Editorial

To the Framingham Data, Turn, Turn, Turn

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Beginning in the mid to late 1960s and continuing to the present, declines in the annual death rates attributed to coronary heart disease (CHD) have been observed in American men and women, reversing previously observed trends of steadily increasing mortality from CHD. Despite these encouraging trends, CHD continues to be a leading cause of morbidity and mortality in American men and women. It has been estimated that almost 1 in every 2 middle-aged American men and 1 in every 3 American woman will develop CHD during their lifetime.

Epidemiologists have provided extensive insights into the predictive and relative importance of a variety of predisposing factors for CHD. This has been accomplished through the conduct of a number of landmark longitudinal studies including the community-based Framingham Heart Study, the migrant Ni-Hon-San Study, and the international Seven Countries Study. Elevated blood cholesterol levels, cigarette smoking, increased levels of blood pressure, diabetes mellitus, the metabolic syndrome, and high fat diets have been consistently linked to the occurrence of CHD. More recent investigations have suggested that there may be other factors involved in the pathogenesis of CHD including cell inflammation, disturbances in clotting and hemostasis, plaque vulnerability, and alterations in autonomic tone of the coronary vasculature.

Concomitant with an enhanced understanding of the risk factors involved in the development of coronary atherosclerosis and its different clinical manifestations, and greater appreciation of the multidecade-long natural history of CHD, remarkable advances have been made in the primary and secondary prevention of acute coronary disease, especially during the past 2 decades.

In the 1960s, prolonged bed rest and treating complications as they occurred were the mainstay approaches used for the treatment of patients with acute myocardial infarction (AMI). In the 1980s, however, coincident with new insights into the underlying pathophysiology of AMI and the results of large-scale clinical trials, the management of patients with AMI evolved from a strategy of watchful waiting and use of supportive therapies to active treatment intervention. The present management of patients with AMI is focused on the prompt restoration and maintenance of the patency of the acutely occluded infarct-related artery through the use of coronary reperfusion and revascularization procedures. Adjunctive therapies that prevent reinfarction/occlusion, favorably impact ventricular remodeling, and promote long-term stabilization of coronary plaques are routinely used treatment regimens.

Given the magnitude of CHD, as well as the morbidity, mortality, and costs associated with this disease, several investigative teams have attempted to thoughtfully sort out the contributions of primary and secondary prevention to declining death rates from CHD observed in this country over the past 40 years. These studies have suggested that efforts of both primary and secondary prevention have been relatively equal contributors to declining CHD death rates, though their relative contributions have changed over time. Favorable alterations in the major coronary risk factors and associated declines in the incidence rates of coronary disease were estimated to have played a more central role in the decline in CHD death rates observed in the United States (US) during the 1960s and 1970s. Improvements in short-term and long-term management have likely translated into the enhanced survival of patients hospitalized with AMI during the past 2 decades.

Assessing secular trends in the death rates attributed to CHD in a large and diverse population such as that of the US is a challenging task because of a multiplicity of contributory factors. Declines in the incidence rates of coronary artery disease would suggest that the decline in death rates due to CHD over the past 40 years is likely due to changes in the frequency and severity of the major coronary predisposing factors. In the face of steady or increasing incidence rates of acute coronary disease during the period of declining CHD death rates, a plausible explanation for the decline in CHD-related mortality would be improvement in the short-term and long-term management of patients with CHD. Changes in how AMI has been diagnosed over time may have also impacted the descriptive epidemiology of CHD. The more widespread adoption of increasingly sensitive cardiac enzyme assays may now allow for the detection of “smaller” acute coronary events that were often previously undetected but likely heralded future larger transmural infarcts that resulted in electrocardiographic changes.

In this issue of *Circulation*, investigators from the Framingham Heart Study (FHS) have provided yet another milestone in the findings from this seminal longitudinal study, furnishing insights into the changing epidemiology of AMI in the US over a 40-year period. Using data from >900 FHS men and women between the ages of 40 and 89 years who experienced an initial AMI between 1960 and 1999, the Framingham investigators characterized these AMIs into...
those that were diagnosed on the basis of ECG findings, irrespective of changes in the serum levels of various biomarkers (n=639) and those that were defined on the basis of elevations in serum biomarkers available at the time the AMI was diagnosed (n=302). In addition to examining multidecade-long trends in the incidence rates of initial AMIs according to varying criteria, the Framingham investigators provided a 4-decade–long perspective into changing 30-day, 1-year, and 5-year death rates after AMI. These data were further examined in several age- and sex-specific strata to provide additional insights into observed trends.

Between 1960 and 1999, the incidence rates of ECG-confirmed AMIs in nearly 10 000 FHS participants declined by approximately one half whereas an approximate doubling occurred in the rates of biomarker-confirmed acute coronary events over this time period. In contrast to these divergent trends, the short (30-day) and more extended (1- and 5-year) death rates after AMI declined markedly over time, ranging from 50% to upwards of 75% during the period under study; these declining death rates were observed in both ECG- and biomarker-confirmed acute coronary events.

