls with Benzodiazepines	67	6	9

Note. *several participants use more than one classification of PIMs to avoid

Table 4. Correlations between Demographic, Health Experience and Health Status Variables and use of PIMs (N=138)

Variable	PIMs to Avoid (r)
Age	0.004
Charlson Comorbidity	0.081
Number of Medications	0.331**
Number of Providers	0.223**
Physical Component Score (S)	-0.193*
Mental Component Score (S)	-0.031
Pittsburgh Sleep Quality Index (S)	0.158[†]
PROMIS Sleep Disturbance (S)	0.073
Total Sleep Time (A)	-0.102
Wake After Sleep Onset (A)	-0.027
Wake % (A)	-0.059

Note. A= Actigraph, S= Self-report, *p<0.05 (2-tailed), **p<0.01 (2-tailed), [†]trend for correlation p<0.20

Table 5. Summary of Binary Logistic Regression Analysis Predicting Probability of use of PIMs

Predictor Variables	Unstandardized B	Standard Error	Wald's X^2	Exponential β Odds Ratio	P value
Number of Medications	0.619	0.224	7.62	1.858*	0.006
Number of Providers	0.220	0.206	1.15	1.247	0.284
Physical Component Score	-0.154	0.202	0.58	0.857	0.446
Pittsburgh Sleep Quality Index	0.180	0.187	0.92	1.19	0.336

Note. Hosmer Lemeshow Test (H-L) model of good fit p>.05
Nagelkerke R^2 = .179, X^2(8)= 14.18 H-L p=.07, *p<.05 (2-tailed)

CHAPTER V: CONCLUSIONS AND DISCUSSION

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Summary

This dissertation study was developed from the progression of knowledge focusing on PIMs use in older adults. Components of this process included formalized coursework and application of this knowledge to scientific inquiry. The following paragraphs are a summary of the knowledge development previously presented in Chapters I-IV followed by a discussion on the dissertation results and findings.

Chapter I was an introduction of the scholarly activities presented in the dissertation. The goal of pharmacological management is to ease symptoms or alleviate disease. Treatment success may depend on patient adherence to the right medication, dosage, at the right time, and frequency. However a problem may arise when the older adult adheres to medications that may be inappropriate. Health professionals and older adults need to understand factors and outcomes associated with PIMs to avoid.

Chapter II presents an integrative literature review on PIMs use. As with any scholarly endeavor, I reviewed previously published literature about PIMs use in older adults. This process allowed me to examine how PIMs have been defined, measured, prospectively and retrospectively analyzed, and led to additional questions to address knowledge gaps. There are plenty of studies on the use of PIMs in long-term care and acute settings, but not in community-dwelling older adults. More studies need to examine the use of PIMs and PIMs to avoid in ambulatory or community-dwelling settings. The concept of PIMs use has not been extensively studied in independent older adults. This presents a problem in methodology of how PIMs are measured. In community-dwelling samples this is especially important because older adults not only take prescribed medications, but also OTC medications. In community-dwelling samples, researchers have examined PIMs operationally in terms of prescribed medications,

overlooking the reality that older adults are independent and may take other medications than what has been prescribed.

Existing studies have provided insight to the awareness and estimated prevalence of the problem of PIMs use. Studies exploring PIMs use have used large databases with lists of prescribed medications. Medication lists may not contain OTC medications, especially if the provider is unaware of their use. Independence of community-dwelling older adults is eliminated when studies only examine PIMs that are prescribed. Are there other factors that are associated with PIMs use that have not been explored? Factors that are associated with PIMs use may be different based on individuality or client singularity factors. In community-dwelling older adults, PIMs use may be underestimated and thus needs to be explored in terms of concept. In addition, interventions have lacked a collaborative model including the patient and nurse as active partners in medication management with health care providers and pharmacists. Interventions targeting the provider or pharmacist may only be effective for prescribed medications, once again leaving out medications that can be purchased OTC in pharmacies, grocers, bulk supply, or online.

Chapter III described sleep and health-related factors in a sample of midlife and older rural women. Through this secondary analysis, I was able to observe the characteristics of specific factors of client singularity (i.e. demographics, sleep, and health status). Chronic conditions and their symptoms such as pain may be caused by poor sleep or cause poor sleep and the following questions arise. Is poor sleep properly managed or treated in this population? Do these individuals self-manage poor sleep? In order to globally capture sleep characteristics and their association with other variables, both subjective and objective instruments are needed. Sleep characteristics are associated with several health-related factors, thus sleep behavior is an important

element in health. The use of nurse-led non-pharmacological interventions may successfully influence patient behavior and lead to improved sleep and physical and mental health.

Building on the knowledge from the integrative review and secondary analysis, I was able to identify possible client singularity factors of independence from Cox's Interaction Model of Client Health Behavior were associated with and predictors of PIMs use in rural community-dwelling older adults. Chapter IV presents the third manuscript for this dissertation study that descriptively analyzed use of PIMs to avoid in rural older adults. Specific aims of the manuscript were:

1) Describe the use of PIMs to avoid in rural community-dwelling older adults ≥ 65 years.

