Spatiotemporal Patterns and Burden of Myocardial Infarction in Florida

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ABSTRACT

Knowledge of spatiotemporal disparities in myocardial infarction (MI) risk and the determinants of those disparities is critical for guiding health planning and resource allocation. Therefore, the aims of this study were to: (i) investigate the spatial distribution and clusters of MI hospitalization (MIHosp) and MI mortality (MIMort) risks in Florida over time to identify communities with consistently high MI burdens, (ii) assess temporal trends in geographic disparities in MIHosp and MIMort risks, and (iii) identify predictors of MIHosp risks.

Retrospective MIHosp and MIMort data for Florida for 2005-2014 and 2000-2014 periods, respectively, were used. Kulldorff's circular and Tango's flexible spatial scan statistics were used to identify spatial clusters, and counties with persistently high or low MIHosp and MIMort risks were identified. Global and local negative binomial models were used to identify predictors of MIHosp risks.

MIHosp and MIMort risks declined by 15%-20% and 48% respectively, but there were substantial disparities in space and over time. Persistent clustering of high MIHosp risks occurred in the Big Bend area, South Central, and Southeast Florida. Persistent clustering of low risks occurred in Southeast and Southwest Florida. Clustering of MIMort risks occurred in the same areas as MIHosp risks, but there was no clustering of high MIMort risks in South Central Florida. The risks declined overall in all clusters over the study period. However, they decreased more rapidly in high-risk clusters during the first four to eight years of study, leading to reduced disparities in the short term. Nevertheless, both MIHosp and MIMort risks for high-risk clusters lagged behind those for low-risk clusters by at least a decade. Significant predictors of MIHosp risks included race, marital status, education level, rural residence and lack of health insurance. The impacts of education level and lack of health insurance varied geographically, with the strongest associations in southern Florida.

In conclusion, MI interventions need to target high-risk clusters to reduce the MI burden and improve population health in Florida. Moreover, the interventions need to consider social contexts, allocating resources based on empirical evidence from global and local models to maximize their efficiency and effectiveness.

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CHAPTER 1
INTRODUCTION

1.1 Background and Justification

Cardiovascular disease (CVD) is the leading cause of morbidity and preventable premature deaths in the US, accounting for more hospital discharges than any other disease category each year, and one in every four fatalities in the country [1,2]. Acute myocardial infarction (MI), or heart attack, contributes significantly to this burden, with an estimated annual incidence of 550,000 new attacks and 200,000 recurrent attacks, 15% of which end in a fatality. An additional 160,000 silent MIs occur each year [3]. Additionally, MI is an economically burdensome disease, with annual direct and indirect costs associated with MI mortality and morbidity estimated at $177.1 billion [4]. Moreover, after three decades of steady decline [5], the countervailing trends in major MI risk factors such as obesity, hypertension, type 2 diabetes [6], and population aging [7,8] are expected to exacerbate the MI burden, which makes MI prevention a continuing priority [6,9].

Since MI is largely preventable, there are concerted efforts to reduce its health and economic impacts through a combination of improved prevention of modifiable risk factors, and treatment of established risk factors at the individual level. Recent studies of temporal trends of MI morbidity [10-20] and mortality [21,22] suggest that interventions targeted to individual-level risk factors may contribute to substantial reductions in the burden of MI and other CVD with similar risk factors as MI [10,23,24]. However, the MI burden remains a major public health challenge in states in the Southeastern US compared to other parts of the country [25,26]. Additionally, there are substantial and persistent spatiotemporal disparities in the distribution of CVD risk factors [26-31] and primary and secondary preventive strategies [32-37] that may lead to widening geographic disparities in cardiovascular health over time, despite overall reductions in the MI burden in all US regions [26,38]. In spite of this, only a few ecologic studies have comprehensively examined changes in geographic disparities in CVD events in the US over time simultaneously [39-46]. Moreover, these studies disregard cases with a secondary MI discharge diagnosis; thus, they may overstate rates of MI declines, thereby underestimating the full MI burden [47]. Thus, additional studies are needed to enhance our knowledge of the extent of geographic disparities, including hot spots of MI morbidity and mortality risks, and the temporal changes in those disparities. This may aid with identification of populations that may have persistently higher MI burdens, and inform planning, implementation, and evaluation of interventions designed to eliminate health disparities and improve the health of all groups, the two overarching goals of the Healthy People 2020 national public health agenda [4].

Individual-level, potentially-modifiable, biological risk factors, such as hypertension, high cholesterol levels, obesity, and diabetes mellitus and behavioral risk factors, such as diet, exercise, smoking, and alcohol intake [48], account for more than 90% of the population-attributable risk for MI [49]. Thus, intervention strategies for CVD prevention have traditionally focused primarily on these risk factors, often without regard for the social environment/contexts in which these risk factors developed [50]. While this prevention strategy focused on downstream MI determinants may have contributed to substantial reductions in the burden of MI and other CVD [10,23,24], the persistence of high MI burden and its risk factors in the Southeastern US [25,26], coupled with the

projected increase by 2030 [6,9] indicate the need for an understanding of the social and economic factors that promote the development of risk factors determining access to preventive and control strategies.

Overwhelming evidence in the literature indicates that the prevalence of population-level factors known as socioeconomic determinants of health (SDoH) can affect the types of exposures and/or access to healthcare, and hence the health of individuals and populations [51]. These include factors such as place of residence; demographic factors such as age, gender, and race; and socioeconomic factors such as marital status, education attainment level, income/poverty level, federal poverty level, home ownership, and unemployment and health insurance rates [2,15,18,44,51-66], among other factors. According to Bookse et al. [67], SDoH are responsible for shaping 40% of the health of a population [67], and they also influence the effectiveness of individually-targeted interventions, specifically as it applies to the initiation of behavior change and adherence [50,68]. Thus, SDoH are largely responsible for pervasive geographic disparities in CVD morbidity and mortality and related risk factors [26,69]. Accordingly, knowledge of, and intervening on, SDoH may hold the greatest prospects for reducing health inequalities and improving cardiovascular health of all populations at the lowest cost [51].

Relationships between health outcomes and SDoH are traditionally investigated using aspatial global models. These models implicitly assume constant effects of explanatory variables across an entire study area. As such, they estimate a single coefficient for each explanatory variable averaged over the entire study area. However, given the inequities in geographic distribution of factors influencing MI risks [26-30,32-37], associations between MI outcomes and SDoH factors would not be realistically reflected by global models. Rather, the influence of SDoH are more likely to vary by geographic location, with some factors being more important determinants at certain locations and less important at other locations [70]. Thus, neglecting the influence of geographic differences in impacts of SDoH factors can lead to inaccurate generalizations. On the other hand, identifying the most important MI determinants for different geographic areas may aid in the development of comprehensive, evidence-driven, location-specific, public health strategies, which is critical for efficient allocation of scarce resources geared towards decreasing the individual, societal, and economic burden of CVD.

1.2 Study Objectives

1.2.1 Overall Objective

The overall goal of this study was to obtain a better understanding of geographic and sociodemographic factors potentially responsible for persistently high MI burden in Florida, and to inform public health planning and the development of needs-based, place-specific strategies for reducing/eliminating health inequities and for improving population health.

1.2.2 Specific Objectives

The specific aims of the study were to:

i. Identify geographic patterns, including clusters, of MI hospitalization risks in Florida between 2000-2014 to identify populations with persistently high MI morbidity;
ii. Assess temporal changes in geographic disparities in MI hospitalization risks;
iii. Estimate the extent to which principal MI hospitalizations may underestimate the disease burden attributable to MI;
iv. Identify geographic patterns, including clusters of MI mortality risks in Florida between 2000-2014 to identify populations with persistently high MI mortality;
v. Assess temporal changes in geographic disparities in MI mortality risks; and
vi. Identify sociodemographic determinants of MI hospitalization risks and explore whether the strength of associations between MI hospitalizations its determinants vary with geographic location in Florida.

1.2.3 Organization

This dissertation comprises three separate but related essays, hence it is organized as a multipart, manuscript format to assist in maintaining consistent format for journal articles. The first is the introductory chapter, which provides an overview of the study, and it comprises background information and the objectives of the study. Chapters 2, 3, and 4 describe the methods and results of studies addressing the specific aims of the study. Chapter 5, the concluding chapter, summarizes major contributions of the dissertation and discusses future research directions.

CHAPTER 2
GEOGRAPHIC CLUSTERS, HEALTH DISPARITIES, AND BURDENS OF PRINCIPAL AND ANY MYOCARDIAL INFARCTION HOSPITALIZATIONS IN FLORIDA, 2005-2014

A version of this chapter “Disparities in Temporal and Geographic Patterns of Myocardial Infarction Hospitalization Risks in Florida, 2005-2014” has been published in Int. J. Environ. Res. Public Health 2019, 16(23), 4734; https://doi.org/10.3390/ijerph16234734

The material presented in this chapter differs substantially from the material submitted for publication. The article only discusses spatiotemporal disparities in hospitalizations with a principal MI discharge diagnosis, but this chapter includes hospitalizations with any (i.e., principal or secondary) MI discharge diagnoses. Moreover, this chapter incudes an estimation of the extent to which the burden of disease attributable to MI may be underestimated by excluding secondary MI cases.

The use of “we” in this chapter refers to co-authors Drs. Nicholas Nagle and Kristina Kintziger, Chris DuClos and myself. As the first author, I designed the study, processed and analyzed the data and wrote the manuscript. Dr. Kintziger was also involved in the design of the study. All authors read and critically revised the manuscript.

2.1 Abstract

Background: Knowledge of geographical disparities in myocardial infarction (MI) is critical for guiding health planning and resource allocation, regardless of whether MI is the primary or secondary cause for hospitalization. The objectives of this study were to (i) identify geographic disparities in hospitalization risks for MI with either principal or principal and secondary (any MI) discharge diagnosis in Florida and (ii) assess temporal changes in MI disparities between 2005 and 2014 (iii) estimate the extent to which principal MI hospitalizations may underestimate disease burden compared to any MI hospitalizations.
Methods: This study used retrospective data on MI principal and secondary hospitalizations that occurred among Florida residents between 2005 and 2014. We identified spatial clusters of MI hospitalization risks using Kulldorff’s circular and Tango’s flexible spatial scan statistics. Counties with persistently high- or low- hospitalization risks were identified.
Results: There was a 20% and 15% decline in hospitalizations with a principal and any MI discharge diagnoses, respectively, during the study period. However, we found persistent clustering of high risks in the Big Bend region, South Central, and Southeast Florida, and persistent clustering of low risks primarily in the south. Risks decreased by 7-21% and 4.6-32% in high-risk clusters of principal and any MI hospitalizations, respectively, and by 10-28% and 6.5-31.6% in principal and any MI low-risk clusters, respectively. Further, MI risks for the high-risk cluster in southeast Florida decreased throughout the study period, while those for the persistent high-risk cluster in the Big Bend area increased during the last four years of study. MI risks in high-risk clusters in the 2013-2014 period were on par with risks in low-risk clusters in the 2005-2006 period. Overall, risks in high-risk clusters lagged behind those of low-risk clusters by at least a decade. Hospitalizations with a principal discharge diagnoses of MI underestimated MI

burden in identified clusters by 13.46 cases/10,000 persons in 2005-2006 and by 10.56 cases/10,000 persons in the 2013-2014 periods.
Conclusion: MI hospitalization risks declined overall during the 10-year study period, but disparities persist geographically and over time. Interventions need to be targeted to counties within high-risk clusters to achieve broader reduction goals and improved health equity. Moreover, studies of MI disparities need to account for secondary MI cases to obtain true estimates of the magnitude of health disparities and MI burden, to achieve broader reduction goals and improved health equity.
Key Words: myocardial Infarction burden; hospitalization risks; geographic disparities; temporal patterns; Kulldorff and Tango's flexible spatial scan statistics

2.2 Introduction

Preventive efforts for myocardial infarction (MI) have resulted in substantial declines in the overall burden of MI hospitalizations among several population groups across the US [11,12,17-19,38,55]. For instance, MI hospitalization rates for individuals aged 35 years and older decreased by at least 20% for 19 out of 20 states in the Centers for Disease Control and Prevention (CDC) Tracking Network between 2000 and 2008, with Florida being the lone state where the rates increased overall. A more recent study found an overall decline in MI hospitalization rates among Florida adults aged 18 years and older from 2000-2013, but the study by Talbott et al. [19] suggests that not all populations have benefited equitably from preventive and control efforts. Moreover, MI remains a leading cause of hospital admissions in Florida, and the US in general, accounting for 42,835 and 608,800 and hospital discharges/stays in Florida and the US, respectively, in 2014 [71-73]. The burden is projected to get worse as major MI risk factors such as diabetes mellitus, obesity, and population aging [12,74,75] become increasingly prevalent in the future [76], ensuring that MI prevention will continue to be a public health priority.

Existing literature shows that the risks of cardiovascular diseases (CVD), including MI [39,40,42,77,78], and major CVD risk factors [26-31], tend to cluster in minority and rural populations in the Southeastern US [28,29,31]. The higher CVD and CVD risk factor burdens notwithstanding, primary and secondary preventive interventions [32,33,35-37,79-81] disproportionately benefit urban and socioeconomically-advantaged communities [32-37,79,82]. Moreover, in addition to being implemented in select places, preventive measures, such as public smoking bans, have not been implemented or adopted at the same time. These spatiotemporal disparities in the prevalence of factors influencing MI hospitalizations risks may lead to widening geographic disparities in cardiovascular health among sub-groups defined by geography and other characteristics, despite overall reductions in the incidence of hospitalized MI in all sub-groups [38]. For instance, Yeh et al. found a 37% increase in geographic disparities in the incidence of hospitalized MIs among Medicare fee-for-service enrollees in US Census Divisions between 2000-2008, despite overall reductions in MI incidence in all regions during the same period [38]. Thus, MI hospitalization risks may vary geographically in Florida and disparities may be widening over time.

Despite the potential for spatiotemporal disparities in MI hospitalization risks, only a few ecologic studies [38,42,43,83] have characterized the geographic and temporal disparities in MI hospitalizations simultaneously. Moreover, those studies excluded hospitalizations with a secondary discharge diagnoses of MI, yet some MIs occur subsequent to admission for other illnesses, rather than being the cause of hospitalization [6]. Further, elderly patients often present with several major comorbidities, complicating the selection of the single most likely underlying cause of hospitalization [6]. Additionally, non-clinical considerations, such as reimbursement, may influence which condition gets coded as principal diagnosis [47]. For these reasons, studies that fail to account for secondary MIs may underestimate the true burden of MI and overstate the success of preventive and control efforts in reducing the health disparities [47]. Secondary MIs were shown to present a substantial and increasing proportion of total MIs [47].

It is strategically advantageous to estimate the extent of morbidity attributable to MI, identify geographic disparities in MI hospitalizations, and investigate how the disparities change over time, regardless of whether MI is the principal or secondary cause of hospitalization. Identifying areas with consistently high MI burdens would enable targeting of intervention strategies to the most affected populations, leading to improved health of all groups and reduced health disparities, which are the overarching goals of the Healthy People 2020 national public health agenda [4]. Monitoring trends in MI disparities over time can provide key insights into the effectiveness of prevention efforts. Moreover, MI overlaps geographically with other cardiovascular diseases, such as stroke, and several of their risk factors, such as hypertension, diabetes mellitus, obesity, etc. [78,84,85]. Consequently, interventions targeting areas with high MI risks may also decrease the burdens of other chronic diseases contributing to the large and growing geographic disparities in life expectancy in Florida [86,87]. Therefore, our objectives were to: (a) identify geographic disparities in hospitalizations with principal and any MI discharge diagnoses in Florida, (b) monitor temporal trends in disparities in MI hospitalization risks from 2005 to 2014, and (c) assess the extent that exclusion of secondary MI cases may underestimate the disease burden attributable to MI.

2.3 Methods

2.3.1 Study Design and Population

This retrospective ecologic study used MI inpatient hospital admissions data for in Florida for the period between 1/1/2005 and 12/31/2014. The study population included all Florida residents with a primary or any (i.e., principal or secondary) discharge diagnosis of acute MI based on the International Classification of Diseases, Ninth Revision, Clinical Modification: ICD-9-CM diagnostic code 410.

2.3.2 Data Sources and Data Preparation

2.3.2.1 Hospital Discharge Data

We obtained individual-level MI hospitalization data collected by the Florida Agency for Health Care Administration (AHCA) from the Florida Department of Health (DOH). The AHCA data includes discharge claims from all Florida hospitals except Veterans Affairs, Indian Health Services, and prison or state-owned facilities; hence, it represents surveillance with 100% coverage among noninstitutionalized hospitals.

We extracted the following variables: ICD-9 codes 410 in the primary field, up to 30 secondary diagnoses to enable extraction of cases with a secondary MI diagnosis, admission date, discharge date, patient age, sex, race, and county of residence.

2.3.2.2 Population Data

We obtained annual county-level population estimates for sex and age categories matching hospitalization data (i.e., 0-34, 35-44, 45-54, 55-64 and ≥65 year-olds) from DOH [88] and used them as denominator data for calculating sex- and age-specific annual MI hospitalization risks. Although the 2000 US standard population is recommended for age-adjustment of age-dependent health events [89], the 2010 US standard population reflects the most recent actual age compositions of the US population, and it also falls within the time period of our included data. Moreover, since the risk of MI increases with age, using a younger population with a lower proportion of older ages (i.e., the 2000 US standard population) could yield lower age-adjusted risks. Therefore, we used the decennial data for 2010 US population from the American FactFinder website [90] for direct age adjustment, as it may provide us with more realistic and more current risk estimates [91], and compared this to the age-adjusted rates using the widely-accepted 2000 US standard population.

2.3.2.3 Cartographic Boundary Files

County-level base maps used for mapping were downloaded from the US Census Bureau website [92].

2.3.3 Descriptive Statistics

We used the county as the geographic unit of analysis. We aggregated the MI data for each county by sex and age (i.e., 0-34, 35-44, 45-54, 55-64 and 65 years and older) by 2-year increments. We then used these counts along with county population estimates and both the 2000 and 2010 US standard populations to calculate sex- and age standardized (per 10,000 population) MI hospitalization risks [89]. We also stratified state-level MI hospitalization data at the beginning (2005-2006) and end of study (2013-2014) by sex, race (non-Hispanic White, non-Hispanic Black, Other), and ethnicity (Hispanic, non-Hispanic) and age-standardized them to both the 2000 and the 2010 US standard

populations. All summary statistical analyses were performed in SAS version 9.4 (SAS Institute; Cary Inc, NC).

2.3.4 Identification of Geographic Clusters

Circular geographic clusters of high or low MI hospitalization risks were detected and identified during each of the 2-year time intervals using Kulldorff's circular spatial scan statistics (CSSS) in SaTScan software version 9.4.0 [93]. Model specifications were: (a) a discrete Poisson probability model; (b) adjustment for both age and sex as confounders; and (c) use of non-overlapping, circular, purely spatial windows. We used a maximum spatial window size of 13.4% of Florida's population. This was chosen to ensure that identified clusters were not unusually large and that the largest county (Miami-Dade) had a chance of being part of a cluster. Likelihood ratio test (LRT) was used to assess statistical significance of potential clusters whose p-values were generated using 999 Monte Carlo replications. We assessed statistical significance of potential clusters using a critical p-value of 0.05.

Irregularly-shaped (non-circular) spatial clusters were detected and identified using Tango's flexible spatial scan statistics (FSSS) in FleXScan software version 3.1.2 [94]. These clusters would not be detected by Kulldorff's CSSS. Model specifications were as follows: (a) age- and sex-adjusted counts; (b) a Poisson probability model; (c) restricted likelihood ratio test (RLRT) to ensure that counties with non-elevated risks were not absorbed into high-risk clusters [95]**;** (d) alpha of 0.2 [96]; and (e) maximum geographic cluster size of 34 counties (equivalent to approximately 50% of the number of counties in Florida).

2.3.5 Mapping of Hospitalization Risks and Clusters

All computed MI hospitalization risks and identified geographical clusters were mapped using ArcGIS Version 10.6.1 [97]. Jenk's optimization classification scheme was used to determine break-points for hospitalization risk maps. Only statistically significant ($p<0.05$) high-risk clusters with relative risks (RR) ≥1.2 (for rural areas) and ≥1.1 (for urban areas) were mapped based on findings by Prates et al. [98]. Similarly, only statistically significant ($p<0.05$) low-risk clusters with RR ≤ 0.8 (for rural areas) and ≤ 0.9 (for urban areas) were mapped.

2.3.6 Temporal Trends

Temporal trends in MI hospitalization risks were investigated using plots of the annual MI hospitalization risks vs. time (in years) for counties within persistent high- or low-risk clusters during the study period. We calculated percentage change in MI hospitalization risks between the time periods 2013-2014 and 2005-2006.

2.3.7 Changes in Geographic Health Disparities

To assess whether geographic disparities in MI hospitalization risks between persistent high- and low-risk clusters widened or narrowed over the study period, we calculated the risk difference (RD) between high-risk clusters and the low-risk cluster with the lowest MI hospitalization risks. We compared the RDs for the 2005-2006 and 2013-2014 study periods.

2.3.8 Comparison of Principal MI and Any MI Burdens

A paired-samples t-test was conducted to compare cluster MI risks for hospitalizations with principal vs. any MI discharge diagnoses, both at the beginning (2005-2006) and end study (2013-2014) periods. We did this to estimate the extent to which exclusion of cases with a secondary discharge diagnosis of MI would underestimate the disease burden attributable to MI.

2.4 Results

2.4.1 Descriptive Analyses of MI Hospitalizations

2.4.1.1 Principal MI Hospitalizations

There were 428,275 inpatient principal MI hospitalization cases in Florida between 2005 and 2014. State-wide, overall, annual, age- and sex-adjusted MI hospitalization risks as estimated using the 2010 US standard were 22.0 (2005-2006), 19.8 (2007-2008), 18.4 (2009-2010), 18.0 (2011-2012), and 17.7 (2013-2014) cases/10,000 population. Those estimated using the 2000 US standard population were 19.9 (2005-2006), 17.9 (2007-2008), 16.6 (2009-2010), 16.3 (2011-2012), and 15.8 (2013-2014) cases/10,000 population. Thus, MI hospitalization risks decreased overall by 20% during the 10-year study period.

Tables 2.1 and 2.2 show state-level MI hospitalization risks adjusted to the age distributions of the 2010 and 2000 US standard populations, respectively, by sex, age group, race, ethnicity, and rurality at the beginning and at the end of the study periods. The highest risks were observed for males, those aged 65 years or older, and non-Hispanic and rural residents both at the beginning (2005-2006) and at the end (2013-2014) of the study periods.

The risks adjusted to the age distributions of the 2010 standard population were higher by 0.9 cases/10,000 persons among White compared to Black residents during the 2005-2006 period, but they were higher by a similar magnitude among Blacks during the 2013-2014 period.

The risks among all groups but the “Other” race category were lower by between 11-24% during the 2013-2014 period compared to the 2005-2006 period. However, MI

Table 2.1. State-level principal myocardial infarction hospitalization risks adjusted to the 2010 US census population age distributions (2005–2006 and 2013–2014).

	% of Total Cases		Age-Adjusted Risks/10,000 persons (95% CI)		
	2005-2006	2013-2014	2005-2006	2013-2014	% Change
Total MI cases	92261	84172	22.0	17.7	20
Sex					
Male	60	61.7	29.7 (29.4, 29.9)	23.9 (23.7, 24.1)	-20
Female	40	38.3	15.7 (15.6, 15.9)	12.1 (12.0, 12.2)	-23
[1]Age (years)					
0–34	1	0.7	0.41 (0.38, 0.45)	0.35 (0.32, 0.38)	-15
35–44	5	3.7	8.1 (7.8, 8.3)	6.5 (6.2, 6.7)	-20
45–54	13	12.9	23.3 (22.9, 23.7)	19.8 (19.4, 20.1)	-15
55–64	19	21.8	43.2 (42.5, 43.8)	36.9 (36.4, 37.4)	-15
≥65	63	61.0	95.4 (94.7, 96.2)	71.8 (71.1, 72.3)	-25
[2]Race					
White	88	80.9	21.1 (22.0, 22.3)	16.5 (16.4, 16.6)	-26
Black	9	10.7	20.2 (19.7, 20.6)	17.4 (17.0, 17.8)	-14
All other races	2	7.2	21.7 (20.8, 22.6)	41.4 (403, 42.4)	+91
[3]Ethnicity					
Hispanic	12	15.3	19.5 (19.2, 19.9)	16.8 (16.5, 17.1)	-14
Non-Hispanic	87	82.2	22.4 (22.2, 22.6)	17.4 (17.3, 17.5)	-22
Rural/Urban					
Rural	6	6.8	24.7 (24.0, 25.4)	21.9 (21.3, 22.5)	-12
Urban	94	93.2	22.1 (21.9, 22.2)	17.4 (17.3, 17.5)	-21

[1]Age-specific risks; [2]Missing race: 2005-2006 = 1248 cases, 2013-2014 = 984 cases; [3]Missing ethnicity: 2005-2006 = 1248 cases, 2013-2014 = 2162 cases.

Table 2.2. State-level principal myocardial infarction hospitalization risks adjusted to the 2000 US census population age distributions (2005–2006 and 2013–2014).

	% of total cases		Age-adjusted Risks/10,000 persons (95% CI)		
	2005-2006	2013-2014	2005-2006	2013-2014	% Change
Total MI cases	92261	84172	20.0	16.0	20
Sex					
Male	60	61.7	26.9 (26.6, 27.1)	21.5 (21.3, 21.66)	-20
Female	40	38.3	14.4 (14.3, 14.6)	11.1 (10.9, 11.2)	-23
[1]Age (years)					
0–34	1	0.7	0.4 (0.4, 0. 5)	0.4 (0.3, 0.4)	-15
35–44	5	3.7	8.1 (7.8, 8.3)	6.5 (6.2, 6.7)	-20
45–54	13	12.9	23.3 (22.9, 23.7)	19.8 (19.4, 20.1)	-15
55–64	19	21.8	43.2 (42.5, 43.8)	36.9 (36.4, 37.4)	-15
≥65	63	61.0	95.4 (94.7, 96.2)	71.7 (71.1, 72.3)	-25
[2]Race					
White	88	80.9	20.1 (20.0, 20.3)	14.9 (14.8, 15.0)	-26
Black	9	10.7	18.3 (17.9, 18.8)	15.8 (15.5, 16.1)	-14
All other races	2	7.2	19.8 (19.0, 20.6)	37.6 (36.7, 38.6)	+90
[3]Ethnicity					
Hispanic	12	15.3	17.7 (17.4, 18.1)	15.2 (14.9, 15.4)	-14
Non-Hispanic	87	82.2	20.4 (20.3, 20.6)	15.8 (15.7, 15.9)	-23
Rural/Urban					
Rural	6	6.8	22.4 (21.8, 23.0)	19.8 (19.2, 20.3)	-12
Urban	94	93.2	20.1 (20.0, 20.2)	15.7 (15.6, 15.9)	-22

[1]Age-specific risks; [2]Missing race 2005-2006 = 1248 cases, 2013-2014 = 984 cases; [3]Missing ethnicity 2005-2006 = 1248 cases; 2013-2014 = 2162 cases.

risks adjusted to the 2000 standard population age distributions were lower than those adjusted to the 2010 US standard population by 1.0-3.8 cases/10,000 persons.

2.4.1.2 Any MI Hospitalizations

There were a total of 645,935 hospitalizations with any MI discharge diagnosis in Florida between 2005-2014. Of these, 217,660 cases had a secondary discharge diagnosis of MI. Thus, hospitalizations with a comorbid diagnosis of MI accounted for 34% of total MIs over the study period. The proportion of MIs with a secondary diagnosis increased from 30% in 2005-2006 to 34% in 2013-2014, which represents a 13% increase over the study period.

Table 2.3 shows the distribution of any MI hospitalization risks by sex, age, race, ethnicity, and rurality at the beginning and at the end of the study periods, adjusted to the 2010 US standard population. The patterns amongst the various demographic groups, as well as the changes in MI risks in between 2005-2006 and 2013-2014 periods are similar to the patterns obtained for principal MIs (Tables 2.1 and 2.2). However, any MI risks were higher than principal MIs by 0.29-48.9 cases/10,000 persons in 2005-2006 and by 0.25-45.5 cases/10,000 persons in 2013-2014.

The largest difference between any and principal MIs was observed in the 65 years and older age group. As a consequence, the percent change in MI risks between 2005-2006 and 2013-2014 were lower for any MIs compared to principal MIs (Tables 2.2 and 2.3).

The risks among all groups with the exception of the “Other” race category were lower by between 6-22% during the 2013-2014 period compared to the 2005-2006 period.

Similar to principal MIs, any MI risks were higher among White residents compared to Black residents in 2005-2006 but the opposite was true during the 2013-2014 period.

2.4.2 Spatial Patterns

2.4.2.1 Age- and Sex-adjusted MI Risks

2.4.2.1.1 Principal MI Hospitalizations

County-specific principal MI hospitalization risks adjusted to the age- and sex-distributions of either the 2000 or the 2010 US standard populations are shown in Figures 2.1 and 2.2, respectively. The highest risks occurred in predominantly rural counties in the Big Bend and South Central regions of Florida, while the lowest risks occurred in mostly urban counties in southern Florida. The risks declined by between 1-42% in most of the counties, but they increased by between 3-51% in 15 primarily rural counties scattered across the northern and middle parts of the state.

