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Spatial Epidemiology and Temporal Trends of Heart Attack and Stroke in Middle Tennessee

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Spatial Epidemiology and Temporal Trends of Heart Attack and Stroke in Middle Tennessee

A Thesis Presented for the Master of Science Degree

The University of Tennessee, Knoxville

Doreen Busingye

December 2011

Dedication

This thesis is dedicated to my parents: my dad, Jerome Byesigwa, and my mom, Rose Mugabe for their constant prayers, encouragement and unwavering faith in me.

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This thesis would not have been completed without the help of many people to whom I owe my deepest gratitude. I've been fortunate to work and learn under the supervision of Dr. Agricola Odoi, a dedicated epidemiologist and a remarkable mentor. His wisdom, patience, extensive knowledge and commitment to the highest standards have inspired and motivated me. Thanks Dr. Odoi, you've truly been a blessing. I would also like to extend my appreciation to Dr. Robert Mee and Dr. Amy Keenum for their willingness to serve on my graduate committee and for their professional and academic support, constructive criticism and interesting perspectives. Thanks are also due to all my friends especially, my colleagues Ashley and Jenny who have always been willing to attend to my many questions. I would also like to thank my parents, siblings, and relatives for always believing in me even when I did not believe in myself. And last but most important of all, I acknowledge my lord, Jesus Christ, my constant source of inspiration.

Abstract

Despite declines in mortality risks of myocardial infarction (MI) and stroke in the US since the 1960's, the burdens of these conditions remain high. These conditions require emergency and specialized care and therefore quick transportation of patients to appropriate hospitals is critical. Geographic disparities in MI and stroke burdens have been consistently reported in the US with the south-east having the highest risks. Most studies of geographic disparities have been performed at county or higher geographic units. Therefore, spatial patterns at neighborhood levels are unclear. Moreover, it's important to investigate disparities at neighborhood levels to better understand neighborhood health needs. Therefore, the goal of this study was to investigate neighborhood disparities associated with MI and stroke in Middle Tennessee. Specific objectives were to investigate: (a) geographic disparities in timely access to emergency care; and (b) geographic disparities in MI and stroke mortality risks.

Street network, hospital, population, and mortality data (1999-2007) were obtained from Streetmap USA, the Joint Commission on Accreditation of Health Organizations, US Census Bureau, and the Tennessee Department of Health, respectively. Network analysis was used to investigate and identify neighborhoods lacking timely access to emergency MI and stroke care. Moran's I and Kulldorff's spatial scan statistic were used to investigate geographic hot-spots of MI and stroke mortality risks at both the county and neighborhood levels. Poisson and negative binomial models were used to investigate predictors of identified geographic patterns.

A temporal increase in the percentage of the population with timely geographic access to stroke and cardiac centers was observed. In 2010, about 5% of the

population, located mainly in rural neighborhoods, lacked timely access to a stroke center. Significant ($p<0.05$) hot-spots of MI and stroke mortality risks were identified at both neighborhood and county levels. However, clusters identified at the neighborhood level were more refined. Neighborhoods with higher proportions of older populations and those with lower education had significantly ($p<0.05$) higher mortality risks.

These findings are vital for guiding health planning, resource allocation and service provision in an effort to provide needs-based services to the population. This is important in reducing/eliminating neighborhood disparities and improving population health.

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List of Abbreviations

ACC - American College of Cardiology
AHA - American Heart Association
ARIC - Atherosclerosis Risk In Communities
ASA - American Stroke Association
BMI - Body Mass Index
BRFSS - Behavioral Risk Factor Surveillance System
CABG - Coronary Artery Bypass Graft
CAD - Coronary Artery Disease
CAS - Carotid Angioplasty and Stenting
CDC - Centers for Disease Control and Prevention
CEA - Carotid Endarterectomy
CHD - Coronary Heart Disease
CK - Creatinine Kinase
CPSS - Cincinnati Prehospital Stroke Scale
CT - Computed Tomography
CVD - Cardiovascular Disease
DALY - Disability-adjusted Life Year
DBP - Diastolic Blood Pressure
DSA - Digital Subtraction Angiography
ECG - Electrocardiogram
ED - Emergency Department
EMS - Emergency Medical Services

EU - European Union

FDA - Food and Drug Administration

GAP - Guidelines in Applied Practice

GIS - Geographical Information Systems

GWTG - Get With The Guidelines

HBP - High Blood Pressure

HDL - High Density Lipoprotein

IAT - Intra-arterial Thrombolysis

ICD - International Classification of Diseases

ICH - Intracerebral Hemorrhage

ICP - Intracranial Pressure

JCAHO - Joint Commission on Accreditation of Health Organizations

LAPSS - Los Angeles Prehospital Stroke Screen

LDL - Low Density Lipoprotein

MHS - Minnesota Heart Survey

MI - Myocardial Infarction

MONICA - Multinational Monitoring of trends and determinants in Cardiovascular disease

MRI - Magnetic Resonance Imaging

NHANES - National Health and Nutrition Examination Survey

NINDS - National Institute of Neurological Disorders and Stroke

PET - Positron Emission Tomography

PCI - Percutaneous Coronary Interventions

SAH - Subarachnoid Hemorrhage

SBP - Systolic Blood Pressure

SES - Socioeconomic Status

SEB - Spatial Empirical Bayesian

tPA - Tissue Plasminogen Activator

UK - United Kingdom

US - United States

WHO - The World Health Organization

CHAPTER 1

1.0 Introduction

Myocardial Infarction (MI), also known as heart attack, occurs as a result of blockage of blood flow to the heart muscle resulting mainly from formation of a blood clot in the coronary artery. Stroke is an acute neurological injury which results from interrupted blood supply to part of the brain. Globally, an estimated 17 million people die annually of Cardiovascular diseases (CVD), particularly MI and stroke [1]. Myocardial infarction, accounts for about 7.2 million deaths globally each year [2] . About 16 million new incidences of stroke occur annually in the world, resulting in a total of 5.7 million deaths [3].

Although the mortality risks from coronary heart disease (CHD) and stroke have declined steadily in the US since the 1960's, heart disease and stroke remain the first and third leading causes of death in the US [4]. Stroke is also the leading cause of adult disability in the US [5]. An estimated 700,000 individuals suffer a stroke each year in the United States. Out of these, about 167,000 die [3] and about 15-30% of the survivors are severely disabled [5]**.** In Tennessee, heart attack accounts for over one-third of all diseases of the heart deaths and results in an average of 5,500 deaths per year [6]. Stroke is also the leading cause of adult disability and third leading cause of death in Tennessee [6]. Additionally, about 20,000 hospitalizations for stroke were recorded each year between 1997 and 2004 in Tennessee [6].

Both MI and stroke are serious conditions that require emergency medical care to reduce chances of complications or death. Percutaneous coronary intervention (PCI), which involves cardiac catheterization, is the recommended treatment for MI. Since timely access to this treatment is critical for good health outcomes [7, 8], quick access to cardiac centers plays an important role in determining patient survival. For acute ischemic stroke, the recommended treatment (administration of thrombolytics) has to be done within 3 hours of symptom onset [9] for better outcomes. There is evidence that half of stroke deaths occur before the patients reach the hospital [10]. Therefore, early transport of patients to appropriate hospitals and early treatment of these patients may prevent or reduce the number of complications, disabilities or deaths [11].

Several factors such as reduction in major population risk factors and improved medical care have been attributed to the decline in the MI and stroke mortality risks [12-15] over the past decades [16-19]. Despite the declines in MI and stroke mortality risks, a disproportionate burden of these conditions is reported to be shouldered by some segments of the population [20]. Significant variability of MI and stroke mortality risks have been observed across geographic regions, races, genders, age groups, and socioeconomic status [14]. The Southeastern United States, also known as the “stroke belt” has about 20% greater average mortality risk than the other regions of the United States [21]. Investigation and identification of these disparities in health outcomes at the local level and identifying determinants for the identified disparities is critical in informing local health planning and policy decisions. Additionally, identification of disparities in geographic access to emergency cardiac and stroke care is a critical step towards reduction and elimination of these disparities, and improving population health. Many past studies assessing geographic access to health services have used straight line/Euclidean distance. However, these methods have inherent limitations as they assume straight line driving and do not adjust for travel impedances. In this study, network analysis was used to estimate travel time. This is better because it accounts for travel impedances such as speed limits and therefore provides a more realistic and accurate measure of geographic accessibility than use of Euclidean distance measures [22].

The objectives of this study were to investigate: (i) spatial and temporal changes in disparities of timely access to emergency heart attack and stroke care in Middle Tennessee (ii) neighborhood geographic disparities and temporal trends in heart attack and stroke mortality risks in Middle Tennessee and identify determinants/predictors of observed disparities. Identification of disproportionately affected neighborhoods will help health planners better target resources and can aid the development of programs better tailored to specific community needs. This is important in addressing one of the overarching goals of the Healthy People 2020 of reducing disparities and improving health of the entire population [23].

This thesis is divided into four chapters. Chapter one includes the introduction of the study as well as literature review. In chapter two, I present results of a study in which network analysis was used to address the first objective of the study and in chapter three, results of a study addressing the second objective are presented.

Chapter four provides a general summary of the thesis, recommendations and concluding remarks.

1.1 Literature Review

1.1.1 Pathophysiology

Myocardial infarction (MI) occurs when a coronary artery supplying the heart becomes occluded. The occlusion impedes the flow of oxygen rich blood to the heart muscle thus causing muscle death. The prognosis of patients after an acute MI is mainly determined by the size of the infarct, which is dependent on the area at risk (determined by localization of coronary occlusion), the duration and severity of ischaemia, as well as the mode of reperfusion [24]. Prompt reperfusion restores blood flow and limits the extent of damage.

Stroke is brain injury caused by interruption of blood supply to the brain, usually as a result of bursting, narrowing or blockage of a blood vessel. Stroke is characterized by rapid onset of neurological symptoms that last at least 24 hours. Blockage of blood supply deprives the brain of necessary oxygen and nutrients resulting in damage to the brain tissue. The impact of stroke is dependent on the part of the brain that is damaged, how quickly blood flow is restored, and how quickly other areas of the brain can compensate for the injury [25]. There are two main types of stroke: hemorrhagic and ischemic. Ischemic stroke, which is the main focus of this study, accounts for 87% of the 780,000 stroke cases that occur annually in the United States [26].

1.1.2 Etiology

A large number of cases of MI occur as a result of coronary artery disease (CAD) [27]. Coronary artery disease results from progressive buildup of fatty deposits, called plaque, on the inner walls of the coronary arteries. This condition is called atherosclerosis and involves the walls of the arteries thickening and accumulating plaque that result in narrowing or blockage of one or more of the arteries supplying a section of the heart muscle. In some cases, rupture of destabilized atherosclerotic plaques inside the arterial wall may trigger the formation of a thrombus which can occlude the artery thus causing cardiac ischemia [28, 29]. Occlusion of the coronary artery impedes blood flow thus causing a heart attack. A heart attack can also occur due to microvascular disease, a condition in which the blood vessels of the heart are very small or microscopic. This condition is believed to be more common in women than in men [27]. A less common cause of MI is severe spasm (tightening) of a coronary artery that cuts off blood flow through the artery. Spasms can also occur in non-atherosclerotic coronary arteries. The causes of coronary artery spasm are not clear, however, they are usually associated with taking certain drugs (such as cocaine), emotional stress or pain, exposure to extreme cold and cigarette smoking.

Ischemic stroke results from occlusion of an artery in the cerebral circulation. The blockages stem from three conditions: (i) formation of a clot within a blood vessel of the brain or neck, called thrombosis; (ii) movement of a clot from another part of the body such as the heart to the neck or brain, called embolism; (iii) severe narrowing of an artery in or leading to the brain, called stenosis. Hemorrhagic stroke occurs when there is bleeding within the brain (intracerebral hemorrhage) or bleeding between the inner (pia mater) and outer (arachnoid mater) layers of the tissue (meninges) covering the brain (subarachnoid hemorrhage). Intracerebral hemorrhage usually results from chronic high blood pressure whereas the most common cause of subarachnoid hemorrhage is rupture of an aneurysm in an artery.

1.1.3 Clinical Presentation

Chest pain or discomfort is the most common symptom of MI [27] . There is discomfort, in the center of the chest, that lasts for more than a few minutes, subsides, and reoccurs. This discomfort may be mild or severe and is characterized by uncomfortable pressure, squeezing, or pain. Heart attack pain sometimes manifests as indigestion or heartburn. Other common signs and symptoms of MI include: upper body discomfort in one or both arms, the back, neck, jaw, or stomach; shortness of breath; nausea, vomiting, lightheadedness or fainting and breaking out in a cold sweat. In women, MI symptoms may be different from the typical symptoms. For instance, some women may experience symptoms such as, shortness of breath, indigestion, or fatigue [25]. This makes diagnosis more complex.

The five main categories of stroke symptoms defined by the American Stroke Association (ASA) are: (i) sudden numbness or weakness of the face, arm or leg, especially on one side of the body; (ii) sudden confusion, trouble speaking or understanding; (iii) sudden trouble seeing in one or both eyes; (iv) sudden trouble walking, dizziness, loss of balance or coordination; and (v) sudden severe headache with no known cause [30]. Other signs that may occur include double vision, drowsiness, and nausea or vomiting. In a multicenter study carried out in Japan, it was found that motor weakness accounted for 70% of all symptoms occurring at the onset of ischemic stroke, speech disturbance (46%), and gait disturbances (37%) [31].

1.1.4 Diagnosis

1.1.4.1 Myocardial Infarction

Patient symptoms, personal and family medical history and results of diagnostic tests form the basis for MI diagnosis. The World Health Organization (WHO) criteria for the diagnosis of MI require that at least two of the following three factors be present: a history of ischemic type chest discomfort, evolutionary changes on serially obtained Electrocardiogram (ECG) tracings, and a rise and fall in serum cardiac markers [32]. The ECG is a test that detects and records the electrical activity of the heart. Injured muscle does not conduct electrical impulses normally, therefore, certain changes in the appearance of the electrical waves on an ECG are strong evidence of a heart attack. Electrocardiography is the most commonly used laboratory procedure for the diagnosis of heart disease [33] and is readily available, non-invasive, and inexpensive. The ECG not only indicates the presence of acute MI, but can also be used for estimation of the size and location of the affected area [34].

Appropriate and accurate interpretation of the ECG recording requires knowledge about its sensitivity and specificity. However, when considering the sensitivity and specificity of the ECG, it is important to recognize that the ECG is composed of a number of waveforms, each with its own sensitivity and specificity, and each influenced differently by a variety of pathologic and pathophysiologic factors [33]. Nevertheless, a study in Scotland reported a 68% sensitivity, 100% specificity and 85% predictive accuracy of ECGs in diagnosing MI [35].

Blood tests such as troponin, creatine kinase (CK) and serum myoglobin tests measure the amount of proteins in the bloodstream released as a result of damaged cardiac muscle cells. Elevated blood levels of these proteins especially, Creatine kinase-myocardial band (CK-MB) isoenzyme, are strong evidence of MI [27, 36]. Recently, troponin I enzyme determinations have become critical in early evaluation of a suspected MI because they rise earlier than the CK-MB isoenzyme and levels may stay elevated for several days. Creatine kinase levels usually rise about 6 hours after an infarction and may return to normal within 48 hours [36]. In a study that compared the diagnostic accuracy of these markers, CK-MB subforms (isoforms) (for example, CK-MB2 and CK-MB1) were most sensitive (91%) and specific (89%) within 6 hours of onset, followed by myoglobin with sensitivity of 78% and specificity of 89%. For late diagnosis, total CK-MB activity (derived from subforms) was the most sensitive (96%) and specific (98%) at 10 hours from onset, followed by troponin I that had a sensitivity of 96% and specificity of 93% at 18 hours, and troponin T with a sensitivity of 87% and specificity of 93% at 10 hours [37]. However, based on the predictive values analysis, Weissler argues that CK-MB subforms have no greater early rule-in power for MI than troponins T and I, CK-MB activity and mass; and that CK-MB subforms have the highest rule-out power only at the sixth hour after chest pain onset [38]. Recently, studies [39-41] have shown that compared to other cardiac biomarkers such as CK-MB and myogloblin, cardiac troponin demonstrates high sensitivity and specificity, with the ability to detect even minor amounts of myocardial damage. Hence, there is evidence to support the role of troponins both in the diagnosis of MI, as well as for post-infarction risk assessment. It is important to note that the sensitivity and specificity of the troponin

I assay depends on the cut-off values. For instance, a study investigating the sensitivity of troponin I, revealed that when a troponin I level greater than 0.6 ng/mL was used as a positive value (cut-off value), the sensitivity was 94% and specificity was 81% using either time zero or 6 hours. Similarly, when troponin I greater than 2.0 ng/mL was used to define a positive test, the sensitivity was 85% and specificity was 91% [42].

Coronary Angiography, a special x-ray exam of the heart and blood vessels, is done in MI patients to help identify blockages in the coronary arteries. A number of sophisticated techniques such as coronary computed tomography, magnetic resonance imaging (MRI) and positron emission tomography (PET) can be used to visualize and identify stenosed or blocked coronary arteries thus help in diagnosis of MI. In a study done in New York, coronary computed tomographic angiography was found to have a sensitivity of 100% and a specificity of 73%, with a positive predictive value of 92%, and a negative predictive value of 100% for diagnosing obstructive CAD [43]. Another study carried out in Switzerland reported that the sensitivity and specificity for ischaemia detection by cardiovascular MRI were 91% and 94%, respectively, and for detection of coronary arteries with ≥50% diameter stenoses, the study found that the sensitivity and specificity of MRI were 87% and 85%, respectively [44]. The average weighted sensitivity of 90% and specificity of 89% was observed for detecting at least one coronary artery with >50% stenosis when PET was used [45]. In the same study, a positive predictive value of 94% and a negative predictive value of 73% was recorded for PET with the overall diagnostic accuracy of 90%.

1.1.4.2 Stroke

Like MI, patient symptoms, personal and family medical history and results of diagnostic tests form the basis for stroke diagnosis. A complete physical and neurological exam, a series of questions and tests to check brain, spinal cord, and nerve function, are performed. The neurological exam checks a person's mental status, coordination, ability to walk, and how well the muscles, sensory systems, and reflexes work. In a community-based study of diagnostic accuracy, primary care physicians practising in an emergency setting had a 92% sensitivity for diagnosis of stroke and transient ischemic attack (TIA) based on physical and neurological examination of patients [46].

A computed tomography (CT) scan of the brain is performed as part of the initial evaluation of a patient with suspected stroke. A CT scan is a brain imaging test that uses low-dose x-rays to show an image of the brain. This test has a low sensitivity to early ischemic changes during acute cerebral ischemia and is usually of little value for establishing the diagnosis of acute stroke. However, the main advantage of this imaging modality is its widespread availability and high sensitivity for hemorrhagic stroke [47]. It is able to eliminate the possibility of intracranial hemorrhage, subdural hematoma, or mass lesion. A study reported a sensitivity of 12% and specificity of 100% of CT in diagnosing acute ischemic stroke within 3 hours of symptom onset [48]. Multimodal imaging techniques such as CT angiography and CT perfusion techniques may also add diagnostic information regarding vascular occlusion but are not widely available on a timely basis at many hospitals [49].

Magnetic resonance imaging is another technique that uses magnetic fields to detect subtle changes in brain tissue and is used to show the location and extent of brain damage. Magnetic resonance imaging based techniques have shown greatly enhanced sensitivity in the early diagnosis of stroke as well as the identification of intracerebral hemorrhage [50]. A study reported a sensitivity of 76% and a specificity of 96% of MRI in diagnosing acute stroke within 3 hours of symptom onset, whereas a sensitivity of 91% and specificity of 98% was reported for the same diagnosis within 12 hours of symptom onset [48]. Additionally, diffusion-weighted imaging (DWI), another MRI imaging technique, is able to demonstrate parenchymal changes early in the presentation of stroke [47]. Magnetic resonance imaging produces sharper and more detailed images than a CT scan so it's often used to diagnose stroke involving small blood vessels [51]. However, as a practical issue, most hospitals do not have these specialized MRI services available in the acute setting, and these diagnostic tools require more advanced interpretations. Therefore, although multimodal imaging techniques may provide valuable information, these diagnostic techniques may be difficult to perform in a timely fashion [47, 49].

Techniques such as transcranial doppler, doppler ultrasound, carotid ultrasound are used to assess blood flow through the vessels in the brain. These tests give information about the condition of arteries. In carotid artery ultrasound scanning, high-pitched sound waves are bounced off the blood vessels and tissues of the neck to create an image of the arteries. Duplex scanning, which is a newer technique than traditional carotid artery ultrasound and now used more often, is able to measure blood flow at many points in the blood vessel at one time. The transcranial doppler is a non-invasive tool for studying the basal cerebral arteries, and has been widely used for evaluating ischemic stroke [52]. Carotid duplex sonography has also been widely used as a tool to evaluate occlusive lesions in the extracranial brain arteries such as the internal carotid artery and vertebral artery [53-55]. The accuracy, sensitivity, and specificity of neurosonography in detection of occlusive vessels in ischemic stroke was found to be 99.6%, 100% and 99.6%, respectively [56]. Additionally, neurosonographic examination is noninvasive, convenient, relatively inexpensive and can be performed at the bedside.

Cerebral angiography (digital subtraction angiography [DSA]) is the gold standard for the detection of many types of cerebrovascular lesions and diseases [57]. Digital subtraction angiography is an invasive test which involves taking an x-ray of the brain arteries after injection of a contrast dye in the vessels. This test gives a picture of the blood flow through the vessels, thus allows identification of the size and location of blockages. In this test, a catheter is inserted into an artery (often in the arm) and threaded through other blood vessels to reach the carotid artery. A dye is then injected through the tube and into the artery. The dye outlines the blood vessel and x-rays are taken to evaluate the degree of narrowing and the condition of a plaque. For most types of cerebrovascular disease, the resolution, sensitivity (95%), specificity (99%) and accuracy (97%) of DSA equal or exceed that of the non-invasive techniques [58-60]. However, a risk of about 1% mortality and serious morbidity has been associated with DSA procedures [61, 62].

Since approximately 20-40% of all ischemic stroke cases are caused by emboli, usually arising from the heart [63], imaging procedures such as transthoracic and transesophageal echocardiography are intended to guide clinical decision making by detecting the cardiac sources of cerebral ischemia or infarction. Both the sensitivity and specificity of transesophageal echocardiography in detecting cardiac anomalies implicated in stroke have been reported to be 99% [64].

1.1.5 Treatment

1.1.5.1 Myocardial Infarction

Limiting the size of the infarct is critical to improving immediate and long-term outcomes and to reducing the incidence and prevalence of heart failure. The primary therapy to limit infarct size in patients with an acute MI is reperfusion by revascularization with a mechanical (percutaneous coronary intervention, also known as, angioplasty) or pharmacological intervention (thrombolysis). Other treatments like pain control, surgical procedures such as coronary artery bypass, and heart transplantations may be performed. Angioplasty is the recommended treatment for MI and is a less invasive procedure that can be used to open coronary arteries that are blocked. During angioplasty, a catheter with a balloon on the end is threaded through a blood vessel to the blocked coronary artery. Then, the balloon is inflated to push the plaque against the wall of the artery thus widening the inside of the artery, restoring blood flow. Sometimes, a small mesh tube called a stent may be inserted into the artery to help keep it open. Insertion of a stent reduces the possibility of the artery narrowing again in the same place (restenosis) but is not associated with significant reductions in death or reinfarction rates [65, 66]. Restenosis occurs in about 40% of patients that undergo angioplasty alone, and in 20% of those that undergo angioplasty with stenting

[25]. Studies have shown that drug-eluting stents reduce the risk of restenosis compared with bare metal stents, without having a significant impact on the risk of stent thrombosis, recurrent myocardial infarction, and mortality [67-69]. Primary PCI approaches a 90% success rate [70] and is effective in securing and maintaining coronary artery patency and prevents some of the bleeding risks associated with fibrinolysis. Several studies have shown the superiority of PCI procedures over thrombolytics in the treatment of acute myocardial infarction [71-74]. There is evidence of reduced mortality and recurrence rates in early catheterization patients as compared to those given thrombolytic therapy. Additionally, lower mortality risks have been observed in patients undergoing primary PCI in centers with a high volume of PCI procedures [75, 76].

Pain control or analgesia is an important element in the management of MI patients, not only for humane reasons but also because the pain is associated with increased sympathetic activation, which causes vasoconstriction and increases the workload of the heart [77]. Intravenous opioids such as morphine are the most common analgesics used. Morphine lessens anxiety and restlessness and reduces sympathetic activation, thus decreasing the workload and oxygen consumption of the heart [78]. Other drugs like nitrates decrease ischemic discomfort through coronary vasodilation which enhances coronary blood flow and also decreases ventricular preload by increasing venous capacitance. Additionally, supplementary oxygen is recommended for most MI patients especially those with breathlessness (shortness of breath) and hypoxia [78]. Thrombolytic therapy is also used and involves administration of thrombolytic agents (clot busters) to dissolve clots in the arteries thus restoring blood flow to the heart tissue. The use of thrombolytics, such as tissue plasminogen activator (tPA), has substantially reduced disability and death from heart attacks [25].

Coronary artery bypass graft (CABG) is a surgical procedure in which a new route is created for blood to flow around or bypass a clogged artery. This is performed to restore adequate blood supply to the heart. This procedure is done by removing a part of a vein from the patient’s leg or thigh, or an artery from the chest wall or arm, and grafting this segment to a blocked coronary artery to form a detour around the blockage. Although the indication of a CABG in the acute phase is limited to a few patients, it may be indicated after failed PCI, coronary occlusion not amenable for PCI, presence of refractory symptoms after PCI, cardiogenic shock, or mechanical complications such as ventricular rupture, acute mitral regurgitation, or ventricular septal defect [79, 80]. Patients that have undergone CABG have been shown to have a long-term survival of 35 years [81, 82].

Cardiac transplantation is indicated for patients with irreversible heart injury from CAD and multiple heart attacks that cannot be treated by any other means. According to a survey conducted by the American Heart Association (AHA), the average survival rates, one year after the transplant are 88% in males, and 86.2% in females. This average has been found to steadily decline as the years progress and so the five year survival rates are found to be 73.1% in males, 69.0% in females [21].

1.1.5.2 Stroke

The treatment for stroke is dependent on the type of stroke (Ischemic or hemorrhagic).

1.1.5.2.1 Ischemic Stroke

Before or on arrival at the hospital, ischemic stroke patients may be given antiplatelet drugs (such as aspirin or clopidogrel) to prevent clotting. The primary treatment for acute ischemic stroke is early administration of thrombolytic medication or “clot-buster” called tissue plasminogen activator (tPA). Tissue plasminogen activator dissolves the clot and restores blood flow to the brain. However, it presents some risk of causing bleeding in the brain in some people. Due to this risk, it is recommended that tPA be administered only by physicians trained in its use and in facilities with the necessary resources to handle the bleeding complications [12]. In the National institute of neurological disorders and stroke (NINDS) tPA stroke study, 50% of tPA treated patients had excellent outcomes compared with 38% of controls at 3 months after treatment [9]. However, the mortality risk at 3 months was not significantly different between the two groups and a higher rate of symptomatic hemorrhage was observed in the tPA group than the control group (6.4% versus 0.6%).

Patients who are beyond the 3-hour window restriction of intravenous tPA treatment may benefit from mechanical thrombolysis. The Concentric Retriever (Concentric Medical, Mountain View, Calif) is the only device currently approved by the U.S. Food and Drug Administration (FDA) for the endovascular treatment of stroke patients [83]. This device is used to mechanically remove occlusions from major cerebral arteries. The device has been reportedly used in patients with occlusion involving either the internal carotid artery, a segment of the middle cerebral artery, the basilar, or vertebral arteries [84].

Intra-arterial thrombolysis (IAT) is a procedure in which recanalization is achieved by direct infusion of a fibrinolytic agent (such as urokinase) into the clot causing the arterial occlusion. This endovascular approach is restricted to the recanalization of major cerebral arteries, most commonly the middle cerebral artery. Lisboa and colleagues [85] reported more favorable outcomes (41.5% versus 23%) and a lower mortality risk (27.2% versus 40%) in IAT treated patients than in the control group. However, symptomatic intracerebral hemorrhage was more frequent in the IAT group compared with the control group (9.5% versus 3%).

Carotid endarterectomy (CEA) is a common surgical procedure performed to prevent or treat stroke in selected patients with high-grade atherosclerotic occlusive disease of one or both carotid arteries [86]. Several controlled trials have provided evidence that carotid endarterectomy is superior to medical therapy in reducing subsequent stroke rates among subgroups of persons at risk [87-90]. For instance, high beneficial effects of CEA were observed in patients with angiographically confirmed high-grade carotid stenosis (70% to 99%) [87]. Although this procedure may reduce the risk of ischemic stroke, it may also trigger a stroke or heart attack by releasing a blood clot or fatty debris. This risk can be reduced by placing filters (distal protection devices) at strategic points in the blood stream to trap any material that may break free during the procedure.

Angioplasty as done in the management of MI can also be done to widen the inside of a plaque-coated artery that supplies blood to the brain. A balloon-tipped catheter is maneuvered into the obstructed area of the artery, and the balloon is inflated compressing the plaques against the artery walls. Sometimes a stent is inserted in the artery to prevent recurrent narrowing. Although carotid angioplasty and stenting (CAS) is a potential alternative treatment to CEA, some randomized trials and meta-analyses have failed to demonstrate that CAS is as safe as CEA with regard to the risks of periprocedural complications [91-95], and current guidelines recommend that CAS should not be used in good surgical candidates [96-98]. Nonetheless, some clinical trials have shown that beyond the perioperative period, the risk of ipsilateral stroke is very low and comparable in CAS and CEA patients [99, 100], suggesting that CAS may be an acceptable option in selected patients who have a low risk of periprocedural complications [101]. Carotid angioplasty and stenting is said to be superior to CEA in certain patient groups, such as those exposed to previous neck surgery or radiation injury, and in patients at high risk of complications with surgical therapy [102]. In their review of literature, Kachel *et al* reported an overall technical success rate of 96.2%, with a 2.1% rate of morbidity, 6.3% rate of transient minor complications, and no deaths for carotid angioplasty procedures [103].