2) Explore individual demographic characteristics (age, gender, income, education, and home location), health experience (comorbidity, number of medications and health providers), and health status factors (physical and mental function, sleep disturbance, sleep quality, and 24 hour sleep-wake patterns) as predictors of use of PIMs to avoid.

An additional manuscript is based on the results of the third aim of the dissertation study. Results can be found in the Appendix A. The third specific aim was:
3) Examine individual demographic characteristics, health experience, health status, and use of PIMs to avoid as predictors of patient-reported ADEs.

The following paragraphs summarize major findings discussed in Chapter IV.

Conclusions and Discussion

Published evidence suggests the need to limit the use of potentially inappropriate medications (PIMs) in older adults. Aim 1 was to describe the use of PIMs in rural community-dwelling older adults ≥ 65 years.

The use of PIMs to avoid was prevalent among this sample of rural community-dwelling older adults. Participants took PIMs at a higher prevalence rate than the national estimated prevalence. Consistent with national results, there was frequent use of NSAIDs and medications with anticholinergic properties (Davidoff et al., 2015; Kachru, Carnahan, Johnson, & Aparasu, 2015). The use of PIMs to avoid was associated with several client singularity factors but higher number of medications was the only significant predictor of an increased probability of PIMs use. The following discussion will focus on the results, conclusions gained from this study, and implications for future research and practice.

The use of prescribed PIMs is important but should not be the primary focus of study in independent older adults. Half of the older adults in this study took at least one prescribed PIM. Providers are prescribing medications that may have more risk than benefit in rural community-dwelling older adults. Older adults in this study had moderate severity of comorbidity, were obese, and had lower than normal self-reported physical and mental health. The high prevalence of prescription PIMs use may reflect the pharmaceutical management of chronic disease in rural areas (National Conference of State Legislatures, 2013; National Rural Health Association, 2014). Community-dwelling older adults in this sample also contribute to the prevalence rates PIMs use. Participants took prescribed and OTC, or primarily OTC PIMs. Consistent with findings by Arcury et al. (2012), participants take OTC medicine to manage symptoms.

Pain was a common symptom; therefore it was not surprising to find the high frequency of participants using PIMs with anti-inflammatory properties. Most of the NSAIDs were obtained OTC and draws attention to the importance of provider pain assessment and prevention of long-term NSAID use. As observed in the study by Gnjidic et al. (2014), long-term use of NSAIDs is discouraged because of the risk of adverse

events. Recommendations may be necessary for anti-inflammatory medications that are similar to warnings associated with acetaminophen toxicity (Kennelty, Parmelee, & Wilson, 2015).

As previously reported, PIMs use was associated with lower physical health (Fu, Liu, & Christensen, 2004). Although older adults tend to score normal on the mental component and poorer on physical component, both were lower than norms for adults ages 65 and older (Ware, Kosinski, & Keller, 1996). No association was found between PIMs use and mental health. This result could be explained by the lack of OTC medications for mood and limited mental and behavioral health specialists in rural areas (Thomas, Macdowell, & Glasser, 2012). The use of PIMs was associated with a higher number of medications and health providers but not with age demographic, gender, or comorbidity (Blalock et al., 2005; Guaraldo, Cano, Damasceno, & Rozenfeld, 2011; Kachru et al., 2015). These results could be explained by the small sample size and incomes above poverty levels. Income was analyzed based on falling above or below federal poverty level guidelines; this may limit our ability for comparison with published literature. Also, comorbidity has not been consistently measured for comparison to previous studies.

Although sleep disturbance was no different than the norm, participants had high minutes awake after falling asleep and poor self-reported sleep quality. Higher minutes awake after falling asleep in this sample may be related to nocturia. Sleep-wake parameters using actigraphy were within normal limits but older adults reported poor sleep quality; consistent with findings from (McCrae et al., 2005).

The use of prescription and OTC sleep medications by this sample is consistent with the sample in the national report (Basu, Dodge, Stoehr, & Ganguli, 2003; Bertisch, Herzig, Winkelman, & Buettner, 2014). Participants in this rural sample used sleep

medications with benzodiazepine and anticholinergic properties that are of concern due to their risk for causing ADEs (Ancoli-Israel, 2005; Ancoli-Israel, 2009; Lee et al., 2013; Radcliff et al., 2015; Steinman, Handler, Gurwitz, Schiff, & Covinsky, 2011). As NSAIDs and medications with anticholinergic properties continue to be available OTC, the use in older adults needs to be monitored.

Aim 2 was to explore individual demographic characteristics (age, gender, income, education, and rural home location), health experience (comorbidity, number of medications and health providers), and health status factors (physical and mental function, sleep disturbance, sleep quality, and 24 hour sleep-wake patterns) as predictors of PIMs use.