MI risks adjusted to the 2010 US population census age- and sex distributions ranged from 12.0-38.7 cases/10,000 population at the beginning of the study to 9.6-56.4 cases/10,000 population at the end of the study. Risks adjusted to the 2000 US census

Table 2.3. State-level any myocardial infarction hospitalization risks adjusted to the 2010 US census population age distributions (2005–2006 and 2013–2014).

	% of total cases		Age-adjusted MI Risks/10,000 persons (95% CI)		
	2005-2006	**2013-2014**	**2005-2006**	**2013-2014**	**% Change**
Total MI Cases	132152	127937	31.0	26.4	15
Sex					
Male	58	59.0	36.9 (36.68, 37.2)	30.9 (30.7, 31.1)	-16
Female	42	41.0	21.6 (21.41, 21.77)	17.8 (17.7, 18.0)	-18
[1]Age (years)					
0–34	1	0.75	0.7 (0.6, 0.7)	0.6 (0.5, 0.6)	-14
35–44	39	3.12	10.1 (9.8, 10.4)	8.3 (8.0, 8.6)	-18
45–54	11	10.86	29.1 (28.6, 29.5)	25.3 (24.9, 25.8)	-13
55–64	17	19.63	57.1 (56.3, 57.8)	50.5 (49.9, 51.2)	-12
≥65	67	65.65	144.4 (143.5, 145.4)	117.3 (116.5, 18.1)	-19
[2]Race					
White	88	81.0	28.5 (28.4, 28.7)	22.3 (22.2, 22.5)	-22
Black	9	11.0	27.5 (26.9, 28.0)	25.0 (24.6, 25.4)	-9
All other races	2	6.9	26.6 (25.7, 27.6)	55.8 (54.6, 56.9)	+109.8
[3]Ethnicity					
Hispanic	11	14.7	23.9 (23.5, 24.2)	22.4 (22.1, 22.7)	-6
Non-Hispanic	88	82.9	29.2 (29.1, 29.4)	23.8 (23.7, 24.0)	-19
Rural/Urban					
Rural	6	6.1	31.6 (30.9, 32.4)	29.6 (28.9, 30.2)	-6
Urban	95	93.9	28.6 (28.4, 28.7)	23.7 (23.5, 23.8)	-17

[1]Age-specific risks; [2]Missing race 2005-2006 = 1539 cases, 2013-2014 = 1374 cases; [3]Missing ethnicity 2005-2006 = 1539 cases; 2013-2014 = 30662162 cases.

age- and sex distributions ranged from 10.7-34.9 cases/10,000 population at the beginning of the study to 8.8-51.4 cases/10,000 population at the end of the study. Thus, MI risks standardized to the 2010 standard population were higher by between 0.8-5.0 cases/10,000 population than those standardized to the 2000 standard population. However, the spatial patterns of MI risks appeared to be similar for both standard populations (Figures 2.1 and 2.2). Thus, the 2010 US standard population was used in all subsequent adjustments.

2.4.2.1.2 Any MI Hospitalization Risks

County-specific, any MI hospitalization risks adjusted to the age- and sex-distributions of the 2010 US standard populations are shown in Figure 2.3. The risks ranged from 17.6-54.7 cases/10,000 population at the beginning of the study to 18.5-69.5 cases/10,000 population at the end of the study.

Similar to the spatial patterns observed for MI hospitalizations with a principal discharge diagnosis, the highest risks occurred in predominantly rural counties in the Big Bend and South Central regions of Florida, while the lowest risks occurred in mostly urban counties in southern Florida. These patterns persisted throughout the study period.

2.4.2.2 Kulldorff's Circular Spatial Scan Statistics (CSSS) Clusters

2.4.2.2.1 Principal MI Hospitalizations Clusters

The geographic location of Kulldorff's CSSS high- and low-risk MI hospitalization clusters, as well as the rural-urban designation of Florida's counties based on DOH Office of Rural Health definition of rural county (i.e., density of less than 100 persons per square mile) [99] are shown in Figure 2.4.

Similar to the visual patterns for age- and sex-adjusted risks (Figures 2.1 and 2.2), we identified three to four large persistent high-risk clusters in Southeast Florida and in predominantly rural counties in the Big Bend area, and two large persistent low-risk clusters in predominantly coastal urban counties designated as retirement designations in Southeast and Southwest Florida.

Over 85% of counties in low-risk clusters in southern Florida and 88% of counties in high-risk counties in 2005-2006 retained their cluster status in 2013-2014. Persistent high-risk clusters in Southeast Florida, the Big Bend area, and South Central Florida accounted for 13%, 11%, and 5% of the total population in the state (Table 2.4), respectively. Persistent low-risk clusters comprised 5-8% of the state's population (Table 2.5).

While some counties retained their status in either low- or high-risk clusters over the study period, a number of counties experienced distinct changes in their risk status by the 2013-2014 period. These changes were most evident in Northwest and Northeast Florida, where 93% of counties in low-risk clusters in the 2005-2006 period transitioned to no cluster status in the 2013-2014 period. Four South Florida counties transitioned from no cluster status in 2005-2006 to low-risk clusters in 2013-2014. Only two counties in South Central Florida transitioned from high-risk to no cluster and vice versa. One county

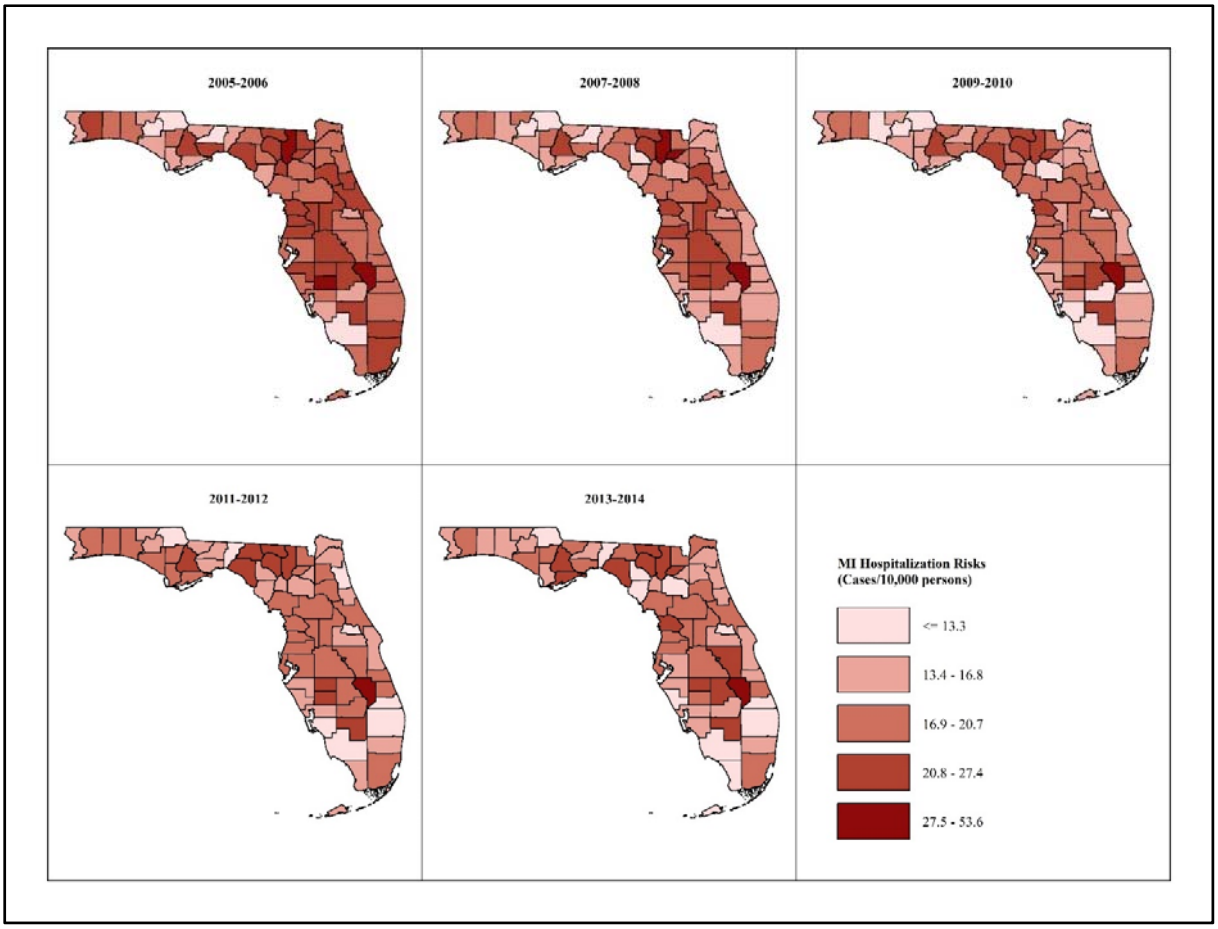


Figure 2.1. Spatial patterns of principal myocardial infarction hospitalization risks adjusted to the age and sex distributions of the 2000 US census population.

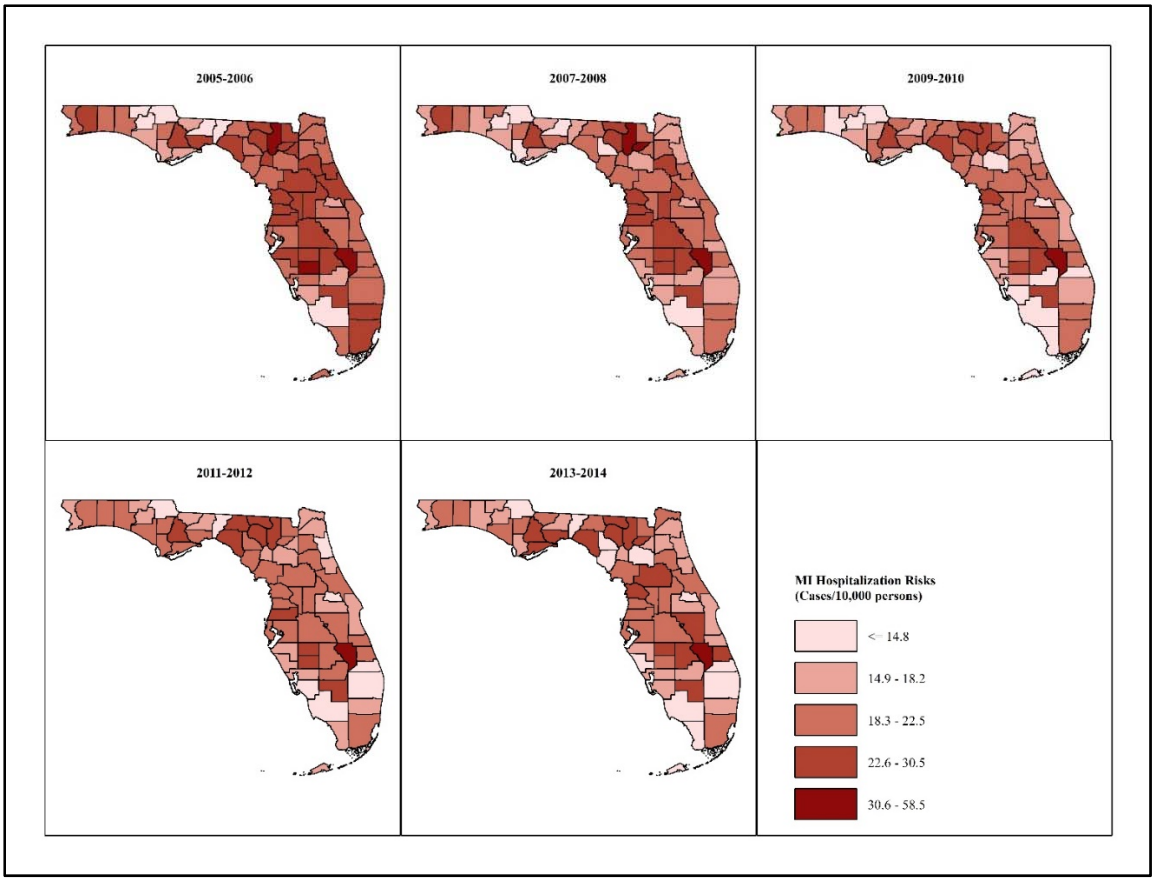


Figure 2.2. Spatial patterns of principal myocardial infarction hospitalization risks adjusted to the age and sex distributions of the 2010 US census population.

transitioned from high- to low-risk cluster, but no county transitioned from low to high-risk status. The RRs for high-risk clusters ranged from 1.1 to 3.3, and from 0.5 to 0.9 among low-risk clusters.

2.4.2.2.2 Any MI Hospitalization Clusters

Figure 2.5 shows the location of Kulldorff's CSSS high- and low-risk clusters for hospitalizations with any MI discharge diagnosis. The distribution of clusters generally mirrored the patterns for principal MI clusters (Figure 2.4), with persistent clustering of high risks occurring in the Big Bend, South Central, and Southeast regions of the state, and persistent clustering of low risks occurring in Southeast and Southwest Florida. The RRs for high-risk clusters ranged from 1.1 to 3.5, and from 0.7 to 0.9 among low-risk clusters. A few notable differences between principal and any MI clusters include:

(i) The transition of the low-risk cluster identified in northwest Florida between 2005-2010 into a high-risk cluster between 2011-2014.
(ii) The absence of clustering of high risks of any MI hospitalizations in Miami-Dade County during the 2007-2008 period.
(iii) Persistent clustering of high any MI hospitalizations risks in Polk and Hardee Counties in South Central Florida throughout the study period.

2.4.2.3 Tango's Flexible Spatial Scan Statistics (FSSS) Clusters

The distributions of Tango's FSSS circular and non-circular clusters for hospitalizations with principal and any MI discharge diagnosis are shown in Figures 2.6 and 2.7, respectively. The spatial patterns of clustering of principal and any MI risks were not different. However, larger primary clusters and more secondary clusters were identified for any MIs than for principal MIs, particularly in Northwest and North Central Florida. For instance, Columbia, Suwannee and Union counties all constituted a single principal MI secondary high-risk cluster in North Central Florida throughout the study period. However, the three counties comprised the secondary any MI cluster in the 2005-2006 period, but they belonged to different clusters in the 2013-2014 period; Columbia and Union counties were a part of a primary cluster, while Suwannee was a part of a secondary cluster.

A comparison of FSSS clusters identified in 2005-2006 with those identified in 2013-2014 shows that 78% (14/18) and 77% (17/22) of counties in high-risk principal and any MI clusters, respectively, in 2005-2006 retained their status in 2013-2014. Most of those counties were located in the middle part of the state. Thirteen and 15 counties transitioned into high-risk principal and any MI hospitalization clusters by the 2013-2014 period, and most of those counties were located in the Panhandle.

The location and the general patterns of clustering of high MI risks for Tango's FSSS clusters were not substantially different than those for Kulldorff's CSSS high-risk clusters (Figures 2.4 and 2.5). However, Tango's FSSS clusters comprised all counties identified using Kulldorff's CSSS, plus additional counties; hence, they tended to be larger

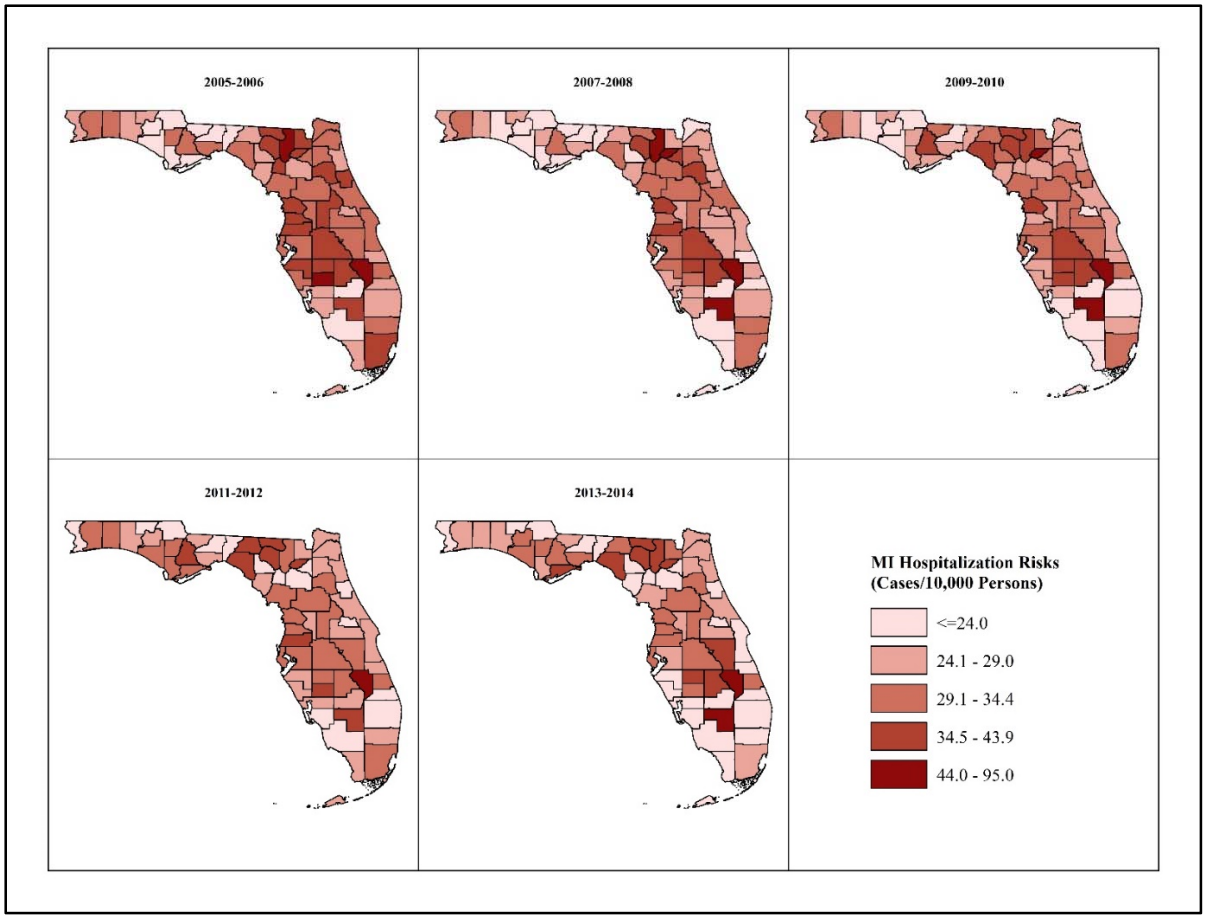


Figure 2.3. Spatial patterns of any myocardial infarction hospitalization risks adjusted to the age and sex distributions of the 2010 US census population.

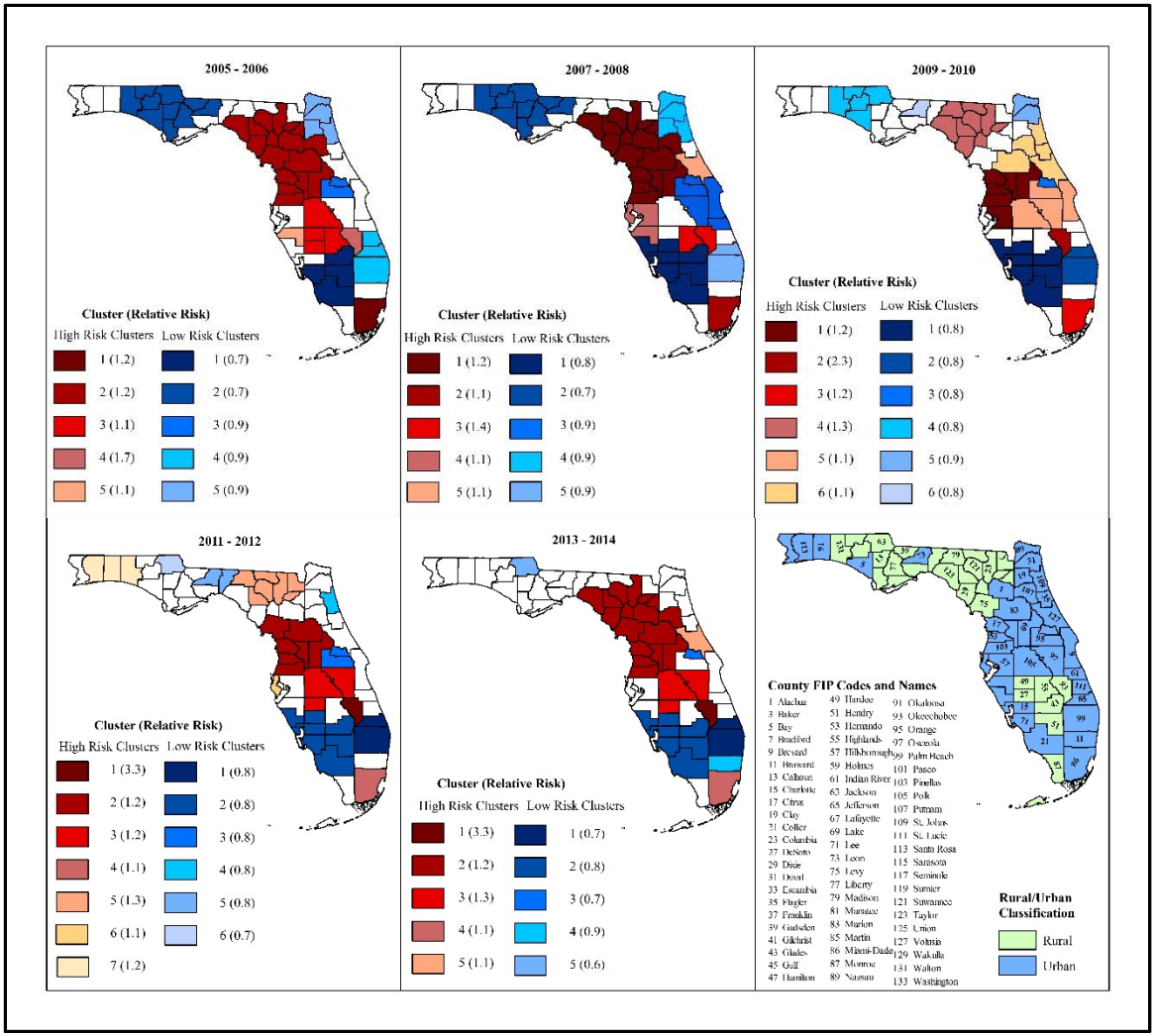


Figure 2.4. Spatial circular clusters of high and low principal myocardial infarction hospitalization risks in Florida between 2005-2014, as well as rural/urban classification of Florida counties.

Table 2.4. Summary statistics for circular high-risk clusters of hospitalizations with a principal myocardial infarction discharge diagnosis in Florida, 2005-2014.

Time Interval	Cluster	County	Cluster population (% of FL population)	Observed # of MIs	Expected # of MIs	MI Cases /10,000 persons	p-value
2005-2006	1	86	4828792 (13.4)	11961	10467.24	28.6	<0.00001
	2	75, 17, 41, 29, 53, 1, 83, 67, 119, 101, 121, 125, 123, 7, 23, 69, 107	3883180 (10.8)	13360	11928.25	26.6	<0.00001
	3	49, 27, 55, 105	1427730 (4.0)	4843	3979.55	31.1	<0.00001
	4	93	77985 (0.2)	319	190.53	42.8	<0.00001
	5	81	620203 (1.7)	2214	1984.07	28.5	0.00013
2007-2008	1	75, 17, 41, 29, 53, 1, 83, 67, 119, 101, 121, 125, 123, 7, 23, 69, 107	4093374 (11.0)	13047	11445.77	26.6	<0.00001
	2	86	4931242 (13.3)	11042	9887.13	26.1	<0.00001
	3	55, 93	278730 (0.8)	1266	902.22	32.7	<0.00001
	4	103, 81, 57	4894293 (13.2)	12315	11451.80	25.1	<0.00001
	5	127	997928 (2.7)	3009	2729.53	25.7	<0.00001
2009-2010	1	93	79951 (0.2)	392	167.89	51.4	<0.00001
	2	75, 17, 41, 29, 53, 1, 83, 67, 119, 101, 121, 125, 123, 7, 23, 69, 107	4154803 (11.1)	12149	10791.06	24.8	<0.00001
	3	105, 49, 97, 57	4241326 (11.3)	9068	7893.89	25.3	<0.00001
	4	86	4982221 (13.3)	10704	9501.80	24.8	<0.00001
2011-2012	1	93	79765 (0.2)	532	163.13	70.6	<0.00001
	2	17, 53, 75, 101, 119, 83, 69	3116403 (8.2)	10296	8600.95	25.9	<0.00001
	3	105, 49, 97	1828195 (4.8)	4359	3630.45	26.0	<0.00001
	4	86	5056071 (13.3)	10495	9565.79	23.8	<0.00001
	5	47, 121, 23, 79, 67, 3, 125	393872 (1.0)	1007	776.93	28.1	<0.00001
	6	103	1836685 (4.8)	5225	4764.21	23.6	<0.00001
	7	91, 131, 113	790131 (2.0)	1730	1498.07	25.0	<0.00001
2013-2014	1	93	79952 (0.2)	532	162.99	70.7	<0.00001
	2	75, 17, 41, 29, 53, 1, 83, 67, 119, 101, 121, 125, 123, 7, 23, 69, 107	4276132 (11.0)	13006	10812.73	26.1	<0.00001
	3	105, 49, 97	1887107 (4.9)	4645	3729.85	27.0	<0.00001
	4	86	5198431 (13.4)	10440	9840.38	23.0	<0.00001
	5	127	1003522 (2.6)	2818	2528.09	24.2	0.00013

Table 2.5. Summary statistics for circular low-risk clusters of hospitalizations with a principal myocardial infarction discharge diagnosis in Florida, 2005-2014.

Time Interval	Cluster	County	Cluster Population (% of FL population)	# Observed MI Cases	# Expected MI Cases	MI Cases/10,000 Persons	p-value
2005-2006	1	51, 43, 21, 71	1853327 (5.1)	4290	5816.98	18.9	<0.00001
	2	63, 13, 133, 59, 39, 77, 5, 131, 45, 73	1308614 (3.6)	1988	2690.58	18.9	<0.00001
	3	117, 95	2977058 (8.2)	4719	5259.91	22.9	<0.00001
	4	85, 111, 99	3353826 (9.3)	9590	10269.14	23.9	<0.00001
	5	31, 89, 19, 109	2487636 (6.9)	4555	4987.02	23.4	<0.00001
2007-2008	1	71, 15, 51, 27, 21, 43, 115	3085443 (8.3)	8078	9688.30	19.5	<0.00001
	2	63, 13, 133, 59, 39, 77, 5, 131, 45, 73	1345777 (3.6)	1940	2582.27	17.5	<0.00001
	3	9, 97, 95, 61, 117	4954523 (13.3)	8728	9708.59	21.0	<0.00001
	4	31, 89, 19, 109	2580453 (6.9)	4141	4843.12	20.0	<0.00001
	5	99, 85	2902376 (7.8)	7241	8075.73	20.9	<0.00001
2009-2010	1	71, 15, 51, 27, 21, 43, 115	3127273 (8.3)	7227	9173.95	17.4	<0.00001
	2	99, 85	2926434 (7.8)	6304	7649.28	18.2	<0.00001
	3	117	844417 (2.2)	1154	1492.38	17.0	<0.00001
	4	133, 59, 5, 63, 131	636666 (1.7)	1029	1327.01	17.1	<0.00001
	5	31, 89	1870728 (5.0)	2890	3234.16	19.7	<0.00001
	6	73	550260 (1.5)	668	805.64	18.3	<0.00001
2011-2012	1	99, 85	2954576 (7.8)	5936	7615.18	16.9	<0.00001
	2	71, 15, 51, 27, 21, 43, 115	3173919 (8.4)	7448	9106.19	17.7	<0.00001
	3	117, 95	3184374 (8.4)	4187	5050.44	18.0	<0.00001
	4	109	391071 (1.0)	659	821.37	17.4	<0.00001
	5	65, 73	582855 (1.5)	725	882.46	17.8	0.00002
	6	63	100092 (0.3)	145	205.78	15.3	0.0022
2013-2014	1	99, 85	3011105 (7.7)	5839	7661.46	16.5	<0.00001
	2	71, 15, 51, 27, 21, 43, 115	3270757 (8.4)	7391	9290.84	17.2	<0.00001
	3	117	868598 (2.2)	1163	1569.40	16.1	<0.00001
	4	11	3582137 (9.2)	6301	7146.82	19.1	<0.00001
	5	63	100080 (0.3)	117	207.34	12.2	<0.00001

fewer, and had lower RRs (1.1-1.7) than Kulldorff's CSSS high-risk (RR=1.1-3.5) clusters. Other notable distinctions between Kulldorff's CSSS and Tango's FSSS clusters include:

(i) The identification of two high-risk circular and non-circular clusters in the Panhandle at the end of the study period (2013-2014). Kulldorff's method identified a large low-risk cluster in those counties during the 2005-2006 period.

(ii) The identification of two distinct FSSS high-risk clusters in the Big Bend area and perisitent clustering of high-risks in DeSoto, Hardee, Highlands, Polk, and Okeechobee Counties in South Central Florida throughout the 10-year study period. In contrast, Kulldorff's method identified one large cluster in the Big Bend area in three out of five of the 2-year intervals assessed, and persistent clustering of high risks in South Central Florida in Polk and Okeechobee Counties only.

(iii) The FSSS high-risk clusters only included counties with elevated risks. Kulldorff's clusters, on the other hand, still included a few counties with elevated risks in low-risk clusters and counties with unelevated risks in high-risk clusters despite using a window with a maximum size of 13.4% of Florida's population. For instance, Hendry County was a part of the persistent low-risk cluster in southeast Florida despite having elevated relative risks ranging from 1.1-1.7 during the study period. Likewise, Sumter County was a constituent of the persistent high-risk cluster in the Big Bend area despite having unelevated relative risks of between 0.98-1.0 during the study period.

