



# The Epidemic of the 20<sup>th</sup> Century: Coronary Heart Disease

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## ABSTRACT

Heart disease was an uncommon cause of death in the US at the beginning of the 20th century. By mid-century it had become the commonest cause. After peaking in the mid-1960s, the number of heart disease deaths began a marked decline that has persisted to the present. The increase in heart disease deaths from the early 20th century until the 1960s was due to an increase in the prevalence of coronary atherosclerosis with resultant coronary heart disease, as documented by autopsy studies. This increase was associated with an increase in smoking and dietary changes leading to an increase in serum cholesterol levels. In addition, the ability to diagnose acute myocardial infarction with the aid of the electrocardiogram increased the recognition of coronary heart disease before death. The substantial decrease in coronary heart disease deaths after the mid-1960s is best explained by the decreased incidence, and case fatality rate, of acute myocardial infarction and a decrease in out-of-hospital sudden coronary heart disease deaths. These decreases are very likely explained by a decrease in coronary atherosclerosis due to primary prevention, and a decrease in the progression of nonobstructive coronary atherosclerosis to obstructive coronary heart disease due to efforts of primary and secondary prevention. In addition, more effective treatment of patients hospitalized with acute myocardial infarction has led to a substantial decrease in deaths due to acute myocardial infarction. It is very likely that the 20th century was the only century in which heart disease was the most common cause of death in America.

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The 20th century was the first century in which heart disease was the most common cause of death in the US, and it may be the last century during which it was the leading cause of death. As shown in **Figure 1**, heart disease was uncommon in the early years of the 20th century.<sup>1</sup> In 1900 it was the fourth most common cause of death, trailing infectious diseases such as pneumonia and tuberculosis.<sup>2</sup> Three decades later, heart disease deaths had increased to become the commonest cause of death in the US.<sup>3</sup> Heart disease deaths continued to increase until the mid-1960s.<sup>1</sup>

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The large majority of cardiac deaths in the US are due to coronary heart disease secondary to coronary atherosclerosis. In 2009 coronary heart disease accounted for 64% of all cardiac deaths.<sup>4</sup>

Many explanations for the increase in coronary heart disease deaths from 1900 to the 1960s have been offered. The marked increase in deaths attributed to heart disease, from 1900 until the late 1960s, was almost certainly due to an increase in the incidence of coronary atherosclerosis, with resultant coronary heart disease.

Americans were living longer due to a decrease in deaths from infectious diseases. Changes in diet led to the consumption of processed foods, more saturated fats, added sugars and other high glycemic index carbohydrates. There was a spectacular increase in cigarette smoking: <5% of Americans were smokers in 1900, compared with 42% in 1965.<sup>5</sup> Others point to a decrease in exercise and regular physical activity as most Americans gained access to automobiles.

Part of the increase in mortality attributed to coronary heart disease was due to increased recognition of myocardial infarction. Herrick, in 1912,<sup>6</sup> was the first to diagnose heart attacks during life, and 6 years later he encouraged the use of the electrocardiogram to diagnose myocardial infarction.<sup>7</sup> The ability to diagnose myocardial infarction during life increased the recognition of coronary heart disease on death certificates.

In the mid-1960s, heart disease deaths began a remarkable and steady decline that has persisted to the present (Figure 1). Coronary heart disease deaths decreased from 466/100,000 in 1965 to 345 in 1980: a 26% relative decrease.<sup>8</sup> From 1980 to 2008, the decrease was 64%: from 345 to 123/100,000.<sup>8</sup>

The reasons for this decline in cardiac deaths are not clear and are likely to be multifactorial, as in the development of coronary heart disease. Was the decline due to better medical and surgical treatment? Primary prevention of coronary atherosclerosis? Secondary prevention of myocardial infarction and sudden death in patients with coronary heart disease? Everyone would like to take credit. As John Kennedy said after the Bay of Pigs debacle: "Victory has a hundred fathers; defeat is an orphan."

Given that coronary heart disease is a complex, multifactorial process, it is unlikely that there is a single explanation for the decline in coronary heart disease deaths in the US over the past 50 years.

What follows here are some possible explanations for the decreasing number of coronary heart disease deaths over the past 5 decades.