These findings suggest that, consistent with improvements in the major risk factors for CHD over time and advances in efforts of primary prevention, the incidence rates of ECG-confirmed AMIs have declined during the past several decades. Marked improvements in the short- and long-term prognosis associated with AMI likely reflect advances in medical care and greater use of evidence-based cardiac therapies. The present findings provide encouragement for advocates sitting on both sides of the CHD prevention aisle, namely proponents of primary prevention as well as advocates of enhanced secondary prevention approaches.

Despite the current magnitude of CHD in the US, the considerable successes that have been made in identifying individuals at increased risk for CHD, and the increasingly effective management of patients hospitalized with AMI, there have been surprisingly few population-based studies that have monitored long-term trends in the magnitude, management, and outcomes associated with AMI, unstable angina, or sudden cardiac death. Furthermore, few studies have examined the impact of changes in the manner in which acute coronary disease has been diagnosed on observed trends, particularly from a multidecades perspective.

The early surveillance studies of CHD, which were carried out in select population or work-site settings during the 1960s and 1970s, were followed by a limited number of community-based monitoring projects in Massachusetts and Minnesota, in the context of a large observational study (Atherosclerosis Risk in Communities), or through the analysis of trends in unvalidated hospital discharge diagnoses or death certificate data.7–10

Although these studies were carried out in populations of varying sizes and characteristics and during differing time periods, the findings from these community-wide investigations generally have shown slight declines in the incidence rates of AMI and changing demographic and clinical characteristics of patients hospitalized with AMI. Differences included the type of AMI and an increasing proportion of patients currently being hospitalized with non–ST-segment elevation AMI, reflecting either changes in the natural history of AMI or, more likely, greater use of increasingly sensitive serum biomarkers of acute myocardial ischemia. Patients are being hospitalized for a first AMI at a considerably older age and with a greater number of important comorbidities present during recent as compared with earlier study years; on the other hand, patients’ acute care-seeking behavior after the onset of acute coronary symptoms has apparently changed little during the past several decades, reinforcing the importance of public education efforts in this important area.

Each of these studies has shown declines in the hospital death rates associated with AMI and, more recently, improvements in the long-term prognosis of discharged hospital patients. In the present FHS investigation, the short and more extended death rates associated with AMI declined markedly over time in both ECG- and biomarker-confirmed acute coronary events. These improving survival trends are consistent with the increased use of timely coronary reperfusion strategies, effective cardiac medications, and increasing adherence to published guideline recommendations.

Investigators from these studies, as well as several expert panels, have, however, struggled with changes in the manner by which AMI has been diagnosed over time, how cases of in- and out-of-hospital acute coronary disease can be systematically captured, and how high-quality information can be collected either directly from patients or through the review of information contained in hospital records for purposes of examining changing trends in the descriptive epidemiology of AMI. Indeed, an expert panel has provided guidance on working case definitions of AMI and approaches to be used for measuring meaningful changes in indicators of acute CHD over time.11

Given the inherent difficulties in the design and interpretation of data assessing changing trends in the major predisposing factors, incidence, and death rates associated with CHD, the FHS data are particularly meaningful and instructive. The present findings further reinforce the importance of population-based monitoring systems that are designed to collect contemporary data in this important area. The capacity of the FHS to present multidecade-long data on AMI defined on the basis of various parameters allows for meaningful examination of the changing epidemiology of AMI and for distinguishing real from artificial changes in incidence and death rates after AMI that would not otherwise be available.

The FHS has proven to be an incredibly rich resource for the study of coronary disease and its antecedents and a fertile source of data for clinical and epidemiological researchers, who, in the words of the 1960s rock hit by the Byrds, have never hesitated to “turn, turn, turn” to this database for new insights into the etiology and prevention of initial and recurrent coronary events and other chronic diseases. It is hoped that the FHS investigators and other cardiovascular epidemiology research teams throughout the US will continue to monitor contemporary trends in patients’ care-seeking behavior in the setting of evolving AMI, use of emergency medical services, the magnitude and prognosis of AMI and its associated complications, the acute management of these high-risk patients, and long-term changes in quality of life and adherence to cardiac medications after AMI.
This information is of crucial importance if we are to continue the identification of patients at increased risk for CHD, less-than-optimal use of effective cardiac therapies, and unsatisfactory short- and long-term patient outcomes. Information from population-based CHD longitudinal studies and surveillance systems will be particularly important to collect over the next several decades given recent increases in the prevalence of several major coronary risk factors, namely diabetes mellitus and obesity, in the American public and the impact of these negative trends and changing treatment practices on AMI incidence rates and related outcomes. These efforts should continue to be encouraged by national funding agencies if we are to sustain and improve on the gains in the prevention and treatment of acute coronary disease that have been previously made. This information will allow researchers and clinicians to more systematically understand the changing epidemiology of acute coronary disease from a “Byrds” eye view and begin to discern differences between the forest and the trees.

Disclosures
None.

References

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