2.4.3 Temporal Trends

2.4.3.1 Principal MI Hospitalizations

The temporal trends in principal MI hospitalization risks among select Kulldorff's CSSS and Tango's FSSS clusters that persisted from 2005-2014 are shown in Figure 2.8. The risks in CSSS clusters declined modestly overall, by 9-21% and 9-28% in high- and low-risk clusters, respectively, between 2005-2006 and 2013-2014. Overall, we observed average rates of decline of 0.9-2.1% per year and 0.9-2.8% per year in high- and low-risk clusters, respectively, with clusters in southeastern Florida showing the largest declines. However, MI risks did not decline uniformly over the 10-year study period. Rather, the risks declined more rapidly during the first six to eight years of study. Thereafter, the rates of decline levelled in low- and high-risk clusters in Southeast Florida, while the trajectory reversed and the risks increased slightly in the high-risk clusters in the Big Bend region.

The risks in persistent Tango's FSSS clusters declined by a similar magnitude (7-21%) as Kulldorff's CSSS high-risk clusters. The temporal trends for risks in FSSS clusters were also similar to those for CSSS clusters, but the upward trend observed for

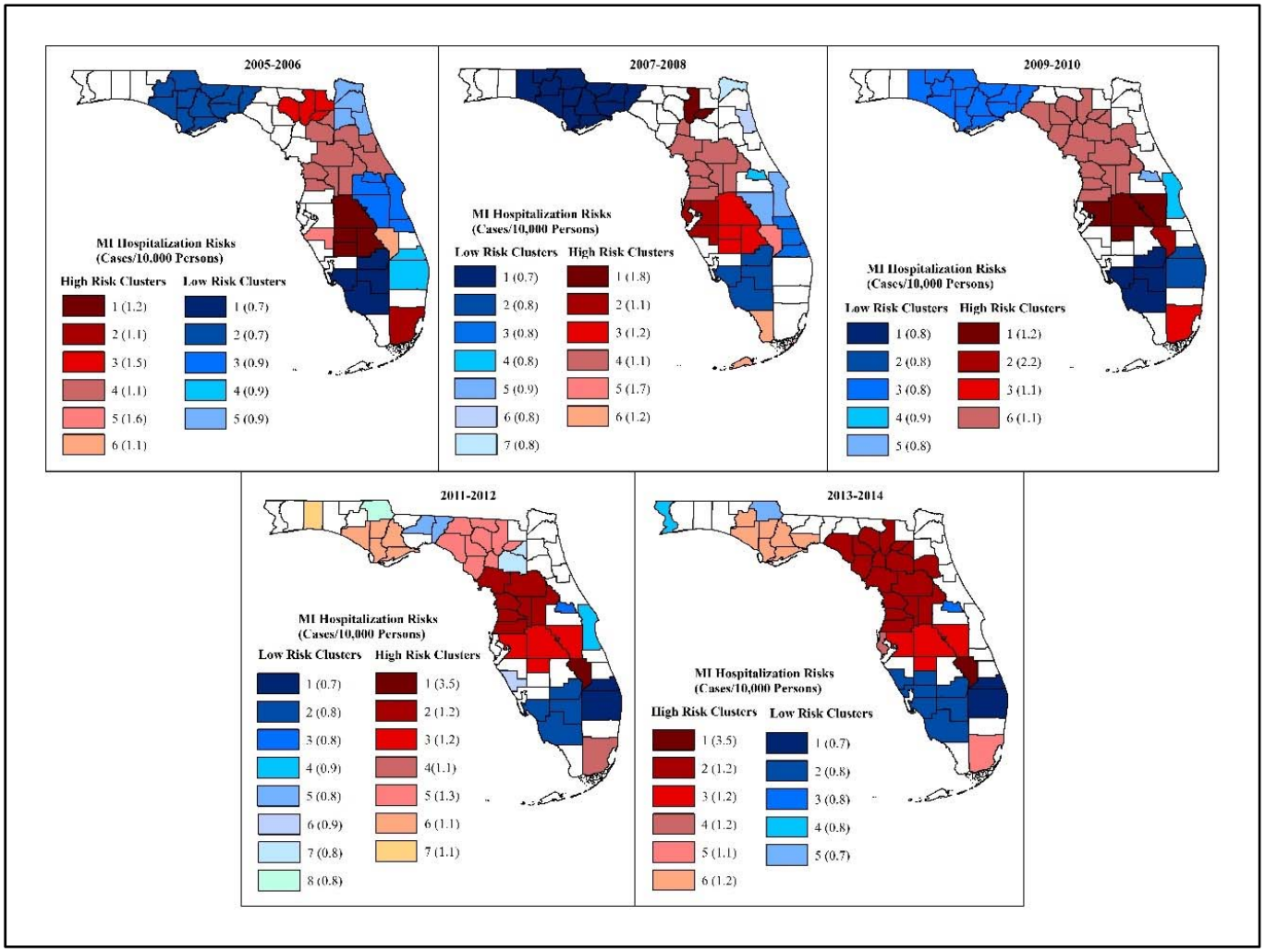


Figure 2.5. Spatial circular clusters of high and low any myocardial infarction hospitalization risks in Florida between 2005-2014.

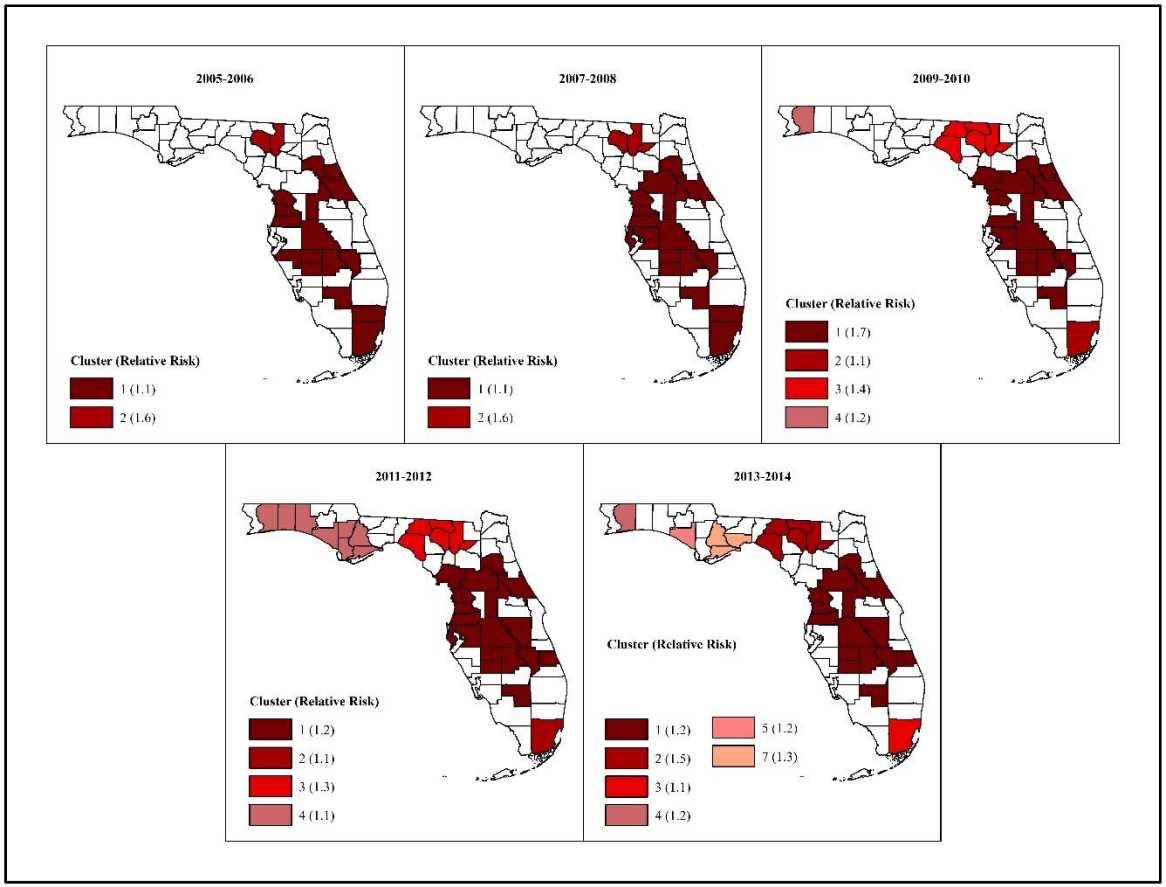


Figure 2.6. Tangos' spatial circular and non-circular high-risk clusters for hospitalizations with principal myocardial infarction discharge diagnosis in Florida, 2005-2014.

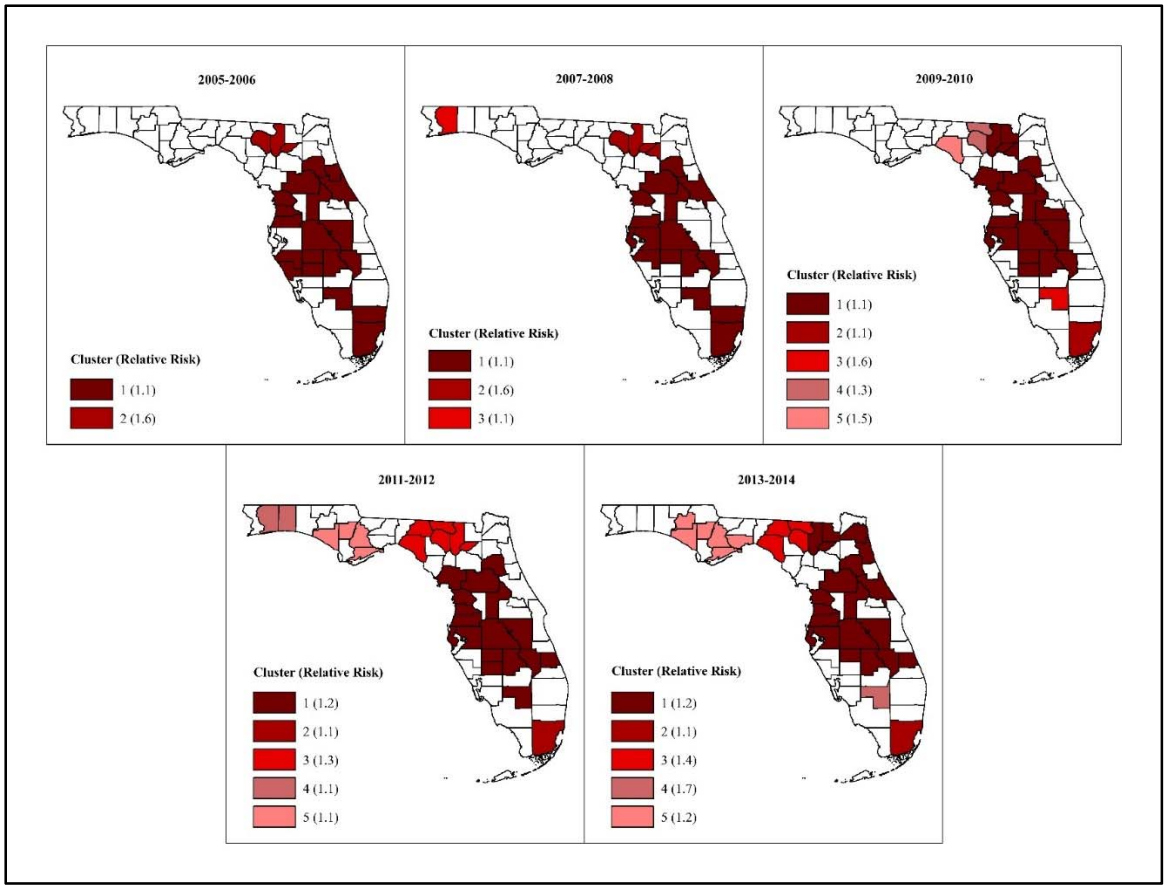


Figure 2.7. Tangos' spatial circular and non-circular high-risk clusters for hospitalizations with any myocardial infarction discharge diagnosis in Florida, 2005-2014.

high-risk clusters in North Central and West Central Florida during the last 4 years of study was more pronounced for FSSS clusters.

2.4.3.2 Any MI Hospitalizations

The changes in any MI risks in persistent in CSSS and FSSS clusters over the study period are displayed in Figure 2.9. The risks decreased by 5%, 16%, and 32% in high-risk CSSS clusters in West Central, South Central, and North Central Florida, respectively, and by 7% and 31% in low-risk clusters in Southwest and Southeast Florida, respectively. Similar to risks for the principal MI clusters, the risks only decreased during the first six to eight years of study, after which no more declines occurred, or the risks actually increased slightly in parts of Northern Florida.

The risks in FSSS clusters decreased overall by 5%, 11%, and 34% in high-risk clusters in West Central, Southeast, and North Central Florida, respectively, but there were disparities in rates of declines in MI risks amongst clusters and over time. The temporal trends in MI risks over the study period generally mirrored the patterns for CSSS high-risk clusters.

2.4.4 Changes in Health Disparities

The low-risk cluster in Southwest Florida (Figures 2.4 and 2.5) had the lowest MI hospitalization risks. Therefore, MI risks for this cluster were used as the baseline/reference for assessing changes in health disparities between circular high- and low-risk clusters at the end of the study (2013-2014) compared to the beginning of the study (2005-2006).

The RD between principal MI risks in the high-risk clusters in North Central, West Central, and Southeast Florida and the referent low-risk cluster were 9.8 cases/10,000 persons, in 2005-2006, and 9.1 cases/10,000 persons in 2013-2014. This resulted in a 7% reduction in health disparities at the end compared to the beginning of the study period. The RD between principal MI risks in the high-risk clusters in Southeast Florida and the referent low-risk cluster were 10.8 cases/10,000 persons in 2005-2006, and 6.4 cases/10,000 persons in 2013-2014, resulting in 41% reduction in heath disparities in the 2013-2014 compared to 2005-2006 periods.

The RD between any MI risks in the high-risk clusters in North Central, South Central, and West Central Florida and the referent low-risk cluster were 27, 11.5, and 16.8 cases/10,000 persons, respectively, in 2005-2006, and 11.5 cases/10,000 persons in 2013-2014. The RD between any MI risks in the high-risk clusters in Southeast Florida and the referent low-risk cluster was 13 cases/10,000 persons in 2005-2006 and 10.2 cases/10,000 persons in 2013-2014. Thus, disparities between high-risk clusters in North Central and South Central and Southeast Florida and the referent low-risk cluster were lower by 57%, 32%, and 22%, respectively, at the end of the study compared to the beginning of the study. However, disparities between the high-risk cluster in West Central Florida and the referent low-risk cluster did not change over the study period.

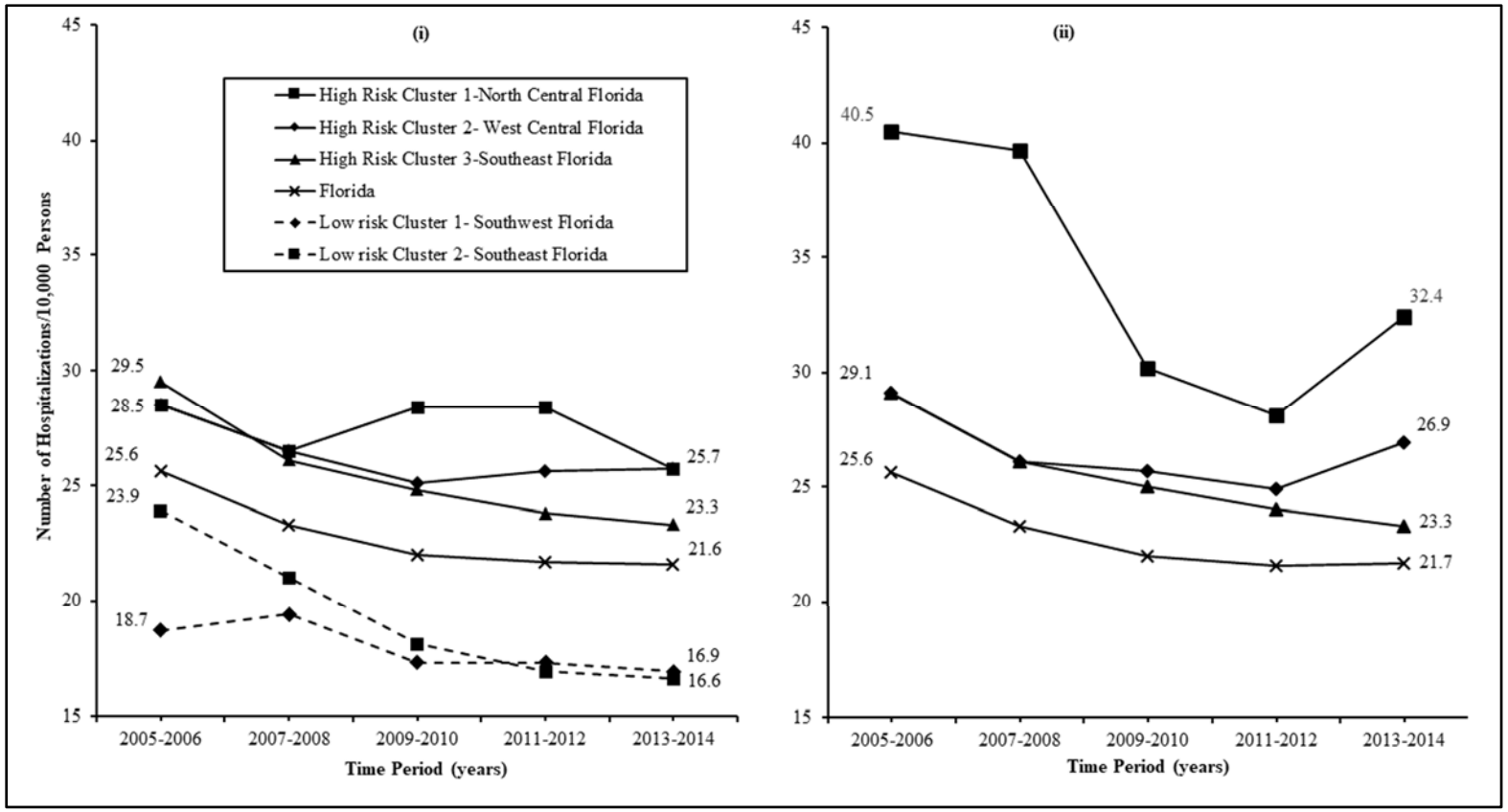


Figure 2.8. Changes in risks of hospitalizations with principal myocardial infarction discharge diagnosis among persistent (i) Kulldorff's circular and (ii) Tango's circular and non-circular clusters in Florida from 2005-2014.

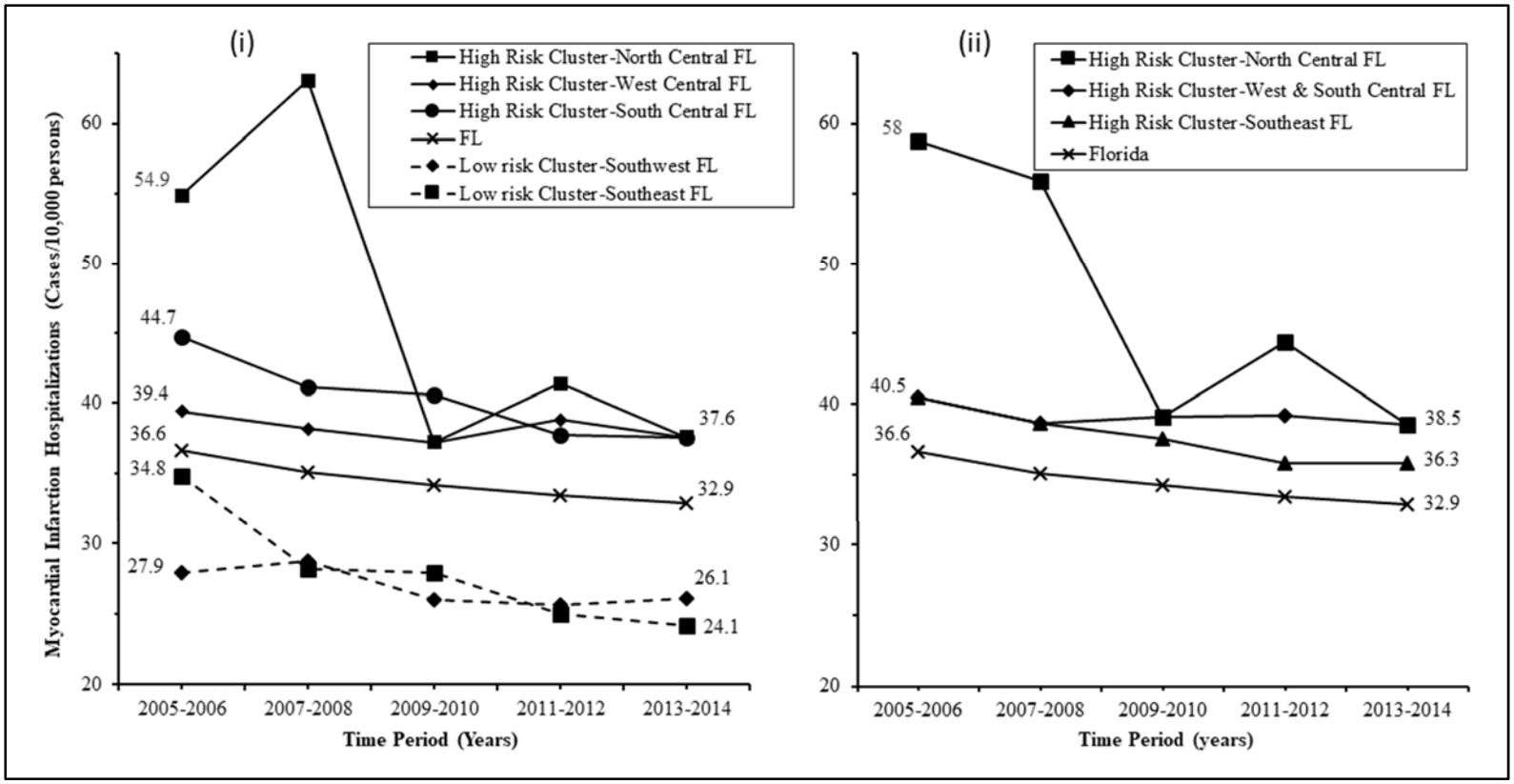


Figure 2.9. Changes in risks for hospitalizations with any myocardial infarction discharge diagnosis among persistent (i) Kulldorff's circular and (ii) Tango's circular and non-circular clusters in Florida from 2005-2014.

Principal and any MI hospitalization risks for the persistent high-risk clusters in Southeast Florida at the end of the study period (23.3 and 36.3 cases/10,000 persons) matched the risks for persistent low-risk clusters at the beginning of the study period (18.7-34.8 and cases/10,000 persons). However, the risks for persistent high-risk clusters in the Big Bend area and South Central Florida at the end of the study period (25.7-114.2 cases/10,000 persons) were equivalent or greater than those for persistent low-risk clusters at the beginning of the study period (18.7-34.8 cases/10,000 persons). Thus, both principal and any M hospitalization risks for counties in high-risk clusters are at least 10 years behind those for counties in low-risk clusters.

2.4.5 Disease Burden Attributable to Principal Versus Any MI Hospitalizations

Hospitalization risks with a principal MI discharge diagnosis compared to those with any MI discharge diagnoses amongst persistent low- and high-risk clusters both at the beginning (2005-2006) and at the end (2013-2014) of study periods are presented in (Table 2.6). Risks for MIs with any discharge diagnoses were higher by between 9.2-26.4 cases/10,000 persons in the 2005-2006 period and by 6.1-13.0 cases/10,000 persons in the 2013-2014 period. The mean difference (i.e. any MI – principal MI) amongst persistent clusters was 13.46 cases/10,000 persons in 2005-2006 (standard error [SE]=1.59; $t(9)=8.46$, $p < 0.0001$) and 10.56 cases/10,000 persons in 2013-2014 (SE=0.77; $t(9)=13.68$, $p < 0.0001$).

2.5 Discussion

We investigated geographic patterns, spatial clusters, and temporal trends of hospitalization with principal and any MI discharge diagnoses in Florida between 2005-2014 to identify communities with consistently high MI burden, so they may be prioritized for interventions to reduce/eliminate health disparities and improve population health for all Floridians. This is amongst a few area-level studies that have comprehensively investigated geographic and temporal disparities in MI/CVD-related hospitalization risks in the US simultaneously [38,42,43,83].

2.5.1 Descriptive Analysis

Our results showing lower MI hospitalization risks for Black residents compared to their White counterparts at the beginning of the study (2005-2006) period but higher risks for Blacks at the end of the study (2013-2014) are consistent with previous studies. For instance, Sacks et al. found higher MI hospitalization risks for Whites than Blacks in a Medicare population in the US between 2002-2006 but higher risks for Blacks by 2011 [55]. Singh et al. [15] examined the temporal trends in MI hospitalization rates among US Medicare beneficiaries hospitalized with MI between 1992 and 2010. They found higher MI hospitalization rates for White women compared to Black women between 1992-1993 but lower rates for White women between 2009-2010. However, MI hospitalization rates

Table 2.6. Hospitalization risks for myocardial infarction hospitalizations with principal versus any discharge diagnoses for persistent low- and high-risk clusters at the beginning (2005-2006) and end (2013-2014) of the study period.

Time Period	2005-2006			2013-2014		
Discharge Diagnoses	Principal MI Cases/10,000 population	Any MI	[1]Difference	Principal MI Cases/10,000 population	Any MI	[1]Difference
[2]CSSS high-risk clusters						
North Central Florida	28.5	54.9	26.4	25.7	37.6	11.6
West Central Florida	28.5	39.4	10.9	25.7	37.6	11.6
South Central Florida	31.0	44.7	13.6	27.0	37.6	10.6
Southeast Florida	29.5	40.9	11.7	23.3	36.3	13.3
[2]CSSS low-risk clusters						
Southwest Florida	18.7	27.9	9.2	16.9	26.1	9.2
Southeast Florida	23.9	34.8	10.9	16.6	24.1	7.5
[3]FSSS high-risk clusters						
North Central Florida	40.5	58.0	17.3	32.4	38.5	5.6
West Central Florida	29.1	40.6	11.6	26.9	38.5	11.6
South Central Florida	29.1	40.6	11.6	26.9	38.5	11.6
Southeast Florida	29.1	40.6	11.4	23.3	36.3	13.0

[1]Any MI risk-Principal MI risk; [2]Circular spatial scan statistics; [3]Flexible spatial scan statistics

for Black men were consistently lower than those for White men throughout the 18-year study period.

Given that MI is a life-threatening health condition requiring immediate catherization within 90 minutes of first medical contact [100], MI hospitalization risk may serve as a proxy for MI morbidity, in which case our results would suggest lower MI morbidity risks for Blacks compared to Whites at the beginning of the study period. However, this interpretation contradicts the well-documented historic racial disparities in the prevalence of ideal cardiovascular health, burdens of CVD and associated risk factors, and prevention and treatment of coronary artery disease, with Blacks having poorer metrics [101-107]. These have been linked to poorer outcomes in Blacks as compared to Whites [108-110]. Area-level factors such as limited access to healthy foods such as fruits and vegetables [36,111,112], high levels of pollution and poor enforcement of environmental regulations [113], low SES, low neighborhood walkability, crime, limited access to green spaces and quality cardiovascular health care [114], and low social cohesion [50] in Black neighborhoods are also related to high MI morbidity risks. Therefore, the lower MI hospitalization risks we observed for Blacks compared to Whites at the beginning of the study do not signify lower MI morbidity risks for Blacks than Whites. Rather, they are indicative of an under-diagnosis of MI among Blacks in the pre-hospital setting due to lower utilization rates for time-sensitive MI care. Underuse of MI care services may be attributed to limited knowledge regarding MI symptoms [115,116], lack of transport and health insurance [117,118], and mistrust of the healthcare system due to negative experiences such as the Tuskegee syphilis study and perceived racial bias that continues to this day [51,119].

2.5.2 Temporal and Spatial Patterns

The encouraging declines we observed in Florida overall and in all demographic groups but the race category coded as “Other” are consistent with other studies of the temporal patterns of MI hospital admissions in disparate US populations [10-20]. The increase in MI hospitalization risks in the “Other” race category suggests that differences in coding ethnicity data within Florida may have affected the trends we observed among racial groups. Potential explanations for the declines in MI hospitalization risks during the study period include changes in the sensitivity of ICD-9-CM codes for MI, increase in out-of-hospital sudden cardiac death, and a decrease in incident and recurrent MIs. However, Chen et al. [10] found concomitant declines in MI and other cardiac conditions that may be coded instead of MI, suggesting no dramatic shifts in coding hospitalizations away from MI to other cardiac conditions. Moreover, the incidence of sudden cardiac death has fallen over time, in parallel with the decline in coronary heart disease mortality [120,121], making this an unlikely explanation for the reductions in MI hospitalization risks. Furthermore, the downward trajectory occurred during a period of increased use of more sensitive troponin biomarker assays, which would be expected to increase the diagnosis of MI and MI discharges [122].

