

CURRICULUM VITAE

Sarah Kathryn Dutcher

Degree and Date to be Conferred: Ph.D., 2014

Education

University of Maryland, Baltimore, 2014
Ph.D., Pharmaceutical Health Services Research

University of Maryland, Baltimore, 2014
M.S., Epidemiology

College of William & Mary, 2006
B.S., Chemistry
Minor: Religious Studies

Fellowships

National Research Service Award Pre-doctoral Research Fellowship, *National Institute on Aging, National Institutes of Health* (F31 AG044091), “Atrial Fibrillation Management and Care Transitions among Nursing Home Residents” 2013–2014

Pre-Doctoral Fellowship in Pharmaceutical Science, *American Foundation for Pharmaceutical Education*, 2012–2014

Pre-doctoral Research Fellowship, Epidemiology of Aging Training Program, *Department of Epidemiology and Preventive Medicine, School of Medicine, University of Maryland Baltimore; funded by the National Institute on Aging, National Institutes of Health* (T32 AG00262), 2009–2012

Professional Experience

Graduate Research Assistant, *School of Pharmacy, University of Maryland Baltimore*, Baltimore, MD

Post-marketing Surveillance of Generic Drug Usage and Substitution, 2013–2014

Principal Investigator: Ilene Zuckerman

Sponsor: Food and Drug Administration

Healthcare claims analysis of Medicare data to estimate generic and brand medication utilization, switchback rates, and healthcare service utilization associated with generic switching; literature review to assess outcomes comparing brand and generic drugs

Long-Term Anticoagulation Therapy After Traumatic Brain Injury in Older Adults, 2012–2013

Principal Investigator: Ilene Zuckerman

Sponsor: National Institute on Aging/National Institutes of Health (R21 AG042768)

Systematic literature review describing use of anticoagulation among patients with traumatic brain injury

Sex Differences in Outcomes of Patients with Alzheimer's Disease, 2011–2013

Principal Investigator: Gail Rattinger

Sponsor: National Institute on Child Health and Human Development/National Institutes of Health (K12 HD043489, Maryland's Organized Research Effort in Women's Health, PI: Patricia Langenberg)

Quantitative research project that described drug use patterns in patients with dementia across care settings, examined the effect of medications commonly used in dementia on functional and cognitive outcomes, and evaluated the use of medications with anticholinergic properties among nursing home residents with dementia

Achieving Maximum Value from Prescription Drug Coverage of Chronically Ill Medicare Beneficiaries, June 2009 – November 2011

Principal Investigator: Bruce Stuart

Sponsor: Commonwealth Fund

Quantitative research projects that examined patterns of medication use and adherence and how adherence influences outcomes in patients with chronic heart failure

Medication Reconciliation during Transitions To/From Long Term Care Settings, February – November 2010

Principal Investigator: Ilene Zuckerman

Systematic literature review detailing medication reconciliation interventions involving long-term care settings

Food and Drug Administration Center for Drug Evaluation and Research Decision Sciences Task Order 1, January – July 2009

Principal Investigator: Frank Palumbo

Sponsor: Food and Drug Administration

Qualitative project that examined the thought processes that guide FDA drug approval decisions

Research Analyst, *Health Economics Research and Quality of Life Evaluation Services, Abt Associates Inc.*, Bethesda, MD, 2006 – 2008

Conducted literature reviews, performed data collection and analysis, developed clinical pathways for economic models, prepared manuscripts and presentations, participated in contract proposals

Teaching Experience

Lecturer, Population-Based Strategies I: Pharmacoepidemiology and Pharmacoeconomics (PHAR 563), *School of Pharmacy, University of Maryland at Baltimore*, Baltimore, MD

“Drug Approval Processes in the United States and Europe,” Fall 2013

“Pharmacoepidemiology Study Designs,” Fall 2012

Lecturer, Research Methodology 1 (PHSR 701), *School of Pharmacy, University of Maryland at Baltimore*, Baltimore, MD

“Causal Hypotheses, Power, & Sample Size,” Fall 2013

Graduate Teaching Assistant, *School of Pharmacy, University of Maryland Baltimore, Baltimore, MD*

Professionalism, Ethics, and Pharmacy Practice (PHAR 502), Fall 2008

Population-Based Medical Information Analysis (PHAR 553), Fall 2008

Professional Publications

Shen X, **Dutcher SK**, Palmer JB, Liu X, Kiptanui Z, Khokhar B, Al-Jawadi MH, Zhu Y, Zuckerman IH. A Systematic Review of Benefits and Risks of Anticoagulation Following Traumatic Brain Injury. *J Head Trauma Rehabil.* Forthcoming 2014.

Dutcher SK, Rattinger GB, Langenberg P, Chhabra PT, Liu X, Rosenberg PB, Leoutsakos JM, Simoni-Wastila L, Walker LD, Franey CS, Zuckerman IH. Effect of medications on physical function and cognition in nursing home residents with dementia. *J Am Geriatr Soc.* Forthcoming 2014.

Rattinger GB, Burcu M, **Dutcher SK**, Chhabra PT, Rosenberg PB, Simoni-Wastila L, Franey CS, Walker LD, Zuckerman IH. Pharmacotherapeutic Management of Dementia across Settings of Care. *J Am Geriatr Soc.* 2013 May;61(5):723-33. PMID: 23590231.

Rattinger GB, **Dutcher SK**, Chhabra PT, Franey CS, Simoni-Wastila L, Gottlieb SS, Stuart B, Zuckerman IH. The effect of dementia on medication use and adherence among Medicare beneficiaries with chronic heart failure. *Am J Geriatr Pharmacother.* 2012 Feb;10(1):69-80. PMID: 22264854; PMCID: PMC3296564.

Chhabra PT, Rattinger GB, **Dutcher SK**, Hare ME, Parsons KL, Zuckerman IH. Medication reconciliation during the transition to and from long-term care settings: A systematic review. *Res Social Admin Pharm.* 2012 Jan;8(1):60-75. PMID: 21511543.

Christensen MC, Valiente R, Sampaio Silva G, Lee WC, **Dutcher S**, Guimarães Rocha MS, Massaro A. Acute treatment costs of stroke in Brazil. *Neuroepidemiology.* 2009;32(2):142-9. PMID: 19088487.

Steadman K, Stein WD, Litman T, Yang SX, Abu-Asab M, **Dutcher SK**, Bates S. PolyHEMA spheroids are an inadequate model for the drug resistance of the intractable solid tumors. *Cell Cycle.* 2008 Mar;7(6):818-29. PMID: 18239467.

Landino LM, Mall CB, Nicklay JJ, **Dutcher SK**, Moynihan KL. Oxidation of 5-thio-2-nitrobenzoic acid, by the biologically relevant oxidants peroxyxynitrite anion, hydrogen peroxide and hypochlorous acid. *Nitric Oxide.* 2008 Feb;18(1):11-8. PMID: 18023374; PMCID: PMC2710247.

Selected Presentations and Posters

Dutcher SK, Zuckerman IH. Quality of Pharmacotherapeutic Management of Atrial Fibrillation for Nursing Home Residents. *The Gerontologist.* 2013 Nov; 53(suppl 1):484.

Palmer J, **Dutcher SK**, Rattinger GB, Walker LD, Liu X, Shen X, Kiptanui Z, Zuckerman IH. Trends in Use of Medications with Anticholinergic Properties among Medicare Beneficiaries with Dementia Residing in Nursing Homes. *AcademyHealth Annual Research Meeting.* June 23-25, 2013. Baltimore, Maryland.

Rattinger GB, **Dutcher SK**, Chhabra P, Zuckerman IH, Langenberg P, Simoni-Wastila L, Walker LD. Burden of medications with anticholinergic effects among nursing home residents with dementia. *The Gerontologist*. 2012 Nov; 52(suppl 1):724. (Podium presentation)

Rattinger GB, **Dutcher SK**, Zuckerman IH, Chhabra P, Langenberg P, Simoni-Wastila L, Walker LD, Franey CS. How does the use of medications for dementia management influence cognition among nursing home residents? Alzheimer's Association International Conference. July 14 - 19, 2012. Vancouver, British Columbia, Canada.

Dutcher SK, Rattinger GB, Zuckerman IH, Chhabra PT, Langenberg P, Simoni-Wastila L, Franey CS, Walker LD. The relationship between medications for dementia management and functional status among nursing home residents. *AcademyHealth Annual Research Meeting*. June 24-26, 2012. Orlando, Florida.

Dutcher SK, Zuckerman IH, Rattinger GB, Chhabra PT, Gottlieb SS, Simoni-Wastila L, Stuart S. Are Medicare beneficiaries with heart failure receiving recommended treatment? *The Gerontologist*. 2011 Nov; 51(suppl 2):9. (Podium presentation)

Dutcher SK, Zuckerman IH, Stuart B, Rattinger GB. Urinary incontinence and falls among older Medicare beneficiaries. *AcademyHealth Annual Research Meeting*. June 12-14, 2011. Seattle, Washington.

Dutcher SK, Rattinger GB, Zuckerman IH, Simoni-Wastila L, Yang HK, Qian J, Stuart B. Impact of dementia on drug use patterns among Medicare beneficiaries with congestive heart failure. *The Gerontologist*. 2010 Oct; 50(suppl 1): 543. (Podium presentation)

Zuckerman IH, **Dutcher SK**, Rattinger GB, Simoni-Wastila L, Gottlieb S, Stuart B. Adherence with recommended medications among Medicare beneficiaries with congestive heart failure. *AcademyHealth Annual Research Meeting*. June 27-29, 2010. Boston, Massachusetts.

Bao Y, Wang Q, Arondekar B, **Dutcher S**, Menditto L, Lee WC, Pashos CL. Adherence and resource utilization of rosiglitazone (RSG) versus sulfonylurea (SU) as an add-on to metformin (MET) monotherapy among patients with type 2 diabetes (441-P). *ADA 68th Scientific Sessions*. June 6-10, 2008. San Francisco, California.

Professional Memberships

AcademyHealth

Secretary, Students United for Policy, Education, and Research, University of Maryland student chapter, 2012–2013

International Society for Pharmacoepidemiology

Vice President, University of Maryland Baltimore student chapter, 2011–2012
Secretary, University of Maryland Baltimore student chapter, 2010–2011

Gerontological Society of America

International Society for Pharmacoeconomics and Outcomes Research

Awards

Award for Excellence in Research in the Field of Aging from the Geriatrics and Gerontology Education and Research Program and the Center for Research on Aging; and Winner: Informatics, Policy, and Social Science session D, for “Quality of pharmacotherapeutic management of atrial fibrillation for nursing home residents.” 35th Annual Graduate Research Conference, University of Maryland Baltimore, 2013

Dr. Arthur Schwartz Memorial Scholarship Award, Pharmaceutical Health Services Research, University of Maryland Baltimore School of Pharmacy, 2012

Award for Excellence in Research in the Field of Aging from the Geriatrics and Gerontology Education and Research Program and the Center for Research on Aging, for “Urinary incontinence and falls among older Medicare beneficiaries.” Graduate Research Conference, University of Maryland Baltimore, 2011

Winner, basic science poster session C, “Impact of Dementia on Medication Use and Adherence among Medicare Beneficiaries with Congestive Heart Failure.” Graduate Research Conference, University of Maryland Baltimore, 2010

Rho Chi Society - Omicron chapter (National Pharmacy Honor Society), 2010

ABSTRACT

Title of Dissertation: Pharmacotherapeutic Management and Care Transitions among Nursing Home Residents with Atrial Fibrillation
Sarah Dutcher, Doctor of Philosophy, 2014
Dissertation Directed by: Ilene Zuckerman, PharmD, PhD

Nursing home (NH) residents are a vulnerable population who experience a high rate of transitions across care settings. This population is also at risk for adverse drug events, given their multimorbidity and polypharmacy. However, the relationship between the quality of medication use and transitions in this population is unknown. This study investigates this relationship in the context of atrial fibrillation (AFIB), as pharmacotherapeutic management of AFIB, especially the use of warfarin, can be problematic, and poor management of AFIB can result in hospitalization.

This study has three specific aims, all conducted among long-stay NH residents with AFIB:

- 1) To describe and identify factors associated with pharmacotherapeutic management of AFIB in the NH;
- 2) To quantify changes in pharmacotherapeutic management for AFIB across a hospital transition;
- 3) To determine the bidirectional relationship between quality of AFIB management and hospital transitions.

This study used 2006-2009 Medicare administrative data, the NH Minimum Dataset, and NH facility data. The first and third aims used a nonconcurrent prospective cohort design

with monthly measures of medication use and hospitalizations. The second aim used a pre-post design to compare medication use before and after a hospitalization.

The cohort comprised 16,174 older, long-stay NH residents with AFIB, contributing 219,571 person-months of observation. Forty-eight percent were receiving any antithrombotic, of which warfarin was a majority (78.0%). Among person-months with warfarin use, 84.3% had regular INR monitoring. Approximately 12% of hospitalized individuals experienced a change in their antithrombotic regimen. A hospitalization was associated with 28% higher odds of warfarin use but 29% lower odds of INR monitoring. Conversely, warfarin use was associated with 10% lower odds of any hospitalization, but not with an AFIB-related hospitalization. INR monitoring was not significantly associated with hospitalization.

Results from this study suggest that targeting clinicians to increase adherence to management guidelines for chronic conditions such as AFIB and expanding medication reconciliation interventions can improve the quality of care for NH residents and avoid unnecessary care transitions.

**Pharmacotherapeutic Management and Care Transitions among Nursing Home
Residents with Atrial Fibrillation**

by

Sarah Dutcher

Dissertation submitted to the Faculty of the Graduate School of the
University of Maryland, Baltimore in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy
2014

©Copyright 2014 by Sarah Dutcher

All rights Reserved

ACKNOWLEDGEMENTS

When I began graduate school, I was told that the dissertation is a lonely process. Fortunately, I have been surrounded by people who have provided support, encouragement and love, making this process as easy as a dissertation can be. Although a countless number of people have influenced me, I would like to specially acknowledge a few:

To my mother, thank you for introducing me to public health and for your unconditional love.

To my father, thank you for always listening and helping me through difficult decisions.

To my sister Lauren, thank you for answering all of my inane questions and telling me the research I do is valuable.

To my husband Dan, thank you for your patience, love, and understanding even when you didn't understand.

To my mentor Ilene, thank you for being a strong role model, for teaching me how to become a researcher, for knowing when to hold my hand and when to push me out of my comfort zone, and for supporting me professionally and personally.

Thank you to my committee members, Drs. Gottlieb, Langenberg, Magaziner, Rattinger, and Simoni-Wastila for your valuable input and guidance.

Thank you to PHSR faculty, staff, and students, for making this department a collaborative and enriching environment. A special thanks to Emily Reese and Michelle Campbell, with whom I have experienced all the ups and downs and who truly understand what this dissertation represents.

I would also like to acknowledge the Bethesda-Chevy Chase YMCA gymnastics team and co-coach Dr. Susan Taymans. For a few hours a week, they reminded me of life outside graduate school and provided a much needed respite.

I would also like to acknowledge several sources of support I received throughout graduate school:

National Institute on Aging/National Institutes of Health Ruth L. Kirschstein National Research Service Award predoctoral fellowship (F31 AG044091; PI: Dutcher)

American Foundation for Pharmaceutical Education Pre-doctoral Fellowship in Pharmaceutical Sciences

National Institute on Aging of the National Institutes of Health Research Training in the Epidemiology of Aging (T32 AG000262; PI: Magaziner)

TABLE OF CONTENTS

CHAPTER 1: INTRODUCTION	1
1.1 Specific Aims	2
1.2 Importance and Significance	4
1.3 Conceptual Model	6
CHAPTER 2: BACKGROUND AND LITERATURE REVIEW	8
2.1 Medication Quality and Care Transitions	8
2.2 Nursing Home Population	17
2.3 Atrial Fibrillation	23
2.4 Summary	35
CHAPTER 3: RESEARCH DESIGN AND METHODOLOGY	38
3.1 Study Cohort	38
3.2 Data Sources	39
3.3 Aim 1 Methods	42
3.4 Aim 2 Methods	50
3.5 Aim 3 Methods	53
CHAPTER 4: RESULTS	58
4.1 Cohort	58
4.2 Aim 1	63
4.3 Aim 2	76
4.4 Aim 3	83
CHAPTER 5: DISCUSSION	91
5.1 Use of AFIB medications	91
5.2 Factors associated with warfarin use and INR monitoring	97
5.3 Medication changes surrounding hospitalizations	101
5.4 The relationship between medications and transitions	104
5.5 Structural equation modeling	108
5.6 Limitations	113
5.7 Strengths	116
5.8 Generalizability	117

CONCLUSION.....	121
APPENDICES	125
REFERENCES	138

LIST OF TABLES AND FIGURES

Figure 1. Conceptual Framework	7
Table 3. Medications used for atrial fibrillation assessed in this study	43
Figure 2. Cohort flowchart for aim 1	59
Table 4. Cohort characteristics	61
Table 5. Monthly prevalence of medications for atrial fibrillation.....	64
Table 6. Cohort characteristics stratified by warfarin use, monthly.....	67
Table 7. Cohort characteristics stratified by INR monitoring, among warfarin users, monthly	70
Table 8. Factors associated with pharmacotherapeutic management of AFIB.....	74
Figure 3. Cohort flowchart for aim 2	77
Figure 4. Cohort flowchart for aim 2 sensitivity analysis.....	78
Table 9. Pre-post comparisons of antithrombotic use surrounding a hospital transition, within each antithrombotic category.....	79
Table 10. Changes in antithrombotic medication use, comparing hospitalized NH residents to control NH residents	82
Table 11. Cohort characteristics stratified by hospitalization, monthly	84
Table 12. Effect of pharmacotherapeutic management of AFIB on risk of transitioning to a hospital.....	87
Table 13. Effect of hospitalization transitions on the pharmacotherapeutic management of AFIB.....	90
Table 14. Quality measures for regular INR monitoring.....	94
Table 15. Use of agents to control heart rate and rhythm in AFIB.....	96
Figure 5. Cross-lagged panel model	109
Table 16. Comparison of the study cohort to published NH study samples.....	118

LIST OF ABBREVIATIONS

ACC: American College of Cardiology
ACOVE: assessing care of vulnerable elders
ACSC: ambulatory care sensitive condition
ADE: adverse drug event
ADWE: adverse drug withdrawal event
AFIB: atrial fibrillation
AHA: American Heart Association
AT: antithrombotic
BB: beta blocker
CAD: coronary artery disease
CCB: calcium channel blocker
CCI: Charlson comorbidity index
CCW: Chronic Condition Data Warehouse
CHF: chronic heart failure
CI: confidence interval
CMS: Centers for Medicare and Medicaid Services
CNA: certified nursing assistant
CPT: current procedural terminology
DUA: data use agreement
FDA: Food and Drug Administration
FTE: full time equivalent
HCBS: home and community based services
ICD-9-CM: International Classification of Disease, 9th revision, Clinical Modification
ICU: intensive care unit
INR: international normalized ratio
IV: intravenous
LIS: low income subsidy
LTC: long term care
LMWH: low molecular weight heparin
LPN: licensed practical nurse
LVH: left ventricular hypertrophy
MAI: medication appropriateness index
MCO: managed care organization
MDS: Minimum Data Set (2.0)
NH: nursing home
NNHS: National Nursing Home Survey
NP: nurse practitioner
NPSG: national patient safety goal
NQF: National Quality Forum
OR: odds ratio
OSCAR: Online Survey Certification and Reporting
PA: physician assistant
PDE: prescription drug event
PDP: prescription drug plan

PT: prothrombin time
RAP: resident assessment protocol
RN: registered nurse
SD: standard deviation
SE: standard error
SEM: structural equation modeling
SNF: skilled nursing facility

CHAPTER 1: INTRODUCTION

Continuity of care for patients who transition between health care settings is vitally important for maintaining high quality health care. High quality medication use across settings of care is a key component of care coordination necessary for producing positive patient outcomes. Nursing home residents experience high rates of hospitalizations and re-hospitalizations for multiple reasons, some of which are preventable with appropriate care coordination. In particular, management of multiple chronic conditions where long-term pharmacotherapy is used for disease management increases NH residents' risk of adverse drug events (ADE) that may result in hospitalizations. Atrial fibrillation (AFIB) is an illustrative example, as appropriate management of AFIB is essential in avoiding negative outcomes such as hospitalizations. At the same time, pharmacotherapeutic management of AFIB, especially the use of warfarin, can be problematic among older adults. However, the relationship between medication quality and transitions to the hospital in the NH AFIB population is unclear, as most research on medication continuity across settings of care focuses on the transition of patients between hospital and community settings. This lack of data on how pharmacotherapeutic management and hospitalizations influence one another, specifically whether a bidirectional relationship exists or one component more strongly influences the other, hinders clinicians and policy makers from knowing where to develop effective interventions that create and maintain a high quality of care for NH residents that avoids both ADEs and unnecessary hospitalizations.

The long term goal of my research is to support the development of interventions that promote high quality continuity of care, especially with respect to pharmacotherapy, for patients moving across settings of care. The objective of this proposed study is to examine the relationship between quality of medication use and transitions between the NH and hospital among long-stay NH residents with AFIB. I hypothesize that there is a bidirectional relationship between poor quality of medication use for AFIB and hospitalization transitions such that each leads to an increased risk of the other. Information on the bidirectional influences of medication quality and hospitalizations among NH residents provides evidence to support future interventions to improve the quality of medication management for AFIB for NH residents that move across settings of care.

1.1 Specific Aims

This study has three specific aims that explore the quality of medication use and its relationship with care transitions among long-stay NH residents with AFIB:

- 1) To describe pharmacotherapeutic management of AFIB in the nursing home
 - a. To quantify the use and quality of pharmacotherapeutic management for AFIB patients who reside in a NH

This aim quantifies the use of medications indicated for the treatment of AFIB (i.e., warfarin, other antithrombotic agents, antiarrhythmic agents, rate control agents) and receipt of international normalized ratio (INR) monitoring for those receiving warfarin.

- b. To identify factors associated with certain management strategies for AFIB

Management strategies include use of warfarin and INR monitoring. Factors studied included both person-level and facility-level characteristics.

- 2) To characterize changes in antithrombotic medication use surrounding transitions experienced by NH residents with AFIB

The following patterns of medication change surrounding a transition were examined: no change, dosage adjustment, initiation of warfarin, discontinuation of warfarin, switch to a different anticoagulant.

- 3) To determine the relationship between quality of AFIB medication use and hospital transitions among long-stay NH residents with AFIB

- a. To quantify the impact of pharmacotherapeutic management of AFIB for NH residents on their risk of transitioning to a hospital

I hypothesized that poorer quality pharmacotherapeutic management of AFIB leads to an increased risk of AFIB-related hospitalization

- b. To quantify the impact of the transition of a NH resident who is hospitalized and transferred back to a facility on the pharmacotherapeutic management of AFIB upon return to the facility

I hypothesized that a hospitalization leads to a change in the quality of AFIB pharmacotherapeutic management upon stabilization of the medication regimen following the return to the NH (i.e., lower use of warfarin, increased INR monitoring for those who are receiving warfarin).

1.2 Importance and Significance

Before examining the cyclical relationship between medication quality and transitions among nursing home residents with AFIB, it is important to describe the quality of medication prescribing in the nursing home. Assessing quality can inform nursing home physicians and pharmacists about areas of medication management that are working well and which areas need improvement (i.e., those that may lead to hospitalizations). The increased regulations, regular supervision, and more intimate caretaking in the NH setting may result in higher quality of care, including pharmacotherapeutic management of chronic conditions, among NH residents compared to their peers who reside in the community. At the same time, NH patients are at increased risk of adverse events as a result of multimorbidity and polypharmacy. These competing situations justify the need for studies in this unique population. In addition, the highly structured and regulated nature of NHs makes them an ideal setting in which to undertake interventions that aim to improve pharmacotherapeutic management and monitoring.

This study is innovative because it explores a bidirectional relationship between medication quality and hospitalizations. Literature exists on the effect of transitions, especially hospitalization, on medication outcomes, and several studies have considered the impact of aspects of medication quality on care transitions. However, most previous research has only tested unidirectional associations, while this study assesses both directions of this hypothesized relationship.

A second novel feature of the study is the linkage of Medicare administrative data and nursing home assessment data (Minimum Data Set) with two databases that contain information on facility providers. This linkage allows this study to describe and account for facility characteristics that influence the relationship between medication quality and setting transitions. Including facility-level information can assist in designing improved medication reconciliation interventions to promote continuity of care across settings for vulnerable populations such as nursing home residents. Specifically, identification of modifiable facility characteristics or policies is important in order to help facilities change and improve their quality, and the identification of non-modifiable characteristics will enable interventions to be targeted toward facilities that will benefit the most from improved medication reconciliation. Further, it has been well documented that a variety of facility characteristics can impact the risk of hospitalization among NH patients and the culture of quality in a facility may influence the quality of management of chronic conditions including AFIB. It is necessary to account for these confounding factors in order to minimize bias, as not controlling for facility-level factors may overestimate the effect of AFIB management on hospitalizations.

In summary, results from this study can lead to the development of valuable, effective, and appropriately placed interventions supporting coordination of care to prevent both ADEs and unnecessary hospitalizations, thus maximizing positive outcomes for older adults with AFIB.

1.3 Conceptual Model

The conceptual model for this study illustrates the hypothesized bidirectional relationship between the quality of medication management among nursing home (NH) residents and transitions across care settings, particularly to and from the hospital (Figure 1).

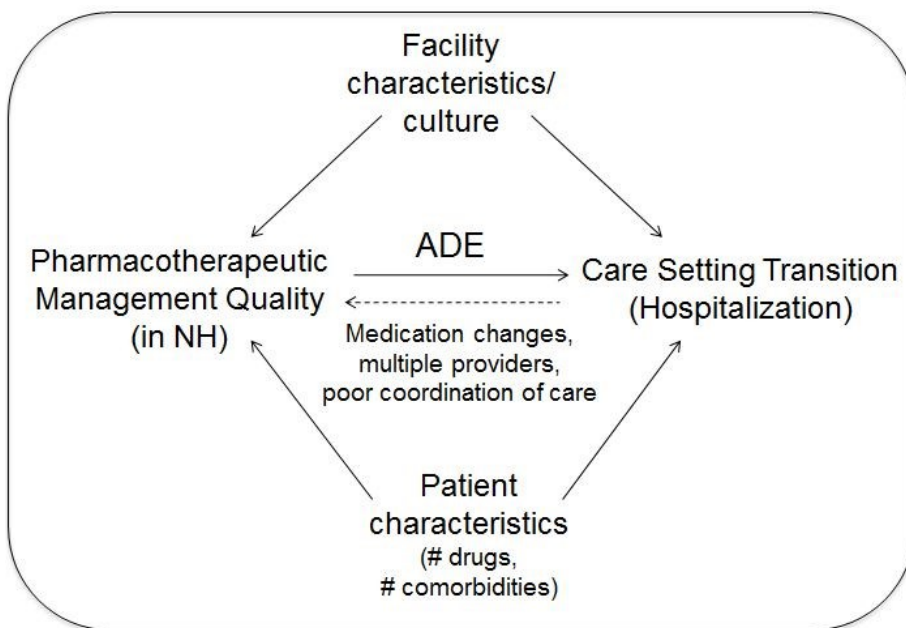
Specifically, poor pharmacotherapeutic management of chronic conditions among NH residents may result in a hospitalization due to an ADE. For example, a NH resident who initiates use of an unnecessary drug may experience an ADE resulting from toxicity or a drug-drug interaction, which could necessitate a visit to the hospital. Similarly, a resident who has had a necessary medication discontinued, another example of poor medication quality, may be hospitalized due to an adverse drug withdrawal event, such as an exacerbation of an underlying chronic condition.

On the other hand, transitions also may negatively influence a patient's quality of care with respect to their medications. Patients often experience multiple medication changes during transitions to the hospital and upon discharge. In addition, multiple providers are often involved in the care of patients who transition between settings, so poor care coordination as a result of potential communication problems between providers may also explain how transitions can influence medication quality. For example, a lack of communication between a hospitalist and those who provide care in the NH may cause a NH resident to inadvertently discontinue a new medication that had been prescribed in the hospital, remain on a medication intended for short term use, or experience therapeutic duplication. Alternatively, a chronic medication for a condition unrelated to a hospitalization that was discontinued upon hospitalization may not be resumed upon

return to the NH. All of these scenarios of poor medication quality may result in a variety of negative outcomes, including hospitalizations, and can prolong the cycle of transitions and poor quality of care.

Many of the same factors that influence medication quality also increase an individual's risk of transitioning to another care setting; these potential confounders have been broadly divided into two categories: patient characteristics and facility characteristics. Patient characteristics may include demographic factors, comorbid conditions, and medications that a resident is receiving. Facility characteristics capture information on the NH facility in which the resident lives. These characteristics may include structural or organizational aspects of the facility (size, ownership, staffing), information on the case-mix of residents, and deficiency history.

Figure 1. Conceptual Framework



CHAPTER 2: BACKGROUND AND LITERATURE REVIEW

2.1 Medication Quality and Care Transitions

2.1.1 Quality of Medication Prescribing

High quality health care is important for ensuring positive patient outcomes, especially with respect to pharmacotherapeutic management of health conditions among older adults. This is particularly important for older adults who are at increased risk of poor medication quality and ADE consequences due to their higher number of comorbid conditions, multiple medications, multiple prescribers/poor coordination of care, age-related changes in the metabolism of drugs, and the “psychological effects of aging on the use of drug therapy.”¹ Pharmacologic interventions are beneficial and often necessary to maintain the health of older adults, but poor quality use of medications can lead to more harm than benefit. This poor quality can be a result of underuse (i.e., an individual who does not receive a medication that is recommended for a given condition), overuse or polypharmacy (e.g., receipt of a medication for which there is no benefit or the benefit is outweighed by the risk of harm due to an ADE), or misuse (i.e., inappropriate prescribing).^{1,2}

Although assessing the quality of medication prescribing among older adults is an important area of research, it is one complicated due to the difficulty of measuring medication quality. Existing literature that examines the quality of medication use in older adults has focused on the use of inappropriate medications^{3,4} or other “...select indicators of medication appropriateness...”¹ One of the most well-known methods for

assessment of medication quality is the Beers criteria, a list of medications that are considered potentially inappropriate for use in older adults.^{3,4} Although the Beers criteria have been used to assess medication quality in the long term care setting, they do not account for individual needs, as some medications on the list may be appropriate for use in some patients.¹ In addition, the list does not include several medications that have been shown to be problematic among older adults, such as warfarin, because the Beers list does not account for the problems that result from inappropriate use of appropriate medications.

