Changing Clinical Presentation and Outcome of Acute Myocardial Infarction

in New Jersey from 1990-2004

by

Yu-Hsuan Shao

A Dissertation submitted to the

School of Public Health

University of Medicine & Dentistry of New Jersey and the

Graduate School-New Brunswick

Rutgers, The State University of New Jersey

In partial fulfillment of the requirements for the degree of

Doctoral of Philosophy

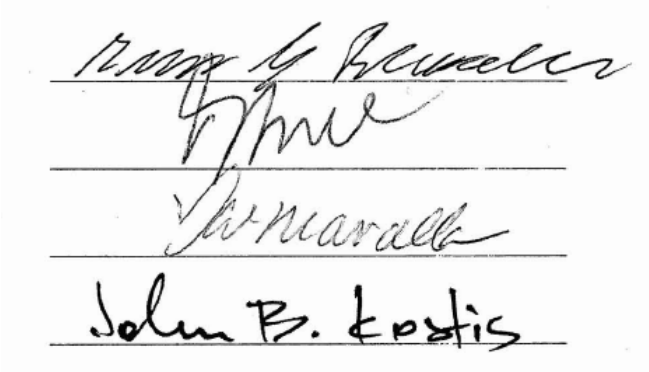
Graduate Program in Public Health

Awarded jointly by these institutions and

written under the direction of

Dr. George G. Rhoads

and approved by



New Brunswick, New Jersey

Oct, 2008

ABSTRACT OF THE DISSERTATION

Changing Clinical Presentation and Outcome of Acute Myocardial Infarction in New Jersey from 1990-2004

By Yu-Hsuan Shao, M.H.S.

Dissertation Director: George G. Rhoads

Over the past few decades, there has been a dramatic decline in coronary heart disease (CHD) mortality in the face of relatively stable incidence of acute myocardial infarction (AMI). However, the clinical presentation of AMI has been changing with more infarcts classified as subendocardial.

Objective

To explore closely the change from 1990 to 2004 in the incidence and presentation of hospitalized AMI, its case fatality, and the relationship of these changes to the decline in overall CHD mortality.

Design, Setting, and Participants

I studied hospitalized AMI cases in New Jersey from 1990-2004 (n=222,944) matched to state death records. The ECG and enzyme presentation of AMI was examined for 1990-1993 and 2001-2004 in 416 patient hospital records.

Results

CHD mortality declined by 40.8% from 1351 to 799 per 100,000, mostly in persons without an AMI hospitalization in the preceding 4-12 years. However, AMI hospitalization rate was relatively stable. The QMI hospitalization rate declined by approximately 50% in every age group; in contrast, the NQMI hospitalization rate increased 2 to 3 fold in each age group. Crude in-hospital case-fatality decreased from 13.4% in 1990 to 8.8% in 2004 for QMI patients while it increased slightly for NQMI. The 1-year case fatality of QMI decreased from 22.5% in 1990 to 17.8% in 2004 but the 1-year case fatality of NQMI patients increased from 18.3% in 1990 to 23.7% in 2004. Hospital record reviews confirmed a substantial decrease in the frequency of ST elevation and Q wave development in AMI admissions across the study period.

A decline in cardiovascular disease (CVD) case-fatality and a marked increase in NCVD case-fatality in four years were observed. The decline in CVD deaths might be attributed by the mix of cases which included milder MIs detected by troponins and possibly more severe cases that underwent revascularization before Q wave develop. One of the contributors to this increasing trend in NCVD deaths might be diabetes, which is known to be associated with higher mortality for both CVD and NCVD. The increasing prevalence of DM may play a significant role in increasing overall deaths, especially among patients following subendocardial infarction.

Conclusion

Changing clinical presentation of AMI and a worsening prognosis of subendocardial infarction suggest that the pathogenesis of CHD changed significantly during the 15 year study period. The worsening prognosis of subendocardial AMI deserves attention.

Acknowledgement

It is a pleasure to thank the many people who made this thesis possible.

I would like to thank my advisors Prof. George Rhoads and Prof. John Kostis for providing me with the opportunity to complete my PhD thesis. I would like to express my gratitude to Dr. Rhoads. Throughout my thesis-writing period, he provided encouragement, sound advice, good teaching, good company, and lots of good ideas. I would have been lost without him. Furthermore, I am grateful to have Dr. Kostis along the way during my PhD study. With his enthusiasm, his inspiration, and his great efforts to explain clinical aspect clearly and simply, he helped to make cardiology fun for me.

I am deeply indebted to Dr. Kitaw Demissie whose help, stimulating suggestions and encouragement helped me in all the time of research for and writing of this thesis. He played a significant role during my PhD study. I would never finish without his encouragement and support.

I would like to thank the many people who have been helped me through: Dr. Stephen Marcella, Dr. Alan Wilson, Nora Cosgrove, Dr. Young Lin and Dr. Samy Selim. For their kind assistance with research, giving wise advice, helping with various applications, and so on, I wish to thank in addition Dr. Elizabeth Marshall, Dr. George Lambert, and Dr. Shou-En Lu for their help in my early years of study.

I wish to thank my best friend in high school (Kohan Lai), and friends in Rutgers community for helping me get through the difficult times, and for all the emotional support, camaraderie, entertainment, caring they provided and for those nights with wine, beer and joke.

Lastly, and most importantly, I wish to thank my family for their never-ended support. To them I dedicate this thesis.

Table of Contents

List of Tables

Chapter 1. Introduction

Mortality and Morbidity

James B. Herrick (1861-1954), an American cardiologist, made a seminal contribution to our understanding of the sequelae of coronary sclerosis when he related coronary thrombosis to the clinical syndrome that is now recognized as a “heart attack” (a term that he coined). While acute myocardial infarction (AMI) was so uncommon and it was not well described before Herrick’s report, its frequency increased rapidly in subsequent years. By the mid twentieth century, coronary heart disease (CHD) had become the most frequent cause of disease in the US [1, 2]. However, mortality from CHD has declined steadily since 1968, except for a relatively small increase in 1993[3, 4]. CHD death decreased by 59 percent from 1950-1999; nonsudden CHD death decreased by 64% and sudden cardiac death by 49% [5]. These trends were seen in both men and women, in subjects with and without a prior history of CHD, and in smokers and non-smokers. However, the incidence of AMI has not declined as much as CHD mortality and the trends have varied by time and among studies. The Minnesota Heart Survey (MHS) found the age adjusted incidence for definite myocardial infarction was similar in 1970 and 1980 (174.2 vs. 179.9 per 100,000)[6]. During the period of 1985 to 1997, the incidence of hospitalized definite AMI decreased by about 10%[7]. The Worcester Heart

Attack study reported a slight increase in initial and recurrent AMIs between 1975 and 1981[8] after which time these rates decreased through 1995 [9, 10]. In Atherosclerosis Risk in Communities (ARIC) study, incidence of hospitalization for AMI increased by 7.4% per year from 1987 to 1994[11]. In the Myocardial Infarction Data Acquisition System (MIDAS) study in New Jersey, there was a decrease in age-adjusted mortality rates from CHD from 1986 to 1996, however the decrease in hospitalized non-fatal events was small[12].

A number of studies have reported significant improvement in short term and long term prognosis after an AMI in the last three decades [13, 14]. The MHS study reported that crude 28-day case-fatality decreased from 18% in 1970 to 13% in 1985 in men[15] and from 27% in 1970 to 18% in 1985 in women. Subsequently, they published a decrease in age-adjusted case-fatality from 13% in 1985 to11% in 1990 to 7% in 1995 in men and from 16% in 1985 to 12% in 1990 to 10% in 1995 in women[7]. In the Ontario myocardial infarction data base, Tu et al [16] reported a modest improvement in the 30-day risk adjusted case-fatality of patients from 15.5% to 14.0% between 1992 and 1996. In Medicare patients in the United States, AMI case-fatality declined from 26% to 23% in 30 days, and from 40% to 36% in 1 year from 1987 to 1990[17]. During 1992-2001, the

adjusted 1 year case-fatality still improved however the crude rate remained high [18]. The decline in case-fatality has been modest after 1990 and there was less improvement in older patients as well as women. Most studies included patients who were younger than 75 years of age and the improved case-fatality may be partially due to exclusion of very old patients [14, 19].

It is generally accepted that reductions in major cardiovascular risk factors such as smoking, cholesterol and blood pressure and rapid growth medical technology and secondary prevention have contributed to the observed declining trends in CHD mortality [4, 19-26]. The computer-simulation estimates suggested that primary prevention accounted for most of the decline in CHD between 1968 and 1974, about 50% of the decline between 1980 and 1990, and about 44% between 1980 and 2000 [27-29]. Other studies concluded that medical care and secondary prevention have the most important roles in this decline due to the absence of a decline in the incidence of CHD and a marked improvement in the case-fatality [11, 28]. It is possible that primary prevention may have affected the severity of AMI and contributed to the lowered case-fatality even though incidence of AMI did not decline much. However, few studies have examined trends in severity of MI and results have been inconsistent. Salomaa et al. reported decreases in the proportion of electrocardiograms coded as definite AMI and in the proportion of individuals with abnormal cardiac enzymes from 1983 to 1990 in the Finnish Monitoring Trends and Determinants in Cardiovascular Disease (FINMONICA)

study[30]. Results from ARIC study provided mixed support for decrease in the severity with worsening ECG indicators, but improving enzyme from 1987 to 1994[31]. The role of reduction in risk factors in changing CHD incidence is generally agreed but its role in reducing case-fatality through changes in the severity of AMI is still unclear. However, trend in severity of AMI after the widespread use of statin has not been studied much[32]. The contribution of statin use and lower cholesterol levels to the manifestation of CHD needs to be further investigated.

Improving treatment may also decrease the re-infarction rate after AMI, which is known to be associated with subsequent increased morbidity and mortality [33, 34] . Before the advent of thrombolytic therapy and revascularization, nearly one-quarter of AMI patients developed a second AMI [35]. Improving secondary prevention with expanded use of aspirin, beta blocker and thrombolytic therapy contributes to a reduction in one year recurrence rates before 1994 [33, 36, 37]. In recent years, an increasing number of patients have undergone percutaneous coronary intervention (PCI) which has been associated with lower recurrence rates than has use of thrombolytics ERA[33].

Patient characteristics

The increasing average age of the population with attendant increased patient co-morbidity, and expanded use of medical treatment has contributed to the changing characteristic of patients with AMI. Many studies have examined the effect of demographic variables, such as age, gender, and co-morbidities on AMI occurrences and outcomes [38-41]. The occurrence of AMI has been pushed from middle-age toward

older ages and less male predominance compared to those who were affected 20 years ago. During the last decade, there has been a substantial rise in the prevalence and incidence of type 2 diabetes mellitus (DM) and an increase in body mass index. The trend in prevalence of DM is expected to continue over the next 25 years[42, 43]. This diabetes epidemic will increase the burden of CHD attributable to diabetes. Ford et al. estimated that increases in the BMI contributed for about 26,000 additional deaths from CHD in 2000 and increases in the prevalence of DM for 33,500 additional deaths. They estimated a total 18% increase in CHD deaths, which offset the improvement in the past two decades. Other studies confirmed the poor prognosis of diabetic patients after AMI particularly in long term [44-46]. Nemetz et al investigated temporal trends in the prevalence of coronary artery disease at autopsy at Olmsted County, Minnesota from 1981-2004 and found that the decline in the atherosclerosis grade of coronary arteries ended after 1995; may have increased since 2000. This increase has been thought to be attributable to the increasing prevalence of obesity and DM[47].

Clinical Presentation

The distinction of Q wave (QMI) and non-Q-wave myocardial infarction (NQMI) remains in clinical use but it is controversial. Researchers have quite different suggestion of the division of QMI and NQMI. Some investigators believe that there is no clinical significance between QMI and NQMI and the division between transmural and subendocardial MIs was meaningless[48] although many anatomic and clinical studies showed that QW MIs were larger and usually more severe[49]. In 2004, Moon and his

colleagues supported the usefulness of the QMI and NQMI distinction examining AMI patients by cardiovascular magnetic resonance (CMR) allowing the precise in vivo detection of the total size, location and transmural extent of MI[50]. They reported the presence of Q wave predicts a lower ejection fraction and a larger MI but the division of MIs into transmural or non-transmural may over-simplify the disease because MIs are rarely exclusively one or the other.

In spite of the controversy about QMI and NQMI, substantial evidence supports the differential prognosis of these two types of AMIs. The incidence of NQMI has been increasing over the past 25 years. The Worcester Heart Attack study found that NQMI constituted 28% of all AMI in 1975, 35% in 1978, and 43% in 1981[51]. In a retrospective study, they reported the incidence of NQMI increased between 1975 and 1997 from 62/100,000 to 131/100,000; in contrast, the incidence of QWMI decreased[52]. In 1993, Wellford et al. reported that in 1985 43% of AMI were NQMI and 71% in 1990, based on more than 1000 hospital discharges each year from Brooke Army Hospital[53]. The increase may partially be due to more sensitive techniques developed for AMI identification[54]. Thus, when the more sensitive CK and CK-MB were used, the attack rates for NQMI were shown to increase between 1975 and 1981. Researchers suggested that the more sensitive detection method identified milder infarctions and thus resulted in lower case-fatality rates during early 1980s. The even more sensitive troponins came into use in 1990s and has resulted in the increased incidence of MI[55].

Early pharmacotherapy may have contributed to the increase in NQMI as well as thrombolysis and acute coronary angioplasty in early AMI with ECG ST segment elevation has probably had an important role in increasing the incidence of NQMI, by achieving early and sustained coronary artery patency with infarction size. Early intervention in an evolving infarct before Q wave develops may affect the course of ECG progression.

In addition to the difference in incidence, the in-hospital case-fatality associated with QWMI and NQMI are not the same. Studies have shown better prognosis of NQMI patients in the short term than that of QMI patients but the advantage disappears in one year. In 1997, Liebson and Klein reported a summary of other researchers' findings that NQMI is usually associated with lower in-hospital mortality than QMI which reflects smaller infarct size and better LV function, but NQMI patients had an earlier trend to reinfarction[56]. The NQMI patients showed an equal to or slightly less long term survival rate than QMI patients. In 2001, Furman et al studied the time trends from 1975 to 1997 showing a decline in-hospital and long term case-fatality of QWMI, in contrast to a steady in-hospital mortality for NQMI[52].

Most of the above reports are mainly concerned with secular trends before the late 1990's, and there is relatively little information available on recent population based trends in the outcomes of patients who had AMI. This study was undertaken to examine the changing trends in CHD over 15 years in a population-based data set in

New Jersey and to study the changing presentation of the disease and factors contributed to the trend. We were able to examine hospital discharge up through 2004.

Chapter 2. Secular changes in acute myocardial infarction mortality and morbidity in New Jersey from 1990 through 2004

Introduction

Although the death rate from coronary heart disease (CHD) in the United States declined by half in the past few decades, it is still a leading cause of death of both men and women above age 40[57]. One-third of CHD deaths are due to acute myocardial infarction (MI). Each year, approximately 865,000 persons in the United States develop acute MI which is fatal in about 38% of cases[57]. It is estimated that, on average, 15 years of life is lost per MI death [57]. A consistent decline in MI incidence and case fatality in the United States has been reported since the late 1960s, but the rate of decline has varied over time [6, 8, 12, 58]. The decline in case-fatality has been attributed to increased use of a variety of preventive and treatment approaches [19, 20, 59]. In spite of the success of these interventions, the decline in incidence and mortality of MI has not been shared equally by all age and gender groups. Better insight into the secular changes in the diagnosis, type [Q-wave (QMI), vs. Non-Q wave (NQMI /subendocardial infarction)], patient characteristics and case-fatality of MI may guide the research agenda and the development of public health measures to further reduce the burden of this disease.

The specific aims of the present study are to examine temporal changes in the incidence of MI by age and type of MI (QMI vs. NQMI) and to investigate secular changes in case-fatality and its determinants during the period between 1990 and 2004.

Methods

Data Sources

The data for this study were obtained from the Myocardial Infarction Data Acquisition System (MIDAS) dataset[12, 60-62]. MIDAS contains information abstracted from hospital discharge data of patients discharged from New Jersey non-federal acute care hospitals with a primary diagnosis of AMI (International Classification of Disease 9th Revision (ICD-9) 410.0-410.9). The database also includes all hospitalization records with any invasive cardiac procedure i.e. cardiac catheterization (CATH), percutaneous coronary intervention (PCI), and coronary artery bypass graft surgery (CABG). Each patient's discharge records were linked across the study period. The patient's initial admission for AMI during the study period was defined as the index admission. Data on the total New Jersey population and age distribution from 1990 to 2004 were obtained from the Population Division of the U.S. Bureau of the Census.

Vital status of subjects who were discharged alive from the hospital was determined by linkage of the MIDAS records with New Jersey death registration, using AUTOMATCH-Generalized Record Linkage System, Version 3.0.[63, 64] The method of determining the sensitivity and specificity of this probabilistic record linkage procedure has been described in a previous report and was found to be 98% and 99%, respectively[65].

Study Subjects

The MIDAS data set includes MI admissions to New Jersey hospitals from 1986 to 2004. This study is based only on patients who were 35 years and older and were discharged from the hospital between January 1, 1990 and December 31, 2004 with acute MI as the primary diagnosis. Only the index admission with the diagnosis of acute MI for each patient was included in the analysis. Acute MI admissions occurring in the four years preceding 1990 (1986-1989) covered by MIDAS but were excluded in order to ensure that patients in this analysis did not have an MI admission in a New Jersey hospital in the four years before their first admission during the study period. In addition, patients with history of old MI (ICD-9 412) in the data base were excluded.