Studies conducted prior to ours showed improvements in awareness, treatment, and control of major CVD risk factors, such as low-density lipoprotein cholesterol, hypertension, and diabetes in US counties [123-127]. A substantial increase in the

utilization of interventional procedures after MI, such as Percutaneous Coronary Intervention (PCI), over the last decade may also have contributed to improved care of MI patients leading to improved outcomes [15,128]. For instance, a self-organizing system based on American College of Cardiology and the American Heart Association (ACC/AHA) guidelines increased the proportion of EMS-transported ST segment elevation MI (STEMI) patients admitted directly to high volume PCI-centers in Florida from 62.4% in 2001 to 89.7% by the first half of 2009 [128]. Based on a study by De Luca et al. [129], this may have led to significantly lower reinfarctions, among other positive outcomes.

The reduction in MI hospitalization risks in our study also coincides with favorable temporal trends noted for behavioral risk factors, such as levels of sufficient physical activity and the prevalence of smoking [130-133]. Additionally, the consistency of the trend over the 10-year study period adds evidence that this is not a statistical artifact. Thus, the progressively lower MI hospitalization risks we observed in Florida over the 10-year study period likely represents a true decrease in incident and recurrent MIs [58,134,135], reflecting gains from improvements in cardiac care through primary and secondary prevention efforts [23].

Despite the overall decrease in MI hospitalization risks in Florida, the striking geographical disparities in MI hospitalization risks we observed across the state, with high-risk clusters occurring in predominantly rural counties in the Big Bend area and South Central Florida, and low-risk clusters in predominantly urban counties in southern Florida, suggested that communities have not benefited equitably from preventive and control efforts. These results corroborate existing research showing place of residence to be an important determinant of cardiovascular health [50,51].

The concentration of high-risk clusters in rural counties, coupled with persistent clustering of high-risks in northern Florida counties, is consistent with clustering of high prevalence rates of MI hospitalizations [26], and historically high stroke and heart disease hospitalization and mortality rates in socioeconomically-deprived areas in the southeastern US, a region that has had persistently high stroke and heart disease rates compared to the rest of the country [15,39,136,137]. This is not coincidental, since northern Florida is demographically and geographically similar to much of the southeastern US. Moreover, the spatial patterns for MI hospitalization risks we observed in this study generally mirror the patterns of clustering previously observed for stroke, heart disease, diabetes, and hypertension rates in various county-level ecologic studies in the US [39,41,42,78,85,138]. The spatial location of clusters with persistently low or high MI hospitalization risks are also remarkably similar to the location of persistent MI mortality risk clusters we identified in Florida between 2000-2014 [77]. The only notable discrepancies between MI hospitalization and mortality clusters were persistent clustering of MI hospitalization risks in South Central Florida and lack of persistent clustering of high MI hospitalization risks in Northwest Florida. Taken together, the concentration of high burdens of MI mortality and hospitalizations in counties previously identified as also having elevated rates of stroke, diabetes, and hypertension suggest that MI preventive and control efforts targeted to those counties would result in reductions in MI-related health disparities, as well as disparities related to stroke, diabetes, and hypertension.

Clustering of high-risk MI hospitalization risks coupled with the lack of clustering of high MI mortality risks in South Central Florida likely reflects improved survival [139].

The clustering of high MI hospitalization risks in rural counties likely reflects several challenges to improving cardiovascular outcomes in those counties including: financial constraints and long travel times due to lower government spending on infrastructural resources in sparsely populated areas compared to more densely-populated areas [140]; unavailability of high-speed broadband internet services [141,142]; lack of health insurance coverage [143]; and inadequate supply of primary care providers [144], cardiologists [80], and PCI-capable hospitals [81]. Consequently, rural counties have limited capacity to implement policies and programs designed to prevent and manage CVD [145,146]. For instance, while the burden of tobacco use is higher in rural counties compared to urban counties [29], tobacco cessation programs and tobacco control policies, such as smoke-free air laws and regulations, sales tax, raising the minimum legal sales age, and restricting the advertising and sale of tobacco products, have limited geographic coverage, with rural populations receiving lower levels of protection [79,82,147]. Accordingly, the prevalence of cigarette use and other CVD risk factors is declining more quickly among high-income urban populations than low-income rural populations [12,43,75,132,148]. Rural communities also tend to have lower prevalence of protective health-related behaviors compared to their urban counterparts [149]. Cultural attitudes towards seeking health care, lower literacy levels, higher unemployment rates, inadequate social support, and higher levels of chronic stress in rural areas may also increase the risk of CVD [51,150] and attenuate the effects of efforts to improve cardiovascular health [151,152]. Variations in exposures such as extreme cold or hot temperature, air pollution, and influenza vaccination may also have contributed to the disparities in MI hospitalization risks [153-155].

Potential causes for persistent clustering of high- or low MI hospitalization risks, or lower rates of decline in MI risks in rural counties in northern Florida during the 10-year study period were not investigated. However, based on similarity of the spatial patterns for MI risks with the geographic patterns for MI risk factors such as cigarette smoking [132], hypertension [156], obesity, and physical inactivity [131] in US counties over time, persistence in MI hospitalization risks may be related to lack of temporal changes in the spatial patterns for MI risk factors. Additionally, recent economic shifts in different regions may contribute to the lag between high- and low-risk clusters [157]. Fueled by agricultural and industrial growth, tourism, retiree migration, and an expanding transportation system, southern Florida counties have undergone rapid urbanization and economic development in recent years, but North Florida has not kept pace [157,158]. Further, urban counties in southern Florida have more resources to invest in the physical and social health environment due to higher levels of government spending in more densely-populated counties. Thus, these counties may have a greater capacity to quickly adopt new models of care delivery, join campaigns for MI prevention, and implement evidence-based primary and secondary prevention strategies. In contrast, counties in the more rural north tend to be chronically under resourced, which could diminish the uptake of new interventions [159]. Thus, cardiovascular risk has been shown to decrease in all US counties, but a low-income level generates latency in this trend [43]. Not coincidentally, we observed persistent clustering of high MI hospitalization risks in counties with

consistently low ranks for health factors and perisitent clustering of low MI risks in counties with consistently high ranks for health factors [160]. In agreement with our study, Schieb et al. [42] found most favorable socioeconomic and healthcare profiles for counties in persistently low-rate clusters of stroke hospitalizations, and least favorable profiles for persistently high-rate counties. Hobbs et al. [161] reported an association of clusters of health behaviors in Queensland adults with different socio-demographic characteristics, with low-risk clusters having the healthiest profile, elevated risk-clusters having a several unhealthy behaviors and moderate-risk clusters having some unhealthy behaviors. White et al. [162] described a cluster of low prevalence for hypertension, which was related to availability of preventive primary care [150].

The identification of the lone high-risk cluster in Miami-Dade County in Southeast Florida, though unexpected, may be attributed to high prevalence of major risk factors for MI including hypertension (32.6%), cholesterol (32.2%) overweight/obesity (87.2%), and physical inactivity (56.7%) [163]. Additionally, Miami-Dade County has large proportions of socioeconomically-disadvantaged Hispanic and Haitian immigrant populations [164,165]. Low social capital is a well-established risk factor MI [51]. Furthermore, utilization rates for low-cost healthcare programs for preventive care, such as the Federally Qualified Health Centers, are very low [165].

Taking MI hospitalization risk as a proxy for morbidity, our results showing clustering of low MI hospitalization risks in rural counties in Northwest Florida between 2005-2010 are suggestive of low prevalence of MI in Northwest Florida during that period. This is inconsistent with the persistent clustering of high MI mortality risks we recently observed throughout most rural counties in northern Florida between 2000 and 2014 [77]. Therefore, the clustering of low MI hospitalization risks we observed in rural counties in Northwest Florida during the first six years of study does not imply lower MI morbidity risks for residents in those counties. Rather, they are likely indicative of higher pre-hospital MI death risks in Northwest Florida, resulting in an under-diagnosis of MI in the pre-hospital setting. Factors that may lead to underuse of cardiac care services, and hence low MI hospitalization risks, in rural counties in Northwest Florida include lack of health insurance due to limited Medicaid eligibility [166,167], scarcity of cardiac specialists [80], lack of emergency medical services to conduct lengthy patient transport on a 24-hour basis [168,169], and poor availability of medical technologies such as broadband internet services [141]. Moreover, as is typical throughout the US [170], high-volume PCI-capable hospitals are clustered in metropolitan and large urban areas on the coastline and along the major interstate highways, with 100% (n=21) of rural/nonmetro counties in Florida lacking a high-volume PCI center [81]. These may result in less frequent interaction with the healthcare system, decreasing the likelihood for diagnosing MI among rural residents. Additionally, mistrust of the healthcare system due to historical events such as the Tuskegee syphilis study [171], perceived racial bias, and discrimination that continues to this day may affect health care-seeking behaviors and lead to underuse of available services [51].

Ironically, the transition of the low-risk cluster we identified in Northwest Florida between 2005-2010 into a high-risk cluster between 2011-2014 may be a reflection of improvements in access to, and utilization of, cardiac care due to mitigation of the above-mentioned barriers over time, thus reducing the risk of sudden cardiac death before

hospitalization and increasing the likelihood for rural residents to be hospitalized when they experience MI [172,173]. These improvements may be attributed to the concerted efforts by Florida Blue Center for Rural Health Research and Policy to improve health care access among underserved communities in rural northern Florida. Efforts of local coalitions throughout Florida have also reduced logistical barriers to timely access to PCI-based reperfusion over time, increasing the proportion of rural MI patients admitted directly to high volume PCI hospitals in Florida [128]. Additionally, increased awareness of and response to heart attack symptoms among high risk groups [174] through educational campaigns by federal agencies such as the CDC and nonfederal partners, such as the American Heart Association, may have reduced pre-hospital delays in seeking timely cardiac care, thereby reducing pre-hospital MI death risks [175-177].

Despite the encouraging modest reductions in MI hospitalization risks in both low- and high-risk clusters, the levelling of MI hospitalization risks in the high-risk cluster in Southeast Florida after an initial period of decline is concerning because it suggests that the Healthy People 2020 [4] target of eliminating health disparities and improving health for all groups by 2020 may not be reached if current trends continue. Moreover, the reversal of the favorable temporal trends in the high-risk clusters in North and West Central Florida in the latter four years of study has the potential to unravel the gains that have been achieved from primary and secondary prevention efforts during recent decades. We observed remarkably similar temporal patterns for MI mortality risks in North Central Florida between 2000-2014 [77].

The reasons for the spatiotemporal trends in MI hospitalization risks discussed above are not clear. However, the trends mirror the slowing in the decline of CVD risk factors and slowing in increase of protective factors for CVD that have been observed in the US. For instance, the management and control of hypertension in the noninstitutionalized US population improved between 1999-2006, but no improvements occurred from 2007 to 2010 [125]. The percentage of US adults with controlled low-density lipoprotein cholesterol increased from 45% in 1999-2000 to 65% in 2005-2006, but it decreased to 64% by 2009-2010 [126]. The prevalence of sufficient physical activity in US counties increased from 2001 to 2009, but there was little progress between 2009 and 2011. Moreover, the increase in level of sufficient physical activity was matched by an increase in prevalence of obesity in almost all counties [131]. An increase in the prevalence of diabetes mellitus may also have contributed to the unfavorable MI trends [12,75,76]. These trends in risk factor management provide circumstantial evidence that the unfavorable trends in MI hospitalizations risks in the high-risk counties in northern Florida in the latter years of study may be due to deteriorating risk factor profiles in some population groups. Moreover, our results showing increasing MI risks in rural counties in North Central and West Central Florida during the last four years of study are consistent with Yeh et al. [12] who showed that the growth of certain CVD risk factors, including obesity and diabetes mellitus, has disproportionately impacted certain geographic regions, particularly rural counties in Southern and Southeastern US. The great economic recession of 2008-2009 may also have resulted in higher unemployment rates in socioeconomically-disadvantaged areas than in areas with high SES, further exacerbating the MI burden in rural areas in Northwest and North Central Florida. Li et al. showed an upward trend in MI occurrences in low-income but not in the high-income in

Raritan Bay region, New Jersey after the onset of the 2008-2009 great recession [178]. More years of data and continued population-based surveillance of MI hospitalizations in those counties are warranted to confirm these trends. Appropriate strategies can then be implemented to prevent a reversal of many of the public health gains of the past decades.

2.5.3 Health Disparities in High-Risk Clusters in 2013-2014 Versus 2005-2006 Time Periods

The fact that MI hospitalization risks for high-risk clusters at the end of the study (2013-2014) were on par with or higher than the risks in low-risk clusters at the beginning of the study (2005-2006) indicates that counties in high-risk clusters would require at least 10 additional years to achieve hospitalization risks seen in low-risk counties during the 2013-2014 period. Delayed declines in MI hospitalization risks in high-risk clusters in the north may be reflective of inequities in the timing of delivery, initiation, and implementation of primary and secondary prevention of MI [179].

2.5.4 Disease Burden of Principal versus Any MI Hospitalizations

Our results showing significantly higher risks in spatial clusters of any MIs than for principal both at the beginning and at the end of the study period suggest that studies that exclude secondary MI hospitalizations may underestimate the current MI burden. In this study, using principal MIs only, on average, underestimated the MI burden by 13.46 cases/10,000 persons in the 2005-2006 period, and by 10.56 cases/10,000 person in the 2013-2014 period. Moreover, the proportion of secondary MIs increased over the study period. Sacks et al. [47] also reported higher disease burden for any MI compared to principal MI hospitalizations in a study of Fee-for-Service Medicare population aged 65 years and older between 2002 and 2011.

2.5.5 Strengths and Limitations

Most recent studies of temporal trends of MI hospitalization risks in the US are typically limited to hospitalizations with a principal MI discharge diagnosis in select populations defined by age or specific socioeconomic, geographic, and racial/ethnic characteristic [10,11,13,18,19,38,83]. Our study included hospitalizations with principal or secondary MI discharge diagnoses for all noninstitutionalized Florida residents. Therefore, our results can be generalized to nearly all patients in Florida and in other southern US states with similar demographic characteristics and healthcare systems as Florida. Moreover, Florida's present racial/ethnic composition, age structure, and healthcare challenges portend the demographic shifts and potential healthcare challenges anticipated for the US by 2030 [180,181]. Therefore, our findings have potential implications for future health care system planning for cardiac care for the rest of the US.

We used MI hospitalization data collected before 2015 (9th Revision Clinical Modification, ICD-9-CM) because subsequent data were collected using ICD 10th Revision Clinical Modification (ICD-10-CM). While our data may not represent the

“current” MI burden in Florida, restricting our study population to the period prior to 2015 ensured that any temporal changes in MI hospitalization risks would be due to changes in disease trends and not due to changes in coding practices. Moreover, using hospitalized cases with principal or any discharge diagnosis for MI allowed us to characterize the burden of MI hospitalizations more fully, and to estimate the extent to which principal MIs may underestimate the disease burden attributable to MI.

The rigorous analytic methods we used enabled us to obtain a more accurate/realistic understanding of disparities in the MI burden in Florida. For instance, the use of a SaTScan window size based on the county accounting for the largest population in Florida instead of the default window size of 50% of the population of Florida reduced the false positive rate, which would result in better targeting, hence more efficient use of scarce resources for MI prevention and control efforts. The use of a flexible spatial scan statistic with a restricted likelihood ratio [182] resulted in the identification of both circular and irregularly-shaped clusters of MI hospitalization risks. Irregularly-shaped clusters would not be identified by Kulldorff’s circular spatial scan statistic, which is the standard method for detecting and identifying spatial clusters. All high risk clusters, regardless of their shape, would be of interest to public health practitioners; hence, the identification of non-circular clusters will reduce the false negative rate [183] and lead to improved control of MI. Thus, while we have confidence in the Kulldorff’s CSS statistic to identify the existence of specific clusters, we have less confidence that it can precisely identify the boundaries of each cluster.

This study has some limitations that suggest important areas for further research. The first limitation arises from the ecologic study design. Although the county is the preferred spatial unit of analysis where public health action is being considered, the study design is prone to ecologic fallacy. Thus, interpretations of specific associations between contextual effects, such as rural residence, and MI hospitalization risks should be made with caution, recognizing that inferences based on aggregate data do not apply to comparable individual-level data [184]. Additionally, geographic analysis of the MI burden at the county-level does not identify within county disparities, which can be large. Therefore, local health planning could benefit from small-area studies at a lower spatial scale, such as the ZIP code, and our study may be used to guide such studies.

Second, it was not possible to differentiate between MI hospital admissions that represent incident cases and those that do not. Therefore, we based MI hospitalization risks on number of hospital discharges rather than patients, hence the data may include multiple admissions for the same individual (i.e., recurrent cases) or the same event (i.e., transfer cases), if the person had more than one hospitalization. Additionally, the AHCA data do not include MI patients who did not seek care, died before hospitalization, or were hospitalized out of state, hence there is potential for selection bias.

Third, we did not investigate the clinical, behavioral, sociodemographic, environmental, and healthcare service factors that might be associated with the spatiotemporal disparities in MI hospitalization risks in Florida. Therefore, follow-up studies will need to identify locally relevant determinants of the MI disparities to enable policy makers to design more effective evidence-based interventions for reducing the MI burden in the most disadvantaged regions. Moreover, investigations of the drivers of MI

risks in counties within persistent low-risk clusters may provide insights regarding the protective factors contributing to low MI hospitalization risks in those counties.

Lastly, the Tango's spatial scan statistic uses a one-tail test, hence it does not detect irregularly-shaped low-risk circular and non-circular clusters. The statistic needs further development to address this shortcoming.

2.6 Conclusions

In general, MI hospitalization risks decreased modestly across Florida over the 10-year study period. However, there are pervasive spatiotemporal disparities, with rural counties in the Big Bend area and South Central Florida having persistently higher MI hospitalization risks and urban counties in southeastern and southwestern Florida having persistently lower risks. Moreover, counties within high-risk clusters in the north lag behind those within low-risk clusters in the south by at least a decade, and there are early signs that the temporal trends have reversed in rural counties in the Big Bend area. Thus, prevention and control strategies should be targeted to high-risk counties to optimize efficiency of interventions geared towards reducing health disparities and improving health for all Floridians.

CHAPTER 3
GEOGRAPHIC DISPARITIES AND TEMPORAL CHANGES IN RISK OF DEATH FROM MYOCARDIAL INFARCTION IN FLORIDA, 2000-2014

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The use of "we" in this chapter refers to co-authors Drs. Nicholas Nagle and Kristina W. Kintziger, Shamarial Roberson and myself. As the first author, I participated in study design, and performed data processing and analysis, interpretation of results and drafted the manuscript. All authors read and critically revised the manuscript.

3.1 Abstract

Background: Identifying disparities in myocardial infarction (MI) burden and assessing its temporal changes are critical for guiding resource allocation and policies geared towards reducing/eliminating health disparities. Our objectives were to: (a) investigate the spatial distribution and clusters of MI mortality risk in Florida; and (b) assess temporal changes in geographic disparities in MI mortality risks in Florida from 2000 to 2014.
Methods: This is a retrospective ecologic study with county as the spatial unit of analysis. We obtained data for MI deaths occurring among Florida residents between 2000 and 2014 from the Florida Department of Health, and calculated county-level age-adjusted MI mortality risks and Spatial Empirical Bayesian smoothed MI mortality risks. We used Kulldorff's circular spatial scan statistics and Tango's flexible spatial scan statistics to identify spatial clusters.
Results: There was an overall decline of 48% in MI mortality risks between 2000 and 2014. However, we found substantial, persistent disparities in MI mortality risks, with high-risk clusters occurring primarily in rural northern counties and low-risk clusters occurring exclusively in urban southern counties. MI mortality risks declined in both low- and high-risk clusters, but the latter showed more dramatic decreases during the first nine years of the study period. Consequently, the risk difference between the high- and low-risk clusters was smaller at the end than at the beginning of the study period. However, the rates of decline levelled off during the last six years of the study, and there are signs that the risks may be on an upward trend in parts of North Florida. Moreover, MI mortality risks for high-risk clusters at the end of the study period were on par with or above those for low-risk clusters at the beginning of the study period. Thus, high-risk clusters lagged behind low-risk clusters by at least 1.5 decades.
Conclusion: Myocardial infarction mortality risks have decreased substantially during the last 15 years, but persistent disparities in MI mortality burden still exist across Florida. Efforts to reduce these disparities will need to target prevention programs to counties in the high-risk clusters.

Key Words: myocardial infarction mortality, geographic clusters, disparities, temporal trend

3.2 Background

The rates of deaths from cardiovascular diseases (CVD), such as coronary heart disease (CHD) and myocardial infarction (MI), have decreased in the US in the last five decades [185]. However, CVD remain the leading cause of preventable premature deaths in the US, accounting for one in every four fatalities in the country [74]. MI, or heart attack,

contributes significantly to this burden, with approximately 14% of the 790,000 people who experience an MI in the US each year dying from it [1].

Cardiovascular diseases also represent a serious economic burden to the US healthcare system, constituting 17% of national health expenditures in 2014 [1], with MI being the most expensive condition to treat [186]. The burden of MI is particularly high in the southeastern US states, including Florida, where 5% and 12% of the adult and elderly (≥65 years) populations, respectively, reported a history of acute MI in 2014 [187]. Moreover, the increase in mean age of the population coupled with an upsurge in risks of obesity and type 2 diabetes [74] are expected to exacerbate the burden of MI and increase its public health and economic costs [9].

Consistent with the trends seen nationally [185], an overall decline in MI/ischemic heart disease mortality risks has been observed in Florida [5,41]. However, it has been shown that population subgroups defined by geography and other factors may show widening disparities in cardiovascular health, despite reductions in overall CVD mortality risks [188]. Additionally, previous studies showing geographic disparities of MI mortality risks at county- [39] and census tract-levels [60,62], suggest that geographic hotspots of MI mortality risks may exist in Florida. Therefore, it is strategically advantageous to identify populations with high MI burdens and investigate how the MI burdens change over time to guide control programs geared towards reducing/eliminating disparities and improving population health. Moreover, understanding how MI burdens change over time may reveal the effectiveness of intervention programs and can be used to guide policy decisions and resource allocation. Unfortunately, no rigorous population-level studies have been conducted to determine if the decreases in MI mortality risks have occurred equitably across all communities in the state. Therefore, our objectives were to: (a) investigate the spatial distribution and clusters of MI mortality risk in Florida; and (b) assess temporal changes in geographic disparities in MI mortality risks in Florida from 2000 to 2014.

3.3 Methods

3.3.1 Study Design and Study Population

This is a retrospective ecologic study using Florida MI mortality data for the period January 1, 2005, to December 31, 2014. The study population included all deceased Florida residents whose underlying cause of death was listed as MI, according to the *International Classification of Diseases*, tenth revision: ICD-10 Code(s): I21 (acute myocardial infarction) and I22 (subsequent myocardial infarction). The variables of interest included age, county of residence, and year of death. We used the county as the geographic unit of analysis.

3.3.2 Data Sources and Data Preparation

We obtained county-level MI mortality data for the age-groups 0-34, 35-44, 45-54, 55-64 and ≥65 year-olds covering the 2000-2014 time period from the Florida Department of Health (DOH) website [5]. Due to a small number of deaths (<25 events) in some

counties, DOH routinely pools age-specific MI death counts by three-year intervals to help stabilize death risks and to maintain patient anonymity and confidentiality.

We also obtained county-level annual population estimates for age categories matching the MI mortality data (i.e., 0-34, 35-44, 45-54, 55-64 and ≥65 year-olds) from DOH [88] and used this as denominator data for calculating age-specific mortality risks. We downloaded county-level cartographic boundary shape files for all cartographic displays from the US Census Bureau website [92].

3.3.3 Descriptive Statistics

MI mortality risks per 100,000 population were calculated and directly age-standardized to the 2000 US Standard Population [89] in SAS v.9.4 (SAS Institute; Cary, NC). Despite pooling death counts by three-year intervals to address the small number problem, a number of rural counties still had <25 MI deaths. According to Curtin and Klien [189], such areas are considered small areas; hence, unsmoothed age-adjusted risks from these areas would be highly unstable due to high variances. Therefore, to minimize the impact of the high variances and adjust for spatial autocorrelation (i.e., clustering), we computed Spatial Empirical Bayes (SEB) smoothed risks using 1st order queen weights in GeoDa [190]. All descriptive analyses were done in SAS v.9.4 (SAS Institute; Cary, NC).

3.3.4 Investigation of Spatial Clusters

We investigated circular spatial clusters of high MI mortality risks using Kulldorff's circular spatial scan statistics (CSSS) implemented in FleXScan v 3.1.2 software, using age-adjusted MI mortality counts and a Poisson probability model specifying restricted likelihood ratio test (RLRT) to preclude absorption of counties with non-elevated risks into high-risk clusters [95]. We specified an alpha of 0.2 [96] and a maximum spatial cluster size of 34 counties, which corresponds to about half the number of counties in Florida. Additionally, we identified non-circular spatial clusters using Tango's flexible spatial scan statistics (FSSS) specifying a Poisson probability model again with a RLRT [182], an alpha of 0.2 and 34 counties as the maximum spatial cluster size. The FSSS generates irregularly shaped windows and is well-suited for irregularly shaped areas such as along Florida's rivers, lakes, and coastline. Clusters occurring in such areas would not be detected by the CSSS. We computed the mortality risks in significant ($p < 0.05$) clusters as the product of standardized mortality ratios and the crude MI mortality risk for Florida.

We investigated circular spatial clusters of low MI mortality risks using CSSS, implemented in SaTScan v 8.0 software. We used a discrete Poisson probability model while adjusting for age as a confounder and specifying non-overlapping, circular, purely spatial clusters of low risks. A maximum window size of 13.4% of Florida's population was used. This choice was based on the population of the largest county (Miami-Dade) to ensure that every county had a chance of being a cluster, while also minimizing the chance of identifying unrealistically large clusters that could comprise counties with high and/or non-elevated risks. Statistical inference was based on likelihood ratio test (LRT),

and the p-value was obtained through 999 Monte Carlo replications. Statistical significance was assessed at an alpha of 0.05.

3.3.5 Cartographic Display

We used ArcGIS Version 10.3.1 (ESRI, 2010) to perform all GIS manipulations, and to display all significant biologically meaningful clusters. Jenk's optimization classification scheme was used to determine the intervals for displaying SEB risks as choropleth maps. According to Prates *et al.* [98], spatial scan statistics has low power to detect clusters in low population density areas. Consequently, the relative risks (RR) for the spatial scan statistic may have an upward (for high-risk clusters) or downward (for low risk-clusters) bias, particularly when the population at risk is small. Accordingly, sparsely populated rural areas require a high RR to accurately detect the correct high-risk cluster, and a low RR to correctly detect low-risk cluster. Therefore, we considered significant high-risk clusters identified in rural and urban counties to be meaningful if the RR value was ≥1.3 and ≥1.2, respectively. On the other hand, we considered significant low-risk clusters identified in rural and urban counties to be meaningful if the RR value was ≤ 0.7 and ≤ 0.8, respectively.

3.3.6 Temporal Changes

We plotted mortality risks against time to examine the temporal trends, and calculated percentage change in mortality risks during the study period by computing the difference between the 2000 and 2014 risks and dividing the result by the 2000 risk. We assessed spatial disparities in MI mortality risks by comparing the magnitude of excess risks (i.e. the risk difference) in high-risk clusters at the beginning and at the end of the study, using the low-risk cluster with the lowest MI mortality risks as the baseline.

3.4 Results

3.4.1 Age-adjusted Risks

There were 58,198 MI deaths in Florida between 2000 and 2014. The overall annual age-adjusted MI mortality risks were 55.5 (2000-2002), 43.8 (2003-2005), 33.1 (2006-2008), 29.8 (2009-2011), and 28.1 (2012-2014) deaths/100,000 population over the study period. This represented an overall decrease of 48% in MI mortality risks during the period of interest.

3.4.2 Spatial Patterns

3.4.2.1 Sex and Age Adjusted Risks

The temporal changes in geographic distribution of SEB risks are shown in Figure 3.1. The risks declined during the study period and ranged from 28.1-149.6 deaths/100,000 population at the beginning of the study to 17.7-56.7 deaths/100,000

population at the end of the study. Although the risks decreased throughout the state during the study period, counties in the north had consistently higher MI mortality risks than those in the south. There was also a clear urban-rural divide, with the rural north having the highest risks and the urban south having the lowest risks throughout the study period. Moreover, the proportion of northern counties in the two highest quintiles increased from 16% in 2000-2002 to 36% in 2012-2014. No such changes were visible in the south.

3.4.2.2 Kulldorff's Circular Spatial Clusters (CSSS)

Figures 3.2 and 3.3 show the geographic distribution circular spatial clusters of high and low MI mortality risks. Consistent with the visual patterns of SEB smoothed risks (Figure 3.1), the Kulldorff's CSSS identified large clusters of high MI mortality risks predominantly in the north (Figure 3.2) and large low-risk clusters predominantly in South Florida (Figure 3.3). A total of 6-11 high-risk clusters were identified during each of the three-year time intervals between 2000 and 2014. The largest high-risk clusters were located in northwest and north central parts of Florida (Figure 3.2), which are predominantly rural (Figure 3.4) based on the Florida Department of Health Office of Rural Health definition of rural areas (i.e. population density < 100 people/sq. mile) [191]. Smaller high-risk clusters were identified in Central, West Central, Northeast, and Southeast Florida, with the urban high-risk cluster in Miami-Dade County being the most prominent (Figure 3.2). A total of 3-6 low-risk clusters, were identified. Large low-risk clusters were located mostly in urban counties in the southeast and southwest (Figures 3.2 and 3.3). A few smaller clusters were identified in Northwest, Northeast, Central, and West Central Florida.