Another method for the assessment of medication quality is the use of quality indicators developed by the Assessing Care of Vulnerable Elders (ACOVE) project. The most recent update, ACOVE-3, contains 392 indicators, of which 24 are related to medications.⁵ In addition to indicators related to use of inappropriate medications, the ACOVE-3 measures include indicators on prescribing of indicated medications, education, continuity, and documentation, and medication monitoring.^{1,5} However, like the Beers criteria, ACOVE indicators do not account for appropriateness related to taking specific medications or for use of effective or necessary drugs at an individual level.¹ A third tool that has been developed to assess medication quality is the Medication Appropriateness Index (MAI).⁶ This tool enables clinicians to classify each individual drug for a given patient based on 10 criteria (indication, effectiveness, dosage, directions, practicality, drug-drug interactions, drug-disease interactions, duplication, duration, and cost), and is much more individualized than other measures. Although comprehensive,

the MAI is burdensome to administer and score, and is therefore not very feasible for use in clinical practice¹ or large population-based research studies.

The Centers for Medicare and Medicaid Services (CMS) includes in its *Guidance to Surveyors for Long Term Care Facilities* a section on unnecessary medications.⁷ CMS states that:

“Each resident’s drug regimen must be free from unnecessary drugs. An unnecessary drug is any drug when used: (i) In excessive dose (including duplicate therapy); or (ii) For excessive duration; or (iii) Without adequate monitoring; or (iv) Without adequate indications for its use; or (v) In the presence of adverse consequences which indicate the dose should be reduced or discontinued; or (vi) Any combinations of the reasons above.”⁷

Unlike each of the above systems for measuring quality, the CMS guidance on unnecessary medications applies specifically to the NH population. However, although examples are given for each of the definitions of an unnecessary drug, the list of examples is not exhaustive. Therefore, applying these broad definitions at an individual level can be difficult and is open to subjectivity both in practice and research.

Measuring quality of medication use is complex, as measures must allow for the individual needs of each patient while at the same time being practical to use. Given the difficulty of this among older adults with many chronic conditions, this study examined the quality of medication use with a focus on one condition, AFIB. Although those with AFIB should have their medication regimens individualized, there are evidence-based

guidelines for the treatment of AFIB that apply nearly universally to all patients with AFIB, such as the use of antithrombotic therapy to reduce the risk of stroke.^{8,9} The measures of medication quality used in the proposed study were based on these guidelines.

2.1.2 The effect of transitions on medication quality

A care transition is defined as “the movement patients make between health care practitioners and settings as their condition and care needs change during the course of a chronic or acute illness.”¹⁰ A hospitalization is the most common example of a care transition. It actually involves two transitions, admission and discharge, both points at which medication changes can occur. A substantial body of literature exists that demonstrates a relationship between care setting transitions and various medication-related outcomes (i.e., regimen modifications, ADEs).¹¹⁻¹⁸ For example, Beers et al. examined the changes in medications surrounding a hospitalization among older adults in a single U.S. hospital, and found that 40% of admission medications had been discontinued upon discharge, while 45% of discharge medications had been new additions during the hospitalization.¹⁹ Similarly, in a study of older adults admitted to an acute geriatric ward in a hospital in Israel, high rates of medication regimen changes were found upon the transition to the hospital: the average in-hospital medication modification rate was 49.8%.¹⁷ In another study of patients admitted to a general internal medicine unit in Canada, 53.6% experienced at least one unintended discrepancy between physicians’ admission medication orders and the patient’s medication history.¹² Over one-third (38.6%) of discrepancies had the potential for moderate or severe discomfort or clinical

deterioration, illustrating the potential impact that these medication discrepancies may have on future quality of care.

A majority of studies that explore how transitions influence medication quality focus on the hospital discharge transition, and several of these studies have focused on discontinuation of chronic medications. Upon discharge from the intensive care unit of one of three hospitals in Canada, 33% of patients had at least one of their medications from six groups of chronic medications discontinued.¹⁵ A study in the Netherlands found 55.2% of hospitalized patients had at least one medication stopped, while only 27.3% of nonhospitalized controls experienced a medication discontinuation.²⁰ After adjustment, hospitalization was still associated with a 1.98 increased odds of having a medication stopped (95% CI 1.85-2.13). One possible reason for discontinuation is poor communication between providers. In a review of studies documenting deficits in communication between hospital physicians and primary care physicians, Kriplani et al. found that between 2% and 40% of discharge summaries lacked information relating to discharge medications,²¹ suggesting that one explanation for the high rates of medication discontinuation following a hospitalization is poor transfer of information between care settings.

Antithrombotic therapy, especially warfarin, is a medication with substantial potential for modifications during a transition. For example, Bell et al. found that 27% and 23% of patients had antiplatelet agents and anticoagulants discontinued after ICU discharge and hospital discharge, respectively.¹⁵ Similarly, 19.4% of hospitalized older adults

experienced discontinuation of their antiplatelet/anticoagulant agents, compared with 11.8% of controls [adjusted OR 1.86 (95% CI 1.77-1.97)].¹⁴ Those with an ICU stay had even higher risk of discontinuation of these agents [adjusted OR 2.31 (95% CI 2.07-2.57)]. Another study found that warfarin discontinuation rates were 11.4% and 7.5% for patients having elective surgical procedures who had overnight hospitalizations and ambulatory procedures, respectively, compared with a discontinuation rate of 4.8% for those with no procedures (control group).¹⁸ Adjusted odds ratios for warfarin discontinuation were 2.6 (95% CI 2.0-3.4) for overnight hospitalizations and 1.6 (95% CI 1.4-1.7) for ambulatory procedures compared to no procedures. The high rate of discontinuation following a hospitalization is not surprising, given the mechanism of action of warfarin and the common need to suspend warfarin during an acute hospitalization. However, attention needs to be paid to the timing of re-initiation of chronic medications such as warfarin following a hospitalization.

Discontinuing medications can be a positive change for a patient who no longer has an indication for the medication. This is particularly true for individuals in the NH setting, as there is a need to reduce polypharmacy. Discontinuations in this setting can be done safely, as residents' health is closely monitored on a daily basis and health care workers can be aware of potential ADEs and disease recurrence.¹³ In addition, regulations require a review of each resident's drug regimen by a pharmacist at least monthly.²² However, one study among long-stay NH residents found that almost half of drug discontinuations within the first six months following admission were followed by an adverse drug

withdrawal event (ADWE),¹³ suggesting that discontinuing medications in this setting requires careful consideration and monitoring.

In addition to discontinuations, other medication discrepancies can result from hospitalizations. Among patients discharged from a large academic medical center who subsequently visited a primary care physician, 42% had at least one medication continuity error, defined as a discrepancy between the discharge medication list from the hospital chart and the primary care physician's medication list.¹¹ In a study of older adults admitted to an acute geriatric ward, the average proportion of the medication regimen that was modified within one month was 36.7% (\pm 25.1%).¹⁶ No medication changes were documented in only 16% of patients. In a similar study, Mansur et al. found a high rate of medication changes during the transition from the hospital to various settings: the medication modification rate at one month post-discharge was 37.5%.¹⁷ In both studies, NH residents represented approximately 13% of both admissions and discharges, and both studies found that patients who were discharged to NHs experienced more medication modifications in the hospital compared with patients discharged to the community, likely because they had more chronic conditions and were more complicated clinically.^{16,17} Only one study examined this relationship entirely in a NH setting, and is described in detail in the section 2.4.²³

2.1.3 The effect of medications on transitioning

Several research studies have explored the reverse relationship between various measures of medication quality and transitions between care settings.^{11,17,24,25} Among ambulatory

older adults who discontinued at least one medication during a health service intervention trial that aimed to optimize medication regimens, 238 drugs were discontinued, 26% (62) of which resulted in ADWEs.²⁵ Of these ADWEs, 36% involved a transition to a hospital, emergency department, or urgent care clinic, suggesting that inappropriate medication discontinuations may result in negative outcomes such as hospitalization. A second study examined factors associated with hospitalization among older, long-stay NH residents.²⁴ Although not focused on the relationship between medications and hospitalizations, Fried et al. found that receiving a new medication in the last 90 days was associated with a 1.25 higher odds of hospitalization (95% CI 1.07 – 1.46).

On the other hand, two studies found no relationship between medication changes and hospitalizations.^{11,17} Mansur et al. found a high rate of modifications to the medication regimen among elderly inpatients, but found no association between in-hospital medication modifications and readmissions within three months post-discharge.¹⁷ Similarly, Moore et al. found that 42% of hospitalized patients experienced at least one medication continuity error during the transition between hospital and primary care.¹¹ However, the association between medication continuity errors and rehospitalizations within three months was not significant [OR 2.5 (95% CI 0.7-8.8)].

To summarize, two of these four studies suggest a positive association between various medication measures and hospitalizations,^{24,25} while two suggest that there is no association.^{11,17} These conflicting results, in addition to the overall lack of information among NH residents, illustrate the need to further explore whether medication quality

impacts transitions, specifically hospitalizations, among a vulnerable population at high risk for both poor medication quality and high rates of hospitalizations.

2.1.4 Medication Reconciliation

The above studies on medications changes and discrepancies that occur during transitions demonstrate the need to improve continuity of care across transitions between healthcare settings, specifically regarding medications. One method to do this is through medication reconciliation. Medication reconciliation is defined as "...the process of creating the most accurate list possible of all medications a patient is taking...and comparing that list against the physician's admission, transfer, and/or discharge orders, with the goal of providing correct medications to the patient at all transition points..."²⁶ The goal of medication reconciliation is to prevent ADEs at all care transitions (i.e., admission, transfer, discharge).

In 2005, The Joint Commission created National Patient Safety Goal (NPSG) 8 (08.01.01-08.04.01) to "accurately and completely reconcile medications across the continuum of care."²⁷ Based on feedback from organizations on the difficulty and complexity of implementing this goal, NPSG 8 was removed and replaced by NPSG 03.06.01 that requires long term care facilities to "maintain and communicate accurate resident medication information," effective July 1, 2011.^{28,29} The revised NPSG is less prescriptive and enables facilities to tailor the medication reconciliation process to meet the needs of their own patients more effectively.²⁹ It is worth noting that this NPSG applies to many different health care settings, including hospitals and long term care

facilities. However, most guidelines and recommendations on medication reconciliation focus on the transition between the hospital and community (i.e., primary care).^{26,30}

2.2 Nursing Home Population

2.2.1 Epidemiology

Currently almost 1.5 million people live in a NH.³¹ Although individuals of all ages reside in NHs, 88% of NH residents are over the age of 65 and 45% are over 85 years.³¹ Not surprisingly, a majority of NH residents are female (71-75%).^{31,32} On a given day, approximately 80% of older NH residents are long-stay residents (stay ≥ 90 days), and over 50% have resided in the NH for at least one year.^{31,33} At admission, Medicaid and Medicare are the primary payers for 35% and 36% of residents, respectively.³¹ However, Medicare benefits only apply to the first 100 days of a qualified skilled nursing facility (SNF) stay, and many long-stay residents must self-pay or switch their primary payer to Medicaid. At the time of the 2004 National Nursing Home Survey (NNHS), Medicaid and Medicare were the primary payers of 60% and 13% of current NH residents, respectively,³¹ reflecting the limited Medicare NH benefits. NH residents often have multiple sources of payment, as illustrated by the 66% who reported having a private source of payment.³¹ Regardless of the primary payor for the NH stay, 81.0% of NH residents are enrolled in Part D for coverage of their prescription drugs.³⁴

2.2.2 Medication use among NH residents

NH residents have a high rate of medication use, reflecting the high number of comorbid conditions among this vulnerable population. In 1997, 94% of residents were receiving

prescribed and nonprescribed medicine services.³² Given that NH residents receive an average of 8.8 medications (5.9 prescription and 2.9 over-the-counter),³⁵ the quality of pharmacotherapy is vital to this population as their high number of medications put them at increased risk of ADEs.^{13,36} Among long-stay residents in two LTC facilities, Gurwitz et al. found a rate of ADEs of 9.8 per 100 resident-months, and a rate of 4.1 preventable ADEs per 100 resident-months.³⁶ Of the ADEs found by investigators, 42% were judged to be preventable. Preventable ADEs are most likely to occur at the ordering and monitoring stages (versus transcription, dispensing, or administration stages).^{36,37} Among ordering errors, wrong dose (63%), known drug interaction (22%), and wrong drug choice (9%) are the most common errors.³⁷

Several studies have identified risk factors for ADEs among NH residents.^{13,36} Common risk factors for ADEs were a higher number of medications^{13,36} and a higher number of diagnoses or comorbid conditions.¹³ Given that NH residents tend to have a substantial number of comorbid conditions and similarly utilize a high number of medications, it is not surprising that they experience a high rate of ADEs. Longer NH stay¹³ and specific medication classes (anticoagulants, antipsychotics, anti-infectives or antibiotics, antiepileptics, antidepressants, sedatives/hypnotics)^{36,37} were also associated with increased risk of ADEs among NH residents. Risk factors for potentially preventable ADEs were similar to those for any ADE: number of comorbid conditions,³⁸ number of medications,³⁸ and specific medication classes (antipsychotics, anticoagulants, diuretics, antiepileptics, anti-infectives or antibiotics, antidepressants, opioids, sedatives/hypnotics).^{36,37} Two risk factors for ADEs related to transitioning were being a

new resident³⁸ and experiencing a hospitalization during the NH stay;¹³ these are described in more detail below.

2.2.3 Care transitions among NH residents

Like ADEs, transitions among health care settings are common among NH residents. Transitions are particularly relevant to NH residents, as those who reside in a facility are more likely to experience multiple transfers to hospitals and SNFs compared with individuals who reside in the community.³⁹ Among those residing in a facility, approximately 40% experience at least one transition within one year, and the large majority of these transitions are to and from the hospital.³⁹ For long-stay residents of US NHs in 1997, a hospital was the most common setting prior to the NH stay (44.5%),³² so that almost half of residents had already experienced at least one transition involving the hospital upon admission to the facility. A study among long-stay residents from four states found that over 15% were hospitalized within 180 days.⁴⁰ Over one-third of these hospitalizations were for an ambulatory-care sensitive condition (ACSC), which the authors suggest represent potentially preventable hospitalizations. Another study among older assisted living residents in a single state found that 20% of hospitalizations were for an ACSC.⁴¹

A review of predictors of hospitalizations among NH residents found wide variation in hospitalization rates, from 9% to 59%.⁴² In a study of long-stay NH residents in four states, hospitalization rates varied from 0 to 41.7% across facilities, reflecting wide variation across geographic areas, nursing home type, patient population, and definition

of hospitalization (e.g., all vs. potentially preventable).⁴⁰ Resident-level characteristics associated with an increased risk of hospitalization among NH residents include: older age, male sex, and new admissions.^{24,41,42} Results regarding the effect of race and ethnicity on hospitalizations are conflicting.^{41,42} Not surprisingly, residents who are more physically or functionally impaired have higher rates of hospitalization,^{24,42} but cognitive impairment is not a consistent predictor of hospitalization, and physically impaired residents are less likely to have a potentially preventable hospitalization.⁴² The overall number of comorbid conditions is positively associated with hospitalizations,⁴¹ and certain health conditions are associated with an increased risk of hospitalization, including heart failure, circulatory problems, respiratory problems, genitourinary problems, and infections.^{24,42} Residents with advance directives (i.e., do not resuscitate, do not hospitalize) have lower hospitalization rates.^{40,42}

In addition to resident-level factors, characteristics of the facility have also been shown to be associated with hospitalizations among NH residents. For example, the relationship between hospitalizations and physician or nursing staffing has been explored, but conflicting results exist. A majority of studies suggest that higher levels of physician and senior-level nursing staff are associated with a reduced risk of hospitalization,^{40,42} but the relationship is thought to be more complex and may be related to the combination of staff rather than the availability of staff.⁴² The size of the facility may also influence hospitalization rates: Intrator et al. found that smaller facilities (<100 beds) had reduced odds of hospitalization.⁴⁰ Other facility-level factors that may influence hospitalization risk are the availability of ancillary services such as IV and respiratory therapy or x-ray

and laboratory services.^{40,42} However, these services are highly correlated with the case-mix of residents and the complexity of the patient population at a given facility, likely explaining the conflicting results found in the literature. It is worth noting that the availability of hospice care is one service that has been clearly associated with a decreased rate of hospitalizations.⁴²

The influence of financial factors on the rate of hospitalization among NH residents has also been examined. For-profit facilities tend to have higher hospitalization rates,^{40,42} as do facilities that are affiliated with a chain.⁴² Payer status can be considered both a person-level or facility-level factor. Regarding the individual, Medicare payer status has been demonstrated to be associated with an increased risk of hospitalization.⁴² At the facility level, the proportion of residents with a certain payer may also influence the facility culture regarding hospitalizations: one study determined that facilities with more than 35% of residents who were private-pay had fewer hospitalizations.⁴⁰

2.2.4 Relationship between medication quality and transitions in the NH population

Most medication reconciliation guidelines and recommendations focus on hospital to home transitions. The Joint Commission NPSG regarding medication reconciliation applies to many settings, including long term care.²⁸ However, only four studies consider the relationship between medication quality and hospitalizations among NH residents,^{13,23,24,38} and it is the focus of only one.²³

Three studies have touched on the impact of transitions on medication quality in the NH population.^{13,23,38} Two studies investigated predictors of ADEs among NH residents.^{13,38} Field et al. found that being a new resident, defined as NH admission within the previous two months, was associated with a 2.8 higher odds of experiencing an ADE (95% CI 1.5-5.2).³⁸ Although new residents had, by definition, experienced a transition within the prior 2 months, the authors did not explore if other transitions, such as hospitalizations during the NH stay, also influenced ADEs. Gerety et al. explored risk factors for ADEs and ADWEs and found that being hospitalized during the NH stay was significantly increased the odds of having at least one ADE or ADWE.¹³

Boockvar et al. performed a study of the influence of medication changes and discontinuations resulting from a transition between a hospital and a NH on ADEs.²³ Among patients transferred between two hospitals and four nursing homes, an average of 3.1 medications were altered during the NH to hospital transition, while 1.4 medications were altered during the hospital to NH transition. Most of these changes were drug discontinuations. ADEs attributable to noted medication alterations occurred in 20% of the bidirectional transfers (14/71), providing an overall 4.4% risk of ADE per drug alteration. Over 50% (8/14) of the medication changes occurred during the hospitalization, but 86% (12/14) of ADEs occurred following readmission to the NH. One major study limitation was that newly prescribed medications were not considered in their assessment of drug alterations, so these results likely underestimate the total number of medication changes, and resulting ADEs, that occur surrounding transitions.

Only one study has considered the impact of medications on the risk of transitioning in a NH population.²⁴ Fried et al. explored how patient-level factors that represent frailty influence hospitalizations among long-stay, older NH residents. The single finding related to medications was a positive association between receipt of a new medication within the last 90 days and hospitalizations: 28% of those who had received a new medication within the previous 90 days were hospitalized, compared with 23% those who had not received a new medication within the previous 90 days ($p < 0.001$), and this effect remained after adjustment [OR 1.25 (95% CI 1.07 – 1.46)].²⁴

2.3 Atrial Fibrillation

2.3.1 Epidemiology

Atrial Fibrillation (AFIB) is a supraventricular tachyarrhythmia characterized by uncoordinated atrial activation with consequent deterioration of atrial mechanical function.^{8,9} AFIB is the most common cardiac arrhythmia, with prevalence estimates ranging from 2.7 to 6.1 million in the United States in 2010.⁴³⁻⁴⁵ A study among Medicare beneficiaries determined that the prevalence of AFIB in that population was 6.0% in 2002.⁴⁶ The incidence and prevalence of AFIB are higher in men than in women and increase with age in both sexes. Given the higher prevalence with age, it is not surprising that between 7.5% and 17% of long-term care residents have AFIB.⁴⁷⁻⁵⁰ The prevalence is projected to increase in the future as individuals are living longer with chronic conditions, especially cardiovascular comorbidities, and the population continues to age.^{43,51} The three types of AFIB are: paroxysmal (self-terminating), persistent (requires termination by pharmacological or electrical means), and permanent (cardioversion is impossible).^{8,9}

However, many patients with AFIB are asymptomatic and therefore undiagnosed, so it is likely that the true prevalence is underestimated.^{43,51,52}

A major concern for individuals with AFIB is an increased risk of thromboembolic events. AFIB is associated with a 4.8-fold increased risk of stroke,⁵³ and this increased risk is the same in patients with paroxysmal AFIB as those with sustained (i.e., persistent or permanent) AFIB.^{45,54,55} Many cardiovascular conditions are a risk factor for AFIB (hypertension, atherosclerosis, myocardial infarction, heart failure); at the same time, AFIB is a risk factor for several cardiovascular conditions (myocardial infarction, heart failure).⁵¹

2.3.2 Pharmacotherapeutic management of AFIB

Management of AFIB with pharmacologic agents plays a central role in preventing strokes and managing symptoms and recurrence. There are three management objectives for patients with AFIB: rate control, rhythm control and maintenance, and prevention of thromboembolism.^{8,9} It is important to note that these three objectives are not mutually exclusive, and that pharmacologic management of AFIB is similar regardless of type of AFIB.^{8,9,51} Rate and/or rhythm control can be maintained using drugs or ablation, or occasionally surgery. However, anticoagulation is necessary regardless of the approach or whether or not sinus rhythm is able to be maintained.^{8,9} As noted by the AFIB Exchange Group, “The day-to-day clinical management of AFIB is complex and variable, reflecting the limitations of currently available therapies as well as the heterogeneous nature of the

patient population and the associated level of risk.”⁵¹ Agents used for the pharmacotherapeutic management of AFIB in the non-acute setting are listed in Table 1.

Table 1. Pharmacologic management of atrial fibrillation in the non-acute setting^{8,9,56}

Drug/Class	Class	Level of Evidence	Indication/Details
Rate Control			
Beta blocker (BB; metoprolol, propranolol, atenolol, esmolol, nadolol) OR Nondihydropyridine calcium channel blocker (CCB; diltiazem, verapamil)	I	B	Rate control (rest) for patients with persistent or permanent AFIB
Digoxin	I	C	Rate control (rest) for patients with CHF, left ventricular dysfunction, or sedentary individuals
Digoxin plus BB OR nondihydropyridine CCB	IIa	B	Rate control (rest and during exercise)
Digitalis	III	B	Should NOT be used as the sole agent for rate control in patients with paroxysmal AFIB
Amiodarone (oral)	IIb	C	Rate control when other measures are not successful or are contraindicated
Preventing thromboembolism			
Aspirin	I	A	Choice (aspirin vs. warfarin) should be based on risk of stroke and risk of bleeding; vitamin K antagonist recommended for patients with >1 moderate risk factor; selection does not depend on type of AFIB (paroxysmal, persistent, permanent)
Vitamin K antagonist (warfarin)	I	A	May be given in combination with aspirin in patients for whom warfarin is unsuitable due to patient preference or physician assessment
Clopidogrel	IIb	B	May be given concurrently with aspirin or warfarin following certain surgical procedures
Low molecular weight heparin	IIb	C	May be given by subcutaneous injection when a surgical procedure requires stopping anticoagulant therapy for >1 week
Dabigatran	I	B	Alternative to warfarin for the prevention of stroke and systemic thromboembolism in patients with paroxysmal to permanent AF IB
Cardioversion			
Dofetilide	I	A	Oral
Flecainide	I	A	Oral or IV
Propafenone	I	A	Oral or IV
			A single oral dose can be used to terminate persistent AFIB outside the hospital once it has used safely in the hospital; BB or nondihydropyridine CCB should be given prior

Drug/Class	Class	Level of Evidence	Indication/Details
Amiodarone	IIa	A	Oral or IV; can be beneficial on an outpatient basis in patients with paroxysmal or persistent AFIB
Digoxin	III	A	
Sotalol	III	A	NOT recommended for cardioversion of AFIB
Maintenance of Sinus Rhythm			
Flecainide	*	*	First-line treatment for those with no/minimal heart disease or those with hypertension but no substantial LVH
Dofetilide	*	*	First-line treatment for those with CAD or heart failure; second-line treatment for those with hypertension but no substantial LVH
Propafenone	*	*	First-line treatment for those with no/minimal heart disease or those with hypertension but no substantial LVH
Sotalol	*	*	First-line treatment for those with no/minimal heart disease or those with hypertension but no substantial LVH or those with CAD
Amiodarone	*	*	First-line treatment for those with hypertension and substantial LVH or those with heart failure; second-line treatment for those with CAD or those with hypertension but no substantial LVH
Disopyramide	*	*	May be considered first-line therapy in vagally induced AFB
Dronedarone	*	*	First-line treatment for those with no/minimal heart disease or those with hypertension but no substantial LVH or those with CAD

BB: Beta blockers; CAD: coronary artery disease; CCB: Calcium channel blockers; LVH: left ventricular hypertrophy

*Class and level of evidence are not provided for section 8.1.6 Pharmacological Agents to Maintain Sinus Rhythm; indications are based on the treatment algorithm presented in the AHA/ACC guidelines^{8,9}

Drugs are typically the first choice for both rate and rhythm control, but the choice of agents for both initial and subsequent management may differ between patients based on individual needs.^{8,9} The goal of agents used for rate control is to slow the heart rate; these agents include beta-adrenergic blockers, calcium channel blockers, and digoxin.^{8,9,56} The goal of agents used for rhythm control is to convert to sinus rhythm, maintain sinus rhythm, and prevent recurrence of AFIB; these antiarrhythmics agents include flecainide, propafenone, amiodarone, sotalol, and dofetilide.^{8,9,56} Electrical cardioversion and ablation techniques are also used in the management of AFIB,⁵⁷ but since they are used for acute conversion and this study aims to focus on chronic management of AFIB, they were not considered in this study.

The use of antithrombotic (AT) therapy is recommended for all patients with AFIB, except those with lone AFIB (i.e., individuals under 60 years of age without clinical or echocardiographic evidence of cardiopulmonary disease, including hypertension) or contraindications.^{8,9} Antithrombotic therapy should be used long-term, regardless of the initial choice to use a rate or rhythm control approach following an AFIB episode, as well as in those who have converted to sinus rhythm.⁵⁶ The two main agents used for prevention of thromboembolism are warfarin and aspirin, and selection of the specific agent should be based on both stroke and bleeding risks for a particular patient.^{8,9} Multiple randomized controlled trials have demonstrated the efficacy of warfarin in preventing stroke compared to no treatment.⁵⁷⁻⁶² Two different meta-analyses have shown that adjusted-dose warfarin significantly reduced the risk of ischemic stroke compared to placebo by 68% (95% CI 50-79%)⁶³ and of ischemic stroke or systemic embolism by

67% (95% CI 55-76%).⁵⁵ Several trials have also demonstrated the efficacy of aspirin versus placebo in preventing stroke^{57,61,62} and a meta-analysis of these trials provided a relative risk reduction of 21% (95% CI 0-38%).⁶⁴ Randomized controlled trials have also directly compared warfarin and aspirin.^{62,65-68} Two meta-analyses demonstrated the superiority of warfarin compared with aspirin, finding relative risk reductions of 52% (95% CI 37-63%) for ischemic stroke,⁶⁹ and 41% (95% CI 14-60%) for ischemic stroke or systemic embolism.⁵⁵ However, meta-analyses comparing warfarin to either no treatment or aspirin demonstrated significantly higher rates of major bleeding among those treated with warfarin.^{55,63,69}

Patients receiving warfarin or another vitamin K antagonist should have their International Normalized Ratio (INR) determined at least weekly during initiation of therapy, and monthly when anticoagulation is stable.^{8,9} INR is a standardized measure derived from the prothrombin time (PT) test that reflects the ability of the blood to clot. The INR therapeutic range for AFIB patients receiving warfarin is between 2.0 and 3.0.^{8,9,56} In CMS' State Operations Manual's Guidance to Surveyors for Long Term Care Facilities, one of the examples listed as a medication issue of particular relevance is appropriate monitoring is for warfarin: "Use must be monitored by Prothrombin Time (PT)/International Normalization Ratio (INR), with frequency determined by clinical circumstances, duration of use, and stability of monitoring results."⁷ Further, a specific example of noncompliance is the "use of warfarin in conjunction with inadequate or absent monitoring of PT/INR during treatment."⁷ Although not as detailed as the clinical

guidelines for AFIB, the guidance from CMS demonstrates the necessity of INR monitoring for those receiving warfarin in the NH setting.

Several new agents have been approved by the Food and Drug Administration (FDA) for prevention of stroke and systemic embolism in patients with non-valvular AFIB: dabigatran,⁷⁰ rivaroxaban,⁷¹ and apixaban.⁷² Dabigatran is a direct thrombin inhibitor that was approved by the FDA on October 19, 2010. A focused update to the 2011 AHA/ACC guidelines recommended that “Dabigatran is useful as an alternative to warfarin for the prevention of stroke and systemic thromboembolism in patients with paroxysmal to permanent AF and risk factors for stroke or systemic embolization...” (class I, level of evidence B).⁷³ Rivaroxaban and apixaban are both factor Xa inhibitors, approved by the FDA on November 4, 2011 and December 28, 2012, respectively. Unlike warfarin, these newer anticoagulants do not require routine monitoring.⁷⁴ However, there are strategies for reversing warfarin-related bleeding (e.g., administration of fresh frozen plasma or vitamin K), while none of the newer oral anticoagulants have a method for reversal of effect.⁷⁴ U.S. guidelines have not yet been updated to reflect the AHA or ACC’s recommendations for the use of these drugs in nonvalvular AFIB. Since the study period for the proposed study ends before any of these newer agents were approved, use of dabigatran, rivaroxaban, and apixaban was not considered in this study.