A regression model was fit to determine predictors of increased probability of the use of PIMs. Higher number of medications was the significant predictor for increased probability of the use of PIMs to avoid. This relationship highlights the necessity to monitor older adults with polypharmacy. Consistent with Maher, Hanlon, & Hajjar (2014) polypharmacy increases the chances of using PIMs, therefore older adults' medications need to be routinely evaluated. Health care professionals need to continuously appraise medications older adults are taking, particularly if they are taking three or more prescribed and OTC medications and supplements. In rural community-dwelling older adults, PIMs use is not only based on the behavior of the prescribing provider; the patient plays also plays a role. As shown by the model, client singularity is an important factor in the use of PIMs. Multi-disciplinary models may guide screening of medications with the patient, in order to promote appropriate medication use behaviors and monitoring of medication management.

Aim 3 was to examine individual demographic characteristics, health experience, health status, and PIMs use as predictors of patient-reported ADEs.

An association was found between PIMs to avoid and patient-reported ADEs. Unlike previous reports, logistic regression results showed the use of PIMs to avoid was not a significant predictor of the increased odds of patient-reported ADEs (Chrischilles, VanGilder, Wright, Kelly, & Wallace, 2009; Lund, Carnahan, Egge, Chrischilles, & Kaboli, 2010). Although this study is unable to declare causality, a trend towards significance is logical. Patient-reported ADEs were CNS disturbances and dry mouth, events that could occur from the use of PIMs with benzodiazepine and anticholinergic properties.

The use of PIMs to avoid as a non-significant predictor was an unexpected finding because the Beers criteria were derived as a resource to prevent incidents such as ADEs. Similar findings have been reported in studies in patients admitted to acute settings (Budnitz, 2011; Hamilton, Gallagher, Ryan, Byrne, & O'Mahony, 2011; Laroche, Charmes, Nouaille, Picard, & Merle, 2007). Studies on PIMs and ADEs are difficult to compare due to a variety of conceptual and operational definitions and measurement.

Older age (79 to 99 years) did not increase the probability of patient-reported ADEs. Older adults may view an ADE as a part of a comorbid condition flare, or just wait to see if things improve. Younger age (65 to 78), lower physical health, and poor sleep quality were significant predictors of the increased odds of patient-reported ADEs. Older adults with lower physical health and poor sleep quality may be susceptible to alterations in pharmacokinetic and pharmacodynamics leading to ADEs (Bressler & Bahl, 2003). Older adults may not report a symptom, it is up to the health care team to frequently evaluate and assess pharmaceutical management. The use of PIMs to avoid showed a trend towards significance to increase the probability of patient-reported ADEs and health care professionals need to consider other aspects of health status when monitoring and evaluating ADEs in older adults.

Limitations

There were several strengths of this study. This study was the first to use Cox's nursing model (1982) to observe factors and outcomes associated with the use of PIMs to avoid. This study sampled rural older adults; a population that has been neglected in prior studies. Rural settings are commonly difficult to recruit and obtain a desired study sample, and this modest sample helped the exploration of the concepts. Community-dwelling older adults were observed, where most studies have assessed those who are hospitalized and or living in long-term care settings. This study is of importance as our baby-boomers are remaining independent in their homes or in community apartment-style settings. Medications were recorded using the participants' actual medication and supplement bottles instead of the medical record or patient lists. In addition to self-reported sleep characteristics, indirect objective measures of activity-rest and sleep-wake were measured. An expert pharmacist in geropharmacology reviewed the medications and patient-reported ADEs.

Despite the strengths, our study is not without limitations. First, a convenience sample that was small in size was used that limited generalizability of the findings. Sampling was performed from only one family practice clinic in one Midwestern rural small town, instead of multiple settings and towns. Selection bias may have occurred as well. Although patients stated that they brought in all medications and supplements for review, there is a chance they did not bring all medications. Furthermore, our study used self-report measures. The Naranjo Algorithm was not used to attribute the use of PIMs to avoid to ADEs, and all patient-reported ADEs could not be verified via medical record (Naranjo et al., 1981).

Implications

There are implications for additional research related to PIMs and optimized medication use in rural community-dwelling older adults. Additional prospective studies could explore the use of PIMs in large samples in outpatient settings and specialties where patients are 65 and older. Studies should not only characterize subjects by age group, but by "medical specialty" to explore if specific specialty clinics have a higher prevalence of the use of PIMs to avoid. Sample sizes need to be large. As our aging population becomes more diverse, studies need to include different ethnicities. It is estimated that the U.S. Hispanic Latino population will become the new majority minority and this population, in addition to the American Indian population, have comorbidities and gaps in care in rural areas.

Interventions not only need to be initiated by physicians or pharmacists but by nurses as well. Nurses can collaborate on a research team to develop interventions to monitor and reduce the use of PIMs to avoid and ADEs. Screening tools for health care staff using updated versions of PIMs, and patient-reported ADEs can be tested in primary care clinics. Interventions can be developed targeting those at risk for using PIMs (i.e. older adults with polypharmacy and poor health status). Randomized controlled trials can be led by nurse scientists that study non-pharmacological interventions that may influence sleep and pain and reduce PIMs use. Studies can compare non-pharmacological interventions to the use or tapering of a pharmacologic intervention.