Study variables

The primary outcome variables were CHD death, MI incidence and MI case-fatality. CHD death was ascertained from the NJ death registration data using the following codes: ICD-9 code 410-414, 429.2 and ICD-10 code I20-I25. Acute MI incidence, in-hospital and 1-year case-fatality were examined in the following age strata: 35-54, 55-64, 65-74, 75-84 and 85 and older, by infarction type (QMI vs. NQMI) and year of admission. For the main analyses patients who were discharged with diagnosis codes 410.0-410.6 were classified as representing QMIs while those with diagnosis code 410.7 were classified as NQMIs. Approximately 9 % of MI patients were discharged with other specified (410.8) and unspecified sites (410.9) diagnostic codes and were excluded from subgroup analyses.

The primary independent variables were calendar year of admission, MI type (QMI vs. NQMI), and age at first acute MI. Covariates included in the presence or absence of co-morbidities, including diabetes, hypertension, chronic obstructive pulmonary disease, chronic liver disease, chronic renal disease, anemia, cerebrovascular disease, and cancer, complications e.g. arrhythmia (ARR), or systolic left ventricular dysfunction (LVD) as well as the use of invasive cardiac procedures (CATH, PCI, CABG) up to 30 days from the date of the index admission (including procedures performed during subsequent admissions during this time interval). Detailed definition of variables has been described elsewhere [62].

Statistical methods

Temporal trends in demographic, clinical and treatment characteristics in hospitalized MI patients were studied separately by MI type (QMI vs. NQMI). For ease of presentation, the 15 study years were aggregated into five periods (1990-1992, 1993-1995, 1996-1998, 1999-2001, and 2002-2004). Because previous findings from this study and others have shown several demographic and clinical factors to predict the survival of AMI patients[12, 60, 62], and because New Jersey MI patients were older and had higher prevalence of co-morbidities during the more recent study years, we controlled for these factors in a series of multiple logistic regression analyses designed to examine changes over time in in-hospital and 1 year case-fatality. The confounders included age, gender, race, diabetes, hypertension, renal disease, anemia, cancer, cerebrovascular disease, ARR and LVD. We compared differences in 1-year survival

following a first MI among five three-year study periods by using the Kaplan-Meier estimates and cumulative mortality curves were tested for statistical significant using the log-rank test.

All statistical analyses were performed by using SAS 9.0 (SAS Institute, Cary, NC). The study was approved by the State of New Jersey Department of Health and Senior Services and the Robert Wood Johnson Medical School Institutional Review Boards.

Results

Incidence of Acute Myocardial Infarction

As shown in Table 2-1, during the fifteen-year period from 1990 to 2004, a total of 222,944 subjects were discharged from New Jersey hospitals with acute MI as the primary diagnosis, with no hospitalization for MI in the preceding four years and with no diagnosis of old MI. The incidence of MI declined from 346.32 (per 100,000) in 1990 to 318.61 in 2004. However, the change was not equal in all age groups. There was a modest decrease in MI incidence in the 35-54 and 65-74 age groups, and a more pronounced decrease in the 55-64 age group. Most of the decline in the incidence of MI in these age groups occurred after 1996. Among subjects aged 85 and older, the MI incidence did not decline; it increased by 23% since 1990.

The clinical characteristics of patients admitted with MI changed significantly during the 15 years under study. Patients admitted in the later years were more likely to be discharged with the diagnosis of subendocardial infarction (NQMI). The incidence of

QMI decreased by approximately 50 % in every age group; in contrast, the incidence of NQMI increased 2 to 2.5 in four younger groups and more than three times in the oldest group (Figure 2-1). These changes in incidence of QMI and NQMI were similar in men and women.

Clinical Characteristics of MI patients

The median age of QMI patients increased from 67 years in 1990-1992 to 68 years in 2002-2004 while it increased from 71 to 74 years for NQMI patients. During the most recent period (2002-2004), about one quarter of the QMI patients (24.4%) were in the group of aged 35-54 and nearly 49% of the NQMI patient were older than 75 years. It compared to 20.3% and 37.8%, respectively for 1990-193. Table 2-2 presents patient characteristic, age-adjusted by the direct method to the age structure of 1990-1992 MIDAS population. Overall, diabetes, hypertension, renal disease, anemia and cancer were coded more frequently among all MI patients in later years even after age-adjustment. Not surprisingly, MI patients admitted in later years were much more likely to have invasive cardiac procedures (CATH, PCI and CABG within 30 days after admission) in later study periods. Compared to QMI patients, NQMI patients had more co-morbidities and were less likely to have CATH and PCI. However, by 2002-2004 almost half of NQMI patients had PCI or CABG.

In-Hospital and 1-Year Case-Fatality

Crude in-hospital case-fatality decreased during the study from 13.42% in 1990 to 8.76% in 2004 for QMI patients while it increased slightly from 5.12% to 6.03% for NQMI. The 1-year case fatality of QMI decreased from 22.54% in 1990 to 17.82% in 2004 but the 1-year case fatality of NQMI patients increased from 18.33% in 1990 to 23.73% in 2004. Compared to patients with QMI, NQMI patients had lower in-hospital case fatality but higher 1 year case-fatality in recent years (Figure 2-2). Crude odds ratios (OR) for death demonstrated a decreasing trend with time among QMI patients, and a significantly increasing trend among NQMI patients for both in-hospital and 1-year case fatality (Table 2-3). These trends persisted after adjustment for age, gender, race, complication, and co-morbidities. The odds of dying in the hospital were significantly lower in later years compared to the odds in the 1990 to 1992 period among QMI patients as well as in 1-year case-fatality among QMI patients in the past 15 years. Among NQMI patients, the case-fatality had no improvement in hospital and increased at 1-year in the 15 years under study. The magnitude of increase in 1 year case-fatality was attenuated but remained statistically significant after adjustment for confounders.

Effects of patient age on 1-year survival.

Figure 3 shows the cumulative mortality of QMI and NQMI patients in two age strata (<75 and >=75). In general, MI patients who were younger than 75, had better survival than those in older age group. QMI patients were more likely than NQMI patients to die within the first month after admission but the chance of dying decreased by the second month. The mortality of these (QMI) patients decreased significantly in the years under

study, especially in the mortality during first month after admission (log rank test, $p<0.0001$). In contrast, the 1-year mortality of NQMI patients did not decrease among those younger than 75 and increased significantly among those aged 75 and older (log rank test, $p<0.0001$). In the older age group, the mortality of NQMI increased while mortality of QMI patients decreased in the later years of the study. In the most recent years (2002-2004), NQMI patients had worse prognosis than QMI patients of the same age group (<75: Q: 9.31%, NQ: 12.1%; >=75: Q: 37.5%, NQ: 37.8%).

State-wide CHD Mortality Trends

In order to understand how mortality following hospitalization for MI related to overall CHD mortality in the state, we examined CHD population mortality adjusted by the direct method to the age and sex structure of 1990-1992 MIDAS population. In New Jersey, CHD mortality declined notably from 1351.58 per 100,000 in 1990 to 798.59 per 100,000 in 2004 (Figure 2-4). There was no increase in mortality from other cardiovascular causes during this period indicating that the decline in CHD mortality was not likely to be explained by changing diagnostic or coding practice.

Among persons dying from CHD in New Jersey, more than 85% had no MI hospital admission in the previous four years. This percentage was a bit higher for MI hospital admission in previous eight and 12 years and remained relatively constant over the period under study. This suggests that more of the decline in CHD mortality has been among persons who did not have an MI hospitalization in the preceding 4-12 years. When deaths among persons with prior MI hospitalization are considered, the

proportion with NQMI almost doubled in the past 15 years, while the rates for QMI and other unspecified MI decreased (Figure 2-5). In 2004, 8.9% of CHD deaths were previous NQWMI hospital admission, in contrast to 2.8% in 1990, after adjusting for age and sex.

Discussion

The results of this population–based study confirm the continuing decline in CHD mortality [66] and highlight three under-appreciated aspects of this remarkable secular change. First, most of the decrease in CHD death rates has occurred in persons who did not have an in-state hospitalization for MI in the preceding four years, or (in 1998-2004) even in the preceding 12 years. Second, among patients hospitalized with MI, there has been a remarkable change in hospital discharge coding from specified location MI toward events discharged as subendocardial MI's. Finally, the increase in mortality seen for NQMI over this period is worrisome and suggests a change in the underlying disease process that is not well understood.

In contrast to the marked decline in mortality, the decrease in acute MI incidence in our study was less striking. Secular trend in acute MI were reported by the Minnesota Heart Survey where the age adjusted incidence of definite myocardial infarction was similar in 1970 and 1980[6] but decreased by about 20% during the period of 1985 to 1997[7, 67]. The Worcester Heart Attack Study reported increasing trends in initial AMIs between 1975 and 1981 but showed a dramatic decline between 1981 and 1984. In MIDAS study, we found a 16% decline in AMI incidence from 1990 to 2004 that mostly occurred after

1996. The decrease was largest among persons aged 55-64, with smaller declines in the other age groups and increased incidence in those aged 85 and older.

The decrease in the AMI incidence was observed occurred for QMI only. The QMI incidence decreased more than 50% in the years under study and the decline was steep after 1996, a trend which was seen in all age and gender groups. The decreased incidence of QMI observed in our study may be related to the reductions in major cardiovascular risk factors such as smoking, serum cholesterol and blood pressure [19-22]. The reduction in risk factors may have diminished the severity of atherosclerosis in large vessels resulting in a less frequent transmural infarction. It was supported by our finding of a lower rate of STEMI patients in 2001-2004 compared to those in 1990-1993.

Contrary to QMI, we observed an increased incidence of NQMI increased in both MIDAS and several previous studies[51-53]. This increase in incidence may be attributed to the change of AMI definition. The advent of more sensitive assays for myocardial injury may be responsible for the increased incidence of NQMI. Edlavitch and his colleagues reported that inclusion of CPK and CPK-MB in diagnostic tests in the Minnesota Heart Study resulted in a 16.8% increase on QMI rates and in a 94.0% on NQMI rates in 1980[54]. In addition, the expanded use of troponins has been reported to have resulted in an increase in recognition of AMI [55, 68, 69]. Salomaa et al. reported a trend in coronary heart disease events in Finland during 1993 -2002 which corrected the effect of troponins and concluded that without troponins incidence rates would have been lower especially in women and older patients[70]. This could help to explain the

dramatic increase in NQMI incidence of patients aged 85 and above after 1998 found in MIDAS. From the result of 191 patient records review in 2001-2004, 15% of patients were documented by troponins only, which was consistent with other study. In addition, among these patients documented by troponins only, the proportion of STEMI was relatively smaller. It is important to point out, however, that these cases added by use of troponins are not necessary to have a benign course and a mixture of these cases had been associated with increased NQMI mortality.

The use of early pharmacotherapy and intervention may have contributed also to the increase in the incidence of NQMI. The use of aspirin, heparin, beta-blocker, ACE inhibitors, thrombolytic agents as well as percutanous coronary intervention in early ST segment elevation MI may have played a significant role in increasing incidence of NQMI by reducing infarct size transforming some QMI to NQMI. The increased use of aspirin, beta-blocker and ACE inhibitors may explain why the increase in NQWMI incidence before the widespread use of thrombolytic agents as reported by Furman and his colleagues in the late 1980s to early 1990s [52] and the observation of similar trends in patients who did not receive thrombolytic agents must be contributed by medication. Therefore, conversion of QMI to NQMI by reperfusion therapy can only partially explain the increased incidence while agents decreasing myocardial oxygen demand may be another explanation.

Presumably, patients with these codes had ECG changes reflecting ischemia in the coded locations, but they may not have really developed Q waves during hospitalization.

For example, an inferior NSTEMI could be classified as 410.7 (subendocardial AMI) or 410.4 (inferior AMI) without really having pathologic Q wave found in ECG. Results from two time points hospitalization records review support the substantial changes in clinical presentation of MI that we observed in state-wide discharge data set. Coding practice may contribute to this change, but it seems like patients were more likely to be discharged from specified locations rather than subendocardial MI which may result in underestimate the incidence of subendocaridal MI.

Despite this ambiguity, the distinction between transmural and subendocardial MIs as defined were meaningful. Besides the difference in incidence trends, the prognosis of QMI and NQMI are different. The decreased mortality for QMI has been broadly studied, especially in-hospital case-fatality[15, 67, 71]. It changed from 13.42% in 1990 to 8.76% in 2004 in MIDAS. In contrast, NQMI patients had a slight increase in in-hospital case-fatality and a marked increase in 1-year case-fatality. This increase remained significant after adjusting for patients' age, race, comorbility, and complications, and was especially marked among patients aged 75 and older. An analysis of the trend in 28-day case-fatality showed that result was similar to that found for in-hospital mortality indicating that changes in length of stay during the 15-year study period did not explain the change in in-hospital case-fatality.

NQMI patients demonstrated better prognosis in short term mortality than QMI patients but the advantage disappears in one year[52, 56]. In MIDAS, we found higher crude 1-year case-fatality in patients with NQMI than that with QMI after 1995. It

appears that the primary prevention has not been as effective in QMI and NQMI in the past 15 years. Also, a larger proportion of NQMI patients developed recurrent AMI in the first few months after discharge[34, 35, 56] which likely affects long term prognosis, particularly among aged 75 and older who comprised the major portion of death after AMI events.

Given the increase in incidence and case-fatality of NQMI observed in our study, it appears that control of traditional risk factors has not efficiently prevented this manifestation of coronary disease. NQMI incidence has probably been augmented by conversion of QMI through coronary interventions and by the introduction of sensitive enzyme detection methods. However, the poor prognosis and somewhat older age may also suggest that different pathphysiologic process may contribute to the development of QMI and NQMI. To further understand this phenomenon, it will be important to verify that the discharge codes used to distinguish QMI and NQMI truly reflect ECG findings. A better understanding of the quantitative contribution of troponins to the increase in NQMI and the disease process that lead to death in these patients would be very helpful. It appears that approaches to preventing and treating NQMI will be keys to the future improvement that will be crucial to the resolution of coronary heart disease epidemic.

Table 2-1 Population AMI incidence from 1990 to 2004 by age group

		Incidence per 100,000				
Year	**Total**	**35-54**	**55-64**	**65-74**	**75-84**	**85+**
1990	346.32	106.50	393.74	631.03	951.59	1255.64
1991	349.93	116.50	394.26	629.82	939.19	1272.32
1992	350.07	113.12	399.55	657.47	934.24	1211.56
1993	360.87	115.44	418.35	665.07	991.50	1269.46
1994	350.07	109.80	411.87	648.67	969.86	1254.41
1995	357.54	113.09	403.37	665.63	1013.16	1339.84
1996	357.00	111.20	418.05	668.66	996.99	1370.57
1997	346.94	107.09	389.75	645.14	998.86	1440.52
1998	351.23	102.25	387.58	631.48	1045.33	1631.63
1999	352.56	96.75	369.87	656.83	1070.22	1717.37
2000	344.24	96.22	362.87	622.95	1056.98	1683.39
2001	355.78	97.62	371.21	648.20	1102.75	1766.40
2002	354.93	101.67	362.11	668.04	1037.82	1778.85
2003	340.07	101.23	344.65	603.07	1017.65	1675.81
2004	318.61	94.56	315.14	569.39	961.71	1544.76
RRR*	-8%	-11%	-20%	-10%	1%	23%
Ave. RRR**	1%	-1%	-3%	2%	6%	19%

* RRR: Relative Rate Reduction to Year 1990 in 2004

**Ave RRR: Average of Relative Rate Reduction in every year to Year 1990

Table 2-2 Distribution of Characteristics in Patients with First Q-wave AMI or non-Q-wave AMI from 1990 to 2004, adjusted by direct method to the age distribution of the 1990/1992 MIDAS population