Figures 3.2 and 3.3 also show that 4-5 high-risk clusters and 2 low-risk clusters persisted throughout the study period. Clusters with persistently high mortality risks were located in the Northwest, North Central, and Southeast Florida. Counties that persisted in the high-risk clusters in the northwest included Holmes, Jackson, and Washington counties. Walton County was part of that cluster in all the three-year time intervals with the exception of the 2006-2008 period. Two persistent high-risk clusters were identified in North Central Florida. The larger cluster comprised Columbia, Dixie, Gilchrist, Hamilton, and Suwannee counties, and the smaller cluster comprised Citrus and Levy counties. The Miami-Dade cluster also persisted throughout the study period. Counties that persisted in the low-risk cluster in Southeast Florida included Indian River, St. Lucie, Martin, and Palm Beach. Collier, Hendry, and Lee counties persisted in the low-risk cluster in Southwest Florida.

Substantial changes in cluster status occurred in North and Central Florida, with several counties that were not a part of any cluster at the beginning of the study transitioning to high-risk clusters by the end of the study. These included Calhoun, Duval, Escambia, Gulf, Lafayette, Madison, Nassau, Okaloosa, and Wakulla counties in North Florida and Lake, Okeechobee, and Volusia counties in Central Florida. The opposite trend was also observed, where some counties in Central (Brevard, Osceola, and Sumter) and Southeast Florida (Broward) transitioned from high-risk clusters at the beginning to not being part of any cluster at the end of the study. Transitions of counties to low-risk

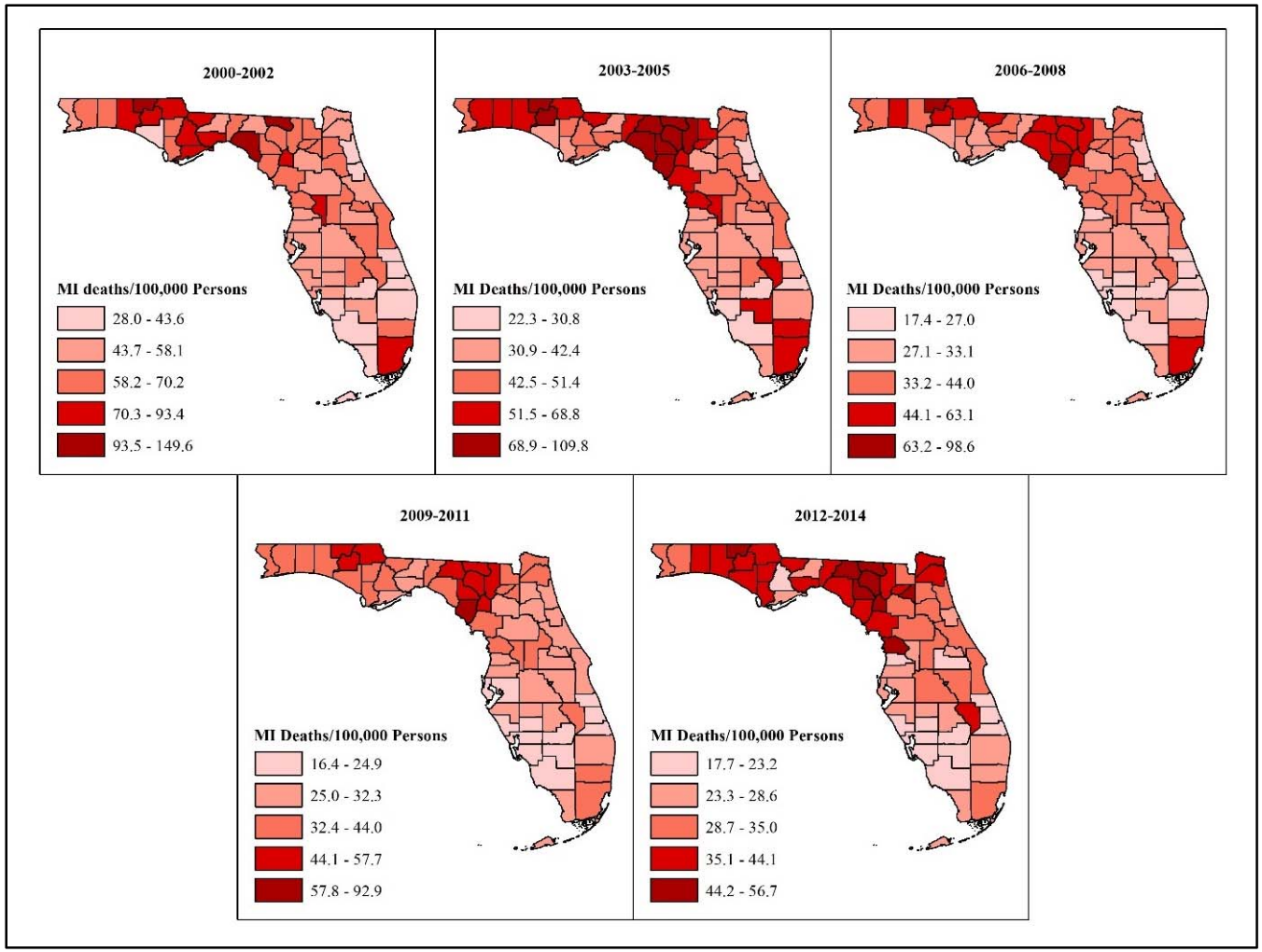


Figure 3.1. County-level age-adjusted Spatial Empirical Bayes smoothed myocardial infarction mortality risks in Florida, 2000-2014.

clusters were less frequent, with only Seminole County in Central Florida transitioning from a high- to low-risk cluster, and Charlotte, DeSoto, Glades, and Sarasota counties in Southwest Florida transitioning from no-cluster to low-risk cluster. The lone low-risk cluster identified in Northwest Florida in Bay County in the 2000-2002 period transitioned to a high-risk cluster by the 2012-2014 period.

There were considerable variations in RRs among the clusters, ranging from 1.2 to 2.4 among the high-risk clusters, and from 0.5 to 0.8 among low-risk clusters.

3.4.2.3 Tango's Circular and Non-circular Spatial Clusters (FSSS)

The geographic distributions of high-risk circular and non-circular clusters identified using Tango's flexible spatial scan statistics are presented in Figure 3.5. While the location of clusters and the general patterns of clustering of MI risks identified using Tango's FSSS (Figure 3.5) mirrored those of clusters identified using Kulldorff's CSSS (Figure 3.2), fewer clusters were identified using FSSS (3-5 clusters) than CSSS (6-11 clusters). The FSSS also resulted in larger clusters, often comprising all counties identified using CSSS plus additional counties. The RRs among clusters identified using FSSS were lower than those identified using CSSS (Figure 3.5).

3.4.3 Temporal Changes

The temporal changes in MI mortality risks among persistent CSSS clusters are shown in Figure 3.6. Overall, MI mortality risks decreased by 48%, which is equivalent to an average rate of decline of 3.2%/year. MI mortality risks decreased more rapidly (4.1%/year) between 2000 and 2008, after which (2009-2014) they decreased by a meagre 0.8%/year.

Declines in MI mortality risks showed considerable variation among clusters and ranged from 35% to 42% in low-risk clusters and from 30% to 61% in high-risk clusters. This resulted in average rates of decline of 2.3-2.8%/year and 2.0-4.1% per year in low- and high-risk clusters, respectively. It is interesting to note that mortality risks in the high-risk cluster in North Central Florida decreased at a lower rate (2.0%/year) than in the two low-risk clusters (2.3%-2.8%). Similar to the temporal pattern observed for the entire, state, there were more dramatic declines in mortality risks in both high- (2.7-4.6%/year) and low-risk (2.3-4.3%/year) clusters during the first nine years of the study. Thereafter, the rates of decline slowed to 0.4-2.3%/year, with the high-risk cluster in North Central Florida showing the slowest rate of decline despite having the highest MI mortality risk.
The patterns of temporal changes in MI mortality risks in high-risk circular and non-circular FSSS clusters that persisted during the study period (Figure 3.6) are generally similar to the patterns observed for high-risk CSSS circular clusters. The largest decline occurred in the high-risk cluster in Northwest Florida (59%), followed by the high-risk cluster in Southeast Florida (51%) and then the high-risk cluster in North Central Florida (42%). As with CSSS clusters, MI mortality risks decreased rapidly during the first nine years of the study, after which they declined at a substantially lower rate. There are early signs that MI mortality risks in the high-risk cluster in North Central Florida could be on an upward trend.

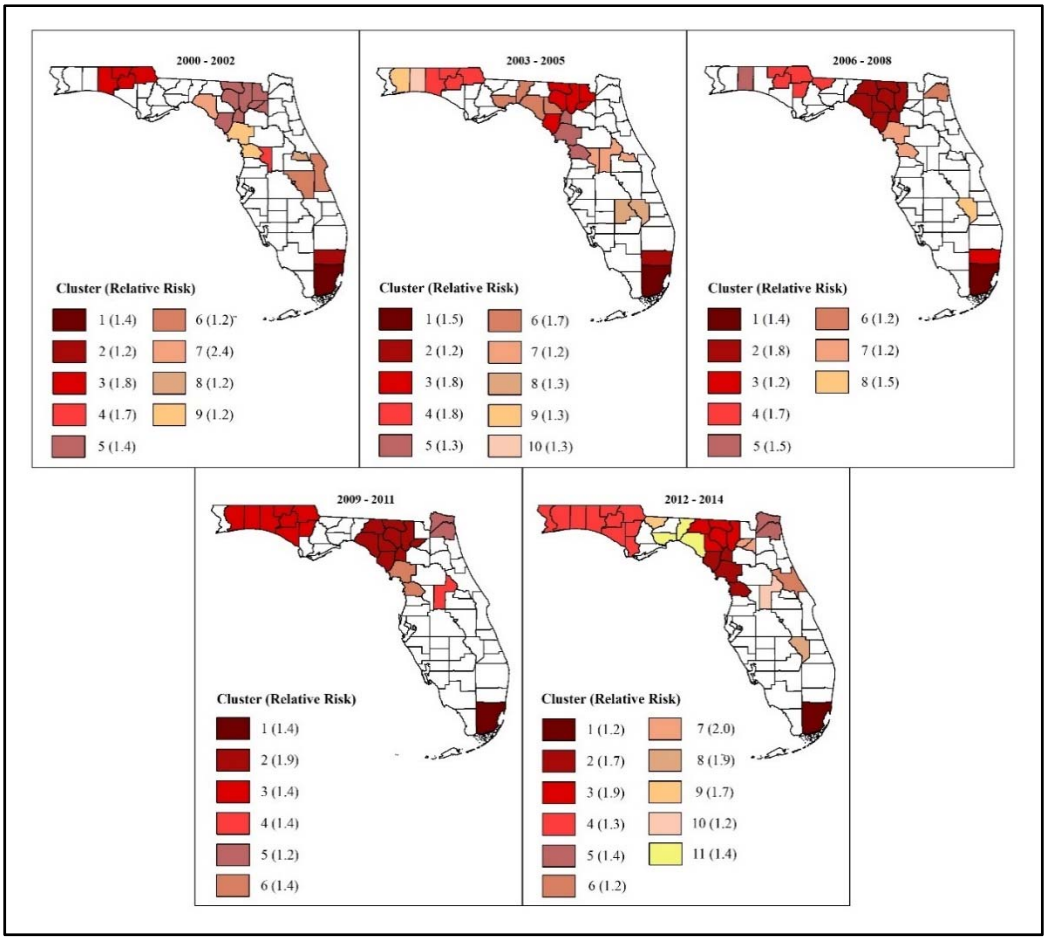


Figure 3.2. Spatial circular clusters of high myocardial infarction mortality risks in Florida, 2000-2014.

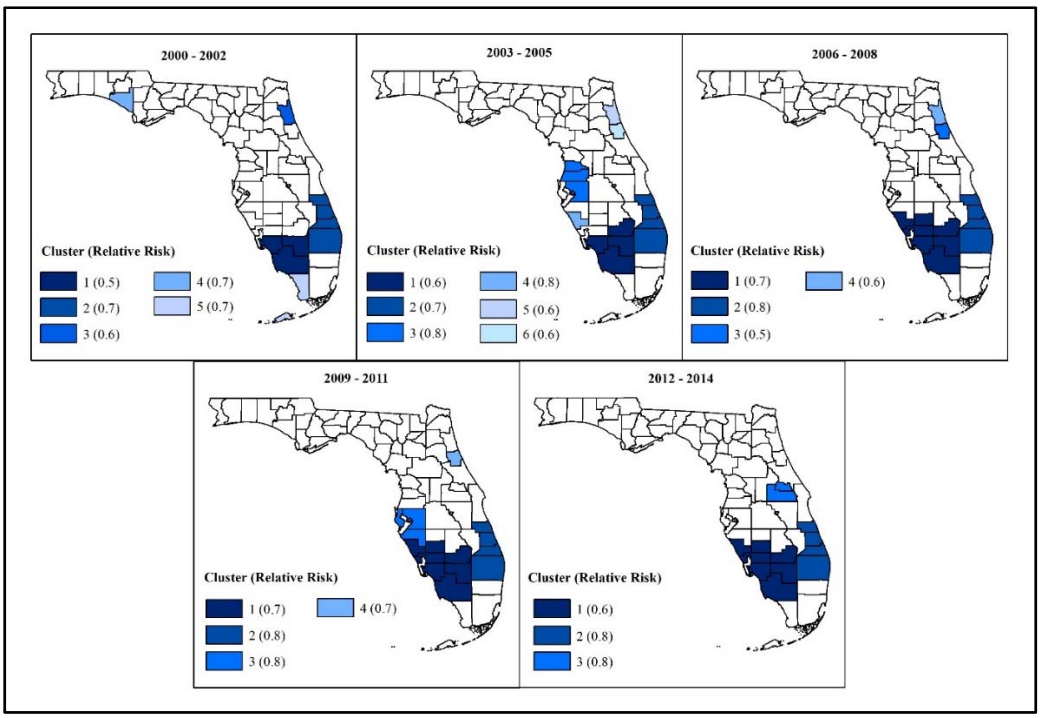


Figure 3.3. Spatial circular clusters of low myocardial infarction mortality risks in Florida, 2000-2014.

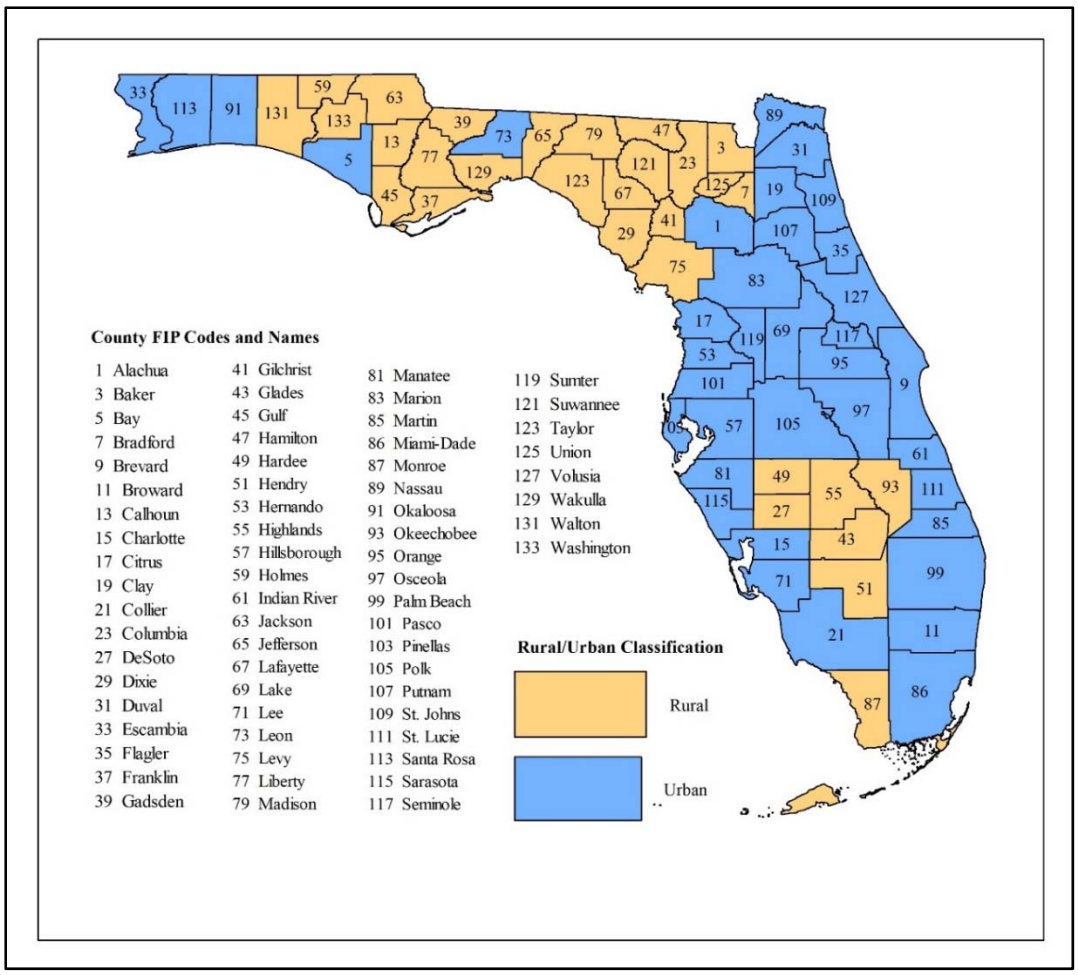


Figure 3.4. Florida counties and their rural/urban classification based on Florida Department of Health Office of Rural Health definition of rural county.

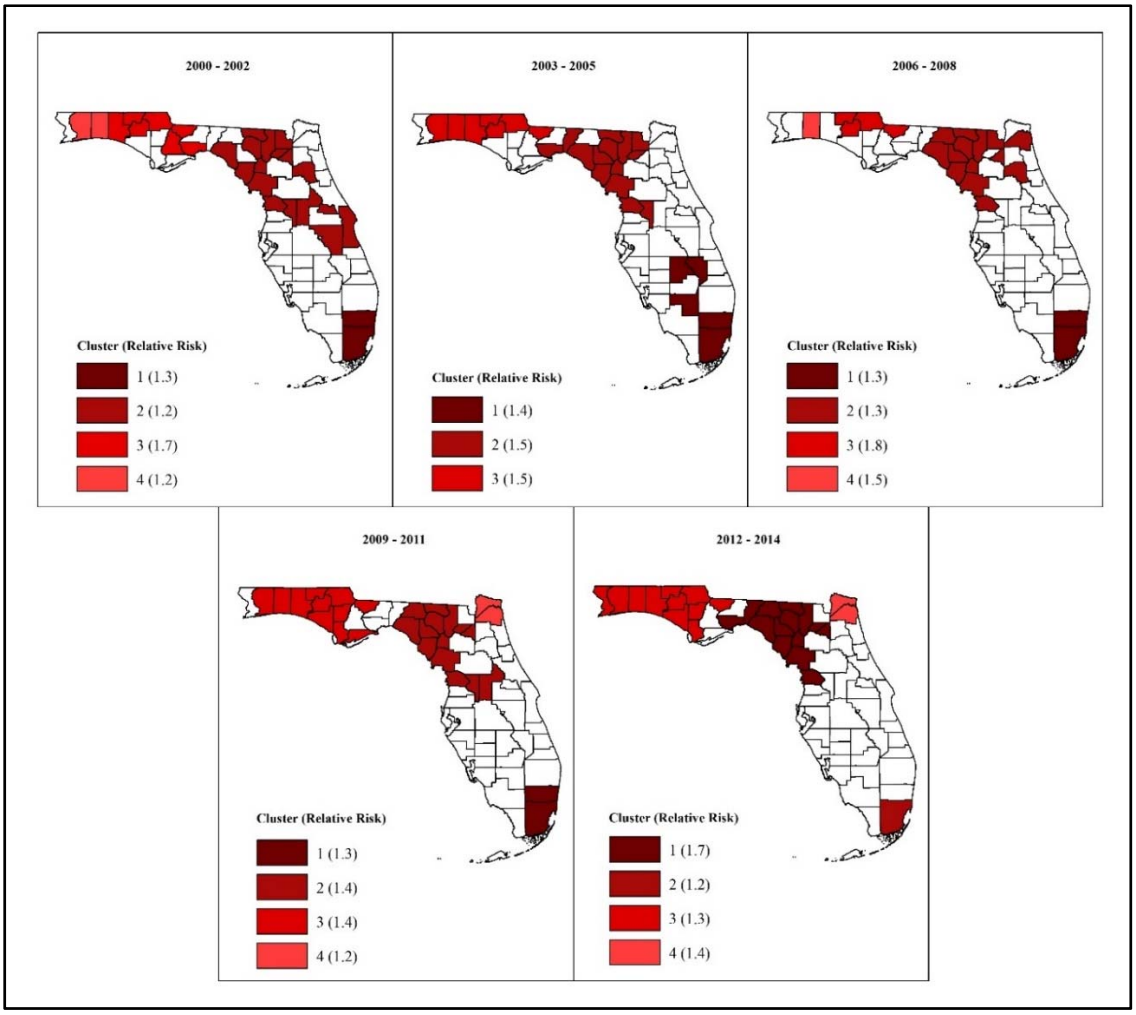


Figure 3.5. Circular and non-circular spatial clusters of high myocardial infarction mortality risks in Florida, 2000-2014.

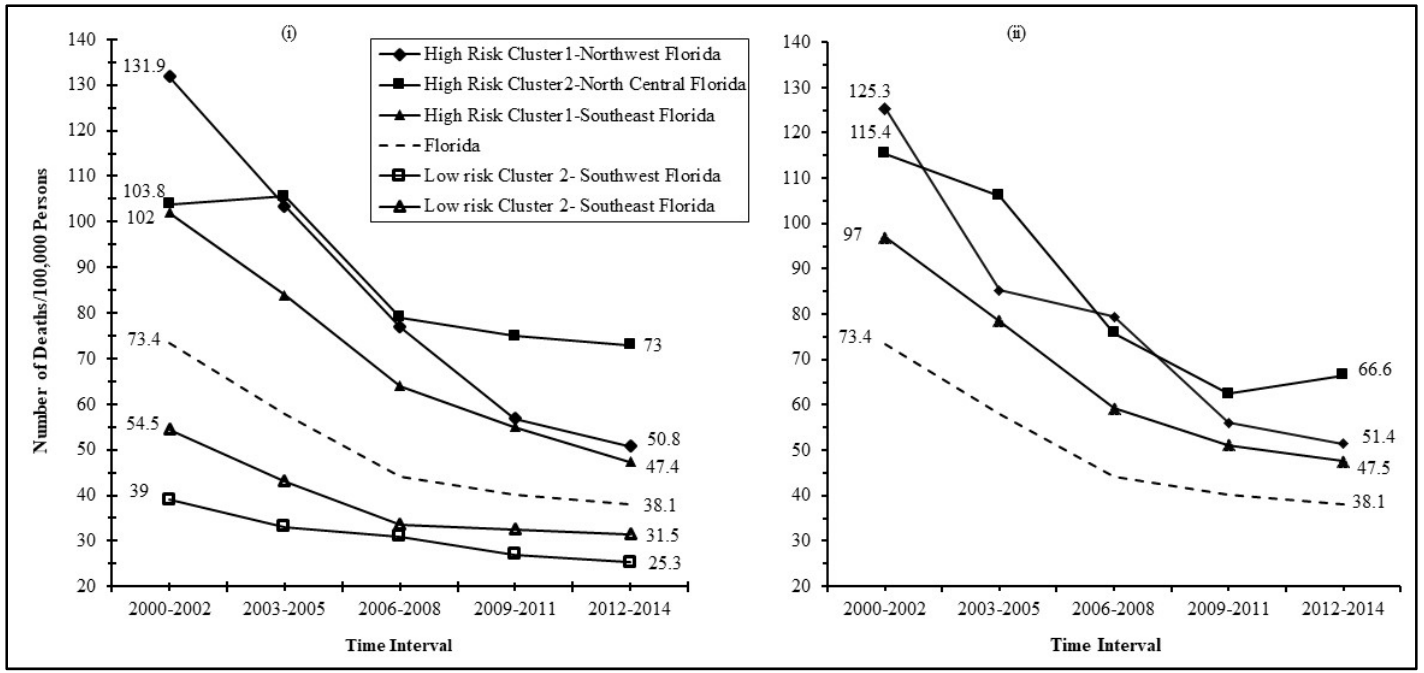


Figure 3.6. Changes in annual myocardial infarction mortality risks in persistent high- and low-risk (i) Kulldorff's circular and (ii) Tango's circular and non-circular spatial clusters, Florida 2000-2014.

Generally, MI mortality risks decreased more rapidly in high- than in low-risk clusters during the early portion of the study (2000-2008), and at a similar rate in both high- and low-risk clusters thereafter (2009-2014). This resulted in lower disparities in MI mortality risks between high- and low-risk clusters at the end than at the beginning of the study period (Figure 3.6). For instance, the risk difference (RD) between the high-risk cluster in Northwest Florida and the referent low-risk cluster in the Southwest Florida decreased by 73% from 92.9 deaths/100,000 persons in 2000-2002 to 25.5 deaths/100,000 persons in 2012-2014. The RD between the high-risk cluster in Southeast Florida and the referent low-risk cluster showed a relatively similar reduction, decreasing by 65% from 63 deaths/100,000 persons at the beginning of the study to 22.1 deaths/100,000 persons at the end of the study. The RD between the high-risk cluster in North Central Florida and the low-risk cluster in Southwest Florida decreased by 26% from 64.8 deaths/100,000 persons at the beginning of the study period to 47.7 deaths/100,000 persons at the end the study.

In spite of the impressive declines, annual MI mortality risks for the high-risk clusters in Northwest and Southeast Florida at the end of the study period (47.4-50.8 deaths/100,000 persons) were at par with mortality risks observed in the low-risk clusters at the beginning of the study period (39.0-54.5 deaths/100,000 persons). This implies that MI mortality risks for counties in high-risk clusters lagged behind those for counties in low-risk clusters by 1.5 decades. Moreover, the annual MI mortality risk observed in the high-risk cluster in North Central Florida at the end of the study period (73 deaths/100,000 persons) was substantially higher than the risk for the referent low-risk clusters (39 deaths/100,000 persons) at the beginning of the study period. Thus, counties in the high-risk cluster in North Central Florida lagged behind counties in the low-risk clusters by over 1.5 decades.

3.5 Discussion

We investigated geographic distribution and spatial clusters of MI mortality risks in Florida over a period of 15 years. We also identified communities with consistently high MI burden over the study period. Study findings will be useful for guiding resource allocation for intervention programs. Florida has a racially and ethnically diverse population with large proportions of minority, immigrant, and elderly populations; hence, it foreshadows the demographic structure projected for the US population by the year 2030 [192]. Therefore, Florida's strategy to address the high MI burden will not only be critical to Florida's future, but it will be instructive for the rest of the US.

Similar to other studies using county-level data to assess cardiovascular mortality disparities across the US [39,41], this study found disparities in the burden of MI across Florida, with the north having the highest mortality risks while the south had the lowest risks. This is consistent with the shift in the concentration of counties with high rates of heart disease-related mortality from Northeastern US to socioeconomically disadvantaged areas in the Deep South that was observed by Casper et al. [39] over a 40-year period.

The identification of high-risk clusters mainly in rural north and low-risk clusters almost exclusively in urban south suggests that different segments of Florida's population

have not benefitted equitably from preventive and treatment efforts. Moreover, these findings mirror those of stroke mortality risks in Florida between 1992 and 2012 [78]. Other studies have also reported disparities in MI/heart disease-related mortality risks in southeastern US based on rurality. For instance, Casper et al. [39] also identified a large persistent low-rate cluster of heart disease mortality in urban counties in southern Florida and 1-2 high-rate clusters in the rural north between 1972 and 2010. Roth et al. [41], also reported clustering of low risks of CVD and ischemic heart disease mortality in South Florida counties and clustering of high risks in North Florida counties in 2014. Odoi and Busigye [60] reported higher MI-mortality risks in rural than in urban neighborhoods in middle Tennessee. Higher mortality rates for CHD, the principal cause for MI, have also been reported for rural/non-metro areas compared to urban/metro areas in southern US [193]. By contrast, Pedigo et al. [62] reported higher odds of urban and suburban neighborhoods being in a high-risk cluster than rural neighborhoods.

We did not investigate the determinants of the identified geographic disparities. However, based on findings from previous studies, the disparities may be associated with disparities in distribution of MI risk factors and access to preventive and treatment services. For instance, rural communities generally have lower prevalence of physical activity [194] and good dietary habits [195] compared to urban populations. Moreover, increased mechanization and automation of farm work has reduced the amount of physically demanding occupations in rural areas [196], making rural lifestyle more sedentary [197]. These contribute to higher risks of obesity, hypertension and diabetes, which lead to higher MI-mortality risks in rural than urban areas. By contrast, the prevalence of nonsmoking, normal body weight, and physical activity, etc., are higher in urban than rural counties in US [149].

Most North Florida counties are rural, sparsely populated, medically underserved [198,199], and have low rates of health insurance coverage [200]. Since health funding is allocated based on population, rural counties tend to have limited resources for adequate prevention and management of CVD and its risk factors [201]. The distribution of health workforce is also geographically skewed, with rural counties having inadequate supply of general practitioners [202] and cardiac specialist [80]. Moreover, cardiac centers tend to be clustered in urban centers [170], leading to long travel times and poor MI outcomes.