The monitoring of medication needs to go beyond medication reconciliation, and promote appraisal. For instance, nurses can assess and notify the health care team on the current use and duration of NSAID use and medications with CNS and anticholinergic effects. Patients need to be monitored for anticholinergic burden from the use of multiple medications. Initial nursing assessments of sleep problems or pain in

older adults may encourage the use pain and sleep diaries to document characteristics of these symptoms. Nurses can promote the use of alternative strategies for problems with pain and sleep. Examples include topical pain preparations and sleep hygiene.

When a provider determines that a PIM is necessary, the nurse needs to contract close follow-up and evaluation of ADEs. Patients need to be educated about PIMs. If patients decide to use PIMs, they also need to be educated about ADEs to report. For example, educate about short term use and potential consequences of use (cardiovascular, cerebrovascular, renal, GI disturbances, dry mouth, dry eyes and impaired gait and risk for dementia) of NSAIDs or medications with CNS or anticholinergic effects. Health care providers need to communicate medication adjustments with specialty providers. Interprofessional teams in rural primary care clinics can develop protocols to manage polypharmacy and imbed updated Beers criteria into screenings. A culture of adhering to current pain and sleep-wake guidelines needs to be enforced in pharmaceutical management in the older adult (Barkin et al., 2010).

In order for these activities to take place, implications for education and policy need to be considered. In terms of education, nursing pharmacology courses need to be more in depth. The Beers criteria need to be included in course content where geriatric considerations are taught. Interprofessional concepts need to be linked into the curriculum to promote a team based approach to geriatric care. This includes pharmacological concepts, where resources such as the Beers criteria are applied in a consistent manner. Nurses may value how other health professions come to decisions about pharmaceutical management, and vice versa; with all developing a healthy respect to the knowledge and skill each profession brings to the team. The Beers criteria are used by the Centers for Medicare and Medicaid Services and insurance companies

to promote appropriate prescribing; however, in terms of policy follow-up has to be done to see if this has made an impact.

This study confirmed that despite the evidence of risk, PIMs use remains prevalent and may be underestimated. In particular, prescribed and OTC PIMs to avoid are being taken by rural community-dwelling older adults. Of notable concern are NSAIDs and medications with anti-cholinergic and sedative properties because of the increased risk of ADEs. Although causality could not be confirmed in our study several ADEs are similar to the effects reported to be caused by frequently used PIMs to avoid.

Chapters I through IV present the gradual building of nursing scholarly inquiry related to PIMs. The use of PIMs to avoid is associated with the number of providers, and self-reported poor physical health in independent older adults but the increased probability of the use of PIMs to avoid is predicted by a high number of medications. Patient-reported ADEs also are associated with client singularity variables but the increased probability is predicted by younger age (65 to 78), self-reported lower physical health, poorer sleep, and the use of PIMs to avoid. The use of PIMs to avoid in rural community-dwelling older adults is an issue that impacts the patient/family, pharmacist, nurse, and prescribing health care providers. The reduction of the use of PIMs to avoid and prevention of ADEs may require interventions that target both prescribing health care providers and independent older adult patients.

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APPENDIX A

Appendix A. Patient-Reported ADEs in Rural Older Adults

Abstract

Adverse drug events (ADEs) are a major contributing factor in the health and safety of older adults. Older adults may experience ADEs that they ignore or self-manage. This behavior can lead to a clinic, emergency or hospital visit, impacting health status and costs. The purpose of this study was to explore the characteristics and predictors of patient-reported ADEs in rural community dwelling older adults. Participants (N=138) underwent one-on-one reviews of all prescribed and over-the-counter medications, vitamins, and supplements. The 2012 Beers Criteria were used to record PIMs to avoid. Data were collected on participant's demographics, subjective physical and mental health and sleep, objective sleep-wake patterns, and patient-reported ADEs. One or more ADEs was reported by 48% of participants. The most frequently reported ADEs by participants were central nervous symptom disturbances (16%), dry mouth (12%), hoarseness, gastrointestinal irritation, and decreased libido (8%). Higher patient-reported ADEs were associated with poor sleep and poor physical health ($p<0.05$). Younger age (65 to 78), poor physical health, and poor sleep quality were significant predictors of an increased probability of patient-reported ADEs ($p<0.05$). These results suggest that health care professionals in rural areas need to use strategies to reduce ADEs in rural community-dwelling older adults. Interventions should engage patients and their families by specifically targeting older adults with poor health status, taking multiple medications, and using PIMs to avoid.