		Q Wave Myocardial Infarction						Non-Q Wave Myocardial Infarction					
		1990/1992	1993/1995	1996/1998	1999/2001	2002/2004		1990/1992	1993/1995	1996/1998	1999/2001	2002/2004	
	N	26123	26294	24489	19702	15863		10392	13587	17277	23855	27569	
		(%)	(%)	(%)	(%)	(%)	p-value*	(%)	(%)	(%)	(%)	(%)	p-value*
Demographic													
Age**	35-54	20.33%	21.07%	21.76%	22.08%	24.41%	<0.0001	13.44%	13.43%	12.75%	11.88%	13.05%	<0.0001
	55-64	22.47%	21.44%	20.76%	21.25%	23.10%		18.86%	17.24%	16.09%	15.48%	16.09%	
	65-74	28.97%	27.83%	25.76%	23.35%	21.02%		29.90%	28.83%	26.25%	23.68%	21.77%	
	75-84	20.98%	21.69%	22.40%	22.88%	21.05%		27.06%	28.70%	30.09%	31.31%	29.82%	
	85+	7.24%	7.96%	9.31%	10.44%	10.42%		10.74%	11.80%	14.82%	17.66%	19.27%	
Sex	Female	39.48%	39.43%	39.41%	38.50%	37.94%	0.0002	42.22%	40.83%	40.58%	41.30%	41.72%	<0.0001
	Male	60.51%	60.57%	60.59%	61.49%	62.05%		57.77%	59.17%	59.42%	58.69%	58.28%	
Race	White	85.66%	87.75%	85.67%	83.84%	79.70%	<0.0001	84.40%	85.63%	83.58%	80.89%	76.73%	<0.0001
	Black	6.25%	6.56%	6.40%	6.80%	6.15%		9.44%	9.63%	9.07%	10.50%	10.14%	
	Others	8.09%	5.68%	7.93%	9.36%	14.14%		7.16%	4.73%	7.35%	8.60%	13.13%	
Comorbidities	Diabetes	23.74%	23.44%	25.08%	24.57%	24.71%	0.0025	28.24%	29.80%	31.83%	33.11%	32.96%	<0.0001
	Hypertension	37.51%	41.78%	46.61%	49.59%	53.57%	<0.0001	45.00%	48.70%	53.14%	56.67%	60.27%	<0.0001
	Renal Disease	4.25%	4.55%	5.07%	5.98%	6.45%	<0.0001	4.88%	6.08%	7.07%	8.03%	9.21%	<0.0001
	Anemia	10.18%	9.97%	10.08%	10.41%	10.72%	0.1128	11.20%	10.84%	11.58%	13.42%	14.01%	<0.0001
	Cancer	1.942%	2.25%	2.39%	2.69%	2.87%	<0.0001	2.16%	2.45%	2.84%	3.11%	3.73%	<0.0001
	Cerebrovascular Dx	4.53%	4.63%	4.67%	4.16%	3.84%	<0.0001	5.16%	5.15%	5.17%	5.79%	5.11%	0.61
Complication	ARRH	26.21%	24.36%	23.55%	20.46%	19.92%	<0.0001	21.36%	19.24%	18.77%	17.09%	16.71%	<0.0001
	LVD	15.56%	14.91%	14.84%	14.84%	14.88%		16.48%	18.53%	19.34%	19.34%	19.80%	
	ARRH and LVD	17.31%	15.92%	14.52%	13.36%	13.10%		13.85%	13.67%	13.31%	12.86%	13.39%	

		Q Wave Myocardial Infarction						Non-Q Wave Myocardial Infarction					
		1990/1992	**1993/1995**	**1996/1998**	**1999/2001**	**2002/2004**		**1990/1992**	**1993/1995**	**1996/1998**	**1999/2001**	**2002/2004**	
Procedures	CATH	42.47%	49.58%	55.41%	61.46%	70.07%	<0.0001	45.11%	51.39%	54.18%	56.37%	61.98%	<0.0001
	PTCA	14.48%	21.84%	31.21%	41.15%	53.32%	<0.0001	12.30%	17.33%	22.22%	26.16%	32.31%	<0.0001
	CABG	8.97%	11.41%	12.93%	14.05%	12.97%	<0.0001	11.55%	13.55%	14.87%	15.09%	13.82%	<0.0001

ARRH: arrhythmia
LVD: left ventricular dysfunction
* From Chi-square test for trend

** Not age-adjusted

Table 2-3 Crude and multivariable-Adjusted* OR of Dying During hospitalization and in 1 year from first Q-wave or Non Q-wave Myocardial infarction

Study Period	Q wave Myocardial Infarction				Non-Q wave Myocardial Infarction			
	Crude OR	Adjusted OR	95% Confidence Interval		Crude OR	Adjusted OR	95% Confidence Interval	
In hospital								
1990-1992	1.0§	1.0§	-		1.0§	1.0§	-	
1993-1995	0.88*	0.88	0.83	0.93	1.11	1.04	0.93	1.16
1996-1998	0.78*	0.76	0.72	0.81	1.05	0.91	0.82	1.02
1999-2001	0.76*	0.74	0.70	0.80	1.14*	0.96	0.86	1.06
2002-2004	0.63*	0.63	0.59	0.68	1.16*	0.93	0.84	1.03
1 year								
1990-1992	1.0§	1.0§	-		1.0§	1.0§	-	
1993-1995	0.94*	0.94	0.89	0.98	1.08*	1.01	0.94	1.08
1996-1998	0.93*	0.91	0.86	0.95	1.24*	1.08	1.01	1.15
1999-2001	0.96	0.95	0.90	1.01	1.45*	1.21	1.14	1.29
2002-2004	0.83*	0.85	0.80	0.90	1.47*	1.20	1.13	1.28

*Adjusted for age, gender, race, diabetes, hypertension, renal disease, anemia, cancer, cerebrovascular disease and complication.

§ Reference category

Figure 2-1 Percentage of 1990 population incidence rate by type of MI and age

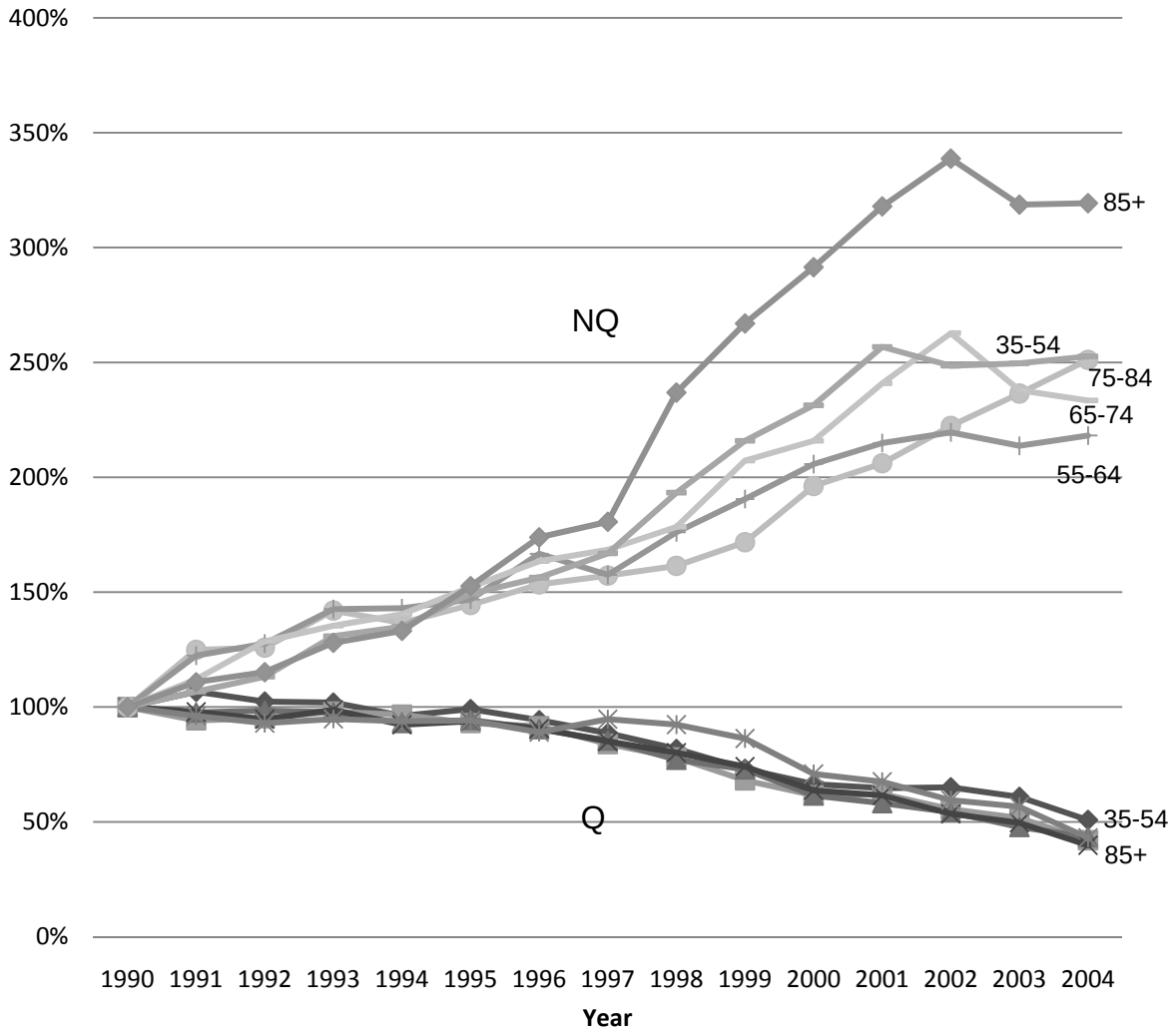


Figure 2-2 In hospital and 1 year case fatality from 1990 to 2004 by type of MI

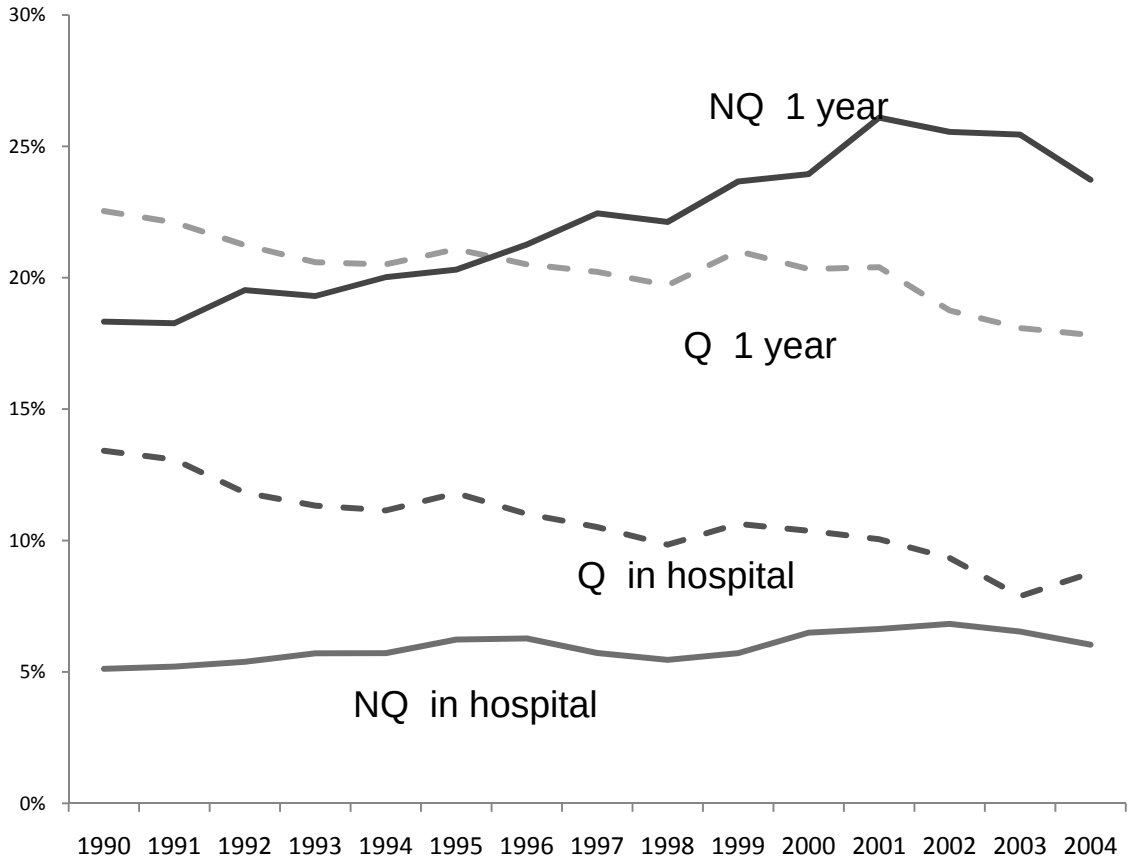


Figure 2-3 One Year Cumulative Mortality by year, type of MI and age strata

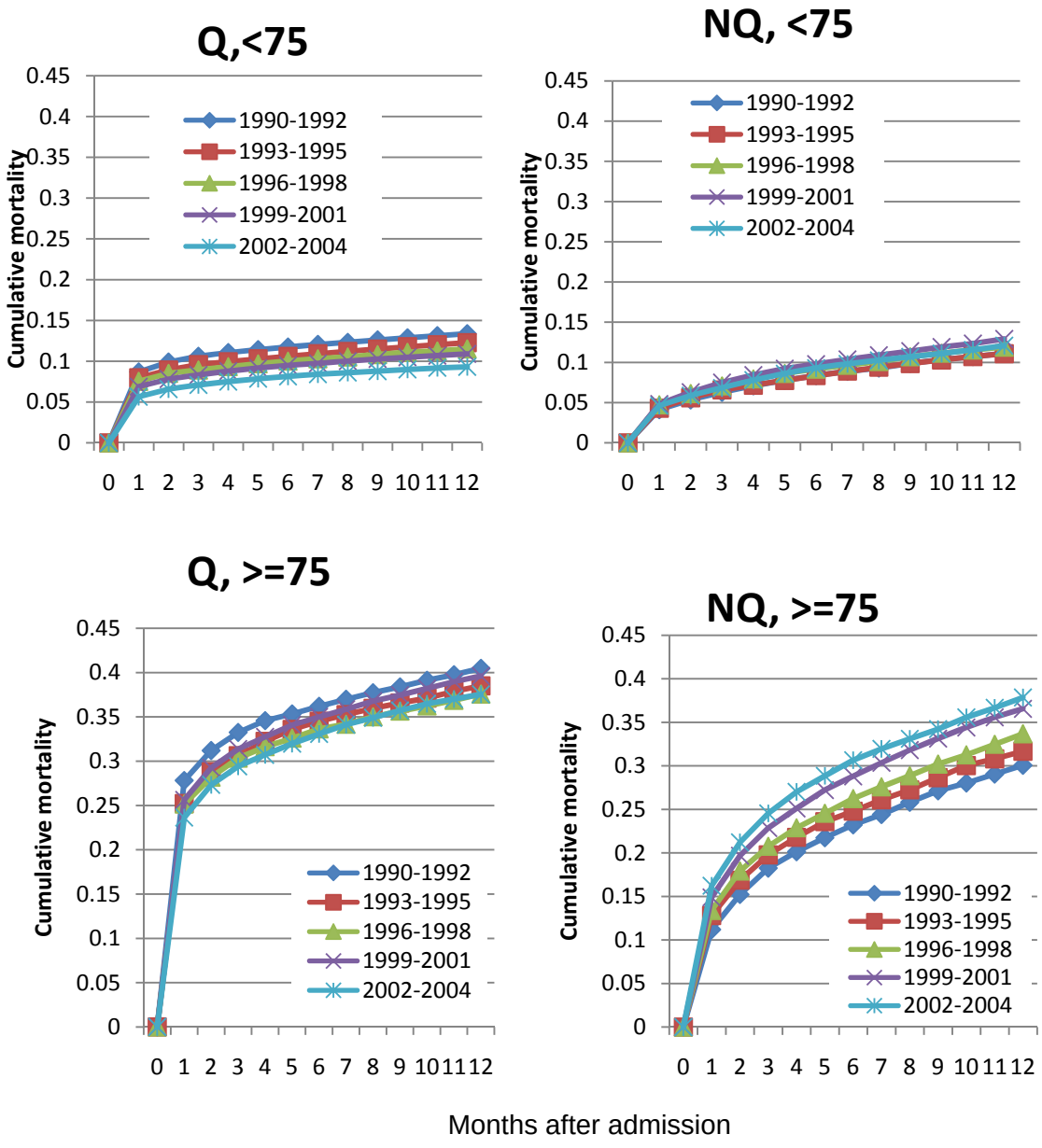


Figure 2-4 Age and sex adjusted CHD population mortality in New Jersey from year 1990 to 2004