1.1.5.2.2 Hemorrhagic Stroke

Intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH) account for about 10% and 3% of all stroke cases in the US, respectively [21]. Potential treatments of hemorrhagic strokes include stopping or slowing the initial bleeding during the first hour after onset; removing blood from the parenchyma or ventricles to eliminate both mechanical and chemical factors that cause brain injury; management of complications of blood in the brain, including increased intracranial pressure (ICP) and decreased cerebral perfusion; and good general supportive management of patients with severe brain injury [104]. Although there is no clear indication from the literature of the optimal treatment for hemorrhagic stroke, surgical treatment is common [105, 106]. The rationale for surgery is evacuation of a hematoma so as to reduce the mass effect, block the release of neuropathic products from the hematoma, and prevent prolonged interaction between the hematoma and normal tissue, which can initiate pathologic processes [107]. In practice, surgery is recommended as a lifesaving measure in patients with large hematomas or in young patients with cortical hemorrhages and secondary neurologic deterioration. Patients with great and prolonged neurologic deficits are considered poor surgical candidates as they are believed to have little chance for functional recovery. Patients with small hemorrhages or minimal neurologic deficits are treated medically and deep hemorrhages are rarely evacuated [104]. Early craniotomy has been recommended in patients with cerebellar hematomas because the rate of neurologic deterioration after cerebellar hemorrhage is very high and unpredictable [108]. Zuccarello *et al* reported a higher likelihood of a good outcome in

ICH patients who underwent surgical evacuation (56%) than in those who received medical treatment alone (36%) [109]. However, the benefits of evacuation of basal ganglionic, thalamic, and pontine hemorrhages through an open craniotomy have been obscured by excessive neural damage incurred during the approach to the hematoma and bleeding recurrence [108]. Additionally, a study reported a higher rate of death or dependency at 6 months associated with this procedure [110].

1.1.6 Timeliness of Access to Myocardial Infarction and Stroke Care

Time is critical in diagnosis and management of MI and stroke. A quick diagnosis enables administration of proper treatment for better outcomes. Therefore, quick recognition of MI and stroke symptoms and timely transportation of the patients, by either Emergency medical services (EMS) or other means, to the nearest cardiac and stroke center is of paramount importance.

Successful use of catheterization, the recommended treatment for MI, depends on the time to treatment. The current American and European guidelines suggest cardiac catheterization be done within 90 minutes of first medical contact [7, 8]. In situations when the time window for cardiac catheterization has been exceeded, it is recommended that thrombolytic therapy be given in the treatment of MI if there are no contraindications [7, 111]. However, for better outcomes, thrombolytic therapy must be administered within 1 hour after the onset of MI symptoms [27]. Thrombolytic therapy has been shown to greatly reduce risk of death in high risk patients presenting within 12 hours of MI symptom onset [112]. Furthermore, it is estimated that thrombolytic therapy prevents about 30 early deaths per 1,000 patients treated, with 20 deaths prevented per 1,000 patients treated between 7 and 12 hours after symptom onset [113].

For ischemic stroke, thrombolytic therapy, the main treatment must be administered intravenously within 3 [13] or 4.5 hours [114] of the onset of stroke symptoms. However, even within the 3-hour recommended treatment window, the odds of improvement decrease as time from symptom onset to treatment increases [14]. Therefore, quick transportation of MI and stroke patients to the appropriate hospitals is very critical in reducing mortality and improving the health outcomes. Moreover, due to the risks involved in thrombolytic therapy, it is recommended that it is administered only by physicians trained in its use and in hospitals with the necessary resources to handle bleeding complications [115]. This implies that not all hospitals can provide appropriate care for these patients. Thus, it's recommended that MI patients be treated in cardiac centers and stroke patients in stroke centers.

1.1.7 Role of Emergency Medical Services in Myocardial Infarction and Stroke Care

Successful MI and stroke care begins with recognizing these conditions as medical emergencies. Therefore, EMS play a key role in the continuum of care for these patients. Emergency medical services respond to, stabilize, and transport patients and therefore play an important role in saving lives and ensuring timely transport of patients in need of life saving cardiac procedures [116] and stroke care [117]. Emergency medical services are the first medical contact for more than half of all patients who have a stroke [118], and EMS transport significantly shortens the arrival time of patients to hospital [117] as well as reduces the time from symptom onset to CT evaluation [119-121]. Studies have also shown that myocardial infarction patients who are transported to the hospital by ambulance rather than by friends or relatives are more likely to receive early reperfusion therapy since they tend to arrive at the hospital earlier [116, 122, 123].

Early identification of MI and stroke symptoms by EMS personnel is a valuable part of optimal care for MI and stroke patients. In order to optimize stroke identification in the field, prehospital professionals are trained in appropriate use of prehospital stroke screening tools, such as the Los Angeles prehospital stroke screen (LAPSS) or the Cincinnati prehospital stroke scale (CPSS). Both of these stroke screening instruments have demonstrated sensitivities of greater than 90% [124-126]. In a study performed in California, the sensitivity, specificity, positive predictive value, and negative predictive value of diagnosing stroke using LAPSS were found to be 91%, 97%, 86%, and 98%, respectively [124]. In another study, the sensitivity and specificity of CPSS in diagnosing stroke was reported as 95% and 54%, respectively [127].

Prehospital notification by EMS personnel of in-bound stroke patients shorten delays from emergency department (ED) arrival until initial neurological assessment and initial brain imaging, and increases the proportion of patients treated with reperfusion therapy [119, 128]. In remote geographical areas without nearby stroke facilities, air medical transport can be used to airlift stroke patients from the field to a facility capable of managing acute stroke patients [129]. Air medical transport reduces transit times, thus may enable more rural residents access to thrombolytic therapy [130], and may be cost effective as well [131, 132].

1.1.8 Role of Specialized Care in Myocardial Infarction and Stroke Care

The creation of cardiac and stroke centers has improved patient outcomes over the years. One of the key components of specialized care for MI and stroke patients is prompt treatment, which increases the likelihood of survival [133, 134].

1.1.8.1 Myocardial Infarction Care

Acute MI is frequently characterized by life-threatening complications. As a result, triage of patients with acute MI to cardiac centers is generally the accepted standard of care [135]. Unfortunately, availability of this optimal strategy is limited because only 25% of hospitals in the United States have the ability to perform PCI [136]. Percutaneous coronary intervention can only be done in hospitals equipped with a catheterization laboratory and a specialized team that must be available 24 hours a day [75].

The AHA and the American College of Cardiology (ACC) have developed guidelines for the treatment of patients with CAD [7, 137]. Despite the wide availability of these guidelines, adherence to them in clinical medicine has been shown to be incomplete, highly variable, and there are frequently missed opportunities to implement this evidence-based care [138-140]. These missed opportunities may adversely affect short-, intermediate-, and long-term patient outcomes which potentially contribute to the high morbidity, mortality, and economic cost resulting from this condition. In order to ensure consistent application of the latest evidence–based scientific guidelines in the treatment of CAD, including MI, the AHA launched the “Get with The Guidelines Coronary Artery Disease” (GWTG-CAD) program [141] which has been instrumental in measuring and improving consistency of healthcare for CAD among participating hospitals in the US [142]. Other programs like the ACC’s Guidelines in Applied Practice (GAP) program were also developed for the same purpose [143]. Hospitals participating in GWTG-CAD have demonstrated improved adherence to national guideline-recommended therapies compared with non-participating hospitals [142, 144]. Moreover, adherence to guideline-based care has shown improved outcomes after acute MI [145].

1.1.8.2 Stroke Care

For optimal acute stroke care, it is essential that all stroke patients are immediately referred to the hospital best equipped to provide the most appropriate acute stroke care. A stroke unit is a hospital unit or part of a hospital unit that exclusively or nearly exclusively takes care of stroke patients. The minimum requirements of stroke centers include 24 hour availability of CT scanning and neurologists or other stroke physicians, presence of specialized staff, and adherence to treatment and management guidelines [146]. In a systematic review report, stroke patients who were treated in a stroke unit had an 18% lower mortality, a 29% lower dependence for activities of daily living, and a 25% lower need of institutional care compared to those treated in a general medical ward [147]. In another study, Asplund *et al* reported that organized stroke unit care resulted in long-term reductions in death, dependency, and the need for institutional care in stroke patients compared with conventional care [148]. The observed benefits were not restricted to any particular subgroup of patients or model of stroke unit care. Even when specialist support is provided, there are substantial differences in management and complications in stroke patients cared for in stroke units and general wards [149]. These may be responsible for the more favorable outcomes seen in patients in stroke units compared to those on general wards. The AHA's "Get with The Guidelines stroke" (GWTG-stroke) program was also developed to ensure consistent application of the latest evidence–based scientific guidelines in the treatment of stroke. Hospitals participating in the AHA/ASA GWTG-Stroke program have been associated with rapid and marked improvements in the quality of care for acute stroke patients during hospitalization [150, 151].

1.1.9 Access to Healthcare

Andersen defines access as the "ability to use health services when and where they are needed" [152]. Access to care can also be defined as "the timely use of personal health services to achieve the best health outcomes" [153]. Receiving medical treatment in a timely fashion can reduce complications, long-term disability, and death from many conditions, including MI and stroke [154]. Access to healthcare has considerable effect on health disparities. The large gap in access to health and healthcare between different groups in developed and developing countries is well documented [153]. There is significant evidence that access to the healthcare system varies by socioeconomic factors (such as, race, age, education, income, sex, culture, ethnicity, and lack of insurance) and geographic location. Individuals with limited or no access to care experience poor health outcomes, as well as worse quality of care [153]. Although socioeconomic factors and health insurance status are significant and powerful predictors of access to healthcare [155], these factors do not explain all of the racial and ethnic disparities in access to care. Evidence shows that even when accounting for insurance and income, disparities in access to care still persist [154].

Location of healthcare services is another important dimension of access to healthcare [156]. Studies reveal the unsurprising fact that utilization of care services tends to decline as the distance traveled to care increases [157]. This may explain why urban residents, who are often also wealthier, use services more than their rural counterparts [158]. Rural residents face travel barriers arising from distance and the lack of public transportation systems. Distance as a barrier to healthcare is not only confined to low- and middle-income countries but is a problem in high-income countries as well. A study of MI patients in the US found that patients living more than 20 miles away from a hospital were much less likely to visit ambulatory services for follow-up [159]. Additionally, reports show that MI patients within close proximity to cardiac centers are more likely to receive cardiac procedures such as PCI compared to those that are further away from the cardiac centers [160, 161]. In Japan, access to follow-up care after stroke treatment was considerably influenced by access to suitable transportation [162]. Location not only influences whether people present for treatment but also how long they wait before seeking treatment. For instance, a study in Vietnam found that location was the main determinant of the delay between onset of illness and presenting for treatment [163]. Transportation barriers to care have also been associated with reduced compliance to treatment regimens, lower rates of preventive care, as well as greater difficulties in accessing emergency healthcare [164, 165].

Despite the fact that most Americans have good access to healthcare that enables them to benefit fully from the Nation's healthcare system, some population groups face barriers that create difficulties in obtaining basic healthcare services [153]. For instance, rural residents often face barriers to accessing high quality care, such as, travelling longer distances to reach healthcare delivery sites [166]. Moreover, rural areas have fewer healthcare resources [156, 166] and yet rural residents report more chronic conditions (such as, heart disease and diabetes) and are generally described in poorer health than urban residents [154]. In Tennessee, disparities regarding geographic access to healthcare in both rural and urban residents have been reported [167]. In a study carried out in East Tennessee, Pedigo and Odoi reported disparities in geographic accessibility to emergency stroke and MI care [22]. Therefore, timely geographic access to appropriate care centers for conditions, such as MI and stroke, that require time sensitive treatments is important for improving patients' health outcomes and reducing mortality.

1.1.10 Burden of Heart attack and Stroke

1.1.10.1 Incidence, Prevalence and Mortality

1.1.10.1.1 Myocardial Infarction

Coronary heart disease, including heart attack, is the leading cause of death in the world with more than 60% of the global burden being shouldered by developing countries [1]. Today, approximately 3.8 million men and 3.4 million women worldwide die each year from CHD [1]. According to the Global Burden of Disease Study, of the 6.2 million global deaths from CHD in 1990, 3.5 million deaths occurred in the developing countries. Future projections estimate that these countries will account for 7.8 million of the 11.1 million deaths due to CHD in 2020 [168]. Coronary heart disease is the single most common cause of death in Europe, accounting for 1.92 million deaths each year and is also the most common cause of death in the European Union (EU) accounting for over 741,000 deaths each year. The EU is currently composed of 27 sovereign Member States: Austria, Belgium, Bulgaria, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Poland, Portugal, Republic of Ireland, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom (UK). Approximately 1.4 million people older than 35 years in the UK have had MI, (970,000 men and 439,000 women). In 2006, CHD accounted for about 94,000 deaths in the UK; that is about 1 in 5 deaths among men and 1 in 7 deaths among women [169]. About 70,000 heart attacks occur in Canada annually, accounting for over 16,000 deaths annually [170]. In China, CHD is also the leading cause of morbidity and mortality in adults. The prevalence of CHD in China in 2003 was 4.6 per 1,000 for all ages [171].

Coronary heart disease is the leading cause of death in the US [21] with 17.6 million Americans having the condition [172]. In 2007, 1 out of every 6 deaths in the US was due to CHD and MI accounted for about 132,968 deaths [21]. On average, a heart attack occurs in the US every 34 seconds. Currently, an estimated 8.5 million people in the US have had a heart attack, and about 610,000 new attacks and 325,000 recurrent attacks are diagnosed annually [5]. In Tennessee, CHD is also the leading cause of death and accounted for about 55% of all the cardiovascular deaths in 2004 [6] as well as 25.8% of total deaths in 2006 [4]. The prevalence of CHD in adult Tennessee residents (≥ 18 years) in 2008 was 5.8% [173].

1.1.10.1.2 Stroke

Approximately 15 million people worldwide suffer a stroke annually. Of these, 5 million die and another 5 million are permanently disabled [1]. Stroke accounts for about 10% of all deaths in developed countries. Stroke is a global problem that is not only limited to the developed or industrialized countries but also affects developing countries. About 85% of all stroke deaths are registered in low- and middle-income countries [174]. In Europe and the EU, stroke is the second most common cause of death accounting for 1.24 million and 508,000 deaths, respectively, each year [169]. In the UK, it is estimated that about 111,000 new stroke cases occur accounting for about 53,000 deaths annually [175]. Stroke is the third leading cause of death in Canada, accounting for about 14,000 deaths annually. An estimated 50,000 stroke cases occur in Canada each year, and about 300,000 Canadians are living with the effects of stroke [169]. Approximately 8 million stroke incidences [176] are said to occur in China annually and more than 1.5 million people die from stroke, three times as many as die from CHD [177].

Stroke is the third leading cause of death and the leading cause of disability in the US. Approximately 6.4 million people in the US have had a stroke [172]. It is also estimated that 795,000 people experience a new or recurrent stroke annually. This implies that on average, every 40 seconds an individual suffers a stroke in the US [21]. In 2007, the overall stroke mortality risk in the US was 42.2 per 100,000 or approximately 1 out of every 18 deaths [21]. In Tennessee, stroke is the third leading cause of death and accounted for 6% of total deaths in 2006 [6]. Tennessee has one of the highest stroke mortality risks in the country and the state's overall mortality risk is usually higher than the national rate. For example, the age-adjusted stroke mortality risk for Tennessee for the period 2005-2007 was 58.1 per 100,000, while that of the whole country was 44.1 per 100,000 persons [21]. Additionally, about 20,000 hospitalizations for stroke were recorded each year between 1997 and 2004 in Tennessee [6]. Three percent of the 2009 Center for Disease Control/Behavioral Risk Factor Surveillance System (CDC/BRFSS) survey respondents from Tennessee reported to have had a stroke [178].

1.1.10.2 Economic Burden

1.1.10.2.1 Myocardial Infarction

Cardiovascular disease is of great economic burden to the healthcare system worldwide. The economic impact of CVD is felt as: the healthcare costs to the individual, family, and government; and costs to the country due to lost productivity [1]. Coronary heart disease is not only the leading cause of death, but is also an important source of disability. Cardiovascular disease accounts for 10% of Disability-adjusted life years (DALYs) in low- and middle-income countries, and 18% in high-income countries [1]. Disability-adjusted life years is a measure of overall disease burden, expressed as the number of years lost due to early death or disability [179]. This is exacerbated in the developing world where cardiovascular disease affects a high proportion of working-age adults [180]. The estimated annual cost of CHD to the EU economy is about €49 billion.

Of this cost, 48% is due to direct healthcare costs (which include the cost of physicians and other health professionals, acute- and long-term care, medications and other medical durables), 34% to lost productivity (due to morbidity and mortality), and 18% to the informal care of CHD patients [181]. In 2006, CHD cost the UK, France, Austria, and Germany healthcare systems about €4.5 billion, €2 billion, 3.5 million, and €8 billion, respectively, in healthcare costs [181]. Cardiovascular disease costs the Canadian economy more than $22.2 billion every year in physician services, hospital costs, lost wages and decreased productivity [170]. In China, annual direct costs are estimated at €30.76 billion or 4% percent of gross national income [180].

The estimated total direct and indirect cost of heart disease in the US for 2007 was $177.5 billion. Direct costs accounted for about 46% of the total cost while indirect costs accounted for about 54% [21]. Heart disease is expected to cost Tennessee an estimated 6.75 billion US dollars in both direct and indirect costs in 2011 [182].

1.1.10.2.2 Stroke

Stroke is a leading cause of morbidity and mortality in the world, imposing an enormous economic burden on individuals, family, and society. The global burden of stroke is projected to rise from 38 million DALYs in 1990 to 61 million DALYs in 2020 [1]. Annually, stroke costs the EU economy an estimated €38 billion, of which, about 49% is due to direct healthcare costs, 23% to lost productivity, and 29% to the informal care of stroke patients [181]. In 2006/07, stroke cost the UK healthcare system about £4.5 billion. Health and social care costs accounted for more than half (56%) of this.

Production losses, and cost of informal care of stroke patients accounted for 21% and 22%, respectively [175]. Stroke costs the Canadian economy about $3.6 billion annually in physician services, hospital costs, lost wages, and decreased productivity [170].

The 2007 total direct and indirect cost of stroke in the US was estimated at $40.9 billion. Direct costs accounted for about 62% of total costs, while the remaining 38% was due to indirect costs [21]. The 2011 total direct and indirect cost of stroke in Tennessee is estimated at $1.38 billion [182]. Direct costs are expected to account for about 39% of total costs, while the remaining 61% will be due to indirect costs.

1.1.11 Temporal Trends

In recent decades, most developed countries have witnessed declines in CVD mortality, including CHD and stroke. However, other parts of the world show different patterns, including high rates of CVD mortality in Eastern Europe that continue to rise and a threatening epidemic of CHD and stroke emerging in developing countries [183]. The increasing trend of CVD burden observed in developing and transitional countries is partly due to increasing longevity, urbanization, and lifestyle changes [1]. The factors essential for decreasing trends in mortality from CHD and CVD, as seen in developed countries are variable and include favorable changes in risk factor exposure, such as decreased smoking, improvements in diet and physical exercise, and better control of hypertension and other risk factors [168, 184]. Advances in treatment and management of patients with CHD and stroke may also account for a substantial proportion of the favorable trends [17]. Despite the observed decline in CVD mortality in recent decades, the WHO predicts that by 2030, CVD will account for about 23.4 million deaths globally [185].

1.1.11.1 Myocardial Infarction

Mortality from CHD has been declining in the US and Japan since the early 1970s and in Western Europe since the mid- to late 1970s. However, in some countries in central and Eastern Europe, CHD death risks have been rising. For instance, death risks for men aged less than 65 years living in Finland and the UK declined by 37% and 42%, respectively, between 1994 and 2004, but rose by 57% for men of the same age living in Albania and by 19% for men living in the Ukraine. For women aged under 65 years living in Finland and the UK, mortality risks fell by 35% and 49%, respectively, but rose by 46% and 19% for women living in Albania and Ukraine, respectively [181]. In the EU, age-adjusted mortality risks from CHD for men rose from 146 per 100,000 persons in 1965–69 to 159 in 1975–79 but declined thereafter to 99.6 in 1995–97. The pattern was similar in women, with a peak at 69 in 1975–79 followed by a decline to 45 in 1995–97 [186]. In the UK, the percentage decline in age-adjusted CHD mortality risks between the periods 1965-1969 versus 1995-1998 was 41% for men and 38% for women. In the Russian Federation, the age-adjusted CHD mortality risk in men increased from 304 per 100,000 persons in the period 1985-1989 to 330 in the period 1995-1998. However, for women in the Russian Federation, the age-adjusted CHD mortality risk decreased from 163 per 100,000 persons to 154 in the same time period [186]. In addition, results from the Monitoring of trends and determinants in Cardiovascular diseases (MONICA) project showed that the incidence and case fatality of CHD were falling rapidly in most Northern, Southern, and Western European countries but not falling as fast in the East and Central Europe populations [181]. The decrease in age-adjusted CHD mortality risks from the late 1960s to mid 1990s were very substantial in Japan. A 29% and 36% decline in age-adjusted CHD mortality risks was observed for both Japanese men and women, respectively, during this time period. In Canada, a 60% and 59% decline in age-adjusted CHD mortality risks was observed for the period 1965-1969 versus 1995-1997 in men and women, respectively [186]. Additionally, in Canada the age- and sex-adjusted in-hospital case fatality rate for acute myocardial infarction declined from 14.5% in 1994 to 9.7% in 2004 [15]. Figures 1.1 and 1.2 show trends in age-adjusted mortality risks from CHD in men and women between 1965 and 1997 [186].

In the US, recent evidence suggests that the decline in CHD mortality since the late 1960s has slowed especially in specific subgroups defined by socioeconomic status, race or ethnicity, and region [183]. For instance, early in the decline of CHD and stroke, CVD death risks in all major demographic groups declined in parallel. However, since the mid-1980s, the documented trends in CHD have differed across race/sex subgroups with the rates of CHD mortality decline being slow in black men and women compared to their white counterparts [187-189]. The age-adjusted CHD mortality risks decreased at >3% per year for the 20-year period between 1970 and 1990. However, for the 7-year period between 1990 and 1997, CHD mortality declined at a rate of 2.7% [183]. Between 1990 and 1994, age-adjusted mortality from CHD among people 35 years of age or older declined by 10.3%; the rate of decline was highest for white men (2.9% per year) and lowest for black women (1.6% per year) [190]. Additionally, Rosamond *et al* reported a decline in mortality due to CHD of 28% for men and 31% for

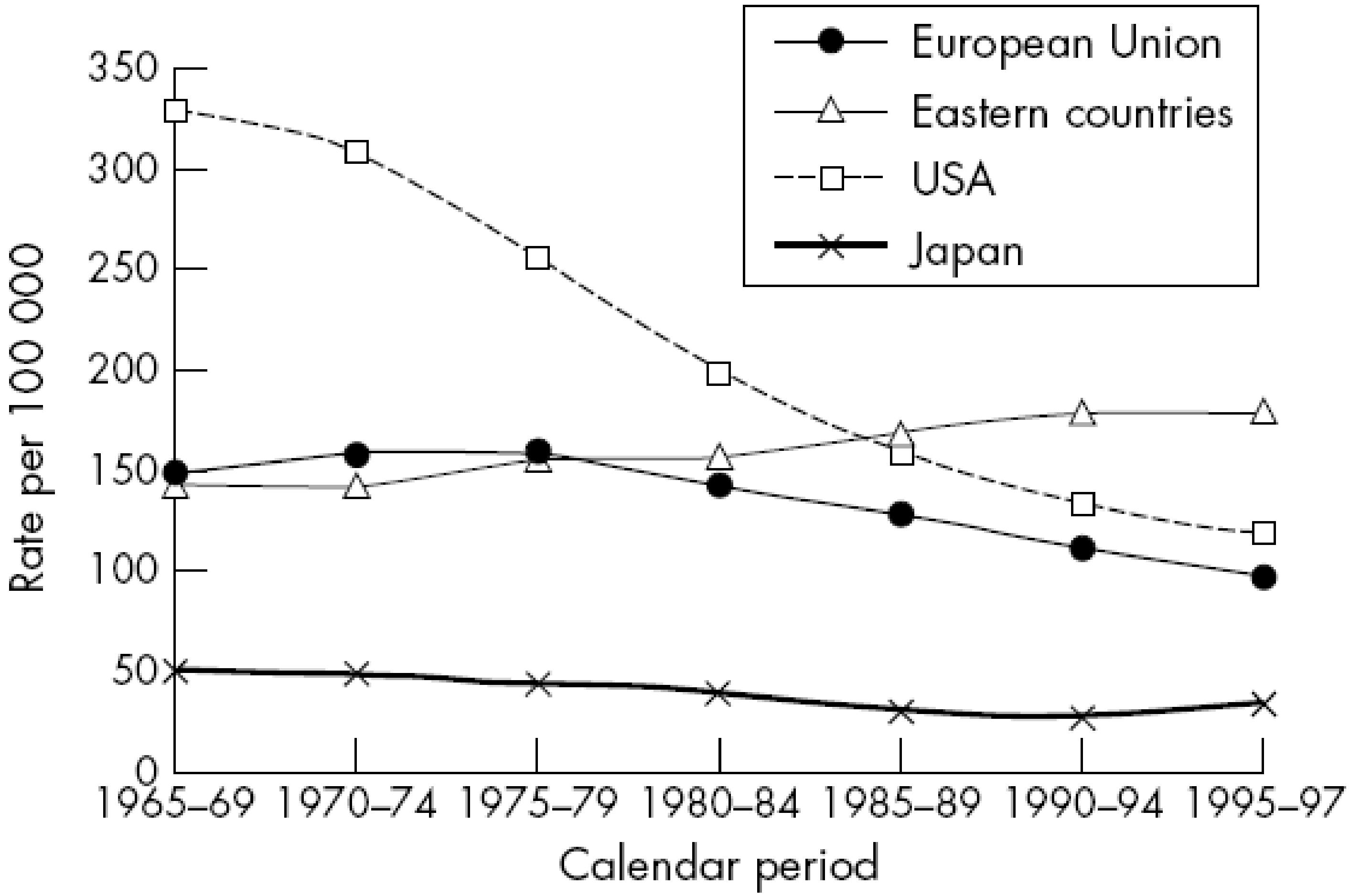

Figure 1.1: Trends in Age-adjusted Mortality Risks from CHD in Men of All Ages from the EU, Eastern European countries, US, and Japan, 1965 to 1997

Source: Levi F, Lucchini F, Negri E, La Vecchia C. Trends in mortality from cardiovascular and cerebrovascular diseases in Europe and other areas of the world. Heart 2002;88(2):119-24

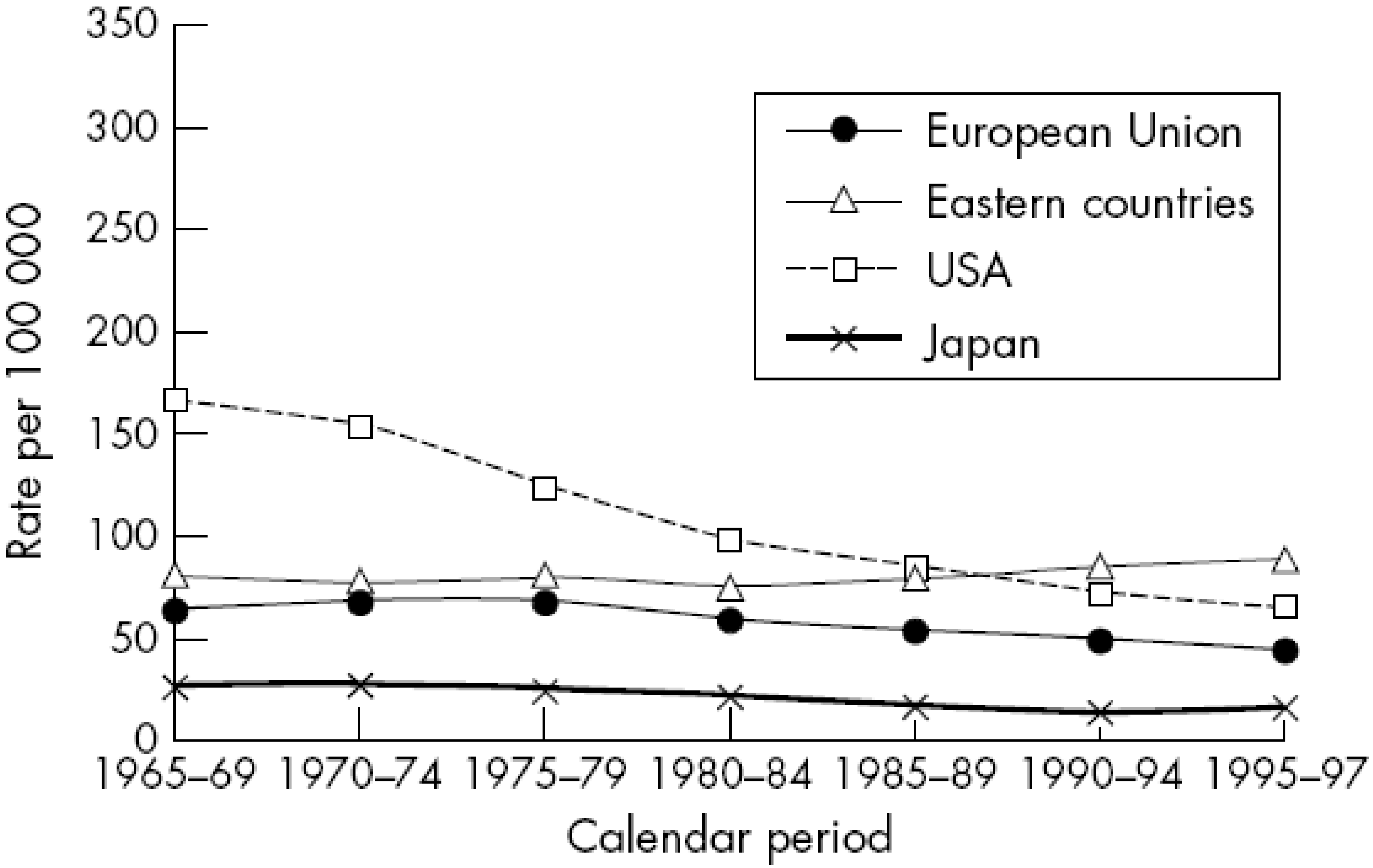

Figure 1.2: Trends in Age-adjusted Mortality Risks from CHD in Women of All Ages from the EU, Eastern European countries, US, and Japan, 1965 to 1997

Source: Levi F, Lucchini F, Negri E, La Vecchia C. Trends in mortality from cardiovascular and cerebrovascular diseases in Europe and other areas of the world. Heart 2002;88(2):119-24

women among 35-74 year old residents of four geographically and ethnically diverse communities in the US from 1987-1994 [191]. In the same study, the decrease in the age-adjusted case fatality rate was 4.1% per year for men and 9.8% per year for women. However, there was no evidence of a decline in the case fatality rate among blacks hospitalized for myocardial infarction. The Minnesota Heart Survey (MHS) study reported that the crude 28-day case-fatality of MI decreased from 18% in 1970 to 13% in 1985 among men and from 27% in 1970 to 18% in 1985 among women [192]. A follow-up study reported a decline in the age-adjusted case-fatality from 13% in 1985 to 11% in 1990, and to 7% in 1995 for men; whereas for women, a decline from 18% in 1985 to 12% in 1990, and to 10% in 1995 was also reported [193].