Keywords: Medications, Adverse Drug Events, Rural, Older adults

Introduction

The prevention of adverse drug events (ADEs) has become a national priority. An ADE is any injury resulting from a pharmaceutical intervention (Institutes of Medicine, 2007; Kohn, Corrigan, & Donaldson, 2000). Reports claim that ADEs result in high morbidity and medical expenditure and the estimates of outpatient ADEs vary with a higher incidence occurring in adults ages 65 and older (Bourgeois, Shannon, Valim, & Mandl, 2010). The estimated prevalence of ADEs related to prescribed medications in older adults has ranged from 18% to 30% (Chrischilles, VanGilder, Wright, Kelly, & Wallace, 2009; Tache, Sonnichsen, & Ashcroft, 2011). Literature is limited about ADEs among older adults in rural community settings because ADEs have primarily been studied in acute care settings (Pretorius, Gataric, Swedlund, & Miller, 2013).

Studies have examined the associations between ADEs and the use of specific medication classes. Community-dwelling older adults have reported adverse events, such as falls, when taking potentially inappropriate medications (PIMs) (Koyama, Steinman, Ensrud, Hillier, & Yaffe, 2014; Landi et al., 2007; Lukazewski, Mikula, Servi, & Martin, 2012; Martin, Tamblyn, Ahmed, & Tannenbaum, 2013). The chronic use of PIMs, such as non-steroidal anti-inflammatory drugs (NSAIDs), has been associated with negative gastrointestinal, renal, cardiovascular, cerebrovascular, and central nervous system events in older adults (Marcum & Hanlon, 2010).

Several studies have refuted the association between ADEs and PIMs use, and concluded that other medications are more of a risk. Other medication categories (i.e. cardiovascular, hypoglycemic, and anticoagulants) have been associated with over 27% of preventable ADEs in a sample of U.S. community-dwelling older adults (Davies & O'Mahony, 2015; Ducoffe et al., 2015; Gurwitz et al., 2003). Compared with other medications, the use of PIMs resulted in fewer emergency department visits for ADEs

(Budnitz, 2011). Other studies reported similar results among older patients admitted into acute care (Hamilton, Gallagher, Ryan, Byrne, & O'Mahony, 2011; Laroche, Charmes, Nouaille, Picard, & Merle, 2007).

ADEs in ambulatory older adults have been reported to be predicted by the use of a higher number of medications, warfarin, and benzodiazepine drugs (Gandhi et al., 2003; Hanlon, Schmader, & Semla, 2013; Pretorius et al., 2013). Several criteria such as the Beers Criteria have been created to help reduce the occurrence of ADEs by targeting PIMs. However, the predictive relationship between ADEs and the use of PIMs is complex. Older adults with multiple comorbidities were found to be at increased risk for ADEs in the ambulatory setting when taking non-opioid analgesics and diuretics (Field et al., 2004). Every increase in one count of inappropriately prescribed medication predicted an increase in the odds of an ADE (OR 1.13) (Lund, Carnahan, Egge, Chrischilles, & Kaboli, 2010). Another study found that those who used inappropriate medications had 2.14 increased odds of developing a self-reported ADE (Chrischilles et al., 2009). Unfortunately, studies have used differing methodologies to measure ADEs which may contribute to the varied results.

Rural community-dwelling older adults are using both prescribed and OTC medications to self-manage health conditions and symptoms (Shade, Berger, Chaperon, Haynatzki, Sobeski, Yates, 2016). A patient symptom could be an ADE that is undetected by health care providers because it is managed by the use of OTC medications and/or other self-care behaviors. Health care providers need to recognize and monitor for risks associated with all prescribed and OTC medications and supplements used by community-dwelling older adults.

PIMs use may be necessary in specific chronic conditions. More studies need to examine the relationship between patient-reported ADEs, PIMs use, and client-

singularity factors such as demographics and self-reported health-status, in rural community-dwelling older adults. Therefore, the dissertation study also examined patient-reported ADEs in rural community-dwelling older adults ≥ 65 years old. In addition to describing patient-reported ADEs, the third specific aim was to: Examine individual demographic characteristics, health experience, health status, and the use of PIMs to avoid as predictors of patient-reported ADEs.

Methods

The detailed methods and procedures are detailed in Chapter IV. The following paragraphs will briefly re-iterate the methods and procedures.

Study Design

This study used an exploratory descriptive study design guided by a derivative of Cox's Interaction Model of Client Health Behavior (IMCHB) (Cox, 1982). Client singularity factors of demographic characteristics, health experience, health status, and PIMs use were examined as predictors of the health outcome of patient-reported ADEs.

Study Sample/Setting

A convenience sample of older adults from a rural family practice clinic in the Midwest was recruited. The rural urban commuting area (RUCA) codes were used to classify rural status. Male and female patients were screened for participation according to inclusion and exclusion criteria.

Inclusion criteria were: men and women ≥ 65 years of age, living independently in the community, took ≥ 3 prescribed medications, scored ≥ 26 on the Montreal Cognitive Assessment (MOCA)(Nasreddine et al., 2005), and available during the data collection period. Exclusion criteria were: older adults not responsible for self-medication, inpatient in acute hospital or living in long-term care facilities, unable to

complete questionnaires, do not read and speak English, and currently taking

medications for cognitive impairment.

Measurements

Demographic Characteristics. Data were collected on participant's age,

gender, education, zip code, marital status, and household income.