2.3.3 Management of AFIB among older adults

There is limited data on the risk to benefit ratio for use of warfarin among older adults.⁷⁵ One randomized controlled trial among older adults (aged >75 years) in the primary care

setting demonstrated that warfarin was more effective in preventing strokes compared with aspirin (RR 0.48, 95% CI 0.28-0.80), while there was no difference in the risk of major bleeding.⁷⁶ Despite these results, older adults are less likely to receive warfarin than younger patients with AFIB. At the same time, older adults may be more likely to benefit, given the higher prevalence of AFIB and increased risk of stroke among older adults.⁷⁵

Several studies suggest that anticoagulation is often underused in the NH population,^{47-49,77} with the use of warfarin in this population ranging from 32% to 57% (Table 2).^{47,78} One of the explanations for the low use of warfarin in these studies is the high rate of discontinuation. Among LTC residents with AFIB who initiated warfarin, 37% discontinued by 90 days and 65% discontinued after 1 year.⁷⁹ Another aspect of the quality of AFIB management is regular INR monitoring. Despite several studies that found high rates of monitoring according to guidelines (Table 2), those who do receive anticoagulation have INR values that are often below the therapeutic range.^{47,49}

Table 2. Antithrombotic management of AFIB among NH residents in the United States and Canada

Author, year	Data Source	N (AFIB)	Proportion of patients receiving			Among patients receiving warfarin	
			Warfarin	Aspirin	Neither	Time INR in range	Monthly INR monitoring
Gurwitz, 1997 ⁴⁷	Medical records (30 LTC facilities in New England, Quebec, Ontario)	413	32%	25% (excluding warfarin users)		39.6%	84% of subjects had INRs monitored \leq every 4 weeks
McCormick, 2001 ⁴⁹	Medical records (21 facilities in Connecticut)	429	42%	29%	32%	51%	90% of INR tests had intervals \leq 30 days
Lau, 2004 ⁷⁸	Administrative databases and medical records (17 LTC facilities in Alberta)	265	57%	30%	20%	64.8%	
Abel Latif, 2005 ⁴⁸	Medical charts, pharmacy records, MDS (6 facilities in Ohio)	117	46%	40% (aspirin or clopidogrel)	21%		
Gurwitz, 2007 ⁸⁰	NH records (25 NHs in Connecticut)	160				49.6%	
Aspinall, 2010 ⁸¹	Medical records (5 VA NHs)	1,767 (warfarin users, 62% with AFIB)				55%	99% of INR tests were repeated within 4 weeks
Ghaswalla, 2012 ⁸²	2004 National Nursing Home Survey	1,767	30%	17% (aspirin or clopidogrel)	54%		
Reardon, 2013 ⁸³	2004 National Nursing Home Survey	1,454	34%	35%			
Reardon, 2013 ⁸³	AnalytiCare database (~200 NHs in 19 states)	3,757	45%	7%			

Many reasons have been suggested to explain the underutilization of warfarin among older adults with AFIB. There are a number of concerns with warfarin, including the narrow therapeutic range of efficacy and safety for all vitamin K antagonists, the substantial interindividual variability in dose response, the need for frequent and long-term monitoring that is required for patients taking the drug, and the existence of numerous food and drug interactions.^{51,55,75} All of these reasons may contribute to “informed dissent” by patients who choose not to initiate warfarin⁵⁵ as well as to poor compliance of patients taking the drug.⁵¹ In practice, there is often inadequate dosing by physicians.⁵¹ One review explains: “Physicians’ reluctance to prescribe warfarin is often due to a perceived greater risk of bleeding, overestimation of the associated risks, underestimation of the stroke risk, and clinical uncertainty or inexperience of warfarin.”⁷⁵

Warfarin is one of the most common agents involved in ADEs.^{51,80} For example, one study among residents in two LTC facilities found that those taking anticoagulants had 2.4 (95% CI 1.7-3.5) higher odds of experiencing any ADE and 2.8 (95% CI 1.6-4.7) higher odds of experiencing a preventable ADE.³⁶ Warfarin was the drug most frequently involved with ADEs, alone being associated with 15% of all ADEs and 12% of preventable ADEs. In a second study among 25 Connecticut NHs, there were 25.5 per 100 resident-month warfarin-related adverse or potential adverse events.⁸¹ Of the serious, life-threatening, or fatal events, 57% were deemed preventable. Given the high rate of adverse events with warfarin, it is not surprising that the Joint Commission has made reducing the likelihood of harm associated with the use of anticoagulant therapy a National Patient Safety Goal for LTC facilities (NPSG 03.05.01).²⁸ Residents with AFIB

are one of the specifically targeted populations for this goal, and elements of the NPSG include education, use of simple dosing methods, monitoring, and documentation.

2.3.4 Transitions among NH residents with AFIB

Prystowsky et al. states that “Fragmentation of care has been cited as a major barrier to the effective implementation of current AFIB treatment guidelines,”⁵¹ suggesting that poor coordination of care resulting from transitions plays an important role in the management of patients with AFIB. This is a substantial issue, as AFIB is positively associated with hospitalizations, a significant care transition. Specifically, AFIB has been demonstrated to be associated with an increased risk of readmission (adjusted HR=2.09; 95% CI 0.94-4.65) among older adults hospitalized for heart failure⁸² and increased odds (OR=1.37; 95% CI 1.15-1.63) of in-hospital mortality or discharge to a long-term care facility among very old patients (≥ 85 years) hospitalized for stroke.⁸³ Among newly admitted NH residents, those with AFIB were 2.6 times more likely to be hospitalized early in their NH stay compared with residents without AFIB.⁸⁴

In light of the substantial number of hospitalizations experienced by NH residents with AFIB, medication reconciliation is a key strategy that should be used for these patients. Specifically, both drugs that are newly prescribed during or following a hospitalization and maintenance medications should be reviewed and potential interactions with warfarin should be considered.⁸⁵ Patients who undergo surgery and are bridged to a parenteral anticoagulant need to be switched back to warfarin; guidelines exist for appropriate methods to do so.⁸⁵ Medication reconciliation can help to ensure that anticoagulant doses

are not omitted or duplicated during a hospital to NH facility transition and are critical to avoid increased stroke or bleeding risks,⁸⁵ potentially resulting in a rehospitalization.

2.4 Summary

Substantial literature has documented various aspects of the relationship between medication quality and care transitions among those who reside in the community. Specifically, many studies have demonstrated that transitions, especially hospitalizations, often result in changes in an individual's medication regimen.^{15-17,20} Regardless of whether or not changes are intentional, transitions are a point at which discrepancies between various providers' documentation of medications occur.^{11,12} Medication changes and poor documentation may result in ADEs. The reverse relationship, the effect of various measures of medication quality on transitions, has been less well-studied and provide mixed results: two studies suggest that medication changes may contribute to hospitalizations,^{24,25} while two other studies suggest that hospitalized patients who experience medication changes or discrepancies do not have an increased risk of rehospitalization.^{11,17}

The body of literature on the relationship between medication quality and care transitions demonstrates the need for medication reconciliation across care settings. However, most medication reconciliation research and practice recommendations focus on the hospital to home transition among community-dwelling individuals. Older NH residents are particularly vulnerable to negative health events given their older age and increased frailty and comorbidity relative to their peers residing in the community. The high

number of medications taken by older adults who reside in NH facilities place them at increased risk of experiencing ADEs. The high frailty and chronic disease burden also place these individuals at risk of care transitions, especially to the hospital.

Although a significant number of studies have documented medication changes resulting from transitions between hospital and community, few have been conducted in a NH population. The few published studies that considered NH residents found a significant number of medication changes take place during a transition, and these changes resulted in ADEs.^{13,23,38} The limited data among this population suggests that care transitions are a place in which change is needed to decrease these adverse events, particularly for a vulnerable population such as NH residents. However, more research is needed to determine how effective interventions can be created and targeted in order to decrease these ADEs.

Patients with AFIB are at significantly increased risk of stroke, which places them at increased risk for transitions including hospitalizations. Antithrombotic agents such as warfarin are recommended to manage stroke risk, particularly among older adults. However, warfarin has a narrow therapeutic window and is the single drug most commonly implicated in ADE-related emergency hospitalizations among older adults.⁸⁰ Substantial underuse of these agents has been documented among NH residents, which also may lead to further hospitalization transitions. On the other hand, antithrombotic agents, specifically antiplatelets and anticoagulants such as warfarin, have been demonstrated to have high rates of change across transitions between care settings.^{14,15,18}

The high rates of hospitalization and medication changes seen with antithrombotic agents, particularly warfarin, make AFIB a practical and relevant population in which to study the relationship between medication use and care transitions.

Most of the research that explores the relationship between medication quality and transitioning focuses on the transition between hospital and primary care settings,^{11,14,18,20,25} and many explicitly exclude those that have come from, or are discharged to, a nursing home.^{12,14,18,86} This has resulted in a gap in the literature on the relationship between medication quality in older adults in the NH and hospitalizations in this setting. AFIB patients are an ideal population in which to study this relationship since AFIB is a common chronic condition among older adults and its management with agents such as warfarin is particularly problematic surrounding transitions. This study investigates the relationships at the intersection of all of these factors by examining the quality of pharmacotherapeutic management and hospitalizations among NH residents with AFIB. Results from this study may suggest that targeting clinicians to increase adherence to guidelines for managing chronic conditions such as AFIB is key in maintaining quality patient care and avoiding unnecessary transitions.

CHAPTER 3: RESEARCH DESIGN AND METHODOLOGY

3.1 Study Cohort

The study population is older, long-stay nursing home residents with chronic AFIB. To identify the study sample, atrial fibrillation was defined by the presence of at least two claims with a diagnosis of AFIB (ICD-9-CM 427.31), at least 30 days apart, of any claim type: inpatient, hospital outpatient, skilled nursing facility, hospice, home health, carrier (physician), and durable medical equipment. Requiring at least two AFIB claims at least 30 days apart served to exclude those with transient AFIB resulting from an acute illness or event,⁸⁷ since recommendations for chronic management do not apply to these patients.⁵² Cohort entry was defined as the date of the first AFIB claim during 2007-2009. Individuals were required to be 65 years of age or older on this date and have full Medicare Parts A and B coverage for 10 of the 12 months prior to this date. Those with valvular AFIB, defined by a claims with a valve-related diagnosis code (see Appendix for ICD-9-CM codes) in the 12 months prior to cohort entry, were excluded. Long-stay nursing home residents were defined as those with at least 4 continuous months of NH residence and for whom at least one of those months was on or after cohort entry. Evidence of NH residence was identified based on the MDS assessment target date, and a gap of up to 120 days between assessments was allowed when classifying a continuous stay. Eligible months were defined as months with NH evidence, excluding those with Medicare-covered SNF days, Medicare Parts A, B, and no C coverage in 10 of the prior 12 months, Medicare Part D (PDP) coverage in the month, and matching to an existing

facility (OSCAR) survey. Individuals were followed until the end of the study period (12/31/2009) or death.

3.2 Data Sources

This study uses the Chronic Condition Data Warehouse (CCW) administrative data linked to the Minimum Data Set (MDS) and to facility-level data. Medicare administrative data from the CCW is linked to the MDS at the patient-level via an encrypted identifier. These data are then linked to facility-level data using the Medicare provider number. All data sources include years 2006 through 2009. Data from 2007-2009 is used for longitudinal follow-up, while data from 2006 is used for baseline information.

3.2.1 CCW administrative data

The CCW database contains Medicare enrollment and claims data linked by beneficiary across the continuum of care.⁸⁸ These administrative data incorporate claims from inpatient, skilled nursing facility, hospital outpatient, carrier (physician), home health, hospice, and durable medical equipment settings. These claims were used to identify the cohort, identify hospitalizations and other health service utilization, and create baseline variables on comorbid conditions and stroke risk factors. Medicare Part D prescription drug events (PDEs) were used to assess use of relevant outpatient prescription drugs.

3.2.2 *Minimum Data Set (MDS)*

The MDS is a 350-item standardized resident assessment that is performed for all residents of Medicare- and Medicaid-certified nursing homes.^{88,89} The MDS contains information on demographics, payer source, physical, cognitive, and social functioning, active medical conditions, services and treatments provided, and admission, hospital transfer, and discharge transitions. The MDS includes different types of assessments, including admission, annual, quarterly, resident assessment protocol (RAP), corrections, and other.^{88,89} Admission, annual, and RAP assessments are all full assessments.

Admission assessments are performed within 14 days of admission to the nursing home. Annual assessments are performed within 365 days of the previous full assessment. RAPs are performed upon a significant change in status, and are triggered by one of many events, including but not limited to falls, pressure ulcers, or use of psychosocial drugs or physical restraints. Quarterly assessments must be performed every 92 days and may contain only a subset of the information contained in a full assessment. Other assessments are those required for the Medicare Prospective Payment System or by the state in which the facility is located. Medicare requires assessments at 5, 14, 30, 60, and 90 days, and upon return to a facility after a discharge. Discharge and reentry assessments are used for tracking purposes, but do not provide clinical or functional information. MDS discharge assessments contain information on discharge status, including: private residence, board and care/assisted living, another nursing facility, hospital, and death. Reentry assessments contain similar information on where the resident is being readmitted from: private residence, board and care/assisted living/group home, another nursing home, or a hospital.

3.2.3 *NH Facility Data*

All facility data is based on CMS-certified NHs. Over 98% of all NHs in the United States are certified by CMS for Medicare and/or Medicaid reimbursement³¹ so facility data represent almost all NHs in the United States. Facility data was obtained from two sources: CMS survey data and LTCfocus. CMS creates provider and deficiency files from standard certification surveys of nursing homes.⁹⁰ These surveys must be performed every 9 to 15 months in order to obtain and maintain Medicare and or Medicaid certification. Annual provider and deficiency files are created from monthly extracts of the Online Survey Certification and Reporting (OSCAR) database. The provider files contain one record for each standard health certification survey and contain basic information on facility size, ownership, staffing, and aggregate resident characteristics. The deficiency files contain one record per deficiency associated with each survey in the corresponding survey file. The provider and deficiency data are used to populate CMS' Nursing Home Compare website.⁹⁰

The LTCfocus data have been created through the Shaping Long-Term Care in America Project being conducted at the Brown University Center for Gerontology and Healthcare Research and supported, in part, by the National Institute on Aging.⁹¹ These data are yearly and is available at the facility, county, and state levels. Facility-level data is pulled from OSCAR, Nursing Home Compare, the MDS (for aggregate resident characteristics), the Residential History File, and the Medicare denominator file. County-level data is pulled from OSCAR and the Area Resource File. State-level data is obtained from a state policy survey and hcbs.org. These data contain some similar elements to CMS' provider

and deficiency files, as well as information on competition, access to NH-related care, and state policies and spending.

3.2.4 Data Procurement and Linkage

Medicare administrative data and the MDS were obtained through a Data Use Agreement with the Centers for Medicare and Medicaid Services (CMS) (DUA # 24275). Provider and deficiency files are publicly available and were downloaded from the CMS website.⁹⁰ LTCFocus data are publicly available after completing a brief form and were downloaded via the LTCFocus website.⁹¹ All facility-level data were non-research identifiable, publicly available, and did not require a DUA.

Medicare administrative data and MDS data were linked by a unique, encrypted beneficiary identifier. Individual-level data were linked with the facility-level data via CMS' NH provider number and by year.

3.3 Aim 1 Methods

3.3.1 Study Design

The first aim uses a retrospective cohort design to describe medication utilization and prescribing quality for AFIB in the nursing home. Observations were monthly and each individual contributed up to 36 months of follow-up data.

3.3.2 Measures

Medication prescribing was assessed at the person-month level using two measures, both based on published guidelines for AFIB:^{8,9}

1) Use of recommended medications (Table 3):

- Any antithrombotic agent
- Warfarin
- Agents for rate control
- Agents for rhythm control (antiarrhythmic)

2) Receipt of regular INR monitoring among those receiving warfarin

Table 3. Medications used for atrial fibrillation assessed in this study

Antithrombotic agents	Rate control agents	Rhythm control agents
Cilostazol	Digoxin	Amiodarone
Clopidogrel	Diltiazem	Dronedarone
Dalteparin (LMWH)	Metoprolol	Disopyramide
Dipyridamole (\pm aspirin)	Propranolol	Dofetilide
Enoxaparin (LMWH)	Verapamil	Flecainide
Fondaparinux		Ibutilide
Heparin		Procainamide
Prasugrel		Propafenone
Ticlopidine		Quinidine
Tinzaparin (LMWH)		Sotalol
Warfarin		

Drug use was measured monthly based on Prescription Drug Event (PDE) records in the Medicare Part D claims. Medication use was defined as availability of the relevant medication during the month based on Part D prescription drug event (PDE) fill dates and days supplied. An individual was considered to have used the drug during the month if the days supply covered at least one day in the month. For those months with a days supply greater than the number of days in the month, it was assumed that the medication

was taken after the current days supply was finished and therefore the days supply was shifted forward.

Guidelines for AFIB management recommend INR monitoring at least monthly for those stabilized on warfarin.^{8,9} Regular INR monitoring was defined as at least one claim for a prothrombin time test within the month and was captured using procedure codes (CPT codes 85610 and 85611) in administrative claims. All claim types were searched for these codes; they appeared only in inpatient, outpatient, carrier, and SNF claims.

3.3.3 *Person-level covariates*

Demographic information was obtained from the Medicare patient denominator file, including sex, age as of the first AFIB diagnosis in 2007-2009, geographic region, and race based on the RTI Institute's algorithm.

Time-varying covariates included month since AFIB diagnosis, LIS and dual eligibility, a flag for incident AFIB, CHADS₂ and HEMORR₂HAGES scores, the Charlson comorbidity index (CCI), and a flag for end of life. A variable counting the months following the first observed AFIB diagnosis was used as the time variable. A monthly LIS flag identified those receiving a low-income subsidy for assistance paying for medications and a monthly dual eligibility flag identified those receiving both Medicare and Medicaid benefits. Both flags were obtained from the Medicare patient denominator file. Incident AFIB was defined for the first 6 months following a person's first observed AFIB diagnosis for those with no AFIB claim during the 12 months prior to that

diagnosis. Stroke risk was assessed using the CHADS₂ index, which was developed to quantify the risk of ischemic stroke in patients with nonvalvular AFIB^{92,93} and is the most commonly used scoring system to assess stroke risk.⁸⁵ Bleeding risk was captured using the HEMORR₂HAGES risk classification scheme, which quantifies hemorrhage risk in older adults with AFIB and has the highest predictive accuracy compared with other schemes.⁹⁴ The CHADS₂ and HEMORR₂HAGES risk scores were calculated by identifying each of the components in administrative claims and summing to calculate a total score for each; the components for each risk scheme are listed in Appendix 2. Each component was identified by the presence of at least one inpatient claim or at least two outpatient (i.e., hospital outpatient or carrier) claims with a relevant ICD-9-CM code in the 12 months prior to each month. The Charlson comorbidity index (CCI) was based on previously published algorithms.⁹⁵⁻⁹⁸ CCI components were identified by the presence of an inpatient claim with a relevant ICD-9-CM code in the 12 months prior to each month. ICD-9-CM codes for each of the components of the CHADS₂, HEMORR₂HAGES, and CCI are provided in Appendix 1. Since healthcare utilization often changes for individuals who are close to death, a flag identifying that a resident was near the end of life was created for the last three months prior to death.

3.3.4 Facility-level covariates

A number of facility characteristics were explored in this study. Organizational facility-level factors included chain affiliation, profit status, and whether or not the facility was hospital-based. Facility size was captured by the total number of beds and the occupancy rate. Variables representing the availability of an Alzheimer's special care unit, the

average number of hospitalizations per resident year, and the average number of medications per resident were also included to capture information about the type of residents in each facility. Facility staffing variables included the availability of a physician extender (i.e., nurse practitioner or physician assistant) and the average direct care (i.e., registered nurse, licensed practical nurse, certified nursing assistant) hours per patient per day.

Deficiency information was captured using six flags that assessed whether or not a facility had:

- Any deficiency
- Any deficiency with a poor scope or severity rating
- Any quality of care deficiency
- Any quality of care deficiency with a poor scope or severity rating
- Any pharmacy-related deficiency
- Any pharmacy-related deficiency with a poor scope or severity rating

Poor scope/severity was defined as any scope causing immediate jeopardy to resident health or safety (J, K, L), a pattern or widespread scope causing actual harm to resident health or safety (H, I), or widespread scope with potential for actual harm to resident health or safety (F).

Scope and Severity Matrix for Nursing Home Deficiencies⁹⁹

Severity	Scope		
	Isolated	Pattern	Widespread
Immediate Jeopardy	J	K	L
Actual Harm	G	H	I
Potential for Actual Harm	D	E	F
Minimal Harm	A	B	C

A quality of care deficiency was defined as an F-tag in the following categories: resident behavior/facility practices, quality of life, or quality of care.⁹⁹ A pharmacy-related deficiency was defined as an F-tag in the pharmacy services category or a subset of F-tags in the quality of care category related to medications (0329, 0330, 0331, 0332, 0333).

LTCFocus incorporates county- and state-level data, and several of these variables were included in this study. The number of hospital beds per 1000 elderly and the number of nurses per 1000 elderly contributed information about the availability of these resources in the county of the facility. In addition, the managed care organization (MCO) penetration rate provided information on the proportion of Medicare beneficiaries in the county enrolled in a Medicare MCO. State level variables provided information on payment policies that affect all facilities in each state. These include the average Medicaid per diem, an indicator of whether or not a state has a Medicaid case mix reimbursement system that adjusts payments based on resident acuity, and the proportion of Medicaid LTC spending on HCBS, which is conversely related to the proportion spent on NH care.

Full definitions and data sources of available facility characteristics are provided in Appendix 3.

3.3.5 Statistical Analysis

Aim 1a

Measures of pharmacotherapeutic management include the use of all recommended medication classes (i.e., antithrombotic agents, agents for rate control, and antiarrhythmic agents) and receipt of regular INR monitoring among those receiving warfarin. These measures are reported as an average monthly prevalence of use. All descriptive statistics are reported as mean and standard deviation (SD) for continuous measures and as number and percent for categorical measures.

A sensitivity analyses was performed by assessing the measures described above in a subset of the cohort in whom warfarin is indicated: high stroke risk (CHADS₂ score ≥ 2) and no major bleeding in the prior year. No additional bleeding risk factors were used as exclusion criteria because they are relative, not absolute, contraindications, and a high bleeding risk score (e.g., HEMORR₂HAGES) should assist in identifying patients who need additional consideration or follow-up rather than avoiding therapy.⁸⁵

Aim 1b

This aim focuses on two specific measures of pharmacotherapeutic management: use of warfarin and receipt of regular INR monitoring among those receiving warfarin. Bivariable analyses were performed at the monthly level to assess the unadjusted

relationships between each of these two binary dependent variables and covariates. To test for statistical significance, chi-square tests were used to compare categorical variables and two-sample (unpaired) t-tests were used for continuous variables.

Multivariable regression quantified the adjusted relationship between each of the measures of pharmacotherapeutic management of AFIB and covariates that were significant in bivariable analyses. These were generalized linear mixed models, specifying a binary distribution and logit link to handle the dichotomous dependent variable. Since there is both correlation between observations within a person and correlation between residents within a facility, hierarchical (e.g., multilevel) models were employed. These models included patient random effects nested within facilities to account for the correlation between repeated observations within a person and facility random effects to account for clustering of patients within each facility:

$$\text{Log} \frac{\text{Pr}(\text{warfarin}_{ijk} = 1)}{\text{Pr}(\text{warfarin}_{ijk} = 0)} = \beta_0 + \beta_1 \text{month}_i + \beta_2 X_{ijk} + \beta_3 X_{jk} + \beta_4 X_k + b_{jk} + b_k + e_{ijk}$$

$$\text{Log} \frac{\text{Pr}(\text{INR}_{ijk} = 1)}{\text{Pr}(\text{INR}_{ijk} = 0)} = \beta_0 + \beta_1 \text{month}_i + \beta_2 X_{ijk} + \beta_3 X_{jk} + \beta_4 X_k + b_{jk} + b_k + e_{ijk}$$

where i=measurement occasion, j=patient, and k=nursing home facility;

warfarin=indicator of warfarin use; INR=indicator of regular INR monitoring;

month=month from AFIB diagnosis; X_{ijk} = time-varying covariates, X_{jk} = person-level

covariates, and X_k = facility-level covariates; b_{jk} is the random patient effect and b_k is the random facility effect.

3.4 Aim 2 Methods

3.4.1 Study Design

This aim uses a pre-post design, comparing drug use before and after a hospitalization.

3.4.2 Specific inclusion criteria

The study population for this aim is the same as in Aim 1: older, long stay NH residents with chronic AFIB. However, since the design is different, inclusion/exclusion criteria were applied differently. All months with an inpatient discharge (i.e., index hospitalization) were selected. The sample was restricted to discharges that occurred at least 6 months after an individual's first observed AFIB diagnosis to ensure that individuals had AFIB prior to the hospitalization and therefore have an indication for AFIB management. Further, hospital discharges were included if they fell between July 2006 and June 2009 to ensure adequate look back and follow-up time, respectively. To avoid a recent or subsequent hospitalization impacting AFIB management, the 6 months prior and 6 months following the hospitalization were required to have no other hospitalizations. At least 3 of the 6 months both prior and following the index hospitalization were required to have evidence of NH residence based on MDS assessments, in order to obtain a sample of long-stay NH residents ("any NH" cohort). A second cohort was created that required at least 6 months of NH residence that excluded months with any SNF coverage ("no SNF" cohort) to ensure that all Part D covered

medications could be observed. For hospitalizations spanning more than one month, the 6-month prior windows ended at the month of the index hospitalization's admission, not discharge, so that the full 6 month period was observable. Lastly, the first eligible observation was selected for this aim, in order to avoid possible correlation between multiple observations of the same person.

A control group was identified for comparison by identifying months with no hospitalization and applying the same criteria as for the study cohort: months between July 2006 and June 2009, months at least 6 months after the first observed AFIB diagnosis, no hospitalization within 6 months prior or following the index month, and at least 3 months of NH residence in each of the prior and following 6 months. Again, the first eligible observation was included for those with more than one eligible month.

A sensitivity analysis was performed among a cohort identified using 3-month windows instead of the 6-month windows described above. This analysis identifies medication use more closely surrounding a hospitalization.

3.4.3 Measures

Hospitalizations were identified via the presence of a Medicare inpatient claim. A flag for each month was created to identify months in which a patient hospitalized. If an inpatient visit spanned more than one month, only the month in which the discharge occurred was flagged. As noted above, each individual could only contribute one observation; the month of the hospital discharge associated with that observation was the index month.

Drug use was measured monthly based on Prescription Drug Event (PDE) records in the Medicare Part D claims. As in aim 1, medication use was defined as availability of the relevant medication during the month based on fill dates and days supplied. An individual was considered to have used the drug during the month if the days supply covered at least one day in the month. For those months with a days supply greater than the number of days in the month, the days supply was shifted forward to the subsequent month.

This aim focused on antithrombotic use, and antithrombotic medications were categorized as follows:

- Warfarin
- Thienopyridines: clopidogrel, prasugrel, ticlopidine
- Low molecular weight heparin (LMWH): dalteparin, enoxaparin, tinzaparin
- Heparin
- Other antithrombotic agents: fondaparinux, dipyridamole, cilostazol

3.4.4 Statistical Analysis

This aim uses descriptive analyses to compare medication use before and after a hospitalization transition. Within each antithrombotic group, the proportion of people who make no change, initiate a drug, or discontinue the drug is reported. Warfarin use was further analyzed by determining the distribution of those who continue warfarin, switch to another drug, or discontinue warfarin after a hospitalization, among those taking warfarin prior to the hospitalization.

A second analysis classified the cohort into the following mutually exclusive groups and report the proportion in each category:

- 1) Maintained on warfarin or another antithrombotic agent
- 2) Maintained on no antithrombotic agent
- 3) Initiation of warfarin or another antithrombotic agent
- 4) Discontinuation of warfarin or another antithrombotic
- 5) Switching to a different antithrombotic

For both the study cohort and the control group, the number and percent of individuals in each of the above categories was determined. The difference in the distribution of these categories between the cohort and controls was tested using a chi-square test of independence.

3.5 Aim 3 Methods

3.5.1 Study Design

Aim 3 uses a retrospective cohort design to determine the bidirectional relationship between pharmacotherapeutic management of AFIB and hospitalizations. The data structure is similar to that used in aim1, where observations were monthly and each individual contributed up to 36 months of follow-up data. Aim 3a assesses the impact of pharmacotherapeutic management of AFIB on hospitalizations, while aim 3b examines the effect of a hospitalization on pharmacotherapeutic management of AFIB.

3.5.2 Measures

Drug Use

In aim 3, measures of pharmacotherapeutic management included binary indicators for warfarin use and INR monitoring among those using warfarin. These measures were operationalized as described in aim 1.

Hospitalizations

Hospitalizations were identified via the presence of a Medicare inpatient claim. A flag for each month was created to identify months in which a patient was hospitalized. If an inpatient visit spanned more than one month, only the month in which the discharge occurred was flagged.

AFIB-related hospitalizations were identified using inpatient claims with a primary diagnosis (i.e., first ICD-9-CM code) of AFIB, ischemic stroke or transient ischemic event, or a major bleeding event (intracranial, gastrointestinal, or other; see Appendix 1 for ICD-9-CM-codes). AFIB-related hospitalizations were used only in aim 3a (as a dependent variable), since it was hypothesized that the quality of pharmacotherapeutic management of AFIB is likely to impact AFIB-related hospitalizations but that any hospitalization transition could influence AFIB management.

Covariates

Aim 3 used the same covariates as presented in aim 1. These covariates included demographic factors, clinical factors, and facility-level factors. Multivariable models

were built by assessing the associations of covariates with the dependent and main independent variables, and by considering the potential clinical or policy relevance of each of the covariates.

3.5.3 Statistical Analysis

Hierarchical generalized linear mixed models

Generalized linear mixed models were employed to determine (a) the effect of AFIB pharmacotherapeutic management on hospitalization and (b) the effect of hospitalization on AFIB pharmacotherapeutic management. These models used a binary distribution and logit link to handle the dichotomous dependent variables. Similar to aim 1, hierarchical (e.g., multilevel) models were used by including patient random effects nested within facilities to account for the correlation between repeated observations within a person and facility random effects to account for clustering of patients within each facility. Variables identified as clinically relevant or significant in aim 1 were included as covariates.

Aim 3a:

$$(1) \text{Log} \frac{\text{Pr}(\text{AFhosp}_{ijk}=1)}{\text{Pr}(\text{AFhosp}_{ijk}=0)} = \beta_0 + \beta_1 \text{warfarin}_{ijk} + \beta_2 \text{month}_i + \beta_3 X_{ijk} + \beta_4 X_{jk} + \beta_5 X_k + b_{jk} + b_k + e_{ijk}$$

$$(2) \text{Log} \frac{\text{Pr}(\text{AFhosp}_{ijk}=1)}{\text{Pr}(\text{AFhosp}_{ijk}=0)} = \beta_0 + \beta_1 \text{INR}_{ijk} + \beta_2 \text{month}_i + \beta_3 X_{ijk} + \beta_4 X_{jk} + \beta_5 X_k + b_{jk} + b_k + e_{ijk}$$

Aim 3b:

$$(3) \text{Log} \frac{\text{Pr}(\text{warfarin}_{ijk}=1)}{\text{Pr}(\text{warfarin}_{ijk}=0)} = \beta_0 + \beta_1 \text{hosp}_{ijk} + \beta_2 \text{month}_i + \beta_3 X_{ijk} + \beta_4 X_{jk} + \beta_5 X_k + b_{jk} + b_k + e_{ijk}$$

$$(4) \text{Log} \frac{\text{Pr}(\text{INR}_{ijk}=1)}{\text{Pr}(\text{INR}_{ijk}=0)} = \beta_0 + \beta_1 \text{hosp}_{ijk} + \beta_2 \text{month}_i + \beta_3 X_{ijk} + \beta_4 X_{jk} + \beta_5 X_k + b_{jk} + b_k + e_{ijk}$$

where i =measurement occasion, j =patient, and k =nursing home facility;

warfarin=indicator of warfarin use; INR=indicator of INR monitoring; AFhosp=indicator of AFIB-related hospitalization in the month; hosp=indicator of any hospitalization in the month; month=month from AFIB diagnosis; X_{ijk} = time-varying covariates, X_{jk} = person-level covariates, and X_k = facility-level covariates; b_{jk} is the random patient effect and b_k is the random facility effect.

Since the data are longitudinal, time (month following first observed AFIB diagnosis) is included in each of the models to control for potential changes over time. However, the coefficient on the time variable is not of interest in this study. Individuals enter the cohort at different points during their AFIB disease progression and NH residence and therefore the month of the first observed AFIB diagnosis at which individuals enter the cohort is not a meaningful time point on which to base comparisons of individual trajectories.