Despite the substantial decline in the CHD mortality observed, the incidence of MI is said not to have declined as much as the mortality, and the trends vary by time and among studies. In the MHS study, the age-adjusted incidence for definite MI was found to be similar in 1970 and 1980 [194]. During the period of 1985-1997, the incidence of hospitalized definite MI decreased by about 10% [193]. The Worcester Heart Attack study reported a slight increase in initial and recurrent MI between 1975 and 1981 [195]. However, after this time period, a decrease in MI rates was observed through 1995 [196, 197]. The Atherosclerosis Risk in Communities (ARIC) study reported an increased incidence (7.4% per year) of hospitalization for MI from 1987-1994 [191]. In Tennessee, a 21% decline in the age-adjusted mortality risk from diseases of the heart was recorded between 1996 and 2005 [6].

1.1.11.2 Stroke

Like CHD, stroke mortality risks have declined in most developed countries [198, 199]. Although the incidence of stroke in developed countries is declining, largely due to efforts to reduce risk factors (such as, high blood pressure and smoking), the overall rate of stroke remains high due to the aging of the population [200]. A decline in stroke incidence has been reported in the United States [201], Asia [202], and Europe [203]. During the 1950s and early 1960s, most developed countries were characterized by increasing trends in stroke mortality. However, since the mid 1960s, stroke mortality rapidly declined for the next 2 decades [204, 205]. On the contrary, most eastern European countries, Portugal and Yugoslavia showed increasing trends in mortality from stroke [204-206]. In the Russian Federation, age-adjusted mortality risks for stroke in both men and women increased between the periods 1985-89 and 1995-98. The Russian rates of 204/100,000 men and 151/100,000 women for stroke recorded between 1995 and 1998 were among the highest registered worldwide [186]. Between 1994 and 2004, the mortality risks for men aged below 65 years decreased by 43% for those living in Germany and by 28% for those in the UK. Similarly, the mortality risks for women aged 65 years and below living in Germany decreased by 37% and by 28% for those in the UK. However, for women living in Albania, the mortality risks increased by 15% [181]. In the EU, age-adjusted mortality risk from stroke for men declined from 103 per 100,000 persons in 1965–69 to 87 in 1975–79 and declined further to 46 in 1995–97. A similar trend was observed for women, declining from 83 per 100,000 persons in 1965-69 to 36 in 1995-97 [186]. In Canada, a decline of 58% for men and 59% for women was observed in the age-adjusted mortality risk for stroke between the time period of 1965-69 and 1995-97. In Japan, the age-adjusted mortality risk for stroke in men decreased from 228 per 100,000 persons in 1965-67 to 61 in 1995-97 whereas that for women decreased from 150 per 100,000 persons to 38 in the same time periods [186]. Figures 1.3 and 1.4 show trends in age-adjusted mortality risks from stroke in men and women from 1965 to 1997 [186].

Like many other developed countries, stroke mortality risks in the US have declined in the past decades. However, substantial geographic, racial, and sex differences in the pattern of the decline of stroke mortality have been reported [207]. For instance, the age-adjusted mortality risks from stroke for men declined from 78 per 100,000 persons in 1965–69 to 29 in 1995–97. A similar trend was observed for women with a 59% decline in the age-adjusted mortality risks between 1965-69 and 1995-97 [186]. Additionally, from 1997 to 2007, the annual stroke mortality risk decreased by 34.3%, and the actual number of stroke deaths declined by 18.8% [21]. Decline in the incidence of stroke has also been reported in the US [201]. In a Framingham Study, the age-adjusted incidence of a first stroke in males declined from 7.6 per 1,000 persons in 1950-1977 to 5.3 in 1990-2004 whereas that of women declined from 6.2 to 5.1 in the same time period [200]. The earliest study looking at trends in stroke incidence reported a decrease of 45% in the average annual incidence of stroke between 1945-1949 and 1975-1979 [208]. Several other studies; including the Honolulu Heart Program [209] and studies from China [176], Denmark [210], Australia [211], Japan [212], Finland [213], England [214], New Zealand [215], and France [216] have reported decreasing or stable incidences mostly attributed to reduction in risk factors over time. Studies have also reported a temporal trend toward decreasing severity and disability from stroke, which

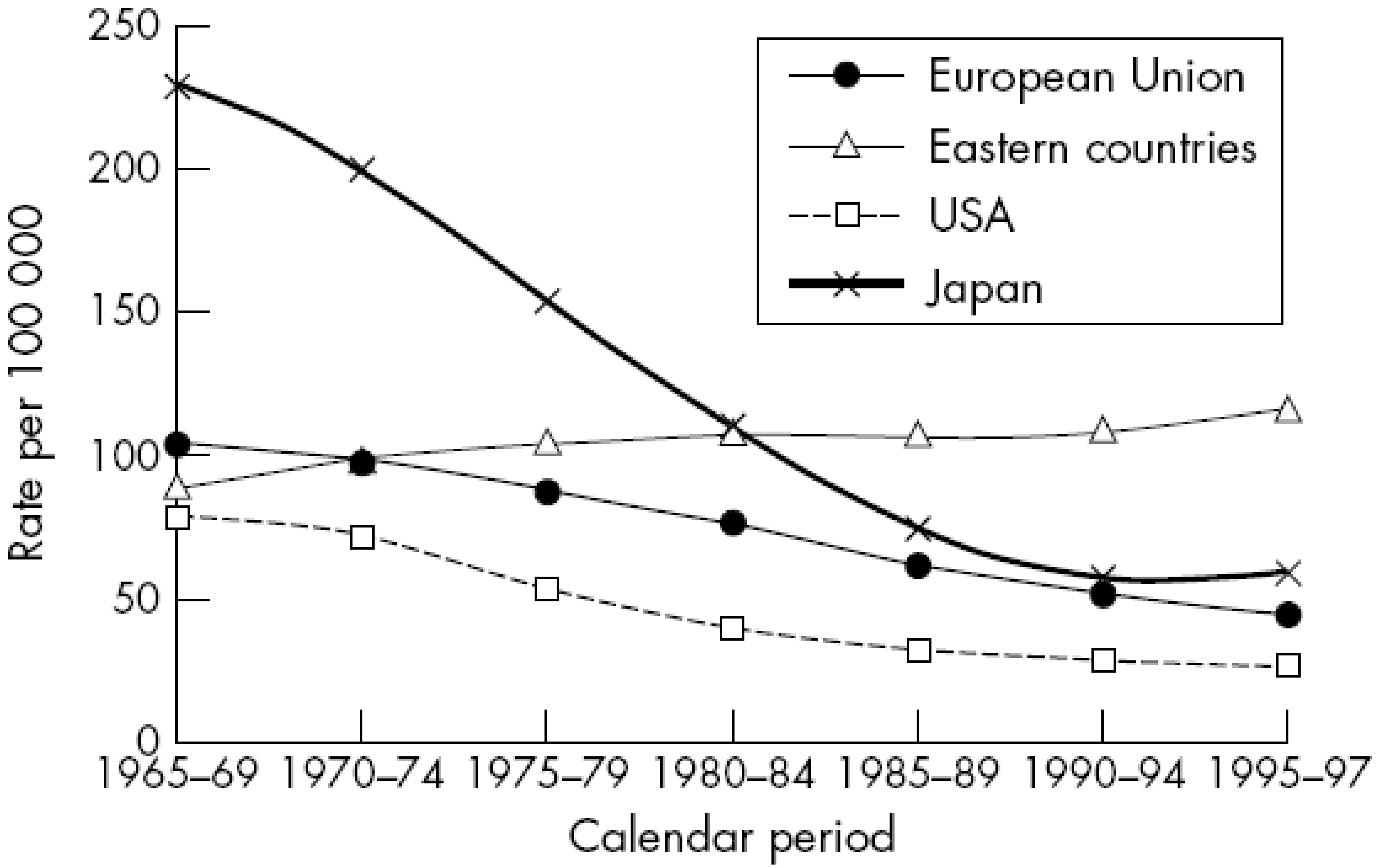

Figure 1.3: Trends in Age-adjusted Mortality Risks from Stroke in Men of All Ages from the EU, Eastern European countries, US, and Japan, 1965 to 1997

Source: Levi F, Lucchini F, Negri E, La Vecchia C. Trends in mortality from cardiovascular and cerebrovascular diseases in Europe and other areas of the world. Heart 2002;88(2):119-24

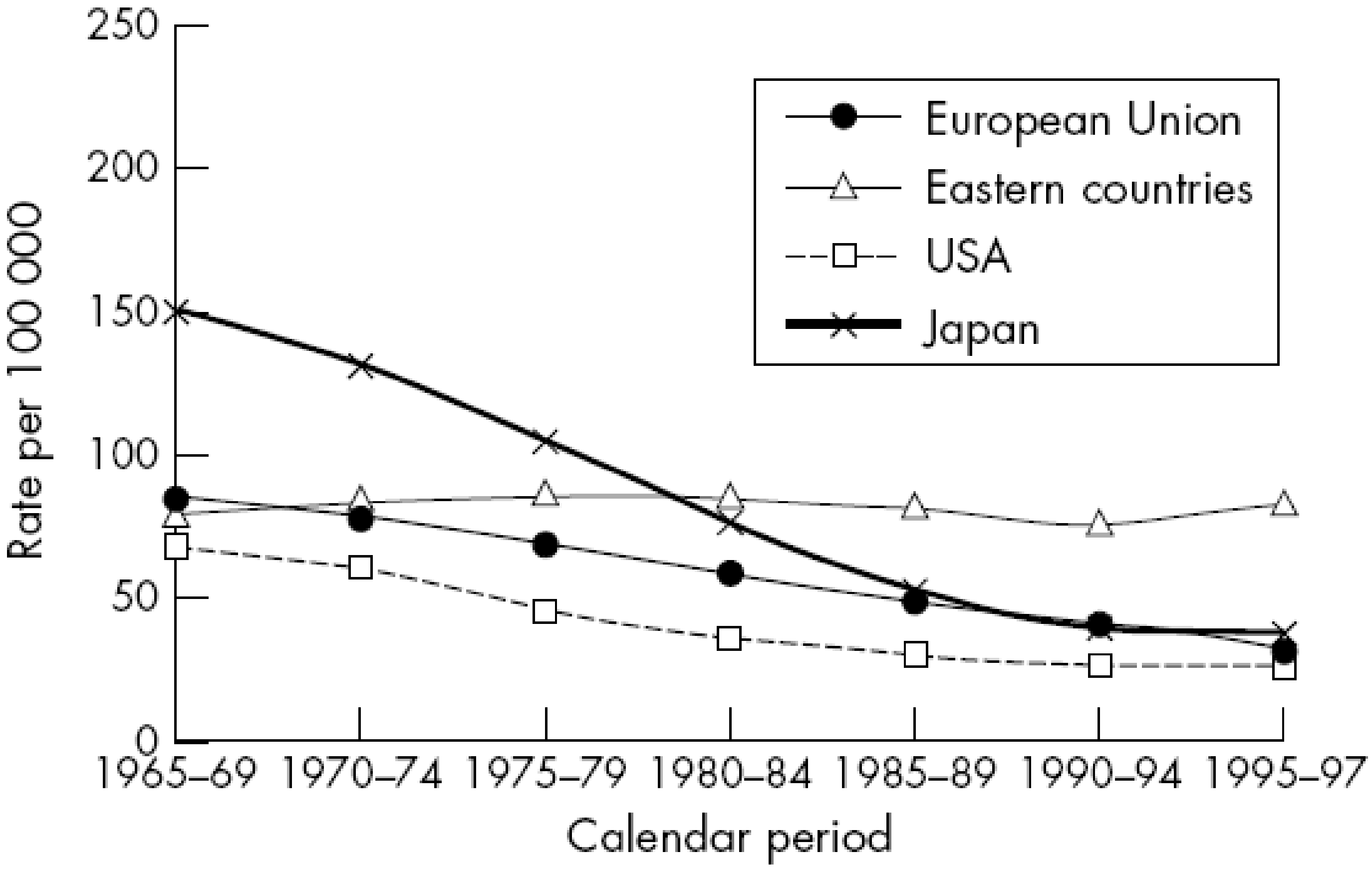

Figure 1.4: Trends in Age-adjusted Mortality Risks from Stroke in Women of All Ages from the EU, Eastern European countries, US, and Japan, 1965 to 1997

Source: Levi F, Lucchini F, Negri E, La Vecchia C. Trends in mortality from cardiovascular and cerebrovascular diseases in Europe and other areas of the world. Heart 2002;88(2):119-24

may be attributed to the increasing sensitivity of imaging techniques such as CT and MRI for identifying stroke thus enabling quick treatment of patients and consequently leads to better outcomes [212, 214, 217]. Although Tennessee has one of the highest stroke mortality risks in the country, the age-adjusted mortality risk from stroke decreased by 23% between 1996 and 2005 [6].

1.1.12 Spatial Patterns

Identifying spatial patterns of disease distribution can help identify possible determinants of disease occurrence. Such factors include risk behaviors, socio-cultural factors, environmental factors, and availability of healthcare resources. Considerable geographic disparities in CVD incidence and mortality have been documented all over the world [183, 218-220]. The highest risks of cardiovascular mortality have been reported in Eastern Europe, Central Asia, the Middle East, and North Africa [221]. Geographic disparities exist between countries as well as within countries. Urban-rural differences in the distribution of cardiovascular disease have also been documented with higher prevalence of coronary heart disease being seen in rural versus urban populations [222, 223]. Geographic comparisons of disease incidence and mortality risks within countries and between countries are valuable for identifying high-risk populations and for generating new hypotheses for defining preventive programs. Although the underlying causes of disparities in stroke and MI mortality are not fully understood, variation in the prevalence of contributing risk factors (such as: smoking, hypertension, hyperlipidaemia, diabetes, overweight; as well as socio-economic factors; lifestyle variables such as diet, alcohol use, physical activity; medical care; genetic factors; and environmental conditions) has been implicated as one of the causes for these disparities [224]. Disparities in awareness as well as access to information and health services are also responsible for the variations in stroke and MI mortality risks [20].

In order to assess the degree of geographical health disparities, small area analyses are recommended because analyses performed at large geographic levels have been shown to mask the underlying patterns of disease thus lead to distortion of the underlying spatial patterns [225]. Secondly, small area data are more likely to be homogenous with respect to population characteristics, thus provide more accurate data for assessing the association between population characteristics and disease. In the US, census tracts have been shown to be good proxies of natural neighborhoods due to their small size and homogenous nature of the population characteristics within them [226].

1.1.12.1 Myocardial Infarction

In Europe, CHD death risks are generally higher in Central and Eastern than in Northern, Southern and Western Europe [181]. Sans *et al* reported a clear north-east to south-west gradient in CHD mortality with the lowest risks for both men and women in France, Spain, Switzerland, and Italy. The highest risks were observed in Central and East European countries such as Ukraine, Bulgaria, or the Russian Federation [219]. The mortality risk for men aged less than 65 years living in Ukraine was 14 times higher than those living in France and for women it was 25 times higher. In addition, the mortality risk for men aged less than 65 years living in Ireland was 1.6 times higher than those in Italy whereas for women it was 1.8 times higher [181]. Regional variations within countries have also been recorded [218, 227, 228]. A north-south gradient has been reported in Britain with higher CVD mortality risks in the north compared to the South [228]. In France, mortality risks due to ischemic heart disease showed a north-south gradient [227]. In India, high CVD mortality risks among middle-aged adults have been observed in Andhra Pradesh, Tamil Nadu, Punjab and Goa whereas low mortality risks have been observed in sub-Himalayan states of Nagaland, Meghalaya, Himachal Pradesh and Sikkim [222] . The CHD mortality risk in China is higher in northern China (Beijing) than in southern China (Shanghai and Guangzhou) and also higher in urban than rural areas [229, 230]. Geographic disparities in CHD have also been reported in Canada [231, 232] and Australia [233].

In the US, substantial geographic disparities in CHD incidence and mortality have also been documented. Coronary heart disease mortality in the United States has revealed a west-to-east gradient with clustering in some states [183]. For example, strong clusters of high CHD mortality risks especially among women have been observed in Mississippi Delta, Appalachia, the Ohio River Valley, the Piedmont areas of Georgia, South Carolina, and North Carolina [183]. Most areas currently observed with high CHD mortality are frequently characterized as rural and poor. Additionally, even within a single population subgroup such as among Native Indians within the US, geographic variations in cardiovascular disease risk exist depending on the State of residence [234]. According to the data from 2009 BRFSS survey of the CDC, the highest MI prevalence was in West Virginia (6.5%) and Kentucky (5.9%) whereas the lowest prevalence was in the District of Columbia (1.9%) [21]. In Tennessee, high CHD mortality risks have been observed in the Appalachian counties compared to other counties in the state. These counties lie in the stroke belt and have higher mortality risks of both CHD and stroke.

1.1.12.2 Stroke

Globally, the highest age- and sex-adjusted mortality risks from stroke have been reported in Eastern Europe, north Asia, central Africa, and the south Pacific whereas the lowest risks have been reported in Western Europe and North America [235]. In Europe, lower stroke mortality risks have been observed in the center of Western Europe with the lowest mortality risks in Switzerland, France, Norway, Spain, the Netherlands, and Italy. Higher mortality risks have been observed in countries in the Central and Eastern part as well as some Mediterranean countries including Greece, Portugal, and certain regions in Southern Spain and Italy [236]. The stroke mortality risk for men less than 65 years of age living in the Russian Federation is said to be 20 times higher than those in Switzerland while that of women of the same age is 15 times higher [181]. Considerable within-country variations in stroke mortality risks have been observed in Italy, Spain, Portugal, and the UK [236]. In the UK [228] and Finland [237], the northern parts of both countries have a higher incidence of stroke than the south. Within Canada, an east-west gradient in CVD mortality risks has been observed with Atlantic Canada having consistently higher risks than Western Canada [238]. Cardiovascular disease mortality risks in 1995 were highest for men and women in Newfoundland and lowest in British Columbia. However, regional differences seem to be more notable with respect to mortality risks from acute MI than to those from stroke [238]. A north-south gradient with significantly higher incidence and mortality risks of stroke in the north compared with the south have been observed in China [177, 239, 240]. In most countries, such as the US [241], Canada [242], Bulgaria [243], and Portugal [244], higher stroke incidence or mortality risks have been observed in rural residents compared to urban residents. However in China, some reports show higher stroke incidence, prevalence and mortality risks in the urban areas compared to rural areas [177, 240].

In the US, stroke incidence and mortality risks are highest in some south-eastern states, referred to as the ‘stroke belt [245]. This area includes the eight southern states of North Carolina, South Carolina, Georgia, Tennessee, Mississippi, Alabama, Louisiana, and Arkansas. The average stroke mortality in the stroke belt is approximately 20% higher than in the rest of the nation [21]. Even within the states (both in the stroke belt and for the rest of the nation), stroke mortality risks vary between regions [246]. For instance, a “buckle” of the stroke belt has been identified in the coastal plain of North Carolina, South Carolina, and Georgia, where the stroke mortality risk is much higher (about 40%) than for the remainder of the nation [21, 247]. Results from the 2009 survey of the CDC/BRFSS, showed that the highest stroke prevalence was in Alabama and Oklahoma (3.9%) and the lowest was in Colorado (1.4%) [178]. In Tennessee, high stroke mortality risks have been observed in the Appalachian counties that lie within the ‘stroke belt’.

1.1.13 Myocardial Infarction and Stroke Risk Factors

Many risk factors are associated with both CHD and stroke [248]. However, the major risk factors are those that meet the following criteria: a high prevalence in many populations; a significant independent impact on the risk of coronary heart disease or stroke; and their treatment and control result in reduced risk of these conditions [1]. The risk factors are divided into modifiable and non-modifiable risk factors. Modifiable risk factors include hypertension (high blood pressure), diabetes, dyslipidemia (high blood cholesterol and triglycerides), smoking, alcohol consumption, poor diet, physical inactivity, stress, obesity, and socioeconomic status. Non-modifiable risk factors include age, sex, race/ethnicity, and genetic factors.

1.1.13.1 Modifiable Risk factors

1.1.13.1.1 Hypertension

Hypertension, also known, as high blood pressure (HBP) is defined as persistent systolic blood pressure (SBP) of at least 140 mmHg and/or diastolic blood pressure (DBP) of at least 90 mmHg, or blood pressure that is controlled to guideline-recommended levels using antihypertensive medication [5, 249]. Blood pressure normally rises with age. Diastolic blood pressure and SBP are associated with cardiovascular risk in people aged up to 50 years, whereas, above this age, SBP is a far more important predictor [1]. High blood pressure means that the heart is pumping harder to move blood through the body thus causing overstretching of the arteries. Overtime, the overstretching creates weak points in the vessels thus making them more prone to ruptures. Overstretching may also cause tiny tears in the blood vessel walls that leave scar tissue. These tears and the scar tissue may trap debris such as cholesterol, plaque or blood cells traveling in the bloodstream. Cholesterol and plaque buildup may cause narrowing or blockage of the arteries thus causing heart attack or stroke. Trapped blood cells can also form clots which may narrow or block the arteries.

High blood pressure is a major independent predictor of cardiovascular events and accounts for about 60% of the population attributable risk of stroke [250, 251]. Additionally, an increment of 20 mmHg SBP doubles the risk of stroke in individuals aged 40–69 years [252]. In one study, the risk of a fatal coronary event was seen to double with each increase in SBP of 20mmHg (or 10mmHg in DBP) [252]. In the same study, it was observed that the risk of adverse outcomes increased with age, such that for any given SBP, the risk of fatal coronary artery disease was 16-fold higher for persons 80-89 years of age than for those 40-49 years of age. Several randomized controlled trials have demonstrated that reduction in mean blood pressure reduces the risk of cardiovascular events [253-256]. One study demonstrated a 35-44% reduction in the incidence of stroke by lowering the blood pressure [254]. Despite the observed improvements in hypertension treatment, awareness and control rates, prevalence of hypertension continues to increase in the general US population. For example, the prevalence of hypertension increased from 24.4% in 1988-1994 to 28.9% in 1999-2004 [257]. The WHO estimates that about 11% of all disease burden in developed countries is due to high blood pressure, and over 50% of CHD and about 75% of stroke burden is due to hypertension [258]. In 2008, 32% of men and 29% of women in England, and 34% of men and 31% of women in Scotland had hypertension [258]. Nineteen percent of Canadian adults have hypertension [170].

Hypertension is one of the most prevalent modifiable risk factors for MI and stroke, and affects at least 65 million people in the United States [5]. On average, 1 in 3 US adults has hypertension [259]. According to the 2007 BRFSS study, the prevalence of hypertension in adults (≥18 years) ranged from 19.7% in Utah to 33.8% in Tennessee [5]. Furthermore, the prevalence of hypertension in Tennessee increased from 26.8% in 1995 to 33.8% in 2007 with the Upper Cumberland region registering the highest prevalence [173]. The prevalence of hypertension in the US is higher among men compared to women under age 55, while women have higher prevalence after age 55 [5]. Blacks also have a higher prevalence than whites [5].

1.1.13.1.2 Diabetes Mellitus

Diabetes mellitus is a condition that develops when the body either does not make enough insulin (type 1) or does not efficiently use the insulin it makes (type 2), a condition known as insulin resistance [25]. Type 2 diabetes mellitus accounts for more than 90% of all diagnosed adult diabetes cases in the US [260]. Patients with diabetes mellitus are at high risk for MI [261] and ischemic stroke, and suffer from a high stroke morbidity and mortality burden [262]. Approximately one third of all acute stroke patients are diabetic, and diabetes is associated with poor outcomes in acute stroke patients [263]. Diabetes affects more women than men, and it's risk is higher among blacks, Hispanics, and Native American people compared to whites [25]. Diabetes doubles CVD risk in men and triples it in women [264]. Diabetes remains a major independent CVD risk factor even when all other risk factors such as, advancing age, hypertension, cigarette smoking, and hypercholesterolemia, are adjusted for. Diabetics have a 2–6 fold increased risk for stroke [265, 266] and 3 fold increased risk for MI [261]. About 65% of people with diabetes mellitus die of heart disease or stroke [5].

The prevalence of diabetes in Europe in 2003 was 7.8% with about 48 million adults (20-79 years) living with diabetes. Currently, the prevalence in Europe is highest in Malta (7.6%) and the Czech Republic (7.2%) [181]. In Canada, 6.6% of the population aged ≥20 years have diabetes [170]. Predictions are that in China, diabetes will increase from 1.4 to 2.4% between 1995 and 2025, whereas in India, the equivalent figures are from 2.1 to 3% [169]. Diabetes is the seventh leading cause of death in the United States and affects about 26 million Americans. The prevalence of diabetes was estimated at 8.3% in 2010 [267]. The incidence of diabetes in the US tripled from 5.6 million in 1980 to 18.1 million in 2008 [268]. In Tennessee, the prevalence of diabetes increased from 6.0% in 1999 to 10.4% in 2008 with Sullivan region having the highest prevalence [173].

1.1.13.1.3 High Cholesterol

Cholesterol, a natural waxy substance, occurs in all body cells and is one of the several types of fats (lipids) that circulate in the bloodstream. At healthy levels, cholesterol is an essential component of cells and blood and is used to form cell membranes as well as make some hormones [25]. Triglycerides are fats that also circulate in blood and together with cholesterol are called plasma lipids. High levels of cholesterol (> 240 mg/dL) and triglycerides (> 150 mg/dL) in the blood lead to buildup of fatty deposits in the blood vessel walls which may restrict blood flow thus predisposing to heart attack and stroke. There are two types of cholesterol, high density lipoprotein (HDL), also known as "good" cholesterol, and low density lipoprotein (LDL), also known as "bad" cholesterol. High levels of one type or deficiency of another predisposes to coronary heart disease, heart attack or stroke. High density lipoprotein helps keep the LDL from getting lodged into the artery walls, and helps prevent atherosclerosis. A healthy level of HDL may also protect against heart attack and stroke, while low levels of HDL (less than 40 mg/dL for men and less than 50 mg/dL for women) have been shown to increase the risk of heart disease [269].

High blood cholesterol is one of the major modifiable risk factors for coronary heart disease, heart attack and stroke [269]. The risk of CHD rises with increased amount of blood cholesterol and this risk is accelerated by presence of other risk factors such as, high blood pressure, diabetes, and tobacco smoke. Although the importance of high total cholesterol as a risk factor for stroke is undeniable, there is still a debate about its role as a risk factor. Several studies have demonstrated the association between high total cholesterol levels with risk of stroke [270-272], whilst others found no clear associations [273-276]. The association between LDL and ischemic stroke has also been reported inconsistently [271, 276]. However, there is evidence of increased risk of ischemic stroke with low levels of HDL [272, 277-279]. Despite the inconsistent or weak association between cholesterol and stroke, a decrease in cholesterol concentrations has been observed to reduce the incidence of stroke in high-risk populations [280]. Whereas the association between high total cholesterol and risk of stroke remains unclear as a result of conflicting results reported in the literature, there is evidence of an association between increased blood cholesterol levels and increased risk of coronary heart disease [281]. Moreover, a 10% decrease in total cholesterol levels of the population is estimated to reduce the incidence of CHD by 30% [282].

According to the WHO, about 60% of CHD and around 40% of stroke burden in developed countries is due to high total blood cholesterol levels [181]. About 57% of men and 61% of women in the United Kingdom; and an estimated 10 million Canadians have high blood cholesterol levels [169]. Approximately 50% of the adults (≥20 years) in the US have total cholesterol concentrations of at least 200 mg/dL [283], the level considered “borderline-high risk” by the National Cholesterol Education Program expert panel [284]. The 2009 data from the BRFSS survey showed that an estimated 37.5% of the adults in the US had been told that they had high blood cholesterol with the highest percentage in South Carolina (41.8%) and the lowest in Tennessee (32.9%) [21]. In 2007, Madison had the lowest prevalence (22.5%) while East region had the highest (41.4%) among the health department regions of Tennessee. The prevalence of high cholesterol in Tennessee increased from 27.5% in 1995 to 34.2% in 2007 [173].

1.1.13.1.4 Cigarette Smoking

Smoking increases blood pressure, decreases exercise tolerance, and increases the tendency for blood to clot. Toxins in the blood, from smoking cigarettes, contribute to the development of atherosclerosis. Inflammation of the artery wall and the development of blood clots can obstruct blood flow and cause MI or stroke. Cigarette smoke also contains nicotine and carbon monoxide which lower oxygen levels in blood cells causing the heart to pump faster in order to keep the oxygen supply adequate. Tobacco smoke decreases the amount of HDL cholesterol in the blood thus increasing the risk of heart disease. Cigarette smoking increases the risk of CHD and stroke by itself, however, the synergistic effect with other risk factors, such as hypertension and diabetes, greatly increases the risk of both CHD and stroke [285]. Smoking nearly doubles the risk of ischemic stroke [5, 248] and also accounts for about 12-14% of all stroke deaths in the United States [286], with the risk being strongly dose-related [287]. The risk of dying from CHD is 2-3 times higher in people who smoke cigarettes compared to those that do not smoke [5]. Additionally, the risk for stroke and CHD is much higher in smokers who are below 50 years of age. Furthermore, women who use oral contraceptives in addition to cigarette smoking have increased risk of stroke and CHD as compared to those that do not take oral contraceptives [285].