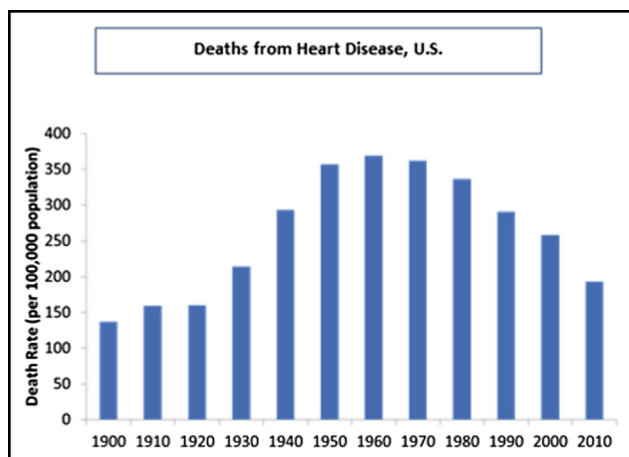


Figure 1 US heart disease deaths/100,000 1900-2010.<sup>1</sup>

### CLINICAL SIGNIFICANCE

- The increase in coronary heart disease deaths in the 1930s, 1940s and 1950s was due to an increase in coronary atherosclerosis.
- A decline in coronary atherosclerosis that began in the late 20th century was associated with decreased smoking and a decrease in cholesterol levels.
- Primary and secondary prevention has decreased the incidence of acute myocardial infarction and sudden cardiac deaths from the mid-1960s to the present.
- More effective treatment of acute myocardial infarction has decreased the number of deaths due to acute myocardial infarction.

## DECREASING INCIDENCE OF CORONARY ATHEROSCLEROSIS

The continuing decline in coronary heart disease deaths could be due to a decreasing prevalence of coronary atherosclerosis, which would lead to a decrease in the prevalence of coronary heart disease.

The Pathobiological Determinants of Atherosclerosis in Youth Study was a multi-institutional study of atherosclerosis in 15- to 34 year-old American men.<sup>9</sup> Investigators from this study reported the results of 2876 autopsies performed in this population between 1987 and 1994. They demonstrated that coronary atherosclerosis begins as fatty streaks at ages 15-25 years and progresses to raised intimal lesions during ages 25-35 years.<sup>9</sup>

The first evidence that the prevalence of coronary atherosclerosis might be decreasing in the US population was based on the autopsy findings of young American servicemen who died during the Korean,<sup>10</sup> Vietnam,<sup>11</sup> and Iraq and Afghanistan<sup>12</sup> wars. The average age of the casualties in the Korean and Vietnam wars was 22;

none were known to have symptoms of coronary heart disease before their wartime deaths.

As shown in Figure 2, in 1951-1953, a relatively small autopsy study of 300 American casualties in the Korean War showed that 77% of the American casualties had some evidence of coronary atherosclerosis.<sup>10</sup> In 35% there was fibrous streaking or intimal fibrous thickening without luminal obstruction. Forty-two percent had plaques causing

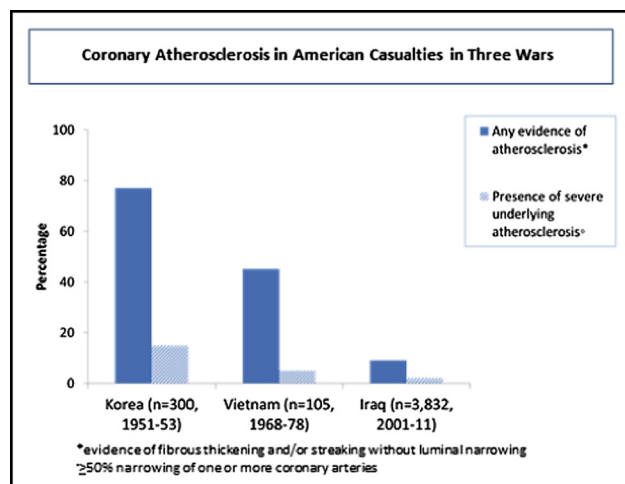


Figure 2 Postmortem evidence of coronary atherosclerosis in American casualties in 3 wars.<sup>10-12</sup>

at least 10% luminal narrowing, and 15% had at least 50% obstruction of one or more coronary arteries.<sup>10</sup>

In the smaller Vietnam War autopsy study (1968-1978), 45% of 105 American casualties had evidence of coronary atherosclerosis.<sup>11</sup> Five percent were judged to have severe disease.

In contrast, postmortem examination of 3832 American casualties in the Iraq and Afghanistan wars (2000-2011) demonstrated evidence of coronary atherosclerosis in only 8.5%, and severe disease (>50% obstruction) in only 2.3% of these young Americans.<sup>12</sup>

As shown in **Figure 2**, evidence of coronary atherosclerosis decreased from 77% in 1950-1953 to 45% in 1968-1978, to <9% in 2001-2011. The numbers of autopsies in the 1950s and from 1968-1978 were relatively small, but the findings are striking and clearly indicate a decrease in the prevalence of coronary atherosclerosis from the 1950s until the early 2000s.

Of particular note is the decrease in the prevalence of atherosclerosis in these young American men from nearly 50% in 1968-1978 to <10% in 2001. As noted in **Figure 1**, the decrease in coronary deaths in the US population began in the mid to late 1960s.