Socioeconomic status (SES) is one of the most reliable predictors of cardiovascular health disparities, with people of low SES experiencing higher mortality from MI and other cardiovascular health outcome [66]. Clustering of CVD risk factors has been reported among US residents with low SES [203]. Socioeconomic status may also contribute to disparities in MI mortality risks by shaping exposure to unhealthy behaviors during childhood [204]. Since a majority of counties in North Florida have poor socioeconomic conditions [205], it is likely that lower SES for rural residents made them less likely to adopt and, therefore, benefit from improvements in prevention and control programs for MI [206], contributing to higher MI mortality risks in rural areas.

The composition of the populations in the different geographic regions is an important factor that may have also contributed to the disparities in MI mortality risks. North Florida has a higher proportion of African Americans than the rest of Florida [207]. African Americans tend to have higher burdens of MI [208] because they are less likely

to receive certain cardiovascular interventions than Whites [209] and as a result of stressors associated with systematic segregation in socioeconomically deprived neighborhoods during critical life stages [210]. In addition to traditional MI risk factors, environmental exposures such as higher, more variable temperatures in the north than the south [211], may have contributed to higher MI mortality risks in the north [212].

The identification of the lone high-risk cluster in Miami-Dade County was surprising because, unlike other persistent high-risk clusters, it occurred in an urban county with a relatively younger population compared to Florida. Additionally, unlike the other persistent high-risk clusters, the Miami-Dade cluster was not identified in earlier county-level studies investigating geographic disparities in heart disease [39] and ischemic heart disease [41] in the US. However, the county has a high prevalence of other major risk factors for MI including hypertension (32.6%), high blood cholesterol (32.2%) overweight/obesity (87.2%), and physical inactivity (56.7%) [163]. Additionally, Miami-Dade County has a high proportion of socioeconomically-disadvantaged, immigrant, minority, uninsured/underinsured population [165]. However, despite the high prevalence of MI risk factors and high under/uninsured rates, utilization rates for low-cost health care programs, such as the Federally Qualified Health Centers, are very low [165]. Therefore, low levels of utilization healthcare services and poorer control of hypertension and other modifiable risk factors for MI may also explain the presence of this cluster.

The reasons for the persistence of some counties in high- or low-risk clusters throughout the 15-year study period are not clear. However, persistence may be reflective of a lack of temporal changes in the geographic patterns for MI risk factors such as prevalence of cigarette smoking [132], hypertension [156], obesity, physical inactivity [131], and socioeconomic factors [213] reported in US counties.

The observed declines in MI mortality risks during the study period imply that population-wide preventive and control efforts to reduce the MI burden have had positive impacts across Florida [23]. These findings are consistent with those of other studies in the US that have shown steady declines in overall MI/CHD-related deaths at the national [21] and regional levels [22]. That a reduction in the prevalence of major risk factors contributed to reduced MI mortality risks in Florida was partly corroborated by a study that reported an 8.8% reduction in MI mortality rates in the state in 2004 following the implementation of the smoke-free ordinance in 2003. Three years prior to the ordinance, the rates declined at only 6.4% per year [214]. However, persistent clustering of MI-mortality risks, coupled with differences in rates of declines among clusters and over time indicate that geographic disparities still exist.

Disparities in geographic patterns and magnitude of rates of declines in MI mortality risks suggest that factors influencing the rates of MI mortality decline are not equitable across the state. According to Phelan et al. [206], the differential rates of decline in MI mortality risks among clusters may be related to disparities in access to social resources that influence adoption and/or the ability to benefit from improvements in MI prevention and control strategies.

The observed decline in MI mortality risks represents remarkable progress in reducing the burden of MI across Florida and is encouraging. However, in light of the fact that elimination of health disparities is one of the goals of the Healthy People 2020 national public health agenda [4], the levelling off of rates of declines from 2009-2014 is

concerning. Thus, the goal of reducing CVD deaths by 20% by 2020 appears elusive. It is interesting to note that these results mirror the recent temporal trends reported for heart disease deaths in the US. For instance, Ma et al. [215] reported an annual rate of decline of heart disease deaths of 3.9% from 2000-2010, and a much slower annual rate of 1.4% from 2010-2013. Sidney et al. [216] reported annual rates of decline of CVD mortality of 3.8% and 0.7% between 2000-2011 and 2011-2014, respectively. Cardiovascular disease death rates decreased at an average of 3.7% per year between 2000 and 2011 and at less than 1%/year between 2012 and 2014, after which the rates actually increased by 1% in 2015 [186]. A deceleration in decrease in CHD mortality rates in the US was also reported between 2012-2015 [24]. These changes in the trajectory of MI and heart disease burden may be due to slowed progression in the favorable trends of MI prevention and/or treatment, coupled with an aging population and dramatic increases in the risks of obesity, hypertension, and diabetes mellitus over the past 25 years [74]. Capewell et al. [217] showed that improvements in survival among CHD patients in the US associated with decreases in the prevalence of CHD risk factors in the wider population were partially offset by increases in the prevalence of obesity and diabetes.

The fact that MI mortality risks for high-risk clusters at the end of the study (2012-2014) were at par with, or higher than the risks in low-risk clusters at the beginning of the study (2000-2002 period) indicates that counties in high-risk clusters lagged behind those in low-risk clusters in the south by at least 1.5 decades in reducing MI-mortality risks. Assuming a continuing downward trend, this implies that high-risk counties would require at least 15 additional years to achieve mortality risks seen in low-risk counties during the 2012-2014 period.

3.6 Strengths and Limitations

This study uses novel analytic methods to obtain a more complete understanding of disparities in the MI burden in Florida. Using SEBs age-adjusted MI mortality risks allows for adjustments for county-level sample size resulting in more stable estimates of MI mortality risks. The use of a FSSS with a restricted likelihood ratio [182] results in the detection of both circular and non-circular clusters. Non-circular clusters would otherwise not be detected by the more common and widely used CSSS. Thus, use of FSSS reduces false negatives in cluster identification [183], and hence potentially results in better targeting of control efforts. Additionally, using a restricted log likelihood ratio test instead of log likelihood ratio limited the number of false positives, which also results in better targeting of preventive and control efforts.

This study is not without limitations. First, we chose to study counties rather than smaller geographic areas such as ZIP codes because the county is the smallest geographic area for which annual population estimates are available from the Florida Legislature's Office of Economic and Demographic Research. The county is also more relevant to policy action steps. However, the choice of the county as the sampling unit means that study design is prone to ecologic fallacy. Thus, study findings need to be interpreted with caution, ensuring that all causal inferences are made at the county level and not at the individual level. Additionally, counties are heterogenous with respect to geographic, socio-demographic, and environmental factors, hence summarizing the data

by county may have masked intra-county disparities in MI mortality risks, which could be large [218]. Therefore, local health planning could benefit from analyses at lower geographic units such as 5-digit zip code or Census tracts or blocks, and this study may be used to guide future small-area studies.

Second, there is potential for geographic variation in diagnosis and reporting of MI as the underlying cause of death, which could lead to misclassification bias [219]. Third, the study did not capture the full burden of MI mortality in Florida, since the analysis was limited to Florida residents, as denominator data were not available to estimate the non-resident population.

Fourth, the study did not investigate the determinants of the observed spatiotemporal disparities in MI-mortality risks. Therefore, follow-up studies will need to identify those factors especially in the high-risk clusters, and to investigate the drivers of the worrisome trends reflecting a stagnation or even a decrease in rates of decline in MI mortality risks in parts of North Florida. Identification of these determinants would provide crucial information for planning and guiding future health policy and control programs for MI and other CVD with similar risk factors as MI. Moreover, investigations of counties within low-risk clusters may provide insights regarding the protective factors contributing to lower than expected MI mortality risks in those counties.

Fifth, due to rapidly changing demographic trends including population aging, changes in racial and ethnic composition of the population, shifts in household and family structures, and rapid population growth, the study results may not accurately reflect the current reality in the State of Florida. Unfortunately, the most current MI mortality data were not available when the study was initiated.

Lastly, the use of the likelihood ratio test to identify low-risk clusters may have resulted in clusters with higher relative risks than would otherwise be obtained with the restricted likelihood ratio test. This implies that the disparities in MI mortality risks between high- and low-risk clusters could actually be larger than estimated. The methodology for detecting circular and non-circular spatial clusters within the FleXScan software needs further development to mitigate this limitation.

3.7 Conclusions

There was substantial progress in reducing the overall MI burden and disparities in MI mortality risks in Florida over time. However, there are persistent geographical disparities, with high-risk clusters occurring primarily in rural northern counties and low-risk clusters occurring exclusively in urban southern counties. Moreover, the reduction in MI death risks in the north lagged behind that in the south by at least 1.5 decades. Since counties within high-risk clusters account for a sizeable proportion of the total population in Florida, prevention and control strategies should be targeted to those counties to maximize efficiency and effectiveness of interventions geared towards reducing health disparities and improving health for all Floridians. Moreover, MI shares similar risk factors with other CVD such as stroke; hence, these health conditions tend to have similar geographic distribution. Thus, public efforts targeting those counties we identified as having persistently high MI risks would address not only MI disparities but also stroke and several of their risk factors such as diabetes, high blood pressure, etc. It is critical that

planning and public health programs need to be guided by empirical evidence such as findings from this study so as to better address issues of health inequity and improve health for all.

CHAPTER 4
SOCIODEMOGRAPHIC DETERMINANTS OF ACUTE MYOCARDIAL INFARCTION HOSPITALIZATION RISKS IN FLORIDA

A version of this chapter was revised and re-submitted to the Journal of American Heart Association on November 7, 2019, and is currently under the second round of review. The abstract is also published in Circulation and is available in: Circulation. Vol 139, Issue Suppl_1: AP208 https://doi.org/10.1161/circ.139.suppl_1.P208.

The use of “we” in this chapter refers to Drs. Nicholas Nagle, Russell Zaretzki and Kristina Kintziger, Melissa Jordan, Chris Duclos, and myself. As the first author, I participated in study design, and performed statistical analyses, interpreted the results and drafted the manuscript. Dr. Kintziger also helped with study design. All authors critically reviewed the study design and analysis plans, as well as the manuscript and provided helpful feedback.

4.1 Abstract

Background: Identifying determinants of myocardial infarction (MI) risks is crucial for guiding efforts to reduce MI disparities. Therefore, our objectives were to identify sociodemographic determinants of MI hospitalization risks and to assess if the impacts of these determinants vary by geographic location in Florida.
Methods: We obtained data for principal and secondary MI hospitalizations that occurred among Florida residents between 2005 and 2014 from the Florida Department of Health, and calculated county-level age-and sex-adjusted MI hospitalization risks. We used a multivariable global negative binomial model to identify sociodemographic determinants of MI hospitalization risks, and then used a local geographically weighted negative binomial model to assess if regression coefficients vary by geographical location.
Results: MI hospitalization risks were significantly greater in counties with high proportions of residents with less than high school education level ($p<0.0001$) and divorced residents ($p=0.018$). However, they were significantly lower in counties with high proportions of rural ($p<0.0001$), African American ($p=0.032$), and uninsured residents ($p=0.040$). The regression coefficients for proportions of uninsured residents and population with less than high school education level varied geographically, with the strongest associations occurring in southern Florida counties.
Conclusions: Race, marital status, education level, rural residence, and lack of health insurance were significant determinants of MI hospitalization risks, but the impacts of education level and lack of health insurance were stronger in southern Florida. Thus, policies and interventions for reducing MI morbidity and improving access to MI care in Florida need to consider social contexts and allocate resources based on empirical evidence from global and local models to maximize their efficiency and effectiveness.
Key Words: myocardial infarction, hospitalization risks, socioeconomic determinants, geographically weighted regression.

4.2 Background

Cardiovascular disease (CVD) is the leading cause of morbidity in the US [1]. Acute myocardial infarction (MI), or heart attack, contributes significantly to this burden, particularly in southeastern US [26,220], such as Florida, where 6.0 and 12% of the state’s

adult and older adult (over 65 years old) populations, respectively, reported a history of acute MI in 2018 [130,187]. By comparison, 5% of the US adult population reported a history of acute MI in 2018 [48,130,221].

Past MI prevention and treatment efforts have resulted in substantial reductions in the overall burden of MI hospitalizations among various population groups across the US [12,17-19,38]. In Florida, age-adjusted MI hospitalization risks decreased by 33% between 2000 and 2014 [222]. However, these declines may overstate the success of preventive and control efforts in reducing the burden of MI morbidity, since the analyses did not consider cases where MI was coded as secondary discharge diagnosis [47]. It is useful to know the extent of morbidity attributable to MI, regardless of whether it is the primary or secondary cause of hospitalization.

Mounting evidence from ecologic studies indicate that the prevalence of area-level socioeconomic determinants of health (SDoH) can affect the types of exposures and/or access to healthcare that one experiences, and hence the risk of MI in a given population [223,224]. According to Bookse et al. [67], SDoH are responsible for shaping 40% of the health of a population, and they also strongly influence health behaviors, the second greatest contributor to health and longevity. Therefore, SDoH are fundamental drivers of persistent health disparities, and are the underlying causes of geographic disparities in MI prevention and treatment [26]. Accordingly, it has been suggested that identifying and dealing with SDoH offers the greatest opportunities for reducing morbidity, deaths and disability from MI and other CVD, and achieving lasting improvements in population health at the lowest cost [223]. Therefore, identifying specific SDoH predictors of MI hospitalizations may provide clues regarding the distal causes of MI and aid in the development of evidence-based strategies for MI prevention leading to reduced health disparities and improved population health.

Studies of associations of health events and SDoH factors are traditionally performed using aspatial global models that implicitly assume constant effects of explanatory variables across the study area. As such, they estimate a single coefficient for each explanatory variable averaged over the entire study area. However, a number of studies have shown that the influence of SDoH factors on the risks of cardiovascular health outcomes [60,225,226] vary by geographic location. Therefore, it is highly unlikely that associations between MI hospitalization risks and SDoH factors would be realistically reflected by global models. Rather, due to substantial local variations in the sociodemographic characteristics of the population in Florida, it is more plausible for the influence of SDoH factors to vary geographically, with some factors being more important determinants of MI hospitalization risks at certain locations but less important at other locations [70]. Therefore, identifying the most important determinants of MI hospitalization risks for different geographic areas may aid in the development of location-specific strategies for MI prevention, which is critical for efficient allocation of scarce resources. Therefore, the objectives of this study were to identify sociodemographic determinants of disparities in MI hospitalization risks and to assess if the effect of these determinants vary by geographic location in Florida.

4.3 Methods

4.3.1 Study Design and Population

This was a retrospective ecologic study using Florida MI hospitalization data for the period January 1, 2005, to December 31, 2014. The study population included all Florida residents with in-patient hospitalizations admitted with any MI discharge diagnosis (i.e., principal or a secondary) *International Classification of Diseases*, ninth revision (ICD-9-CM) diagnostic code 410, but it did not include Veterans Affairs, Indian Health Services, prison populations, or state-owned facilities.

4.3.2 Data Sources and Data Preparation

4.3.2.1 Hospital Discharge Data

Individual-level MI hospitalization data, collected by the Florida Agency for Health Care Administration (AHCA), were obtained from the Florida Department of Health (DOH). We extracted the following variables: admission date, discharge date, primary diagnosis and up to 30 secondary diagnoses to enable extraction of cases with a secondary MI diagnosis, patient age, sex, race/ethnicity, and county of residence. We used the county as the geographic unit of analysis.

The MI data for Florida and each county were aggregated by sex and age (i.e., 0-34, 35-44, 45-54, 55-64 and ≥65 years) for each year and for the entire 10-year study period, respectively. These data were used as numerator data for calculating both sex- and age-specific MI hospitalization risks and for risk-adjustment. To assess seasonal trends, the state-level MI data for each year were also aggregated by season and year.

4.3.2.2 Population Data

We downloaded annual population estimates by sex, race/ethnicity, and age groups matching the MI hospitalization data from DOH [88]. We used these as denominator data for calculating attribute-specific MI hospitalization risks for Florida for the entire study period. Annual county-level population estimates for age and sex categories matching hospitalization data (i.e., 0-34, 35-44, 45-54, 55-64 and ≥65 year-olds) were also obtained from DOH [88] and used as denominator data for calculating age- and sex-adjusted annual MI hospitalization risks. We downloaded 2000 and 2010 decennial data for the US population from US Census Bureau, American FactFinder website [90].

4.3.2.3 Cartographic Boundary Files

We downloaded county-level cartographic boundary shape files for 2010 from the US Census Bureau website [92]. These were used as base maps for all cartographic displays.

4.3.2.4 Socioeconomic and Demographic Data

Five-year (2008-2012) American Community Survey estimates for several sociodemographic variables related to race/ethnicity, marital status, place of residence, education level, health insurance, employment and economic status of the population in each county were also pulled from the US Census Bureau via the American FactFinder website [227]. We used 5-year estimates for the 2008-2012 period because it is in the middle of our study period, hence we deemed data for this period best suited to match the MI hospitalization data.

4.3.3 Conceptual Model Used to Guide Selection of Potential Determinants of MI

We built a conceptual causal web model (Figure 4.1) to guide the selection of potential SDoH study variables. The variables of interest were selected based on hypothesized associations with MI hospitalization risks and they included: proportion of population with less than high school education; proportion of population living below poverty level; median income; proportion of population living in owner-occupied housing; unemployment rate for population aged ≥16 years old; proportion of uninsured population; proportion of population classified as rural/urban; proportion of population aged 65 years and older; proportion of population classified as White, African American or Hispanic; proportion of widowed, married, divorced, separated, and never married populations; and proportion male population.

4.3.4 Statistical Analysis

4.3.4.1 Summary Statistics

We computed the percent of MI hospitalizations by age (0–34, 35–44, 45–54, 55–64, and ≥65 years), gender (male and female), and ethnicity (White, Hispanic and Black), as well as factor-specific MI hospitalization risks for the different demographic groups. We also computed summary statistics including median or mean, minimum and maximum values for all SDoH variables. All descriptive statistics were done in SAS v.9.4 (SAS Institute Inc., Cary, NC).

Myocardial infarction hospitalization risks were age- and sex-adjusted to the 2010 US Census standard population [89] to allow for valid comparisons of risks across different counties and years. We used the 2010 US census population for risk adjustment. This is because while the 2000 US population is recommended for age-adjustment of age-dependent health events [89], the 2010 US population represents the most recent actual age compositions of the US population, and it also falls within the range of our data collection. Moreover, since the risk of MI increases with age, using a standard population with a lower proportion of older ages could yield lower age-adjusted risks [91]. Thus, 2010 US census population may provide us with more realistic and more current risk estimates.

Finally, we computed seasonal MI hospitalization risks by defining seasons: winter (December 1 to Feb 28/29); spring (March 1 to May 31); summer (June 1 to August 31); fall (September 1 to November 30).

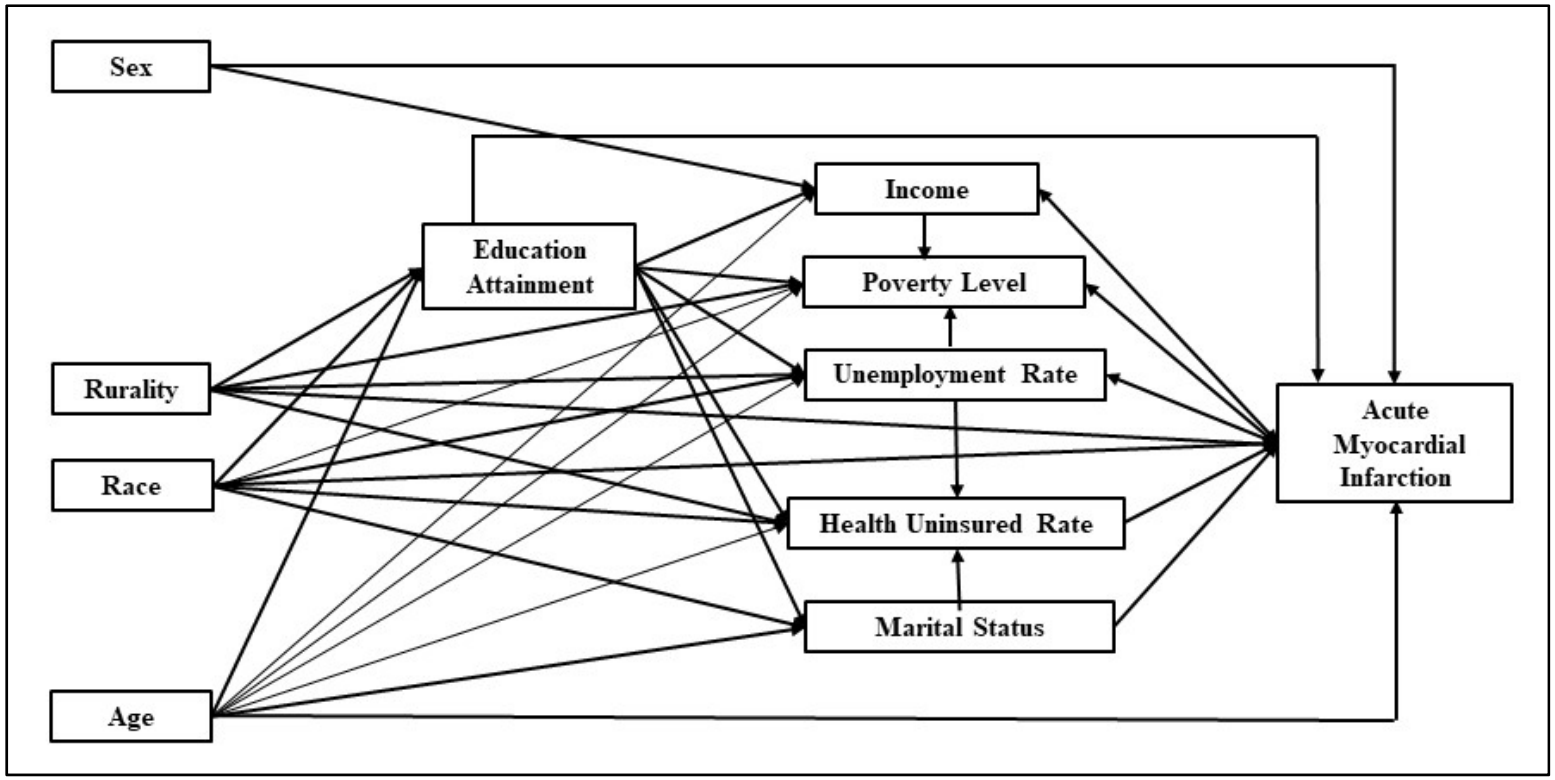


Figure 4.1. Causal web model used to guide selection of sociodemographic determinants of myocardial infarction hospitalization risks.

4.3.4.2 Model Building Process to Identify Sociodemographic Determinants of MI Hospitalizations Risks

Spearman's rank pairwise correlations were used to screen highly correlated ($r \geq 0.7$) SDoH variables to avoid multicollinearity issues. We chose a cut-off correlation coefficient of 0.7 or higher based on a study by Fotheringham et al. [228] showing geographically weighted regression to be highly robust to moderate levels of collinearity between explanatory variables. Only one variable of a pair of highly correlated variables was retained for subsequent analysis. The choice of variable for retention was based on statistical and biological considerations.

Uncorrelated variables were then investigated for potential associations with MI hospitalization risks in two steps. First, the relationship between MI risks and all potential predictors of interest was assessed by fitting univariable ordinary Poisson regression models to the data using the generalized linear model procedure, PROC GENMOD in SAS v.9.4 (SAS Institute Inc.; Cary, NC). The dependent variable was the expected MI hospitalization count in each county based on age and sex adjustment, and the offset was the natural log of the 2005-2014 period county population estimates. Second, variables which had potentially significant associations with MI hospitalizations based on a liberal p-value of 0.15 in the univariable model were included for assessment in a multivariable Poisson regression model. The multivariable model was built using a manual backward elimination approach, specifying a 5% significance level. Overdispersion of the final model was assessed using the ratio of deviance to degrees of freedom of the final model. Ratios >1 imply significant overdispersion. The value of the overdispersion parameter was 95.93 indicating overdispersion.

Since the Poisson regression model had significant overdispersion, a negative binomial (NB) model was fit to the data, using PROC GENMOD. As with the Poisson regression model, the dependent variable was the expected MI hospitalization count obtained from the direct age and sex standardization of risks in each county, and the offset was the natural log of the 2005-2014 period population for each county. Significant SDoH variables from the multivariable Poisson model were entered into a full global NB model, and manual backward elimination was used to select significant ($p<0.05$) determinants, using the likelihood ratio test to assess variable significance. Confounders were identified by assessing the change of parameter estimates of variables in the model with and without the suspected confounder. Variables whose removal resulted in a change of at least 20% in the parameter estimates of any significant variable in the model were considered as important confounders and were retained in the model. All biologically-plausible, two-way interaction terms between significant variables in the final model were explored, and significant ones retained.

We assessed multicollinearity in the final model through the variance inflation factor and tolerance using PROC REG and the natural log of age- and sex-adjusted MI hospitalization risks as the dependent variable. Variance inflation factor above 10 and tolerance values < 0.1 indicate presence of multicollinearity. Goodness-of-fit for the final NB model was assessed using the deviance and Pearson X^2 goodness-of-fit tests. Standardized Pearson's residuals and Cook's Distance were used to assess for presence of outliers and influential points, respectively. Standardized Pearson residuals were

assessed for spatial autocorrelation using Global Moran's I in Geoda [190], specifying 1st order queen spatial weights. The conceptual model for potential sociodemographic determinants of MI hospitalizations was revised based on the results of the global NB model.

4.3.4.3 Geographically Weighted Negative Binomial (GWNB) Regression

Global models, such as the multivariable NB regression model above, estimate a single coefficient averaged over all locations for each of the explanatory variables. As such, they have limited ability to take local variations into account. By contrast, the Geographically Weighted Negative Binomial (GWNB) regression model [229], estimates as many regression coefficients as the number of geographic locations in the study area. Thus, it enables the investigator to assess whether relationships between the dependent and explanatory variable(s) vary with geographic location. Thus, we used the GWNB regression model proposed by Silva and Rodrigues [229], to assess if the strength of relationships between MI hospitalization risks and significant SDoH determinants varied by geographic location. This was implemented in SAS using a set of SAS/IML© macros developed by Silva and Rodrigues [230]. Briefly, the procedure accounts for spatial dependency and overdispersion of residuals by fitting a Geographically Weighted Negative Binomial regression model (i) with spatially varying regression coefficients (βs) and a single global overdispersion parameter, (α), which is equivalent to the α value in the non-spatial NB regression model. Here,

$$E(y_j) \sim NB\left[t_j \, exp\left(\sum_k \beta_k(\mu_j, \upsilon_j) x_{jk}\right), \alpha\right] \quad \text{(i)}$$

where:

y_j is the j-th dependent variable for j = 1, ……, n,

NB represents Negative Binomial,

t_j is an offset variable,

β_k is the parameter related to the SDoH variable, x_k, for k = 1,……., K,

(μ_j, υ_j) are the location coordinates of data points j, for j = 1,……., n, and

α is the overdispersion parameter.

Similar to the global NB model, the dependent variable in the GWNB model was the age- and sex-adjusted MI hospitalization count, $E(y_j)$, with j indicating one of the 67 counties, and the log of 2005-2014 period population for each county was used as the offset, t_j, as noted above. The biquadratic kernel weighting function was used to determine the geographical weighting to estimate local coefficients; see Silva and Rodrigues [230].

A major concern when applying a biquadratic kernel weighting function is the choice of bandwidth. According to Fotheringham et al. [231], a small bandwidth would result in large standard errors for the coefficients, and make spatial patterns difficult to detect. A large bandwidth, on the other hand, would yield over-smoothed local extremes, and lead to biased local estimates [232]. Since Florida comprises both densely populated

urban counties and sparsely populated rural counties, the adaptive method, where the size of the bandwidth varies to adapt to the variations in the density of observations, was used to adjust for the differences in population density, shapes, and sizes of counties in the state. The optimum kernel bandwidth was determined by minimizing the bias-corrected Akaike Information Criteria (AICc). The AICc was also used to compare the performance of the global NB and GWNB regression models. Mean absolute deviance (MAD) and mean absolute percentage error (MAPE) were also used to compare the model fits. These were computed as:

$$MAD = \frac{1}{n}\sum_{i=1}^{n} |y_i^{obs} - y_i^{pred}|$$

$$MAPE = \frac{1}{n}\sum_{i=1}^{n} |\frac{y_i^{obs} - y_i^{pred}}{y_i^{obs}}|$$

Where:
n is the number of counties in Florida,
y_i^{obs} and y_i^{pred} are the observed and expected number of hospitalizations respectively, in each county. Lower AICc, MAD or MAPE values all indicate a better model fit.

As with the NB model, the Pearson standardized residuals for the GWNB were assessed for spatial autocorrelation using Global Moran's I in Geoda [190]. Non-stationarity of the coefficients for the GWNB model was assessed using the randomization non-stationarity test [233] based on 999 replications. This was also implemented in SAS v.9.4 using the macros developed by Silva and Rodrigues [230]. A family-wise error rate was used to correct for multiple testing [234]. The non-stationarity of the local regression coefficients for the GWNB were also assessed by comparing the interquartile range (IQR) of the local regression coefficients with the standard error estimates of the global NB model. Any local regression coefficient whose IQR was larger than twice the standard error of the regression coefficient from the global NB model was considered non-stationary across the study area [70,231]. The regression coefficients for non-stationary SDoH variables were displayed as choropleth maps in ArcGIS using Jenk's classification scheme to determine the break-points.

4.3.5 Mapping of Spatial Patterns

We used ArcGIS Version 10.3.1 (ESRI, 2010) to perform all GIS manipulations, and to display the spatial distributions of MI hospitalization risks, SDoH factors and regression coefficients for non-stationary SDoH variables. Jenk's optimization classification scheme was used to determine the intervals for displaying MI hospitalization risks and SDoH factors as choropleth maps.