Aim 3 also proposed to use structural equation modeling, specifically the cross-lagged panel model, to assess the hypothesized reciprocal relationship between pharmacotherapeutic management of AFIB and hospital transitions. It was determined

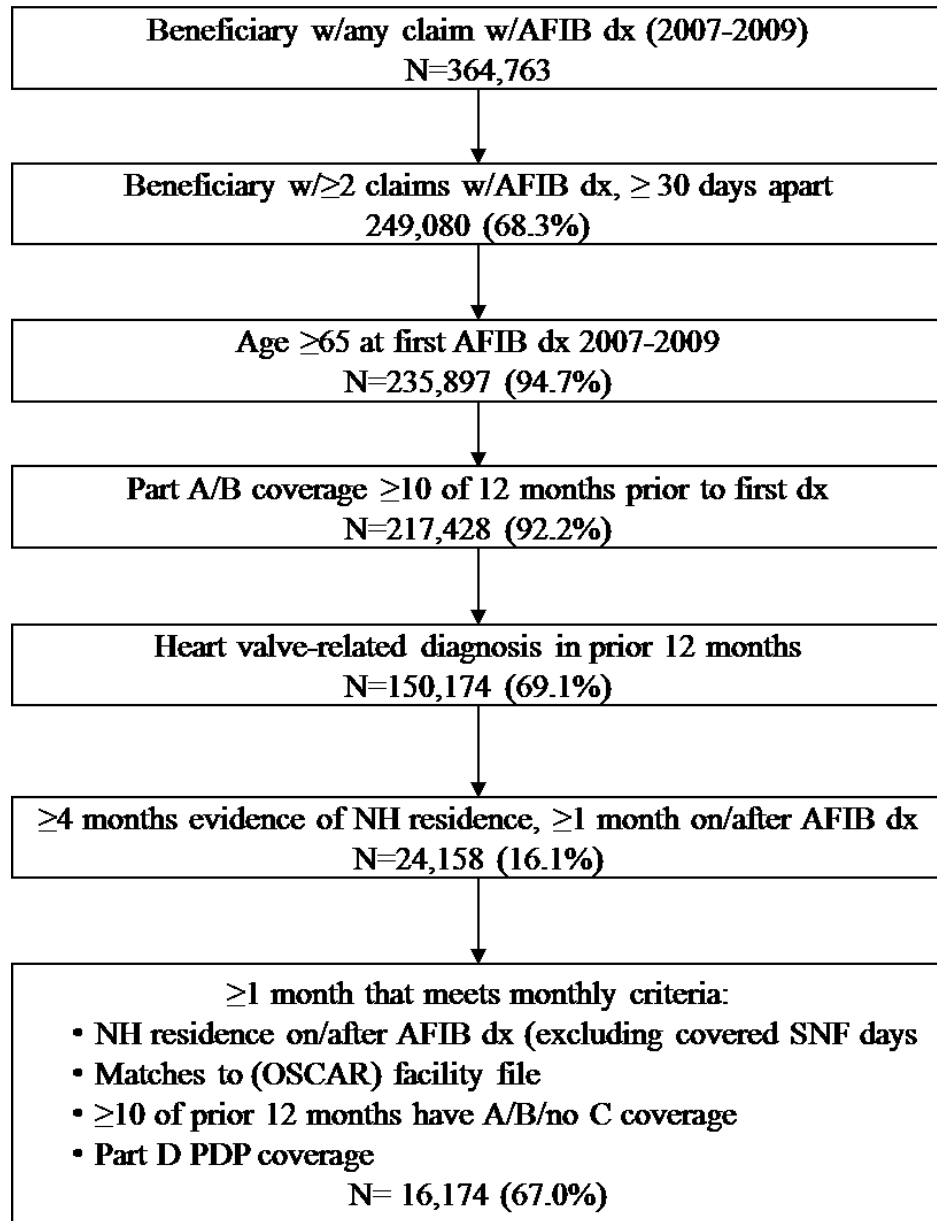
that this analysis was not feasible. A discussion of this method is presented in the Results section.

CHAPTER 4: RESULTS

4.1 Cohort

A total of 364,763 individuals were identified as potentially having AFIB based on at least one claim of any type (inpatient, outpatient, skilled nursing, home health, hospice, carrier, durable medical equipment) with an AFIB diagnosis code (ICD-9-CM 427.31) in 2007-2009 (Figure 2). At least 2 AFIB claims, at least 30 days apart, were required in order to remove those with a single “rule-out” diagnosis or those with transient AFIB after a procedure (N=249,080, 68.3%). A majority of these individuals were at least 65 years old at their first AFIB diagnosis (N=235,897, 94.7%). Individuals were required to have Medicare Part A and B coverage for at least 10 of the 12 months prior to the first AFIB diagnosis (N=217,428, 92.2%) in order to have a sufficient look-back period in which to determine prior conditions and 150,174 (69.1%) were identified as having non-valvular AFIB based on an absence of valve-related claims during those prior 12 months. The most restrictive criteria was long-stay nursing home residents (N=24,158, 16.1%). Of these, 16,174 individuals (67.0%) had at least one eligible month of observation and comprised the final study sample (Figure 2).

Figure 2. Cohort flowchart for aim 1



On average, individuals had over 13 months of follow-up (± 10 , range 1-36) (Table 4).

The first follow-up month was the same month as the first observed AFIB diagnosis during the study period for 41.7% of the cohort, while 27.7% had over 6 months between the first observed diagnosis and first follow-up month. The average (SD) age was 84.5

years (± 7.4), 76.4% were female, and 88.3% were white race. During the first month of observation, over three-quarters of the cohort were receiving a low-income subsidy (LIS) for assistance paying for medications. Over one-third of the cohort had newly-diagnosed AFIB, and over half died during the follow-up period. A large majority of the cohort had a high risk of stroke, defined as a CHADS₂ score ≥ 2 (91.9%). The average HEMORR₂HAGES score was 3.9 (± 1.5) and the average CCI was 2.0 (± 2.1). Common comorbid conditions included chronic heart failure (53.2%), dementia (52.1%), and anemia (47.0%).

Table 4. Cohort characteristics (N=16,174)*

Characteristic	Number	%
Number of follow-up months (mean, SD)		13.6 (10.3)
Months between first observed diagnosis and first follow-up month		
0	6,751	41.7
1-6	4,943	30.6
≥7	4,480	27.7
Age		
Mean, SD		84.5 (7.4)
65-74	1,775	11.0
75-84	5,742	35.5
≥85	8,657	53.5
Female	12,352	76.4
Race		
White	14,273	88.3
Black	1,172	7.3
Hispanic	453	2.8
Other†	276	1.7
Region		
Northeast	4,089	25.3
Midwest	4,667	28.9
West	1,806	11.2
South/Other	5,612	34.7
LIS	12,252	75.8
Dual eligibility	11,866	73.4
Died during follow-up	8,277	51.2
Newly-diagnosed AFIB‡	5,596	34.6
Hospitalization in prior 12 months	11,178	69.1
Charlson comorbidity index		
0	5,795	35.8
1	2,315	14.3
2	2,588	16.0
≥3	5,476	33.9
CHADS ₂ score		
0	70	0.4
1	1,246	7.7
2	3,798	23.5
3	5,101	31.5
4	3,376	20.9
5	1,771	11.0
6	812	5.0
HEMORR ₂ HAGES score (mean, SD)		3.9 (1.5)
Individual comorbid conditions§		
Ischemic event	4,369	27.0
Diabetes	6,087	37.6
Chronic heart failure	8,597	53.2
Hypertension	13,555	83.8
Major bleed	2,288	14.2
Liver or kidney disease	3,482	21.5
Alcohol abuse	221	1.4

Characteristic	Number	%
Cancer	1,582	9.8
Reduced platelet count or function	538	3.3
Anemia	7,599	47.0
Dementia	8,430	52.1
Increased fall risk	9,122	56.4
Facility characteristics**††		
For profit	10,783	66.7
Chain affiliated	8,542	52.8
Hospital-based facility	774	4.8
Any “poor” deficiency	3,582	23.1
Quality of care “poor” deficiency	554	3.6
Any pharmacy-related deficiency	7,247	46.7
Dedicated Alzheimer’s unit	3,624	22.7
Available physician extender (NP, PA)	5,357	33.5
Direct care hours/patient/day (mean, SD)		3.3 (1.1)
Bed size (mean, SD)		141 (88)
Occupancy rate (mean, SD)		87 (13)
Hospitalizations/patient/year (mean, SD)		0.95 (0.52)
Average number of medications/patient (mean, SD)		10.8 (1.4)
County- and state-level characteristics		
# hospital beds/1000 elderly (county) (mean, SD)		26 (20)
# nurses/1000 elderly (county) (mean, SD)		44 (32)
MCO penetration rate (county) (mean, SD)		16.6% (12.8%)
Average Medicaid per diem (state) (mean, SD)		\$158 (\$33)
Medicaid LTC spending on HCBS (state) (mean, SD)		28.4% (13.0%)
Case-mix adjustment (state)	11,637	72.9

*All time-varying variables are based on the first month of observation

†Other race category includes: Asian, Pacific Islander, American Indian, Alaska Native, self-identified other race, and unknown

‡Newly-diagnosed AFIB: No evidence of AFIB for the 12 months prior to the first observed AFIB diagnosis and the first observation month is within 6 months of the first AFIB diagnosis

§Risk factors all measured in the 12 months prior to the first observed month

**Frequencies and means for facility characteristics are based on the facility in which a resident resides during the first month of observation

††Sample sizes for facility characteristics were different due to missing values: for-profit, chain affiliated, hospital based (N=16,168); deficiency variables (N=15,521), Alzheimer’s unit, specialty unit, physician extender (N=15,998), direct care hours/patient/day (N=15,947); bed size, occupancy rate (N=16,168), hospitalizations/patient/year (N=15,895), medications/patient (N=15,770), county-level variables (N=15,994), state-level variables (N=15,964)

The cohort resided in 9,133 unique facilities, with between 1 and 12 residents in the cohort residing in each facility. At the first month of observation, two-thirds of the cohort resided in a for-profit facility and just over half of facilities were part of a chain. The average size of facilities was 141 beds, with an average occupancy rate of 87%. Almost one-quarter of residents resided in a facility that had received at least one “poor”

deficiency citation in the most recent survey, and 3.4% were in facilities with a “poor” deficiency related to quality of care. Physician extenders (e.g., nurse practitioners, physician assistants) were available in 33.5% of facilities. The average number of medications for all residents in facilities represented by NH residents in this study was 10.8 (± 1.4).

4.2 Aim 1

4.2.1 Aim 1a: Pharmacotherapeutic management of AFIB

Under half of the observed person-months (48.0%) were receiving any antithrombotic, of which warfarin made up a large majority (78.0%) (Table 5). The second-most common antithrombotic class was the thienopyridines (9.8%), followed by other antithrombotic agents (1.9%), low molecular weight heparin (0.9%) and heparin (0.4%). Among those person-months on warfarin (n=82,215), 84.3% had at least one INR test in the month, indicative of regular INR monitoring.

Rate control agents were used in 61.2% of person-months (Table 5). Beta-blockers, calcium channel blockers, and digoxin were taken by 30.8%, 14.4%, and 28.6%, respectively. Rhythm control agents were used much less frequently, used in only 8.1% of person-months. Amiodarone was the most common rhythm-control agent (5.6%), followed by sotalol (1.6%). Class 1c agents, class 1a agents, dronedarone, and dofetilide were each used in less than 1% of person-months.

Table 5. Monthly prevalence of medications for atrial fibrillation (N=219,571)

Agent	Average Monthly Prevalence	
	N	(%)
Antithrombotic agents		
Any antithrombotic	105,368	48.0
Warfarin	82,215	37.4
Thienopyridines*	21,422	9.8
Low molecular weight heparin†	1,886	0.9
Heparin	875	0.4
Other antithrombotic agent‡	4,090	1.9
INR monitoring (N=82,215)	69,310	84.3
Rate control agents		
Any rate control agent	134,393	61.2
Digoxin	62,790	28.6
Beta blockers§	67,673	30.8
Calcium channel blockers**	31,658	14.4
Rhythm control agents		
Any rhythm control agent	17,764	8.1
Amiodarone	12,183	5.6
Dronedarone	10	<0.1
Dofetilide	35	<0.1
Sotalol	3,478	1.6
Rhythm1a††	499	0.2
Rhythm1c‡‡	1,860	0.9

*Thienopyridines: clopidogrel, prasugrel, ticlopidine

†Low molecular weight heparin: dalteparin, enoxaparin, tinzaparin

‡Other antithrombotic agent: fondaparinux, dipyridamole, cilostazol

§Beta blockers: propranolol, metoprolol

**Calcium channel blockers: verapamil, diltiazem

††Rhythm1a: disopyramide, procainamide, quinidine

‡‡Rhythm1c: flecainide, propafenone

Since warfarin may not be indicated in all of the studied individuals, a sensitivity analyses was performed that restricted the sample to those at high risk of stroke (CHADS₂ ≥2) and no prior major bleed (N=180,802, 82.3%). Among these person-months in whom warfarin is indicated, just under half were receiving any antithrombotic (49.9%). Of the antithrombotic medication groups, warfarin use was highest (38.8%), followed by thienopyridines (10.2%). Use of LMWH, heparin, and other ATs (fondaparinux, dipyridamole, cilostazol) remained low, with use in 0.8%, 0.4%, and 1.9%

of person-months, respectively. Lastly, 85.2% of person-months received INR monitoring.

4.2.2 Aim 1b: Factors associated with pharmacotherapeutic management of AFIB

Bivariable analyses: factors associated with warfarin use

Table 6 presents person- and facility-level factors stratified by months of warfarin use. In bivariable analyses, use of warfarin was associated with the following: younger age, White race, Northeast and Midwest regions. There was a lower proportion of warfarin use among person-months receiving a low-income subsidy, those with newly-diagnosed AFIB, and those at the end of life. Higher CHADS₂ scores were associated with warfarin use, as were each of the individual conditions included in the CHADS₂ calculation (i.e., diabetes, CHF, hypertension, ischemic events). There was a lower proportion of warfarin use among those with each of the elements in the HEMORR₂HAGES score calculation except cancer, hypertension, and ischemic events (i.e., hepatic or renal disease, alcohol abuse, decreased platelet count or function, anemia, dementia or other fall risk, and history of major bleed).

Facility characteristics positively associated with warfarin use include: being a hospital-based facility, higher occupancy rate, higher average number of medications taken per resident, and facilities in a state with a case-mix adjustment system. Lower warfarin use was observed in for-profit facilities, those with “poor” or pharmacy-related deficiencies. There were a number of other facility characteristics statistically significantly related to warfarin use, but the small actual differences make it unlikely that the differences are

clinically meaningful. At the county level, warfarin user resident-months had a lower average lower number of hospital beds and lower number of nurses per 1000 elderly in the county, and a lower proportion of elderly enrolled in managed-care organizations. Warfarin use had a positive association with facilities in states with a case-mix adjustment system and a negative association with facilities in states with a lower proportion of LTC spending on HCBS (and therefore higher spending on NH services).

Table 6. Cohort characteristics stratified by warfarin use, monthly (N=219,571)

Characteristic	No warfarin use (n=137,356)		Warfarin use (n=82,215)		p-value
	Number	%	Number	%	
Age					
Mean, SD		85.3 (7.4)		83.5 (7.0)	<0.001
65-74	12,737	9.3	9,849	12.0	
75-84	44,869	32.7	32,600	39.7	<0.001*
≥85	79,750	58.1	39,766	48.4	
Female	107,985	78.6	64,501	78.5	0.37
Race					
White	120,511	87.7	73,934	89.9	
Black	10,358	7.5	5,283	6.4	<0.001
Hispanic	4,001	2.9	1,944	2.4	
Other†	2,486	1.8	1,054	1.3	
Region					
Northeast	34,969	25.5	22,808	27.7	
Midwest	37,769	27.5	25,378	30.9	<0.001
West	14,743	10.7	8,066	9.8	
South/Other	49,875	36.3	25,963	31.6	
LIS	115,303	83.9	68,587	83.4	0.001
Dual eligibility	112,484	81.9	67,208	81.8	0.39
Newly-diagnosed AFIB	14,457	10.5	5,613	6.8	<0.001
End of life	16,023	11.7	7,562	9.2	<0.001
Charlson comorbidity index					
0	73,096	53.2	45,141	54.9	
1	15,326	11.2	8,272	10.1	<0.001*
2	16,996	12.4	9,757	11.9	
≥3	31,938	23.3	19,045	23.2	
CHADS ₂ score					
0	738	0.5	309	0.4	
1	12,362	9.0	5,290	6.4	
2	37,255	27.1	19,026	23.1	
3	44,003	32.0	25,307	30.8	<0.001*
4	25,851	18.8	18,858	22.9	
5	11,878	8.7	9,170	11.2	
6	5,269	3.8	4,255	5.2	
HEMORR ₂ HAGES score (mean, SD)		3.7 (1.4)		3.6 (1.4)	<0.001
Individual comorbid conditions					
Ischemic event	30,085	21.9	23,782	28.9	<0.001
Diabetes	49,912	36.3	33,675	41.0	<0.001
Chronic heart failure	67,240	49.0	44,962	54.7	<0.001
Hypertension	111,348	81.1	67,508	82.1	<0.001
Major bleed	14,155	10.3	6,531	7.9	<0.001
Liver or kidney disease	25,566	18.6	14,307	17.4	<0.001
Alcohol abuse	1,271	0.9	522	0.6	<0.001
Cancer	10,235	7.5	5,996	7.3	0.17
Reduced platelet count or function	3,144	2.3	1,662	2.0	<0.001
Anemia	63,744	46.4	34,521	42.0	<0.001

Characteristic	No warfarin use (n=137,356)		Warfarin use (n=82,215)		p-value
	Number	%	Number	%	
Dementia	83,146	60.5	42,284	51.4	<0.001
Increased fall risk	73,970	53.9	43,037	52.4	<0.001
Facility characteristics‡					
For profit	91,848	66.9	53,427	65.0	<0.001
Chain affiliated	71,464	52.0	42,618	51.8	0.36
Hospital-based facility	6,246	4.6	4,228	5.1	<0.001
Any “poor” deficiency	31,541	23.0	17,390	21.2	<0.001
Quality of care “poor” deficiency	5,241	3.8	2,633	3.2	<0.001
Pharmacy-related deficiency	63,924	46.5	35,846	43.6	<0.001
Dedicated Alzheimer’s unit	30,710	22.6	18,652	23.0	0.04
Available physician extender	47,631	35.0	27,998	34.5	0.007
Bed size (mean, SD)		141 (90)		140 (93)	<0.001
Occupancy rate (mean, SD)		87.4 (12.0)		87.6 (12.0)	<0.001
Hospitalizations/patient/year (mean, SD)		0.93 (0.48)		0.91 (0.51)	<0.001
Average number of medications/patient (mean, SD)		10.9 (1.4)		11.0 (1.4)	<0.001
Direct care hours/patient/day (mean, SD)		3.3 (1.0)		3.3 (0.9)	0.004
County- and State-level characteristics‡					
Number of hospital beds/1000 elderly (county) (mean, SD)		25.9 (19.8)		25.4 (20.0)	<0.001
Number of nurses/1000 elderly (county) (mean, SD)		44.0 (32.0)		42.9 (33.8)	<0.001
MCO penetration rate (county) (mean, SD)		18.5% (12.5%)		17.8% (12.3%)	<0.001
Average Medicaid per diem (state) (mean, SD)		\$159 (\$34)		\$159 (\$34)	0.85
Proportion of Medicaid LTC spending on HCBS (state) (mean, SD)		29.3% (12.9%)		28.5% (12.7%)	<0.001
Case-mix adjustment (state)		97,572 72.0		61,654 75.9	<0.001

*Significance for bivariable analyses with age, CCI, and CHADS₂ was tested using the Cochran-Armitage test for trend.

†Other race category includes: Asian, Pacific Islander, American Indian, Alaska Native, self-identified other race, and unknown

‡Sample sizes for facility characteristics were different due to missing values: for-profit, chain affiliated, hospital based (N=219,529); deficiency variables (N=219,571), Alzheimer’s unit, physician extender (N=217,234), direct care hours/patient/day (N=216,856); bed size, occupancy rate (N=219,529), hospitalizations/patient/year (N=216,317), medications/patient (N=215,263), county-level variables (N=217,192), state-level variables (N=216,780)

Bivariable analyses: Factors associated with INR monitoring, among warfarin users

Table 7 presents person- and facility-level factors stratified by INR monitoring, among warfarin users. Age and sex were not predictive of INR monitoring, but a higher proportion of those of white race and those residing in the Northeast and Midwest regions

had regular INR monitoring. Those with newly-diagnosed AFIB were more likely to have INR monitoring, while those at the end of life were less likely to have INR monitoring. Those with a higher number of comorbid conditions were less likely to receive regular INR monitoring, as were those with individual risk factors for stroke and/or bleeding. Interestingly, CHADS₂ score was not consistently associated with INR monitoring.

A number of facility characteristics were negatively associated with INR monitoring, including for profit facilities, those affiliated with a chain, those with “poor” deficiencies, an available physician extender, larger bed size, and those with a higher rate of hospitalizations. Facilities with an Alzheimer’s special care unit and those with higher occupancy had higher proportions of resident-months with INR monitoring. At the county level, a higher availability of hospital beds and a lower MCO penetration rate were associated with INR monitoring. States with a lower proportion of LTC spending on HCBS (and therefore a higher proportion on NHs) and those with a case-mix adjustment system also had a higher proportion of resident-months with INR monitoring.

Table 7. Cohort characteristics stratified by INR monitoring, among warfarin users, monthly (N=82,215)

Characteristic	No INR monitoring (n=12,905)		INR monitoring (n=69,310)		p-value
	Number	%	Number	%	
Age					
Mean, SD		83.5 (7.3)		83.5 (7.0)	0.70
65-74	1,761	13.7	8,088	11.7	
75-84	4,703	36.4	27,897	40.3	0.82*
≥85	6,441	49.9	33,325	48.1	
Female	10,135	78.5	54,366	78.4	0.81
Race					
White	11,293	87.5	62,641	90.4	
Black	968	7.5	4,315	6.2	<0.001
Hispanic	380	2.9	1,564	2.3	
Other†	264	2.1	790	1.1	
Region					
Northeast	3,323	25.8	19,485	28.1	
Midwest	3,502	27.1	21,876	31.6	<0.001
West	1,519	11.8	6,547	9.5	
South/Other	4,561	35.3	21,402	30.9	
LIS	10,713	83.0	57,874	83.5	0.17
Dual eligibility	10,410	80.7	56,798	82.0	0.001
Newly-diagnosed AFIB	771	6.0	4,842	7.0	<0.001
End of life	2,044	15.8	5,518	8.0	<0.001
Charlson comorbidity index					
0	6,105	47.3	39,036	56.3	
1	1,546	12.0	6,726	9.7	<0.001*
2	1,559	12.1	8,198	11.8	
≥3	3,695	28.6	15,350	22.2	
CHADS ₂ score					
0	53	0.4	256	0.4	
1	869	6.7	4,421	6.4	
2	2,711	21.0	16,315	23.5	
3	4,120	31.9	21,187	30.6	0.006*
4	2,990	23.2	15,868	22.9	
5	1,456	11.3	7,714	11.1	
6	706	5.5	3,549	5.1	
HEMORR ₂ HAGES score (mean, SD)		3.8 (1.5)		3.6 (1.4)	<0.001
Individual comorbid conditions					
Ischemic event	3,794	29.4	19,988	28.8	0.20
Diabetes	5,469	42.4	28,206	40.7	<0.001
Chronic heart failure	7,212	55.9	37,750	54.5	0.003
Hypertension	10,714	83.0	56,794	81.9	0.003
Major bleed	1,641	12.7	4,890	7.1	<0.001
Liver or kidney disease	2,655	20.6	11,652	16.8	<0.001
Alcohol abuse	82	0.6	440	0.6	0.99
Cancer	1,163	9.0	4,833	7.0	<0.001

Characteristic	No INR monitoring (n=12,905)		INR monitoring (n=69,310)		p-value
	Number	%	Number	%	
Reduced platelet count or function	328	2.5	1,334	1.9	<0.001
Anemia	5,895	45.7	28,626	41.3	<0.001
Dementia	6,804	52.7	35,480	51.2	0.001
Increased fall risk	6,933	53.7	36,104	52.1	0.001
Facility characteristics‡					
For profit	8,759	67.9	44,668	64.5	<0.001
Chain affiliated	7,311	56.7	35,307	50.9	<0.001
Hospital-based facility	668	5.2	3,560	5.1	0.85
Any “poor” deficiency	2,929	22.7	14,461	20.9	<0.001
Quality of care “poor” deficiency	475	3.7	2,158	3.1	0.001
Pharmacy-related deficiency	5,783	44.8	30,063	43.4	0.003
Dedicated Alzheimer’s unit	2,641	20.7	16,011	23.4	<0.001
Available physician extender	4,768	37.4	23,230	33.9	<0.001
Bed size (mean, SD)	142 (95)		139 (93)		0.001
Occupancy rate (mean, SD)	87 (12)		88 (12)		<0.001
Hospitalizations/patient/year (mean, SD)	0.96 (0.57)		0.90 (0.49)		<0.001
Average number of medications/patient (mean, SD)	11.0 (1.4)		11.0 (1.4)		0.80
Direct care hours/patient/day (mean, SD)	3.3 (1.1)		3.3 (0.9)		0.028
County- and State-level characteristics‡					
Number of hospital beds/1000 elderly (county) (mean, SD)	24.8 (19.0)		25.5 (20.1)		<0.001
Number of nurses/1000 elderly (county) (mean, SD)	42.9 (35.0)		43.0 (33.6)		0.76
MCO penetration rate (county) (mean, SD)	18.6% (12.4%)		17.6% (12.3%)		<0.001
Average Medicaid per diem (state) (mean, SD)	\$160 (\$33)		\$159 (\$34)		0.13
Proportion of Medicaid LTC spending on HCBS (state) (mean, SD)	28.9% (13.0%)		28.5% (12.6%)		<0.001
Case-mix adjustment (state)	9,475	74.4	52,179	76.2	<0.001

* Significance for bivariable analyses with age, CCI, and CHADS₂ was tested using the Cochran-Armitage test for trend.

† Other race category includes: Asian, Pacific Islander, American Indian, Alaska Native, self-identified other race, and unknown

‡ Sample sizes for facility characteristics were different due to missing values: for-profit, chain affiliated, hospital based, bed size, occupancy rate (N=82,208); Alzheimer’s unit physician extender (N=81,247), direct care hours/patient/day (N=81,112); hospitalizations/patient/year (N=80,840), medications/patient (N=80,422), county-level variables (N=81,225), state-level variables (N=81,196)

Multivariable analyses: Factors associated with warfarin use and INR monitoring among warfarin users

Results from adjusted models that identify factors associated with warfarin use and INR monitoring are shown in Table 8. Factors that were highly nonsignificant in unadjusted

analyses were not included in adjusted models. Correlation between certain variables was also examined in order to avoid collinearity in the model. Since all examined correlations were statistically significant due to the large sample size, the actual Pearson correlation coefficient was considered in model building:

CHADS₂ and CCI: $r = 0.37$

CHADS₂ and age: $r = -0.02$

CHADS₂ and HEMORR₂HAGES: $r=0.51$

Any “poor” deficiency and any “poor” quality of care deficiency: $r = 0.36$

Any “poor” deficiency and any pharmacy-related deficiency: $r = 0.13$

Any “poor” quality of care deficiency and any pharmacy-related deficiency: $r = 0.08$

HEMORR₂HAGES was not included in the model because it was highly correlated with the score, likely due to the three overlapping components of each scheme (i.e., age, hypertension, ischemic stroke). The non-overlapping components of the HEMORR₂HAGES score were included individually. Since CHADS₂ and CCI were moderately correlated, a second model was performed that included the individual CHADS₂ items instead of the score. Lastly, each model included an indicator of either any “poor” deficiency or any “poor” quality of care deficiency, depending on which was more strongly associated in bivariable analyses.

The multivariable models used the SAS procedure for generalized linear mixed models (GLIMMIX) with the following specifications: binary distribution, logit link, residual pseudo-likelihood estimation technique, between-within degrees of freedom method, sandwich estimator for fixed effects SE adjustment.

Due to missing data for some of the facility-level factors, 214,554 of the 219,571 cohort person-months were used for the model predicting warfarin use (97.7%). Both the random intercept for facility (covariance parameter estimate: 0.52, SE: 0.17, $p=0.002$) and the random intercept for person (covariance parameter estimate 13.83, SE: 0.25, $p<0.001$) were significant, indicative of significant correlation between observations within a person and between people within a facility.

In adjusted analyses, age was strongly negatively associated with warfarin use, while females and those of white race were more likely to receive warfarin (Table 8). There were 33% lower odds of warfarin use during months following a new diagnosis of AFIB, and 30% lower odds of use during months toward the end of life. Those with a higher number of comorbid conditions were more likely to receive warfarin. There was a trend toward higher use of warfarin with higher CHADS₂ scores, but it was not significant. Certain conditions known to have an increased risk of bleeding were associated with lower warfarin use, including bleeding (OR 0.64) and dementia (OR 0.81). Only a few facility-level factors were associated with warfarin use: MCO penetration rate, case-mix adjustment, and the proportion of Medicaid LTC spending on HCBS ($p=0.015$). In a model replaced the CHADS₂ score with its individual components, CHF (OR=1.36) and prior ischemic events (OR=1.46) were associated with increased warfarin use.