Exposure to environmental tobacco smoke (secondhand smoke) has also been identified as a risk factor for heart disease [288] as well as stroke [289]. Short exposure to secondhand smoke has immediate adverse effects on the cardiovascular system, interfering with the normal functioning of the heart, blood, and vascular systems in ways that increase the risk of heart attack. Studies have shown that non-smokers who are exposed to secondhand smoke have a 25-30% increased risk of CHD [290] . An estimated 126 million children and nonsmoking adults were exposed to secondhand smoke in the US between 1999 and 2002 [21]. Enactment of laws enforcing smoke-free workplaces and public places have had a significant positive impact on reduction of exposure to secondhand smoking. For example, the percentage of the US population exposed to secondhand smoke declined from 52.5% in 1999-2000 to 40.1% in 2007-2008 [21].

Tobacco use kills 5.4 million people a year and accounts for 1 in 10 adult deaths worldwide. The WHO estimates that by 2020, tobacco is expected to be the single greatest cause of death and disability worldwide, accounting for about 10 million deaths per year [169]. Annually, smoking kills over 1 million people in Europe (453,000 from CVD) and about 654,000 people in the EU (183,000 from CVD) [181]. In Canada, 19% of the population smoke, and 14.5% of heart disease and stroke deaths are attributed to smoking [169].

Cigarette smoking is the most important modifiable risk factor contributing to premature morbidity and mortality in the US, accounting for approximately 443,000 deaths annually [291]. In 2009, an estimated 46.6 million (20.6%) of US adults were cigarette smokers; of these, 36.4 million (78.1%) smoked every day, and 10.2 million (21.9%) smoked on some days. Men had a higher (23.1%) prevalence of smoking compared to women (17.9%) [291]. In the same year, among adults (≥18 years), West Virginia had the highest percentage (25.5%) of cigarette smokers and Utah the lowest (9.8%) [21]. Additionally, the percentage of US adults (≥18 years) who were cigarette smokers declined from 24.1% in 1998 to 20.6% in 2009. However, the percentage of smokers did not change significantly from 2005 to 2009 [291]. In 2008, the prevalence of cigarette smoking among adults (≥18 years) in Tennessee was 23.1%, however, there was no significant change in prevalence over the period 1999 to 2008 [173].

1.1.13.1.5 Obesity and Overweight

Obesity as defined by the WHO is having a body mass index (BMI) of 30 or more while overweight is having a BMI of 25 to 29.9 (Table 1.1). Body mass index is a simple index of weight-for-height that is commonly used to determine whether one has a healthful or unhealthful percentage of total body fat [292]. It is calculated by dividing the individual’s weight in kilograms by the square of the height in meters (kg/m^2). The BMI

Table 1.1: International Classification of Adult Underweight, Overweight and Obesity Using Body Mass Index

Classification	BMI (kg/m^2)	
	Principal Cut-off Points	Additional Cut-off Points
Underweight	<18.50	<18.50
Severe thinness	<16.00	<16.00
Moderate thinness	16.00 - 16.99	16.00 - 16.99
Mild thinness	17.00 - 18.49	17.00 - 18.49
Normal range	18.50 - 24.99	18.50 - 22.99; 23.00 - 24.99
Overweight	≥25.00	≥25.00
Pre-obese	25.00 - 29.99	25.00 - 27.49; 27.50 - 29.99
Obese	≥30.00	≥30.00
Obese class I	30.00 - 34.99	30.00 - 32.49; 32.50 - 34.99
Obese class II	35.00 - 39.99	35.00 - 37.49; 37.50 - 39.99
Obese class III	≥40.00	≥40.00

Source: World Health Organization. BMI classification 2006 [Accessed May 31, 2011]; Available from: http://apps.who.int/bmi/index.jsp?introPage=intro_3.html values for most adults correlate with their amount of body fat. However, BMI does not directly measure body fat thus may not correspond to the same degree of fatness in different individuals and populations due to different body proportions [293]. Body mass index values for adults are usually age-independent and apply to both men and women. On the other hand, in children and teens BMI ranges are defined such that they take into account normal differences in body fat between boys and girls and differences in body fat at various ages [294]. Age and gender growth charts are used to determine the BMI percentile in which the child or teen falls. A BMI percentile of greater than or equal to 85, but less than 95 is categorized as overweight, and a BMI percentile of greater than or equal to 95 is considered obese [295, 296].

Other methods such as waist circumference measurement have been recommended for use as predictors of obesity. The National Heart, Lung, and Blood Institute/North American Association for the Study of Obesity committee recommends using waist circumference cut points of 40 inches (102 cm) for men and 35 inches (88 cm) for women as a measure of ‘central obesity’ [297]. Research shows that waist circumference is a better predictor of obesity-related diseases than overall obesity assessed by using BMI [298, 299]. Moreover, it’s high predictive value for future health risks, ease of measurement, and understanding by the general public make waist circumference measurement an equally or more useful tool than BMI [297-299].

Excess abdominal fat is an important, independent risk factor for disease. A disproportionate amount of body fat that is especially distributed around the waist, creates a greater risk of developing high blood pressure, high blood cholesterol, diabetes, heart disease, and stroke [25]. Independently, obesity seriously increases the risk of developing CVD. Obesity is associated with high levels of LDL and triglyceride levels, lower levels of HDL, higher blood pressure, and diabetes [25, 300]. A high BMI (BMI≥25) is associated with an increased risk of stroke in men [301, 302] and women [303, 304]. In addition, there is a dose-response relationship between ischemic stroke risk and BMI [301, 303, 305]. Abdominal adiposity (measured by waist-to-hip ratio) has been found to be associated with increased stroke rate than overall body mass (measured by BMI) [303, 306, 307]. Although no clinical trial has tested the effects of weight reduction on stroke outcomes, weight reduction is associated with a lowering in blood pressure [308] and may therefore contribute to a reduced stroke risk.

Obesity and overweight are strongly related to early age occurrence of first MI in individuals [309, 310]. However, several studies have reported an apparent paradoxical effect of BMI on outcomes. Body mass index seems to be associated with better survival as obese and overweight patients showed better survival compared to those with normal BMI [311, 312]. In patients with acute MI, high BMI appears to have an unexplained protective effect on survival [313-315]. This obesity paradox continues to invoke debate about the importance of increased BMI as an independent risk factor for coronary heart disease.

Although overweight and obesity were once considered a problem only in high-income countries, these conditions are now dramatically on the rise in low- and middle-income countries, particularly in urban settings. The WHO projections suggest that the number of overweight people globally will increase to 2.3 billion and more than 700 million will be obese by 2015 [169]. In 2008, the prevalence of overweight in England among men was 42% while that among women was 32%. An additional 25% of men and 28% of women in England were obese [258]. About 14.1 million Canadians are overweight or obese, and of these, about 5.5 million are obese [170].

Obesity in the US has reached epidemic proportions. Between 1980 and 2002, obesity prevalence doubled in adults (≥20 years) and overweight prevalence tripled in children and adolescents aged 6-19 years [316-318]. In 2008, about 68% of US adults (≥20 years) were either overweight or obese. Of these, about 34% were obese. The prevalence of overweight and obesity among children 2-19 years of age was 31.9% and 16.3%, respectively [21]. Additionally, the prevalence of obesity among men rose from 28% between 1999 and 2000 to 32% between 2007 and 2008, whereas the prevalence among women rose from 33% to 36% in the same period. According to the CDC/BRFSS 2008 data, the prevalence of obesity ranged from 19.1% in Colorado to 33.3% in Mississippi [319]. Among adults, women have higher obesity risks than men and non-Hispanic Black and Mexican American women have higher risks than non-Hispanic White [317]. Approximately 68% of adults (≥18 years) in Tennessee were overweight or obese in 2008. The prevalence of overweight adults in Tennessee did not change significantly between 1999 and 2008. However, the percentage of obese adults increased from 20.5% to 31.2% during this period [173].

1.1.13.1.6 Sedentary Lifestyle

Lack of exercise or a sedentary lifestyle is a risk factor for CHD. The risk of a fatal heart attack is nearly doubled in sedentary people than active people [292]. Results of a meta- analysis study showed that highly physically active individuals had a lower risk of stroke and lower stroke mortality than those with low activity, who in turn had a lower risk of stroke than those who are inactive [320]. Maintaining a healthful activity level gives the heart capacity to pump blood efficiently and reduces the risk of dying from heart disease. Exercise also helps to reduce other stroke and CAD risk factors such as lowering total cholesterol and triglyceride levels and increases protective HDL cholesterol levels, it lowers the blood sugar thus protects from development of type 2 diabetes, it reduces the risk of developing high blood pressure as well as promoting weight loss [25, 292]. In addition, patients with established CAD can lower their risk of cardiac death through regular physical exercise. All individuals regardless of body weight are advised to live a physically active life as a way of reducing the risk of CVDs [292]. The AHA recommends at least 30 minutes of physical activity most days of the week for adults [321].

Physical inactivity accounts for 20% of CHD and 10% of stroke burden in developed countries [181]. Only 42% of men and 31% of women in England met the government’s physical activity guidelines in 2008 [258]. In Canada, nearly half of the adults (≥12 years) are physically inactive and only 43% of people over the age of 65 are active [170]. Most of the population of the United States is sedentary. More than 60% of American adults and about 50% of adolescents do not get the recommended amount of physical activity [321, 322]. Physical inactivity is most common among women, black and Hispanic adults, older individuals, and less affluent people [322]. According to the National Health and Nutrition Examination Survey (NHANES) data, between 1988-1994 and 2001-2006, the proportion of adults who engaged in >12 bouts of physical activity per month declined from 57% to 43% among men and from 49% to 43% among women [21]. In Tennessee, the prevalence of physical inactivity in 2009 was reported to be 31% [323].

1.1.13.1.7 Alcohol Consumption

The relationship between alcohol intake and cardiovascular health is complex, involving both protective and harmful effects, depending on the amount and pattern of consumption. Excessive alcohol intake increases the risk of high blood pressure, raises the level of harmful triglycerides, adds empty calories that contribute to overweight or obesity and thus increases the risk of CHD and stroke [324]. Research also shows an association between frequent heavy drinking, especially over a lifetime, with development of insulin resistance syndrome, a dangerous combination of risk factors for heart disease [25]. Despite the fact that the risk of CHD increases with heavy drinking [325], a substantial body of literature also indicates that CHD risk is lower among moderate drinkers compared to non-drinkers [326, 327]. In one study, moderate drinkers were found to have a better prognosis following a complicated MI than heavy drinkers and non-drinkers [328]. Studies have shown that moderate alcohol consumption (not more than one drink for women, and two drinks for men a day) raises HDL cholesterol level, helps prevent blood clots thus reducing the risk of heart attack and ischemic stroke [25].

A meta-analysis of 35 observational studies found an increased risk of ischemic stroke in people that consume more than 60g of ethanol/day (approximately six drinks) [329]. In the same study, light to moderate alcohol consumption was associated with a reduction in ischemic stroke risk. The apparently positive effect of light to moderate alcohol consumption is associated with beneficial effects on lipids and hemostatic factors [330]. The flavonoids of red wine are said to be involved in preventing the formation of atherosclerotic plaques [331]. On the other hand, heavy alcohol intake and binge drinking increase blood pressure and the risk of hypertension, thereby increasing the risk of stroke [332, 333] and CHD. Heavy long term alcohol consumption (>36g/day or more than three drinks/day) and episodic heavy drinking increase the risk of atrial fibrillation, a major risk factor of stroke [334].

About 2% of CHD and about 5% of stroke burden in men in developed countries is attributed to excessive alcohol consumption [181]. Thirty seven percent of men and 29% of women in Great Britain were reported to have exceeded the recommended amount of alcohol consumption in 2008 [258]. Excessive alcohol use is the third leading preventable cause of death in the US [335] and was responsible for approximately 79,000 deaths and 2.3 million years of potential life lost in the US each year during 2001-2005 [336]. Binge drinking, defined as consuming ≥4 alcoholic drinks on one or more occasions for women and ≥5 drinks on one or more occasions for men, was responsible for more than half of these deaths [337]. Of the 52% US adults (≥18 years) reported to be regular drinkers in 2009 [338], 15.2% indulged in binge drinking [339]. The prevalence of binge drinking among men (20.8%) was twice as high as that among women (10.0%) [339]. Geographically, 49% of adults living in the South were current regular drinkers, in contrast to 52% in the West, 55% in the Midwest, and 56% in the Northeast [338]. In Tennessee, 10.5% of the adults (≥18 years) reported binge drinking in 2008 and 3.5% reported heavy drinking (defined as men having more than 2 drinks per day and women having more than 1 drink per day) [173].

1.1.13.1.8 Socioeconomic Factors

Indicators of socioeconomic status (SES), such as, education, income, and occupation have been associated with coronary heart disease morbidity and mortality [340-343]. These SES indicators are likely independent risk factors for heart disease [344-351]. Studies have reported inverse associations between education [352, 353], income [353], and occupation [354] with incident fatal and non-fatal MI events as well as higher MI risks among middle-aged persons living in socially deprived neighborhoods [347, 355]. Kelly and Weitzen found that people with less than a high school education were more likely to have MI as compared to college graduates [352]. In the same study, prevalence of MI decreased with increase in the life time level of education. In another study, individuals residing in neighborhoods with low median incomes had significantly higher risk of MI compared to those living in neighborhoods with high median income [356]. There is also evidence of inverse associations between stroke mortality risks [357-359] and incidence rates [360-363] with socioeconomic status of individuals. The mechanisms by which socioeconomic status influences stroke and MI risk are not entirely understood. Potential explanations include differences in major stroke risk factors [342, 364], and in access to and use of medical care [365, 366]. Inverse relationships between SES and blood pressure, smoking, diabetes, physical inactivity, and obesity (particularly for women) have been widely reported [367-369].

Socioeconomic deprivation in early life has been associated with increased risk of stroke [370-374] and CHD [374-378] in adulthood. The life course concept considers the social and physical hazards, and the resulting behavioral, biological and psychosocial processes, that act across all stages of the life span (gestation, infancy, childhood, adolescence, young adulthood and midlife) to affect risk of disease later in life [379]. Disadvantageous in-utero conditions have been shown to biologically imprint or program disease and illness susceptibility during fetal development [380] leading to permanent alteration of cardiovascular, endocrine, and metabolic systems thus increasing the risk for obesity, hypertension, diabetes, and CHD in adulthood [381]. Childhood deprivation may restrict opportunities for social mobility (e.g., educational attainment) and access to the goods and services necessary to promote and maintain good health [382, 383]. Other findings indicate that children from disadvantaged families learn poorer health behaviors than their better-off counterparts and are more likely to smoke, have a poor diet, and low physical activity levels in adulthood [383] which may increase the risk of MI and stroke. These findings imply that childhood deprivation may act with other social and behavioral events across the life course and that social mobility and healthy behaviors may effectively mediate the adverse relationship between childhood deprivation and CHD [381, 382].

1.1.13.2 Non-Modifiable Risk Factors

1.1.13.2.1 Age

The prevalence of CVD, predominantly ischemic heart disease and stroke, increases exponentially with age, and CVD remains an important cause of morbidity and mortality up to the oldest age categories [384]. Age tends to weaken the heart's function. The heart is less able to pump blood, the heart walls may thicken, and the artery walls may stiffen and become narrow. The increase in hypertension with age may compound the problem, thus predisposing to MI and stroke [25]. About 82% of people who die of CHD are 65 years or older [385]. Men over age 45 and women over age 55 are at increased risk of CAD [292]. The prevalence of MI is known to be higher in the older population and is associated with high long-term morbidity and mortality [386, 387]. Age is probably the most important determinant of stroke as the risk of stroke doubles for each successive decade after age 55 years [388, 389].

1.1.13.2.2 Sex

Stroke occurs in both men and women but is more prevalent in men than women [388] especially men within the age range of 45-84 years [390]. Myocardial infarction is also more prevalent in men than women [391]. The differences in stroke and MI risks for both men and women may reflect differential exposure to stroke [392] and MI [393] risk factors or differences in the relative magnitude of these risk factors for men and women. Although women develop CAD about 10 years later in life than men [292, 393], they have a higher mortality after MI than men mainly due to the older average age at which women develop MI [394]. Additionally, men are more likely to suffer from MI at a younger age while women are generally protected from heart disease by their sex hormones until menopause [25, 292]. However, after menopause, a woman's risk of heart disease starts to rise and after age 65 the risk of having CAD is about the same as for men, and after age 75, a woman is at greater risk than a man [25]. Even though sex hormones seem to render some sort of protection against heart disease in women, there is still controversy surrounding the effect of hormone replacement therapy (estrogen and/or progestin) in reduction of the risk of heart disease in post menopausal women [292]. Some observational studies [395, 396] have shown beneficial effects of hormone replacement therapy on clinical endpoints for CHD whereas contrasting evidence of no beneficial effect has come from some randomized clinical trials [397-399].

1.1.13.2.3 Race/Ethnicity

The association between race/ethnicity, and stroke and CHD risks may be difficult to interpret. Globally, stroke mortality does not follow any ethnic patterns [400]. However, the incidence of MI in the UK is higher in South Asians than in non-South Asians for both sexes; and the incidence of stroke is higher in blacks than in whites for both sexes [401]. Clear ethnic group differences exist in Canada with First Nations people (Aboriginals) and those of African or South Asian descent having a greater risk of heart disease and stroke than the general population [402]. In the US, clear ethnic group differences also exist with blacks [390, 403] and some Hispanic Americans [404, 405] having higher stroke incidence and mortality risks compared to whites. Blacks also have a higher risk of heart disease [385]. Higher prevalence of hypertension, obesity, and diabetes within the black population are possible reasons for the higher incidence and mortality risk of stroke [406, 407] and heart disease [385]. Incidence data from the Northern Manhattan Stroke Study demonstrated race/ethnic differences in stroke incidence with blacks having a 2.4-fold higher annual stroke incidence, and Caribbean

Hispanics having a 2-fold higher annual stroke incidence compared to whites living in the same community [390].

1.1.13.2.4 Genetic Factors

Both paternal and maternal history of stroke and MI are associated with an increased risk of stroke [408-410] and CAD [25, 292]. Parental CHD occurring at less than 60 years of age has been accepted as a marker of increased CHD risk in the offspring [411]. An individual's risk of CAD is considered to be above average if their father/brother developed CAD before age 55 or if their mother/sister developed it before age 65 [292]. In a recent Framingham study, results showed that offsprings with documented parental history of any stroke type by 65 years of age had a 2-3 fold higher risk of stroke [412]. Moreover, offspring with positive paternal history of stroke were 4 times more likely to develop a stroke by 65 years of age.

In the past, studies indicated that increased stroke risk was not necessarily due to "stroke genes" but may have been mediated through one or more mechanisms, including: (1) genetic heritability of stroke risk factors, (2) genetic susceptibility to these risk factors, (3) familial sharing of cultural/environmental and lifestyle factors associated with stroke, and (4) the interaction between genetic and environmental factors [413]. However, recent genome-wide association analyses have suggested that several putative genes may be responsible for this genetic risk [414, 415]. Some risk factors that can be inherited from parents include tendency toward moderately high cholesterol levels, high blood pressure, obesity or diabetes [292]. Genetic variation at the chromosome 9p21.3 region has consistently been associated with increased risk of

CHD and MI [416-419]. However, the potential mechanism by which variants in this chromosome 9 region increase risk of CHD is still unclear [418, 419].

1.1.14 Vital Statistics

Vital statistics are those related to births (natality), deaths (mortality), marriages, health, and disease (morbidity). In the US, vital statistics are obtained from the official records of live births, deaths, fetal deaths, marriages, divorces, and annulments [420]. The official recording of these events resides individually with the states and independent registration areas (District of Columbia, New York City, and territories) in which the event occurs [420]. The vital statistics for the entire US are then published by the National Center for Health Statistics and can be obtained from the CDC, state health departments, county health departments and other agencies.

Mortality data provide important source of demographic, geographic, cause-of-death information, and are valuable for surveillance of cause-specific mortality. In this study, MI and stroke mortality data obtained from Tennessee vital statistics are used to determine the mortality risks of neighborhoods in Middle Tennessee as well as identify high risk neighborhoods. Additionally, vital statistics provide one of the few sources of health-related data that can be analyzed at the small geographic area level and are available for long periods thus important in assessment of temporal trends in cause specific mortality. This is evident in this study as temporal trends of MI and stroke mortality risks across the study period were computed. These data can also be used to present the characteristics of individuals dying of specific diseases (which is important in determining potential predictors of disease), to determine life expectancy, and to compare mortality trends with other countries [421]. Mortality data are also widely used as indicators of health status or for healthcare needs evaluation [156]. High mortality risks are indicative of a high burden of disease. Thus, mortality data can be used to identify geographical areas in which healthcare resources are most needed. Therefore, vital statistics records provide a rich source of data to epidemiologists and other health and medical investigators for health research.

1.1.15 Summary

Disparities in access to healthcare services and the resulting adverse health outcomes are major public health priorities. Distance to healthcare is one of the most important geographic factors that may affect access to care and therefore health outcomes [156]. Although there is an overwhelming amount of research about MI and stroke disparities in healthcare access and health outcomes, research linking mortality risks of specific regions of the country to access to healthcare services is important in providing information to guide health programs intended to reduce these disparities.

Currently, most population health planning interventions are based on disease spatial patterns observed at the county level or higher geographic units. However, the use of such a large unit of analysis limits the ability to identify specific disease spatial patterns at the lower levels, such as neighborhoods. In the current study, neighborhoods lacking timely access to MI and stroke care were identified. Furthermore, MI and stroke mortality data of neighborhoods in Middle Tennessee were used to investigate and identify MI and stroke high risk clusters. Research relating mortality data to the geographical location of healthcare services is vital in helping healthcare planners and policy makers achieve equitable distribution of resources. Additionally, assessment of temporal trends in mortality risks and disparities in access to healthcare is important in evaluation of intervention strategies and in implementation of needs-based population health planning and service provision. This is important for reducing the burden of MI and stroke in high risk populations thus improving the health of the entire population.

CHAPTER 2

2.0 Temporal Changes in Geographic Disparities in Access to Emergency Heart Attack and Stroke Care: Are We Any Better Today?

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2.1 Abstract

The objective of this study was to investigate temporal changes in geographic access to emergency heart attack and stroke care. Network Analysis was used to compute travel time to the nearest emergency department (ED), cardiac, and stroke centers in Middle Tennessee. Populations within 30, 60, and 90 minutes driving time to the nearest ED, cardiac and stroke centers were identified. There were improvements in timely access to cardiac and stroke centers over the study period (1999-2010). There were significant increases in the proportion of the population with access to cardiac centers within 30 minutes from 29.4% (1999) to 62.4% (2009) while that for stroke changed from 5.4% (2004) to 46.1% (2010). Most (96%) of the population had access to an ED within 30 minutes. Access to care has improved in the last decade but more still needs to be done to address disparities in rural communities.

2.2 Introduction

Coronary heart disease, including heart attack, is the leading cause of death in the United States while stroke is the leading cause of adult disability and third leading cause of death [12]. Out of 700,000 individuals that have stroke in the United States each year, 167,000 die [422] and about 15-30% of the survivors are severely disabled [12]. Heart attack, also known as myocardial infarction (MI) and stroke are of great economic burden to the US health system. The estimated combined direct and indirect costs of MI and stroke in 2010 was an astounding 250.8 billion dollars [12].

Myocardial infarction occurs as a result of blockage of blood flow to the heart muscle mainly due to formation of a blood clot in the coronary artery. Treatments for MI include, but are not limited to, pain control, use of thrombolytics, surgical procedures including coronary artery bypass, and heart transplantations. Other procedures such as percutaneous coronary interventions (PCI), which involve cardiac catheterization, are increasingly being used [423]. For these treatments to be successful, it is critical that they are given as soon as possible after onset of symptoms. The current American and European guidelines suggest cardiac catheterization be done within 90 minutes of first medical contact [424, 425]. Moreover, it is recommended that these procedures be done in hospitals equipped with a catheterization laboratory and specialized team that must be available 24 hours a day [75]. Therefore, not every hospital can appropriately perform these procedures, and so some patients have to travel long distances to get access to a hospital with these facilities and personnel. Long distances and travel times may therefore have a significant impact on patient survival. For instance, out of 1.2 million people who suffer an acute MI each year in the United States, more than 50% die before reaching a hospital or in an emergency department [422]. It has been reported that prolonged transport time to an appropriate cardiac center is one of the factors that contributes to these deaths [426]**.** Moreover, studies have shown that MI patients who live in close proximity to cardiac centers are more likely to receive invasive cardiac procedures such as cardiac catheterizations compared to those that are further away from the cardiac centers [161, 427]**.** Unfortunately, only about 25% of the hospitals in the United States are capable of performing cardiac catheterization [428]. This limitation places a barrier in receiving this intervention for some MI patients, and therefore highlights the need for quick transportation of patients to the few available cardiac centers.

Stroke is an acute neurological injury that results from interrupted blood supply to part of the brain. The primary treatment for acute ischemic stroke is early administration of thrombolytics. However, due to the risks involved in thrombolytic therapy, it is recommended that it is administered only by physicians trained in its use and in centers with the necessary resources to handle complications [115]. Better health outcomes have been observed in patients when thrombolytic treatment is administered intravenously within 3 hours of symptom onset [429]. Even within the 3-hour recommended treatment window, the odds of improvement decrease as time from symptom onset to treatment increases [430]. It is reported that half of stroke deaths occur before the patients reach the hospital [10, 431]. Therefore, early transport to appropriate hospitals and early treatment of these patients would prevent or reduce the number of deaths, disabilities or complications [432]. This emphasizes the need for quick transportation of patients to appropriate stroke centers.

The recommended 90- and 180-minute treatment windows for MI and stroke, respectively, place geographic limits on the distance a patient can be located from a cardiac or stroke center. This indicates that travel time considerations are of paramount importance in accessing stroke and cardiac care. Identification of disparities in geographic access to emergency cardiac and stroke care is the first step towards reduction and elimination of these disparities and improving the health of the population.

Most past studies of geographic access to health services have used straight line or Euclidean distance [433, 434]. More recent studies have used road network based travel time to assess geographic disparities in access to care [22, 435]. Travel time estimated from road networks has increasingly become a popular method because it accounts for travel impedances such as speed limits and therefore provides a more realistic and accurate measure of geographic accessibility [22]. It is also considered a better measure of geographic accessibility because of several reasons: (i) people relate more easily to travel time than to geographic distance when making decisions on seeking care, (ii) speed of access to care in an emergency is often assessed in time, (iii) travelling time is a more sensitive measure than distance as it considers transportation mode (air, ground or water transport) [436].

The American Heart Association/American Stroke Association's Get With the Guidelines (GWTG) program for coronary artery disease (CAD) and stroke established in 2001 and 2004, respectively, was to ensure consistent application of the latest evidence–based scientific guidelines in the treatment of stroke and CAD, including heart attack [437]. With more hospitals adopting the GWTG programs and achieving accreditation status, there is bound to be changes in disparities of timely access to emergency care over time. Therefore, in this study we used network analysis to investigate temporal changes in geographic disparities of timely access to emergency stroke and heart attack care. To the best of our knowledge, this is the first study to use network analysis to investigate temporal changes in geographic disparities of access to health care in the US. Identification of geographic disparities in access to care services is useful for guiding equitable resource allocation and policy decisions geared towards achieving one of the Healthy People 2020 objectives of elimination of health access disparities [438] thus improving the health of the entire population.

2.3 Methods

2.3.1 Study Area

Middle Tennessee is used as a case study in this research although the methodology is applicable to any other geographical region. Thus the current study was carried out in 30 counties of Middle Tennessee (Figure 2.1) using data for 1999-2010. Most of the counties in this area lie in the “stroke belt” of Tennessee, a region with high stroke and MI prevalence. The area consists of 250 census tracts and spans about 12,045 square miles with a total population of approximately 1.2 million people. It was important to include a 4-8 county “buffer” around the study area to allow for the fact that some residents may seek care in neighboring counties (outside the study area) (Figure 2.1). The geographic size of the neighboring counties influenced the number of buffer counties included in the analysis. Thus, in areas where most of the counties were of small geographic size, more counties were included, whereas in areas where the neighboring counties were relatively geographically large, fewer counties were included in the “buffer.”

2.3.2 Data Sources and Preparation

2.3.2.1 Hospital Data

Geographic location data of accredited cardiac and stroke centers as well as other hospitals with an emergency department (ED) were obtained from the Joint Commission on Accreditation of Health Organizations (JCAHO) Web site [439]. The JCAHO is a body responsible for accreditation of care centers that meet specific criteria for providing specialized medical services. Cardiac centers were defined as hospitals

Figure 2.1: Map of Study Area and Neighboring (Buffer) Counties

capable of providing percutaneous coronary intervention services whereas stroke centers were defined as those that comply with the Brain Attack Coalition guidelines [440]. The EDs were defined as hospitals capable of providing emergency care. The street addresses of all the qualifying care centers were geocoded using batchgeo [441] and mapped using ArcGIS Version 9.3 [442]. Hospitals were contacted to determine the initial year of accreditation. In order to assess temporal changes in disparities of access to timely emergency stroke and heart attack care, analyses were performed for each year when there were changes in the number of care centers of interest (cardiac or stroke) during the study period. For cardiac centers this occurred in 1999, 2007, 2009, and 2010 while for stroke centers it was in 2004, 2005, 2006, 2007, and 2010. For ED, two analyses were performed, in 1999 and 2010.

2.3.2.2 Street Network Data

The street network dataset was obtained from Streetmap USA [443]. These data provided segment-by-segment information on street names, legal speed limits, distance, road connectivity and turn impedances, which are required to perform realistic travel time calculations. The North American Datum 1983 State Plane coordinate system with the high accuracy reference network for Tennessee was the reference system used because it uses Lambert conformal conic projection, which minimizes scale distortion allowing for accurate distance computations. Travel time for each street segment was calculated using the field geometry calculator in ArcGIS 9.3, as follows: travel time (minutes) = length of the segment (miles)/speed limit (miles/minute).

2.3.2.3 Cartographic Boundary Files

The cartographic boundary files for census tracts were downloaded from the US Census Bureau [444]. These data were used for overlaying the street dataset and the care center locations. The main geographic unit of analysis used was a census tract. Census tracts are small, county statistical subdivisions that contain between 2,500 and 8,000 people. In this study, census tracts were used to represent neighborhoods because they are good proxies of natural neighborhood boundaries and are homogenous with respect to population characteristics [226].