4.4 Results

4.4.1 Descriptive Statistics

There was a total of 645,935 MI hospitalizations in Florida during the 10-year study period, of which 66% had a principal MI discharge diagnosis, with the rest being secondary diagnoses. Males accounted for a larger (58%) proportion of total MI hospitalizations than females (42) (Table 4.1). The MI hospitalization risks for men (40.9 cases/10,000 persons) were significantly greater ($p < 0.0001$) than those for women (28 cases per 10,000 persons). Among the different ethnic groups, Whites accounted for the largest (74%) proportion of MI-related hospitalizations followed by Hispanics (12%) and then Blacks (10%) (Table 4.1). Whites had the highest MI hospitalization risks, followed by Blacks and Hispanics, respectively. The median age of hospitalized patients was 72 years (Interquartile Range=22 years), and 66% of hospitalizations occurred in individuals 65 years and older. The highest MI hospitalization risks (130.2 cases per 10,000 persons) was observed in the ≥65-year age group while the lowest (0.6 cases per 10,000 persons) was observed in the 0–34-year-old age group.

There were gradual declines in annual MI hospitalization risks (Figure 4.2), with risks for MI with any and principal discharge diagnoses declining by 15% and 20%, respectively. There was a distinct seasonal pattern, with highest risks occurring in winter and lowest risks occurring in summer seasons throughout the 10-year study period. Winter, spring, summer, and fall seasons accounted for 27%, 26%, 23% and 24% of total MI hospitalizations, respectively.

Summary statistics for the 23 SDoH variables considered potential determinants of MI hospitalization risks are presented in Table 4.2, and the spatial distributions of MI hospitalization risks and selected SDoH factors are shown in Figure 4.3. Age- and sex-adjusted MI hospitalization risks (Figure 4.3) varied widely across Florida, ranging from 18.49 cases per 10,000 persons in Jackson County to 69.48 cases per 10,000 persons in Okeechobee County. The median MI hospitalization risk was 28.18 cases/10,000 persons. In general, high MI hospitalization risks were observed in counties in northern central, western, and southern central parts of Florida.

With respect to demographic factors, 50% of the counties had at least 16% of their population aged 65 years and older. The distributions of male and female residents across the state were relatively similar.

Florida is predominantly white, with 50% of the counties having at least 74% of their population being white. However, a number of counties in the north and south have large proportions of minority populations (Figure 4.3). Most of the state's population reside in urban counties, with 50% of the counties having at least 76% of their population classified as urban (Table 4.2). A large proportion of the urban population reside in counties in southern Florida, while Northern and south-central Florida counties comprised mostly rural populations (Figure 4.3). The proportion of the population with less than high school education level varied widely across the state (7-37%) (Table 4.2), but it was highest in rural counties in the Panhandle, north-central and south-central Florida (Figure 4.3). On average 18% of the population in Florida counties live below the federal poverty level. The unemployment rates and proportion of the population without health insurance

Table 4.1. Myocardial infarction attribute-specific hospitalization risks for Florida, 2005-2014.

Variable	Percentage of cases	Hospitalization risk (per 10,000 persons)
Sex		
Male	58	40.9 (40.8-41.0)[1]
Female	42	28.2 (28.1-28.3)
Age-group (years)		
0–34	1	0.6 (0.6-0.7)
35–44	4	9.2 (9.1-9.2)
45–54	11	27.0 (26.8-27.2)
55–64	18	52.0 (51.7-52.3)
≥65	66	130.2 (129.9-130.6)
[2]Race/Ethnicity		
Non-Hispanic White	74	43.3 (43.3-43.5)
Hispanic Latino	12	18.9 (18.8-19.0)
Non-Hispanic Black	10	21.4 (21.3-21.6)
All other races	3	23.6 (23.2-23.9)

[1]95% confidence limit of the mean; [2]Cases with missing Race/Ethnicity = 10645.

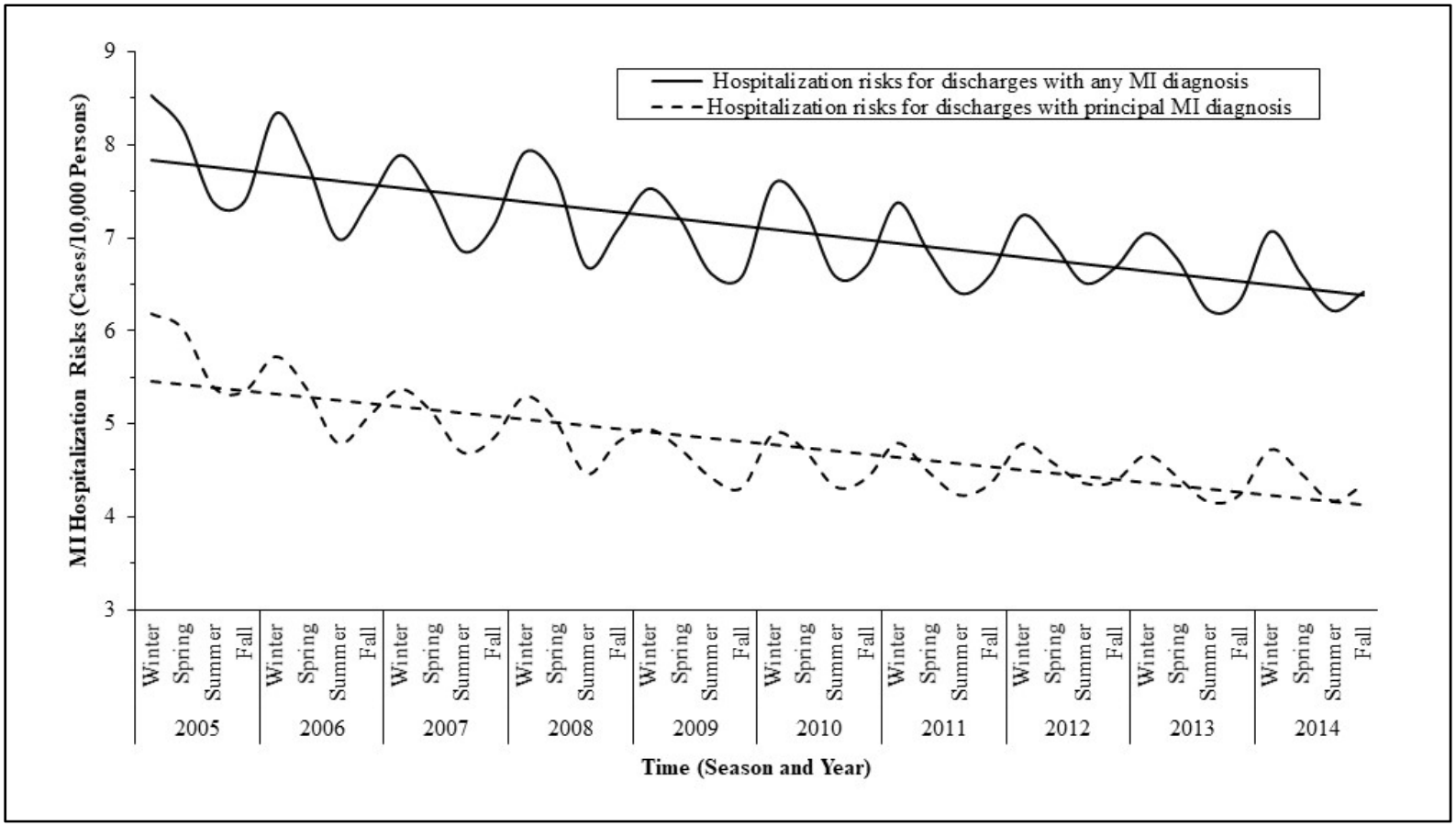


Figure 4.2. Temporal trends of age- and sex-adjusted myocardial infarction hospitalization risks with any and principal discharge diagnosis, Florida, 2005-2014.

Table 4.2. Summary statistics for sociodemographic assessed for potential associations with myocardial infarction hospitalization risks.

Category	[1]Sociodemographic Variable	Mean	Std Dev	Median	Min	Max
Age	≥ 65 years old (Pop ≥ 65 years)	0.18	0.07	0.16	0.09	0.43
Gender	Male (Male Pop)	0.51	0.04	0.49	0.48	0.65
Race/ethnicity	African American (Black Pop)	0.14	0.09	0.11	0.03	0.55
	Hispanic (Hispanic Pop)	0.14	0.12	0.10	0.03	0.65
	White (White Pop)	0.70	0.15	0.74	0.16	0.90
Marital status	Divorced (Divorced Pop)	0.13	0.02	0.13	0.07	0.21
	Separated (Separated Pop)	0.02	0.01	0.02	0.01	0.04
	Widows (Widowed Pop)	0.07	0.02	0.07	0.02	0.11
	Never married (Never Married Pop)	0.28	0.06	0.28	0.15	0.47
Rural/urban status	Rural (Rural Pop)	0.38	0.32	0.24	0.00	1.00
	Urban (Urban Pop)	0.62	0.32	0.76	0.00	1.00
Education level	< High school education (< High Sch. Educ. Pop)	0.17	0.07	0.15	0.07	0.37
	High school education (High Sch. Educ. Pop)	0.34	0.06	0.35	0.20	0.48
	Some college education (Some Coll. Educ. Pop)	0.22	0.03	0.22	0.16	0.26
	Associate degree (Associate Deg. Pop)	0.08	0.02	0.08	0.16	0.26
	Bachelor's degree (Bachelor's Deg. Pop)	0.13	0.05	0.13	0.05	0.27
	Graduate degree (Graduate Deg. Pop)	0.07	0.04	0.06	0.02	0.20
Economic status	Median income $ (/10,000)	4.39	0.74	4.38	3.25	6.43
	Living below poverty (Below Poverty Pop)	0.18	0.05	0.17	0.10	0.30
	Owner-occupied housing units (Owner-occupied Pop)	0.73	0.07	0.75	0.55	0.90
Employment rate	Unemployment rate for ≥16 years old (Unemployment Rate)	0.12	0.03	0.12	0.07	0.23
Health insurance	Uninsured rate for ≤ 64 years old (Uninsured Pop)	0.13	0.03	0.12	0.07	0.22

[1]All variables but median income are expressed as proportions of county population
Data source: US Census Bureau, 2010 and American Community Survey (2005-2008).

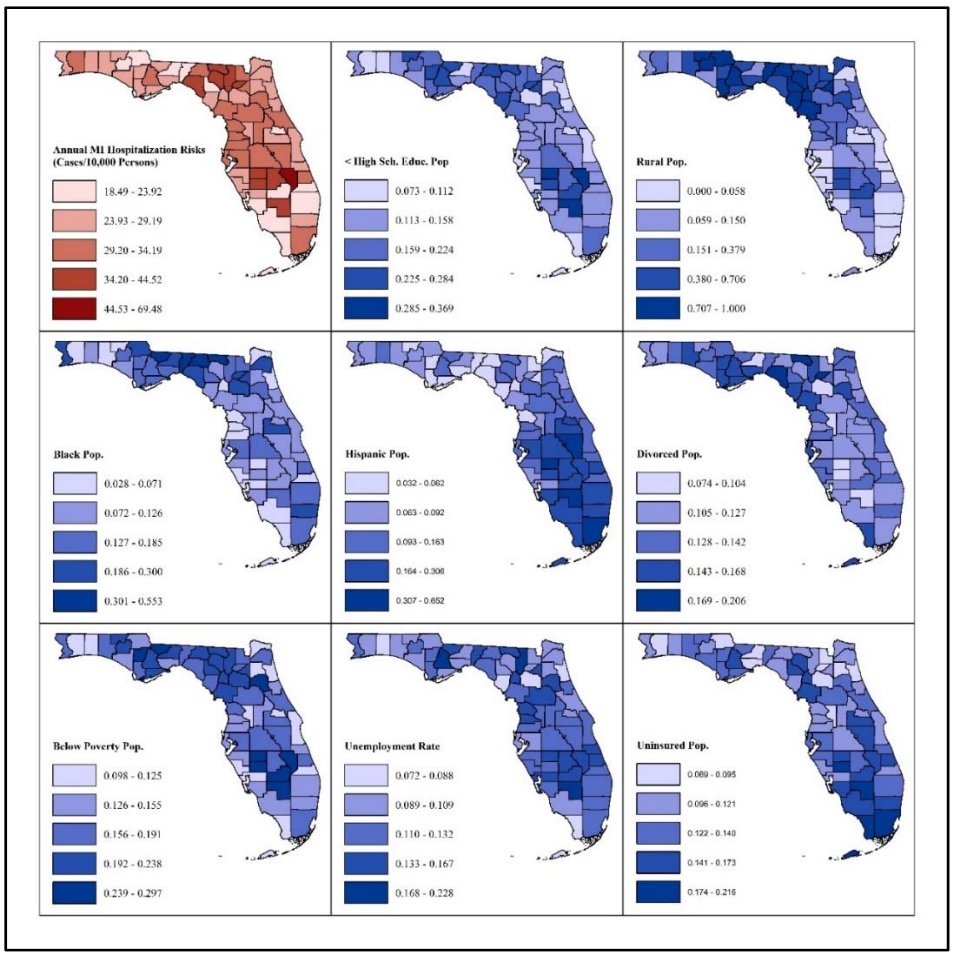


Figure 4.3. Spatial distribution of myocardial infarction hospitalization risks and selected sociodemographic determinants in Florida, 2005-2014.

varied widely across the state, with some counties having up to 23% and 22% of their population being unemployed and lacking health insurance, respectively. These counties were predominantly located in southern Florida (Table 4.2, Figure 4.3).

Counties with a high prevalence of risk factors (Figure 4.3) also appeared to have high MI hospitalization risks, suggesting potential associations between MI hospitalization risks and SDoH factors.

4.4.2 Spearman Rank Correlations and Simple Associations

Several SDoH variables had high (r≥0.70) pairwise correlations. The proportion of the population with less than high school education level was highly correlated with several variables including all variables related to education attainment (r=-0.72 to -0.86), the proportion of population living below poverty (r=0.78) and the median income (r=-0.81).

Other highly correlated variables included the proportion of widows and the proportion of population ≥65 years old (r=0.82), proportion of male population and proportion of population living in rural areas (r=0.72), the median house value and unemployment rate (r=-0.71), proportions of never married and married populations (r=-0.91), and the proportion of population living in rural and those living in urban areas (r=-1).

Only 12 out of the 23 initial sociodemographic variables considered as potential determinants of MI hospitalization risks were uncorrelated and had potentially significant (p<0.15) univariable associations with MI hospitalization risks (Table 4.3).

4.4.3 Sociodemographic Determinants of MI Hospitalizations Risks

4.4.3.1 Global Multivariable Negative Binomial (NB) Regression model

The coefficients for the final multivariable NB model for the estimated global relationship between MI hospitalization risks and significant SDoH variables are presented in Table 4.4. There were significant positive associations between MI hospitalization risks and proportions of divorced residents (p<0.018) and population with less than high school education (p<0.0001). Surprisingly, counties with high proportions of rural and African American populations tended to have significantly lower (p<0.0001 and p=0.032, respectively) MI hospitalization risks than counties with low proportions of these. Counties with high proportions of population lacking health insurance were marginally (p<0.040) associated with low MI hospitalization risks.

Based on the results of the global NB model, the conceptual causal model for sociodemographic determinants of MI was revised to show only those variables that were significantly associated with MI hospitalization risks in Florida (Figure 4.4).

The tolerance values and the variance inflation factors for all the explanatory variables in the final NB model (Table 4.4) were above 0.1 and below 10, respectively, indicating lack of multicollinearity. The p-values for both the Pearson and Deviance Chi-Square goodness-of-fit tests were large (0.22572 and 0.27616, respectively) indicating a good fit for the NB model.

Table 4.3. Univariable associations of uncorrelated sociodemographic determinants with myocardial infarction hospitalization risks in Florida.

[1]Sociodemographic variable	Coefficient (CI)[2]	[3]LRT p-value
Male (Male Pop)	1.27 (1.08 - 1.46)	<0.0001
≥65 years old (≥65 years Pop)	-0.23 (-0.27 - 0.18)	<0.0001
African American (Black Pop)	-0.17 (-0.20 - 0.13)	<0.0001
Hispanic (Hispanic Pop)	0.17 (0.15 - 0.19)	<0.0001
Divorced (Divorced Pop)	1.43 (1.22 - 1.63)	<0.0001
Separated (Separated Pop)	9.18 (8.67 - 9.68)	<0.0001
Rural (Rural Pop)	0.18 (0.16 - 0.19)	<0.0001
<High school education (<High Sch. Educ. Pop)	1.64 (1.58 - 1.70)	<0.0001
Some college education (Some Coll. Educ. Pop)	-0.96 (-1.05 - -0.86)	<0.0001
Owner occupied housing (Owner-occupied Pop)	-0.14 (-0.17 - -0.10)	<0.0001
Unemployment rate for ≥16 years old (Unemployment Rate)	2.64 (2.47 - 2.81)	<0.0001
Health uninsured rate for ≤ 64 years old (Uninsured Pop)	0.76 (0.69 - 0.84)	<0.0001

Univariable results are for a model with Poisson error distribution.
[1]All variables except median income are expressed as proportions of county population
[2]95% Confidence limit of the coefficient estimate
[3]Log Likelihood Ratio

Table 4.4. Final negative binomial model showing significant sociodemographic determinants of myocardial infarction hospitalization risks in Florida.

Sociodemographic Variable	Coefficient (CI)[1]	[2]LRT p-value	[3]VIF	Tolerance
< High Sch. Educ. Pop.	3.23 (2.30, 4.18)	<0.0001	2.559	0.391
Divorced Pop.	2.53 (0.44, 4.64)	0.0181	1.176	0.850
Rural Pop.	-0.38 (-0.56, -0.19)	0.0001	2.309	0.433
Uninsured Pop	-1.76 (-3.41, -0.09)	0.0395	1.506	0.664
Black Pop.	-0.50 (-0.93, -0.04)	0.0323	1.119	0.895
Intercept	-6.27 (-6.62, -5.95)	[4]<0.0001	0	.

[1]CI = Confidence Interval; [2]Likelihood Ratio Test; [3]Variance Inflation Factor; [4]Wald P value.

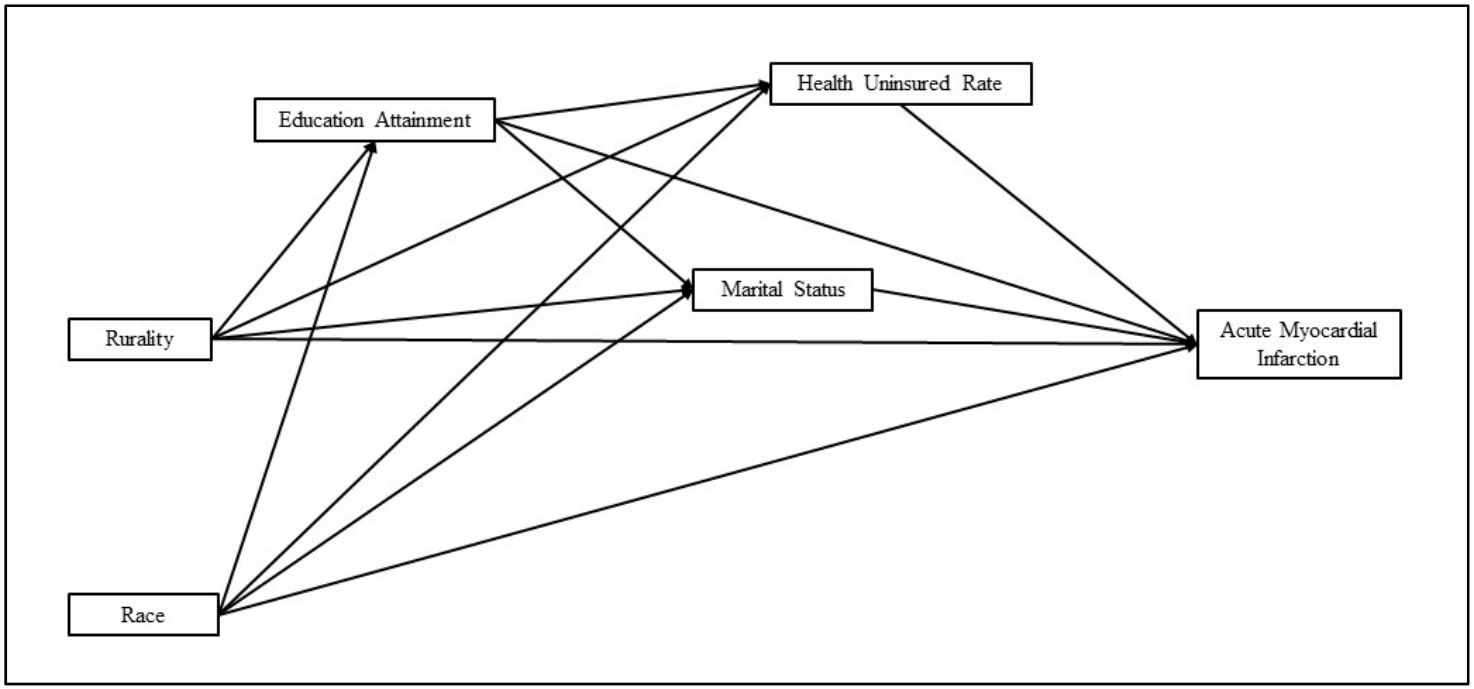


Figure 4.4. Conceptual causal model for sociodemographic determinants of myocardial infarction hospitalization risks in Florida based on the final global multivariable negative binomial model.

4.4.3.2 Local Geographically Weighted Negative Binomial (GWNB) Model

4.4.3.2.1 Stationarity of Regression Coefficients

The results for assessment of stationarity of GWNB model regression coefficients are shown in Table 4.5. There is evidence of non-stationarity of relationships between MI hospitalization risks and the proportions of population with less than high school education level and population with no health insurance coverage ($p<0.05$). However, the coefficients for proportions of divorced, African American, and rural populations were stationary ($p>0.05$).

The interquartile ranges of local coefficients for proportions population with less than high school education level and population with no health insurance coverage were larger than twice the standard error of the coefficients of the global NB model, but those for the proportions of divorced, African American, and rural populations were not (Table 4.5). This provided corroborating statistical evidence to reject the null hypothesis of stationarity of associations between MI hospitalization risks and its SDoH predictors across Florida. Thus, the associations between MI hospitalization risks and the proportions of population with less than high school education level and uninsured population varied based on location in Florida.

4.4.3.2.2 Spatial Distribution of Non-stationary Regression Coefficients

The spatial distribution of the local regression coefficients provides visual evidence for variability of the local relationships between MI hospitalization risks and proportions of population without high school diploma and uninsured population (Figure 4.5). Thus, the effects of education level and lack of health insurance varied considerably across Florida, with a strong north-south gradient. Low education levels were significantly associated with high MI hospitalization risks throughout Florida, but stronger associations were observed in southern Florida. On the other hand, counties with high proportions of uninsured population tended to have low MI hospitalization risks, but this association was only significant in southern Florida.

4.4.3.2.3 Performances of Global and Local Regression Models

The AICc, MAD, and MAPE values used to compare the performances of global and local models are presented in Table 4.6. Moran's I statistics indicating the extent of spatial autocorrelation of residuals are also presented in Table 4.6. According to Fotheringham et al. [231,235], the difference between AICc scores for any two models needs to be at least 3 units for the performance the two models to be considered different. Based on this rule, the Poisson regression model had the worst fit, but the NB and GWNB models had similar fit. However, based on MAD and MAPE criteria, the spatial GWNB model outperformed the global Poisson and NB models. Moreover, minimal clustering of residuals for the GWNB model (Moran's I statistic=-0.102, $p=0.116$), coupled with non-stationarity of education level and lack of health insurance coefficients indicate that the GWNB model is more appropriate for modeling of these data than the global NB model.

Table 4.5. Results of assessment of stationarity of coefficients of Geographically Weighted Negative Binomial model.

Variable	[1]NB [3]SE	[1]NB [3]SE*2	[2]GWNB [4]IQR	Is regression coefficient for [2]GWNB non-stationary?	[2]GWNB [5]P-value
< High Sch. Educ.	0.4735	0.947	1.178	Yes	0.043
Divorced Pop	1.0556	2.1112	0.298	No	0.776
Rural Pop	0.0934	0.1868	0.045	No	0.766
Uninsured Pop	0.8360	1.672	2.351	Yes	0.001
Black Pop	0.2242	0.4484	0.092	No	0.559
Intercept	0.1697	0.3394	0.069	No	0.751

[1]NB = Global Negative Binomial Regression Model.
[2]GWNB = Geographically Weighted Negative Binomial Model fitted with a global overdispersion parameter (α = 0.0256).
[3]SE = Standard Error of the coefficients for the Negative Binomial Regression model.
[4]IQR = Interquartile range for the coefficients for the Geographically Weighted Negative Binomial models. An IQR of local regression coefficients > 2*SE of global NB model is evidence for non-stationarity.
[5]P-value based on randomization test (m = 999 replications).

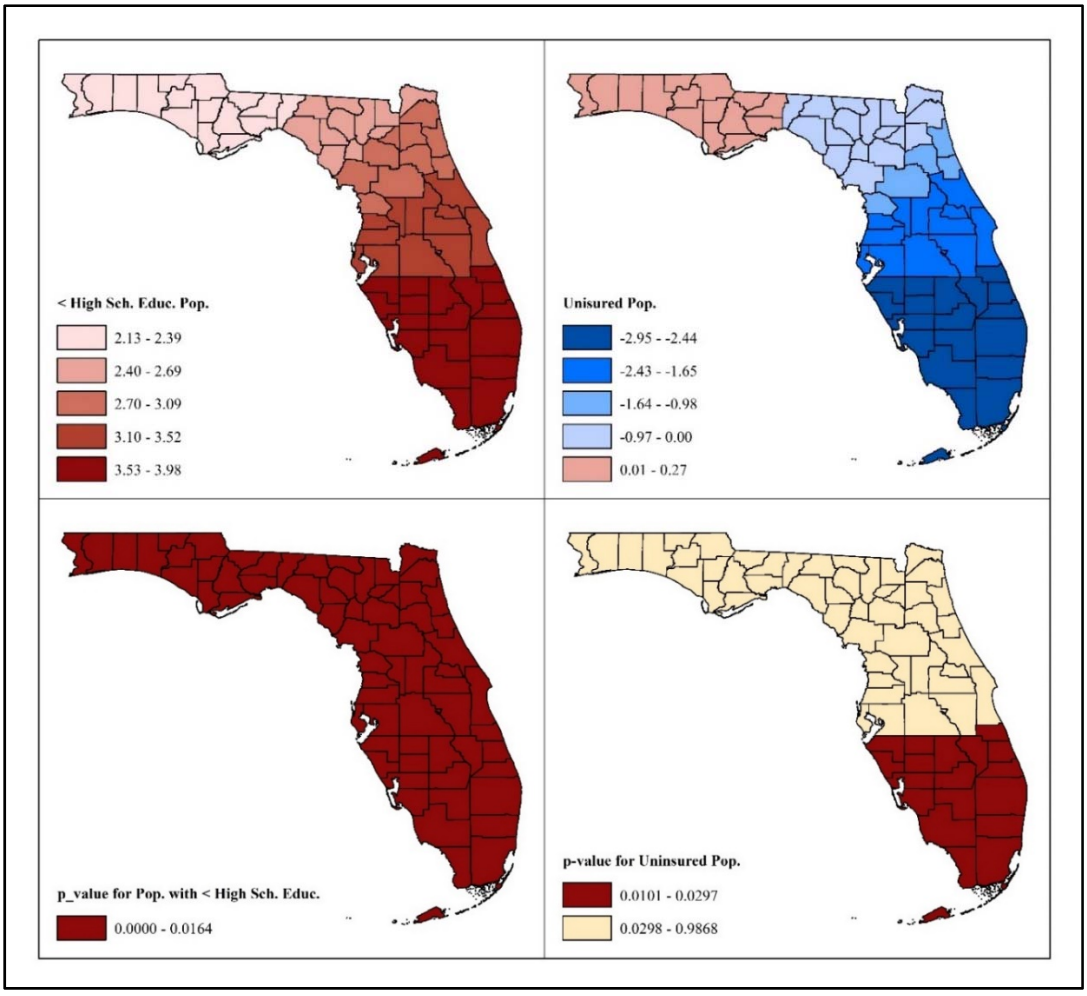


Figure 4.5. Spatial distributions of non-stationary regression coefficients and associated family-wise p-values.

Table 4.6. Goodness-of-fit and Moran's I statistics for global Poisson, global Negative Binomial (NB), and Geographically Weighted Negative Binomial Regression (GWNB) models.

Model	Bandwidth	Number of Parameters	[1]AICc	[2]MAD	[3]MAPE (%)	Moran's I ([4]p-value)
Poisson	-	10	5865.3	714.1	13.5	0.156 (0.023)
[5]NB	-	6	1034.9	613.2	12.4	-0.113 (0.1)
[6]GWNB	65	10.09	1032.0	580.8	11.4	-0.102 (0.116)

[1]Small sample bias-corrected Akaike's Information Criteria.
[2]Mean absolute deviance
[3]Mean absolute percentage error
[4]p-value based on Monte Carlo simulations (rep = 9999)
[5]Global Negative Binomial Regression model
[6]Geographically Weighted Negative Binomial Regression model fitted with a global overdispersion parameter, $\alpha = 0.0256$

4.5 Discussion

4.5.1 Descriptive Statistics

In this study, we identified the sociodemographic determinants of myocardial infarction (MI) hospitalization risks among Florida residents from 2005-2014. We then assessed if model regression coefficients varied by geographic location to identify the most important determinants of MI hospitalization risks for different geographic areas in Florida. Since SDoH factors are responsible for shaping 40% of the health of a population [67], study findings will aid in the development of evidence-based, location-specific strategies for reducing the high MI burden in Florida. Moreover, MI shares similar risk factors with other CVD such as stroke, hence these health conditions tend occur together geographically. Thus, public efforts targeting MI risk factors would address the burdens of MI and stroke and several of their risk factors such as diabetes, high blood pressure etc. Additionally, since Florida's current age structure and race/ethnic composition portend the changes projected for the US population by the year 2030 [192], Florida's strategy to address the high MI burden will also be instructive for the rest of the US.