Table 8. Factors associated with pharmacotherapeutic management of AFIB

Characteristic	Warfarin use (N=214,554)*		INR monitoring among warfarin users (N=80,692)*	
	OR	99% CI	OR	99% CI
Month following AFIB diagnosis (per month)	0.97	0.96 – 0.99	0.96	0.95 – 0.97
Age, years (reference: 65-74)				
75 – 84	0.75	0.55 – 1.03	1.25	0.98 – 1.59
≥85	0.32	0.23 – 0.43	1.01	0.79 – 1.30
Female (reference: Male)	1.22	0.99 – 1.51	0.89	0.75 – 1.06
Race (reference: White)				
Black	0.60	0.42 – 0.85	0.85	0.63 – 1.16
Hispanic	0.63	0.37 – 1.06	0.83	0.53 – 1.28
Other	0.56	0.27 – 1.13	0.74	0.38 – 1.45
Region (reference: South)				
Northeast	1.72	1.31 – 2.26	1.43	1.13 – 1.82
Midwest	1.59	1.25 – 2.03	1.32	1.07 – 1.63
West	1.99	1.33 – 2.97	0.96	0.69 – 1.35
LIS	0.88	0.67 – 1.17		Not included
Dual eligibility		Not included	1.19	1.00 – 1.42
Newly-diagnosed AFIB	0.67	0.53 – 0.85	1.22	0.96 – 1.54
End of life	0.70	0.60 – 0.82	0.33	0.28 – 0.38
Charlson comorbidity index (reference:0)				
1	1.18	0.91 – 1.54	0.70	0.56 – 0.88
2	1.22	0.94 – 1.57	0.84	0.68 – 1.05
≥3	1.38	1.08 – 1.78	0.83	0.68 – 1.02
CHADS ₂ score (reference: 0)				
1	0.99	0.20 – 4.86	0.61	0.25 – 1.49
2	1.13	0.22 – 5.68	0.72	0.30 – 1.76
3	1.31	0.26 – 6.56	0.69	0.28 – 1.69
4	1.46	0.29 – 7.39	0.73	0.29 – 1.80
5	1.84	0.36 – 9.43	0.74	0.30 – 1.85
6	2.55	0.49 – 13.3	0.69	0.27 – 1.76
Individual comorbid conditions				
Major bleed	0.64	0.49 – 0.85	0.50	0.40 – 0.64
Liver or kidney disease	0.96	0.75 – 1.23	0.85	0.70 – 1.04
Alcohol abuse	0.57	0.20 – 1.60		Not included
Cancer		Not included	0.77	0.59 – 0.99
Reduced platelet count or function	0.86	0.48 – 1.54	0.81	0.53 – 1.24
Anemia	0.98	0.81 – 1.19	0.96	0.82 – 1.12
Increased fall risk	0.97	0.81 – 1.15	0.97	0.84 – 1.12
Dementia	0.81	0.66 – 0.98	0.92	0.79 – 1.08
Facility characteristics†				
For profit	0.85	0.65 – 1.10	0.95	0.77 – 1.17
Chain affiliated		Not included	0.85	0.70 – 1.02
Hospital-based facility	0.82	0.37 – 1.81		Not included
Bed size (per 10 beds)	0.99	0.98 – 1.00	1.00	0.99 – 1.01
Occupancy rate (per 1%)	1.00	0.99 – 1.01	1.00	1.00 – 1.01
Hospitalizations/patient/year (per 0.1	1.00	0.97 – 1.02	0.98	0.96 – 0.99

Characteristic	Warfarin use (N=214,554)*		INR monitoring among warfarin users (N=80,692)*	
hosp/pt/yr)				
Average number of medications/patient (per 1 medication)	1.06	0.97 – 1.16	Not included	
Any “poor” deficiency	Not included		1.02	0.86 – 1.21
Quality of care “poor” deficiency	1.06	0.70 – 1.61	Not included	
Pharmacy-related deficiency	0.88	0.74 – 1.04	0.96	0.83 – 1.11
Available physician extender	1.08	0.87 – 1.34	0.99	0.83 – 1.18
Dedicated Alzheimer’s unit	Not included		1.03	0.83 – 1.28
Direct care hours/patient/day (per 1 hour)	0.98	0.87 – 1.11	0.97	0.88 – 1.06
County- and State-level characteristics				
Number of hospital beds/1000 elderly (county) (per 10 beds)	0.99	0.92 – 1.07	1.01	0.97 – 1.06
Number of nurses/1000 elderly (county) (per 10 nurses)	0.99	0.94 – 1.04	Not included	
MCO penetration rate (county) (per 1%)	0.99	0.98 – 1.00	0.99	0.98 – 1.00
Case-mix adjustment (state)	1.34	1.07 – 1.68	0.94	0.76 – 1.15
Average Medicaid per diem (state) (per \$10)	Not included		Not included	
Proportion of Medicaid LTC spending on HCBS (state) (per 1%)	0.99	0.98 – 1.00	1.00	0.99 – 1.01

*Sample size is smaller due to observations with missing values for some facility effects

Specification for the multivariable model predicting monthly INR monitoring among warfarin users was the same as described above for the model predicting warfarin use. Due to missing data for some of the facility-level factors, 80,692 of the 82,215 cohort person-months were used for the model predicting INR monitoring (98.1%). The covariance parameter estimates for the facility random intercept (estimate: 1.34, SE: 0.12, $p < 0.001$) and the person random intercept (estimate 2.06, SE: 0.11, $p < 0.001$) were significant, indicative of significant correlation between observations within a person and between people within a facility.

Unlike the results for factors associated with warfarin use, age, sex, and race were not predictive of INR monitoring among warfarin users (Table 8). Months with dual Medicare/Medicaid eligibility had 19% higher odds of INR monitoring. Months

immediately following a new AFIB diagnosis had 22% higher odds of INR monitoring, while months toward the end of life had a 67% lower odds of monitoring. Those with at least one comorbidity were less likely to receive INR monitoring, and specific conditions associated with lower odds of INR monitoring included major bleeding (OR 0.50) and cancer (OR 0.77). Similar to the results for the overall CHADS₂ score, none of its individual components were associated with INR monitoring. Individuals in facilities that were part of a chain (p=0.024), facilities with higher average number of hospitalizations per patient per year, and facilities in states with higher MCO penetration were less likely to have INR monitoring.

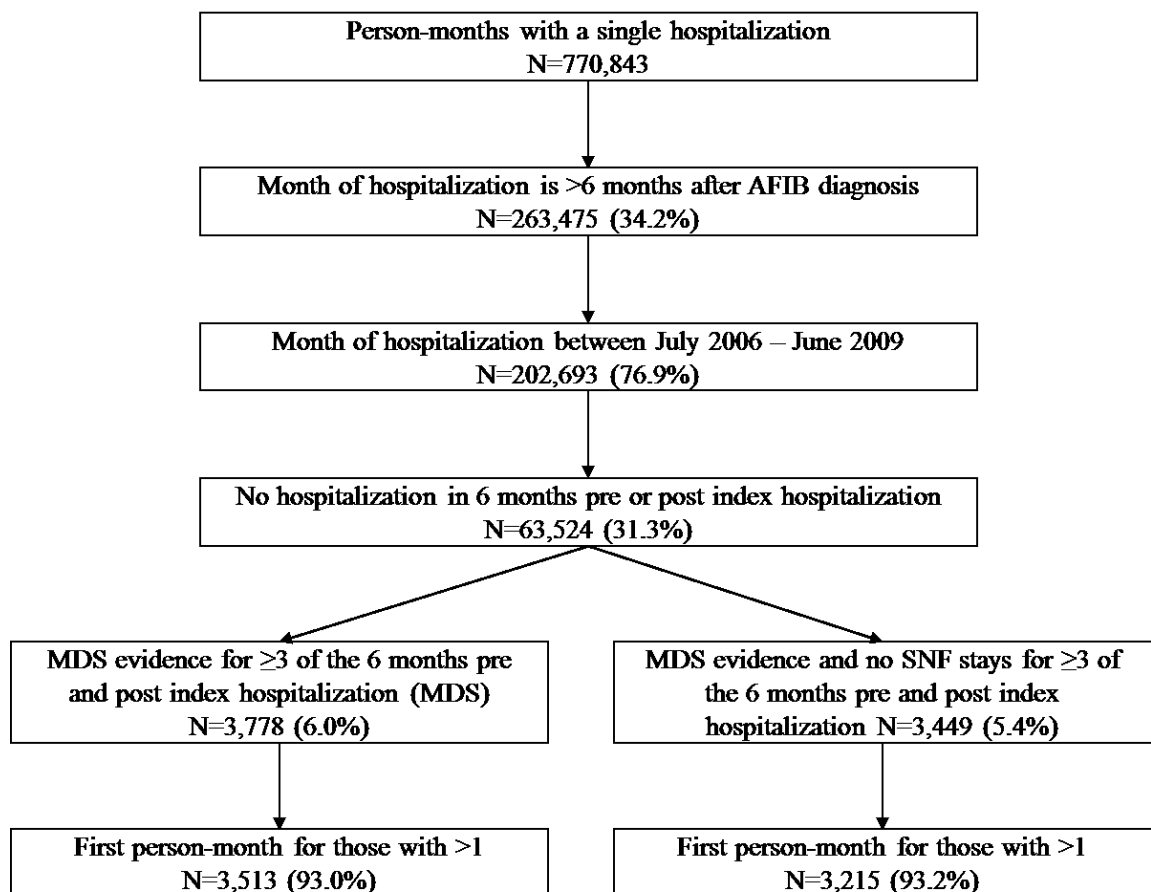
4.3 Aim 2

4.3.1 Aim 2 cohort

Using data from the years 2006-2009, 770,843 person-months with a single (“index”) hospitalization were identified (Figure 3). Those with more than one hospitalization in a month were not included because it is harder to accurately determine what changes in medication use occur surrounding multiple hospitalizations. In order to restrict the cohort to AFIB patients with stable management and to ensure adequate windows in which to identify drug use, months with a hospitalization were included if they were at least 6 months following the first observed AFIB diagnosis during the study period and were at least 6 months from the beginning or end of the study period. Those with another hospitalization in the 6 months before or after the index hospitalization were excluded so that AFIB management would be uninterrupted and observable during those periods. To restrict the sample to long-stay NH residents, at least 3 of the 6 months both before and

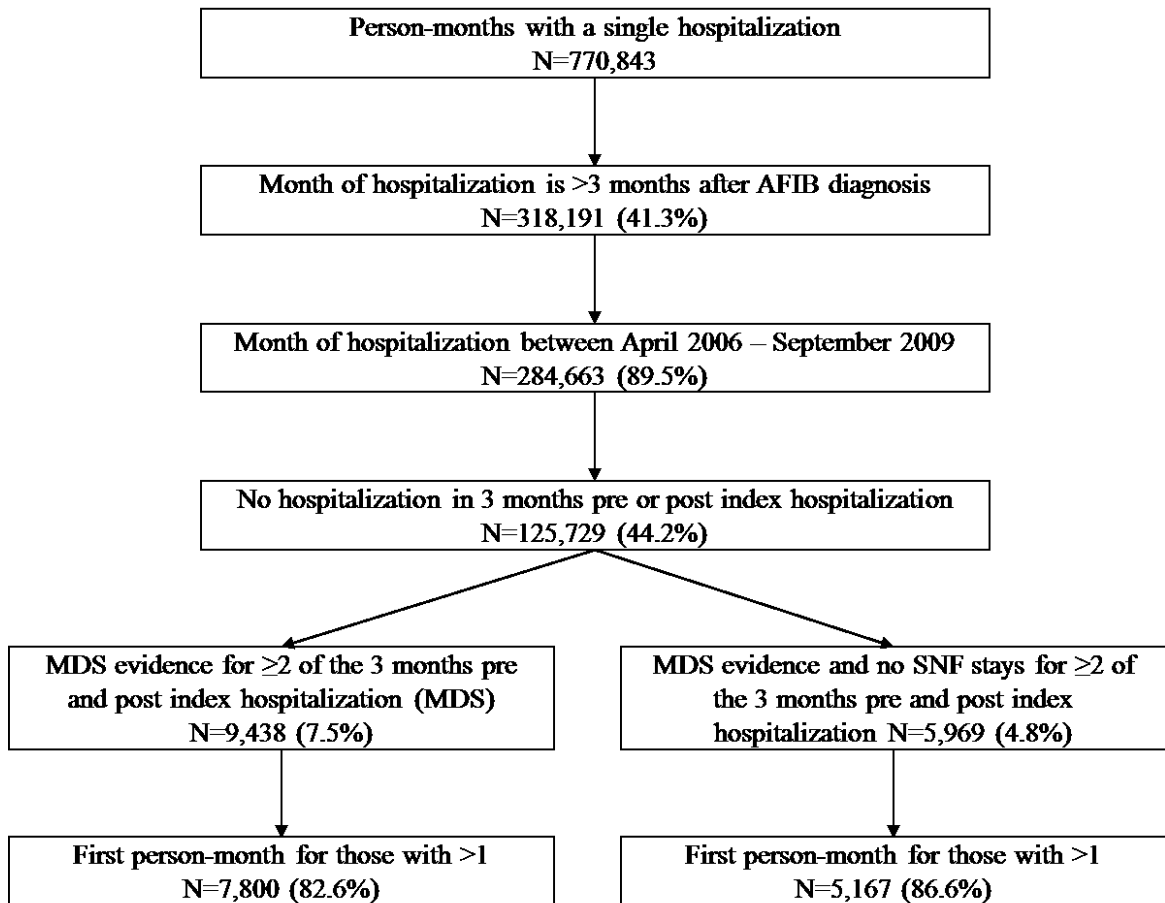
following a hospitalization were required to have evidence of NH residence based on MDS assessments. A second cohort was identified restricting eligible NH months to those with no SNF days, in order to ensure that all medication use was observable. Lastly, if an individual had more than one eligible index month, the first index month was chosen. A cohort of 3,513 individuals were identified who met the inclusion criteria (“any NH”) (Figure 3). A second cohort excluding NH residents with SNF months was slightly smaller: 3,215 (“no SNF”).

Figure 3. Cohort flowchart for aim 2



A second cohort was created in which to conduct a sensitivity analysis (Figure 4). This cohort was identified by using 3-month windows instead of 6-month windows. For the secondary analyses using 3-month windows, the any NH and no SNF cohorts comprised 7,800 and 5,167 individuals, respectively.

Figure 4. Cohort flowchart for aim 2 sensitivity analysis



4.3.2 Pre-post comparisons within antithrombotic groups

The majority of individuals did not use any antithrombotic prior to or following a hospitalization (Table 9). For warfarin, thienopyridines, and other antithrombotic agents, most individuals with any exposure took the drug both prior to and following a

hospitalization (e.g., continuation). On the other hand, there were higher proportions of initiators and discontinuers compared to continuers for LMWH and heparin. For all antithrombotic drug classes, the proportion of those imitating and the proportion of those discontinuing within each class were similar. Results were fairly similar between the any NH and no SNF cohorts.

Table 9. Pre-post comparisons of antithrombotic use surrounding a hospital transition, within each antithrombotic category

Antithrombotic category	Continuation on no drug (%)		Continuation on drug (%)		Initiation (%)		Discontinuation (%)	
	Any NH	No SNF	Any NH	No SNF	Any NH	No SNF	Any NH	No SNF
<i>6-month windows</i> (any NH, N=3,513; no SNF, N=3,215)								
Warfarin	65.0	64.5	28.9	29.6	3.0	2.9	3.2	2.9
Thienopyridine	88.5	88.6	6.9	6.9	2.2	2.2	2.4	2.3
LMWH	99.2	99.1	0.1	0.2	0.5	0.5	0.2	0.2
Heparin	99.3	99.2	0.2	0.3	0.3	0.3	0.2	0.2
Other antithrombotic agents	97.8	97.8	1.1	1.2	0.5	0.5	0.6	0.6
<i>3-month windows</i> (any NH, N=7,800; no SNF, N=5,167)								
Warfarin	66.5	65.7	26.8	28.6	3.4	3.1	3.4	2.6
Thienopyridine	88.5	88.2	6.2	7.5	2.1	2.1	3.3	2.2
LMWH	99.1	98.9	0.2	0.2	0.5	0.6	0.3	0.3
Heparin	99.2	99.2	0.2	0.3	0.4	0.3	0.2	0.2
Other antithrombotic agents	97.7	97.6	1.2	1.5	0.4	0.4	0.7	0.5

In sensitivity analysis, using 3-month windows to examine drug use also gave similar results (Table 9). There were slightly larger discrepancies between the any NH and no SNF cohort results using 3-month windows, which are to be expected since SNF stays are 100 days or less, and would be captured in the “post” window since they immediately follow a hospitalization. The no SNF cohort tended to show slightly higher proportions of continuers on a drug and slightly lower proportions of initiation, discontinuation, and continuation of no drug.

Changes in warfarin use surrounding a hospitalization

Among those on warfarin for at least 3 of the 6 months prior to a hospitalization, the majority remained on warfarin for at least 3 of the 6 months following the hospitalization (90.1%), but 9.9% discontinued warfarin. Of those who continued warfarin following the hospitalization, most continued on warfarin only (94.9%), while some individuals added another antithrombotic agent: 3.6% added a thienopyridine, 0.5% added LMWH or heparin, and 1.1% added another antithrombotic agent. Among those who discontinued warfarin, most did not initiate another antithrombotic drug (83.8%). A thienopyridine was the most common drug added following discontinuation of warfarin (10.8%); LMWH, heparin, and other antithrombotic agents were initiated by 0.2% each. Results were similar for the cohort of those excluding SNF months and in sensitivity analyses using 3-month windows.

4.3.3 Pre-post comparisons across antithrombotic groups

Taking all antithrombotic classes into account, individuals were categorized by comparing their antithrombotic use prior to the index month with their antithrombotic use following the index month (Table 10). Over half of individuals did not receive any antithrombotic before or after a hospitalization. Over one-third of individuals maintained use of their previously used antithrombotic agent following a hospitalization.

Approximately 5% each initiated and discontinued an antithrombotic, while less than 1% switched to a different antithrombotic agent. Since individuals could be receiving medications in more than one antithrombotic category in the pre and/or post periods, extra categories were created to represent these individuals: just under 1% maintained

one agent and initiated another agent, and similarly, just under 1% maintained one agent and discontinued another agent).

Patterns were significantly different compared with controls (Table 10). Control individuals more often maintained use of no antithrombotic agent, while a higher proportion of individuals in each of the cohorts initiated, switched, or discontinued an antithrombotic agent following a hospitalization. There was a slightly higher proportion of cohort individuals who maintained use of an antithrombotic compared with controls. The differences between cohort and control were statistically significant and consistent across all cohorts tested (i.e., any NH and no SNF cohorts, using both 6-month and 3 month windows; all $p < 0.001$).

Table 10. Changes in antithrombotic medication use, comparing hospitalized NH residents to control NH residents

	Study group (hospitalized)		Control group (no hospitalization)	
	N	%	N	%
6-month windows				
Any NH cohort*	(N=3,513)		(N=16,265)	
Maintained AT	1,214	34.6	5,366	33.0
Maintained on no AT	1,873	53.3	9,728	59.8
Initiation of AT	169	4.8	467	2.9
Discontinuation of AT	175	5.0	531	3.3
Switch to a different AT †	22	0.6	34	0.2
Maintained AT & initiate AT	29	0.8	45	0.3
Maintained AT & discontinue AT	31	0.9	94	0.6
No SNF cohort*	(N=3,215)		(N=16,201)	
Maintained AT	1,137	35.4	5,362	33.1
Maintained on no AT	1,700	52.9	9,683	59.8
Initiation of AT	153	4.8	459	2.8
Discontinuation of AT	149	4.6	524	3.2
Switch to a different AT †	19	0.6	32	0.2
Maintained AT & initiate AT	28	0.9	46	0.3
Maintained AT & discontinue AT	29	0.9	95	0.6
3-month windows				
Any NH cohort*	(N=7,800)		(N=26,156)	
Maintained AT	2,512	32.2	7,773	29.7
Maintained on no AT	4,232	54.3	15,881	60.7
Initiation of AT	404	5.2	1,492	5.7
Discontinuation of AT	493	6.3	719	2.8
Switch to a different AT †	42	0.5	58	0.2
Maintained AT & initiate AT	51	0.7	93	0.4
Maintained AT & discontinue AT	66	0.9	140	0.5
No SNF cohort*	(N=5,167)		(N=25,033)	
Maintained AT	1,832	35.5	8,194	32.7
Maintained on no AT	2,748	53.2	15,153	60.5
Initiation of AT	251	4.9	680	2.7
Discontinuation of AT	226	4.4	722	2.9
Switch to a different AT †	29	0.6	57	0.2
Maintained AT & initiate AT	43	0.8	79	0.3
Maintained AT & discontinue AT	38	0.7	148	0.6

AT: antithrombotic

*Comparison between cohort and controls is statistically significant at $p < 0.001$

†Individuals who switched from one antithrombotic agent to another while maintaining a different antithrombotic agent were included in the switch to a different agent category due to the small number of people in which this occurred (<0.05% in all cases).

4.4 Aim 3

In order to determine relevant factors to include in the multivariable analyses, the association between hospitalization and person- and facility-level characteristics was also examined (Table 11). Hospitalization was associated with male sex, non-white race, newly diagnosed AFIB, and months at the end of life. Surprisingly, those at older ages and those receiving a low-income subsidy were less likely to be hospitalized. Higher stroke and bleeding risk scores were positively associated with hospitalization, as were all of the individual comorbid conditions included in the stroke or bleeding risk schemes. Facility characteristics with a higher proportion of hospitalization included for-profit and hospital-based facilities, and those with a “poor” deficiency related to quality of care. The average facility bed size was higher among person-months with a hospitalization, but the occupancy rate was significantly lower. Not surprisingly, the facility’s average rate of hospitalization per patient per year was higher among those hospitalized. Increased availability of hospital beds and nurses were both positively associated with hospitalizations.

Table 11. Cohort characteristics stratified by hospitalization, monthly (N=219,571)

Characteristic	No hospitalization (n=210,548)		Hospitalization (n=9,023)		p-value
	Number	%	Number	%	
Age					
Mean, SD		84.7 (7.3)		82.5 (7.7)	<0.001
65-74	210,040	10.0	1,546	17.1	
75-84	73,862	35.1	3,607	40.0	<0.001*
≥85	115,646	54.9	3,870	42.9	
Female	165,949	78.8	6,537	72.5	<0.001
Race					
White	187,085	88.9	7,360	81.6	
Black	14,586	6.9	1,055	11.7	<0.001
Hispanic	5,567	2.6	378	4.2	
Other†	3,310	1.6	230	2.6	
Region					
Northeast	55,500	26.4	2,277	25.2	
Midwest	60,764	28.9	2,383	26.4	<0.001
West	21,949	10.4	860	9.5	
South/Other	72,335	34.4	3,503	38.8	
LIS	176,589	83.9	7,301	80.9	<0.001
Dual eligibility	172,808	82.1	6,884	76.3	<0.001
Newly-diagnosed AFIB	18,482	8.8	1,588	17.6	<0.001
End of life	20,414	9.7	3,171	35.1	<0.001
Charlson comorbidity index					
0	115,917	55.1	2,320	25.7	
1	22,560	10.7	1,038	11.5	<0.001*
2	25,406	12.1	1,347	14.9	
≥3	46,665	22.2	4,318	47.9	
CHADS ₂ score					
0	1,015	0.5	32	0.4	
1	17,204	8.2	448	5.0	
2	54,710	26.0	1,571	17.4	
3	66,487	31.6	2,823	31.3	<0.001*
4	42,558	20.2	2,151	23.8	
5	19,828	9.4	1,220	13.5	
6	8,746	4.2	778	8.6	
HEMORR ₂ HAGES score (mean, SD)		3.6 (1.4)		4.4 (1.7)	<0.001
Individual comorbid conditions					
Ischemic event	51,018	24.2	2,849	31.6	<0.001
Diabetes	79,123	37.6	4,464	49.5	<0.001
Chronic heart failure	106,414	50.5	5,788	64.2	<0.001
Hypertension	170,852	81.2	8,004	88.7	<0.001
Major bleed	18,805	8.9	1,881	20.9	<0.001
Liver or kidney disease	36,930	17.5	2,943	32.6	<0.001
Alcohol abuse	1,665	0.8	128	1.4	<0.001
Cancer	15,213	7.2	1,018	11.3	<0.001
Reduced platelet count or function	4,306	2.1	500	5.5	<0.001
Anemia	92,862	44.1	5,403	59.9	<0.001

Characteristic	No hospitalization (n=210,548)		Hospitalization (n=9,023)		p-value
	Number	%	Number	%	
Dementia	120,458	57.2	4,972	55.1	<0.001
Increased fall risk	111,342	52.9	5,665	62.8	<0.001
Facility characteristics‡					
For profit	139,042	66.1	6,233	69.1	<0.001
Chain affiliated	109,506	52.0	4,576	50.7	0.017
Hospital-based facility	9,969	4.7	505	5.6	<0.001
Any “poor” deficiency	46,868	22.3	2,063	22.9	0.18
Quality of care “poor” deficiency	7,456	3.5	418	4.6	<0.001
Pharmacy-related deficiency	95,640	45.4	4,130	45.8	0.52
Dedicated Alzheimer’s unit	47,652	22.9	1,710	19.3	<0.001
Available physician extender	72,644	34.9	2,985	33.6	0.017
Bed size (mean, SD)		140 (91)		145 (92)	<0.001
Occupancy rate (mean, SD)		87.5 (12.0)		86.6 (12.8)	<0.001
Hospitalizations/patient/year (mean, SD)		0.91 (0.48)		1.10 (0.59)	<0.001
Average number of medications/patient (mean, SD)		10.9 (1.4)		10.9 (1.5)	0.33
Direct care hours/patient/day (mean, SD)		3.3 (1.0)		3.3 (1.1)	<0.001
County- and State-level characteristics					
Number of hospital beds/1000 elderly (county) (mean, SD)		25.6 (19.8)		27.1 (20.8)	<0.001
Number of nurses/1000 elderly (county) (mean, SD)		43.5 (32.5)		45.7 (36.8)	<0.001
MCO penetration rate (county) (mean, SD)		18.2% (12.4%)		18.6% (12.7%)	0.002
Average Medicaid per diem (state) (mean, SD)		\$159 (\$34)		\$158 (\$35)	0.001
Proportion of Medicaid LTC spending on HCBS (state) (mean, SD)		29.0% (12.8%)		29.1% (12.8%)	0.31
Case-mix adjustment (state)		152,780 73.5		6,446 72.7	0.11

*Significance for bivariable analyses with age, CCI, and CHADS₂ was tested using the Cochran-Armitage test for trend.

†Other race category includes: Asian, Pacific Islander, American Indian, Alaska Native, self-identified other race, and unknown

‡Sample sizes for facility characteristics were different due to missing values: for-profit, chain affiliated, hospital based (N=219,529); deficiency variables (N=219,571), Alzheimer’s unit, physician extender (N=217,234), direct care hours/patient/day (N=216,856); bed size, occupancy rate (N=219,529), hospitalizations/patient/year (N=216,317), medications/patient (N=215,263), county-level variables (N=217,192), state-level variables (N=216,780)

4.4.1 *Aim 3a: Effect of pharmacotherapeutic management of AFIB on hospitalization transitions*

Pharmacotherapeutic management: warfarin use

Using the SAS procedure for generalized linear mixed models (PROC GLIMMIX), there was difficulty regarding model convergence for the model specified in equations (1) and (2), perhaps due to the rare nature of the event (i.e., hospitalizations). Various model specification options were attempted and model convergence was obtained using the Laplace approximation for model estimation, where the SAS procedure approximates the marginal likelihood using Laplace's method. Those models that required this specification are noted below and in Table 12. Otherwise, models used the default pseudo-likelihood estimation method (METHOD=RSPL).

In unadjusted analyses, there was a negative relationship between warfarin use and any hospitalization: the proportion of those hospitalized is lower among those with prior warfarin use (3.8%) compared to those with no prior warfarin use (4.3%) ($p < 0.001$), giving an odds ratio of 0.87 (99% CI 0.82 – 0.92) (Table 12). In an unadjusted model that used random effects to take into account the hierarchical data structure, warfarin use was associated with a 17% lower odds of any hospitalization (99% CI 0.75 – 0.92; Laplace approximation). Significance was maintained after adjusting for confounders (OR 0.90, 99% CI 0.83 – 0.98; Laplace approximation), suggesting a protective effect of warfarin against hospitalizations.

Table 12. Effect of pharmacotherapeutic management of AFIB on risk of transitioning to a hospital

Independent variable	Model	Any hospitalization		AFIB-related hospitalization	
		Odds Ratio	99% CI	Odds Ratio	99% CI
Warfarin use	Unadjusted (N=219,571)	0.87	0.82 – 0.92	0.88	0.74 – 1.04
	Unadjusted, multilevel* (N=219,571)	0.83†	0.75 – 0.92	0.84†	0.61 – 1.17
	Adjusted, multilevel‡ (N=215,607)	0.90†	0.83 – 0.98	0.89†	0.65 – 1.23
INR monitoring	Unadjusted (N=81,679)	0.68	0.60 – 0.76	0.81	0.57 – 1.17
	Unadjusted, multilevel* (N=81,679)	0.78†	0.67 – 0.92	0.83	0.58 – 1.20
	Adjusted, multilevel§ (N=80,233)	0.91	0.80 – 1.04	1.03	0.71 – 1.49

*Multilevel models include person and facility random effects

†The Laplace estimation method was used because convergence could not be obtained with the default pseudo-likelihood (RSPL) estimation method

‡Model adjusted for: time (months following first observed AFIB diagnosis), sex, age, race, geographic region, CHADS₂ score, CCI, new AFIB diagnosis, end-of-life, major bleed, dementia; facility: profit status, hospital-based, “poor” quality-of-care deficiencies, bed size, occupancy rate, hospitalizations/patient/year, physician extender, direct care hours/patient/day, hospital beds/1000 elderly, nurses/1000 elderly, MCO penetration rate, Medicaid per diem, proportion of Medicaid LTC spending on HCBS, case-mix adjustment

§ Model adjusted for: time (months following first observed AFIB diagnosis), sex, age, race, geographic region, dual eligibility, CHADS₂ score, CCI, new AFIB diagnosis, end-of-life, major bleed, hepatic or renal disease, cancer, reduced platelet function, anemia, dementia; facility: profit status, chain affiliated, “poor” deficiencies, bed size, occupancy rate, hospitalizations/patient/year, physician extender, hospital beds/1000 elderly, nurses/1000 elderly, MCO penetration rate, Medicaid per diem, proportion of Medicaid LTC spending on HCBS, case-mix adjustment

Results were similar for AFIB-related hospitalization, although statistical significance was not obtained (Table 12). A completely unadjusted model suggested that warfarin use may be associated with fewer hospitalization (OR 0.88, 99% CI 0.74 – 1.04). However, accounting for the hierarchical nature of the data and adjusting for confounders resulted in non-significance (OR 0.89, 99% CI 0.65 – 1.23).

In all of the models testing the effect of warfarin use on hospitalization (any and AFIB-related), the facility random effect was not significant. This suggests that the likelihood of hospitalization does not vary across facilities, controlling for the person and facility factors in the model. However, most of the models do have significant person random effects, indicating that the likelihood of hospitalization does differ across individuals.

Pharmacotherapeutic management: INR monitoring

In unadjusted analyses, receipt of INR monitoring in the month (among months with warfarin use) was associated with significantly lower odds of any hospitalization (OR 0.68, 99% CI 0.60 – 0.76) (Table 12). In an adjusted random-effects model, INR monitoring was still indicative of fewer hospitalizations, although the effect was not statistically significant (OR 0.90, 99% CI 0.79 – 1.03).

Receipt of INR monitoring among warfarin users was not predictive of AFIB-related hospitalizations. Unadjusted analyses gave an odds ratio of 0.81 (99% CI 0.57 – 1.17) (Table 12). Accounting for correlation within individuals and within facilities and adjusting for confounders gave an odds ratio of 1.00 (99% CI 0.69 – 1.46).

In unadjusted and adjusted models of the effect of INR monitoring on AFIB-related hospitalization, neither the person random effect nor the facility random effect were significant, suggesting a similar likelihood of AFIB-related hospitalization across individuals and across facilities. However, the person random effect was statistically

significant in models of the effect of INR monitoring on any hospitalization, indicating a varying likelihood of hospitalization across individuals.