Health Experience. Participants were asked about the number of medications

taken and their current number of health providers. Data on medications taken in the last

month included: prescribed, over the counter, herbal, vitamin, and supplements. Names

of drugs, dosage, frequency, and length of use were verified with patient records.

Additional information such as the routine for taking medications and pharmacies used

were recorded. Medical diagnoses were recorded from each participant's medical

records. The Charlson Comorbidity Index was used to assess comorbidity (Charlson,

Szatrowski, Peterson, & Gold, 1994; Charlson, Pompei, Ales, & MacKenzie, 1987).

Health Status. The 12-Item Medical Outcomes Survey (MOS) Short Form (SF-

12) was developed to describe patient-reported physical and mental health status and to

measure health related QOL (Ware, Kosinski, & Keller, 1996). The tool has established

reliability and validity in the older adult (Cernin, Cresci, Jankowski, & Lichtenberg, 2010;

Jakobsson, 2007). The Cronbach's alpha for this study was 0.82.

Sleep. Sleep was observed using both subjective and objective instruments. The

Pittsburgh Sleep Quality Index (PSQI) and Patient Reported Outcomes Measurement

Information System (PROMIS)-Sleep Disturbance SF-8A measured self-reported sleep

quality and disturbance (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989; Cella et al.,

2010). The Cronbach's alphas for this study were 0.74 and 0.88, respectively. Sleep-

wake patterns were measured by wrist actigraphy. The GT3X wrist actigraph by

Actigraph ® (Pensacola, FL) is a non-invasive method of indirectly estimating sleep-wake and activity-rest patterns (Actigraph, 2016). Total sleep time (TST), wake after sleep onset (WASO), and wake percent were obtained (Berger et al., 2008).

Potentially Inappropriate Medications (PIMs). All prescribed, OTC home medications and supplements taken within the month were brought to the clinic for review. Participant medications were compared to the 2012 Beers criteria. The criteria are based on a Delphi method of expert evidence base (American Geriatrics Society 2012 Beers Criteria Update Expert Panel, 2012). Chronic medication use was defined as the weekly use of a medication for the past 3 months. The PIMs used were recorded on an investigator-derived PIMs use log.

Patient-Reported Adverse Drug Events (ADEs). For this study, ADEs were defined as any injury resulting from a pharmacological medical intervention (Institute of Medicine, 2007; Kohn et al., 2000). ADEs were explained to the participant as any unintended, undesirable, or harmful effect resulting from the treatment of a medication (Bates et al., 1995; Gandhi et al., 2003). Participants were given an adapted version of an adverse event questionnaire with drug-related symptoms (Corso, Pucino, DeLeo, Calis, & Gallelli, 1992). The questionnaire contained 23 dichotomous (yes/no) questions that assess participant ADE's from the previous month. A pharmacist with expertise in geropharmacology to review recorded PIMs and patient-reported ADEs.

Procedures

Approval of the study was obtained from the Institutional Review Board. After enrollment, each participant was taught how to complete the questionnaires, sleep diary, properly wear the wrist actigraph, and was given instructions on what to bring to the clinic for follow-up. Participants were instructed to bring prescribed, OTC medications, vitamins, and herbal supplements taken in the last month from home in the red bag(s).

Participants were given a reminder call two days prior to the follow-up visit (Shade et al., 2016).

After 1 week, participants returned the binder of completed questionnaires, sleep diary, wrist actigraph, and red bag(s) of home medications, vitamins, and supplements. Private office space in the medical clinic was used to conduct an in-person medication review. The investigator recorded medications in the red bag(s). All medications, vitamins, and supplements were returned to the participant along with information about medication safety and a $25 gift card. Participants' primary care providers at the medical clinic were given a medication update form in a binder that listed 1) all reviewed medications taken in the last month, 2) medications on the medical record, and 3) the 2012 Beers Criteria medications (Shade et al., 2016).

Statistical Analysis

For aim 3 univariate descriptive statistics were performed to analyze predictor variables of demographic characteristics, health experience, and health status factors. Chrischilles et al. (2009), found a one-year self-reported ADE prevalence of 30% in older adults who were prescribed at least one PIM. Patient-reported ADEs was estimated to be higher for this study because a larger percentage of participants used PIMs to avoid.

Demographic characteristics were coded as dummy variables (male=1, female=2; married or cohabitating=1, single or widowed=2; high school graduate=1, college and above or trade school=2; below poverty level=1, above poverty level=2; small rural town=7, rural=10). Age was divided into 2 groups (65 to 78, and 79 to 99) by a median split. The number of medications and health providers were counted, and values (rather than dummy variables) were used from subjective questionnaires and actigraphy instruments. Chi square tests and point biserial correlations were performed to explore relationships between variables. We used a less stringent p value of 0.20 to

screen and explore potential relationships. A binary logistic regression analysis was performed to determine which statistically significant variables predict the probability of the use of PIMs to avoid. The dependent variable was coded as ADEs: (yes=1 and no=0). Due to the variation of units, the other numerical predictor variables were transformed into standardized form so that all units were standard deviations. An evaluation was performed on the overall model fit. The Hosmer-Lemeshow test for logistic regression was performed to test the goodness of fit for the overall model. A Hosmer-Lemeshow test with a p-value greater than 0.05 indicates adequate model fit (Lemeshow & Hosmer, 1982).