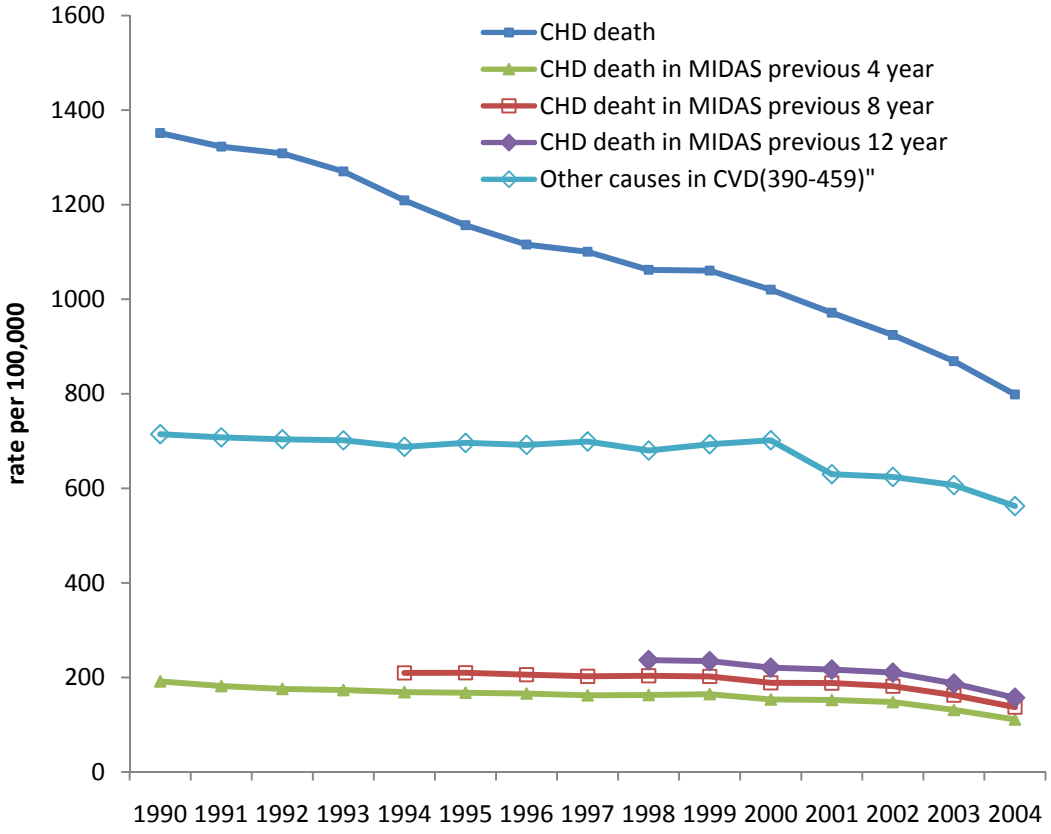
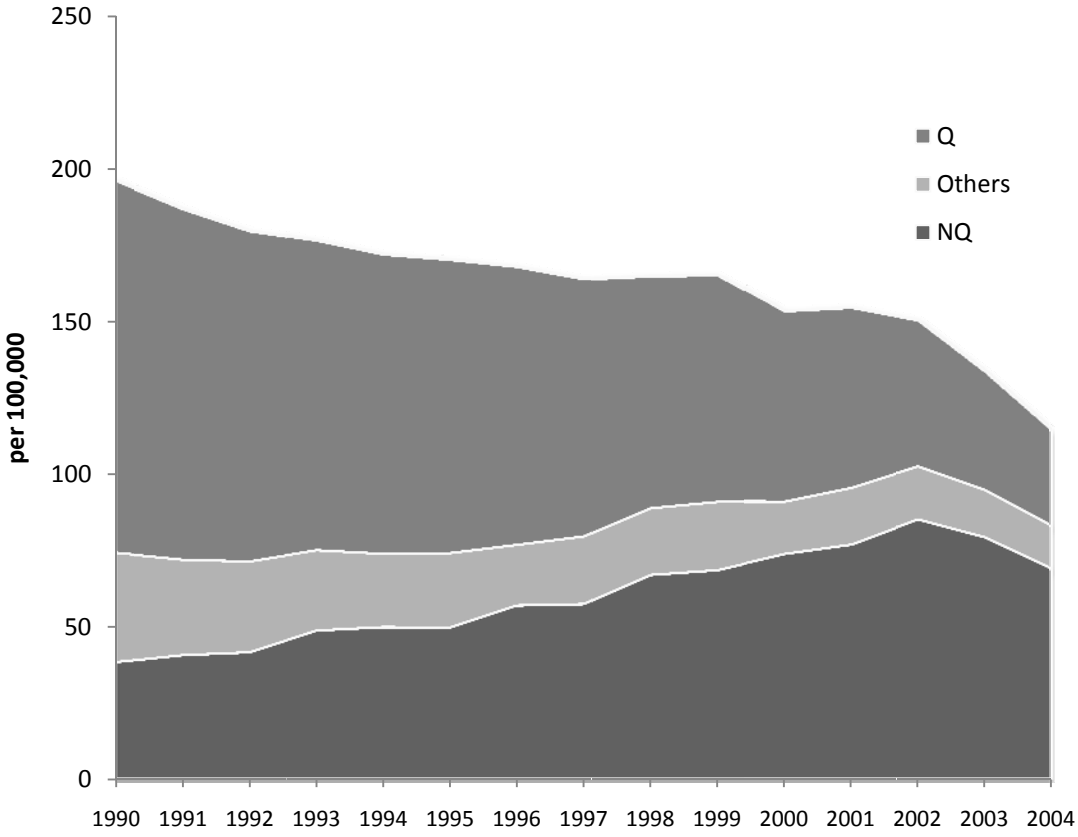


Figure 2-5 Age and gender standardized CHD mortality contributed by persons hospitalized with Q-wave, non-Q-wave and other unspecified MI in the preceding four years (1990-2004).



Chapter 3. Changes in clinical presentation of acute myocardial infarction from 1990 to 2004 in New Jersey.

Introduction

A decline in myocardial infarction (MI) in the United States has been reported since the late 1960s, but the rate of decline has varied over time [6, 8, 12, 58]. The Minnesota Heart Survey reported that age adjusted incidence of definite myocardial infarction was similar in 1970 and 1980[6] but decreased by about 20% during the period from 1985 to 1997[7, 67]. The Worcester Heart Attack Study reported increasing trends in initial AMIs between 1975 and 1981 but a dramatic decline between 1981 and 1984. Our results from MIDAS, a population based data set with 205,673 AMI patients in New Jersey, found a 8% decline in AMI incidence from 346 per 100,000 in 1990 to 319 per 100,000 in 2004; the decline mostly occurred after 1996.

Within this decreasing MI incidence trend, a substantial change in patients' clinical presentation was observed. In the MIDAS study, we found a marked decline in incidence of patients being discharged with MI in specified locations (ICD-9, 410.0-410.6, anterolateral, other anterior, inferolateral, other lateral, inferoposterior, and posterior locations) from 226 per 100,000 in 1990 to 91 per 100,000 in 2004. The incidence of patients discharged from 410.0-410.6 decreased more than 50% in the years under study and the declining trend was seen in Whites and in African Americans, and in all age and gender groups.

Contrary to the decreasing trend for patients discharged with codes 410.0-410.6, there was an increased incidence of patients discharged with subendocardial infarction (ICD-9, 410.7) , which went from 70 per 100,000 in 1990 to 170 per 100,000 in 2004 in the MIDAS study. A similar increase has been reported by several previous studies [51-53] suggesting that this phenomenon is by no means limited to New Jersey. This increase in incidence may be attributed, at least in part, to changes in AMI definition. The advent of more sensitive enzyme assays for myocardial injury may contribute to the increased incidence of subendocardial infarction. Edlavitch et al reported that inclusion of CPK and CPK-MB in diagnostic tests in the Minnesota Heart Study resulted in a 16.8% increase in Q wave MI (QMI) rates and in a 94.0% in non-Q wave MI rates in 1980[54]. More recently, the introduction of troponins has been reported to have resulted in a further increase in the recognition of AMI [55, 68, 69]. Salomaa et al. reported a trend in coronary heart disease events in Finland during 1993 -2002 which corrected the effect of troponins and concluded that without troponins incidence rates would have been lower especially in women and older patients[70]. Importantly, those cases confirmed mainly or exclusively by troponins may have higher subsequent death rates than other MI patients.

In order to verify that the decreased trend in discharge codes for specified location MIs and the increase in coded subendocardial MIs reflect real changes in ECG, we reviewed the clinical records of 381 AMI patients in two New Jersey hospitals.

Methods

Inclusion criteria

For 1990-1993 and 2001-2004, we obtained a random list of 416 patients 55-84 years old who were discharged from 2 hospitals contributing records to the MIDAS data set. We included patients admitted to the hospitals from the emergency room or by physician referral only (hospital transfers excluded).

Patient Record abstraction

The medical records of the selected patients were abstracted according to a written protocol by two trained persons. Information was obtained on sign and symptoms, medical history, cardiac enzyme levels and therapy. Two types of information were abstracted: 1) Validation information: medical record number, name and birthday were first abstracted to ensure records being reviewed correspond to the patient sampled from the MIDAS data set. Other demographic information, for example, race, ethnicity, gender, insurance status are included in MIDAS data set already; 2) Medical information: time of symptom onset (chest pain), weight in pounds, height in inches, smoking (current/ cigarettes per day, past/ months since stop smoking , never and not mentioned), diabetes (yes/ no/ not mention, treatment: no medication, insulin or oral only), hypertension (yes/ no/ not mention, treatment yes/no) and high cholesterol (yes/

no/ not mention, treatment yes/no); laboratory data: first three and the highest enzyme levels and time measured during hospitalization (CK-MB from 1990-1993 and 1999-2002 and Troponin from 1999-2002) usually being measured by every 6 or 8 hours, it may vary by hospitals, first available level of total cholesterol, high density lipoproteins (HDL) and low density lipoproteins (LDL); interventional procedures (CATH/PCI reports, CABG operation report) and discharge status (discharge alive or expired); medication use prior to hospitalization (which usually is described in the history section of patient charts), medication during hospitalization and time of first dose of medication (ER record medication/treatment section and medication administration record), and medication after discharge (physician discharge order). A check list of medications was provided to the chart reviewers and included aspirin, clopidogrel, anticoagulants, beta-blockers, ACE inhibitors, lipid lowering agents, thromboytic agents, nitroglycerin and calcium channel blockers. All patients' electrocardiograms (ECGs) during hospitalization were photocopied and brought back for reading.

ECG reading

Electrocardiograms (ECGs) were read blindly by one cardiologist. Up to four ECGs

including the first and the last were reviewed for each hospitalization. The ECGs were read independently one at a time, to minimize bias in the ascertainment of Q waves. Only Q waves that developed during hospitalization were considered as definite QWMI. The reading were guided by the following ECG criteria which were published in a recent consensus statement.[72]

ST segment elevation (STEMI)

New or presumed new ST segment elevation at the J point in two or more contiguous leads with the cut-off points ≥0.2 mV in leads V_1, V_2, or V_3 and ≥0.1 mV in other leads (contiguity in the frontal plane is defined by the lead sequence aVL, I, inverted aVR, II, aVF, III).

No ST segment elevation (NSTEMI)

a. ST segment depression

b. T wave abnormalities only

New or presumed new ST segment depression or T wave abnormalities, or both, should be observed in two or more contiguous leads. Also, new or presumed new symmetric inversion of T waves ≥1 mm should be present in at least two contiguous leads.

Q-wave

Any Q wave in leads V_1 through V_3, Q wave > or = to 30 ms (0.03 s) in leads I, II, aVL, aVF, V_4, V_5, or V_6. (The Q wave changes must be present in any two contiguous leads, and be > or = to 1 mm in depth.)

Variable Definitions

For the main analyses patients were classified by ECG's (as read one at a time blindly) as: 1)STEMI or NSTEMI; 2) Q wave or non-Q wave. Patients admitted into the hospitals with

a Q wave were excluded from the analysis if the Q was present in the same location on the first ECG.

Abnormal level of CK-MB and troponins followed the laboratory standard in each hospital. Patients discharged in 1999-2002 were categorized into four groups by level of troponins and CK-MB: 1) Abnormal troponin and CK-MB [Tn (+), CK-MB (+)]; 2) Abnormal troponin and normal CK-MB [Tn (+), CK-MB (-)]; 3) Normal troponin and abnormal CK-MB [Tn (-), CK-MB (+)]; 4) normal troponin and CK-MB [Tn (-), CK-MB (-)]. Patients discharged in 1990-1993 were categorized into 1) CK-MB (+); 2) CK-MB(-) since level of troponin were most likely unavailable.

Patients were coded as having diabetes mellitus, hypertension, or hyperlipidemia if the conditions were recorded in the written history or if patients took related medication before hospitalization. Other risk factors were defined as: 1) body mass index (BMI); 2) smoker (present or past). When risk factors were not recorded in the charts, the patient was grouped into “no” or “never” category during analysis. We also abstracted patients’ gender, age, race and insurance status (commercial, medicare/Medicaid, uninsured), and the discharge diagnostic code from the MIDAS dataset.

Statistical Analysis

All analyses were conducted using SAS (SAS Institute, Cary, NC). Descriptive analyses were focus on percentages to describe ECG characteristics by calendar year. We compared the two time periods, 1990-1993 and 2001-2004, as the primary focus. Data were summarized as frequencies and percentages for categorical variables. Continuous variables were presented as medians or means.

We accessed the differences in proportion of these with STEMI and those with new Q waves between the two calendar periods. We compared demographics, risk factors, medical history, use of revascularization, enzyme categories, Q wave, and medications for STEMI and NSTEMI patients within each period. Chi-square test or Fisher's exact test for categorical data was used to test statistical significant of categorical data and the Wilcoxon rank-sum test was used similarly for continuous data. We measured the time from symptom onset to the first ECG during the two time periods to check for any systematic secular change between the two periods that could be a said of bias. Second, the percentage of patients defined by abnormal troponin and normal CK-MB [Tn (+), CK-MB (-)] was estimated. By diagnostic code 410.7, the percentage of these patients that had evolving Q wave in ECGs was also reported. We compared the percentage of

non-Q-wave patients that had a primary discharge diagnostic code 410.7 between two time periods.

Other analyses examined whether there were any important differences between charts not available for review and those successfully reviewed in discharge diagnoses or demographic variables recorded in MIDAS.

Results

For 1990-1993 and 2001-2004, we reviewed hospitalization records of 416 patients. Compared to all MI discharges from two contributing hospitals in MIDAS, our samples in 1990-1993 were more likely to be male, older and to have higher case-fatality; the sampled records in 2001-2004 were more likely to be women, and more likely to have higher 1 year case-fatality than overall MIDAS (Table 3-1). Because these differences were small, we did not do any adjustments for them. Of these 416 patients, 35 patients were excluded due to ECG's that were uninterpretable for ST segment elevation , such as patients with pace maker, left bundle branch block (LBBB), right bundle branch block (RBBB) or poor quality of ECGs. A total of 381 patients, 190 from 1990-1993 and 191 from 2001-2004, were reviewed to examine whether the increase in the discharge code 410.7 (subendocardial MI) was accompanied by the expected changes in ECG's and enzyme evidence.

Results showed that 51% of patients presents with ST segment elevation in their ECG during a hospitalization in 1990-1993 compared to only 24% in 2001-2004 (Table 3-2). Also, the percentage of patients presenting with ST segment depression or T wave abnormanities was lower in 2001-2004. The proportion of patients developing a new Q wave during hospitalization was 31% in 1990 -1993 compared to 19% in 2001-2004 and they were higher among STEMI patients in both time periods. The results are very similar even if MI's confirmed only by troponins are excluded from the second time period. Proportion of male patients decreased from 61.1% in 1990-1993 to 53.9% in 2001-2003. It decreased from 63.6% to 50% among STEMI patients and changed only slightly from 58.5% to 55.2% among NSTEMI patients. Compared to patients in the first time period, there were fewer current smokers, but more former smokers in second time period. Among STEMI patents, there were more patients who were either current or former smokers, compared to NSTEMI, in both time periods. Patients' mean cholesterol level declined from 201.4 in 1990-1993 to 177.5 in 2001-2004. This decrease was observed in both STEMI and NSTEMI patients. The percentage of patients who had diabetes or hypertension was higher in the later calendar period, but these increases were likely due to changes in the definition of those conditions. The increased trend in diabetics was observed in NSTEMI patients only.

As shown in Table 3-3, there were 22 patients documented by troponins, which were about 8.9% of total patients in 2001-2004. Of these, 17 patients (16 NSTEMI and 1 STEMI) were documented by troponins only and did not develop a pathologic Q wave in

their ECGs during hospitalization. There were 51 more NSTEMI patients in the second time period, an increase from 94 in 1990-1993 to 145 in 2001-2004. The 16 NSTEMI patients documented by positive troponins only, contributed to 31.4% of the total increase in NSTEMI from 1990-1993 to 2001-2004.

The percentage of patients developing a Q wave MI declined from 34% in 1990-1993 to 23% in 2001-2004. In Figure 3-1, the percentages developing Q waves were compared between patients who had procedures (either PCI of CABG) and those who did not. During 1990-1992, there were only 20 patients having a procedure in the same hospitalization, and 10% of them developed Q wave within 7 days of admission. This compared to 57 patients in 2001-2004 having procedures during the same hospitalization, of whom 25% developed Q wave within 7 days. In contrast, among patients not having a procedure during hospitalization, the percentage developing Q wave decreased from 27% (47 out of 172) to 16% (22 out of 134) for the two time periods ($P<.05$). Among patients without procedures, the decline in the percentage developing a Q wave in ECG demonstrated changes of AMI presentation over time. In the second time period, the proportion of patients who underwent either PCI or CABG during hospitalization nearly tripled, but the increase in Q wave occurrence following there procedures suggests that less stringent criteria were used in the second time period. The decrease in percentage of those developing Q wave between the two time periods was mostly attributed to the decline among patients not having procedure in the same hospitalization.

Medications taken prior to hospitalization, in-hospital and at discharge is shown in Table 3-5. Prior to admission, aspirin was taken by 9.47% of patients in 1990-1993 and by 25.65% in 2001-2004. Beta-blockers were taken by 15.26% and by 23.04% in these time periods, respectively. Lipid lowing agents were taken by 3.68% of patients in 1990-1993 and by 27.75% in 2001-2004. Overall, medications were administered to more patients in the second time period. However, within the same calendar period, there was no difference in medication use between STEMI and NSTEMI. At hospital discharge, the rate of the use of aspirin, beta-blocker, ACE-inhibitors and lipid lowing agents increased relative to their use at admission in both the STEMI and NSTEMI population.

ECGs were categorized into two groups 1) STEMI or Q wave MI, and 2) neither. The correspondence of ECG and discharge code was examined by Kappa statistic. In 1990-1993, two thirds of patients presented with either STEMI or Q wave in their ECGs but this declined to one third in 2001-2004 (Table 3-4). The changing presentation of patients was prominent. However, the agreement between ECG finding and discharge code was only fair. With a kappa of 0.41 (95% CI: 0.27-0.56) in 1990-1993 and 0.37 (95% CI: 0.23-0.51) in 2001-2004. Despite the lack of good case by case agreement between the presence of Q waves and low STEMI and specified location MI at discharge, both methods of classifying MI's showed a major shift between two time periods. The proportion of MIs with Q wave or STEMI fell from 65% to 26% across time periods, while the proportion with a specified location MI fell from 74% to 34%.