2.3.2.4 Population Data

Census tract and block group-level population data were obtained from the 2000 Census summary file 3 [445]. In this study, population weighted centroids of census tracts (based on block group-level population data) were used instead of simple geographic centroids because they correspond to the approximate locations that are closest to where most residents in the census tract live. Census tract population characteristics (potential risk factors for MI and stroke), such as, proportion of individuals aged ≥65 years, below poverty level, with utmost elementary education, as well as the median household income and the median housing value were also obtained from the 2000 Census summary file 3 [445].

2.3.2.5 Mortality Data

The MI and stroke mortality data used to calculate mortality risks for neighborhoods within each travel time was obtained from the Tennessee Department of Health. Only mortality data for the years 1999-2007 was available for the study. Deaths from stroke and MI were defined on the basis of underlying cause of death. The International Classification of Diseases, Tenth Revision (ICD-10) codes used were I21-I22 for MI and I63-I64 for stroke. Cases were geocoded based on their residential addresses.

2.3.3 Network Analysis

This technique uses road network data to calculate distances between points or nodes on a network. Hence, the first step was to build a network dataset of the study area. Network datasets consist of a series of segments or links that are joined by nodes (intersections), and each link is assigned a travel cost, which in this case was time (measured in minutes). Nodes represent a point (care center or population centroid of a census tract) of interest within the network whereas links are the connections (roads) that allow flow between the nodes. Each road segment in the network has a known length/distance and associated speed limit that allow for calculation of travel time. Therefore, travel time (in minutes) for each road segment in the study area was determined. Travel time from each neighborhood population centroid to the nearest cardiac or stroke center along the road network was calculated using network analyst's service area solver function. This function uses Dijkstra's shortest path algorithm [446] to compute the shortest path between each population centroid and the closest cardiac or stroke center. This algorithm works by first computing travel times along all possible routes connecting the origin (neighborhood population centroids) and destinations (cardiac and stroke centers) within a given travel time limit, which was 30, 60, and 90 minutes in this study. The travel time is minimized by hierarchical routing where driving on higher-level roads (interstate highways) is preferable to driving on lower-level roads (local roads) [447]. Thus, the service area solver function generated travel time zones within the specified travel time limits: 30, 60, and 90 minutes in this study. A travel time zone represents the area that can be reached by road within specified time limits. For example, the 30-minute travel time zone for a hospital includes all the areas that can reach the hospital within 30-minutes travel time [446]. Separate analyses of the 30-, 60-, and 90-minute travel time zones for stroke, cardiac and emergency departments were performed. In order to assess temporal changes in access, analyses were performed for each of the years during which there were changes in the number of accredited care centers. For cardiac centers, these occurred in 1999, 2007, 2009, and 2010 while for stroke centers it was 2004, 2005, 2006, 2007, and 2010. Analyses of access to stroke centers began in 2004 because accreditation of stroke centers began in 2003 [448]. For ED, analyses were performed for 1999 and 2010 because only 1 ED was added to the study area and 1 to the buffer counties between 1999 and 2010. Neighborhoods (census tracts) whose population-weighted centroids were within a specified travel time zone boundary were allocated to that travel time zone. The percentage of the population that had access to ED, stroke, and cardiac centers within 30, 60, and 90 minutes travel time at each of the time periods was estimated. Population characteristics of the populations within the different cardiac and stroke travel time zones at each of the study periods were also computed.

2.3.4 Statistical Analysis of Mortality Risks and Temporal Changes in Access

Age- and sex-adjusted mortality risks for neighborhoods in each of the travel time periods for the years 1999-2007 (for MI) and 2004-2007 (for stroke) were computed.

The Tennessee 2000 census population was used as the standard population for direct standardization of the mortality risks.

To assess temporal changes in timely access, the percentage of the population with timely access to ED, cardiac and stroke centers were computed for each time period when changes occurred. Two-way comparisons between proportions of adjacent time periods were then performed using two-sample test of proportions in Stata version 11.0 (Stata Corp., College Station, TX). Simes method was used to adjust for multiple comparisons. To assess temporal trends, tests for trend in the proportions of populations and mortality risks for both MI and stroke were performed.

2.4 Results

2.4.1 Distribution of Care Centers

The number of accredited cardiac and stroke centers in the study area increased over time (Tables 2.1 and 2.2). The number of cardiac centers in the study area increased from 2 in 1999 to 7 in 2010 (Table 2.1; Figures 2.2 and 2.3). The lowest (7) number of cardiac centers in the buffer counties was observed in 1999 while the highest (35) was in 2010 (Table 2.1). Of the 7 cardiac centers in the study area in 2010, 3 were located in Hamilton county, 2 in Rutherford, and one in each of Coffee and Putnam counties (Figure 2.3b). It is worth noting that all the stroke centers were also cardiac centers. The distribution of stroke centers followed a similar temporal trend with the lowest number of stroke centers in both the study area and buffer region recorded in

Table 2.1: Changes in the Number of Cardiac Centers, Neighborhoods and Populations with Access to Emergency Cardiac Care at Different Times in Middle Tennessee, 1999-2010

Year	Number of Cardiac Centers		Travel Time (min)	Number of Neighborhoods	Number of People	% Pop
	Study Area	Buffer Counties				
1999	2	7	0 - 30	60	352,807	29.4
			>30 - 60	50	222,542	18.6
			>60 - 90	103	433,213	36.2
			>90	37	189,419	15.8
2007	3	12	0 - 30	128	657,753	54.9
			>30 - 60	58	275,581	23.0
			>60 - 90	49	208,878	17.4
			>90	15	55,769	4.7
2009	6	26	0 - 30	147	748,018	62.4
			>30 - 60	86	387,276	32.3
			>60 - 90	17	62,687	5.2
			>90	0	0	0
2010	7	35	0 - 30	148	751,391	62.7
			>30 - 60	88	396,085	33.1
			>60 - 90	14	50,505	4.2
			>90	0	0	0

Table 2.2: Changes in the Number of Stroke Centers, Neighborhoods and Populations with Access to Emergency Stroke Care at Different Times in Middle Tennessee, 1999-2010

Year	Stroke Center Number		Travel Time (min)	Neighborhoods	Number of People	% Pop
	Study Area	Buffer Counties				
2004	0	1	0 - 30	9	63,679	5.4
			>30 - 60	41	233,931	19.5
			>60 - 90	62	277,891	23.2
			>90	138	622,480	51.9
2005	0	5	0 - 30	12	79,095	6.6
			>30 - 60	44	239,580	20.0
			>60 - 90	60	281,927	23.5
			>90	134	597,379	49.9
2006	0	11	0 - 30	44	195,195	16.3
			>30 - 60	84	451,042	37.7
			>60 - 90	81	403,427	33.7
			>90	41	148,317	12.3
2007	1	15	0 - 30	67	341,999	28.5
			>30 - 60	94	458,760	38.3
			>60 - 90	71	332,708	27.8
			>90	18	64,514	5.4
2010	2	21	0 - 30	107	551,956	46.1
			>30 - 60	70	328,824	27.4
			>60 - 90	56	256,783	21.4
			>90	17	60,418	5.1

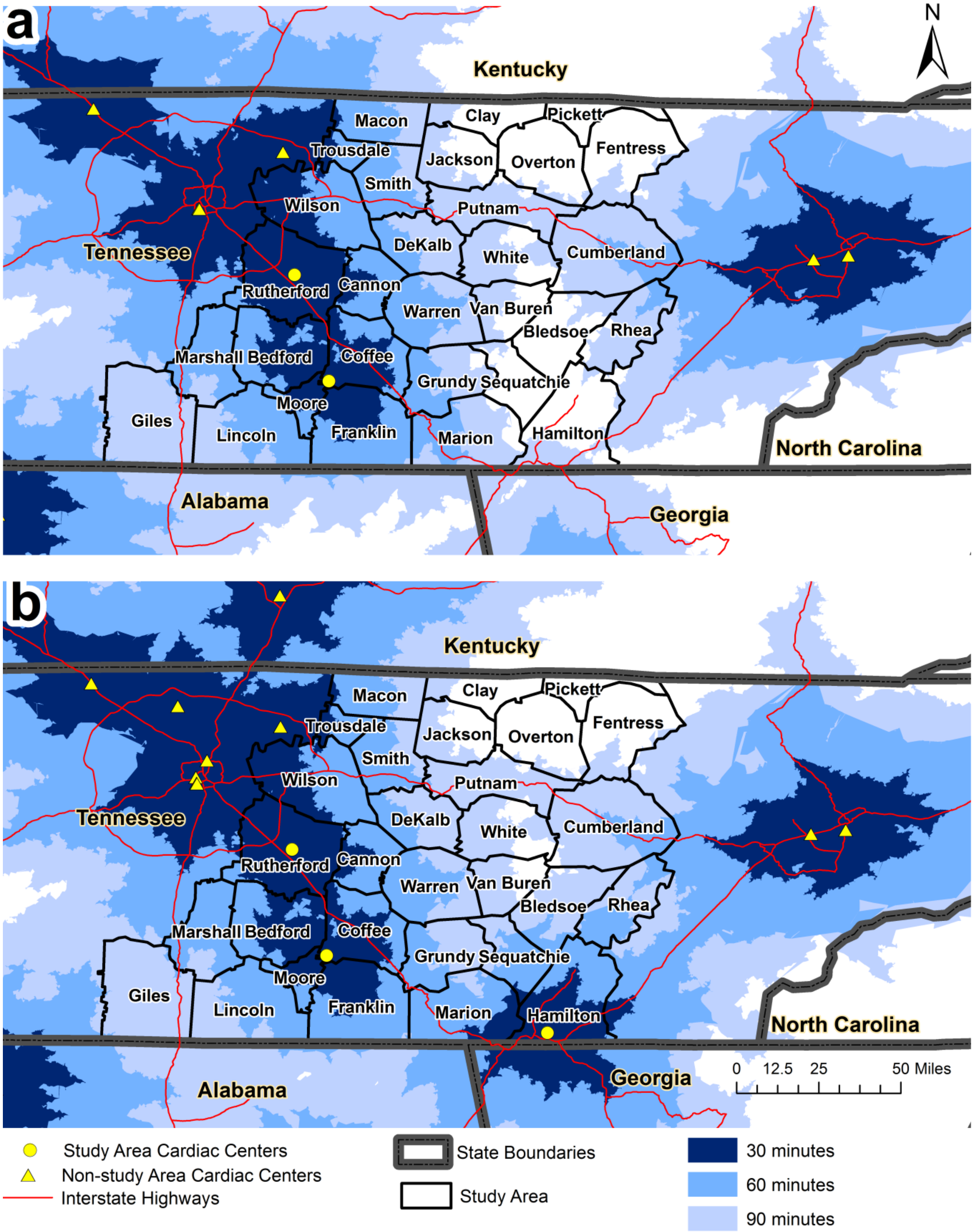

Figure 2.2: Travel Time to Cardiac Centers in Middle Tennessee in (a) 1999 and (b) 2007

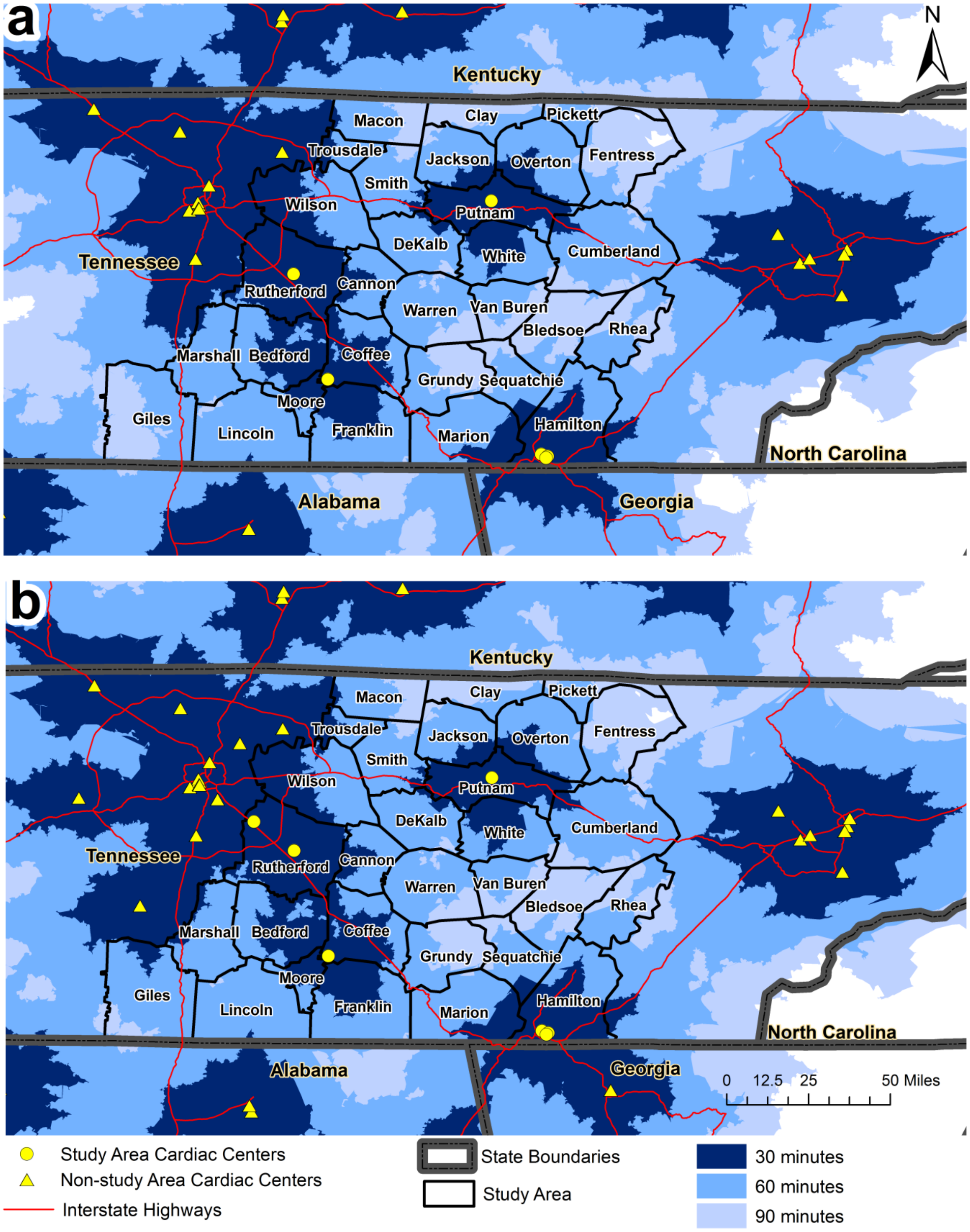

Figure 2.3: Travel Time to Cardiac Centers in Middle Tennessee in (a) 2009 and (b) 2010

2004 and the highest in 2010 (Table 2.2). Notably, there were no accredited stroke centers in the study area until 2007 (Table 2.2 and Figures 2.4 and 2.5). However, a number of stroke centers were located in the buffer counties from 2004 through 2010 (Table 2.2 and Figures 2.4, 2.5, and 2.6). As expected, most of the cardiac and stroke centers were located in the major cities. For instance, the only 2 stroke centers in the study area in 2010 were located in the two major cities; Murfreesboro (Rutherford County) and Chattanooga (Hamilton County) (Figure 2.6). The number of EDs in both the study area and the buffer counties did not change significantly between 1999 and 2010. Only two EDs were added during the study period; one in the study area in 2003 and the other in the buffer county in 2002. There were 35 hospitals with EDs in the study area and 69 in the buffer counties in 2010 (Figure 2.7). The spatial distribution of EDs followed a similar trend as for the cardiac and stroke centers with 7 of the 8 EDs in Hamilton County located in Chattanooga and 2 of the 3 EDs in Rutherford County located in Murfreesboro. Unfortunately, some counties, such as Grundy, Jackson, Moore, Sequatchie, Pickett, and Van Buren did not have any hospitals with an emergency department for the entire study period (Figure 2.7).

2.4.2 Disparities in Geographic Access

Generally, the population with timely access to emergency care for the two conditions increased over time. There were significant ($p<0.0001$) increases in the percentages of the population that had access to cardiac and stroke centers at different travel time intervals (30, 60, and 90 minutes) over the study period. Most evident was a

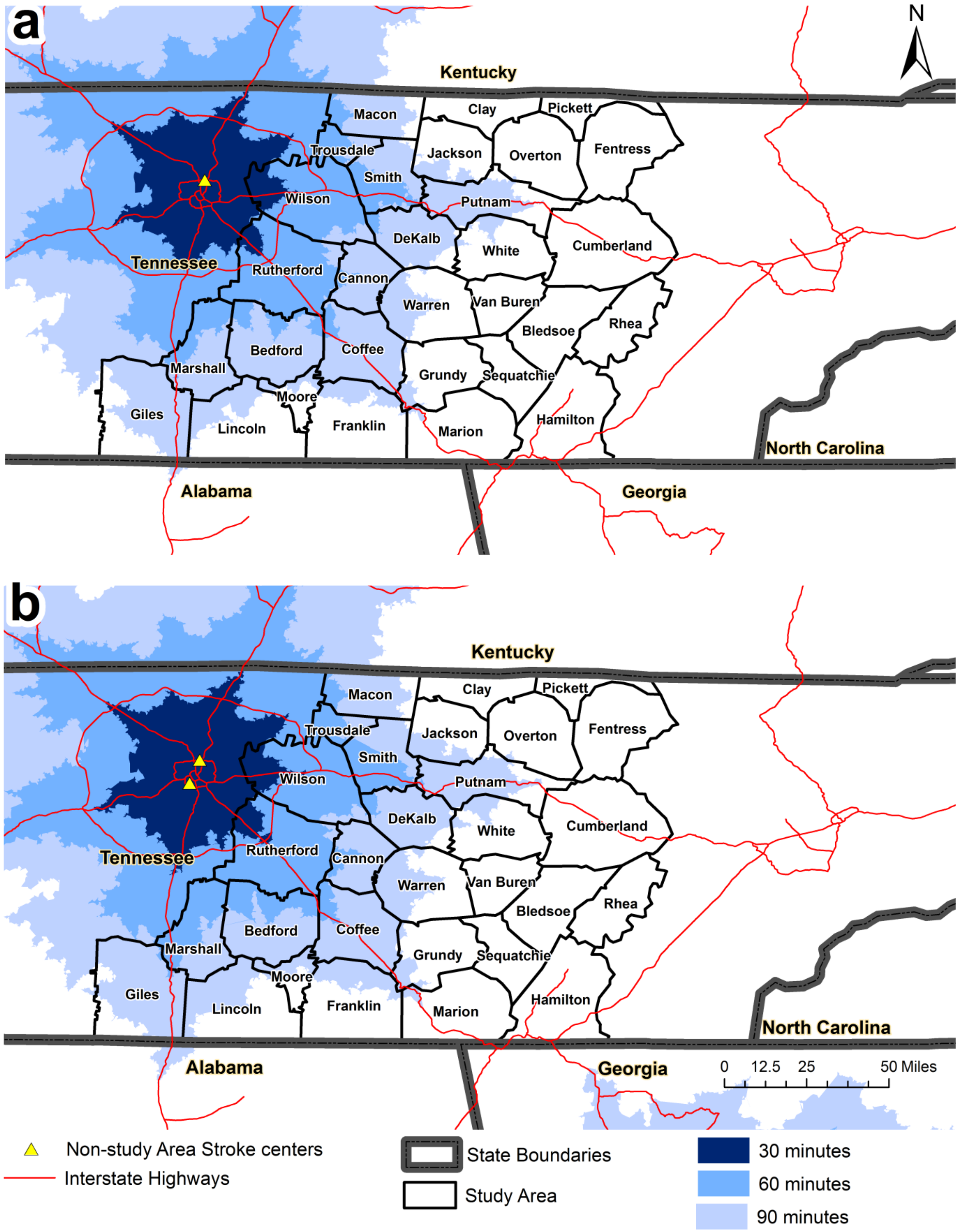

Figure 2.4: Travel Time to Stroke Centers in Middle Tennessee in (a) 2004 and (b) 2005

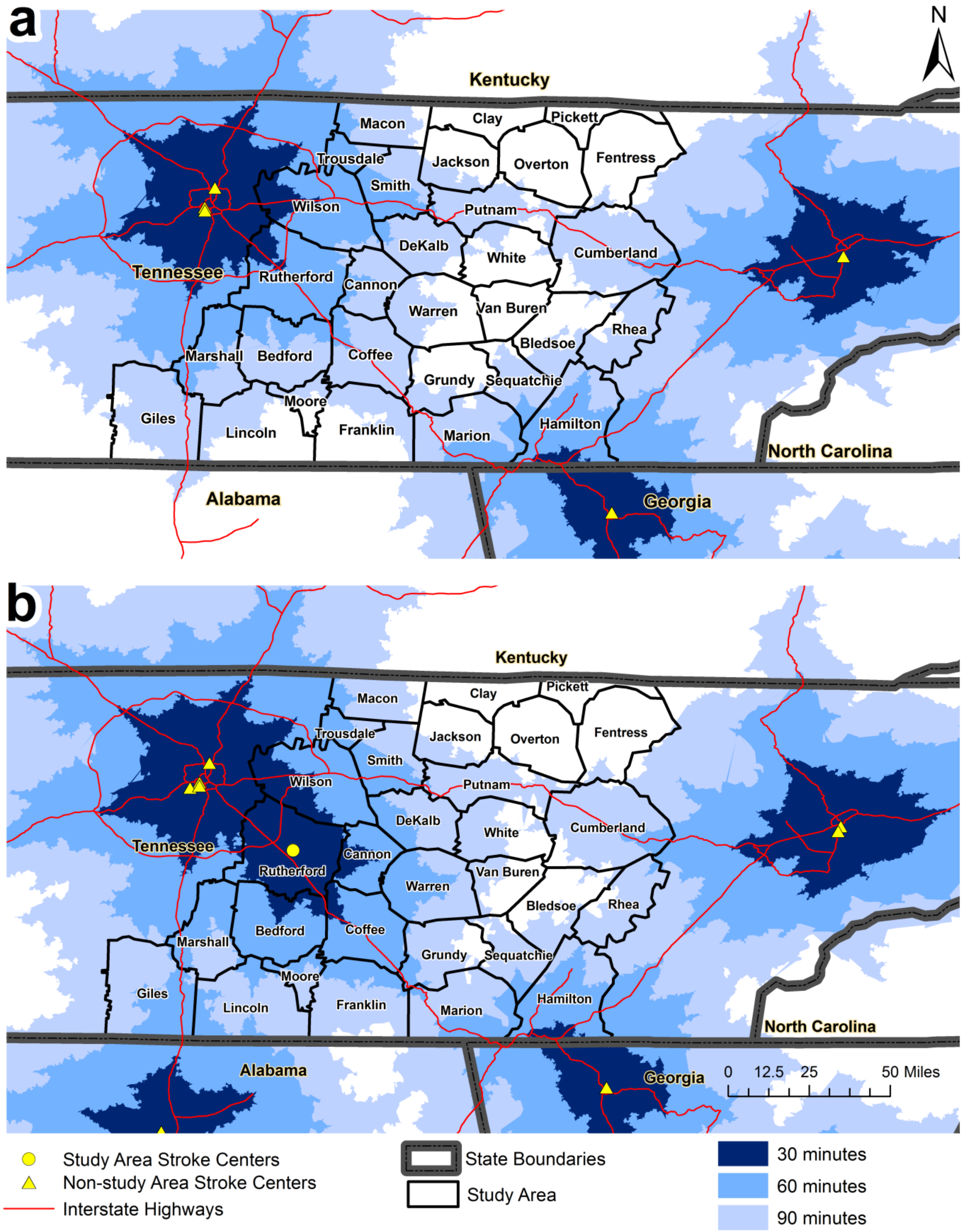

Figure 2.5: Travel Time to Stroke Centers in Middle Tennessee in (a) 2006 and (b) 2007

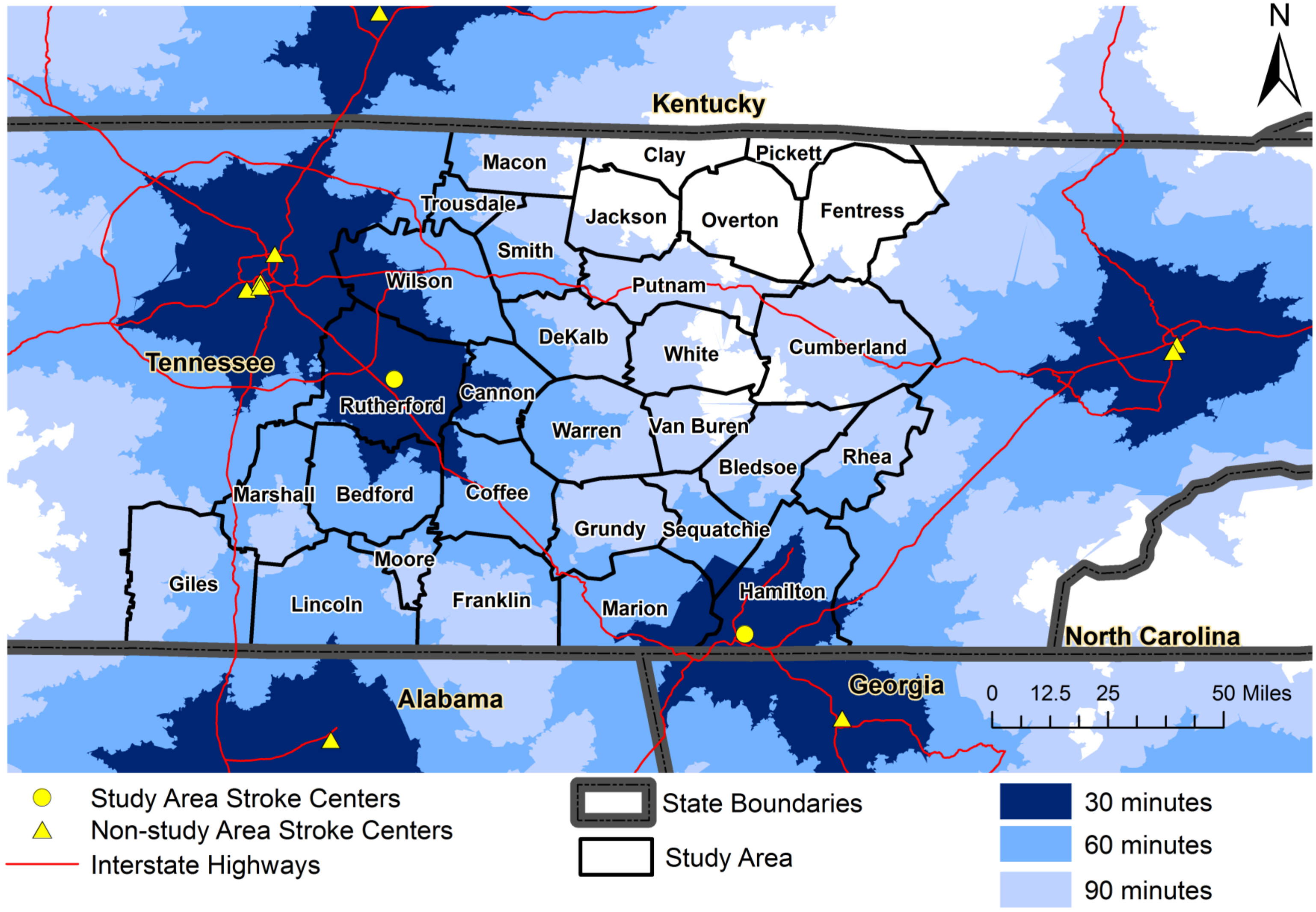

Figure 2.6: Travel Time to Stroke Centers in Middle Tennessee, 2010

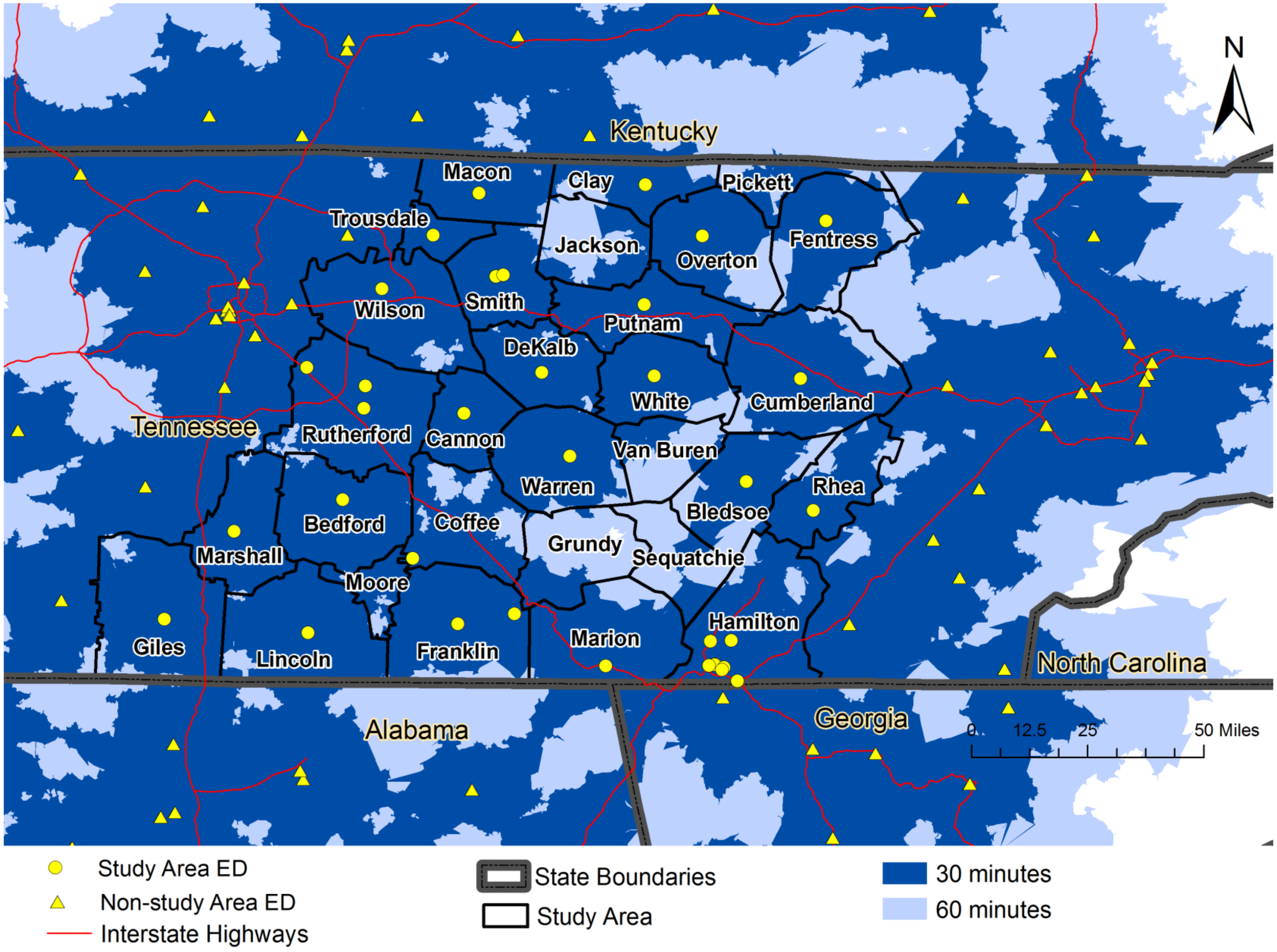

Figure 2.7: Travel Time to Hospitals with an Emergency Department in Middle Tennessee, 2010

temporal increase in the number of neighborhoods and the percentage of the population that had timely geographic access to cardiac (Table 2.1) and stroke (Table 2.2) centers over the study period. The number of neighborhoods with access to a cardiac center within 90 minutes rose from 213 in 1999 to 235 in 2007 (Table 2.1). With the exception of a few neighborhoods in Fentress County, most neighborhoods in the study area had access to a cardiac center within 90 minutes in both 2009 and 2010.