4.4.2 Aim 3b: Effect of hospitalization transitions on pharmacotherapeutic management of AFIB

Pharmacotherapeutic management: warfarin use

For the reverse relationship, unadjusted analyses suggest a hospitalization in the prior month was weakly associated with warfarin use: the proportion of warfarin users is lower among those with a previous hospitalization (36.3%) compared to those with no previous hospitalization (37.5%) ($p=0.013$). In other words, the odds of warfarin use was 0.95 (99% CI 0.90-1.00) comparing those with a hospitalization in the prior month to those with no prior hospitalization (Table 13). However, adding random effects resulted in an estimate suggesting that a hospitalization increased the odds of warfarin use (OR 1.33, 99% CI 1.16 – 1.53). In a fully adjusted model, a hospitalization increased the odds of warfarin use by 28% (99% CI 1.11 – 1.46).

In both unadjusted and adjusted models for the effect of hospitalization on warfarin use, the person and facility random effects were statistically significant, with the person effects being substantially stronger than the facility effects. Therefore, the likelihood of warfarin use varied significantly across facilities, and varied more significantly across individuals, even after adjusting for covariates.

Table 13. Effect of hospitalization transitions on the pharmacotherapeutic management of AFIB

Model	Warfarin use (N= 214,682)		INR monitoring among warfarin users (N=80,303)	
	OR	99% CI	OR	99% CI
Unadjusted	0.95	0.90 - 1.00	0.54	0.49 – 0.59
Unadjusted, multilevel*	1.33	1.16 – 1.53	0.60	0.51 – 0.69
Adjusted, multilevel†	1.28	1.11 – 1.46	0.71	0.61 – 0.82

*Multilevel models include person and facility random effects

†Models adjusted for: time (months following first observed AFIB diagnosis), sex, age, race, geographic region, CHADS₂ score, CCI, new AFIB diagnosis, end-of-life, major bleed, dementia; facility: profit status, hospital-based, “poor” quality-of-care deficiencies, bed size, occupancy rate, hospitalizations/patient/year, physician extender, direct care hours/patient/day, hospital beds/1000 elderly, nurses/1000 elderly, MCO penetration rate, Medicaid per diem, proportion of Medicaid LTC spending on HCBS, case-mix adjustment

Pharmacotherapeutic management: INR monitoring among warfarin users

The proportion of those with INR monitoring was lower among those with a prior hospitalization (74.9%) compared to those who did not experience a prior hospitalization (84.7%) ($p < 0.001$). Therefore, those with a previous hospitalization had 0.54 the odds of receiving INR monitoring in the following month compared to those with no hospitalization (99% CI 0.49 – 0.59) (Table 13). Results were similar in an unadjusted random effects model (OR 0.60, 99% CI 0.51 – 0.69). In a fully adjusted model, a hospitalization reduced the odds of receiving INR monitoring in the following month by 29% (99% CI 0.61 – 0.82).

In both unadjusted and adjusted models, the person and facility random effects were statistically significant. In other words, the likelihood of INR monitoring varied significantly across individuals and across facilities.

CHAPTER 5: DISCUSSION

5.1 Use of AFIB medications

5.1.1 Use of warfarin and INR monitoring

The average monthly prevalence of warfarin use was 37.4% in this study among NH residents with AFIB. These results are consistent with other studies that have reported warfarin usage rates among NH residents ranging from 30% to 57%.^{78,100} Despite being consistent with that described in other studies, the level of antithrombotic use in this study is not in line with guidelines for the management of chronic AFIB; current guidelines strongly recommend warfarin for those with a CHADS₂ score of 2 or higher.^{8,9,52} In this study, 91.5% of person-months were in this high risk category. In a sensitivity analysis among those with high stroke risk (CHADS₂ ≥2) and which further excluded those with a prior major bleed, a significant relative contraindication to warfarin, use of warfarin was similar to the overall study population (38.8% vs. 37.4%). Low use was consistent across all antithrombotic groups in the sensitivity analysis.

The choice to use an antithrombotic should be made by a physician and patient on an individual basis, and there are some relative contraindications that may influence this decision. In the NH setting, patients often have little say in treatment decisions. Long-stay residents are less likely to be married and more likely to have cognitive impairment,^{101,102} so their treatment decisions may more often be made by a physician and less often are influenced by patient or family member preferences. A study examining physician and patient acceptance of stroke and bleeding risk with

anticoagulation found, compared to physicians, patients had a significantly lower threshold of acceptable stroke risk, but a significantly higher threshold of bleeding risk that they were willing to accept with warfarin.¹⁰³ Therefore, patients placed more importance on avoiding strokes and less on avoiding bleeding, suggesting a preference toward using warfarin to manage stroke risk in AFIB. It is unlikely that individual contraindications and patient preference led to the treatment decision in the 52% of time that an antithrombotic was not used in this study, suggesting that antithrombotics remain underused in this high risk population of long-stay NH residents with AFIB.

Although warfarin use was low in this study, over 84% of person-months with warfarin use had at least one INR test in the month. Results from this study were in accordance with previous estimates ranging from 84% to 90%,^{47,49} although lower than the most current study where 99% of INR tests were repeated within 4 weeks.¹⁰⁴ There is no accepted threshold for what level of INR monitoring represents high quality, but these findings suggest that NH residents with AFIB are receiving adequate monitoring.

During the past several years, the Food and Drug Administration approved three new agents to reduce the risk of stroke in patients with nonvalvular AFIB: dabigatran (approved in 2010),⁷⁰ rivaroxaban (approved in 2011),⁷¹ and apixaban (approved in 2012).⁷² One advantage of these drugs over warfarin is the absence of the need to regularly monitor patients, since they are all fixed-dose medications. The finding in this study that over 84% of person-months receiving warfarin had an INR monitoring test suggests that INR monitoring is not particularly burdensome among NH residents with

AFIB. This may not be the case for community-dwelling warfarin users, who must travel to have their INR testing. However, NH residents appear to be easy to monitor, likely because they reside in the same place in which medical care is given. Unlike warfarin, newer agents have no antidote to reverse their effect if a patient bleeds and there is very limited information on long-term safety of these medications. Despite the availability of these newer agents, the lack of burden of INR monitoring, the ability to reverse warfarin during a bleeding episode, and the higher level of long-term safety information suggest that warfarin will likely continue to remain a highly relevant medication to manage thromboembolic risk among NH residents with AFIB.

The use of warfarin among AFIB patients and receipt of at least one monthly INR monitoring test among warfarin users were defined as a quality measures in this study. Since warfarin is not indicated in all individuals with AFIB, sensitivity analyses were conducted among the subset of those with high risk of stroke and low risk of bleeding, where the use of warfarin may be a more appropriate measure of quality. In this subset of the population, warfarin use remained low: 38.8%. Although not a widespread quality measure, the American College of Cardiology and the American Heart Association published Clinical Performance Measures for Adults with Nonvalvular AFIB or Atrial Flutter, in which they identified chronic anticoagulation therapy as a quality measure.¹⁰⁵ This was defined as the proportion of patients with nonvalvular AF or atrial flutter at high risk for thromboembolism (according to risk stratification and defined in the 2006 guidelines⁹) who are prescribed warfarin during the reporting year. Given the well-documented underuse of warfarin in the NH setting,^{47-49,78,100,106} and the substantial

evidence supporting the efficacy of warfarin in reducing risk of stroke,^{55,57-63,65,69} the use of warfarin in patients at or above a certain risk of stroke should be considered as a quality measure for NH residents.

The use of INR monitoring as a quality measure is less controversial, since regular INR monitoring is recommended in all patients taking warfarin, without exception. Prior studies have used 28- and 30-day intervals to assess regular INR monitoring,^{47,49,104} and several quality measure schemes use quality measures assessing the receipt of INR monitoring approximately monthly (Table 14). CMS uses a quality measure for INR monitoring in the ambulatory care setting, but does not include it as a quality measure for NH residents.¹⁰⁷

Table 14. Quality measures for regular INR monitoring

Quality Measure	Definition	Source
Lack of Monthly INR Monitoring for Individuals on Warfarin (NQF-0555)	Average percentage of monthly intervals in which individuals with claims for warfarin do not receive an INR test during the measurement period	Centers for Medicare & Medicaid Services (process measure for the ambulatory care setting); endorsed by National Quality Forum as a patient safety measure ¹⁰⁷
Monthly INR measurement	Percentage of calendar months during the reporting year during which patients with a diagnosis of nonvalvular AF or atrial flutter, receiving warfarin therapy, have at least one INR measurement made	American College of Cardiology (ACC), American Heart Association (AHA) ¹⁰⁵
Therapeutic Monitoring of Warfarin Therapy	IF a vulnerable elder is prescribed warfarin, then an INR should be determined within 4 days after initiation of therapy and at least every 6 weeks thereafter	Assessing Care of Vulnerable Elders (ACOVE)-3 medication quality indicator ⁵

Nursing Home Compare is an online, publicly-available resource that contains information on all CMS-certified NH facilities, including staffing, deficiencies, and quality measures.¹⁰⁸ This research provides evidence to support the inclusion of warfarin use among those with a high risk of stroke and the use of monthly INR monitoring among warfarin users as potential quality measures for Nursing Home Compare, since appropriate management of AFIB can reduce the risk of stroke and unnecessary hospitalizations.

5.1.2 Use of agents for rate and rhythm control

The use of agents to control heart rate and heart rhythm in AFIB patients is not as well documented as use of warfarin. Among the few published studies, estimates for use of rate and rhythm control agents vary widely (Table 15). Among patients with new-onset AFIB enrolled in a prospective, multicenter registry covering the United States and Canada, rate-controlling and rhythm-controlling agents were used by 68% and 48% of patients within the first year, respectively.¹⁰⁹ More recently, a study among Medicare beneficiaries with prevalent AFIB enrolled in Part D found that use of rate-control and rhythm-control agents was 74% and 19%, respectively.¹¹⁰ In this study, the use of rate-control agents was slightly lower (61.2%), but the use of rhythm control agents was substantially lower (8.1%) than found in these prior studies. However, the patterns of use of specific antiarrhythmic agents observed in this study were consistent with published studies,^{110,111} with amiodarone contributing the most to antiarrhythmic use, followed by sotalol and agents in class IC.

Table 15. Use of agents to control heart rate and rhythm in AFIB

Drug	Zimetbaum, 2012¹¹¹	Zimetbaum, 2003¹⁰⁹	Piccini, 2012¹¹⁰
Rhythm control agents (class)	(% of annual antiarrhythmic prescriptions)	(% of rhythm-control drugs during first year of new-onset AFIB)	(% of patients with prevalent AFIB)
Any			19.1%
Quinidine (1A)	“Rarely used for AF”		
Disopyramide (1A)	1-2%	14% (class 1A)	0.4% (class 1A)
Procainamide (1A)			
Propafenone (1C)	10%	29% (class 1C)	3.9% (class 1C)
Flecainide (1C)	10%		
Sotalol (III)	26%	23%	5.1%
Dofetilide (III)	2%	N/A*	0.5%
Amiodarone (III)	45%	34%	9.4%
Dronedarone (III)		N/A*	N/A*
Rate control agents		(% of rate-control drugs during first year of new-onset AFIB)	(% of patients with prevalent AFIB)
Any			74.0%
Beta blockers		36%	53.7%
Calcium channel blockers		32%	18.6%
Digoxin		34%	29.4%
≥2 agents		41%	

*Approved after the study period

One of the potential reasons for the low use of agents to control and maintain sinus rhythm in NH residents may be a low occurrence of specialty physician visits.

Zimetbaum et al found that management by a cardiologist or electrophysiologist (vs. internist) was associated with higher antiarrhythmic utilization.¹⁰⁹ If NH residents are less likely to see cardiac-related specialty physicians, this also may explain the lower use of antiarrhythmic agents seen in this study. Another potential reason for the low use of antiarrhythmic treatment is the accumulating evidence that a rate control strategy is equivalent to a rhythm control strategy. A meta-analysis of randomized trials found no statistical difference in mortality between rate- and rhythm-control strategies (pooled OR:

0.87, 95% CI: 0.74-1.02).¹¹² In fact, the trend was toward rate control as superior to rhythm control.¹¹²

In both published studies and the current study, the use of rate control agents is much higher than use of rhythm control agents. Since agents used for rate control are indicated for a variety of cardiovascular conditions (e.g., chronic heart failure, hypertension), many of which tend to be comorbid conditions among those with AFIB, it is not surprising that a high proportion of AFIB patients are taking these medications.

Some of the differences between utilization in this study and estimates from published studies are likely due to the different populations. To my knowledge, no published studies were conducted in a NH population. The current study adds to the literature by providing utilization estimates for agents to control heart rate and rhythm among NH residents with AFIB.

5.2 Factors associated with warfarin use and INR monitoring

Several studies have examined factors associated with warfarin use,¹¹³⁻¹¹⁶ although only a subset are in a NH population.^{48,49,78,100} The factors most commonly studied as potential indicators of warfarin use are those related to risk of stroke. However, there are mixed results in the literature regarding the relationship between stroke risk and warfarin usage. Several studies supported a positive relationship between higher stroke risk and likelihood of warfarin use.^{49,106,113,114} A couple of other studies found no relationship between CHADS₂ score and receipt of warfarin.^{115,116} Interestingly, one study found a

negative relationship where anticoagulation therapy was less frequent with increasing CHADS₂ scores, ranging from 62.1% among those with a CHADS₂ score of 0 to 49.4% among those with a CHADS₂ score of 6 ($p < .001$). In this study among NH residents with AFIB, CHADS₂ score was not significantly associated with warfarin use. The finding in some studies, including this one, in which recommended management was not aligned with an individual's risk of stroke, is known as the risk-treatment paradox.^{110,115} The CHADS₂ score was developed in order to predict risk of ischemic stroke,⁹² and recommendations for the choice of antithrombotic agent are based on the CHADS₂ score.^{8,9,52} However, several factors included in the CHADS₂ score are also risk factors for bleeding (older age, hypertension, ischemic stroke), so individuals with a higher CHADS₂ score also have an increased risk of bleeding. The fact that the CHADS₂ score predicts an increased risk of both ischemic stroke and hemorrhagic events in practice may explain the risk-treatment paradox reproduced in this study in which stroke risk, measured using the CHADS₂ score, did not significantly predict warfarin use.

In this study, history of a major bleed and dementia were the only two bleeding risk factors negatively associated with warfarin use. In general, those with a higher number of bleeding risk factors are less likely to use warfarin.^{49,106} Specifically, those with a history of gastrointestinal bleeding had lower odds of warfarin use.^{48,100} Impaired cognition was also seen as predictive of lower warfarin use,⁴⁸ supporting the results of this study.

As seen in prior studies,^{100,113} age had a strong negative association with warfarin use, despite age being a significant risk factor for stroke. However, older NH residents on

warfarin had similar likelihood of receiving regular monitoring, regardless of age.

Similarly, residents of non-white race were less likely to receive warfarin than those of white race, but those that did had no significant disparity in INR monitoring. There was also significant geographic variation, with those in the Northeast and Midwest regions having higher quality both in terms of higher warfarin use and increased likelihood of INR monitoring.

The current study found that NH residents with prevalent AF were significantly more likely to be using warfarin than incident users. This is surprising, and is an opposite finding to previously published studies. Zimetbaum et al. studied a group of commercially-insured adults with AFIB and found that warfarin was prescribed more often to those with newly-diagnosed AFIB (49.6%) than to those with pre-existing AFIB (39.5%).¹¹⁶ In a cohort of patients with new onset AFIB, the proportion of those using warfarin declined from 65% at study enrollment to 49% and 44% at 12 months and 30 months, respectively,¹¹⁷ also suggesting a decline in use over the disease progression. This may indicate a delay in AFIB management among NH residents and could be a target for future interventions to improve AFIB care in this population.

Among NH residents with AFIB, the 3 months at the end of life were associated with a 30% lower odds of warfarin use and 67% lower odds of INR monitoring. Similarly, a study among LTC residents from the 2004 NNHS found that a lower proportion of warfarin users were hospice or had less than 6 months to live compared to warfarin nonusers.¹⁰⁶ This finding has face validity, as many medications are stopped when a

patient and/or physician knows that the end of life is close and goals are changed from chronic disease management to palliative care.

Only one study was found that examined factors associated with INR monitoring quality, specifically predicting those with at least 50% or more time in the therapeutic range.¹⁰⁴ They found that earlier initiation of warfarin was associated with higher odds of INR in the therapeutic range, while history of stroke was negatively associated with having greater time in the therapeutic range. This study did not find stroke, or any other stroke risk factors, to be predictive of INR monitoring. However, the outcomes related to quality of INR monitoring are different between the study by Aspinall et al. and this study, and the lack of information on factors associated with INR monitoring reveals this to be an area that requires further research.

Facility characteristics were examined in this study to capture the quality of care culture within NHs, since these factors likely influence management of residents' chronic conditions. However, most facility characteristics were not significant predictors of warfarin use or INR monitoring and those that were had small effect sizes. Residents in states with a case mix reimbursement system had 34% higher odds of warfarin use. These facilities receive payments weighted by resident acuity level and therefore may have more funding to improve quality of care for patients. Similarly, residents in facilities with a lower proportion of Medicaid LTC spending on home and community-based services had lower use of warfarin; these facilities then have higher funding directed toward NHs, which also may improve quality of care in those facilities. However, neither of these

factors was associated with INR monitoring. Facilities that were part of a chain and those with higher average hospitalization rates were associated with lower INR monitoring, suggesting that these might be indicators of poor quality. MCO penetration rate the only facility-level factor associated both with lower warfarin use and with lower INR monitoring, suggesting that higher use of managed care organizations is indicative of poorer quality of AFIB management.

5.3 Medication changes surrounding hospitalizations

In the analysis of changes surrounding a hospitalization within each group of antithrombotic agents, the majority of individuals continued on the agent they were taking prior to the hospitalization, or maintained use of no antithrombotic agent. Within each antithrombotic group, similar proportions of individuals initiated and discontinued a given antithrombotic agent following a hospitalization (Table 9). Published studies that examine medication modifications due to a hospitalization focus on discontinuation of medications,^{14,15,18,20} but initiation of new drugs and switching to a different agent are just as important to consider when undergoing a smooth care transition. Compared to warfarin and thienopyridines, changes were more likely for LMWH and heparin, as evidenced by the higher number of initiators and discontinuers compared to those continuing surrounding the hospitalization. Further, LMWH was the only group of antithrombotic agents with a substantially higher proportion of initiators compared with discontinuers.

Few studies have specifically considered modifications of antithrombotic agents surrounding care transitions.^{14,15,18} These studies found that hospitalized patients are significantly more likely to discontinue anticoagulant medications compared with nonhospitalized patients,¹⁴ with discontinuation rates for these medications ranging from 11%¹⁸ to 23%¹⁵ among hospitalized patients. Two of these studies explicitly excluded LTC residents,^{14,18} and NH residents made up less than 5% in the third.¹⁵ The current study found that 10% of those who were taking warfarin prior to a hospitalization discontinued the medication after. Since hospitalized patients discharged to a NH experience more medication regimen changes than patients discharged home,¹⁶ the lower estimate found in this study of NH residents compared to prior ones is surprising. The difference may be due to different definitions of medication use and discontinuation.

The use of a control group in this analysis was a strength that helped separate medication changes due to a hospitalization from adjustments occurring during the typical course of management. Since in any given month, one could expect some amount of medication changes, differences between the studied cohort and control group could then be attributed to the hospitalization transition. In the comparison of antithrombotic use before and after a hospitalization, a notable percentage of individuals experienced a medication change (i.e., initiation, discontinuation, switch) surrounding a hospitalization: 12.2%, 11.8%, 13.5%, and 11.3% for the 6-month any NH, 6-month no SNF, 3-month any NH, and 3-month no SNF cohorts, respectively (Table 10). Since the control patients experienced fewer medication changes in any given month (7.2%, 7.1%, 9.6%, and 6.8%,

respectively), it can be inferred that the difference represents the medication changes in the study cohort due to hospitalization.

Overall, sensitivity analyses using 3-month assessment windows gave results consistent with results obtained with 6-month windows. The discrepancies between the any NH and no SNF cohort results were more pronounced using 3 month windows, although still not large. This difference is expected since SNF stays are 100 days or less and are captured in the “post” window since they immediately follow a hospitalization. Since the no SNF cohorts excluded all months with any SNF stays, medication use in the remaining months is more likely to be observed. However, this discrepancy was minimized by using thresholds for defining medication use: at least 3 of 6 months for 6-month windows and at least 2 of 3 months for 3-month windows.

The one major difference seen in the sensitivity analysis using 3-month instead of 6-month windows is that initiation of an antithrombotic agent in the controls (5.7%) was similar to the study cohort (5.2%) for the any NH cohort only, whereas it was lower in all of the other analyses (Table 10). This may be a cohort selection issue and not indicative of what is truly occurring, since this pattern was not seen in the no SNF cohort that used 3-month windows. Since the first eligible month was chosen for individuals with more than one, that first month may be sooner after NH entry, and is more likely to be a SNF month in which medications are not observed. Since SNF stays only last up to 100 days, any medication use would be more likely to show up in the “post” period, indicating drug initiation rather than continuation.

Dosage changes were not considered because of the limitations in accurate assessment using claims. If a physician determines that warfarin dosage needs to be changed based on an INR result, s/he may tell the patient to take half of a pill or two pills, rather than give a new prescription for a different dose. Therefore, dosage adjustments would be underestimated in this study.

5.4 The relationship between medications and transitions

Hospitalizations are common among individuals with AFIB. Among older Medicare beneficiaries with chronic AFIB, approximately one-third experienced a hospitalization within one year, about half of which were cardiovascular-related.¹¹⁸ In a population of managed care patients, over 10% were readmitted to the hospital within a year for an AFIB-related reason following an initial AFIB-related hospitalization.¹¹⁹ Since the cohort in the study by Kim et al. is significantly younger and community-based, readmissions are likely higher among older NH residents. The current study did not differ between a “new” hospitalization and readmissions, but examines medication use surrounding all hospital transitions. Over an average follow-up of 13.6 months, 35.2% of the cohort experienced at least one hospitalization, and 5.5% experienced an AFIB-related hospitalization.

In aim 3a, the effects of warfarin use and INR monitoring on AFIB-related hospitalizations were nonsignificant. However, the equivalent models for any hospitalizations gave more significant results, suggesting that warfarin use and INR

monitoring were protective against all-cause hospitalizations. This refutes the hypothesis that appropriate AFIB management results in fewer AFIB-related hospitalizations. The nonsignificant association of both warfarin use and INR monitoring with AFIB-related hospitalization may be due to the heterogeneity in the operational definition of AFIB-related hospitalizations (inpatient visits with a primary diagnosis of AFIB, an ischemic event, or a hemorrhagic event). Although appropriate management of AFIB with warfarin and INR monitoring may be expected to reduce hospitalizations due to ischemic events, warfarin use may increase the risk of bleeding events. Including these opposing outcomes may have resulted in the null effect that was observed. Further, a hospitalization with a primary diagnosis of AFIB may be due to symptoms, which are managed with rhythm and rate control agents, not antithrombotic agents, so there is likely to be no effect of warfarin on hospitalizations with a primary AFIB diagnosis.

The finding of a protective effect of warfarin use and the trend toward significance with INR monitoring against any hospitalizations may be indicative of better management of chronic conditions as a whole. A NH resident with AFIB being treated with warfarin and receiving regular INR monitoring may be more likely to receive better management of other conditions, thus avoiding any-cause hospitalizations. While these analyses controlled for potential facility-level variables, unmeasured quality of care factors may still be influencing these results.

Among emergency hospitalizations due to adverse drug events, warfarin was the most commonly indicated drug (33.3%) and oral antiplatelet agents were the third most

common (13.3%).⁸⁰ Further, it has been well-documented that a substantial proportion of time on warfarin is spent below the therapeutic range,^{47,49,81,104} and that inadvertent discontinuation and poor adherence to anticoagulants are common causes of hospital readmissions.^{14,25,85} Since this study did not take into account therapeutic failures (e.g., under-dosing), there may be additional ADE-related hospitalizations due to inappropriately low use of warfarin not captured in this study. Therefore, the finding of warfarin not being a significant predictor of AFIB-related hospitalizations may be due to a combination of reduced hospitalizations from the protective effect of warfarin and the increased hospitalizations due to adverse drug events related to warfarin misuse.

In aim 3b, a hospitalization was associated with 28% higher odds of warfarin use. However, there were 29% lower odds of INR monitoring following a hospitalization. These results refute the original hypothesis that a hospitalization would lead to lower warfarin use due to the potential medication changes inevitable during a hospitalization, but higher INR monitoring among users due to heightened awareness of potential adverse events. The results of higher warfarin use following a hospitalization suggest that some individuals may be initiated on warfarin following a hospitalization or that other individuals already receiving warfarin are more likely to immediately fill a new prescription. The lower INR monitoring caused by a hospitalization is cause for concern, and may reflect lower monitoring among new users or poor communication between hospital physicians who initiate or refill warfarin and NH providers who must perform the drug monitoring. These findings suggest the need to expand medication reconciliation interventions in both scope and time. The process of medication reconciliation should

include information on medications a patient is taking as well as on any monitoring required for those medications. Further, medication reconciliation should be expanded in time to include more rigorous follow-up once the patient has returned to the NH, in order to ensure that appropriate monitoring is being conducted for medications, particularly ones that have been recently initiated.

In aim 3, I encountered difficulty in estimating the random effects models. This is likely due to the large sample size, unbalanced design, and two random effects with a large number of clusters with small cluster sizes. Specifically, there were 16,174 individuals with cluster sizes ranging from 1 to 36, and there were 9,133 unique facilities, with cluster sizes ranging from 1-12. Various options were attempted to improve model specification; the between-within method for computing denominator degrees of freedom and re-specifying character IDs as numeric and sorting substantially improved efficiency. Using the Laplace estimation method (versus the default pseudo-likelihood method) allowed those models that still did not converge to do so. Although results from models with different estimation methods cannot be directly compared, the results are largely similar, as evidenced by those models that were able to converge using both methods. For example, in Aim 3b, the odds ratios for the unadjusted effect of a hospitalization on INR monitoring were 0.60 and 0.59 using the default pseudo-likelihood and Laplace methods, respectively. The equivalent results from adjusted models were 0.71 and 0.68, respectively. For the effect of a hospitalization on warfarin use, the Laplace estimation method gave somewhat larger estimates for the unadjusted (OR 1.73) and adjusted models (OR 1.48) than for the default method (unadjusted OR 1.33, adjusted OR 1.28).

However, these estimates are all consistent with a conclusion of a positive association between hospitalization and warfarin use.

5.5 Structural equation modeling

5.5.1 Overview

Structural equation modeling (SEM) is a multivariate statistical method that tests relationships between concepts, represented as both measured variables and latent constructs.¹²⁰ SEM requires the user to specify a model a priori, based on prior experience, knowledge, and research.^{120,121} The goal of a specified model is to account for as much variation and covariation of measured variables as possible. Estimates are obtained by simultaneously solving multiple equations of the specified relationships.¹²⁰

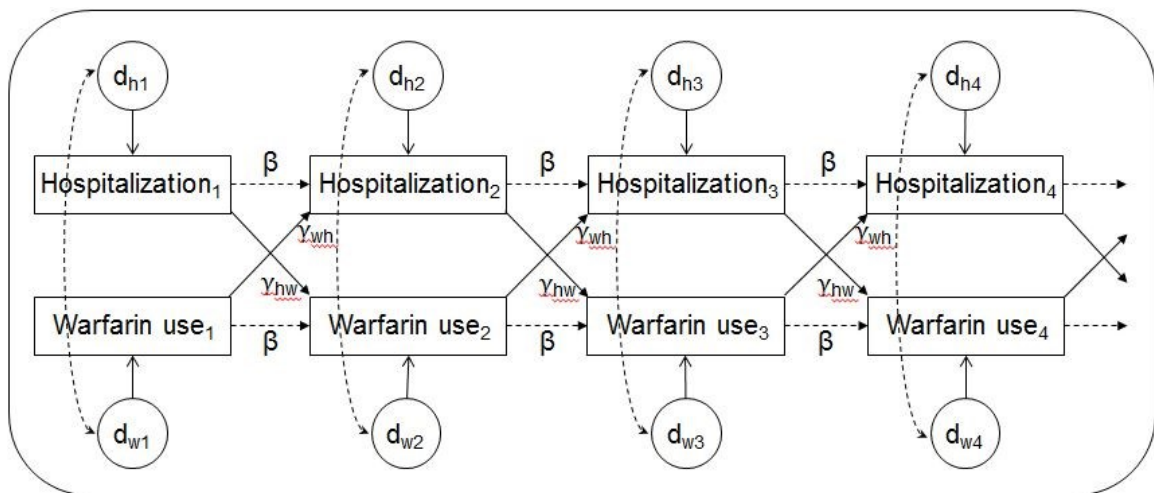
One specific type of SEM is path analysis, where directional relationships between measured variables are hypothesized (specified) and tested. Regression analysis is similar, and is actually a special case of SEM. While SEM can handle measurement error by explicitly specifying it using latent variables, path analysis is similar to regression in its (somewhat unrealistic) assumption that all variables are measured without error.^{120,121} Therefore, consequences of this reliability assumption are the same for path analysis as for regression.

5.5.2 Cross-lagged panel model

Most SEM studies use cross-sectional rather than longitudinal data.¹²¹ One specific model that handles longitudinal data is the panel model, with multiple measurements of a set of variables over time. In this study, a cross-lagged relationship was hypothesized and is

represented in Figure 5. In this model, two endogenous variables, hospitalization and use of warfarin, are specified to have both lagged (β) and cross-lagged (γ) effects. The path coefficient represented by β estimates the lagged effect of one variable on itself at a later time. For example, one would expect that prior hospitalizations would influence the likelihood of future hospitalizations. The path coefficient represented by γ estimates the cross-lagged effects and corresponds to the research questions: γ_{hw} estimates the effect of a prior hospitalization on subsequent warfarin use; γ_{wh} estimates the effect of prior warfarin use on a hospitalization in the following month. All path coefficients are hypothesized to be equal, since the relationships are hypothesized to be cyclical and stable.

Figure 5. Cross-lagged panel model



The errors are included in this model as disturbances, represented as d_h and d_w for hospitalizations and warfarin, respectively. Since these variables are endogenous, the unexplained variance due to omitted causes and measurement error is included using disturbances rather than errors. At each time point, these errors are hypothesized to be

correlated. Since warfarin use and hospitalizations are thought to causally influence one another, it makes sense to think that there are also unmeasured variables that may influence both of these variables (i.e., confounders).¹²¹ These correlated disturbances result in the model being nonrecursive.

5.5.3 Limitations and Practical Challenges

Specification of reciprocal effects, such as that hypothesized in the cross-lagged panel model, is not simple and makes a model more difficult to analyze. The nonrecursive nature of the model is more statistically demanding and is more likely to encounter a technical problem in the analysis.¹²¹ In addition, several features of the data and proposed analyses for this study would further complicate the SEM analysis: the dichotomous nature of the endogenous variables, the hierarchical (clustered) nature of the data, and the inclusion of covariates.

Dichotomous variables

Most SEM software packages use maximum likelihood to estimate parameter estimates, but this method is only appropriate for normally distributed data. In the past, categorical data have been treated as if they were normally distributed and the traditional maximum likelihood approach used because there were no alternatives.¹²² However, this approach results in attenuated parameter estimates, downwardly biased standard errors, and incorrect data-model fit indices.^{123,124} Variables that are further from normality, like the dichotomous variables used in the current study, would generate greater bias in the results.