Results

Characteristics of Patient-Reported ADEs

Table 1 lists the frequency of participants who reported ADEs. One or more ADE was reported by 48% of participants. As seen in Table 1 the most frequently reported ADEs were CNS disturbances (16%), dry mouth (12%), and hoarseness, gastrointestinal irritation, and decreased libido (all 8%). Of those who used at least one PIM, 59% of participants had at least one patient-reported ADE. Demographic variables of patients who reported ADEs were different based on age (X^2= 4.1; p=0.04) and PIMs use (X^2= 7.3; p=0.007). Participant-reported ADEs were no different based on gender, rural home location, highest education achieved, or income (p>0.05).

As shown in Table 2, there was a trend for association between patient-reported ADEs and higher number of medications and lower mental component score. Higher number of patient-reported ADEs was weakly associated with poorer sleep quality [PSQI (r=0.233, p=0.006)] and with sleep disturbance [PROMIS (r=0.231, p=0.006)] and poor physical health status (r=0.336, p=0.0001). Patient-reported ADEs were not associated with comorbidity or sleep-wake parameters from actigraphy (p>0.05).

Table 3 presents a logistic regression analysis conducted to predict the probability of patient reported ADEs. The number of medications, age by median split, PCS, MCS, PSQI, and use of PIMs to avoid were predictors. The overall model was examined for fit and 26% of the variance of the use of PIMs to avoid was explained by this model. The odds of patient reported ADEs are 0.4 less or 60% decreased in those aged (79-99); than those who are 65-78 95% CI [0.20, 0.96].

The odds of patient reported ADEs are 0.4 less or 60% decreased with a standard deviation decrease of physical component score; than those with higher physical component scores or poorer physical health, 95% CI [0.32, 0.74]. Higher PSQI score was the significant predictor of the increased probability of patient reported ADEs. Every standard deviation increase in PSQI score increased the odds of patient reported ADEs by 1.5 or 57%, 95% CI [1.0, 2.4]. The use of PIMs to avoid was not a significant predictor of patient-reported ADEs (OR 2.06, p= 0.06), but showed a strong trend. The odds of patient reported ADEs are 2.0 more in those who use PIMs to avoid; than those who do not use PIMs to avoid.

Discussion

The older adults in this sample reported ADEs such as CNS disturbances, dry mouth, and GI irritation. Patient-reported ADEs were associated with age, physical health, sleep quality, sleep disturbances, and the use of PIMs to avoid. Younger age (65 to 78), poor physical health, and poor sleep quality were significant predictors of the increased probability of patient-reported ADEs. The following discussion highlights the study's results and provides implications for research and practice.

This study found 48% of older adults reported ADEs. Previous prevalence estimates are lower and may be attributed to studies examining ADEs associated only with prescribed medications (Chrischilles et al., 2009; Tache et al., 2011). Previous

studies examined the association of ADEs with specific medications. Complimentary to Marcum et al. (2010) Chapter IV results confirmed participants' use of anticholinergic medications and other PIMs to avoid such as short acting benzodiazepine and NSAIDs. This study was unable to determine the causality of ADEs, yet several risks associated with the use of these medications are frequent patient-reported ADEs.

There was a difference in patient-reported ADEs based on age. Patient-reported ADEs were associated with lower physical health, poor sleep quality, sleep disturbances, and the use of PIMs to avoid. Older age (79-99) was did not increase the probability of reported ADEs. Older adults may view an ADE as a part of a comorbid condition flare, may wait to see if things improve, or exhibit stoicism and not report an event.

This study did not predict patient-reported ADEs based on specific medication class as previous studies (Gandhi et al., 2003; Hanlon et al., 2013; Pretorius et al., 2013). Lower physical health and poor sleep quality were significant predictors of the increased odds of patient-reported ADEs. Results reinforce older adults' susceptibility to the alterations in pharmacokinetic and pharmacodynamics factors that are associated with ADEs (Bressler & Bahl, 2003; Field et al., 2004).

Unlike previous reports the use of PIMs to avoid only had a predictive trend to increase the odds of patient-reported ADEs (p=0.06) (Chrischilles et al., 2009; Lund et al., 2010). Similar findings have been reported in patients admitted to acute settings (Budnitz, 2011; Hamilton et al., 2011; Laroche et al., 2007). Although we are unable to declare causality, the trend towards significance is logical because several patient-reported ADEs were CNS disturbances and dry mouth, all events that could occur from the use of PIMs with benzodiazepine and anticholinergic properties. Although the Beers Criteria were derived as a resource to prevent incidents such as ADEs, other factors

such as physical health, sleep quality, and age may be important variables to consider while preventing ADEs.