The percentage of the population that had access to a cardiac center within 30 minutes rose from 29.4% in 1999 to 62.7% in 2010 (Table 2.1). A total of 37 and 15 neighborhoods representing 15.8% and 4.7% of the study population had no access to a cardiac center within 90 minutes in 1999 and 2007, respectively (Table 2.1). Most of these neighborhoods were consistently located in the more rural counties of Bledsoe, Clay, Fentress, Jackson, Overton, Pickett, Sequatchie, Van Buren, and White.

Although access to stroke centers was more limited, a similar increasing temporal trend was observed over the study period. The percentage of the population that had access to a stroke center within 30 minutes rose from 5.4% in 2004 to 46.1% in 2010 (Table 2.2). Several neighborhoods had no access to a stroke center within 90 minutes throughout the study period (Table 2.2 and Figures 2.4, 2.5, and 2.6). However, it is interesting to note that the percentage of the population that had no access to a stroke center within 90 minutes declined from 51.9% in 2004 to 5.1% in 2010 (Table 2.2). The proportion of the population with access to stroke centers was similar for 2008 through 2010.

The percentage of the population with access to an ED was similar for both 1999 and 2010. Most (96%) of the study population could access a hospital with an emergency department within 30 minutes and the entire study area population had access to an ED within 60 minutes. Some areas of Grundy, Sequatchie, Jackson, Overton and Van Buren counties had no access to an ED within 30 minutes (Figure 2.7). Since the results for both 1999 and 2010 were similar, we present only the results of 2010. Additionally, since all neighborhoods were within 60 minutes of an ER, the map of access to an ER does not include the 90 minutes travel time zone (Figure 2.7).

2.4.3 Population Characteristics of Neighborhoods Within Travel Time Zones

The proportions of the population within 60 minutes of a cardiac center that were 65 years and older, living in rural areas, below poverty level, and had utmost elementary education increased between 1999 and 2007 (Table 2.3). Similar changes were observed for stroke with respect to neighborhoods that had access within 30 minutes of a stroke center. On the other hand, there were decreasing proportions of those with access to stroke centers over 90 minutes (Table 2.4). Interestingly, for all the study periods considered, neighborhoods within 30 minutes of cardiac care had the highest median household income and median housing value (Table 2.3) implying that neighborhoods with lower income tended to be further away from cardiac centers. Similarly, with the exception of the 2006 study period, median household income and median housing value tended to be lower in neighborhoods that had longer travel times to a stroke center (Table 2.4).

2.4.4 Age- and Sex-adjusted Mortality Risks Across Travel Time Zones

There was a total of 9,822 MI and 4,919 stroke deaths over the study period. Mortality risk for MI was lower in neighborhoods that were within 30 minutes of a cardiac

Table 2.3: Socioeconomic and Demographic Characteristics of Populations with Different Levels of Access to Cardiac Centers in Middle Tennessee, 1999-2010

Year	Travel Time (Min)	Pop 65 Years and Above		Pop in Rural Areas		Pop Below Poverty		Pop with Utmost Elementary Education		Median Household Income	Median Housing Value
		Number	%	Number	%	Number	%	Number	%		
1999	0 - 30	35,382	22.9	139,728	24.8	34,184	22.9	15,640	19.5	42,808	97,850
	>30 - 60	30,811	19.9	154,731	27.4	30,886	20.7	19,421	24.2	34,696	80,000
	>60 - 90	64,373	41.8	167,893	29.7	63,640	42.6	30,691	38.2	31,006	74,500
	>90	23,743	15.4	101,970	18.1	20,716	13.8	14,626	18.1	31,689	73,200
2007	0 - 30	77,819	50.4	165,075	29.2	70,609	47.3	27,236	33.9	37,755	88,950
	>30 - 60	37,055	24.0	197,859	35.1	37,843	25.3	24,150	30.0	34,076	78,500
	>60 - 90	30,806	20.0	148,755	26.4	30,875	20.7	20,239	25.2	30,291	73,500
	>90	8,629	5.6	52,633	9.3	10,099	6.7	8,753	10.9	25,813	60,700
2009	0 - 30	89,922	58.3	213,479	37.8	83,711	56.0	35,168	43.8	37,134	87,500
	>30 - 60	55,766	36.1	293,790	52.1	54,681	36.6	37,251	46.3	31,746	74,550
	>60 - 90	8,621	5.6	57,053	10.1	11,034	7.4	7,959	9.9	28,607	61,500
	>90	0	0	0	0	0	0	0	0	0	0
2010	0 - 30	90,319	58.5	216,852	38.4	84,040	56.2	35,362	44.0	37,173	87,400
	>30 - 60	57,320	37.1	296,974	52.6	55,859	37.4	37,935	47.2	31,747	74,550
	>60 - 90	6,670	4.3	50,496	9.0	9,527	6.4	7,081	8.8	27,962	57,150
	>90	0	0	0	0	0	0	0	0	0	0

Table 2.4: Socioeconomic and Demographic Characteristics of Populations with Different Levels of Access to Stroke Centers in Middle Tennessee, 1999-2010

Year	Travel Time (Min)	Pop 65 Years and Above		Pop in Rural Areas		Pop Below Poverty		Pop with Utmost Elementary Education		Median Household Income	Median Housing Value
		Number	%	Number	%	Number	%	Number	%		
2004	0 - 30	3,776	2.4	8,493	1.5	3,242	2.2	1,507	1.9	54,213	120,800
	>30 - 60	21,525	14.0	108,447	19.2	21,625	14.5	10,535	13.1	44,507	103,600
	>60 - 90	38,747	25.1	160,641	28.5	39,884	26.7	22,626	28.1	34,652	78,700
	>90	90,261	58.5	286,741	50.8	84,675	56.7	45,710	56.9	30,882	71,700
2005	0 - 30	4,827	3.1	10,960	1.9	4,014	2.7	1,852	2.3	55,888	122,450
	>30 - 60	23,583	15.3	114,905	20.4	23,641	15.8	11,991	14.9	40,133	101,250
	>60 - 90	39,693	25.7	167,800	29.7	40,618	27.2	22,802	28.4	33,646	77,500
	>90	86,206	55.9	270,657	48.0	81,153	54.3	43,733	54.4	31,038	72,350
2006	0 - 30	21,904	14.2	13,389	2.4	22,232	14.9	6,834	8.5	36,447	87,750
	>30 - 60	51,845	33.6	157,181	27.9	44,433	29.7	20,512	25.5	40,509	93,950
	>60 - 90	58,760	38.1	261,467	46.3	59,016	39.5	34,727	43.2	31,938	76,600
	>90	21,800	14.1	132,285	23.4	23,745	15.9	18,305	22.8	28,490	68,300
2007	0 - 30	34,983	22.7	76,697	13.6	36,336	24.3	12,380	15.4	39,470	92,900
	>30 - 60	60,821	39.4	190,763	33.8	51,543	34.5	26,189	32.6	36,825	83,950
	>60 - 90	48,803	31.6	235,432	41.7	50,108	33.5	31,801	39.6	30,865	74,500
	>90	9,702	6.3	61,430	10.9	11,439	7.7	10,008	12.5	25,941	60,350
2010	0 - 30	62,327	40.4	112,748	19.9	56,245	37.6	19,888	24.7	39,871	92,900
	>30 - 60	44,215	28.7	218,105	38.6	43,360	29.0	26,265	32.7	35,019	77,950
	>60 - 90	38,417	24.9	176,135	31.2	38,979	26.1	24,686	30.7	30,491	74,550
	>90	9,350	6.0	57,334	10.2	10,842	7.3	9,539	11.9	25,902	60,700

center compared to those that were within >30-60 minutes (Figure 2.8a). Generally, MI mortality risks decreased over the study period with risks in neighborhoods that were within 30 minutes decreasing from 88.7 in 1999 to 67.1 in 2007 while that for neighborhoods that were within >30-60 minutes travel time decreased from 116.7 in 1999 to 89.5 in 2007 (Figure 2.8a). Although the pattern of change in the stroke mortality risks of the neighborhoods in the travel time zones was not consistent across the study periods, the mortality risks recorded in 2007 were lower than those recorded in 2004 for all the travel time zones (Figure 2.8b). Other graphs showing the temporal changes in the mortality risks for neighborhoods within different travel time zones for both MI and stroke can be found in appendix 1 and appendix 2, respectively. The tests for trend in the proportions of populations and mortality risks for both MI and stroke were significant (p<0.0001) implying significant changes during the study period.

2.5 Discussion

The results of this study undoubtedly depict significant temporal changes in geographic disparities of access to stroke and cardiac centers. Despite important improvements observed in geographic access to stroke and cardiac centers during the study period, disparities in geographic access still exist especially for emergency stroke care. Not surprisingly, clear differences were apparent between urban and rural areas, with drive times to care centers being generally longer in rural neighborhoods because most of the care centers were located in urban areas. This is in agreement with several other studies [22, 449-452] that have documented inequitable distribution of health services between rural and urban populations. Pedigo and Odoi [22] investigated

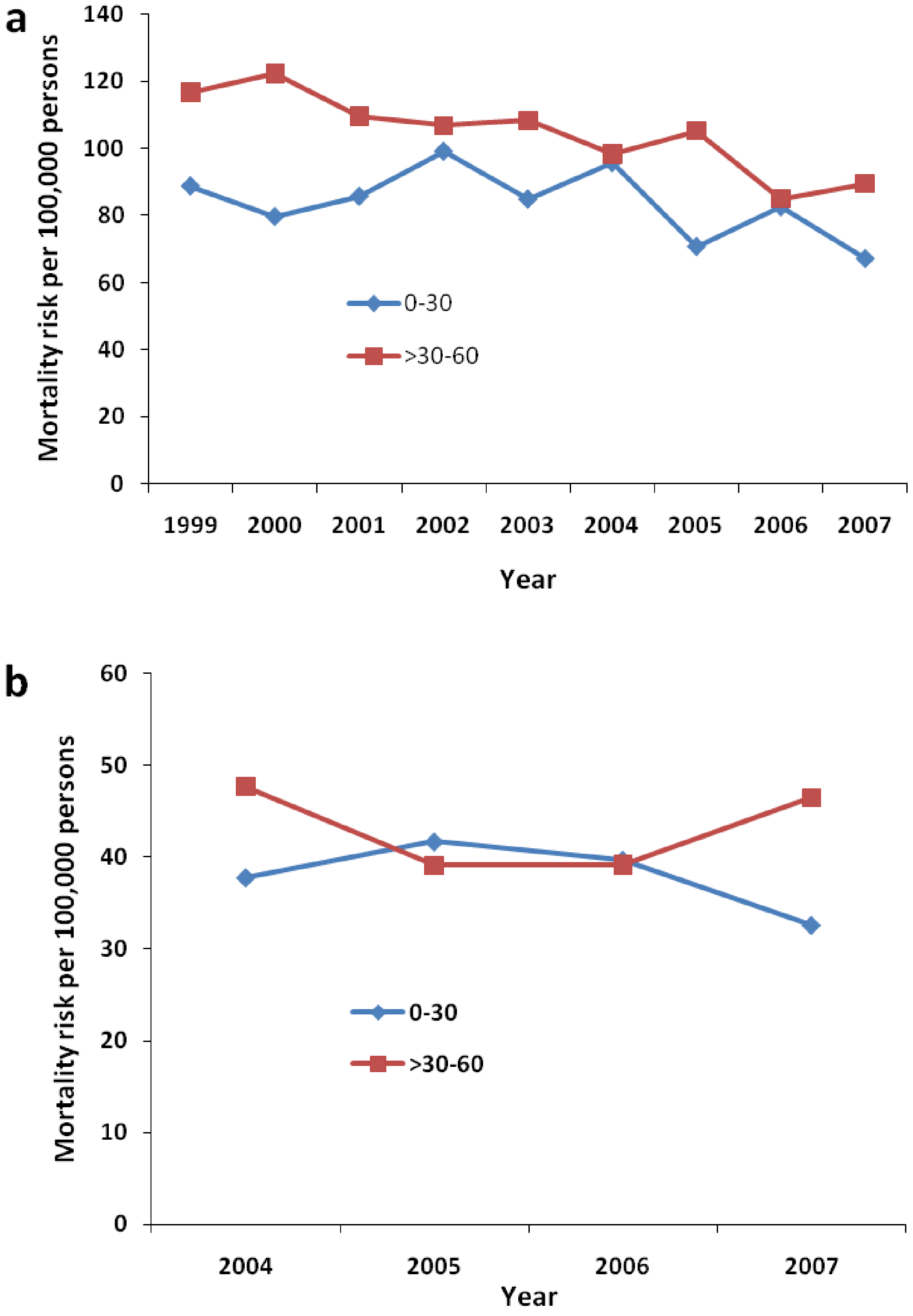

Figure 2.8: Temporal Changes in the Mortality Risks of Neighborhoods with Access to a (a) Cardiac Center and (b) Stroke Center within 30 and 60 Minutes

disparities in access to heart attack and stroke care in East Tennessee and found that most of the neighborhoods with poor access were those in the rural mountaneous parts of the study area. Their study did not investigate changes in disparities of access overtime; however, they found that 8% and 15% of the study population did not have timely access to emergency stroke and MI care by road ambulance, respectively. They also observed that travel by air ambulances greatly improved access to both MI and stroke resulting in all neighborhoods (both urban and rural) having access to appropriate care within 30 minutes. They argued that although it may not be practical or cost effective to add additional stroke or cardiac centers, in order to improve access for rural communities, use of air ambulances may be quite beneficial for these neighborhoods. Similar to our study, they found that 96% of their study area population had access to an ED within 30 minutes. These together with the use of telemedicine, could play a key role in stabilizing the patients before or during transportation to appropriate cardiac and stroke centers. This finding is important for public health planning and resource allocation.

Significant improvements in access to care centers were observed as the number of JCAHO accredited centers increased significantly during the study period. It is important to note that whereas in 1999 most of the potential high risk populations (those aged ≥65 years, below poverty level, and those with utmost elementary education) were not within 60 minutes of a cardiac center and 90 minutes of a stroke center, in 2010 most of them had access to cardiac and stroke care within 60 and 90 minutes, respectively. This is indicative of the progress that has been made to improve access to emergency health services over time. This improvement can in part be attributed to the AHA/ASA and other organizations that have made efforts to improve stroke and heart attack treatments and outcomes in patients. In particular, the AHA's GWTG program which has been shown to not only improve patient outcomes but also earn participating hospitals national recognition as centers of excellence in the treatment of stroke and cardiac events [437]. This has motivated more hospitals to implement their programs as a way of achieving recognition and excellence. Hospitals that implement the GWTG programs are most likely to be accredited by the JCAHO since most performance measures for the two programs are similar [141, 437]. An increase in the number of accredited centers implies that more patients can access the time sensitive treatments as observed in the study. For ED, the percentage of the population with access did not change between 1999 and 2010 (even with addition of one ED in the study area in 2003), because this ED was located in the urban area of Murfreesboro which already had another ED center thus did not create any changes as regards to timely accessibility since both EDs were located in the same area.

A very interesting finding of this study was that for all the study periods for both MI and stroke (except 2006), neighborhoods furthest away from cardiac and stroke centers had the lowest median household income and median housing value. This gives evidence that economically disadvantaged neighborhoods are normally faced with geographic accessibility problems compared to the affluent ones. Moreover, mortality risks also tended to be lowest among neighborhoods closest to the care centers compared to those that were much further away. This helps strengthen the evidence that geographic access to care impacts health outcomes observed at the neighborhood level and therefore should impact health planning strategies.

The MI guidelines suggest that the estimated door-to-treatment time (that is, time required for initial evaluation of a heart attack patient, performing the electrocardiogram, laboratory tests, and mobilizing the catheterization team) should not exceed 30 minutes [425, 453]. Since the maximum allowable time for cardiac catheterization is 90 minutes [424, 425], this leaves, on average, only 60 minutes as the maximum travel time for a patient to reach a cardiac center in order to receive therapy in the recommended time frame. Interestingly, in 2009 and 2010, 94.7% and 95.8% of the population in the study had access to cardiac care within 60 minutes, respectively. These percentages are similar to that reported by Pedigo and Odoi [22], where about 98% of the population in East Tennessee had access to cardiac care within 60 minutes. However, the observed percentages are greater than the one reported by Nallamothu [454], in which 80% of the entire United States population had access to cardiac care within 60 minutes. In contrast, the 80% reported by Nallamothu is greater than the 48% and 77.9% recorded in the periods of 1999 and 2007, respectively. Additionally, it is not surprising that for the entire study period, neighborhoods within the 60 minute travel time zone had higher mortality risks compared to those that were within the 30 minute travel time zone. Reports have revealed that utilization of care services tends to decline as the distance traveled to care increases [157] and this may explain the observed high MI mortality risk. Moreover, studies have shown that MI patients within close proximity of cardiac centers are more likely to receive cardiac procedures such as PCI compared to those that are further away from the cardiac centers [160, 161]**.**

The recommended ideal door-to-treatment time (that is, time for emergency department evaluation, computerized tomographic scan, required laboratory tests and thrombolytic initiation) for stroke patients is 60 minutes [455]. Since the maximum allowable time for thrombolysis is 180 minutes [429], this leaves 120 minutes for travel and symptom recognition. However, the time needed for symptom recognition may vary depending on symptom presentation, time when the symptoms occur, reoccurrence of stroke or knowledge of stroke symptoms by the patients or family members [456]. Based on the variable nature of the time from onset to symptom recognition, we determined that on average, the patient would need a maximum of 90 minutes of travel time in order to be on time for thrombolytic therapy. It is therefore worthwhile to note that 51.9%, 49.9%, 12.3%, 5.4%, and 5.1% of the population in the study area could not access a stroke center within 90 minutes in 2004, 2005, 2006, 2007, and 2010, respectively. These percentages are greater than the one reported by Pedigo and Odoi [22], where only about 1% of the population in East Tennessee did not have access to stroke care within 90 minutes. Most of the population that had no access to a stroke center within 90 minutes in 2010 was mainly from the rural counties of Clay, Fentress, Jackson, Overton, and Pickett. However, the percentage of the population with access to a stroke center within 90 minutes in 2006 (87.7%), 2007 (94.6%), and 2010 (94.9%) was higher than that of a Canadian study reported by Scott [452], where only 78.2% of the total Canadian population had access to stroke care within 90 minutes. In contrast, the 78.2% reported by Scott is much higher than the 48.1% and 50.1% observed in the current study during the years 2004 and 2005, respectively.

In this study, we use travel time calculations that are based on road networks and actual speed limits of each road segment, which provide more realistic estimates of travel times and therefore helps to more accurately identify neighborhoods without timely access to emergency care. This technique provides a much better estimate of travel times than Euclidean distance methods that have been used by some studies in the past [457, 458]. Euclidean distance methods have been shown to underestimate actual travel times at lower travel speeds whereas they overestimate actual travel times at higher travel speeds [22, 459]. This reaffirms the superiority of road network based travel time over Euclidean distance derived travel time in measuring geographic accessibility to healthcare. Therefore, this analytical technique provides a useful measure of geographical access to healthcare. The results are useful for guiding health planning decisions aimed at reduction of health disparities in neighborhoods. With the increasing availability of network analysis tools (such as ESRI's network analysis extension), health planners should be able to apply these techniques to better inform planning decisions. Moreover, these analyses can be iteratively performed to reflect changes in road networks (such as construction of new roads and changes in speed limits of road segments). However, this technique is not without limitations. Firstly, ambulances may not travel at the legal speed limits (on which we based our travel time estimates) and are also exempted from restrictions, like traffic lights. Additionally, changes in driving conditions such as periods of traffic congestion affect driving speeds and therefore travel times. These factors were not adjusted for in the model because several attempts to acquire information regarding the actual travel speeds of ambulances (that is, how fast above the legal speed limits) were unsuccessful. Nevertheless, considering about 50% of MI [460] and stroke [461] patients use self-transport and are therefore subjected to the standard traffic laws used in this analysis, we believe that study findings will be quite applicable and useful to inform planning decisions. Data on travel impedances which may affect travel speed, such as, traffic congestion, weather conditions, and time of day were not available thus were not adjusted for. Secondly, due to financial constraints, the Streetmap USA version of 2007 was used for all the study periods. Although some changes may have occurred in the road network, we believe that these changes had minimal effects on the results. Lastly, network analysis technique is quite computer intensive and requires relatively high-end computers when dealing with a large number of nodes and geographical units. However, with the increased availability of more powerful computers at more affordable prices, this will not be a problem in the future.

The above limitations notwithstanding, our results show improved geographic access to stroke and cardiac centers over the study period although gaps in geographic access to stroke care particularly in rural neighborhoods still exist. Hence, there is still need for strategies to improve geographic access to emergency care for cardiac and stroke patients. This will play a vital role in achieving the Healthy People 2020 [438] goals of reducing disparities in access. Addressing disparities in timely access to emergency care will require a multifaceted approach involving increased use of air ambulance, telemedicine and education of the public on symptoms of stroke and MI. Reducing the time from symptom occurrence to treatment will be achieved through prompt recognition of symptoms and seeking early treatment. Early recognition of symptoms reduces part of the pre-hospital delay and thus ensures arrival of the patients to care centers in time to receive therapy. Instead of calling the primary physicians first, the public should be educated to call emergency medical services (EMS) immediately stroke or heart attack symptoms are observed. This action also reduces pre-hospital delays and ensures timely arrival at the hospital. In one study potential stroke patients who first called their primary physician arrived at the emergency department within a mean time of 379 minutes, compared with a mean time of 155 minutes for patients who called EMS right away [460]. In the same study, only 50% of heart attack patients were found to use EMS in a pre-hospital setting. Due to financial implications involved in using EMS, patients and caregivers tend to self transport instead of using an ambulance. Moreover, use of EMS has been shown to reduce pre-hospital delay and is recognized to be the most optimum means of providing emergency care [462]. Therefore, the public should be educated on the time-sensitive nature of stroke and heart attack treatments and the EMS’s ability to deliver the patients to care centers faster than self transport. This will in turn guide patients and care givers in making decisions deemed best for improving health outcomes for stroke and cardiac patients.

Increased use of air ambulances can be critical in remote, rural or areas with difficult terrain that make access by road ambulances challenging. This observation was also made by Pedigo and Odoi [22]. This implies that neighborhoods in middle Tennessee would benefit from increased use of air ambulances. Moreover, some studies have shown that air transport can be cost effective [131, 132]. In addition, increased use of telemedicine is a feasible solution to bridge the gap in delivery of cardiac and stroke care in geographic settings where timely access to cardiac and stroke centers is otherwise not possible. Telemedicine is “the use of medical information exchanged from one site to another via electronic communications to improve patients’ health status” [463]. Technically, it encompasses all aspects of medicine practiced at a distance, including use of telephone, fax, and electronic mail technology, as well as the use of interactive full motion video and audio, that brings together patients and providers separated by distance. Therefore, since the majority of the population in the study area had access to an emergency department within 30 minutes, incorporation of telemedicine in some of the hospitals would improve access to cardiac and stroke care without necessarily transporting patients to cardiac and stroke centers. Moreover, use of telemedicine facilities during ambulance transport would shorten the time that would otherwise be spent in diagnosis at the hospital since use of telemedicine between EMS and neurologists/cardiologists would enhance diagnosis during transport and hence minimize time spent in diagnosis on arrival at the hospital. Telemedicine also has the ability to link rural hospitals with regional acute stroke centers of excellence, thus enhancing standardized, streamlined care throughout a system’s care facilities [464].

2.6 Conclusions

These data demonstrate temporal improvement in geographic access to stroke and cardiac centers across the study period. The research further shows that currently, a large percentage of the population in Middle Tennessee has access to cardiac and stroke care, however, gaps still exist in accessing stroke care, especially in rural areas. Timely access to care is essential for delivery of definitive treatments for stroke and MI in order to reduce complications and death. The study has also demonstrated the usefulness of network analyses in investigating temporal changes in geographic access to healthcare as well as in identifying underserved populations. The findings are useful for guiding health planning programs, policy decisions and health resource allocation and are instrumental in tailoring interventions targeted at reducing/eliminating health disparities at the neighborhood level with the view to improving health of the entire population.

CHAPTER 3

3.0 Neighborhood Geographic Disparities and Temporal trends in Heart attack and Stroke Mortality

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This chapter is a manuscript that has been submitted for peer review to the International Journal for Equity in Health. Peer review comments have been received and are currently being addressed. My contributions to this paper include data preparation, analysis, gathering and reviewing of literature, formulation of discussion topics, and drafting the manuscript.

3.1 Abstract

Despite significant declines in coronary heart disease and stroke mortality risks over the past years, coronary heart disease, particularly myocardial infarction (MI), and stroke continue to be the first and third leading causes of death in the U.S. Some population groups continue to have a disproportionate burden of MI and stroke mortality risks. Therefore, the objective of this study was to investigate neighborhood geographic disparities and temporal trends in MI and stroke mortality risks in Middle Tennessee and identify predictors of observed disparities so as to guide neighborhood health planning programs.

Descriptive, temporal, and spatial analyses were performed on MI and stroke mortality data obtained from the Tennessee Department of Health for the period 1999-2007. Global Moran’s I and Kulldorff’s spatial scan statistic were computed at both the county and census tract/neighborhood levels to investigate and identify geographic hot spots of high MI and stroke mortality risks. Negative binomial model was used to investigate predictors of the identified geographic patterns.

Decreasing temporal trends were observed in mortality risks for both MI and stroke. Significant ($p<0.05$) differences in mortality risks for sex, race, age group and educational level categories were observed. Seven and 13 significant ($p<0.05$) high risk clusters of MI mortality were identified at the county and neighborhood levels, respectively. For stroke, 2 significant ($p<0.05$) high mortality risk clusters were identified at the county level whereas 6 were identified at the neighborhood level. Neighborhoods

with higher proportions of the older population and those with higher proportions of individuals with low education were associated with high MI and stroke mortality risks.

Although a decreasing temporal trend was observed, substantial disparities in MI and stroke mortality risk still exist. Identification of high risk neighborhoods is essential for targeting resources and will aid the development of more needs-based prevention programs. This is crucial in addressing one of the goals of the Healthy People 2020 of reducing disparities and improving health of the entire population.

3.2 Background

Stroke and coronary heart disease (CHD), particularly myocardial infarction (MI), are the leading causes of death and disability among adults in the United States [21]. Despite significant declines in CHD and stroke mortality risks over the past decades, these conditions continue to be the first and third leading causes of death in the U.S [21] and Tennessee [465]. Stroke, which is the leading cause of adult disability in the United States, accounted for approximately 1 out of every 18 deaths (136,000 deaths) in 2007 [21]. Myocardial infarction, also known as heart attack, is responsible for approximately 17 years of life lost in the US and also accounted for about 133,000 deaths in 2007 [21].

Over the past decades, a decline in coronary heart disease and stroke mortality risks have been observed in the United States [12-15]. For example, from 1997 to 2007, the annual mortality risk due to CHD declined by 26.3% while that of stroke decreased by 34.3% [21]. These decreases are attributed to reduction in major population risk factors as well as improved medical care [16-19]. Ford *et al* reported that approximately 47% of the decrease in CHD deaths was attributable to increased use of evidence-based medical therapies and 44% to changes in risk factors in the population due to lifestyle and environmental changes [19]. However, evidence shows that not all Americans have benefited from the improved stroke and heart attack outcomes as some segments of the population have a disproportionate burden of these conditions [20]. Considerable variability has been observed in the degree to which heart disease and stroke contribute to the overall burden of death across geographic regions, races, genders, age groups, and socioeconomic status [14]. For instance, a consistent pattern of marked geographic variation in stroke mortality within the United States has been observed, with very high risks reported in the southeast Atlantic coastal plain and very low risks in the mountain census division [466]. The Southeastern United States, also known as the “stroke belt” has about 43% greater age-adjusted mortality risk than the other regions of the United States [467]. Additionally, strong clusters of high CHD mortality risks especially among women have been observed in Mississippi Delta, Appalachia, the Ohio River Valley, the Piedmont areas of Georgia, South Carolina, and North Carolina [183]. Marked race variations in stroke and MI mortality risks have also been documented in the US with blacks having higher mortality from both diseases compared with whites [14] and non-Hispanic populations also having relatively high CHD mortality than whites [183]. Additionally, great disparities in stroke and heart disease mortality have been observed across socioeconomic status, as measured by education, income, or occupation with higher risks reported among the poor and under-educated compared to the wealthy and well-educated individuals [183].