Discussion

The results of this chart review study confirm our findings of secular change in acute MI from the MIDAS data set. There has been a substantial change in ECG presentation from ST elevation and Q wave toward subendocardial infarction. Our results found a 27% decline in STEMI patients while the decrease in Q wave patients was only 12%. The larger decline in patients presenting ST elevation in their ECG may indicate that the changing manifestation of the coronary heart disease has been primarily contributed by the reduction of traditional CHD risk factors[19-22], which would be expected to diminish the severity of atherosclerosis in the larger coronary vessels. Results from the ARIC study which examined the severity of AMI from 1987 to 1994 provided mixed support for a decrease in MI severity with worsening ECG indicators, but improving enzymatic indicators [31]. However, we included patients after 1994, which was after the widespread introduction of statins. The decrease in mean total cholesterol level and a large increase in use of lipid lowering agent prior to hospitalization in the second time period were prominent and they may have contributed most to this change after 1994. The change is not easily to be explained by the increasing use of revascularization since ST segment elevation is usually observed on the first ECG during hospitalization. The decrease in percentage developing Q wave was observed in the group of patients not undergoing procedures as well.

Our results are not much explained by the contribution of troponins to the increasing incidence of subendocardial infarction. In our review of 191 patient records in 2001-

2004, only 17 patients were documented by troponins only, which is only a modest part of the two fold increase that we observed in MIDAS data set. However, almost all cases documented by troponins only were NSTEMI, which contributed one-third of the overall increase we found for NSTEMI in the second time period. Nearly 88% (14 out of 16) of them were discharged as subendocardial infarction.

The shift in ECG presentation from STEMI to NSTEMI in this random sample over time was substantial and this change supports the validity of our findings for a the shift from transmural MI to subendocardial MI that we observed in the discharge data set, although we did not find a perfect agreement between discharge code and ECG finding. However, discharge coding practice could have introduced bias by coding patients with STEMI but not Q waves with response to a specific anatomic location rather than subendocardial MI. This would underestimate the proportion of subendocardial infarction, especially in recent years. It is generally agreed that the reduction in risk factors have contributed to the decline in CHD, but the role of risk factor change in reducing case-fatality through changes in the severity of AMI has not been proven. The introduction of troponins in the second period added to the proportion of mild MIs that were detected, which were mostly NSTEMI and did not develop Q waves. Perhaps this was because the same patients with subendocardial infarction would have developed Q waves had they not been revascularized.

In conclusion, this review of a sample of 381 medical charts for AMI events recorded in MIDAS reflects the main MIDAS data set in showing a subendocardial decline in

specified location discharge codes (410.1-410.6) and a corresponding increase in subendocardial codes (410.7). A parallel decrease in Q waves was seen in the overall sample, in patients discharged with a specified location and in those not receiving revascularization procedures. Troponins made only a small contribution to this increase in subendocardial MI. Finally, we found a substantial increase in the use of aspirins, anticoagulatants, beta-blocker and statins among patients admitted with AMI.

These chart review strongly suggest that the major secular changes in AMI presentation seen in MIDAS represent a biological change and are not due to diagnostic or coding shifts.

Table 3-1 Comparison of characteristics of sample selected for medical record review with all MI discharges in two New Jersey hospitals.

		1990-1993		2001-2004	
		Sample	MIDAS*	Sample	MIDAS*
	N	203	1123	213	1252
Sex					
	Female	37.93%	42.30%	46.48%	42.01%
	Male	62.07%	57.70%	53.52%	57.99%
Age					
	55-64	25.62%	27.60%	28.64%	27.16%
	65-74	39.41%	39.45%	32.86%	33.47%
	75-84	34.98%	32.95%	38.50%	39.38%
Discharge Code	4101-4106	65.52%	62.15%	29.58%	31.47%
	4107	24.14%	29.47%	64.79%	64.14%
	4108-4109	10.34%	8.37%	5.63%	4.39%
Case-fatality					
	30 days	14.78%	12.38%	10.80%	9.90%
	1 year	25.62%	21.55%	22.07%	18.93%

* Total MI admission in two selected hospitals

Table 3-2 Distribution of demographics, coronary heart disease risk factors and ECG characteristics by status of STEMI and year

	Total			STEMI			NSTEMI		
	1990-1993	2001-2004	P-value*	1990-1993	2001-2004	P-value	1990-1993	2001-2004	P-value
N	190	191		96	46		94	145	
Demographics									
Men (%)	61.1 %	53.9 %	0.031	63.6 %	50 %	0.146	58.5 %	55.2 %	0.689
Median Age for men	68	66	0.153	68	64	0.106	70	67	0.390
Median age for women	74	74	0.777	74	73	0.412	74	74	0.667
Mean BMI	26.29	27.77	0.018	26.22	28.08	0.007	26.36	27.67	0.409
CHD risk factors									
Smoking									
current	29.5 %	18.8 %	0.028	33.3 %	21.7 %	0.242	25.5 %	17.9 %	0.246
former	26.8 %	36.1 %		27.1 %	39.1 %		26.6 %	35.2 %	
Diabetes	30 %	34 %	0.061	31.3 %	28.3 %	0.846	28.7 %	35.9 %	0.323
Hypertension	54.2 %	67.5 %	0.002	55.2 %	63 %	0.468	53.2 %	69 %	0.018
Mean cholesterol	201.4	177.5	<.0001	199.8	168	0.004	203.1	180.2	<.0001
Mean LDL	-	102.27		-	100.31		-	102.83	
Mean HDL	-	43.17		-	46.21		-	42.3	
ECG characteristics									
Q-wave	31.1 %	18.8 %	0.002	38.5 %	30.4 %	0.455	23.4 %	15.2 %	0.125
ST-depression	55.8 %	40.8 %	0.001	66.7 %	56.5 %	0.267	44.7 %	35.9 %	0.179
T abnormanalities	70.5 %	57.6 %	0.003	71.9 %	63 %	0.334	69.1 %	55.9 %	0.043
ST-elevation	50.5 %	24.1 %	<.0001						

* p-value from fisher exact test for categorical variables and Wilcoxon rank test for continuous variables

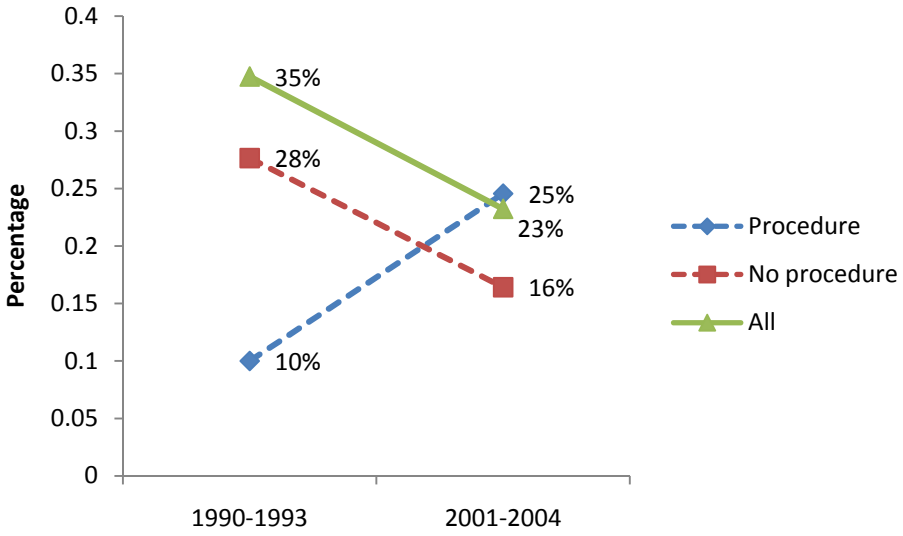
Table 3-3 Distribution of enzymatic indicators by status of STEMI and year

	1990-1993			2001-2004		
	Total	STEMI	NSTEMI	Total	STEMI	NSTEMI
Total	**190**	**96**	**94**	**191**	**46**	**145**
CK(+) Tn(+)				152	40	112
CK(+) Tn(-)				7	1	6
CK(-) Tn(+)	2	1	1	22	2	20
CK(-) Tn(-)				5	1	4
CK(+)	162	81	81	3	1	2
CK(-)	26	14	12	2	1	1

Table 3-4 Distribution of ECG reading and discharge diagnosis code by year.

	Discharge Code	ECG					
		STEMI or Q	Neither	Total	Kappa	Sensitivity	Specificity
1990-1993	4101-4106	97	29	126	0.41 (0.27-0.56)	87.4%	51.7%
	4107	14	31	45			
		111	60	171			
2001-2004	4101-4106	37	24	61	0.37 (0.23-0.51)	56.9%	79.5%
	4107	28	93	121			
		65	117	182			

Figure 3-1 Percentage developing Q wave by status of procedure in 1990-1993 and 2001-2004.



	1990-1993		2001-2004	
	Q	NQ	Q	NQ
All	49	141	36	155
no procedure	47	123	22	112
Procedure	2	18	14	43

Table 3-5 Percentage of medication use prior to admission, in hospital and at discharge

	All		STEMI		NSTEMI	
Prior	**1990-1993**	**2001-2004**	**1990-1993**	**2001-2004**	**1990-1993**	**2001-2004**
Aspirin	9.47%	25.65%	4.17%	28.26%	14.89%	24.83%
Plavix	-	5.76%	-	0.00%	-	7.59%
Anticoagulation	2.63%	8.38%	3.13%	8.70%	2.13%	8.28%
Beta-Blocker	15.26%	23.04%	17.71%	21.74%	12.77%	23.45%
ACE	11.58%	19.90%	12.50%	19.57%	10.64%	20.00%
Lipid	3.68%	27.75%	1.04%	15.22%	6.38%	31.72%
Thromboytic	1.58%	0.52%	3.13%	0.00%	0.00%	0.69%
Nitro	17.89%	8.90%	17.71%	4.35%	18.09%	10.34%
Calcium channel	24.74%	18.85%	19.79%	10.87%	29.79%	21.38%
In hospital						
Aspirin	73.68%	87.43%	81.25%	84.78%	65.96%	88.28%
Plavix	-	52.36%	-	54.35%	-	51.72%
Anticoagulation	66.84%	70.68%	73.96%	73.91%	59.57%	69.66%
Beta-Blocker	40.53%	71.73%	47.92%	69.57%	32.98%	72.41%
ACE	26.32%	41.88%	27.08%	32.61%	25.53%	44.83%
Lipid	4.21%	45.55%	2.08%	36.96%	6.38%	48.28%
Thromboytic	18.42%	5.24%	29.17%	15.22%	7.45%	2.07%
Nitro	92.63%	68.06%	94.79%	73.91%	90.43%	66.21%
Calcium	55.26%	20.94%	52.08%	8.70%	58.51%	24.83%
Discharge						
Aspirin	46.32%	68.59%	45.83%	60.87%	46.81%	71.03%
Plavix	-	51.31%	-	47.83%	-	52.41%
Anticoagulation	13.16%	15.71%	12.50%	19.57%	13.83%	14.48%
Beta-Blocker	31.58%	70.16%	34.38%	65.22%	28.72%	71.72%
ACE	18.95%	42.93%	14.58%	32.61%	23.40%	46.21%
Lipid	3.16%	50.26%	1.04%	36.96%	5.32%	54.48%
Thromboytic	1.58%	1.05%	2.08%	2.17%	1.06%	0.69%
Nitro	54.21%	32.46%	50.00%	26.09%	58.51%	34.48%
Calcium	40.53%	12.04%	32.29%	4.35%	48.94%	14.48%

Chapter 4. Changes in short term and long term mortality after acute myocardial infarction from 1990-2003 in New Jersey

Introduction

The prognosis following acute myocardial infarction (AMI) has improved since 1970[6, 7, 9, 12, 15]. The decline in AMI death rates has been attributed to the progress in primary and secondary prevention, including reduced coronary risk factors, effective cardiac medications and interventional cardiology [19, 21, 73]. Despite these encouraging changes, the magnitude of decline has been modest since 1990 and has differed by gender and age [74].

Because the decline in AMI incidence has been proportionally greater at younger ages, the average age at first MI has been increased. A growing proportion of AMI is occurring among women and diabetics. In addition, troponins, which have been widely used since the late 1990s, may identify a considerable new group of MI patients that might contribute to an altered average prognosis [75]. The above factors have been shown to be associated with AMI prognosis.

Most information about prognosis following AMI comes from subjects studies conducted before 2000 or relatively young study populations (typically excluding those over 75 years of age) [14, 19]. Moreover, few data describe the long-term prognosis of AMI patients after 2000. Given changing patient characteristics and diagnostic methods and criteria, we underlook a new study of short-term and long-term case-fatality following first AMI in New Jersey from 1990 to 2004. We sought to evaluate the effect of key factors known to influence survival: age, diabetes and interventional procedures.

Methods

Data Sources

The data for this study were obtained from the Myocardial Infarction Data Acquisition System (MIDAS) [12, 60-62]. MIDAS contains information abstracted from hospital discharge summaries of patients discharged from New Jersey non-federal acute care hospitals with a primary diagnosis of AMI (International Classification of Disease 9th Revision (ICD-9) 410.0-410.9). The database also includes all hospitalization records with any invasive cardiac procedures, cardiac catheterization, percutanuous cardiovascular Intervention (PCI), and coronary artery bypass graft surgery (CABG). Each patient's discharge records were linked across the study period. The patient's initial admission for AMI during the study period was defined as the index admission.

Vital status of subjects who were discharged alive from the hospital was determined by linkage of the MIDAS records with New Jersey death registration, using AUTOMATCH-Generalized Record Linkage System, Version 3.0.[63, 64] The method of determining the sensitivity and specificity of this probabilistic record linkage procedure has been described in a previous report and was found to be 98% and 99%, respectively[65]. All subjects were matched up to year 2004 and the longest follow-up time was 15 years. The analyses in this study were confined to patients discharged between January 1990 and December 2003. This allowed patients to be followed up for a minimum of 1 year.

Study variables

The primary outcome variable was cause-specific death. Cause of death was determined from NJ death registration data which including cardiovascular disease deaths (ICD-9 code 390-459 and ICD-10 code I00-I25) and others. AMI patients' case-fatality was examined by infarction type (QW vs. NQW), presence of diabetes and calendar year. The QW, NQW AMI and diabetes were defined by the discharge diagnosis code (QW: 410.0-410.6, NQW: 410.7, Diabetes: 250).

The primary independent variables were calendar year of admission, MI type (QW vs. NQW), and diabetes. Covariates included the presence or absence of comorbidities, including hypertension, chronic obstructive pulmonary disease, chronic liver disease, chronic renal disease, anemia, cerebrovascular disease, and cancer, arrhythmia, left ventricular dysfunction as well as the use of catheterization, PCI and CABG up to 30 days from the date of admission (including procedures performed during a subsequent admission within 30 days). Detailed definition of variables has been described elsewhere [62].

Statistical method

Temporal trends in survival following first MI over the 14 year study period were compared by using the Cox Proportional Hazard model to estimate the survival experience after controlling for the effect of age. The 14 individual study years were aggregated into three periods for analysis (1990-1994, 1995-1999, and 2000-2003) by length of follow-up time for ease of presentation.

Cause-specific standardized case-fatality in 30 days, 1 year and 4 year were examined by type of MI and diabetes. All rates were adjusted by the direct method to the age structure of 1990-1992 MIDAS population. Multiple logistic regression analyses were conducted to examine changes over time in 30 day, 1 year and 4 year case-fatality. The confounders included age, gender, race, diabetes, hypertension, renal disease, anemia, cancer, cerebrovascular disease, type of insurance, severity, type of hospital and hospital area.

Temporal trends in the distribution of demographic, clinical and treatment characteristics in hospitalized patients were studied separately for diabetics and non-diabetics. The risk of dying in 30 days, 1 year and 4 year among patients with and without diabetes were examined by multiple logistic regression analysis. Due to the high correlation of diabetes with other coexisting conditions during hospitalization, only age, gender and race were included in the model.

All statistical analyses were performed by using SAS 9.0 (SAS Institute, Cary, NC). The study was approved by the State of New Jersey Department of Health and Senior Services and the Robert Wood Johnson Medical School Institutional Review Boards.

Results

All cause and Cardiovascular Disease Death

This study includes 222,944subjects from 1990 to 2004 discharged with a primary diagnosis of AMI in New Jersey. Figure 4-1 shows the temporal trends in age-adjusted

long-term survival of hospitalized patients following initial AMI. About 20% of AMI patients died within 12 months after admission. Another 15% of patients died in 5 year after an AMI. The one year survival rate hardly changed over the study periods; 82% for patients hospitalized in 1990-1994, 82% in 1995-1999 and 81% in 2000-2004. The five year survival rate was 68% in 1990-1994 and 66% in 1995-1999. The 10 year survival rate was 50% for patients hospitalized during 1990 to 1994. During the 15 year study period, age-adjusted overall survival rate declined over time; however, the cardiovascular death rate improved. Approximately 80% of deaths in 1 year were cardiovascular disease deaths and 68% of deaths at 4 year and 10 year were cardiovascular deaths. The proportion of AMI patients who died from non cardiovascular causes increased from 4% for patients hospitalized in 1990-1994, 6% in 1995-1999 to 8% in 2000-2004 after 1 year even after controlling for the effect of age.