Strengths and Limitations

This study was the first to use Cox's nursing model to describe factors associated with patient-reported ADEs. Most prior studies have been conducted in acute settings and this study was performed in a rural community-setting. Commonly rural settings are difficult to recruit and a modest sample was obtained. Instead of using lists, data were recorded from participants' medications and supplement bottles. This study measured both self-reported and indirect objective activity-rest and sleep-wake patterns. A pharmacist with expertise in geropharmacology reviewed PIMs and patient-reported ADEs.

The study also had limitations. A small mostly Caucasian convenience sample in a farming community in the Midwest limits the generalizability of the findings. The recruitment of participants from one clinic in a small rural town may have resulted in selection bias. Patients may have forgotten to bring in all medications and supplements for review. The study did not use the Naranjo Algorithm to determine if the ADEs were due to medication rather than other health-related factors (Naranjo et al., 1981).

Implications

There are several implications for nursing research. Comparing results from studies about ADEs is difficult due to the variety of conceptual and operational definition and measurement of PIMs and ADEs. We recommend using the use of the definition developed by the Institute of Medicine (2007). When appropriate, studies need to use the Naranjo Algorithm to determine the probability of a medication causing an ADE. Future studies need to be performed in multiple community settings. Large longitudinal

studies can explore patient-reported ADEs further examining older adult and family member knowledge about ADEs and self-efficacy with medication management. To reduce ADEs, team-based interventions need to be developed that target older adults with poor physical health and poor sleep quality.

There also are implications for nursing practice. Nursing professionals in rural settings can help develop a family/caregiver resources or tools to help recognize ADEs. Nurses can help educate older adults about the importance of communicating with the provider regarding falls or sudden symptoms. Those who are older may not report a problem and nurses as part of the health care team need to frequently evaluate and assess problems with pharmaceutical therapies. The Beers Criteria may be beneficial but health care professionals also need to consider other aspects of health status when monitoring older adults for ADEs.

Conclusion

Patient-reported ADEs are prevalent in rural community-dwelling older adults. Events such as CNS disturbances and GI irritation may lead to additional negative health outcomes in older adults, including falls, hospitalization or increased health costs. The results of this study suggest that health care professionals need to develop strategies to prevent ADEs in rural community-dwelling older adults by targeting older adults with poor health status, taking multiple medications, and using PIMs to avoid. Engagement of the patient and family as full partners with the health care team is vital.

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Table 1. Characteristics of Patient-Reported ADEs (N=138)

	Number of Participants	% of Participants
Ecchymosis	9	6
Arthralgia and Myalgia	7	5
Xerophthamia and Vision disturbance	3	2
Rhinorrhea or Epistaxis	3	2
Xerostoma	16	12
Dysgeusia	5	4
Hoarse	11	8
Gastrointestinal Irritation	11	8
Bowel (constipation or diarrhea)	10	7
Urination (increased frequency)	7	5
Decreased libido or sex organ dysfunction	11	8
CNS disturbance (dizziness, sleepy)	22	16
Total	115*	83*

Note. 66 participants (48%) had patient-reported ADEs and 59% of those taking 1 or more PIMs to avoid had at least one patient-reported ADE
*Some participants had more than one classification of patient-reported ADE

Table 2 Correlations between Patient-Reported ADEs and Demographic, Health Experience, Health Status Variables, and use of PIMs to Avoid (N=138)

Variable	Patient-Reported ADEs (r)
Age	-0.087
Charlson Comorbidity	-0.100
Number of Providers	0.108
Number of Medications	0.151
Physical Component Score (S)	-0.336**
Mental Component Score (S)	-0.113[†]
Pittsburgh Sleep Quality Index (S)	0.233**
PROMIS Sleep Disturbance (S)	0.231**
Total Sleep Time (A)	0.020
Wake After Sleep Onset (A)	-0.057
Wake % (A)	-0.032

Note. A= Actigraph, S= Self-report; *p<.05 (2-tailed), **p<.01 (2-tailed), [†]trend for correlation p<0.20

Table 3 Summary of Binary Logistic Regression Analysis Predicting Probability of Patient-Reported ADEs

Predictor Variables	Unstandardized B	Standard Error	Wald's X^2	Exponential β Odds Ratio	P value
Number of Medications	-.149	0.218	0.467	0.861	0.494
Age (79 to 99)	-0.807	0.395	4.16	0.446*	0.041
Physical Component Score	-0.716	0.212	11.42	0.489*	0.001
Mental Component Score	-0.121	0.209	0.332	0.886	0.565
Pittsburgh Sleep Quality Index	0.451	0.219	4.26	1.57*	0.039
PIMs to Avoid	0.727	0.400	3.30	2.06[†]	0.069

Note. Hosmer Lemeshow (H-L) test for good model fit p>0.05.
Nagelkerke R^2 = .265, X^2(8) = 12.0 H-L p=.150, *p<.05 (2-tailed), [†]trend
Younger age (65 to 78) was a significant predictor of higher probability of patient-reported ADEs.