Generally, the underlying causes of disparities in stroke and MI mortality are not fully understood. However, variation in the prevalence of contributing risk factors has been implicated as one of the causes for these disparities. It is also known that there is little data in support of this ‘risk factor’ theory [224]. Disparities in awareness as well as access to information and health services are also responsible for the variations in stroke and MI mortality risks [20]. Since many risk factors are involved in determining the observed disparities, it is likely that some risk factors may play more important roles in disease burdens in some communities than in others. Therefore, investigation of the geographic patterns in mortality risks, and identification of specific risk factors responsible for observed patterns would aid in better guiding needs-based health planning and service provision.

Traditionally, spatial patterns of disease risks have been displayed at larger geographical units such as state and county levels. However, it has been shown that analyses performed at large geographic levels may mask the underlying patterns of disease thus lead to distortion of the underlying spatial patterns [225]. Therefore, use of finer geographic units such as census tracts may be necessary for more efficient visualization of the spatial patterns and to better guide disease control efforts and resource allocation. Thus the objective of this study was to investigate neighborhood geographic disparities and temporal trends in heart attack and stroke mortality risks in middle Tennessee and identify determinants/predictors of observed disparities so as to guide neighborhood health planning programs. Identification of disproportionately affected neighborhoods will help health planners better target resources and can aid the development of programs better tailored to specific community needs. This will play a key role towards addressing one of the goals of the Healthy People 2020 [438] of reducing disparities and improving health of the entire population.

3.3 Methods

3.3.1 Study Area

The study was performed in 30 counties of middle Tennessee (Figure 3.1). Most of these counties lie in the “stroke belt” of Tennessee, a region with high stroke and MI prevalence. The area consists of 250 census tracts and spans about 12,045 square miles with a total population of approximately 1.2 million people of which about 88% are white, about 9% are black and 3% is comprised of other races. Approximately 49% of the population is male. About 48% of the population is aged between 0 and 34 years. Sixteen percent, 14%, 9%, and 13% of the population are aged 35-44, 45-54, 55-64, and ≥65 years, respectively. The region has a mixture of urban and rural areas with Hamilton being the most urbanized (and most populated) and Pickett least urbanized (and least populated) counties (Figure 3.1).

3.3.2 Data Sources

3.3.2.1 Mortality and Population Data

Stroke and MI mortality datasets for the period January 1999 through December 2007 were obtained from the Tennessee Department of Health. Deaths from stroke and MI were defined on the basis of underlying cause of death. The International Classification of Diseases, Tenth Revision (ICD-10) codes used were I21-I22 for MI and

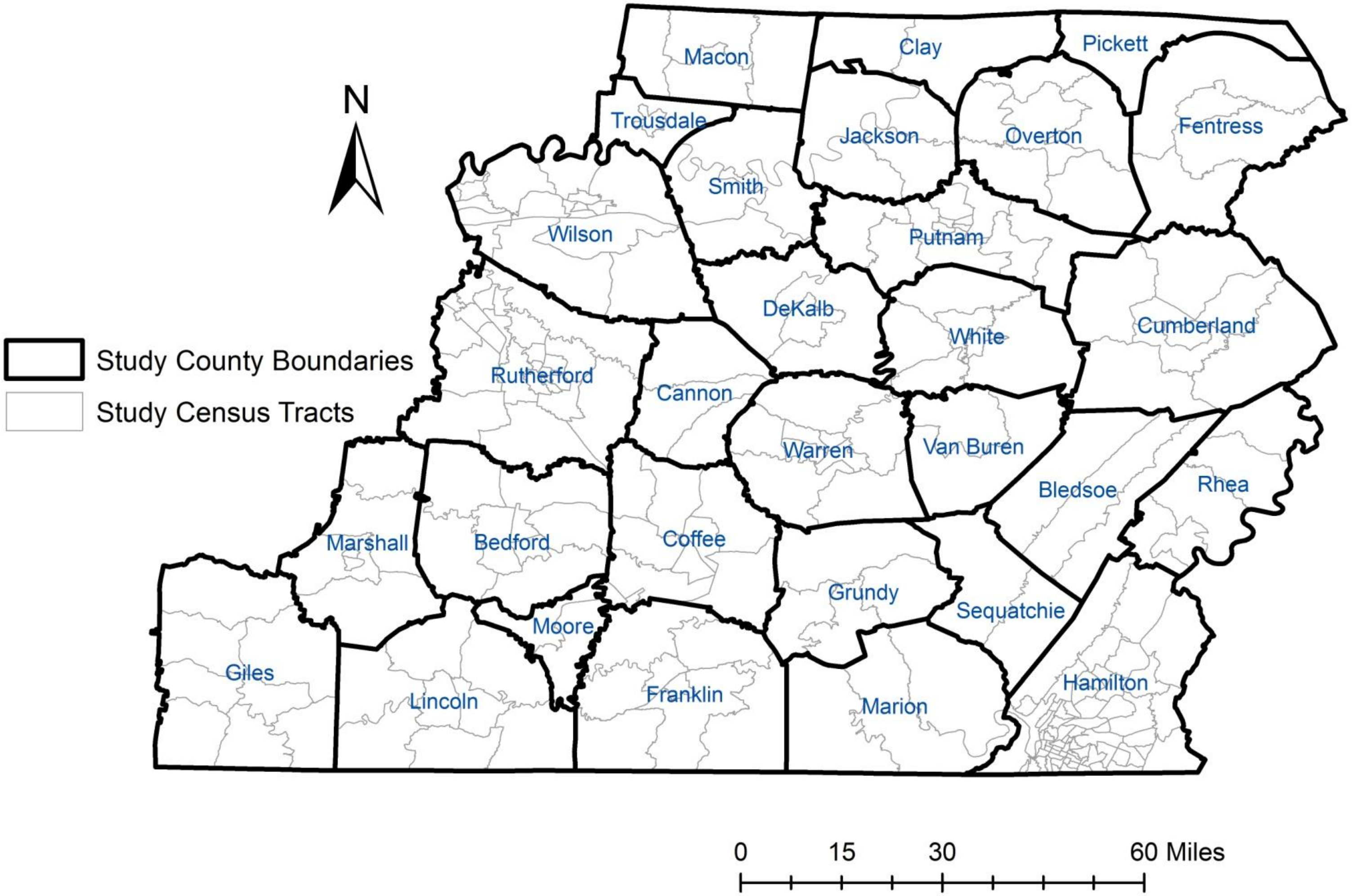

Figure 3.1: Map of Middle Tennessee Showing Study Counties and Census Tracts (Neighborhoods)

I63-I64 for stroke. For each record, we obtained data on address of residence, age, race, sex, level of education, year of birth, and year of death. These variables were used for calculation of attribute-specific mortality risks. Cases were geocoded based on their residential addresses.

The Tennessee 2000 census population, used as the standard population for direct standardization of the mortality risks, was obtained from the US Census Bureau [445]. The 2000 US census population estimates were also obtained from the US Census Bureau and provided denominators used in the computation of the MI and stroke mortality risks.

3.3.2.2 Cartographic Boundary Files

The cartographic boundary files for counties and census tracts were downloaded from the US Census Bureau [468] and used for displaying spatial patterns of mortality risks. Counties are administrative and statistical subdivisions of a state whereas census tracts are small, county statistical subdivisions that contain between 2,500 and 8,000 people. In this study we use census tracts as proxies for neighborhoods because past studies have shown that they are good proxies of natural neighborhood boundaries and are also homogenous with respect to population characteristics [226].

3.3.3 Data Preparation and Statistical Analysis

All the variables in the mortality dataset were assessed for completeness and accuracy. Impossible entries were identified and corrected, where possible, or otherwise omitted from further analyses.

3.3.3.1 Mortality Risk Calculation and Standardization

Attribute-specific mortality risks were computed for the following attributes: sex, race, education level and age-groups (0-34, 35-44, 45-54, 55-64, 65-74, 75-84, and ≥85 years). Age- and sex-standardized mortality risks were computed by the direct method using the 2000 Tennessee population as the standard population and expressed as the number of cases per 100,000 persons. Average annual mortality risks and their 95% confidence intervals were also computed. All statistical analyses were performed in Stata version 11.0 (Stata Corp., College Station, TX).

3.3.3.2 Descriptive Statistics

The Shapiro-Wilk test was used to assess the normality of continuous variables. Since all the continuous variables were not normally distributed, median, minimum and maximum values were used to summarize the data. Comparisons of the mortality risks across age groups, sex, race, and education levels were performed using “prtesti” command in Stata for comparing two proportions. Simes method was used to adjust for multiple comparisons. Seasonal mortality risks were computed to assess seasonal differences in MI and stroke mortality risks. Months were aggregated into the traditional seasons: spring (March, April, and May); summer (June, July, and August); fall (September, October, and November); and winter (December, January, and February).

3.3.4 Geographic Analysis and Cluster Detection

Spatial empirical Bayesian (SEB) smoothing [225, 469-471], using inverse distance spatial weights was used to adjust mortality risks for spatial autocorrelation and variance heterogeneity resulting from inhomogeneous population distribution at the census tract and county levels. The spatial empirical Bayesian computed risks enable better visualization of the spatial patterns compared to the unsmoothed risks when working with data from small areas [472]. Global Moran's I was used to assess for evidence of significant spatial autocorrelation of the raw (unsmoothed) mortality risks. Statistical significance of global Moran's I was tested using 9,999 permutations using GeoDa Version 0.9.5i [473].

Spatial clusters of high MI and stroke mortality risks were detected and identified using Kulldorff's spatial scan statistic [474] implemented in SaTScan [475]. Poisson probability models were used to identify geographical areas (counties and census tracts) with statistically significant high mortality risks. The maximum spatial cluster size was set at 5% for the total study population. All cartographic displays were done using Arc View GIS 9.3 [442].

3.3.5 Investigation of Predictors of Spatial Disparities of MI and Stroke Mortality

Predictors of the geographic distribution of MI and stroke mortality risks were investigated at the census tract spatial scale. Sociodemographic variables considered for potential association with MI and stroke mortality risks were: sex (proportion of male and female), race (proportion of white, black, and other), age group (proportion of individuals in 0-34, 35-44, 45-54, 55-64, ≥65 years categories), marital status (proportion of single, married, divorced, and widowed), education (proportion of the population with utmost elementary education, high school, and college education), rural (proportion of population living in rural areas), poverty (proportion of population living below poverty level), median household income and median housing value of neighborhoods. First, a Poisson model was fit using stepwise backwards elimination procedure to identify the best main effects model. All possible two-way interaction terms of variables included in the main effects model were then assessed for significance and the significant ones were retained in the final model. The final Poisson model was then assessed for overdispersion using the Pearson and deviance dispersion parameters. Significant overdispersion for MI (Pearson $X^2 = 6.25$; $p < 0.0001$ and Deviance $X^2 = 6.29$; $p < 0.0001$) and stroke (Pearson $X^2 = 2.93$; $p < 0.0001$ and Deviance $X^2 = 2.96$; $p < 0.0001$) models were identified and therefore negative binomial models were fit to the data using the variables retained in the final Poisson models. Goodness of fit of the negative binomial models were assessed using Pearson and deviance goodness-of-fit statistics. Overdispersion of the final negative binomial model was assessed using the likelihood ratio test ($\alpha=0$, where α is the dispersion parameter) which compares the Poisson model to the negative binomial model. Residual diagnostics were performed using analysis of standardized deviance and Anscombe residuals. All modeling was done using Stata version 11.0 (Stata Corp., College Station, TX).

3.4 Results

3.4.1 Descriptive Analyses of Cases

3.4.1.1 Age Distribution

A total of 14,741 deaths, 9,822 (66.6%) MI and 4,919 (33.4%) ischemic stroke were recorded in the study area from January 1999 to December 2007. Myocardial infarction mortality cases ranged in age from 8 to 113 years, with 77% of the deaths occurring in individuals 65 years and older. The median age for women was significantly ($p<0.0001$) higher (82 years) than that for men (72 years). Stroke mortality cases ranged in age from 18 to 107 years with 91% of the deaths occurring in individuals 65 years and older. Similar to MI, the median age of death from stroke for women was significantly ($p<0.0001$) higher (84 years) than that for men (79 years).

3.4.1.2 Attribute Specific Mortality Risks

The age-adjusted mortality risk for MI was significantly ($p<0.0001$) higher in men (45.6 per 100,000 persons) than women (42.2 per 100,000 persons) (Table 3.1). In contrast, the age-adjusted mortality risk for stroke was significantly ($p<0.0001$) higher in women (28.4 per 100,000 persons) than men (15.5 per 100,000 persons) (Table 3.2). The highest sex-adjusted age-specific mortality risk for MI (25.9 per 100,000 persons) was observed in the 75-84 year age group while the lowest (0.4 per 100,000 persons) was observed in the 0-34 year old age group (Table 3.1). Similar patterns were observed for stroke with the lowest sex-adjusted age-specific mortality (0.2 per 100,000 persons) being observed in the 0-34 year age group and highest (18.5 per 100,000 persons) among the 85+ year olds (Table 3.2).

Not surprisingly, the age- and sex-adjusted mortality risks for blacks for both MI (94.7 per 100,000 persons) and stroke (52.5 per 100,000 persons) were significantly ($p<0.0001$) higher than those for whites (68.9 per 100,000 persons for MI and 39.6 per 100,000 persons for stroke) (Tables 3.1 and 3.2). The age- and sex-adjusted education-specific mortality risk for MI was highest among those with utmost elementary school

Table 3.1: Myocardial Infarction Attribute-specific Mortality Risks for Middle Tennessee, 1999-2007

Variable	Percentage of Cases	Mortality Risk (Per 100,000 persons)	95% Confidence limits of mortality risk
Sex			
Male	52.7	45.6	44.4 - 46.8
Female	47.3	42.2	40.9 - 43.2
Age-group (years)			
0-34	0.4	0.4	0.3 - 0.5
35-44	2.2	2.0	1.7 - 2.3
45-54	7.0	6.3	5.9 - 6.8
55-64	13.9	12.1	11.5 - 12.7
65-74	19.7	16.9	16.1 - 17.6
75-84	29.3	25.9	25.0 - 26.8
≥85	27.5	23.9	23.1 - 24.8
Race			
Black	7.3	94.7	87.9 - 101.5
White	83.7	68.9	67.4 - 70.5
All other races	9.0	648.8	615.2 – 682.4
Education			
Utmost Elementary	35.9	182.1	175.0 - 189.2
High school	45.1	115.3	111.9 - 118.6
College and above	15.6	62.5	59.3 - 65.7
Missing	3.4		
Season			
Winter	27.9	25.4	24.5 - 26.4
Spring	25.1	22.9	21.9 - 23.8
Summer	23.1	21.0	20.2 - 21.9
Fall	23.9	21.8	20.9 - 22.7

Table 3.2: Stroke Attribute-specific Mortality Risks for Middle Tennessee, 1999-2007

Variable	Percentage of Cases	Mortality Risk (Per 100,000 persons)	95% Confidence limits of mortality risk
Sex			
Male	36.0	15.5	14.8 - 16.2
Female	64.0	28.4	27.5 - 29.4
Age-group (years)			
0-34	0.4	0.2	0.09 - 0.23
35-44	0.8	0.4	0.3 - 0.5
45-54	1.8	0.8	0.7 - 1.0
55-64	6.1	2.6	2.3 - 2.9
65-74	13.6	5.9	5.4 - 6.3
75-84	34.9	15.6	14.8 - 16.3
≥85	42.4	18.5	17.8 - 19.3
Race			
Black	8.2	52.5	47.4 - 57.5
White	82.6	39.6	38.4 - 40.8
All other races	9.2	383.1	356.7 - 409.5
Education			
Utmost Elementary	38.0	84.8	80.5 - 89.1
High school	41.5	52.4	50.2 - 54.7
College and above	16.5	37.3	34.7 - 39.8
Missing	4.0		
Season			
Winter	27.6	12.6	11.9 - 13.3
Spring	25.7	11.7	11.1 - 12.4
Summer	23.0	10.5	9.9 - 11.1
Fall	23.7	10.8	10.2 - 11.4

education (182.1 per 100,000 persons) and lowest among those with college education and above (62.5 per 100,000 persons) (Table 3.1). Similar trends were observed for stroke (Table 3.2).

3.4.2 Temporal Patterns

Generally, there was a gradual decline in the annual mortality risk for MI over the 9 year study period (Figure 3.2). The highest mortality risk was observed in 1999 at 107.5 per 100,000 persons (95% CI: 101.7-113.6) and the lowest was in 2007 at 78.2 per 100,000 persons (95% CI: 73.3-83.4). Although the pattern of change in the stroke mortality risk over the 9 year period was not very consistent, there was a general decreasing temporal trend (Figure 3.2). The highest mortality risk being recorded in 2000 at 51.7 per 100,000 persons (95% C1: 47.7-55.9) and the lowest in 2005 at 40.4 per 100,000 persons (95% CI: 36.9-44.2). The highest mortality risk for MI was observed in winter (25.4 per 100,000 persons) and the lowest in summer (21.0 per 100,000 persons) (Table 3.1). Similarly, the highest mortality risk for stroke was registered during winter (12.6 per 100,000 persons) and the lowest during summer (10.5 per 100,000 persons) (Table 3.2). For both conditions, the differences between winter and summer risks were statistically significant ($p<0.05$).

3.4.3 Spatial Patterns

Spatial Empirical Bayes smoothed risks for MI ranged from 53.3 to 197.6 per 100,000 persons (for counties) and 10.3 to 300.3 per 100,000 persons (for census tracts) (Figure 3.3a-b). At the county level, the highest risks of MI were observed in the northeastern, southwestern and some counties in the central region (Figure 3.3a). In

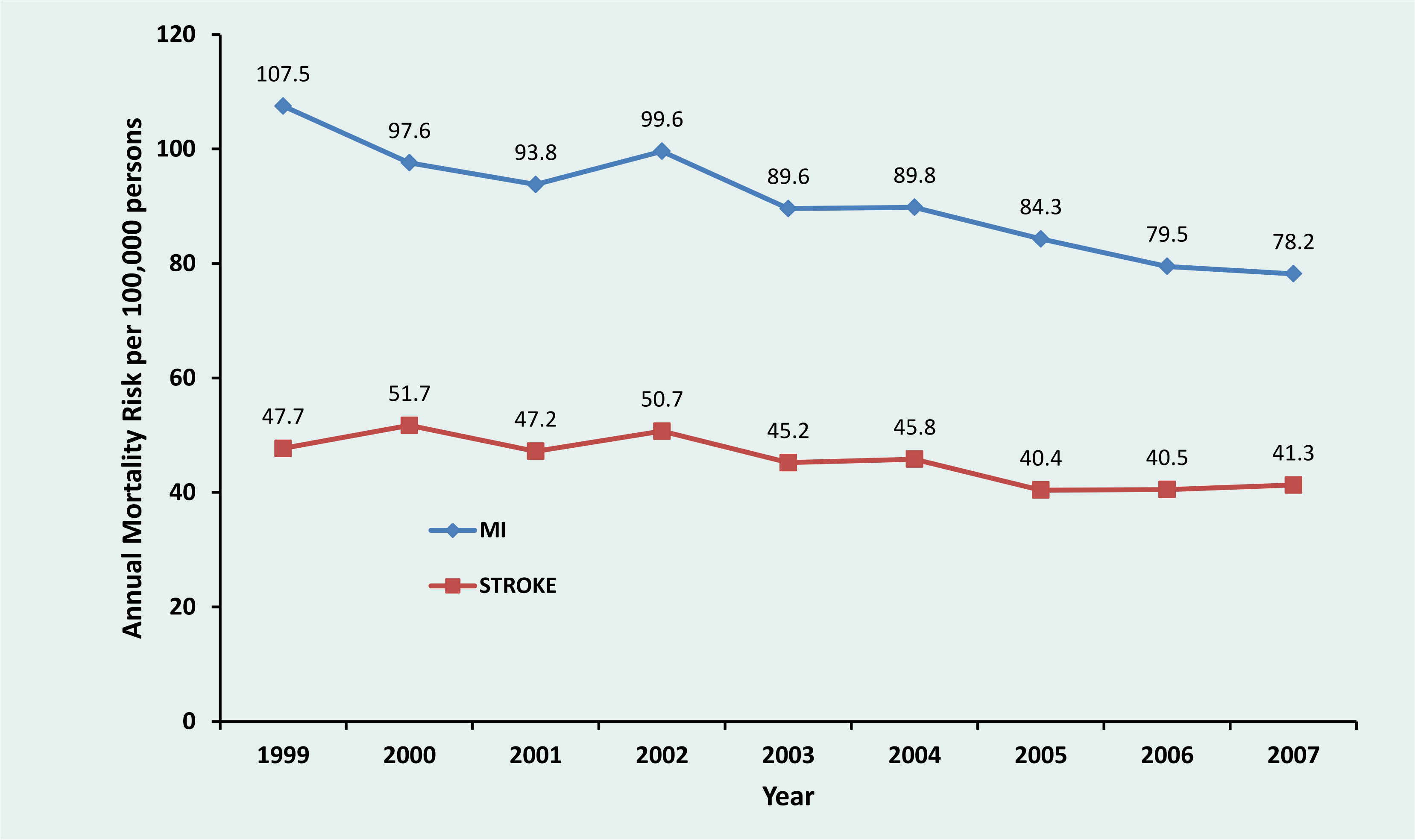

Figure 3.2: Annual Mortality Risk for MI and Stroke in Middle Tennessee, 1999-2007

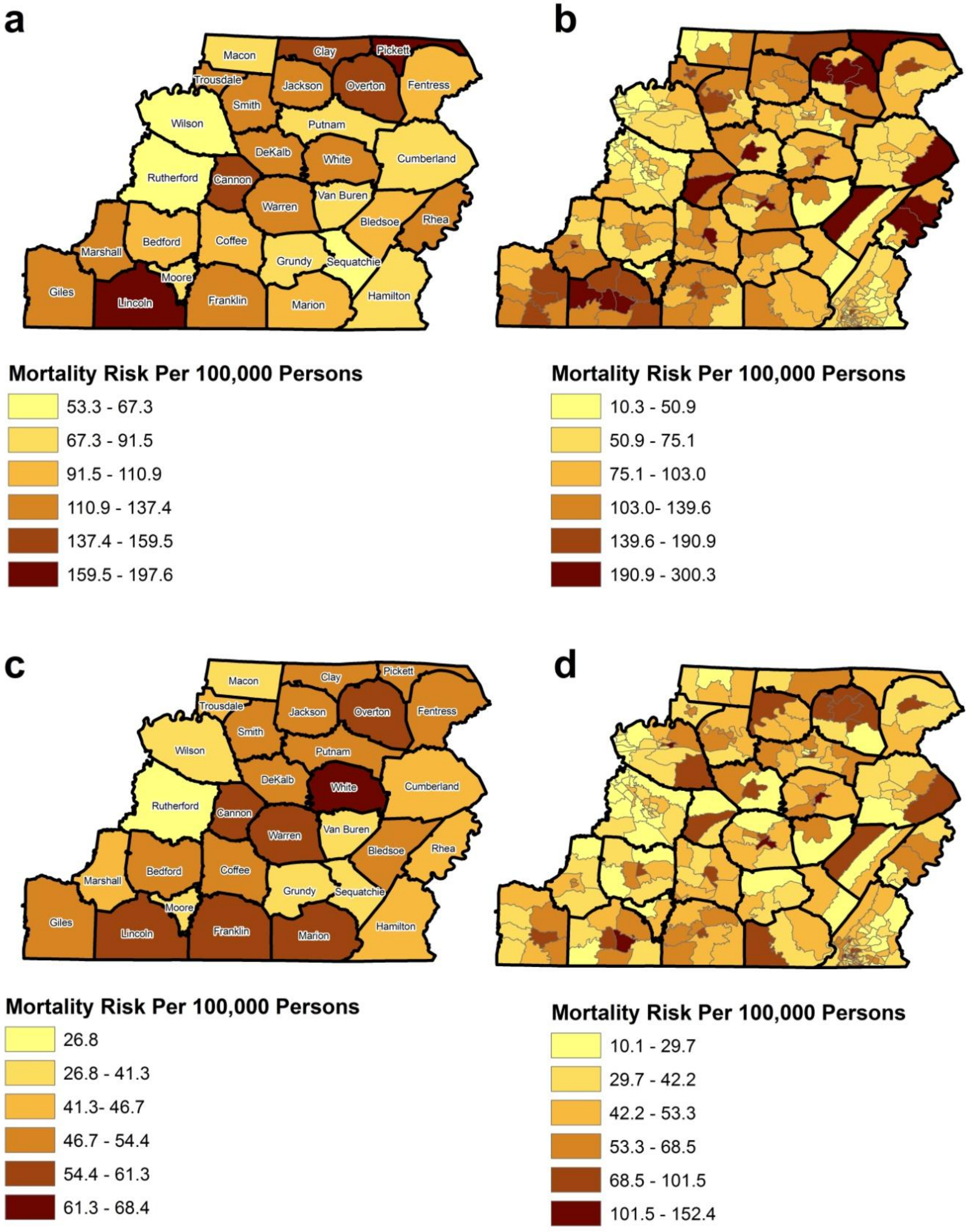

Figure 3.3: The Spatial Empirical Bayesian Smoothed Mortality Risks of MI at (a) County and (b) Census Tract/Neighborhood Levels; and of Stroke at (c) County and (d) Census Tract/Neighborhood Levels in Middle Tennessee, 1999-2007

addition to the above areas, high mortality risks of MI were also evident in the eastern part of the study area at the census tract/neighborhood level. Interestingly, high risk neighborhoods were observed in some seemingly low risk counties. For example, although Bledsoe, Cumberland, and Rhea counties did not have high MI mortality risks, they had some neighborhoods with the highest MI mortality risks in the study area (Figures 3.3a and 3.3b).

For stroke, the SEB smoothed risks ranged from 26.8 to 68.4 (per 100,000 persons) and 10.1 to 152.4 (per 100,000 persons) for counties and neighborhoods, respectively. Counties with the highest stroke mortality risks were observed mainly in the south, central and one in the northeast (Figure 3.3c). Similar to MI, seemingly low risk counties contained some of the very high risk neighborhoods. An example is seen in Wilson and Cumberland counties (Figure 3.3c and 3.3d).

No evidence of spatial clustering was detected by the global Moran's I analysis at the county level for both MI and stroke. Nevertheless, significant global clustering was detected at the neighborhood level for both MI (Moran's I = 0.181; p = 0.0001) and stroke (Moran's I = 0.090; p = 0.014). However, for both conditions, significant local clusters ($p < 0.05$) of high risk were identified at both the county and the neighborhood levels using Kulldorff's spatial scan statistic (Figure 3.4). For MI, a significant ($p<0.0001$) high-risk primary cluster comprising of one county (Lincoln) was identified (Figure 3.4a). This cluster had a relative risk of 1.9, implying that the mortality risk of MI was 1.9 times higher in this county than other counties in the study area (Table 3.3 and Figure 3.4a). Six significant ($p<0.05$) high risk secondary clusters were also identified at the county

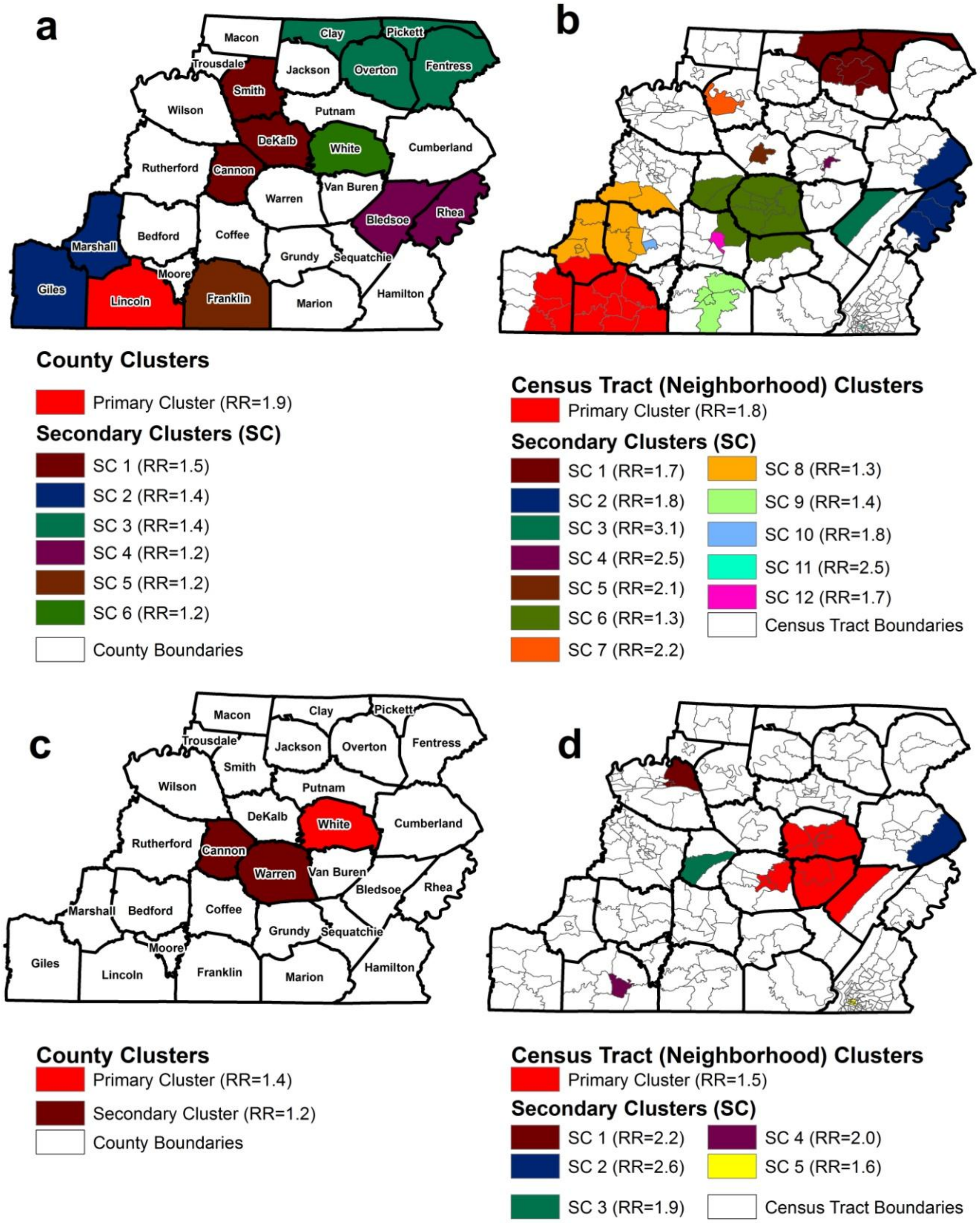

Figure 3.4: Spatial Clustering of Mortality Risks of MI at (a) County and (b) Census Tract/Neighborhood Levels; and Stroke at (c) County and (d) Census Tract/Neighborhood Levels in Middle Tennessee, 1999-2007

Table 3.3: High Risk Clusters of MI Identified at Both the County and Census Tract (Neighborhood) Levels in Middle Tennessee, 1999-2007

Geographic Unit	Clusters	No. of locations in cluster	Mortality Risk	Relative Risk	p-value
	Primary Cluster	1	160.3	1.9	<0.0001
	Secondary Clusters				
County Level	1	3	126.9	1.5	<0.0001
	2	2	121.9	1.4	<0.0001
	3	4	120.8	1.4	<0.0001
	4	2	105.9	1.2	0.0027
	5	1	104.2	1.2	0.010
	6	1	106.6	1.2	0.037
	Primary Cluster	13	151.8	1.8	<0.0001
	Secondary Clusters				
Census tract Level	1	6	147.2	1.7	<0.0001
	2	4	153.4	1.8	<0.0001
	3	1	273.0	3.1	<0.0001
	4	1	214.4	2.5	<0.0001
	5	1	184.1	2.1	<0.0001
	6	13	114.1	1.3	<0.0001
	7	1	189.4	2.2	<0.0001
	8	10	111.6	1.3	0.0001
	9	4	118.6	1.4	0.0025
	10	1	152.9	1.8	0.0066
	11	1	220.2	2.5	0.010
	12	1	147.4	1.7	0.012

level (Figure 3.4a, Table 3.3). At the neighborhood level, a significant (p<0.0001) high-risk primary cluster was identified in Giles, Lincoln, and Marshall Counties (Figure 3.4b and Table 3.3). Several significant (p<0.05) high risk secondary clusters were also identified at the neighborhood level (Figure 3.4b and Table 3.3). The relative risks for clusters at the county level ranged from 1.2 to 1.9 while those at the neighborhood level ranged from 1.3 to 3.1 (Table 3.3).