Table 4-1 presents the secular change in age-adjusted case-fatality rates from all cause, cardiovascular disease death and non-cardiovascular disease following acute myocardial infarction. The all cause 30-day case-fatality decreased from 14.65% in 1990 to 9.76% in 2004; one-year case-fatality decreased from 22.93% to 19.33%, while the 4 year all cause case-fatality was steady during study period. There was a decline in cardiovascular disease case-fatality in each of the follow-up periods, but it was offset by the increase in non cardiovascular deaths. The NCVD-case-fatality increased by 0.64%, 3.15% and 5.37% for 30 day, 1 year and 4 year, respectively.

Transmural and Subendocardial infarction

The decrease in CVD case-fatality and increase in NCVD case-fatality were observed in patients both with transmural and subendocardial infarctions but in different magnitude (Table 4-2). Compared to a steeper decrease in CVD deaths among transmural infarction patients, a modest decrease was found among subendocardial infarction patients. The 30 day age-adjusted CVD case-fatality decreased from 1990 to 2004 by 25%, by 27% at 1 year from 1990 to 2003 and by 23% at 4 years from 1990 to 2000 among patients with a transmural infarction. From 1990-2004, the age-adjusted , among subendocardial infarction patients, a slight increase by 11.1% in 30 days, and a decrease by 7.4% in 1 year and 0.2% in 4 year were observed. In contrast, the NCVD case-fatality was increased by 167% in 30 days, by 64% in 1 year and by 54% in 4 year among transmural infarction patients, and by 293% in 30 days, by 103% in 1 year and by 61% in 4 year among subendocardial patients.

Patient characteristics by diabetic status

During 1990-2003, there were 60,692 diabetics and 162,252 non-diabetics in our study. The proportion of acute MI patients who had diabetes as a coexisting condition during hospitalization increased from 25.02% in 1990-1993 to 29.95% in 2002-2004. This constituted 12% overall increase which ranged between 16 and 21% in different age groups. The largest increase was found in the age group 55-64, which increased from 26% in 1990-1991 to 32% in 2002-2003. Generally, AMI patients who had diabetes were more likely to be female and less likely to develop Q-waves than were those without diabetes during hospitalization (Table 4-3). Diabetic patients had higher

prevalence of hypertension, renal disease, anemia and cerebrovascular disease than non-diabetic patients and the prevalence of above conditions increased over time. Moreover, diabetics had more left ventricular dysfunction but less arrhythmia.

Diabetetes and Subendocardial Infarction

The trend in age-adjusted case-fatality was examined separately in four strata: subendocardial infarction patients with or without diabetes and transmural infarction patients with or without diabetes. These strata were used to explore the association between increasing prevalence in diabetes and lack of improvement in CVD death among subendocardial MI patients during study period (Figure 4-2). In the short term, patients with transmural MI had higher case-fatality rate than those with subendocardial MI regardless of diabetes. In the long-term, the difference in case-fatality between patients with and without diabetes was more prominent. The decrease in CVD case-fatality was found in both diabetic and non-diabetic among patients with transmural MI at every follow-up time. Among subendocardial patients, the increased mortality in diabetics appeared mainly after 1 year. At four years, case-fatality among diabetic patients with subendocardial MI was close to diabetic patients with transmural MI. Long-term prognosis through 7 and 10 years was more strongly influenced by diabetes than type of MI. We observed similar relationship between diabetes and patient prognosis in all-cause case-fatality among these four groups. The impact of diabetes was stronger for all cause case-fatality than for CVD case-fatality, which

implied that diabetes increase the risk of dying not only from CVD but also in NCVD in long-term.

Odds Ratios from a multiple logistic regression, adjusting for sex, age and race, showed a consistently higher risk of dying among diabetics than non-diabetics during the study period (Table 4-4). Diabetics had 65% greater risk of dying by 4 years than non-diabetics after controlling the effect of age, gender and race. During the 15 year study period, the prevalence of diabetes was 26.5% on average. The population attributable risk suggested that the proportion of deaths following AMI in 4 years explained by diabetes was 14.7%.

Revascularization

CVD case-fatality among patients with or without receiving cardiac revascularization (PCI or CABG) within 30 days was compared. Age-adjusted CVD case-fatality was 15% higher among patients who did not receive revascularization (PCI or CABG) within 30 days than in those who received procedures. This high risk was saw at 30 days through 4 years follow-up. This suggests that the expansion of utilization of cardiac procedures over time was positively associated with reduction in CVD death in AMI patients.

Discussion

Between 1990 and 2004, short-term and long-term CVD case-fatality following first AMI admission fell steeply after adjusting for age. These decreases observed in our study were consistent with other US studies [13, 15-17]done in 1990s earlier. We found that

for 30 day and one year case-fatality decline continued through 2004. Most studies also reported a decline in long-term all cause mortality following MI. In contrast, we only observed a decrease in CVD mortality not in four year all cause mortality. Three factors might explain this difference. In MIDAS, we included every patients older than 35 years of age and did not exclude the elderly, which was not common in other studies[14, 15, 19]. Our follow up time is longer than other studies [7]. Finally, MIDAS includes cases occurring after 1998, when the increase in NCVD mortality became more prominent.

Our data was consistent with the suggestion that modern medical treatments have had an important impact on reducing death. The improvements in short-term case-fatality suggested the importance of new technologies, primarily angioplasty and stent placement which were rare before 1990[6, 14, 76-78]. Pharmacological therapy including ACE inhibitors and aspirin may also play a role [52, 76]. In addition, we found a steady decline in recurrence of infarction during the study period (data not shown) which is consistent with the longer term benefit of the pharmacologic interventions or with effectiveness of reperfusion therapies.

While newer interventions are an obvious likely explanation for improved survival following AMI, we argued in chapter 1 that there is also substantial evidence that the underlying disease profile has become less severe. This is evidenced by a substantial drop in ischemia and other heart diseases declined over the study period, with most of the decline occurring in persons who had not had a hospitalization for MI in many years or ever. In addition, among hospitalized MI there has been a swift toward

subendocardial infarction that are likely associated with smaller vessel diseases than are the previous more common transmural infarct. A swift in the underlying vascular pathology could also affect prognosis in the MI's that occur.

In the US and other countries, the population age-standardized coronary heart disease mortality has dropped almost continuously since 1970. Declines in out-of-hospital death have contributed the most [79-81]. In spite of the success in reducing out-of-hospital death, the AMI admission rate has not fallen as much. Perhaps some of the persons who previously would have died as outpatients are admitted to hospital with less severe infarctions of coronary disease. It is also likely that the increased sensitivity of diagnostic enzyme have led to the inclusion of milder AMI cases and resulted in decreasing CVD case-fatality [21, 54]. As noted in chapter 3, we think troponins have made only a modest contribution to coded MI incidence.

A large increase (81%) in four year age-adjusted NCVD mortality among AMI patients has offset the success in reducing CVD death, resulting in no improvement in all cause four year case-fatality during the study period. About 40% of these deaths occur in the first year and the rate of increase both in first year deaths and in deaths in year 2-4 appeared to accelerate after 1995.

We hypothesized that this increase might be due to an increased prevalence of diabetes which is a well established risk factor for cardiovascular mortality and morbidity, and has been increasing in prevalence [43, 83]. However, within MIDAS patients, there was only a 3.6 percent increase in prevalence of diabetes from 25.2% in 1990-1992 to 28.8%

in 2002-2004. Ford et al. studied the decline in US coronary heart disease death and reported that the reduction of death in coronary heart disease in the past two decades was partially offset by increases in body-mass-index and the prevalence of diabetes[27]. Ten percent of the CHD mortality was attributed to the increased prevalence of diabetes. Our result supports this suggestion and found a similar attributable risk of diabetes of 14.6%.

Given the increasing prevalence of diabetes over time, the impact of diabetes to the long-term prognosis of AMI patients will increase further. Moreover, the high case-fatality of diabetic subendocardial infarction patients after 30 days may partially explain the worse long term prognosis of patients with subedocardial infraction. The growth in the proportion of subendocardial infarction patients with worse prognosis may result in lack of improvement in AMI case-fatality in the future.

Figure 4-1 Age-adjusted All cause and CVD survival curves up to 10 years from acute myocardial infarction patients from 1990-2004.

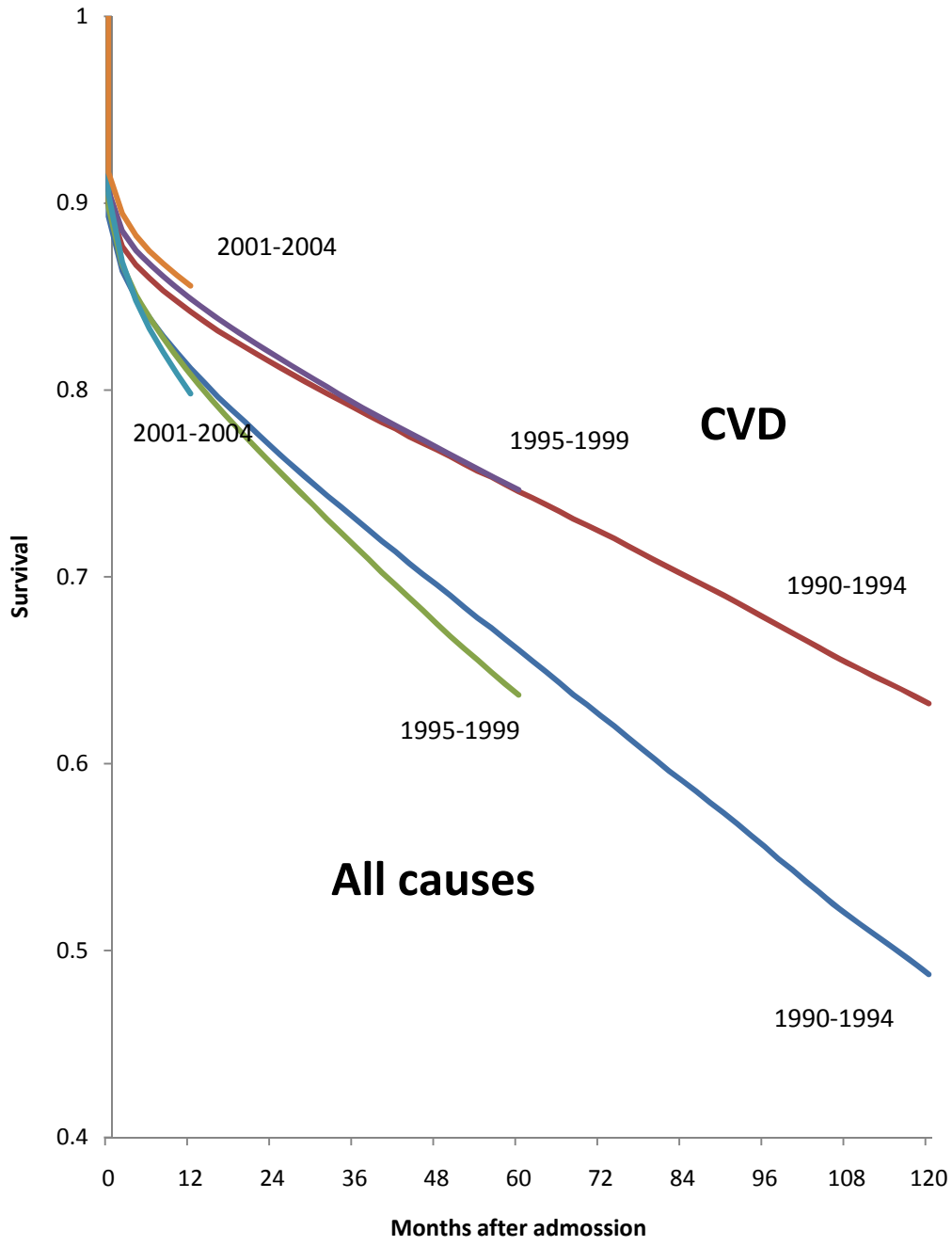


Table 4-1Age adjusted case-fatality in 30 days, 1 year and 4 year following acute myocardial infarction in New Jersey from 1990 to 2003.

	CVD			NCVD			all cause		
	30 day	**1 year**	**4 year**	**30 day**	**1 year**	**4 year**	**30 day**	**1 year**	**4 year**
1990	14.38%	20.31%	27.65%	0.27%	2.62%	6.66%	14.65%	22.93%	34.31%
1991	13.74%	19.95%	27.25%	0.30%	2.63%	7.07%	14.04%	22.57%	34.32%
1992	12.57%	19.02%	26.79%	0.32%	2.72%	7.30%	12.89%	21.74%	34.09%
1993	12.02%	18.36%	26.22%	0.32%	2.64%	7.60%	12.34%	21.00%	33.82%
1994	12.21%	18.35%	25.52%	0.32%	2.95%	8.08%	12.53%	21.30%	33.60%
1995	12.38%	18.05%	25.58%	0.37%	3.08%	8.38%	12.75%	21.13%	33.96%
1996	12.05%	17.77%	25.06%	0.55%	3.38%	8.79%	12.60%	21.15%	33.85%
1997	11.66%	17.36%	24.72%	0.62%	3.70%	9.20%	12.28%	21.06%	33.92%
1998	10.37%	16.08%	23.25%	0.53%	3.86%	10.22%	10.90%	19.94%	33.47%
1999	10.60%	16.81%	24.23%	0.80%	4.53%	11.13%	11.40%	21.34%	35.35%
2000	10.50%	16.33%	23.28%	0.71%	4.56%	11.37%	11.21%	20.89%	34.65%
2001	10.17%	16.59%	22.56%	0.89%	5.36%	12.03%	11.06%	21.95%	34.60%
2002	9.72%	15.19%		0.94%	5.71%		10.66%	20.90%	
2003	9.04%	14.94%		0.85%	5.52%		9.88%	20.46%	
2004	8.85%	13.56%		0.91%	5.77%		9.76%	19.33%	
Dif*	**-5.53%**	**-6.75%**	**-5.09%**	**0.64%**	**3.15%**	**5.37%**	**-4.89%**	**-3.60%**	**0.29%**

*difference between 1990 and 2004

Table 4-2 Age adjusted case-fatality in 30 days, 1 year and 4 year following acute myocardial infarction in New Jersey from 1990 to 2003 by type of MI.

		CVD		NCVD		All cause	
30 days		**Q**	**NQ**	**Q**	**NQ**	**Q**	**NQ**
	1990	15.7%	6.0%	0.2%	0.3%	15.9%	6.2%
	1991	15.3%	6.1%	0.3%	0.4%	15.6%	6.5%
	1992	13.9%	6.0%	0.3%	0.3%	14.2%	6.3%
	1993	13.4%	6.1%	0.4%	0.3%	13.8%	6.4%
	1994	13.6%	6.6%	0.3%	0.3%	13.9%	6.9%
	1995	13.7%	7.0%	0.3%	0.3%	14.1%	7.4%
	1996	13.7%	7.3%	0.5%	0.6%	14.2%	7.8%
	1997	13.3%	6.9%	0.6%	0.6%	13.9%	7.6%
	1998	12.1%	6.2%	0.5%	0.5%	12.6%	6.7%
	1999	12.6%	6.4%	0.7%	0.9%	13.3%	7.3%
	2000	12.6%	7.2%	0.5%	0.8%	13.1%	8.0%
	2001	12.7%	7.2%	0.7%	0.9%	13.4%	8.2%
	2002	11.8%	7.4%	0.7%	1.0%	12.5%	8.4%
	2003	10.3%	7.2%	0.5%	1.0%	10.8%	8.2%
	2004	11.7%	6.6%	0.6%	1.1%	12.4%	7.7%
		-25.2%	**11.1%**	**167.3%**	**293.1%**	**-22.2%**	**23.2%**

		CVD		NCVD		All cause	
1 year		**Q**	**NQ**	**Q**	**NQ**	**Q**	**NQ**
	1990	20.9%	12.9%	2.2%	3.4%	23.1%	16.3%
	1991	20.8%	13.3%	2.1%	3.5%	22.9%	16.8%
	1992	19.4%	13.8%	2.3%	3.7%	21.7%	17.5%
	1993	18.8%	13.7%	2.2%	3.4%	21.0%	17.2%
	1994	18.7%	13.9%	2.5%	3.8%	21.2%	17.7%
	1995	18.8%	13.5%	2.5%	4.0%	21.3%	17.5%
	1996	18.3%	14.0%	2.8%	4.3%	21.1%	18.4%
	1997	17.6%	14.4%	2.8%	5.0%	20.4%	19.4%
	1998	16.7%	12.9%	3.0%	4.7%	19.7%	17.7%
	1999	17.5%	13.4%	3.2%	5.6%	20.8%	19.0%
	2000	17.0%	13.8%	3.4%	5.4%	20.4%	19.2%
	2001	17.2%	14.7%	3.6%	6.6%	20.7%	21.3%
	2002	15.5%	13.9%	4.1%	6.6%	19.6%	20.5%
	2003	14.7%	13.8%	3.9%	6.5%	18.6%	20.3%
	2004	15.3%	11.9%	3.6%	6.9%	18.9%	18.9%
		-27.0%	**-7.4%**	**63.9%**	**103.3%**	**-18.3%**	**15.8%**

Table 4-2 Age adjusted case-fatality in 30 days, 1 year and 4 year following acute myocardial infarction in New Jersey from 1990 to 2003 by type of MI.