In the most common approach to handling nonnormal data, categorical variables are assumed to have an underlying continuous latent variable, and the categorical variables result from categorizing values of the underlying variable based on given thresholds. The joint distribution of two variables is given by a correlation: tetrachoric (two binary variables), polychoric (two categorical variables), or biserial or polyserial (one categorical and one continuous variable). Then, a maximum likelihood, weighted least squares, or diagonally weighted least squares (recommended) approach can be taken to estimate the model using these correlations.¹²³⁻¹²⁶ One issue with this approach is that not all categorical variables can truly be assumed to have an underlying continuous and normally distributed scale.¹²⁶ Using the current study as an example, health status may be an underlying latent concept that influences hospitalization, but the “decision” to be hospitalized is a discrete event and should be represented as such. Similarly, this study could use a continuous concept, such as adherence, to measure warfarin use. However, measures of adherence such as the medication possession ratio or proportion of days covered are not necessarily normally distributed and are, based on the author’s experience with these data, highly left-skewed.

On the practical side, methods to handle categorical data have not been fully established in SEM. Although SAS has an SEM procedure (PROC CALIS), it cannot handle analyses using dichotomous data. Further, a textbook on “applied, intermediate-level” issues in SEM handles nonnormally distributed and ordered categorical data, but ignores nonordered categorical data such as dichotomous variables.¹²⁵

Multilevel Modeling

As in multivariable regression, SEM typically assumes independence between observations. Ignoring clustering in SEM can create inappropriately small standard errors, giving incorrectly large chi-square values¹²³ and therefore increasing the probability of type I error. Although a hierarchical data structure can be handled in SEM more easily than some of the above-mentioned challenges, it does add a layer of complexity to an already complicated model.

Covariates

Although SEM can technically handle covariates, most models use one or two in practice. Unlike regression, where a large number of covariates can be included in a model, SEM becomes more complicated as the number of variables increases. This is even more difficult in a panel model with repeated measures and time-varying covariates.¹²¹ The correlated disturbances shown in the cross-lagged panel model (Figure 5) capture the unexplained variance due to confounders not included in the model, but since this study has a number of known and measured covariates, it does not make sense to exclude them from the model.

5.5.4 Summary

After working with the data and evaluating the abilities of SEM (and the researcher), it was determined that SEM was not feasible for this analysis. The author of a textbook on SEM states:

There is no “embarrassment” in using a simpler statistical technique over a more complicated one, especially if the simpler technique is sufficient to test your hypothesis and if your comprehension of the more complex method is not strong. In general, it is better to resist the temptation to use the “latest and greatest” (i.e., more complicated) statistical technique when a simpler method will accomplish the task.¹²¹ For this study, the hypothesized bidirectional relationship was tested using hierarchical generalized linear mixed models. Although these relationships were not tested simultaneously, the “simpler” technique answered the research questions and hypotheses.

5.6 Limitations

This study has a number of limitations. Aspirin is recommended as the anticoagulant of choice for those with a low risk of stroke (CHADS₂ score of 0) and is an option for patients with a moderate risk of stroke (CHADS₂ score of 1).^{8,9} However, Medicare Part D claims data do not include over-the-counter medications such as aspirin or other non-steroidal anti-inflammatory drugs so the use of these medications could not be assessed. Several studies among NH residents with AFIB have found prevalence estimates of aspirin use ranging from 8% to 37.6%,^{47-49,78,100} with a small number of individuals taking both aspirin and warfarin concomitantly. Therefore, it can be expected that some of the individuals in this study were prescribed aspirin instead of warfarin for their AFIB. Despite the lack of information on aspirin use in this study, 82.3% of the cohort had a high risk of stroke (CHADS₂ score ≥ 2) and no history of major bleeding, and therefore should be receiving warfarin, not aspirin, according to published guidelines.^{8,9}

A second medication-related limitation is the inability to capture medication prescribing during a SNF stay, since medications are bundled into the Part A payment. This includes periods immediately after a NH resident's return from the hospital for those residents whose stay qualifies. Restricting the study sample to long-stay residents excludes those who are only in a NH for SNF services. For aims 1 and 3, individual months with any SNF covered days were excluded (i.e., censored) so that medication use could be appropriately assessed in all included months. Although this study cannot answer the question of medication use during a SNF stay, it limits the potential bias that would exist if SNF months were included. For aim 2, 6-month windows are used for both the pre and post periods, which are broad enough to capture medication use outside of any SNF stays, which are up to 100 days. Since it may take time for an individual's regimen to stabilize after an acute event such as a hospitalization, the 6-month window following hospitalization is broad enough to capture medication use upon stabilization of the medication regimen. To further address the inability to observe drug use during a SNF stay, a secondary cohort was restricted to individuals with NH residence not covered under a SNF stay. The similar results between the any NH and no SNF cohorts indicates that the potential issue of not observing drug use during a SNF stay does not cause significant bias in this study.

A third limitation is the inability to determine if residents are maintaining INR levels within the therapeutic range, as claims data does not provide INR test results. This study makes the assumption that practitioners who are conducting regular INR tests to monitor patients' INR levels are following up with patients and adjusting the warfarin dose

appropriately to maintain the patient in the therapeutic range. Despite this limitation, the use of regular INR monitoring among those being treated with warfarin is a published quality measure (Table 14)^{5,105,107} and is an important assessment of a facility's processes.

The use of ICD-9-CM codes on administrative claims to identify risk factors and comorbid conditions is challenging for several reasons. First, there is always a chance that a physician does not include a diagnosis on a claim or includes an incorrect diagnosis. Second, a diagnosis that is no longer relevant may "follow" a person if physicians see a prior diagnosis and continue to include it on claims. While not a substantial concern for many chronic conditions (e.g., CHF, hypertension) that rarely resolve entirely, these diagnoses may cause an individual to be misclassified for more acute events such as bleeding despite appropriate management. In this study, major bleeding and ischemic events, acute occurrences that can be mitigated with appropriate management, were both defined solely on inpatient claims, which are less likely to have older diagnoses unless they contribute to the current hospitalization.

Lastly, this study proposed to apply the cross-lagged panel model to assess the bidirectional association between the quality of AFIB management and hospitalizations. However, this method was unfeasible for this type of analysis using these data. Although not performed in a single analysis, results from aims 3a and 3b provide information on each of the hypothesized directions of association.

5.7 Strengths

This is the first study, to my knowledge, that uses Medicare Part D data to examine treatment patterns among NH residents with AFIB. Many prior studies have been restricted to a small number of nursing homes in limited geographic areas.^{48,49,78,104}

Although two studies used the NNHS to describe use of warfarin,^{100,106} none have examined medication use in NH residents following the implementation of Medicare Part D. Two studies that examined use of medications to manage AFIB among Medicare beneficiaries with Part D coverage found higher rates of use compared to those found in this study: 74% were taking rate-control agents,¹¹⁰ 19% were taking rhythm control agents,¹¹⁰ and 59%¹¹⁰ and 67%¹¹³ were using warfarin. The higher use observed in these studies likely represents differences in AFIB management between community-dwelling individuals and NH residents, a disparity that this study begins to inform.

Another strength of the study is the ability to control for characteristics of the facility in which the resident lives using the CMS provider and deficiency files and the LTCfocus.org database. Most published studies examining factors associated with AFIB management have focused on person-level factors.^{41,42} Some facility characteristics that were associated with an increased risk of hospitalization in this study have been shown to be associated with hospitalizations among NH residents in previous studies, including for profit status, larger bed size, staffing levels, and Medicaid per diem reimbursement.^{40,42} Since many factors that were associated with hospitalization also were seen to influence treatment patterns of NH residents in the current study, ignoring these facility-level confounders may overestimate the relationship between AFIB management and

hospitalizations. As hypothesized, the culture of a NH and its quality of care, represented through facility characteristics, influence both AFIB management and transitions between care settings, and this study accounted for these important confounders

The use of repeated measures allowed for the assessment of changes in AFIB management across transitions, as well as the impact of transitions on AFIB management over time. The longitudinal study design ensured temporality, a major limitation in cross-sectional studies, and provides added statistical power compared with cross-sectional studies, as a result of having multiple data points per person. The knowledge of when medication changes occur provides information regarding points at which interventions can be anticipated to improve patient care.

5.8 Generalizability

A benefit to using the chosen data sources is that this study cohort was selected from the 5% random sample of Medicare beneficiaries, a nationally representative sample. Due to exclusion criteria, the study sample may not be fully generalizable to the national NH population. A comparison of the demographics of the study sample to other studied NH samples is provided in Table 16. The age ≥ 65 and long-stay criteria result in a sample that is older than the general population of NH residents. The Medicare coverage and long-stay requirements resulted in a study sample with a higher proportion of dual (Medicare/Medicaid) eligibility; this is expected, since NH patients with longer stays are more likely to have spent down their assets and rely on Medicaid.³³ However, the study includes individuals from all 50 states, is similar to the general NH population in terms of

sex and region, and is only slightly less racially diverse than the general NH population. Since the study sample was older and likely more frail, the use of warfarin in this study may be lower, and the rate of hospitalization higher, than that found in younger and healthier NH residents. However, there is no reason to believe that there is a substantial difference in the relationship between pharmacotherapeutic management and hospitalization among a broader population of NH residents with AFIB. Therefore, results should provide a reasonable representation for the population of older NH residents with AFIB.

Table 16. Comparison of the study cohort to published NH study samples

Characteristic	Study sample: Older, long-stay NH residents with AFIB	2004 NNHS population ³¹	2004 NNHS: older long-stay residents ³³
Female	76.4%	71.2%	76.1%
Age			
<65	0*	11.7%	0*
65-74	11.0%	11.7%	12.6%
75-84	35.5%	31.4%	34.1%
≥85	53.5%	45.2%	53.4%
Race			
White	88.3%	85.5%	N/A
Black	7.3%	12.5%	N/A
Other	1.7%	2.0%	N/A
Hispanic	2.8%	3.8%†	N/A
Region			
Northeast	25.3%	22.2%	N/A
Midwest	28.9%	30.0%	N/A
South	34.7%	33.6%	N/A
West	11.2%	14.2%	N/A
Dual eligibility	73.4%	59.7%‡	68.8%§

*NH residents under 65 years of age were excluded from the sample

†Persons of Hispanic or Latino origin may be of any race; only the race categories of White, Black, and Other are mutually exclusive.

‡The proportion of all current residents using Medicaid as a source of payment at the time of interview

§The proportion of all current residents using Medicaid as a primary payment source in the past month

Despite having external validity to older, long-stay NH residents, results from this study are likely not generalizable to a younger population, community-dwelling individuals, or those with other chronic conditions. Younger adults tend to be healthier, take fewer medications, and experience fewer transitions, so the results found in this cohort of older adults cannot be applied to a younger population. Further, management of each chronic condition is different and medications to treat other conditions have varying effectiveness and strength of recommendations. Therefore, the relationship between the quality of pharmacotherapeutic management and transitions is likely also different in individuals with conditions other than AFIB, and is an area for future study.

Further, long-stay NH residents are very different from both short-stay residents and those who reside in the community. Long-stay residents are significantly older and have higher rates of certain chronic conditions including stroke compared with short-stay residents,¹⁰¹ putting them at higher risk for sequelae of inappropriate treatment for chronic conditions such as AFIB. In addition, the management of long-stay residents should be relatively stable, given the longer nature of their residence in the NH, so adverse drug events that results in hospitalizations may be preventable. Second, the greater amount of time spent in a facility by long-stay residents puts them at increased risk for experiencing multiple transitions. Although short-stay residents are more likely to be admitted to a NH following a hospitalization, a transition to and back from an acute care setting within 90 days of NH admission is highly predictive of being a long-stay resident¹⁰² Multiple transitions may result in changes to the medication regimens, causing the individual to become involved in a cycle of transitions and poor medication quality.

Lastly, short-stay residents are often in a skilled nursing facility (SNF) stay where the nursing home is reimbursed under Medicare Part A for up to 100 days for all costs related to the care of a patient, including medications.¹²⁷ Since medications are not billed separately under Medicare Part D during a SNF stay and therefore are not able to be observed using claims data, short-stay residents were excluded from this study. For all of these reasons, improving medication quality and understanding the relationship with transitions in order to reduce them is more relevant to a long-stay population in order to ultimately achieve more efficient health care.

CONCLUSION

This study explored the quality of medication use and its relationship with care transitions among long-stay NH residents with AFIB. This study found that antithrombotic agents were underused in this population, with only 37.4% receiving warfarin. However, a large majority of those taking warfarin were receiving INR monitoring in accordance with guideline recommendations.^{8,9} Therefore, NH interventions should focus on improving provider education and awareness of the need for anticoagulation in AFIB, and less on the need for monitoring since that recommendation appears to have been more widely adopted. In light of the strong recommendations for use of warfarin in high risk patients such as NH residents, and the requirement for INR monitoring at least monthly, both of these should be considered as quality measures among NH residents with AFIB. Although there are new agents available to reduce thromboembolic risk in AFIB, it is likely that warfarin will remain a preferred medication among physicians that manage NH residents due to the observed low burden of INR monitoring, the ability to reverse warfarin during a bleed, and the availability of long-term safety information.

A number of factors were associated with lower warfarin use, which can help identify subgroups in which interventions to increase warfarin use may be most effective. These include the oldest old, those of nonwhite race, and those with incident AFIB. Further, CHADS₂ score should be considered more strongly in treatment decisions, as those with higher stroke risk scores were not significantly more likely to receive warfarin. Although

INR monitoring rates are above 80%, they could continue to be improved by targeting individuals with a higher number of comorbid conditions, particularly conditions that increase bleeding risk.

Individual differences played a greater role in treatment decisions than facility-level factors, evidenced by the larger effect sizes seen with individual-level factors. Most general facility characteristics and potential indicators of the quality culture at the NH were not associated with AFIB management, so future research should examine additional facility factors that may help identify facilities that need improvement. However, certain facility factors that were predictive of warfarin use were related to reimbursement (i.e., MCO penetration rate, case-mix adjustment, and the proportion of Medicaid LTC spending on HCBS). Therefore, policy makers at the county and state levels need to consider unintended consequences relating to the quality of care for residents when creating reimbursement policies.

Deitelzweig states that “Anticoagulation requires close monitoring and adjustment depending on clinical circumstances as the patient moves through various care settings. Good communication and the continuity of care among providers are key in mitigating risk”⁸⁵ Communication between providers in different care settings is a necessary aspect of continuity of care. NH residents with AFIB experience a high rate of transitions across care settings, particularly hospitalizations. Following a hospitalization, this study found a substantial proportion of individuals experienced medication changes (i.e., initiation, discontinuation, switching) for antithrombotic medications (aim 2), and found a 28%

higher odds of warfarin use specifically associated with a prior hospitalization (aim 3b). Despite these changes, a hospitalization was associated with significantly lower INR monitoring (OR=0.71), a concerning finding. This suggests that, while NH residents may be treated with warfarin for their AFIB, the monitoring of this medication, which is known for a high rate of ADEs, is suboptimal. NH residents who have recently transitioned from hospital to NH are a population that should be targeted for future interventions to improve medication monitoring.

Only two studies to my knowledge have explored the potential *bidirectional* relationship between pharmacotherapeutic management and transitions,^{11,17} and neither focuses on this relationship in a NH population. Among NH residents included in this study, the reverse relationship, the effect of medication use on hospital transitions, was also examined (aim 3a). Warfarin use and INR monitoring were associated with lower odds of hospitalization. These findings support AFIB guidelines which recommend use of warfarin and regular INR monitoring.^{8,9} However, these results were not duplicated for AFIB-related hospitalizations, possibly due to the inclusion of opposing ischemic and hemorrhagic outcomes. The lower risk of any hospitalization may indicate that use of warfarin and INR monitoring are indicators of other aspects of quality at the physician or NH facility level that reduces the likelihood of hospitalizations overall.

It has been recommended that the transition between hospital and LTC setting be treated similarly to the transfer between hospitals, and that systematic procedures, including medication reconciliation, exist for these complicated handoffs.⁸⁵ Given the high rate of

transitions and polypharmacy found among NH residents, expanded interventions aiming to improve medication-related quality of care would be particularly beneficial for this population. These interventions should target increased use of antithrombotic agents among older, long stay NH residents with AFIB, and improved medication monitoring for these individuals who transitions across care settings. Future research should continue to explore different measures of medication quality. Additional facility-level factors that aim to capture the culture of quality in a facility should also be investigated, in order to continue guiding the creation, implementation, and targeting of improved medication reconciliation interventions.

APPENDICES

Appendix 1. ICD-9-CM codes used to define comorbid conditions

Appendix 2. Calculation of CHADS₂, HEMORR₂HAGES, and Charlson Comorbidity Index

Appendix 3. Study variable list

Appendix 1. ICD-9-CM codes used to define comorbid conditions

Medical Condition	Study Application(s)	ICD-9-CM codes	References ^{16,90,95,98-100,128-131}
Valvular disease	Exclusion criteria	Diagnosis codes: V42.2, V43.3, 093.2x, 394.x, 395.x, 396.x, 397.x, 398.9, 424.0, 424.1, 424.2, 424.3, 424.9x, 746.0x-746.7 Procedure codes: 35.0x, 35.1x, 35.2x, 35.3x, 35.4x, 35.5x, 35.6x, 35.7x, 35.8x, 35.9x CPT codes: 33400-33417, 33420-33430, 33460-33468, 33470-33478, 33496, 33600, 33602, 33660-33670, 33684	Birman-Deych 2005, Bocuzzi 2009, Boulanger 2006, Mercaldi 2011, Casciano 2013
Chronic heart failure	CHADS ₂ , CCI	398.91, 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 404.03, 404.13, 404.93, 425.x, 428.x	Birman-Deych 2005, Lakshminarayan 2006, Casciano 2013
Hypertension	CHADS ₂ , HEMORR ₂ HAGES	401.x, 402.x, 403.x, 404.x, 405.x, 437.2	Birman-Deych 2005, Mercaldi 2011, Lakshminarayan 2006, Casciano 2013
Mild/moderate diabetes	CHADS ₂	250.0x, 250.1x, 250.2x, 250.3x, 250.8x, 250.9x	Birman-Deych 2005, Lakshminarayan 2006, Casciano 2013, Deyo 1992, Romano 1993, Quan 2005
Diabetes w/complications		250.4x, 250.5x, 250.6x, 250.7x	
Ischemic stroke	CHADS ₂ , HEMORR ₂ HAGES	433.x1, 434.x, 436, 437.1x	Gage 2001, Birman-Deych 2005, Mercaldi 2011, Lakshminarayan 2006, Casciano 2013
Transient ischemic attack		435.x	
Cerebrovascular disease	CCI	Diagnosis codes: 430, 431, 432, 433, 434, 435, 436, 437, 438, 362.34 Procedure codes: 38.12, 38.42	Deyo 1992, Romano 1993, Quan 2005
Myocardial infarction	CCI	410.x, 412	Deyo 1992, Romano 1993, Quan 2005

Medical Condition	Study Application(s)	ICD-9-CM codes	References ^{16,90,95,98-100,128-131}
Peripheral vascular disease	CCI	Diagnosis codes: 440.x, 441.x, 442.x, 443.x, 447.1, 785.4, V43.4 Procedure codes: 38.13, 38.14, 38.16, 38.18, 38.33, 38.34, 38.36, 38.38, 38.43, 38.44, 38.46, 38.48, 39.22-39.26, 39.29	Deyo 1992, Romano 1993, Quan 2005
	CCI	290.x, 294.x, 331.0, 331.1x, 331.2	Mercaldi 2011, Deyo 1992, Romano 1993, Quan 2005
Dementia	HEMORR ₂ HAGES	E880.x, E881.x, E882, E883.x, E884.x, E885.x, E886.x, E887, E888.x, 291.x, 292.x, 293.x, 295.x, 296.x, 297.x, 311, 332.x, 334.x, 357.x, 458.0, 780.4, 781.2	Mercaldi 2011
	CCI	416.8, 416.9, 490, 491, 492, 493, 494, 495, 496, 500, 501, 502, 503, 504, 505, 506.4, 508.1	Deyo 1992, Romano 1993, Quan 2005
Chronic obstructive pulmonary disease	CCI	710.x, 714.x, 725	Deyo 1992, Romano 1993, Quan 2005
Rheumatologic disease	CCI	531.x, 532.x, 533.x, 534.x	Deyo 1992, Romano 1993, Quan 2005
Peptic ulcer disease	CCI	070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6, 070.9, 570, 571.x, 573.x	Mercaldi 2011, Deyo 1992, Romano 1993, Quan 2005
Mild liver disease	CCI	Diagnosis codes: 572.2, 572.3, 572.4, 572.8, 456.0, 456.1, 456.2x Procedure codes: 39.1, 42.91	Mercaldi 2011, Deyo 1992, Romano 1993, Quan 2005
Moderate/severe liver disease	HEMORR ₂ HAGES	Diagnosis codes: 582.x, 583.0, 583.1, 583.2, 583.4, 583.6, 583.7, 585.x, 586, 588.x, V42.0, V45.1x, V56.x Procedure codes: 39.27, 39.42, 39.93, 39.94, 39.95, 54.98	Mercaldi 2011, Deyo 1992, Romano 1993, Quan 2005
Renal disease	CCI		

Medical Condition	Study Application(s)	ICD-9-CM codes	References ^{16,90,95,98-100,128-131}
Hemi-/paraplegia	CCI	342.x, 343.x, 344.x	Deyo 1992, Romano 1993, Quan 2005
Malignancy	HEMORR ₂ HAGES	140.x, 141.x, 142.x, 143.x, 144.x, 145.x, 146.x, 147.x, 148.x, 149.x, 150.x, 151.x, 152.x, 153.x, 154.x, 155.x, 156.x, 157.x, 158.x, 159.x, 160.x, 161.x, 162.x, 163.x, 164.x, 165.x, 170.x, 171.x, 172.x, 174.x, 175.x, 176.x, 179, 180.x, 181, 182.x, 183.x, 184.x, 185, 186.x, 187.x, 188.x, 189.x, 190.x, 191.x, 192.x, 193.x, 194.x, 195.x, 200.x, 201.x, 202.x, 203.x, 204.x, 205.x, 206.x, 207.x, 208.x, 273.0, 273.3	Mercaldi 2011, Deyo 1992, Romano 1993, Quan 2005
	CCI		
Metastatic solid tumor	CCI	196.x, 197.x, 198.x, 199.x	Deyo 1992, Romano 1993, Quan 2005
AIDS	CCI	042, 043, 044	Deyo 1992, Romano 1993, Quan 2005
Alcohol abuse	HEMORR ₂ HAGES	303.x, 305.0, V11.3	Mercaldi 2011
Decreased platelet function	HEMORR ₂ HAGES	287.x	Mercaldi 2011
Anemia	HEMORR ₂ HAGES	280.x, 281.x, 282.x, 283.x, 284.x, 285.x	Mercaldi 2011
Bleeding ("rebleed risk")	HEMORR ₂ HAGES	Intracranial bleeding: 430, 431, 432, 800.2x, 800.3x, 800.7x, 800.8x, 801.2x, 801.3x, 801.7x, 801.8x, 803.2x, 804.2x, 852.0x, 852.1x, 852.2x, 852.3x, 852.4x, 852.5x, 853.0x, 853.1x Gastrointestinal bleeding: 448.0, 448.9, 455.x, 456.0, 456.20, 459.0, 530.21, 530.7, 530.82, 531.0x, 531.2x, 531.4x, 531.6x, 532.0x, 532.2x, 532.4x, 532.6x, 533.0x, 533.2x, 533.4x, 533.6x, 534.0x, 534.2x, 534.4x, 534.6x, 535.x, 537.83, 537.84, 562.02, 562.03, 562.12, 562.13, 568.81, 569.3, 569.85, 569.86, 578.x	Bocuzzi 2009, Boulanger 2006, Mercaldi 2011, Casciano 2013

Medical Condition	Study Application(s)	ICD-9-CM codes	References ^{46,90,95,98-100,128-131}
		Other bleeding: 008.04, 077.4, 078.6, 246.3, 286.5, 360.43, 362.43, 362.81, 363.6x, 363.72, 364.41, 372.72, 374.81, 376.32, 377.42, 379.23, 386.8, 388.69, 423.0, 593.81, 596.7, 596.8, 599.7, 602.1, 626.6, 627.1, 719.1x, 782.7, 784.7, 784.8, 786.3, 958.2, 998.1x, E934.0, E934.1, E934.2, E934.3, E934.4, E934.5, E934.6, E934.7, E934.8, E934.9	

Appendix 2. Calculation of CHADS₂, HEMORR₂HAGES, and Charlson Comorbidity Index

CHADS₂⁹²

Element	Weight
Chronic heart failure	1
Hypertension	1
Age ≥75	1
Diabetes	1
Stroke/TIA	2

HEMORR₂HAGES⁹⁴

Element	Weight
Hepatic or renal disease	1
Ethanol abuse	1
Malignancy	1
Older: age >75	1
Reduced platelet count or function	1
Rebleeding risk	2
Hypertension	1
Anemia	1
Genetic factors*	N/A
Excessive fall risk	1
Stroke	1

*Genetic factors cannot be identified in administrative claims. Gage et al. did not have capture genetic risk factors for bleeding and therefore validated the HEMORR₂HAGES score excluding the genetic factors item.⁹⁴

Charlson Comorbidity Index⁹⁵⁻⁹⁸

Element	Weight
Myocardial infarction	1
Chronic heart failure	1
Peripheral vascular disease	1
Cerebrovascular disease	1
Dementia	1
Chronic pulmonary disease	1
Rheumatologic disease	1
Peptic ulcer disease	1
Mild liver disease	1
Diabetes (mild/moderate)	1
Diabetes with chronic complications	2
Hemi/paraplegia	2
Renal disease	2
Malignancy	2
Moderate/severe liver disease	3
Metastatic solid tumor	6
AIDS	6

Appendix 3. Study variable list

Variable	Definition	Source ^{91,93,94}
Month	Measure of time, calculated as the number of months between cohort entry (i.e., first observed AFIB diagnosis) and the current month	N/A
Resident demographics		
Age	Beneficiary's age at cohort entry, calculated based on the date of birth	Medicare denominator file
Sex	Beneficiary's sex	Medicare denominator file
Race	Beneficiary's race, based on the RTI race variable, an enhanced race/ethnicity designation based on first and last name algorithms	Medicare denominator file
Region	Census regions based on the beneficiary's state of residence (Midwest, Northeast, South, West); "Other" locations not in one of the 50 states were grouped with the South region	Medicare denominator file
Dual eligibility	A monthly flag identifying those receiving both Medicare and Medicaid benefits; time-varying	Medicare denominator file
Low income subsidy	A monthly flag identifying those receiving a low-income subsidy for assistance paying for medications; time-varying	Medicare denominator file
End of life	A flag for the last three months prior to death and the month of death, based on the beneficiary date of death; time-varying	Medicare denominator file
Resident Clinical information		
Charlson comorbidity index	Score to capture comorbidity burden; range 0-33; each component was identified by the presence of at least one inpatient claim with a relevant ICD-9-CM code in the 12 months prior to each month; time-varying; see Appendix 1	Medicare administrative claims (inpatient)

Variable	Definition	Source ^{91,93,94}
CHADS ₂	<p>for component ICD-9-CM codes and Appendix 2 for score calculation</p> <p>Score to predict risk of stroke, range 0-6; each component was identified by the presence of at least one inpatient or two outpatient (hospital outpatient or carrier) claims with a relevant ICD-9-CM code in the 12 months prior to each month; time-varying; see Appendix 1 for component ICD-9-CM codes and Appendix 2 for score calculation</p>	Medicare administrative claims (inpatient, hospital outpatient, carrier)
HEMORR ₂ HAGES	<p>Score to predict risk of bleeding, range 0-11; each component was identified by the presence of at least one inpatient or two outpatient (hospital outpatient or carrier) claims with a relevant ICD-9-CM code in the 12 months prior to each month; time-varying; see Appendix 1 for component ICD-9-CM codes and Appendix 2 for score calculation</p>	Medicare administrative claims (inpatient, hospital outpatient, carrier)
Newly diagnosed AFIB	<p>A flag for the first 6 months following a person's first observed AFIB diagnosis for those with no AFIB claim (ICD-9-CM 427.31; any claim type) during the 12 months prior to that diagnosis; time-varying</p>	Medicare administrative claims (inpatient, skilled nursing facility, hospital outpatient, home health, hospice, carrier, durable medical equipment)
Drug information		
Drug use	<p>Indicator of availability of the relevant medication during the month based on PDE fill dates and days supplied, if the days supply covered at least one day in the month; for months with a days supply greater than the number of days in the month, it was assumed that the medication was taken after the current days supply was finished and the days supply was shifted forward; time-varying</p>	Medicare administrative claims (Part D prescription drug events)

Variable	Definition	Source^{91,93,94}
Hospitalizations		
Any hospitalization	Indicator for a hospitalization in the month based on the discharge date in a Medicare inpatient claim	Medicare administrative claims (inpatient)
AFIB-related hospitalization	Indicator for a hospitalization in the month that may be due to AFIB, based on the discharge date in a Medicare inpatient claim with a primary diagnosis of AFIB, ischemic stroke or transient ischemic event, or a major bleeding event (intracranial, gastrointestinal, or other); see Appendix 1 for IC9-CM-codes	Medicare administrative claims (inpatient)
General facility characteristics		
For profit	Indicates whether or not the facility is for-profit (individual, partnership, or corporation)	CMS provider/deficiency files & LTCfocus*
Chain affiliated	Indicates whether or not facility is part of a chain	CMS provider/deficiency files & LTCfocus*
Hospital-based facility	Indicator of whether or not facility is hospital-based	CMS provider/deficiency files & LTCfocus*
Bed size	Total number of beds as reported on the annual survey, imputed from the previous year if necessary	CMS provider/deficiency files & LTCfocus*
Occupancy rate	Number of occupied beds in facility divided by the total number of beds	CMS provider/deficiency files & LTCfocus*
Dedicated Alzheimer's unit	Indicator of whether or not facility has a special care unit for residents with Alzheimer's disease	LTCFocus
Dedicated specialty unit	Indicator of whether or not facility has any Special Care Unit (SCU) beds, excluding ventilator beds	LTCFocus
Hospitalizations per patient-year	Number of hospitalizations from the facility in the calendar year for every 365 nursing home resident days	LTCFocus

Variable	Definition	Source^{91,93,94}
Average number of medications per patient	Average number of medications in the past 7 days per resident in the facility on the 1st Thursday in April	LTCFocus
Facility Deficiencies		
Any deficiency	Facility contained ≥ 1 deficiency	CMS provider/deficiency files
Any “poor” deficiency†	Facility contained ≥ 1 deficiency with a poor scope/severity rating	CMS provider/deficiency files
Quality of care deficiency‡	Facility contained ≥ 1 quality of care deficiency	CMS provider/deficiency files
Quality of care “poor” deficiency††	Facility contained ≥ 1 quality of care deficiency with a poor scope/severity rating	CMS provider/deficiency files
Pharmacy-related deficiency§	Facility contained ≥ 1 pharmacy-related deficiency	CMS provider/deficiency files
Pharmacy-related “poor” deficiency†§	Facility contained ≥ 1 pharmacy-related deficiency with a poor scope/severity rating	CMS provider/deficiency files
Facility Staffing		
Available physician extender	Indicator of whether or not facility has a physician extender, meaning a nurse practitioner (NP) or physician's assistant (PA)	LTCFocus
Direct care hours/patient/day	Direct-care staff hours per resident day, calculated by dividing the total number of registered nurse (RN) plus licensed practical nurse (LPN) plus certified nursing assistant (CNA) hours by the number of residents in the facility	LTCFocus
Ratio of RN/nurse hours	Ratio of number of RN FTEs divided by number of RN FTEs plus LPN FTEs	LTCFocus

Variable	Definition	Source ^{91,93,94}
County-level information		
Number of hospital beds per 1000 elderly	Number of hospital beds in the county for every 1000 persons age 65 or older	LTCFocus
Number of nurses per 1000 elderly	Number of nurses (RNs & LPNs) in the county for every 1000 persons age 65 or older	LTCFocus
MCO penetration rate	The MCO penetration rate is drawn originally from the Area Resource File and is defined as the proportion of all Medicare beneficiaries in the county who are enrolled in a Medicare MCO	LTCFocus
State-level information		
Case mix adjustment	Indicator of whether or not state has a case mix reimbursement system used to adjust payments to nursing homes based on resident acuity level	LTCFocus
Average Medicaid per diem	Total Medicaid nursing home spending in the state divided by the total number of Medicaid days in nursing homes	LTCFocus
Proportion of Medicaid LTC spending on HCBS	Medicaid LTC spending on HCBS, calculated from hcbs.org and defined as the proportion of state Medicaid long-term care dollars spent on home and community based services; all other LTC spending is on NH care	LTCFocus

*For data contained in both CMS' provider/deficiency files and in the LTCfocus data, variables were coded to reflect provider-deficiency files if available; LTCfocus data was used only where data were missing. This was done because data in the provider-deficiency files are directly from OSCAR and are at the survey-level, whereas LTCfocus data are only available yearly and it is unclear how situations where there were no surveys or more than one survey in a given year were handled.