A significant (p=0.007) high risk primary cluster for stroke was found in White county (Figure 3.4c and Table 3.4). The risk of stroke mortality in this county was 1.4 times higher than that in other counties in the study area. A high risk secondary cluster consisting of Cannon and Warren counties was also identified (Figure 3.4c and Table 3.4). Additionally, a significant (p=0.0001) high risk primary cluster located in White, Warren, Van Buren, and Bledsoe counties was identified at the neighborhood level (Figure 3.4d, Table 3.4). Five other high risk secondary clusters were also identified (Figure 3.4d and Table 3.4). It is worth noting that analysis at the neighborhood level revealed that stroke clusters identified in White, Cannon and Warren counties only involved one neighborhood in each of the counties and does not involve the whole of the counties as suggested by the results of the county analysis. Similar situations were evident for MI clusters at the county and neighborhood levels.

Table 3.4: High Risk Clusters of Stroke Identified at Both the County and Census Tract (Neighborhood) Levels in Middle Tennessee, 1999-2007

Geographic Unit	Clusters	No. of locations in cluster	Mortality Risk	Relative Risk	p-value
County Level	Primary Cluster	1	58.4	1.4	0.0070
	Secondary Cluster	2	52.2	1.2	0.038
Census tract Level	Primary Cluster	11	62.9	1.5	<0.0001
	Secondary Clusters				
	1	2	95.2	2.2	<0.0001
	2	1	110.2	2.6	<0.0001
	3	1	82.1	1.9	0.0075
	4	1	83.2	2.0	0.024
	5	6	70.0	1.6	0.045

3.4.4 Regression Modeling

The likelihood ratio test of α=0 was significant for both MI (p<0.001) and stroke (p<0.001) models implying that the negative binomial model seems to fit the data well. The Pearson and deviance goodness of fit statistics were not significant for both MI (Pearson p = 0.63 and Deviance p = 0.17) and stroke (Pearson p = 0.48 and Deviance p = 0.31) models thus confirming that the negative binomial model fits the data well. No significant outliers and influential observations were observed from residual analyses.

As expected, high MI and stroke mortality risks tended to occur in neighborhoods with high proportions of the population 65 years and older (Table 3.5). Neighborhoods with high proportions of individuals with utmost elementary education had higher mortality risks of MI and stroke (Table 3.5). For MI, neighborhoods that had high proportions of individuals living in rural areas had high mortality risks while neighborhoods with high median housing value tended to have lower mortality risks (Table 3.5). Additionally, neighborhoods in which high proportions of the population were married tended to have low stroke mortality risks (Table 3.5). More information on the negative binomial models for MI and stroke can be found in appendix 3 and appendix 4, respectively.

3.5 Discussion

Results of this study demonstrate spatial disparities of MI and stroke mortality risks among neighborhoods and population subgroups. For both conditions, women had

Table 3.5: Negative Binomial Model Results Investigating Predictors of MI and Stroke Mortality Risks at the Census Tract (Neighborhood) Level in Middle Tennessee, 1999-2007

	Variable	Parameter Estimate	Standard error	p-value	95% Confidence Interval
MI	Population Aged ≥65years	5.446	0.622	<0.0001	4.227 - 6.666
	Utmost Elementary Education	2.605	0.818	0.001	1.003 - 4.207
	Living in Rural areas	0.493	0.129	<0.0001	0.239 - 0.746
	Median housing value	-0.435	0.119	<0.0001	-0.669 - -0.201
Stroke	Population Aged ≥65years	6.512	0.581	<0.0001	5.372 - 7.650
	Utmost Elementary Education	1.495	0.389	<0.0001	0.731 - 2.258
	Population Married	-0.640	0.257	0.013	-1.144 - -0.137

a higher median age of death than men because women tend to live longer than men [392]. Previous studies have shown that over 81% of all CHD [21] and approximately 89% of all stroke [476] deaths occur in individuals that are 65 years and older. Our study confirms these findings with 77% and 91% of MI and stroke deaths, respectively, occurring in this age group. Age tends to weaken the heart's function as a result of thickened heart walls as well as thickened and stiffened artery walls. These tend to increase hypertension which eventually compounds the problem, thus predisposing to heart attack and stroke [25].

Similar to findings from other reports [12], men had a higher (45.6 per 100,000 persons) age-adjusted mortality risk for MI compared to women (42.2 per 100,000 persons). Evidence shows that men are more likely to suffer a heart attack at a younger age than women. After 40 years, men have a 49% risk of developing CHD compared to women (32%) [477]. It is also known that women are protected from heart disease earlier in life by their sex hormones. However, after menopause the risk of heart disease in women starts to rise and by 75 years, the risk is equal to or greater than that of men [25]. In contrast to MI, women had a higher (28.4 per 100,000 persons) age-adjusted mortality risk of stroke than men (15.5 per 100,000 persons). The differences in stroke and MI mortality risks for both men and women may reflect differential exposure to stroke [392] and MI [478] risk factors.

Our results show lowest mortality risk for both stroke and MI in populations that had college education. This is consistent with other studies that have reported that indicators of socioeconomic status, such as, level of education are associated with MI

[352, 353] and stroke [479, 480] mortality in populations. Kelly and Weitzen found that people with less than a high school education were more likely to have a myocardial infarction as compared to college graduates [352]. In the same study, prevalence of MI was seen to decrease with increase in the life time level of education. Education influences mortality primarily through factors such as health behavior. The higher an individual's level of education, the more likely that individual is to exercise, drink moderately, receive preventive medical care, and less likely to smoke [481].

The temporal decreases in MI (27.3%) and stroke (13.4%) mortality risks between 1999 and 2007 were lower than those recorded nationally (35.3% for MI and 31.5% for stroke) in the same time period [482]. The temporal decrease in the mortality risk for both MI and stroke may be attributed to improved quality of preventive care and health services, changes in risk factors and increased awareness of MI symptoms [16-18, 483]. Prompt recognition of symptoms and seeking early treatment is essential for better health outcomes. It is also known that every 30 minutes that elapse before an MI patient receives treatment increase the mortality risk [21]. Findings of this study are in agreement with several other studies that have reported high mortality risks from MI [484-487] and stroke [486, 488-491] during winter and lower mortality risks during summer. The seasonal variations in mortality have been associated with ambient temperatures. It is hypothesized that exposure to cold temperatures in winter may induce physiological stresses such as, sympathetic activation, and hypercoagulability, which may increase the incidence of MI and stroke [492]. Consistent with findings from other studies [14, 183, 493], our results show that blacks had a higher mortality risk than whites for both MI and stroke.

Significant high-risk clustering was observed at both the county and neighborhood levels, however, high risk clusters were more refined at the neighborhood level compared to the county level. For instance, some seemingly low risk counties contained high risk neighborhoods and within some high risk counties only one or two neighborhoods had high risks (not the whole county). This implies that assessment of spatial patterns at larger geographic units tends to mask underlying spatial patterns that would otherwise be evident at a finer/smaller geographic unit. This result reaffirms that a smaller geographic unit such as the census tract/neighborhood is better for investigation of spatial patterns of disease distribution. Moreover, application of these strategies will enable targeting of limited resources to the highest risk groups thus aid the development of more needs-based prevention programs. The MI and stroke spatial patterns observed at the county level are similar to those that have been observed in other reports [494, 495]. The identified high risk neighborhoods form a baseline for future interventions and continued surveillance.

The regression modeling results suggest that neighborhoods with higher proportions of the older population and those with higher proportion of the population with low education attainment tended to have high MI and stroke mortality risks. The observed high MI and stroke mortality risks in neighborhoods with high proportions of individuals aged 65 years and older is not surprising. The association between education attainment and MI and stroke mortality risk is similar to findings from other studies [479, 480, 496]. In addition to the above mentioned sociodemographic factors, marital status was also a predictor of stroke mortality risk. The low risk of stroke mortality in populations with a high proportion of married individuals could be due to the fact that marriage provides social support/security resulting into less distress and healthier lifestyles [497-499]. It is worthwhile to note that neighborhoods with high median housing value, another indicator of socioeconomic status, tended to have lower MI mortality risks compared to those with low median housing value. This reiterates the importance of socioeconomic status as a risk factor for MI and stroke. As has been reported by other studies [187], neighborhoods in rural areas were associated with higher MI mortality risks. Lower socioeconomic status of rural populations and lack of access to quality care may be responsible for the higher mortality risks in these rural areas [500]. Lower standards of living and socioeconomic restrictions, in most rural areas, lead to higher prevalence of CHD risk factors, such as cigarette smoking, poor dietary habits, sedentary lifestyles, and obesity [501]. Many rural neighborhoods face barriers such as shortages of health professionals, lack of health insurance, transportation difficulties, and geographic distance, which impede accessing medical care, an important determinant of CHD case fatality rates [187] .

Results of this study highlight the need to reduce disparities in stroke and MI mortality risks among population subgroups and neighborhoods in Middle Tennessee. Identification and continued monitoring of high risk neighborhoods is an important component for stroke and MI prevention and treatment efforts. The findings will be useful for helping public health officials better target resources and control efforts to the highest risk areas. Health programs targeting high risk neighborhoods should focus on education on symptom recognition and the importance of seeking treatment promptly for better health outcomes. Since the treatments for both stroke [429] and MI [424, 425] are very time sensitive, emergency care treatment guidelines and protocols must also ensure that proper diagnosis and evaluation be performed in a timely manner for patients with stroke and MI symptoms.

3.6 Conclusion

Although the results of this study indicate a decreasing temporal trend in MI and stroke mortality risks, substantial disparities still exist in some populations and neighborhoods in the study area. These findings are useful for guiding health planners in targeting resources and in the development of more needs-based prevention programs aimed at reducing the burden of MI and stroke in high risk neighborhoods and improving population health.

CHAPTER 4

4.0 Summary, Conclusions and Recommendations

This chapter reviews the specific objectives of the study, summarizes the key findings and provides conclusions and recommendations for future research. The main goal of the thesis was to investigate neighborhood disparities associated with MI and stroke in Middle Tennessee. Specific study objectives were to: (i) investigate temporal changes in geographic disparities of timely access to emergency heart attack and stroke care in Middle Tennessee, (ii) investigate neighborhood geographic disparities and temporal trends in heart attack and stroke mortality risks in middle Tennessee and identify determinants/predictors of observed disparities.

Timely access to MI and stroke care improved over the study period (1999-2010). There were significant increases in the percentage of the population that had access to cardiac centers within 30 minutes from 29.4% in 1999 to 62.7% in 2010 while that for stroke changed from 5.4% in 2004 to 46.1% in 2010. The percentage of the population that did not have access to cardiac care within 90 minutes decreased from about 16% in 1999 to zero in 2010 while that for stroke decreased from approximately 52% in 2004 to 5% in 2010. Most (96%) of the population had access to an ED within 30 minutes in 2010. Increase in the number of accredited care centers over the study period was responsible for the observed increase in access to MI and stroke care. Whereas most neighborhoods had access to a cardiac center within 90 minutes by 2009, some neighborhoods in Clay, Fentress, Overton, Pickett, Cumberland, Jackson, Van Buren and White counties did not have access to a stroke center within the same travel time in 2010. Most of these neighborhoods were located in the rural areas where there were fewer care centers. The number of accredited cardiac centers in the study area increased from 2 in 1999 to 7 in 2010. Notably, there were no accredited stroke centers in the study area until 2007 and by 2010 there were only 2 stroke centers in the entire study area. Although the number of cardiac and stroke centers in the study area increased across the study period, most of the cardiac and stroke centers were located in the major cities, such as Chattanooga and Murfreesboro.

There was a general decreasing temporal trend of annual mortality risks for both MI and stroke over the study period. There was approximately a 27% decrease in MI mortality risk from 107.5 per 100,000 in 1999 to 78.2 in 2007 while that of stroke decreased by about 9.6% from 47.7 to 43.1 in the same time period. Higher mortality risks for both MI and stroke were recorded during the winter season. Significant differences in mortality risks for sex, race, age group and educational level categories were observed. The MI mortality risk was higher among men than women, whereas stroke mortality risk was higher among females. For both conditions, individuals ≥65 years, black, and those with utmost elementary education had the highest mortality risks.

Spatial empirical Bayesian (SEB) risks were computed because they enable better visualization of spatial patterns compared to unsmoothed (raw) risks as spatial autocorrelation and variance heterogeneity (resulting from inhomogeneous population distribution) are adjusted for. The SEB risks for MI ranged from 53.3 to 197.6 per 100,000 persons (for counties) and 10.3 to 300.3 per 100,000 persons (for neighborhoods) whereas those for stroke ranged from 26.8 to 68.4 (per 100,000 persons) and 10.1 to 152.4 (per 100,000 persons) for counties and neighborhoods, respectively. Clusters of high MI and stroke mortality risks were identified at both the county and neighborhood levels. However, the spatial patterns observed at the neighborhood level were more refined than those observed at the county level. Some seemingly low risk counties contained high risk neighborhoods and within some high risk counties only one or two neighborhoods had high risks. This implies that spatial patterns observed at lower geographic levels may be more informative for health planning and resource allocation since they tend to be more refined, thus enable targeting of limited resources to high risk neighborhoods. Furthermore, high MI and stroke mortality risks were observed in neighborhoods with high proportions of older individuals and those with high proportions of individuals with less than high school education. Additionally, neighborhoods with high proportions of married individuals had a low mortality risk for stroke. Intervention programs should target these high risk neighborhoods so as to reduce MI and stroke risk and improve the health of the population.

Since MI and stroke require time sensitive treatments in order to improve health outcomes and reduce mortality, identification of neighborhoods without timely access to care and those with high mortality risks of these conditions is important for needs-based health planning programs. This will play a major role in achieving one of the goals of the Healthy people 2020 of reducing health disparities and improving the health of the entire population. In addition, identification of high risk neighborhoods also ensures continued community surveillance of MI and stroke burden trends needed to evaluate the effects of new health programs and policies.

Currently, most public health intervention programs are based on disease distribution patterns observed at either the county level or other higher geographic levels. However, the results of chapter 3 have demonstrated that neighborhoods provide a more accurate picture of the geographic distribution of mortality risks, thus reduce the chances of missing disease clusters. To better target high risk populations and neighborhoods, it would be beneficial for health planners to use neighborhood/census tract spatial patterns as the baseline for health programs in order to better guide resource allocation and disease control efforts.

Disparities in geographic access to stroke care particularly in rural neighborhoods may be addressed by increased use of telemedicine and air ambulances. Telemedicine programs for stroke care have been shown to be safe, feasible, reliable, acceptable, and lead to improved health outcomes [502-504]. Therefore, encouraging increased use of telemedicine can help bridge the gap in delivery of cardiac and stroke care in geographic settings where timely access to cardiac and stroke centers is otherwise not possible. Increased use of air ambulances may be necessary in remote areas or those in which the terrain makes accessibility by road ambulances challenging. A study carried out in East Tennessee reported that all neighborhoods had access to MI and stroke care within 30 minutes when air ambulances were used [22]. Although there may be issues associated with availability and maintenance of aircrafts, air transport has been reported to be cost effective [131, 132]. This implies that emergency air ambulances can be used to improve geographic accessibility to MI and stroke centers in the study area.

Education has been shown to influence MI and stroke mortality risk primarily by influencing health behaviors such as smoking, high alcohol consumption and inactivity. Since level of education attained was a significant predictor of both MI and stroke mortality risks in the neighborhoods, education programs (especially targeting populations with low education attainment) on symptom recognition as well as the importance of seeking treatment promptly would be beneficial. As well, health programs targeting high risk neighborhoods should bolster efforts directed towards education on benefits of moderate alcohol consumption, physical activity, and smoking cessation.

Further detailed research into the underlying reasons of the observed differences in MI and stroke mortality between neighborhoods in Middle Tennessee would be beneficial to further guide health planning and policy. Multilevel analyses combining individual patient level data with aggregate data is a valuable approach to identify both individual and area risk factors important in determining most neighborhood variations in risk. Preventive programs may then focus resources on risk factors with the highest population attributable fraction so as to reduce disparities and improve health of the entire population. Thus reduction of MI and stroke burden in Tennessee will be more efficiently achieved when resources are focused on those risk factors with the highest attributable risks.

In conclusion, the identified temporal changes in geographic disparities help highlight progress in access to emergency health services over time as well as identify communities that are still underserved. Moreover, the variation in geographical patterns of MI and stroke mortality risks can help identify and target high risk neighborhoods for disparity reduction. This is vital for guiding planning and policy decisions aimed at improving population health.

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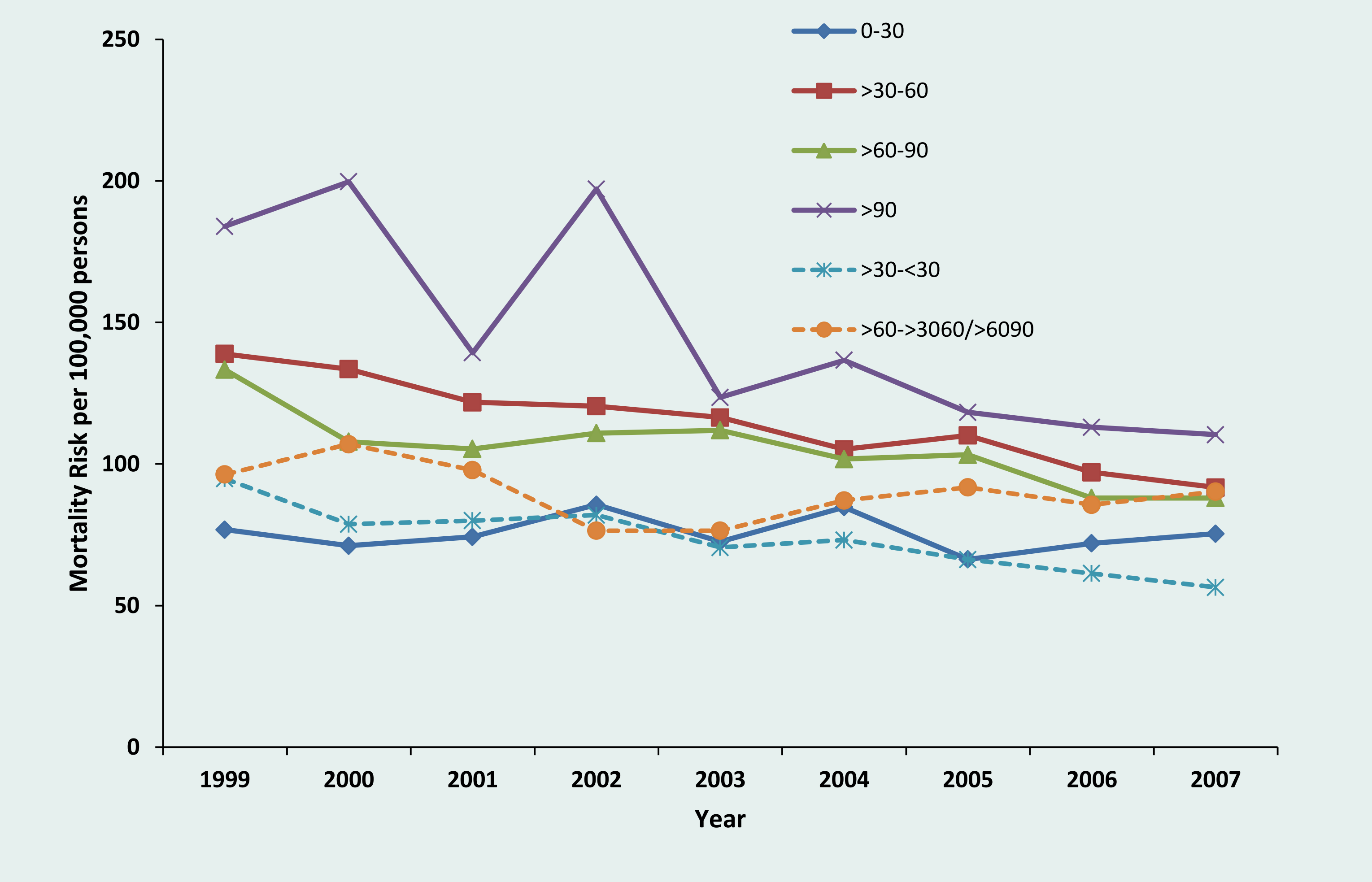
APPENDICES

Appendix 1: Temporal Changes in the Mortality Risks of Neighborhoods with Access to a Cardiac Center within Different Travel Time Zones



Where,

0-30 – Neighborhoods that were within 30 minutes of driving to a cardiac center the entire study period.

>30-60 – Neighborhoods that were within >30-60 minutes of driving to a cardiac center the entire study period.

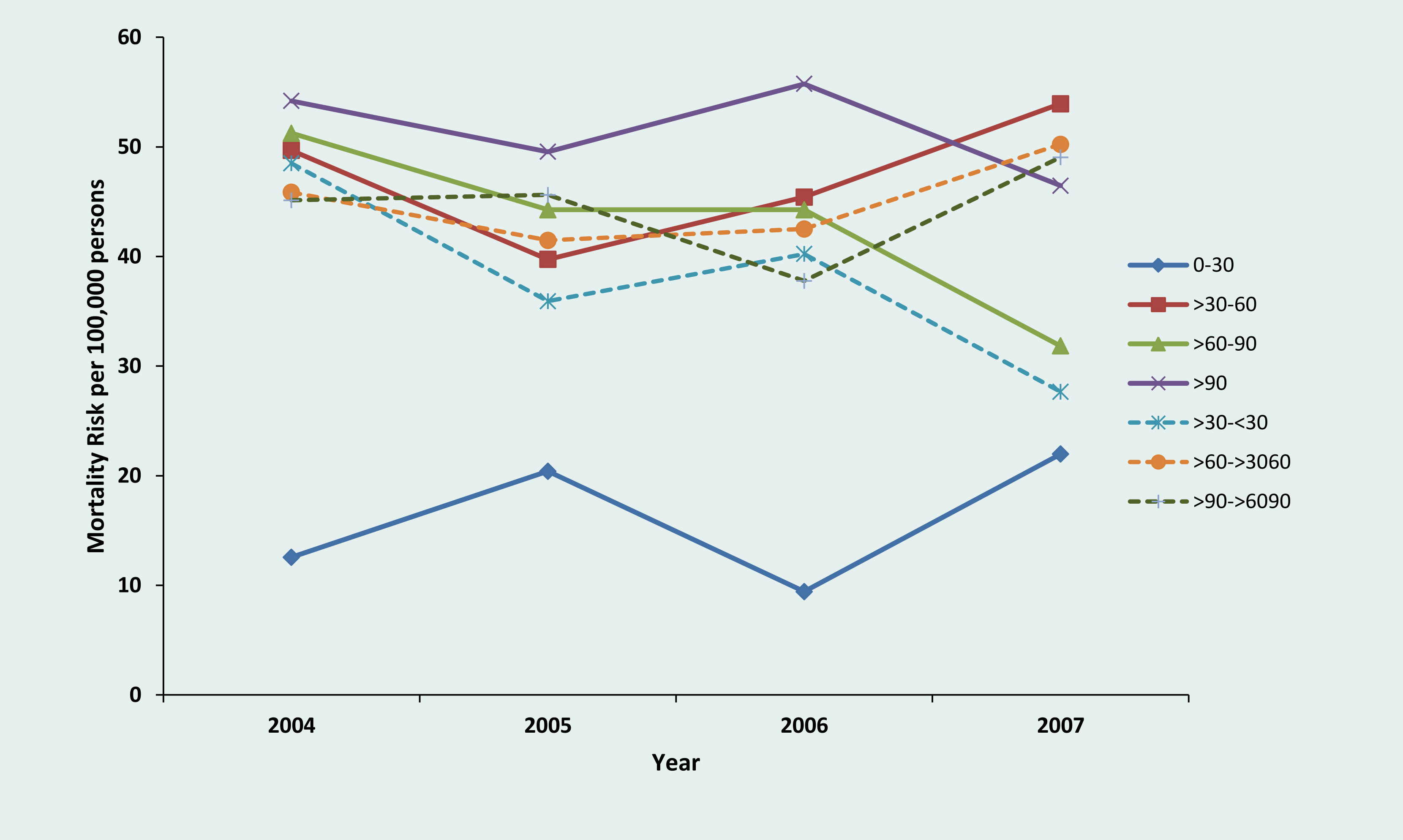
>60-90 – Neighborhoods that were within >60-90 minutes of driving to a cardiac center the entire study period.

>90 – Neighborhoods that were not within 90 minutes of driving to a cardiac center the entire study period.

>30-<30 – Neighborhoods that initially were not within 30 minutes of driving to a cardiac center and at the end had access to a cardiac center within 30 minutes.

>60->3060/>6090 – Neighborhoods that initially were not within 60 minutes of driving to a cardiac center and at the end had access to a cardiac center within >30-60 and >60-90 minutes.

Appendix 2: Temporal Changes in the Mortality Risks of Neighborhoods with Access to a Stoke Center within Different Travel Time Zones



Where,

0-30 – Neighborhoods that were within 30 minutes of driving to a stroke center the entire study period.

>30-60 – Neighborhoods that were within >30-60 minutes of driving to a stroke center the entire study period.

>60-90 – Neighborhoods that were within >60-90 minutes of driving to a stroke center the entire study period.

>90 – Neighborhoods that were not within 90 minutes of driving to a stroke center the entire study period.

>30-<30 – Neighborhoods that initially were not within 30 minutes of driving to a stroke center and at the end had access to a stroke center within 30 minutes.

>60->3060 – Neighborhoods that initially were not within 60 minutes of driving to a stroke center and at the end had access to a stroke center within >30-60 minutes.

>90->6090 – Neighborhoods that initially were not within 90 minutes of driving to a stroke center and at the end had access to a stroke center within >60-90 minutes.

Appendix 3: Negative Binomial Model showing the Probability of Death from Heart Attack in the Lowest and Highest Risk Neighborhoods

$$Y = -5.557 + 5.446 * \text{AGE65OVER} + 2.605 * \text{UTMELEM} + 0.493 * \text{RURAL} - 0.435 * \text{MHVALUE} - 2.329 * \text{RURALUTMELEMT}$$

NEIGHBORHOODS	AGE65 OVER	UTMELEMT	MHVALUE	RURAL	RURAL UTMELEM	Y	PROBABILITY OF DEATH
Lowest risk							
1	0	0.533	1.21400	0	0	-4.697	0.009
2	0.134	0.221	0.49200	1	0.221	-4.488	0.011
Highest risk							
1	0.212	0.230	0.68400	0.302	0.069	-4.113	0.016
2	0.214	0.137	0.77600	0.492	0.068	-4.289	0.014

Where,

Y – Predicted Mortality risk

AGE65OVER – Proportion of population in the neighborhood above 65 years

UTMELEMT – Proportion of population in the neighborhood with utmost elementary Education

MHVALUE – Median housing value of neighborhoods

RURAL – Proportion of population in neighborhoods living in rural area

RURALUTMELEM – Interaction between rural and utmost elementary Education

For the 9 year study period, the probability of death from a heart attack in the neighborhood with the lowest mortality risk was 0.009 whereas that for the neighborhood with the highest mortality risk was 0.016.

Appendix 4: Negative Binomial Model showing the Probability of Death from Stroke in the Lowest and Highest Risk Neighborhoods

Y= -6.169 + 6.512*AGE65OVER + 1.495*UTMELEM – 0.640*MARRIED

NEIGHBORHOODS	AGE65OVER	UTMELEMT	MARRIED	Y	PROBABILITY OF DEATH
Lowest Risk					
1	0	0.053	0.364	-6.323	0.0018
2	0.134	0.221	0.611	-5.357	0.0047
Highest Risk					
1	0.212	0.230	0.524	-4.779	0.0084
2	0.208	0.177	0.479	-4.857	0.0078

Where,

Y – Predicted Mortality risk

AGE65OVER – Proportion of population in the neighborhood 65 years and above

UTMELEMT – Proportion of population in the neighborhood with utmost elementary Education

MARRIED – Proportion of population in the neighborhood that is married

For the 9 year study period, the probability of death from a stroke in the neighborhood with the lowest mortality risk was 0.0018 whereas that for the neighborhood with the highest mortality risk was 0.0084.

VITA

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