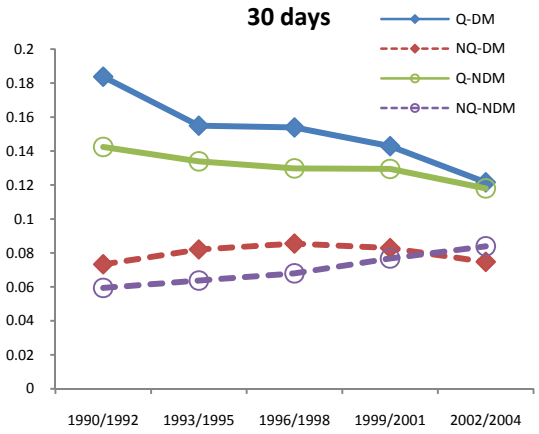
		CVD		NCVD		All cause	
4 year		**Q**	**NQ**	**Q**	**NQ**	**Q**	**NQ**
	1990	27.4%	22.2%	5.8%	9.0%	33.1%	31.1%
	1991	27.3%	22.5%	6.0%	9.0%	33.3%	31.5%
	1992	26.1%	23.6%	6.8%	8.9%	32.9%	32.4%
	1993	25.6%	23.2%	6.8%	9.3%	32.4%	32.5%
	1994	25.0%	22.6%	6.7%	10.6%	31.7%	33.2%
	1995	25.1%	22.9%	7.0%	10.8%	32.1%	33.7%
	1996	23.9%	23.9%	7.5%	10.7%	31.4%	34.6%
	1997	23.6%	23.8%	7.3%	12.0%	30.8%	35.7%
	1998	22.5%	21.4%	8.7%	12.2%	31.2%	33.6%
	1999	22.9%	22.5%	8.7%	13.6%	31.6%	36.1%
	2000	22.1%	22.1%	8.7%	13.7%	30.8%	35.8%
	2001	21.2%	22.1%	8.9%	14.4%	30.0%	36.5%
		-22.7%	**-0.2%**	**53.9%**	**60.7%**	**-9.4%**	**17.3%**

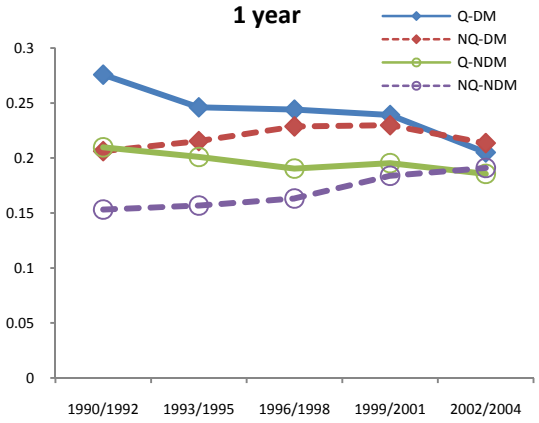
Table 4-3 AMI patient characteristics by diabetes and year

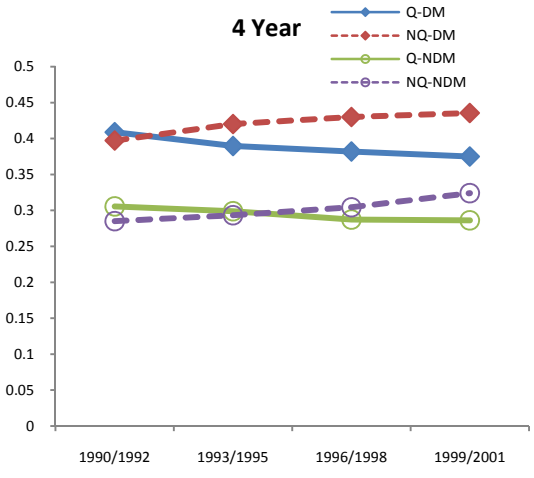
	Diabetics			Non-Diabetics		
	1990/1994	**1995/1999**	**2000/2004**	**1990/1994**	**1995/1999**	**2000/2004**
	n=17447	n=20591	n=22654	n=51384	n=54713	n=56155
Characteristic						
Female	47.18%	46.57%	45.15%	37.89%	39.20%	41.32%
Race						
white	81.54%	81.68%	76.44%	87.08%	86.50%	82.30%
black	10.13%	10.24%	10.97%	6.58%	6.38%	7.07%
others	8.33%	8.09%	12.58%	6.33%	7.11%	10.63%
Age						
Median age	69	71	71	69	70	72
35-54	12.56%	12.42%	12.32%	19.35%	19.14%	18.30%
55-64	21.40%	19.74%	20.18%	20.06%	17.82%	17.46%
65-74	34.37%	30.87%	27.04%	26.91%	23.99%	19.92%
75-84	24.90%	27.70%	28.82%	23.49%	25.47%	26.52%
85+	6.76%	9.27%	11.64%	10.18%	13.57%	17.80%
MI type						
Q-wave	58.71%	47.67%	29.88%	65.01%	55.93%	38.53%
Non-Q-wave	31.74%	44.57%	62.17%	26.42%	36.90%	53.63%
Co-morbidity						
Hypertension	49.78%	57.96%	65.73%	37.52%	45.01%	51.82%
Renal disease	8.12%	10.08%	11.33%	3.82%	4.90%	7.49%
Anemia	10.72%	11.91%	15.04%	10.33%	10.87%	12.71%
Cancer	1.93%	2.25%	2.98%	2.29%	2.97%	3.55%
Cerebrovascular Dx	5.62%	6.16%	5.73%	4.71%	4.80%	4.97%
Complication						
ARRH	18.78%	16.40%	14.66%	25.78%	23.32%	20.09%
LVD	23.88%	26.05%	27.39%	13.64%	14.50%	15.84%
ARRH and LVD	17.99%	16.10%	14.16%	16.09%	15.16%	15.27%
Procedure						
CATH	40.64%	48.70%	55.88%	45.42%	52.19%	58.08%
PCI	12.27%	20.98%	30.31%	16.56%	27.17%	36.04%
CABG	10.73%	14.31%	14.68%	10.02%	12.32%	11.86%

Figure 4-2 Acute myocardial infarction patients age-adjusted all cause and CVD case – fatality in 30 days, 1-year, 4-year, 7-year and 10-year by type of MI and Diabetes from 1990 to 2003.

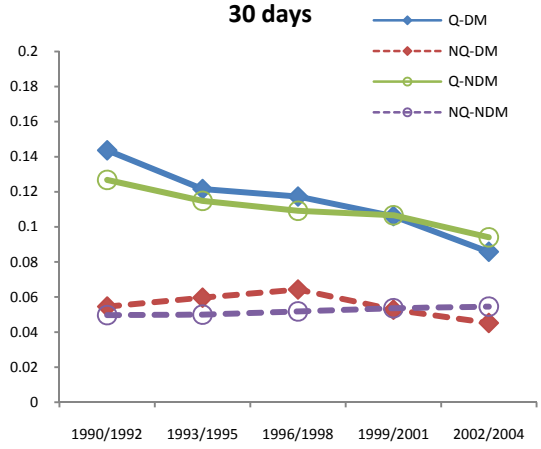
ALL CAUSES

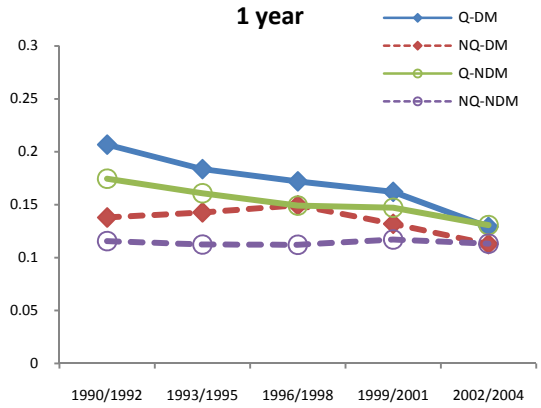






CVD





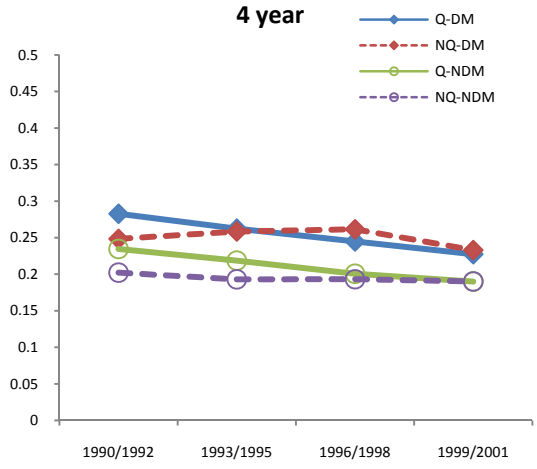
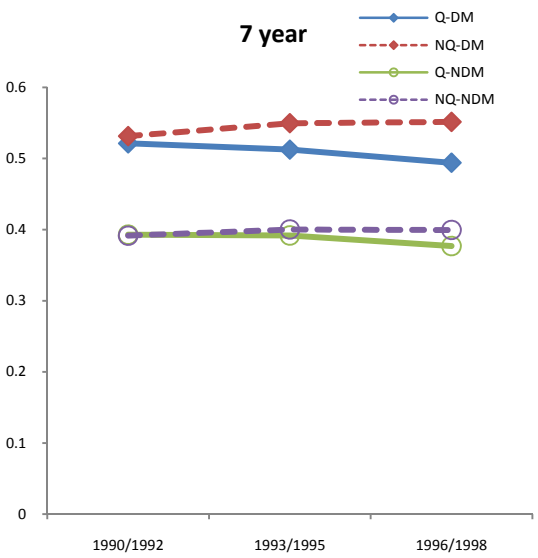
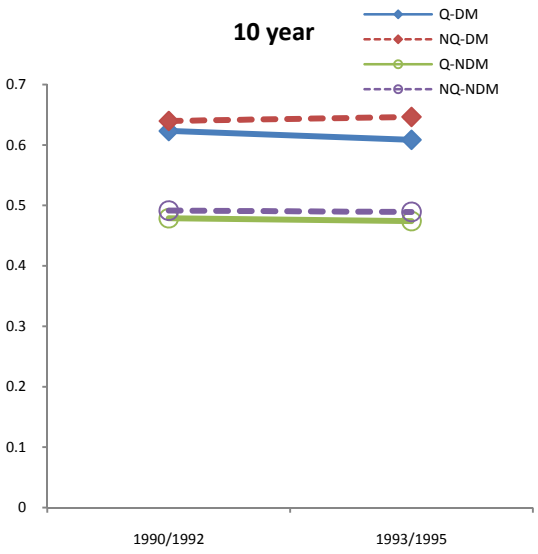


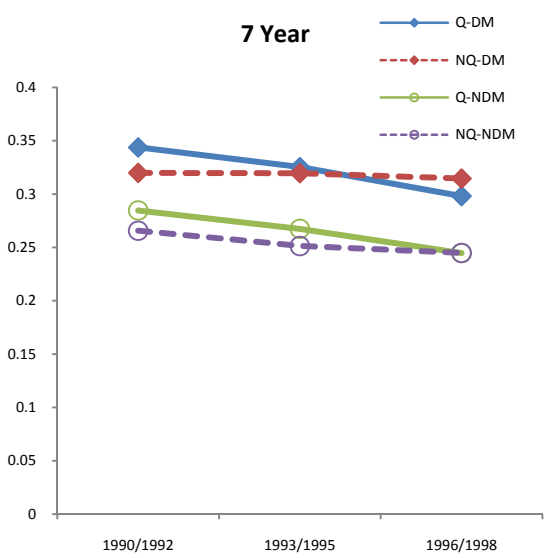
Figure 4-2 Acute myocardial infarction patients age-adjusted all cause and CVD case – fatality in 30 days, 1-year, 4-year, 7-year and 10-year by type of MI and Diabetes from 1990 to 2003.

All Cause





CVD



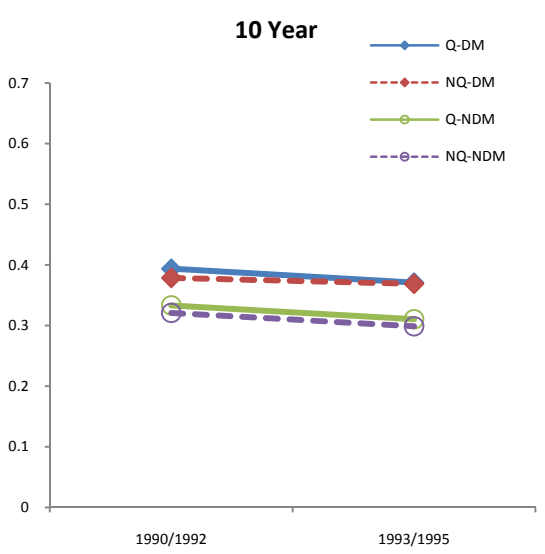


Table 4-4 Adjusted odds ratio of dying in CVD or NCVD in 30 days, 1 year and 4 year in Diabetics vs. non-diabetics by year, adjusted for sex, age and race

	CVD	NCVD
	30 days	
	OR	OR
1990/1992	1.10*	2.45*
1993/1995	1.00	2.06*
1996/1998	1.03	1.60*
1999/2001	0.90*	1.40*
2002/2004	0.82*	1.01*
	1 year	
	OR	OR
1990/1992	1.24*	2.00*
1993/1995	1.16*	1.81*
1996/1998	1.20*	1.73*
1999/2001	1.08*	1.53*
2002/2004	0.94*	1.27*
	4 year	
	OR	OR
1990/1992	1.35*	1.90*
1993/1995	1.30*	1.79*
1996/1998	1.35*	1.70*
1999/2001	1.24*	1.59*

* p-value <0.05

Chapter 5. Conclusion

The results of this population–based study confirm the continuing decline in CHD mortality [66] and demonstrated a shift in AMI patients' demographic and clinical profiles. In New Jersey, the CHD mortality dropped by 40% from 1990 to 2004. Most of the decrease has occurred in persons who did not have an in-state hospitalization for AMI in the previous four years or even in the preceding 12 years.

Among patients presenting with MI, there has been a remarkable change in clinical presentation from events characterized by ST elevation and the development of Q waves toward events characterized as subendocardial MI's that are mainly confirmed by blood enzyme levels and do not have these pathonomonic ECG characteristics. These trends are related to changes in known risk factors for CHD during study period. While the decrease in Q wave MI's could be related to the sharp increase in revascularization procedures, this does not easily explain the decrease in the proportion with ST elevation which usually is seen on the first ECG.

Efforts in primary prevention may have contributed to the decreasing trend in STEMI and lower case-fatality among Q wave patients through a decrease in the severity of the disease. However, reduction of risk factors cannot easily explain the trends in incidence of hospitalized MI and increase in case-fatality seen for subendocardial infarction. The adoption of troponins as one of the enzymatic indicators in MI diagnosis during the latter half of 1990s has contributed modestly to these changes. It is generally known

that, because of their greater sensitivity, troponins can detect MIs that cannot be detected with CKMB.

In MIDAS, we observed a declining CVD case-fatality but a marked increase in NCVD case-fatality in four years. The decline in CVD deaths might be attributed by the mix of cases which included milder MIs detected by troponins and possibly more severe cases that underwent revascularization before Q wave develop. One of the contributors to this increasing trend in NCVD deaths might be diabetes, which is known to be associated with higher mortality for both CVD and NCVD. The increasing prevalence of DM may play a significant role in increasing overall deaths, especially among patients following subendocardial infarction.

A limitation of this study is that myocardial infarctions occurring outside of New Jersey would not be in our data base. While this obviously introduces some error in the data presented here, we doubt inclusion of out-of-state MI's would affect the results substantially.

In summary, the changes in the clinical presentation of MI, the increase in lethality of subendocardial events, and the striking decrease in CHD mortality that has occurred in persons not recently hospitalized with MI all argue that the underlying pathological processes for CHD are changing in New Jersey (and presumably other states). The nature and causes of these changes need to be better understood to address the increasing problem of subendocardial MI.

Chapter 6. Reference

1. *Health, United States, 2006 with Chartbook on trends in the health of Americans*. 2006: National Center on Health Statistics.

2. Rosamond, W., et al., *Heart Disease and Stroke Statistics--2008 Update: A Report From the American Heart Association Statistics Committee and Stroke Statistics Subcommittee.* Circulation, 2008. **117**(4): p. e25-146.

3. NCHS, *Deaths: Final Data for 2005.* NVSR, 2008. **56**(10): p. 2008-1120.

4. Luepker, R.V., et al., *Trends in Blood Pressure, Hypertension Control, and Stroke Mortality: The Minnesota Heart Survey.* The American Journal of Medicine, 2006. **119**(1): p. 42-49.

5. Fox, C.S., et al., *Temporal Trends in Coronary Heart Disease Mortality and Sudden Cardiac Death From 1950 to 1999: The Framingham Heart Study.* Circulation, 2004. **110**(5): p. 522-527.

6. Burke, G.L., et al., *Trends in CHD mortality, morbidity and risk factor levels from 1960 to 1986: the Minnesota Heart Survey.* International Journal of Epidemiology, 1989. **18**(3 Suppl 1): p. S73-81.

7. McGovern, P.G., et al., *Trends in acute coronary heart disease mortality, morbidity, and medical care from 1985 through 1997: the Minnesota heart survey.* Circulation, 2001. **104**(1): p. 19-24.

8. Goldberg, R.J., et al., *Recent changes in attack and survival rates of acute myocardial infarction (1975 through 1981). The Worcester Heart Attack Study.* JAMA: The Journal Of The American Medical Association, 1986. **255**(20): p. 2774-2779.

9. Goldberg, R.J., et al., *Incidence and case fatality rates of acute myocardial infarction (1975-1984): The Worcester Heart Attack Study.* American Heart Journal, 1988. **115**(4): p. 761-767.