We found that 66% of the MI hospitalizations had a principal MI discharge diagnosis, with the rest being coded as secondary MI. Thus, including only MI cases with a principal diagnosis in the analysis would have excluded a substantial burden of MI hospitalizations from the study. Sacks et al. [47] also reported a similar proportion of principal MI hospitalizations in a study of Fee-for-Service Medicare population aged 65 years and older. Acute MI is a serious clinical condition requiring percutaneous coronary intervention (PCI) in a specialized cardiac center within 90 minutes of disease onset to prevent adverse consequences on patient outcomes [100]. Therefore, hospitalization may be used as a proxy of morbidity, in which case the decline in MI hospitalization risks observed during the 10-year study period may represent declining MI morbidity risks in Florida over time. These secular decreases are consistent with decreases in the prevalence of CVD risk factors at the individual and community levels, primarily smoking [132], exposure to secondhand smoke [236]. and physical inactivity [131]. Broad application of evidence-based primary prevention measures for CHD with aspirin and statins [237] and improvements in air quality [238] may also have contributed to reduced MI morbidity risks. However, MI hospitalization is not necessarily equivalent to a morbidity measure [239], particularly for populations with limited access to resources for appropriate cardiac care such as to PCI-capable hospitals and health insurance coverage. In this instance, MI hospitalization risks are a proxy of utilization rates for MI care, in which case declining MI hospitalization risks would be reflective of reduced rates of utilization for MI care.

The annual rate of decline in MI hospitalization risks with any discharge diagnoses reported in our study (1.6% per year) is lower than the 2.5% annual rate reported for a Medicare population aged ≥65 years [47]. However, the annual rate of decline of MI hospitalization risks with a principal discharge diagnosis in our study (2.3% per year) is close to rates reported in recent studies considering only acute MI hospitalizations with a principal MI diagnoses. For instance, age- and sex-adjusted incidence rates of acute MI hospitalization decreased by an average of 3.8% per year among US adults aged >25

years [17]. Yeh et al. [12] found a 2.75% per year rate of decline of incident MI hospitalizations in a ≥30 years old community-based population over a 10-year period. In contrast, Talbott et al. [19] reported an overall 7.6% increase in principal MI hospitalization risks among Florida residents 35+ years of age between 2000 and 2008. In general, our results, together with those of other studies, suggest that studies that consider only a section of the population, or fail to account for both principal and secondary MI hospitalizations may underestimate the current MI burden.

4.5.2 Seasonal Trends

Myocardial infarction hospitalization risks showed seasonal fluctuations, with highest hospitalization risks during the winter months and lowest risks during the summer. Seasonality of MI hospitalizations with winter peaks and summer troughs have been observed in other studies. Spencer et al. [240] observed a marked winter increase or summer decrease, or both, in the number of acute MI cases reported in a large, prospective US registry of acute MI cases, irrespective of geographic area, age or gender. Bhaskaran et al. [241] reported elevated risks of MI morbidity at colder temperature in eight out of 12 studies with data from the winter season.

The higher MI hospitalization risks we observed during winter than summer seasons may partly be attributable to the “snowbird” phenomenon, whereby elderly individuals, who experience more morbidity from MI, migrate from the Northern hemisphere into Florida and other states on east coast of the US during the winter and migrate out during the summer [242]. This is corroborated by a nation-wide study showing a predominance of inpatient NSTEMI admissions during winter in warmer southern states but not in cooler northern states [243]. However, there is evidence that the seasonal migration of elderly individuals may not substantially contribute to the seasonal variations we observed. For instance, similar temporal patterns as those we observed have been reported for coronary heart disease (CHD) deaths in Los Angeles County, California, where the “snowbird” phenomenon is not prevalent and temperatures tend to be mild throughout the year [242-244]. Moreover, higher MI hospital admission rates during winter compared to summer seasons have also been observed for younger (<70 years old) and older (≥70 years old) groups in both northern (snowbird source states) and southern (snowbird destination states) states [245]. Other potential explanations for the seasonal patterns we observed include higher respiratory infections, such as the influenza [242,246,247], and increased cardiac workload caused by increased blood pressure, hemoconcentration and vascular thromboses during the winter season [153].

4.5.3 Spatial Distribution of MI Hospitalization Risks and its Sociodemographic Determinants

This study shows that MI hospitalization risks were high in counties with large proportions of population with less than high school education level and high divorce rates, and low in counties with large proportions of rural, African American, and uninsured populations. However, only the effects of education attainment and uninsured rate varied

with geographic location, with stronger impacts being observed in southern compared to northern counties.

4.5.3.1 Education Level

Our results showing higher MI hospitalization risks in counties with high proportions of population with less than high school education are consistent with previous area-level studies showing higher CVD risks in areas with low education attainment [54,57,62,248]. These results may be attributable to higher burdens of CVD risk factors such as hypertension [249]. diabetes mellitus [250], and obesity [251], and risky behaviors such as unhealthy southern dietary patterns [252], cigarette smoking and alcohol consumption [253]; and lower prevalence of protective healthy behaviors such as fruit/vegetable consumption [254,255], non-smoking [256], and regular exercise [257] in counties with low education levels. This is not unexpected since health literacy has been shown to mediate the association between education level and health behaviors [258,259]. In fact, low education attainment may confer a cardiovascular risk that is equivalent to traditional risk factors [260,261]. Accordingly, counties with low education levels may have low health literacy levels, resulting in a large proportion of their population having limited ability to obtain, process, and understand basic health-related information needed to communicate, navigate health systems and to make decisions regarding lifestyle and personal health behaviors [262,263].

Education level is a proxy for socioeconomic status (SES) [264], and low neighborhood SES is an independent risk factor for a higher MI incidence and CVD risk factors [68]. Thus, the higher MI hospitalization risks in counties with low education levels may be related to lower accumulation of, and access to, material, economic and social resources for MI prevention in those counties [213,265]. For instance, supermarkets, which offer a wide variety of healthy foods at lower prices, tend to be concentrated in affluent neighborhoods. Living in a socioeconomically advantaged area is associated with greater fruit and vegetable consumption [254], which is inversely associated with the risk of CVD [266]. On the other hand, fast food outlets and small corner grocery convenience stores offering limited selections of lower quality foods and at substantially higher prices predominate in poor neighborhoods [112]. Thus, low SES neighborhoods devoid of supermarkets, referred to as ‘Food desserts’, may lack equal access to the variety of healthy food choices that are available to wealthy communities [36]. Furthermore, residents in low SES neighborhoods lack transport, hence they are less likely to travel to a supermarket outside of their neighborhood [36].

The distribution of physical activity resources, such as walking trails, is also skewed, with resources being concentrated in neighborhoods with high SES [33]. Long-term exposure to environments with limited access to physical activity resources and healthy nutritious food has been linked to higher incidence/prevalence of chronic diseases that are precursors of MI such as diabetes, obesity and hypertension [68,267]. Additionally, low SES neighborhoods tend to have high income inequality, which is associated with disinvestment in social capital, which is in turn linked with increased deaths from CHD, among other causes [268-270]. Low social capital has also been linked

with elevated biological stress i.e. allostatic load [57,251,271] and subsequently poor CVD outcomes [270].

4.5.3.2 Marital Status

The high MI hospitalization risks we observed for counties with a high proportion of divorced residents is consistent with previous reports of negative impacts of divorce, and other disruptive events such as separation or being widowed on cardiovascular health, including increased risk of MI [272]. Venters et al. found higher rates of hospitalization for MI/stroke for separated/divorced persons than for married and widowed persons [273]. A recent study found that multiple divorce experiences increased the risks of MI, and especially in women with multiple divorces [274].

Divorce is a stressful event that often involves adjustments to a new social role, identity, and living arrangement, and is associated with increased psychological distress and a decline in the availability of financial and social capital [275]. Therefore, the high MI hospitalization risks we observed in counties with a high proportion of divorced residents may be attributable to losses of income and health insurance, resulting in decreased ability to prevent, detect, and treat illness [276,277]. The acute and chronic stress associated with divorce may also play a role [278]. Moreover, many individuals respond to stress and depression with unhealthy coping habits/behaviors such as smoking and alcohol use, among others further exacerbating the risk of MI [276]. By contrast, married individuals tend to have stronger social support, less stress, better mental health status, healthier lifestyles [279], and greater access to medical insurance, prescription drugs, and overall higher quality of health care [280].

At the ecologic level, neighborhood social capital, defined as social resources inherent within community networks, and consisting of social support, social leverage, informal social control, and neighborhood organization and participation [281]. may exert a contextual effect on cardiovascular health by: promoting more rapid diffusion of health information thereby increasing the likelihood for healthy norms of behavior to be adopted; exerting social control over deviant and unhealthy behavior; providing emotional or material support and mutual respect based on social network and participation, and promoting access to local services and amenities [282]. Thus, neighborhood social cohesion is recognized as an important neighborhood social environment indicator [223].

Marital and family disruption may decrease informal social controls at the community level and lead to more disorder and lower social capital or social cohesion [269]. Thus, counties with a large proportion of divorced residents may lack collective social control which has been linked to higher alcohol consumption, smoking and crime rates [283]. These can increase social disorganization and are associated with depression, lower levels of physical activity [284-286] reduced access to preventive care [287]. and decreased efficiency and effectiveness of intervention programs [282]. All these are associated with adverse health outcomes, including diabetes mellitus [68,288,289] and higher CVD risks [290]. Thus, low social capital may have contributed to the high MI hospitalization risks in counties with high divorce rates. On the other hand, based on a study by Saudquist et al. [291], that showed protective effects of social capital

on hospitalizations for CHD, the contextual protective effects of social capital may have contributed to lower MI hospitalization risks in counties with low divorce rates.

4.5.3.3 Rural Population

Our results showing lower MI hospitalization risks in counties with high proportions of rural populations compared to those with low proportions of rural populations are inconsistent with recent ecologic studies showing higher mortality risks from MI [77], and heart disease and ischemic heart disease in rural counties compared to urban counties in Florida [39,41] and in southeastern US in general [292]. Our results are also inconsistent with lower SES [141,143] lower prevalence of protective health-related behaviors [149] and higher prevalence of several MI risk factors reported for rural counties in Florida and in US in general compared to urban counties. These include unhealthy behaviors/lifestyles such as smoking, physical inactivity and unhealthy eating patterns [29,30,111,194,195]; being overweight and/or obese [27,197,293,294]; hypertension [295]; and diabetes [28,296]. It is worth noting that food deserts tend to be concentrated in rural neighborhoods, which together with the low SES of these neighborhoods limits accessibility of healthy foods to rural communities [36,111,112]. Additionally, despite the additional burden of risk factors in rural areas, area-level primary and secondary interventions for MI, such regulations around taxation or smoking restrictions, the sale and marketing of tobacco products [82,297,298], distribution of primary care providers [144] and cardiologists [80], disproportionately benefit urban areas [82,297,298]. Moreover, targeted marketing of tobacco products in rural areas can reinforce pro-tobacco norms in those areas [299].

The foregoing discussion suggests that it is highly unlikely that the lower MI hospitalization risks we observed for counties with high proportions of rural residents compared to those with low proportions these reflect low MI morbidity risks for rural populations. Rather, similar to undiagnosed hypertension which has been reported to be more prevalent in some rural western Panhandle counties [85], undiagnosed MI may be more prevalent in rural counties where the level of knowledge regarding the five classic symptoms of heart attack [115], tend to be lower. Furthermore, cardiac centers/PCI-capable hospitals tend to be clustered in metropolitan and large urban areas [81], thereby impeding timely access to emergency cardiac care [300]. These factors may exacerbate tendencies for rural residents to delay or forgo health care altogether and contribute to the lower MI hospitalization risks and disproportionately higher pre-hospital MI death rates in rural counties compared to urban counties [301,302]. Thus, higher out-of-hospital MI death risks may potentially explain the lower MI hospitalization risks we estimated in counties with high proportions of rural populations.

4.5.3.4 African American Population

The lower MI hospitalization risks we observed for counties with higher proportions of Black residents are inconsistent with previous reports of higher burdens of CVD and traditional CVD risk factors [303], and lower prevalence of ideal cardiovascular health metrics among non-Hispanic Black compared to White populations [48,304].

Furthermore, these risk factors often cluster in African Americans, due to generally low SES for that population [303]. Additionally, African American populations are disproportionately and adversely impacted by unfavorable neighborhood features such as limited access to healthy foods such as fruits and vegetables [36,111,112], racial segregation [305], high levels of industrial pollution and poor enforcement of environmental regulations [113], high crime leading to low neighborhood walkability, limited access to green spaces and quality cardiovascular health care [114], and low social cohesion [50]. All these factors would be expected to increase MI morbidity risks in predominantly Black counties. Moreover, disproportionate burdens of pre-hospital mortality from MI/coronary heart disease [301] and CVD in general [292,306], have been reported among non-Hispanic Black compared to White populations. Therefore, lower MI hospitalization risks for counties with high proportions of Black residents may be due to an under-diagnosis of MI in Blacks in the pre-hospital setting due to lower rates of utilization for cardiac care services. Lower rates of utilization for cardiac care by Black residents may be attributed to limited knowledge regarding symptom recognition [115,116], lack of access to quality cardiac care [81,117,118], and mistrust of the health care system stemming from historical events such as the Tuskegee syphilis study [171], and is reinforced by perceived racial discrimination [307].

4.5.3.5 Lack of Health Insurance

The lower MI hospitalization risks observed for counties with high proportions of uninsured population are consistent with the findings of a study by Talbott et al. [19] which found a positive association between health care coverage and acute MI hospitalization rates. In that study, a large proportion of the population in the New England/Mid-Atlantic region reported that they had health insurance, yet they had the highest acute MI hospitalization rates. Talbott et al. [19] also found a negative association between acute MI mortality rates and health care coverage.

Taking MI hospitalization risk as a proxy for MI morbidity, the lower MI hospitalization risks for counties with high proportion of uninsured population would suggest lower MI morbidity risks for those counties. However, this is highly unlikely, since lack of health insurance not only impedes timely access to cardiac care when needed, but also reduces access to necessary preventive and therapeutic care to minimize future illness [308]. On the other hand, having health insurance leads to higher rates of MI diagnoses and therapeutic cardiac procedures [309,310], thereby reducing the risks of major cardiac events. Thus, the disease is more likely to be identified/diagnosed and controlled among the insured. Moreover, it is more difficult to obtain off-site specialty cardiovascular services, including referrals, for the uninsured compared to those with health insurance [311]. Therefore, the association of low MI hospitalization risks with high uninsured rates is a reflection of lower rates of utilization of cardiac care services in counties with high proportions of uninsured populations [308].

The stronger association between the proportion of population lacking health insurance and MI hospitalization risks in southern Florida counties may be due to a large proportion of low-income minority population, particularly Haitian, Non-Hispanic Blacks and Hispanic immigrants, in that part of the state [165,312,313]. These demographic

groups have been disproportionately impacted by Florida's decision not to expand Medicaid under the Affordable Care Act, hence they have double the likelihood to fall into the "coverage gap" compared to their uninsured White counterparts [117]. Community health centers, such as Federally Qualified Health Centers (FQHCs) provide a safety net for the under and uninsured on income-based sliding-fee scales [314], but they are highly underutilized [311,313], hence they have not been successful in reducing socioeconomic barriers to advanced treatment for heart disease for the under and uninsured in southern Florida.

To summarize, the results from the NB model suggest that for certain populations, MI hospitalization is not necessarily equivalent to a morbidity measure [239]. Rather, MI hospitalization risks are a proxy of utilization rates for MI care. In our study, this was particularly true for Black, rural, and uninsured populations, due to limited access to resources for cardiovascular health such as health insurance and specialized cardiac centers.

4.5.4 Non-Stationarity of Regression Coefficients

The local GWNB model allowed geographically varying relationships between MI hospitalization risks and its sociodemographic determinants to be modelled through spatially varying parameter estimates. Our results showing geographic variations of associations between MI hospitalization risks and education and health uninsured rates corroborate findings from previous ecologic studies [60,225,226,315] that showed that the impacts of SDoH factors on the risks of cardiovascular health outcomes vary based on geographic location. For instance, all the coefficients for the relationships between sex, race, age, education and rural residence and MI/stroke mortality risks varied with location in middle Tennessee [60]. Ford and Highfield [315] showed significant spatial association between CVD mortality and social deprivation in Harris County in Texas.

Stationarity of regression coefficients for proportions of rural, African American and divorced residents suggest that global relationships between MI hospitalization risks and these determinants may be generalized to every county in Florida (the effects of these three determinants were constant across Florida). Conversely, variation in the associations between MI hospitalization risks and the proportion of population with less than high school education and uninsured rates based on geographic location suggest that a global relationship between MI hospitalization risks and these determinants cannot be generalized to every county in Florida.

These findings have several policy implications. First, the results imply that "one size fits all" approaches would not be suitable for addressing high MI morbidity risks and inequitable utilization of MI care services in Florida. Rather, different parts of the state require slightly different strategies. Therefore, planning for MI control and prevention efforts will need to use a needs-based approach informed by empirical evidence from global regression models supplemented with local models. Specifically, policies for addressing inequitable utilization of MI care services by improving health insurance coverage rates need to focus on Southern Florida counties where low MI hospitalization risks may reflect low utilization rates for MI care services. Likewise, policies focusing on

reducing MI hospitalization risks by improving literacy levels should pay extra attention to counties within southern Florida which have low education attainment.

4.5.5 Strengths and Limitations

The data we used were collected using a consistent set of case definitions and included MI admissions for all institutionalized hospitals in the state of Florida, thus allowing us to explore temporal trends and assess geographic variation of MI risks for the entire state of Florida. In this study, secondary MIs accounted for a 1/3 of MI-related hospital admissions in Florida. Thus, using hospitalized cases with principal or secondary discharge diagnosis for MI allowed us to characterize the burden of MI hospitalizations more fully, regardless of whether MI was the principal or secondary diagnosis.

The use of a geographically weighted regression model to account for potential local variations in the strength of associations between MI hospitalization risks and its sociodemographic determinants enabled identification of location-specific strategies that may be used to reduce the burden of MI and to increase equitable utilization of MI care in Florida. Without the place-specific perspective of GWNB model, the local associations between MI hospitalization risks and education level and uninsured rates would not be apparent, which would suggest a uniform/“one size fits all” control strategy for the entire state. This is an unrealistic proposition, given the wide variabilities in socioeconomic and environmental conditions that exist within Florida. Moreover, correction for multiple hypothesis testing avoided false positives in geographically weighted regression.

The findings of this study have some limitations that suggest important areas for future research. This being an ecologic study, there is potential for ecological fallacy, since individuals diagnosed with MI may not be the same people who were exposed to the SDoH factors we investigated at the county level. Therefore, interpretations of specific associations between contextual variables and MI hospitalization risks should be made with caution, recognizing that inferences based on aggregate data do not apply to comparable individual-level data [184]. Moreover, there is potential for substantial within-county variations in sociodemographic factors due to the heterogeneous nature of the counties. Thus, a change in spatial unit of analysis (e.g. ZIP code or census tract) may alter our findings due to the modifiable areal unit problem [316]. Nonetheless, we chose to study counties rather than a smaller geographic area such as a 5-digit zip code or US census tracts or blocks because the former is more relevant to policy action steps.

We based MI hospitalization risks on events rather than individuals due to lack of personal identifiers in the data. As such, multiple admissions for the same individual for the same event may be included in the data. Additionally, we lacked statistically robust data at the county level to adjust for important behavioral, clinical, and environmental factors, and our MI data do not include subclinical MIs, patients who never sought care or may have died before hospitalization. Accordingly, there is potential for confounding and selection bias, which may result in inaccurate estimation of the true associations between MI hospitalization risks and its sociodemographic predictors.

The American Community Survey (ACS) has collected 1-, 3- and 5-year estimates for sociodemographic data since 2005. We selected a time frame for SDoH data based on what was available. Although people may have been exposed much earlier and could

have resided in a different county than where the first signs of the MI occur, our analysis did not consider the lag-time between potential exposure and the occurrence of the disease symptoms. This may have results in misclassification of some exposures, with consequent underestimation or overestimation of associations between SDoH factors and MI risks.

These limitations notwithstanding, our results are consistent with a broad range of causal biological processes, and with studies showing strong associations between cardiovascular events and area-level sociodemographic predictors even after adjusting for relevant confounders [54,68]. Thus, study findings may be useful for guiding policies directed toward reducing disparities related to education attainment, lack of health insurance coverage, divorce rates, rural residence and race. This would go a long way towards reducing MI morbidity risks or increasing utilization rates for cardiovascular care in Florida. Moreover, the results identify specific areas that may benefit most from place-based public health interventions that address low education levels and high uninsured rates to improve cardiovascular health in Florida.

4.6 Conclusions

Race, marital status, rurality, education level, and lack of health insurance were significant predictors of MI hospitalization risks in Florida. The influence of race, divorce rate and rurality were constant across Florida. However, the influence of education level and uninsured rate varied based on geographic location in the state, with their influence being strongest in counties in the south. These results indicate that global models supplemented with local models are more appropriate for exploring the associations between MI hospitalization risks and its demographic and socioeconomic predictors. Study findings may help state and local public health entities allocate scarce resources more efficiently to reduce cardiovascular health disparities and improve population health for all Floridians.

CHAPTER 5
CONCLUSIONS

5.1 Summary of Dissertation Research

This dissertation addresses issues related to spatiotemporal disparities and burden of myocardial infarction (MI) in Florida using geospatial methods. Understanding these disparities has great relevance for public health because MI remains the leading cause of morbidity and premature mortality in Florida, despite overall reductions in MI risks in the state over time.

An innovative contribution of this work is the integration of spatial scan statistics, spatial modeling, and Geographic Information System (GIS) to investigate spatiotemporal disparities in risks of principal and any (i.e. principal or secondary) myocardial infarction hospitalizations and mortality, and the contextual social demographic factors that may be related to MI hospitalizations. Specifically, my dissertation is composed of three major themes.

5.1.1 Theme 1. Investigation of Geographic Distribution and Spatial Clusters of MI Hospitalization and Mortality Risks Over Time

Identifying areas that may have consistently high MI burdens is the first step towards understanding the MI burden in Florida. Both Kulldorff''s and Tango's circular and flexible spatial scan statistics were used for cluster detection and identification. The use of the flexible spatial scan statistic was important because it enabled the identification of irregularly-shaped high-risk clusters that were otherwise excluded by the circular spatial scan statistic, which is the standard methodology for detection of geographic clusters. All high-risk clusters, regardless of their shape, would be of interest to public health practitioners interested in health disparities, hence the identification of irregularly-shaped clusters is expected to result in improved control of MI. Additionally, basing statistical inference on a restricted log likelihood ratio test, instead of a log likelihood ratio test, resulted in identification of more homogenous clusters, which may lead to more precise targeting of strategies for MI control, allowing more efficient use of scarce public health resources. The results indicated substantial geographic disparities in MI hospitalization and mortality risks in Florida, with persistent clustering of high MI hospitalization risks occurring in the Big Bend area and in South Central and Southeast Florida, and persistent clustering of low risks occurring in Southeast and Southwest Florida. Low and high MI mortality clusters occurred in the same areas as MI hospitalization clusters, but there were no high-risk clusters of MI mortality in South Central Florida. Thus, high-risk clusters need to be prioritized for interventions to achieve health equity and broader reduction goals.

5.1.2 Theme 2. Investigation of the Temporal Changes in MI Hospitalization and Mortality Risks in Persistent Clusters

Monitoring trends in MI risks may reveal whether health disparities have widened or narrowed over time, thereby providing insights into the effectiveness of prevention efforts. Disparities in MI hospitalization and mortality risks were assessed by computing the risk difference between the high-risk clusters and the low-risk cluster with the lowest

MI hospitalization risk, both at the beginning and at the end of the study periods. The results showed that disparities narrowed in the short term, but counties in perisitent high-risk clusters are only now achieving MI risks seen in low-risk counties at the beginning of the study. Concerning trends, where risks appeared to trend upwards in parts of northern Florida during the latter years of study, were identified. The results indicate the need for acceleration of intervention efforts in counties within high-risk clusters.

5.1.3 Theme 3. Investigation of Potential Sociodemographic Determinants of MI Hospitalization Risks

Identifying the most important determinants of MI for different geographic areas may lead to the development of evidence-driven strategies for reducing/elimination health disparities and improved population health. These factors account for 40% of the health of a population; hence, their identification offers the greatest opportunities for reducing morbidity and disability from MI and achieving lasting improvements in population health at the lowest cost.

A global negative binomial model identified that race, marital status, education level, lack of health insurance, and rural residence were important sociodemographic drivers of MI hospitalization risks in the state. A geographically weighted negative binomial model showed that the impacts of education and health insurance varied by geographic location, with the impacts being strongest in southern Florida.

Geographic differences in the impacts of education and health insurance signify that the negative binomial model, and other global regression models that estimate a single coefficient for each predictor for the entire study area, may not capture the unique health needs at the local level in Florida. Thus, a “one size fits all” strategy would not be sufficient for addressing MI disparities in Florida. Rather, different parts of the state require slightly different strategies, informed by empirical evidence from global regression models supplemented with local models.

The findings in this dissertation will be used to target resources for MI control to high-risk areas as a part of a needs-driven prevention/control strategy geared towards reducing the MI burden in Florida. Thus, the findings have direct relevance to public health efforts aimed at addressing MI-related health disparities in Florida, and can be expected to have a significant impact on resource allocation, health program planning, and advocacy for high risk populations. Moreover, MI shares common risk factors with other cardiovascular diseases such as stroke, and also tends to overlap geographically with these health conditions. Thus, interventions targeting MI risk factors would address the burdens of MI and stroke and several of their associated risk factors (e.g., diabetes, high blood pressure) and lead to reduced cardiovascular health inequities and improved population health for all communities in Florida. Furthermore, Florida’s current demographics and healthcare challenges mirror those for states in the southern US such as Alabama, Mississippi, Oklahoma, and Tennessee, given their failure to expand Medicaid [117]. They also foreshadow the changes projected for the US population in the future. Thus, the results for this study have important implications for local, regional and national health policy.

5.2 Future Research Directions

The findings and the limitations identified in chapters 2, 3 and 4 in this dissertation suggest potential avenues for further research.

An ecological study design was used because the interest was to investigate spatiotemporal patterns and burdens of MI hospitalization and mortality, as well as potential sociodemographic predictors of MI hospitalization risks at the county level. The county is more relevant to policy action steps. However, geographic analysis of the MI burden at the county-level does not identify within county differences which can be large. For instance, while perisitent clustering of high MI risks in predominantly rural counties argue convincingly for the need for additional research and intervention efforts in these specific areas, some areas within rural counties could have low MI risks. Thus, additional studies limited to high-risk clusters, with high-risk counties partitioned further into ZIP codes may help identify specific ZIP codes within high-risk counties that have highest risk for MI deaths. Interventions may then be targeted to those ZIP codes and these may have a higher success rate in improving cardiovascular health than generalized interventions targeted at the county level. Additionally, perisitent clustering of low-risks in urban counties may mask high risks in socioeconomically-disadvantaged inner-city populations in those counties, which do not appear as hot spots in county-level maps. Thus, public health officials or policy makers using these data may not identify or target these inner-city populations as needing intervention to reduce MI risk. Therefore, health programs could benefit from small-area studies at the ZIP code or the census tract levels.

Contextual sociodemographic features of county populations were investigated for potential associations with MI hospitalization risks across Florida counties. However, there is potential for substantial within-county variations in sociodemographic factors due to the heterogeneous nature of the counties. Thus, a change in spatial unit of analysis may alter the spatial patterns due to the modifiable areal unit problem. From a research policy perspective, this is good cause to avail individual-level data to designated researchers, with appropriate safe guards for confidentiality, to investigate the role of geography in the etiology of MI.

Potential confounding factors such as clinical (obesity, diabetes, and hypertension), behavioral (lack of physical activity, poor diet, smoking, and alcohol consumption), physical environmental (built environment, safety, walkability) and healthcare access factors (i.e. location of primary care physicians and cardiac specialists, transportation system, and travel distance to cardiac centers) that might be associated with the spatiotemporal disparities in MI-hospitalization risks in Florida were not investigated this study. Therefore, future studies will need to include these variables, to enable policy makers to design more effective evidence-driven interventions for reducing the MI burden in the most disadvantaged regions. Moreover, investigations of the drivers of MI risks in counties within persistent low-risk clusters may provide us with insights regarding the protective factors responsible for the lower than expected MI risks in those counties.

The distinct seasonal patterns observed for MI hospitalizations, with higher risks for winter months than for summer months suggest that weather may contribute substantially to MI burden/morbidity in Florida. Additional studies of associations of heat

and cold exposure and MI, adjusting for $PM_{2.5}$ and O_3 levels and other confounding effects, may lead to improved strategies for MI prevention.

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