†Poor scope/severity was defined as any scope causing immediate jeopardy to resident health or safety (J, K, L), a pattern or widespread scope causing actual harm to resident health or safety (H, I), or widespread scope with potential for actual harm to resident health or safety (F) (see shaded areas below).¹⁰²

Severity	Scope		
	Isolated	Pattern	Widespread
Immediate Jeopardy	J	K	L
Actual Harm	G	H	I
Potential for Actual Harm	D	E	F
Minimal Harm	A	B	C

‡ A quality of care deficiency was defined as an F-tag in the following categories: resident behavior/facility practices: (0221, 0222, 0223, 0224, 0225, 0226), quality of life (0240, 0241, 0242, 0243, 0244, 0245, 0246, 0247, 0248, 0249, 0250, 0251, 0252, 0253, 0254, 0255, 0256, 0257, 0258), or quality of care (0309, 0310, 0311, 0312, 0313, 0314, 0315, 0316, 0317, 0318, 0319, 0320, 0321, 0322, 0323, 0324, 0325, 0326, 0327, 0328, 0329, 0330, 0331, 0332, 0333, 0334).¹⁰²

§ A pharmacy-related deficiency was defined as an F-tag in the pharmacy services category ('0425', '0426', '0427', '0428', '0429', '0430', '0431', '0432') or a subset of F-tags in the quality of care category ('0329', '0330', '0331', '0332', '0333').

**Some resident characteristics had two measures in the LTCFocus data: one based on the number of NH admissions in a year and one based on the NH population on a given day during the year (first Thursday in April) (prevalence). For these variables, the prevalence measure was used when available; the admissions measure was used only where the prevalence measure was missing.

REFERENCES

1. Roth MT, Weinberger M, Campbell WH. Measuring the quality of medication use in older adults. *Journal of the American Geriatrics Society*. Jun 2009;57(6):1096-1102.
2. Hanlon JT, Schmader KE, Ruby CM, Weinberger M. Suboptimal prescribing in older inpatients and outpatients. *Journal of the American Geriatrics Society*. Feb 2001;49(2):200-209.
3. Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. An update. *Archives of internal medicine*. Jul 28 1997;157(14):1531-1536.
4. Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. *Archives of internal medicine*. Dec 8-22 2003;163(22):2716-2724.
5. Shrank WH, Polinski JM, Avorn J. Quality indicators for medication use in vulnerable elders. *Journal of the American Geriatrics Society*. Oct 2007;55 Suppl 2:S373-382.
6. Hanlon JT, Schmader KE, Samsa GP, et al. A method for assessing drug therapy appropriateness. *Journal of clinical epidemiology*. Oct 1992;45(10):1045-1051.
7. Centers for Medicare & Medicaid Services (CMS). State Operations Manual Appendix PP - Guidance to Surveyor for Long Term Care Facilities 2011.
8. Fuster V, Ryden LE, Cannom DS, et al. 2011 ACCF/AHA/HRS focused updates incorporated into the ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation*. Mar 15 2011;123(10):e269-367.
9. Fuster V, Ryden LE, Cannom DS, et al. ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Circulation*. Aug 15 2006;114(7):e257-354.
10. Division of Health Care Policy and Research, School of Medicine, University of Colorado Denver. The Care Transitions Program. 2007; <http://caretransitions.org/definitions.asp>. Accessed February 11, 2014.

11. Moore C, Wisnivesky J, Williams S, McGinn T. Medical errors related to discontinuity of care from an inpatient to an outpatient setting. *Journal of general internal medicine*. Aug 2003;18(8):646-651.
12. Cornish PL, Knowles SR, Marchesano R, et al. Unintended medication discrepancies at the time of hospital admission. *Archives of internal medicine*. Feb 28 2005;165(4):424-429.
13. Gerety MB, Cornell JE, Plichta DT, Eimer M. Adverse events related to drugs and drug withdrawal in nursing home residents. *Journal of the American Geriatrics Society*. Dec 1993;41(12):1326-1332.
14. Bell CM, Brener SS, Gunraj N, et al. Association of ICU or hospital admission with unintentional discontinuation of medications for chronic diseases. *JAMA : the journal of the American Medical Association*. Aug 24 2011;306(8):840-847.
15. Bell CM, Rahimi-Darabad P, Orner AI. Discontinuity of chronic medications in patients discharged from the intensive care unit. *Journal of general internal medicine*. Sep 2006;21(9):937-941.
16. Mansur N, Weiss A, Hoffman A, Gruenewald T, Beloosesky Y. Continuity and adherence to long-term drug treatment by geriatric patients after hospital discharge: a prospective cohort study. *Drugs & aging*. 2008;25(10):861-870.
17. Mansur N, Weiss A, Beloosesky Y. Relationship of in-hospital medication modifications of elderly patients to postdischarge medications, adherence, and mortality. *The Annals of pharmacotherapy*. Jun 2008;42(6):783-789.
18. Bell CM, Bajcar J, Bierman AS, Li P, Mamdani MM, Urbach DR. Potentially unintended discontinuation of long-term medication use after elective surgical procedures. *Archives of internal medicine*. Dec 11-25 2006;166(22):2525-2531.
19. Beers MH, Dang J, Hasegawa J, Tamai IY. Influence of hospitalization on drug therapy in the elderly. *Journal of the American Geriatrics Society*. Aug 1989;37(8):679-683.
20. Stuffken R, Heerdink ER, de Koning FH, Souverein PC, Egberts AC. Association between hospitalization and discontinuity of medication therapy used in the community setting in the Netherlands. *The Annals of pharmacotherapy*. Jul 2008;42(7):933-939.
21. Kripalani S, LeFevre F, Phillips CO, Williams MV, Basaviah P, Baker DW. Deficits in communication and information transfer between hospital-based and primary care physicians: implications for patient safety and continuity of care. *JAMA : the journal of the American Medical Association*. Feb 28 2007;297(8):831-841.
22. The Lewin Group. CMS Review of Current Standards of Practice for Long-Term Care Pharmacy Services: Long-Term Care Pharmacy Primer. 2004;

<http://cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/downloads/lewingroup.pdf>.

23. Boockvar K, Fishman E, Kyriacou CK, Monias A, Gavi S, Cortes T. Adverse events due to discontinuations in drug use and dose changes in patients transferred between acute and long-term care facilities. *Archives of internal medicine*. Mar 8 2004;164(5):545-550.
24. Fried TR, Mor V. Frailty and hospitalization of long-term stay nursing home residents. *Journal of the American Geriatrics Society*. Mar 1997;45(3):265-269.
25. Graves T, Hanlon JT, Schmader KE, et al. Adverse events after discontinuing medications in elderly outpatients. *Archives of internal medicine*. Oct 27 1997;157(19):2205-2210.
26. 5 Million Lives Campaign. Getting Started Kit: Prevent Adverse Drug Events (Medication Reconciliation) How-to Guide. 2008; <http://www.ih.org/resources/Pages/Tools/HowtoGuidePreventAdverseDrugEvents.aspx>.
27. Eldridge N, Revere A. JCAHO National Patient Safety Goals for 2005. *Topics in Patient Safety, VA National Center for Patient Safety*. 2005;5(1).
28. The Joint Commission. Long Term Care (Medicare/Medicaid): 2014 National Patient Safety Goals 2014.
29. The Joint Commission. Revised NPSG on medication reconciliation is approved. *Joint Commission Online*. 2010.
30. Kripalani S, Jackson AT, Schnipper JL, Coleman EA. Promoting effective transitions of care at hospital discharge: a review of key issues for hospitalists. *Journal of hospital medicine : an official publication of the Society of Hospital Medicine*. Sep 2007;2(5):314-323.
31. Jones AL, Dwyer LL, Bercovitz AR, Strahan GW. The National Nursing Home Survey: 2004 overview. *Vital Health Stat 13*. Jun 2009(167):1-155.
32. Gabrel CS. Characteristics of elderly nursing home current residents and discharges: data from the 1997 National Nursing Home Survey. *Advance data*. Apr 25 2000(312):1-15.
33. Kasper J, O'Malley M. Changes in Characteristics, Needs, and Payment for Care of Elderly Nursing Home Residents: 1999 to 2004. *Kaiser Commission on Medicaid and the Uninsured, The Henry J. Kaiser Family Foundation*. 2007.
34. Briesacher BA, Soumerai SB, Field TS, Fouayzi H, Gurwitz JH. Nursing home residents and enrollment in Medicare Part D. *Journal of the American Geriatrics Society*. Oct 2009;57(10):1902-1907.

35. Simoni-Wastila L, Stuart BC, Shaffer T. Over-the-counter drug use by medicare beneficiaries in nursing homes: implications for practice and policy. *Journal of the American Geriatrics Society*. Oct 2006;54(10):1543-1549.
36. Gurwitz JH, Field TS, Judge J, et al. The incidence of adverse drug events in two large academic long-term care facilities. *The American journal of medicine*. Mar 2005;118(3):251-258.
37. Gurwitz JH, Field TS, Avorn J, et al. Incidence and preventability of adverse drug events in nursing homes. *The American journal of medicine*. Aug 1 2000;109(2):87-94.
38. Field TS, Gurwitz JH, Avorn J, et al. Risk factors for adverse drug events among nursing home residents. *Archives of internal medicine*. Jul 9 2001;161(13):1629-1634.
39. Sato M, Shaffer T, Arbaje AI, Zuckerman IH. Residential and health care transition patterns among older medicare beneficiaries over time. *The Gerontologist*. Apr 2011;51(2):170-178.
40. Intrator O, Zinn J, Mor V. Nursing home characteristics and potentially preventable hospitalizations of long-stay residents. *Journal of the American Geriatrics Society*. Oct 2004;52(10):1730-1736.
41. Becker M, Boaz T, Andel R, DeMuth A. Predictors of avoidable hospitalizations among assisted living residents. *Journal of the American Medical Directors Association*. May 2012;13(4):355-359.
42. Grabowski DC, Stewart KA, Broderick SM, Coots LA. Predictors of nursing home hospitalization: a review of the literature. *Medical care research and review : MCRR*. Feb 2008;65(1):3-39.
43. Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. *JAMA : the journal of the American Medical Association*. May 9 2001;285(18):2370-2375.
44. Miyasaka Y, Barnes ME, Gersh BJ, et al. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. *Circulation*. Jul 11 2006;114(2):119-125.
45. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics--2012 update: a report from the American Heart Association. *Circulation*. Jan 3 2012;125(1):e2-e220.
46. Lakshminarayan K, Solid CA, Collins AJ, Anderson DC, Herzog CA. Atrial fibrillation and stroke in the general medicare population: a 10-year perspective

- (1992 to 2002). *Stroke; a journal of cerebral circulation*. Aug 2006;37(8):1969-1974.
47. Gurwitz JH, Monette J, Rochon PA, Eckler MA, Avorn J. Atrial fibrillation and stroke prevention with warfarin in the long-term care setting. *Archives of internal medicine*. May 12 1997;157(9):978-984.
 48. Abdel-Latif AK, Peng X, Messinger-Rapport BJ. Predictors of anticoagulation prescription in nursing home residents with atrial fibrillation. *Journal of the American Medical Directors Association*. Mar-Apr 2005;6(2):128-131.
 49. McCormick D, Gurwitz JH, Goldberg RJ, et al. Prevalence and quality of warfarin use for patients with atrial fibrillation in the long-term care setting. *Archives of internal medicine*. Nov 12 2001;161(20):2458-2463.
 50. Aronow WS, Ahn C, Gutstein H. Prevalence and incidence of cardiovascular disease in 1160 older men and 2464 older women in a long-term health care facility. *The journals of gerontology. Series A, Biological sciences and medical sciences*. Jan 2002;57(1):M45-46.
 51. Prystowsky EN, Camm J, Lip GY, et al. The impact of new and emerging clinical data on treatment strategies for atrial fibrillation. *Journal of cardiovascular electrophysiology*. Aug 1 2010;21(8):946-958.
 52. Singer DE, Albers GW, Dalen JE, et al. Antithrombotic therapy in atrial fibrillation: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest*. Jun 2008;133(6 Suppl):546S-592S.
 53. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke; a journal of cerebral circulation*. Aug 1991;22(8):983-988.
 54. Hart RG, Pearce LA, Rothbart RM, McAnulty JH, Asinger RW, Halperin JL. Stroke with intermittent atrial fibrillation: incidence and predictors during aspirin therapy. Stroke Prevention in Atrial Fibrillation Investigators. *Journal of the American College of Cardiology*. Jan 2000;35(1):183-187.
 55. Lip GY, Edwards SJ. Stroke prevention with aspirin, warfarin and ximelagatran in patients with non-valvular atrial fibrillation: a systematic review and meta-analysis. *Thrombosis research*. 2006;118(3):321-333.
 56. Stanley JM. Pharmacological treatment of persistent atrial fibrillation in the older adult: evidence-based practice. *Journal of the American Academy of Nurse Practitioners*. Mar 2011;23(3):120-126.
 57. Secondary prevention in non-rheumatic atrial fibrillation after transient ischaemic attack or minor stroke. EAFT (European Atrial Fibrillation Trial) Study Group. *Lancet*. Nov 20 1993;342(8882):1255-1262.

58. Ezekowitz MD, Bridgers SL, James KE, et al. Warfarin in the prevention of stroke associated with nonrheumatic atrial fibrillation. Veterans Affairs Stroke Prevention in Nonrheumatic Atrial Fibrillation Investigators. *The New England journal of medicine*. Nov 12 1992;327(20):1406-1412.
59. Connolly SJ, Laupacis A, Gent M, Roberts RS, Cairns JA, Joyner C. Canadian Atrial Fibrillation Anticoagulation (CAFA) Study. *Journal of the American College of Cardiology*. Aug 1991;18(2):349-355.
60. The effect of low-dose warfarin on the risk of stroke in patients with nonrheumatic atrial fibrillation. The Boston Area Anticoagulation Trial for Atrial Fibrillation Investigators. *The New England journal of medicine*. Nov 29 1990;323(22):1505-1511.
61. Stroke Prevention in Atrial Fibrillation Study. Final results. *Circulation*. Aug 1991;84(2):527-539.
62. Petersen P, Boysen G, Godtfredsen J, Andersen ED, Andersen B. Placebo-controlled, randomised trial of warfarin and aspirin for prevention of thromboembolic complications in chronic atrial fibrillation. The Copenhagen AFASAK study. *Lancet*. Jan 28 1989;1(8631):175-179.
63. Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation. Analysis of pooled data from five randomized controlled trials. *Archives of internal medicine*. Jul 11 1994;154(13):1449-1457.
64. The efficacy of aspirin in patients with atrial fibrillation. Analysis of pooled data from 3 randomized trials. The Atrial Fibrillation Investigators. *Archives of internal medicine*. Jun 9 1997;157(11):1237-1240.
65. Warfarin versus aspirin for prevention of thromboembolism in atrial fibrillation: Stroke Prevention in Atrial Fibrillation II Study. *Lancet*. Mar 19 1994;343(8899):687-691.
66. Bleeding during antithrombotic therapy in patients with atrial fibrillation. The Stroke Prevention in Atrial Fibrillation Investigators. *Archives of internal medicine*. Feb 26 1996;156(4):409-416.
67. Gullov AL, Koefoed BG, Petersen P, et al. Fixed minidose warfarin and aspirin alone and in combination vs adjusted-dose warfarin for stroke prevention in atrial fibrillation: Second Copenhagen Atrial Fibrillation, Aspirin, and Anticoagulation Study. *Archives of internal medicine*. Jul 27 1998;158(14):1513-1521.
68. Hellemons BS, Langenberg M, Lodder J, et al. Primary prevention of arterial thromboembolism in non-rheumatic atrial fibrillation in primary care: randomised controlled trial comparing two intensities of coumarin with aspirin. *BMJ (Clinical research ed.)*. Oct 9 1999;319(7215):958-964.

69. van Walraven C, Hart RG, Singer DE, et al. Oral anticoagulants vs aspirin in nonvalvular atrial fibrillation: an individual patient meta-analysis. *JAMA : the journal of the American Medical Association*. Nov 20 2002;288(19):2441-2448.
70. Prescribing information for Pradaxa (R) (dabigatran etexilate mesylate) (product label): Boehringer Ingelheim Pharmaceuticals, Inc.; 2010.
71. Prescribing information for Xarelto (R) (rivaroxaban) (product label): Janssen Pharmaceuticals, Inc.; 2011.
72. Prescribing information for Eliquis (R) (apixaban) (product label): Bristol-Myers Squibb Company; 2012.
73. Wann LS, Curtis AB, Ellenbogen KA, et al. 2011 ACCF/AHA/HRS focused update on the management of patients with atrial fibrillation (update on Dabigatran): a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation*. Mar 15 2011;123(10):1144-1150.
74. Kim D, Barna R, Bridgeman MB, Brunetti L. Novel Oral Anticoagulants for Stroke Prevention in the Geriatric Population. *American journal of cardiovascular drugs : drugs, devices, and other interventions*. Nov 14 2013.
75. Lane DA, Lip GY. Barriers to anticoagulation in patients with atrial fibrillation: changing physician-related factors. *Stroke; a journal of cerebral circulation*. Jan 2008;39(1):7-9.
76. Mant J, Hobbs FD, Fletcher K, et al. Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial. *Lancet*. Aug 11 2007;370(9586):493-503.
77. Osborne CA, Hooper R, Swift CG, Jackson SH. Explicit, evidence-based criteria to assess the quality of prescribing to elderly nursing home residents. *Age and ageing*. Jan 2003;32(1):102-108.
78. Lau E, Bungard TJ, Tsuyuki RT. Stroke prophylaxis in institutionalized elderly patients with atrial fibrillation. *Journal of the American Geriatrics Society*. Mar 2004;52(3):428-433.
79. Patel AA, Reardon G, Nelson WW, Philpot T, Neidecker MV. Persistence of warfarin therapy for residents in long-term care who have atrial fibrillation. *Clinical therapeutics*. Nov 2013;35(11):1794-1804.
80. Budnitz DS, Lovegrove MC, Shehab N, Richards CL. Emergency hospitalizations for adverse drug events in older Americans. *The New England journal of medicine*. Nov 24 2011;365(21):2002-2012.

81. Gurwitz JH, Field TS, Radford MJ, et al. The safety of warfarin therapy in the nursing home setting. *The American journal of medicine*. Jun 2007;120(6):539-544.
82. Ahmed A, Thornton P, Perry GJ, Allman RM, DeLong JF. Impact of atrial fibrillation on mortality and readmission in older adults hospitalized with heart failure. *European journal of heart failure*. Jun 2004;6(4):421-426.
83. Tabereaux PB, Brass LM, Concato J, Bravata DM. Hospital admissions for stroke among the very old in the USA. *Neuroepidemiology*. 2008;31(2):93-99.
84. Boockvar K, Lachs M. Hospitalization risk following admission to an academic nursing home. *Journal of the American Medical Directors Association*. May-Jun 2002;3(3):130-135.
85. Deitelzweig S. Care Transitions in Anticoagulation Management for Patients With Atrial Fibrillation: An Emphasis on Safety. *The Ochsner journal*. Fall 2013;13(3):419-427.
86. Gleason KM, McDaniel MR, Feinglass J, et al. Results of the Medications at Transitions and Clinical Handoffs (MATCH) study: an analysis of medication reconciliation errors and risk factors at hospital admission. *Journal of general internal medicine*. May 2010;25(5):441-447.
87. Boulanger L, Hauch O, Friedman M, et al. Warfarin exposure and the risk of thromboembolic and major bleeding events among medicaid patients with atrial fibrillation. *The Annals of pharmacotherapy*. Jun 2006;40(6):1024-1029.
88. Centers for Medicare & Medicaid Services (CMS). Chronic Conditions Data Warehouse. 2014; <https://www.ccwdata.org>.
89. Crystal S, Gaboda D, Lucas J, Gerhard T, Chakravarty S. Assessing medication exposures and outcomes in the frail elderly: assessing research challenges in nursing home pharmacotherapy. *Medical care*. Jun 2010;48(6 Suppl):S23-31.
90. Centers for Medicare & Medicaid Services (CMS). Five-star quality rating system: NHC provider and deficiency files 2006-2011. 2013; <https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/CertificationandCompliance/Downloads/NHCProviderAndDeficiencyFiles.zip>.
91. Brown University, Center for Gerontology and Healthcare Research. LTC Focus. 2013; <http://lctfocus.org/>.
92. Gage BF, Waterman AD, Shannon W, Boehler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *JAMA : the journal of the American Medical Association*. Jun 13 2001;285(22):2864-2870.

93. Oldgren J, Alings M, Darius H, et al. Risks for stroke, bleeding, and death in patients with atrial fibrillation receiving dabigatran or warfarin in relation to the CHADS2 score: a subgroup analysis of the RE-LY trial. *Annals of internal medicine*. Nov 15 2011;155(10):660-667, W204.
94. Gage BF, Yan Y, Milligan PE, et al. Clinical classification schemes for predicting hemorrhage: results from the National Registry of Atrial Fibrillation (NRAF). *American heart journal*. Mar 2006;151(3):713-719.
95. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *Journal of clinical epidemiology*. Jun 1992;45(6):613-619.
96. Romano PS, Roos LL, Jollis JG. Adapting a clinical comorbidity index for use with ICD-9-CM administrative data: differing perspectives. *Journal of clinical epidemiology*. Oct 1993;46(10):1075-1079; discussion 1081-1090.
97. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Medical care*. Nov 2005;43(11):1130-1139.
98. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *Journal of chronic diseases*. 1987;40(5):373-383.
99. Levinson DR, Inspector General. Memorandum Report: "Trends in Nursing Home Deficiencies and Complaints," OEI-02-08-00140. In: Office of Inspector General, Department of Health & Human Services, ed2008.
100. Ghaswalla PK, Harpe SE, Slattum PW. Warfarin use in nursing home residents: results from the 2004 national nursing home survey. *The American journal of geriatric pharmacotherapy*. Feb 2012;10(1):25-36 e22.
101. Kasper J. Who Stays and Who Goes Home: Using National Data on Nursing Home Discharges and Long-Stay Residents to Draw Implications for Nursing Home Transition Programs. *Kaiser Commission on Medicaid and the Uninsured, The Henry J. Kaiser Family Foundation*. 2005.
102. Gassoumis ZD, Fike KT, Rahman AN, Enguidanos SM, Wilber KH. Who transitions to the community from nursing homes? Comparing patterns and predictors for short-stay and long-stay residents. *Home Health Care Serv Q*. 2013;32(2):75-91.
103. Devereaux PJ, Anderson DR, Gardner MJ, et al. Differences between perspectives of physicians and patients on anticoagulation in patients with atrial fibrillation: observational study. *BMJ (Clinical research ed.)*. Nov 24 2001;323(7323):1218-1222.

104. Aspinall SL, Zhao X, Handler SM, et al. The quality of warfarin prescribing and monitoring in Veterans Affairs nursing homes. *Journal of the American Geriatrics Society*. Aug 2010;58(8):1475-1480.
105. Estes NA, 3rd, Halperin JL, Calkins H, et al. ACC/AHA/Physician Consortium 2008 clinical performance measures for adults with nonvalvular atrial fibrillation or atrial flutter: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures and the Physician Consortium for Performance Improvement (Writing Committee to Develop Clinical Performance Measures for Atrial Fibrillation): developed in collaboration with the Heart Rhythm Society. *Circulation*. Feb 26 2008;117(8):1101-1120.
106. Reardon G, Nelson WW, Patel AA, Philpot T, Neidecker M. Warfarin for prevention of thrombosis among long-term care residents with atrial fibrillation: evidence of continuing low use despite consideration of stroke and bleeding risk. *Drugs & aging*. Jun 2013;30(6):417-428.
107. Centers for Medicare & Medicaid Services (CMS). Quality Measures. 2013; http://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/QualityMeasures/index.html?redirect=/qualitymeasures/03_electronicSpecifications.asp 2013.
108. Centers for Medicare & Medicaid Services (CMS). Medicare.gov Nursing Home Compare. 2014; <http://www.medicare.gov/NursingHomeCompare/About/Quality-Measures-Info.html>, 2014.
109. Zimetbaum P, Ho KK, Olshansky B, et al. Variation in the utilization of antiarrhythmic drugs in patients with new-onset atrial fibrillation. *The American journal of cardiology*. Jan 1 2003;91(1):81-83.
110. Piccini JP, Mi X, DeWald TA, Go AS, Hernandez AF, Curtis LH. Pharmacotherapy in Medicare beneficiaries with atrial fibrillation. *Heart rhythm : the official journal of the Heart Rhythm Society*. Sep 2012;9(9):1403-1408.
111. Zimetbaum P. Antiarrhythmic drug therapy for atrial fibrillation. *Circulation*. Jan 17 2012;125(2):381-389.
112. de Denus S, Sanoski CA, Carlsson J, Opolski G, Spinler SA. Rate vs rhythm control in patients with atrial fibrillation: a meta-analysis. *Archives of internal medicine*. Feb 14 2005;165(3):258-262.
113. Raji MA, Lowery M, Lin YL, Kuo YF, Baillargeon J, Goodwin JS. National utilization patterns of warfarin use in older patients with atrial fibrillation: a population-based study of Medicare Part D beneficiaries. *The Annals of pharmacotherapy*. Jan 2013;47(1):35-42.
114. Samsa GP, Matchar DB, Goldstein LB, et al. Quality of anticoagulation management among patients with atrial fibrillation: results of a review of medical

records from 2 communities. *Archives of internal medicine*. Apr 10 2000;160(7):967-973.

115. Sandhu RK, Bakal JA, Ezekowitz JA, McAlister FA. Risk stratification schemes, anticoagulation use and outcomes: the risk--treatment paradox in patients with newly diagnosed non-valvular atrial fibrillation. *Heart (British Cardiac Society)*. Dec 2011;97(24):2046-2050.
116. Zimetbaum PJ, Thosani A, Yu HT, et al. Are atrial fibrillation patients receiving warfarin in accordance with stroke risk? *The American journal of medicine*. May 2010;123(5):446-453.
117. Reynolds MR, Shah J, Essebag V, et al. Patterns and predictors of warfarin use in patients with new-onset atrial fibrillation from the FRACTAL Registry. *The American journal of cardiology*. Feb 15 2006;97(4):538-543.
118. Naccarelli GV, Johnston SS, Dalal M, Lin J, Patel PP. Rates and implications for hospitalization of patients ≥ 65 years of age with atrial fibrillation/flutter. *The American journal of cardiology*. Feb 15 2012;109(4):543-549.
119. Kim MH, Lin J, Hussein M, Battleman D. Incidence and temporal pattern of hospital readmissions for patients with atrial fibrillation. *Current medical research and opinion*. May 2009;25(5):1215-1220.
120. Suhr D. The basics of structural equation modeling. 2006; <http://www.lexjansen.com/wuss/2006/tutorials/tut-suhr.pdf>.
121. Kline RB. *Principles and Practice of Structural Equation Modeling*. Third ed. New York: The Guilford Press; 2011.
122. Kupek E. Beyond logistic regression: structural equations modelling for binary variables and its application to investigating unobserved confounders. *BMC Med Res Methodol*. 2006;6:13.
123. Hancock GR. Introduction to Structural Equation Modeling (short course notes). College Park, MD: University of Maryland College Park; 2014.
124. Allison P. Introduction to Structural Equation Modeling (short course notes). Chicago, IL: Statistical Horizons LLC; 2013.
125. Hancock GR, Mueller RO. *Structural Equation Modeling: A Second Course*. 2nd edition ed. Charlotte, NC: Information Age Publishing Inc.; 2013.
126. Byrne BM. *Structural Equation Modeling with Mplus*. New York: Taylor & Francis Group; 2012.
127. Centers for Medicare & Medicaid Services (CMS). Medicare Coverage of Skilled Nursing Facility Care. *CMS Publication No. 10153* 2007.

128. Birman-Deych E, Waterman AD, Yan Y, Nilasena DS, Radford MJ, Gage BF. Accuracy of ICD-9-CM codes for identifying cardiovascular and stroke risk factors. *Medical care*. May 2005;43(5):480-485.
129. Boccuzzi SJ, Martin J, Stephenson J, et al. Retrospective study of total healthcare costs associated with chronic nonvalvular atrial fibrillation and the occurrence of a first transient ischemic attack, stroke or major bleed. *Current medical research and opinion*. Dec 2009;25(12):2853-2864.
130. Casciano JP, Dotiwala ZJ, Martin BC, Kwong WJ. The costs of warfarin underuse and nonadherence in patients with atrial fibrillation: a commercial insurer perspective. *Journal of managed care pharmacy : JMCP*. May 2013;19(4):302-316.
131. Mercaldi CJ, Ciarametaro M, Hahn B, et al. Cost efficiency of anticoagulation with warfarin to prevent stroke in medicare beneficiaries with nonvalvular atrial fibrillation. *Stroke; a journal of cerebral circulation*. Jan 2011;42(1):112-118.