10. Goldberg, R.J., et al., *A two-decades (1975 to 1995) long experience in the incidence, in-hospital and long-term case-fatality rates of acute myocardial infarction: a community-wide perspective.* Journal of the American College of Cardiology, 1999. **33**(6): p. 1533-1539.

11. Rosamond, W.D., et al., *Trends in the incidence of myocardial infarction and in mortality due to coronary heart disease, 1987 to 1994.* N Engl J Med, 1998. **339**(13): p. 861-7.

12. Kostis, J.B., et al., *Time trends in the occurrence and outcome of acute myocardial infarction and coronary heart disease death between 1986 and 1996*

(a New Jersey statewide study). The American Journal of Cardiology, 2001. **88**(8): p. 837-841.

13. Dauerman, H.L., et al., *Ten-year trends in the incidence, treatment, and outcome of Q-wave myocardial infarction.* The American Journal of Cardiology, 2000. **86**(7): p. 730-735.

14. McGovern, P.G., et al., *Recent trends in acute coronary heart disease--mortality, morbidity, medical care, and risk factors. The Minnesota Heart Survey Investigators.* New England Journal of Medicine, 1996. **334**(14): p. 884-90.

15. McGovern, P.G., et al., *Trends in survival of hospitalized myocardial infarction patients between 1970 and 1985. The Minnesota Heart Survey.* Circulation, 1992. **85**(1): p. 172-9.

16. Tu, J.V., C.D. Naylor, and P. Austin, *Temporal changes in the outcomes of acute myocardial infarction in Ontario, 1992-1996.* CMAJ Canadian Medical Association Journal, 1999. **161**(10): p. 1257-61.

17. Pashos, C.L., J.P. Newhouse, and B.J. McNeil, *Temporal changes in the care and outcomes of elderly patients with acute myocardial infarction, 1987 through 1990.* JAMA, 1993. **270**(15): p. 1832-1836.

18. Franklin, K., et al., *Implications of Diabetes in Patients With Acute Coronary Syndromes: The Global Registry of Acute Coronary Events.* Arch Intern Med, 2004. **164**(13): p. 1457-1463.

19. Tunstall-Pedoe, H., et al., *Contribution of trends in survival and coronary-event rates to changes in coronary heart disease mortality: 10-year results from 37 WHO MONICA project populations. Monitoring trends and determinants in cardiovascular disease.* Lancet, 1999. **353**(9164): p. 1547-57.

20. Capewell, S., C.E. Morrison, and J.J. McMurray, *Contribution of modern cardiovascular treatment and risk factor changes to the decline in coronary heart disease mortality in Scotland between 1975 and 1994.* Heart, 1999. **81**(4): p. 380-6.

21. Capewell, S., et al., *Explanation for the decline in coronary heart disease mortality rates in Auckland, New Zealand, between 1982 and 1993.* Circulation, 2000. **102**(13): p. 1511-6.

22. Fichtenberg, C.M. and S.A. Glantz, *Association of the California Tobacco Control Program with Declines in Cigarette Consumption and Mortality from Heart Disease.* N Engl J Med, 2000. **343**(24): p. 1772-1777.

23. Arnett, D.K., et al., *Fifteen-year trends in cardiovascular risk factors (1980-1982 through 1995-1997): the Minnesota Heart Survey.* American Journal of Epidemiology, 2002. **156**(10): p. 929-35.

24. Iribarren, C., et al., *Twelve-year trends in cardiovascular disease risk factors in the Minnesota Heart Survey. Are socioeconomic differences widening?* Archives of Internal Medicine, 1997. **157**(8): p. 873-81.

25. Kuulasmaa, K., et al., *Estimation of contribution of changes in classic risk factors to trends in coronary-event rates across the WHO MONICA Project populations.* Lancet, 2000. **355**(9205): p. 675-87.

26. Luepker, R.V., et al., *Cardiovascular risk factor change-1973-1974 to 1980-1982: the minnesota heart survey.* Journal of Clinical Epidemiology, 1988. **41**(9): p. 825-833.

27. Ford, E.S., et al., *Explaining the Decrease in U.S. Deaths from Coronary Disease, 1980-2000.* N Engl J Med, 2007. **356**(23): p. 2388-2398.

28. Hunink, M.G., et al., *The recent decline in mortality from coronary heart disease, 1980-1990. The effect of secular trends in risk factors and treatment.* JAMA, 1997. **277**(7): p. 535-42.

29. Goldman, L. and E.F. Cook, *The decline in ischemic heart disease mortality rates. An analysis of the comparative effects of medical interventions and changes in lifestyle.* Ann Intern Med, 1984. **101**(6): p. 825-36.

30. Salomaa, V., et al., *Diagnostic features of acute myocardial infarction--changes over time from 1983 to 1990: results from the FINMONICA AMI Register Study.* J Intern Med, 1995. **237**(2): p. 151-9.

31. Goff, D.C., Jr., et al., *Trends in severity of hospitalized myocardial infarction: the atherosclerosis risk in communities (ARIC) study, 1987-1994.* Am Heart J, 2000. **139**(5): p. 874-80.

32. Ma, J., et al., *National Trends in Statin Use by Coronary Heart Disease Risk Category.* PLoS Medicine, 2005. **2**(5): p. e123.

33. Donges, K., et al., *Incidence, determinants, and clinical course of reinfarction in-hospital after index acute myocardial infarction (results from the pooled data of the maximal individual therapy in acute myocardial infarction [MITRA], and the myocardial infarction registry [MIR]).* American Journal of Cardiology, 2001. **87**(9): p. 1039-44.

34. Hollander, G., et al., *High mortality early reinfarction with first nontransmural myocardial infarction.* American Heart Journal, 1984. **108**(6): p. 1412-6.

35. Berger, C.J., et al., *Prognosis after first myocardial infarction. Comparison of Q-wave and non-Q-wave myocardial infarction in the Framingham Heart Study.[see comment]*. JAMA, 1992. **268**(12): p. 1545-51.

36. Kornowski, R., et al., *Predictors and long-term prognostic significance of recurrent infarction in the year after a first myocardial infarction.* The American Journal of Cardiology, 1993. **72**(12): p. 883-888.

37. Volpi, A., et al., *Predictors of nonfatal reinfarction in survivors of myocardial infarction after thrombolysis. Results of the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI-2) Data Base.* Journal Of The American College Of Cardiology, 1994. **24**(3): p. 608-615.

38. Rich, M.W., et al., *Is age an independent predictor of early and late mortality in patients with acute myocardial infarction?* The American Journal of Medicine, 1992. **92**(1): p. 7-13.

39. Greenland, P., et al., *In-hospital and 1-year mortality in 1,524 women after myocardial infarction. Comparison with 4,315 men.* Circulation, 1991. **83**(2): p. 484-491.

40. Naylor, C.D. and E. Chen, *Population-wide mortality trends among patients hospitalized for acute myocardial infarction: The Ontario experience, 1981 to 1991.* Journal of the American College of Cardiology, 1994. **24**(6): p. 1431-1438.

41. Wilkinson, P., et al., *Acute myocardial infarction in women: survival analysis in first six months.* BMJ (Clinical Research Ed.), 1994. **309**(6954): p. 566-569.

42. King, H., R.E. Aubert, and W.H. Herman, *Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections.* Diabetes Care, 1998. **21**(9): p. 1414-31.

43. Wild, S., et al., *Global prevalence of diabetes: estimates for the year 2000 and projections for 2030.* Diabetes Care, 2004. **27**(5): p. 1047-53.

44. Donahoe, S.M., et al., *Diabetes and mortality following acute coronary syndromes.* JAMA, 2007. **298**(7): p. 765-75.

45. Cubbon, R.M., et al., *Temporal trends in mortality of patients with diabetes mellitus suffering acute myocardial infarction: a comparison of over 3000 patients between 1995 and 2003.* Eur Heart J, 2007. **28**(5): p. 540-5.

46. Mukamal, K.J., et al., *Impact of diabetes on long-term survival after acute myocardial infarction: comparability of risk with prior myocardial infarction.* Diabetes Care, 2001. **24**(8): p. 1422-7.

47. Nemetz, P.N., et al., *Recent Trends in the Prevalence of Coronary Disease: A Population-Based Autopsy Study of Nonnatural Deaths.* Arch Intern Med, 2008. **168**(3): p. 264-270.

48. Phibbs, B., *"Transmural" versus "subendocardial" myocardial infarction: an electrocardiographic myth.* Journal Of The American College Of Cardiology, 1983. **1**(2, Part 1): p. 561-564.

49. Klein, L.W. and R.H. Helfant, *The Q-wave and non-Q wave myocardial infarction: differences and similarities.* Progress In Cardiovascular Diseases. **29**(3): p. 205-220.

50. Moon, J.C.C., et al., *The Pathologic Basis of Q-Wave and Non-Q-Wave Myocardial Infarction: A Cardiovascular Magnetic Resonance Study.* Journal of the American College of Cardiology, 2004. **44**(3): p. 554-560.

51. Goldberg, R.J., et al., *Non-Q wave myocardial infarction: recent changes in occurrence and prognosis--a community-wide perspective.[erratum appears in Am Heart J 1987 Dec;114(6):1535].* American Heart Journal, 1987. **113**(2 Pt 1): p. 273-9.

52. Furman, M.I., et al., *Twenty-two year (1975 to 1997) trends in the incidence, in-hospital and long-term case fatality rates from initial q-wave and non-q-wave myocardial infarction: a multi-hospital, community-wide perspective.* Journal of the American College of Cardiology, 2001. **37**(6): p. 1571-1580.

53. Wellford, L., et al., *Changing presentation of coronary heart disease in an inpatient population within the U.S. military health care system.* Military Medicine, 1993. **158**(9): p. 598-603.

54. Edlavitch, S.A., et al., *Secular trends in Q wave and non-Q wave acute myocardial infarction. The Minnesota Heart Survey.* Circulation, 1991. **83**(2): p. 492-503.

55. Bertoni, A.G., et al., *Acute coronary syndrome national statistics: Challenges in definitions.* American Heart Journal, 2005. **149**(6): p. 1055-1061.

56. Liebson, P.R. and L.W. Klein, *The non-Q wave myocardial infarction revisited: 10 years later.* Progress In Cardiovascular Diseases, 1997. **39**(5): p. 399-444.

57. Rosamond, W., et al., *Heart Disease and Stroke Statistics--2007 Update: A Report From the American Heart Association Statistics Committee and Stroke Statistics Subcommittee*. 2007. p. e69-171.

58. Cooper, R., et al., *Trends and disparities in coronary heart disease, stroke, and other cardiovascular diseases in the United States: findings of the national conference on cardiovascular disease prevention.* Circulation, 2000. **102**(25): p. 3137-47.

59. Ford, E.S., et al., *Explaining the Decrease in U.S. Deaths from Coronary Disease, 1980-2000,* in *N Engl J Med*. 2007. p. 2388-2398.

60. Kostis, J.B., et al., *Sex differences in the management and long-term outcome of acute myocardial infarction. A statewide study. MIDAS Study Group. Myocardial Infarction Data Acquisition System.* Circulation, 1994. **90**(4): p. 1715-1730.

61. Abbud, Z.A., et al., *Effect of diabetes mellitus on short- and long-term mortality rates of patients with acute myocardial infarction: A statewide study.* Am Heart J, 1995. **130**(1): p. 51-58.

62. Kostis, W.J., et al., *Weekend versus Weekday Admission and Mortality from Myocardial Infarction.* N Engl J Med, 2007. **356**(11): p. 1099-1109.

63. Jaro, M., *Advances in record-linkage methodology as applied to matching the 1985 census of Tampa, Florida.* J Am Stat Assoc, 1989. **84**: p. 414-420.

64. Jaro, M., *AUTOMATCH Generalized Record Linkage System Version 3.0 Manual.* 1995.

65. Gregory, P., et al., *Impact of availability of hospital-based invasive cardiac services on racial differences in the use of these services.* American Heart Journal, 1998(138): p. 507-517.

66. Hoyert DL, H.M., Murphy SL, Kung HC., *Deaths: final data for 2003.* Natl Vital Stat Rep, 2006. **54**(13): p. 1-120.

67. McGovern, P.G., et al., *Trends in Acute Coronary Heart Disease Mortality, Morbidity, and Medical Care From 1985 Through 1997 : The Minnesota Heart Survey*, in *Circulation*. 2001. p. 19-24.

68. Roger, V.L., et al., *Redefinition of Myocardial Infarction: Prospective Evaluation in the Community*. 2006. p. 790-797.

69. Alpert, J.S., *A call for universal definitions in cardiovascular disease.* Circulation, 2006. **114**(8): p. 790-797.

70. Salomaa, V., et al., *The effects of cprrcting for troponins on trends in coronary heart disease events in Finland during 1993-2002: the FINAMI study.* European Heart Journal, 2006. **27**: p. 2394-2399.

71. Goldberg, R.J., et al., *Trends in community mortality due to coronary heart disease.* American Heart Journal, 2006. **151**(2): p. 501-507.

72. Antman, E., et al., *Myocardial infarction redefined--a consensus document of The Joint European Society of Cardiology/American College of Cardiology committee for the redefinition of myocardial infarction: The Joint European Society of Cardiology/ American College of Cardiology Committee.* J Am Coll Cardiol, 2000. **36**(3): p. 959-969.

73. Ford, E.S., et al., *Explaining the Decrease in U.S. Deaths from Coronary Disease, 1980-2000*. 2007. p. 2388-2398.

74. Rosamond, W.D., et al., *Coronary heart disease trends in four United States communities. The Atherosclerosis Risk in Communities (ARIC) study 1987-1996.* Int J Epidemiol, 2001. **30 Suppl 1**: p. S17-22.

75. Salomaa, V., et al., *A new definition for myocardial infarction: what difference does it make?* Eur Heart J, 2005. **26**(17): p. 1719-25.

76. Botkin, N.F., et al., *Changing trends in the long-term prognosis of patients with acute myocardial infarction: A population-based perspective.* American Heart Journal, 2006. **151**(1): p. 199-205.

77. Haim, M., et al., *Prognosis of patients with a first non-Q-wave myocardial infarction before and in the reperfusion era. SPRINT and the Israeli Thrombolytic Survey Groups. Secondary Prevention Reinfarction Israeli Nifedipine Trial.* American Heart Journal, 1998. **136**(2): p. 245-51.

78. Perschbacher, J.M., et al., *Evidence-based therapies for myocardial infarction: secular trends and determinants of practice in the community.* Mayo Clin Proc, 2004. **79**(8): p. 983-91.

79. Chambless, L., et al., *Population versus clinical view of case fatality from acute coronary heart disease: results from the WHO MONICA Project 1985-1990. Multinational MONItoring of Trends and Determinants in CArdiovascular Disease.* Circulation, 1997. **96**(11): p. 3849-59.

80. Luepker, R.V., *Population versus clinical views in coronary disease: can epidemiological data be useful to clinicians?* Circulation, 1997. **96**(11): p. 3836-7.

81. Salomaa, V., et al., *Decline in Out-of-Hospital Coronary Heart Disease Deaths Has Contributed the Main Part to the Overall Decline in Coronary Heart Disease Mortality Rates Among Persons 35 to 64 Years of Age in Finland: The FINAMI Study.* Circulation, 2003. **108**(6): p. 691-696.

82. Kuch, B., et al., *What is the real hospital mortality from acute myocardial infarction?. Epidemiological vs clinical view.* Eur Heart J, 2002. **23**(9): p. 714-720.

83. CDC. *Crude and Age-Adjusted Prevalence of Diagnosed Diabetes per 100 Population, United States, 1980–2005*. 2007 [cited; Available from: http://www.cdc.gov/diabetes/statistics/prev/national/figage.htm.

Curriculum Vita

Yu-Hsuan Shao
Ph.D, Epidemiology
Email: shaoyu@umdnj.edu

EDUCATION

UNIVERSITY OF MEDICINE AND DENTISTRY OF NEW JERSEY Piscataway, USA
PhD in Epidemiology, SPH, 2003 - 2008

THE JOHNS HOPKINS UNIVERSITY Baltimore, USA
Master of Health Science in Public Health, June 2000

TAIPEI MEDICAL COLLEGE Taipei, Taiwan
Bachelor of Science in Public Health, June 1998

EXPERIENCE

UMDNJ, Robert Wood Johnson Medical School, Department of Medicine
Graduate Assistant, October '04 - Present
Rutgers University, Environmental and Occupational Health Safety Institute
Graduate Assistant, January '03 – September '04
National Cheng Kung University, Taiwan
Research Assistant, July '00 – November '02
TAIPEI MEDICAL COLLEGE
Research Assistant, July '98 – July '99

PUBLICATION

Prevalence of Self-Reported Work-Related Skin Conditions in Taiwanese Working Population. **Yu-Hsuan Shao**, Wen-Yu Yeh, Chiou-Jong Chen, Chun Wan Chen, Yue-Liang Guo. *Journal of Occupational Health. 2001 43; 5:238-242.*

Number of boys born to men exposed to polychlorinated byphenyls. Iliana del Rio Gomez, Tom Marshall, Peichien Tsai, **Yu-Shuan Shao** and Yueliang Leon Guo. *Lancet. 2002 13; 360(9327):143-4.*

Weekend versus Weekday Admission and Mortality in Patients with Myocardial Infarction. Kostis WJ, Demissie K, Marcella SW, **Shao Y-H**, Wilson AC, Moreyra AE for the Myocardial Infarction Data Acquisition System Study Group. N Engl J Med *2007 356; 1099-109*.