Autopsies present the opportunity to assess trends in the prevalence of symptomatic and asymptomatic coronary atherosclerosis in a population; however, autopsy rates in the US civilian population declined in the last half of the 20th century<sup>13</sup> and these rates vary widely across the nation. In 1975, <20% of deaths in the US had a postmortem examination.<sup>14</sup> However, in that same year, postmortem examinations were performed in 50% of all deaths that occurred in Olmsted County, Minnesota, home of the Mayo Clinic and the longitudinal Rochester Epidemiology Project.<sup>15</sup>

A study by Mayo Clinic investigators<sup>15</sup> reported the incidence of significant coronary atherosclerosis in 5558 postmortem examinations performed from 1950 to 1979. This represented autopsies on 50% of all deaths in Olmsted County during these 3 decades. The proportion of autopsies with significant coronary atherosclerosis (obstruction of >50% of one or more arteries) increased progressively from 23% in 1950-1954 to 33% in 1960-1964, to 51% in 1975-1979; representing a 122% relative increase from 1950-1954 to 1975-1979.<sup>15</sup> These findings are consistent with the increase in coronary heart disease deaths from 1950 until the mid-1960s, as shown in **Figure 1**.

A follow-up study from the Mayo Clinic<sup>16</sup> described trends in the prevalence of coronary atherosclerosis in Olmsted County, Minnesota from 1979 until 1994. During this more recent period, 2562 (27%) of 9312 deaths had a postmortem examination. The investigators found a decrease in the prevalence of significant coronary atherosclerosis (>75% narrowing of one or more arteries) in individuals younger than 60 years of age: from 38% in 1979-1983 to 27% in 1990-1994, a 29% decrease. However, there was an insignificant decrease in individuals older than 60 years: 61% had significant coronary

atherosclerosis in 1979-1983, compared with 59% in 1990-1994.<sup>16</sup>

These reports from the population-based Olmsted County Epidemiology Project<sup>15,16</sup> and from the American war casualties<sup>10-12</sup> are highly consistent with the observed increase in coronary heart disease deaths from 1950 until the mid-1960s and the substantial decrease since the mid-1960s, as shown in **Figure 1**.

These data indicate that the decline in coronary heart disease deaths since the mid-1960s was due in part to a decrease in the prevalence of coronary atherosclerosis. This decline in coronary atherosclerosis may have occurred because of population-wide efforts in primary prevention. Since the seminal Surgeon General's report in 1964, the prevalence of cigarette smokers that had peaked at 42% in 1965 has progressively decreased to 18% in 2012.<sup>5</sup>

The average serum total cholesterol levels of American men and women as measured in a number of nationally representative National Health and Nutrition Examination Surveys<sup>17,18</sup> consistently decreased between 1960 and 2010. The average cholesterol level in men decreased from 217 mg/dL in 1960-1962 to 194 in 2007-2010. The decrease in women over the same time period was from 222 to 198. The decrease in population cholesterol levels after statins were introduced in 1987<sup>19</sup> was nearly the same as the decrease in the 20 years before their introduction. This decrease in serum cholesterol levels occurred despite the fact that the percent of saturated fat in the average US diet was the same (14%) in 1993<sup>20</sup> as it was in 1975.<sup>21</sup>

Secondary prevention including dietary changes, statin therapy, aspirin therapy, earlier detection and treatment of hypertension, decreased smoking, and increased physical activity could also have prevented or impeded the progression of minor (nonobstructive) coronary disease to obstructive coronary heart disease.

## DECREASING PREVALENCE OF CORONARY HEART DISEASE?

The total prevalence of obstructive (symptomatic and asymptomatic) coronary heart disease in the US is unknown.

The Centers for Disease Control and Prevention (CDC) estimates the prevalence of coronary heart disease by compiling data from the Behavioral Risk Factor Surveillance System, which carries out telephone surveys of the noninstitutionalized US civilian population aged 18 years and older. They ask each survey respondent if a doctor, nurse, or other health professional has ever told them that they had a heart attack, myocardial infarction, angina, or coronary heart disease. Those who answer yes to this single question are defined as having self-reported coronary heart disease.<sup>21</sup> Using this technique, the CDC reported that the prevalence of age-adjusted self-reported coronary heart disease decreased from 6.7% in 2006 to 6.0% in 2010.<sup>22</sup> However, these estimates do not include the very substantial number of individuals with asymptomatic (and therefore undiagnosed) coronary heart disease.

In a report by Kuller et al,<sup>23</sup> only half of 489 patients with sudden cardiac death outside hospitals were known to have coronary heart disease before their death.<sup>23</sup>

In the Mayo clinic report of autopsies performed from 1979 until 1994, 37% of those without a history of coronary heart disease had significant coronary heart disease (75% narrowing of one or more arteries) at postmortem.<sup>16</sup>

In the Worcester Heart Attack Study, only 17% of men with their first myocardial infarction and 22% of women were known to have coronary heart disease before their acute myocardial infarction.<sup>24</sup>

An accurate determination of the prevalence of silent obstructive coronary heart disease would require coronary arteriography of a very large and representative number of men and women at various ages without clinical evidence of coronary heart disease. Such an investigation is highly unlikely.

Another Mayo Clinic study reported 2 decade-long trends in the incidence of coronary disease in Olmsted County, between 1979 and 1998.<sup>25</sup> The Mayo Clinic and the Olmstead Medical Center provide nearly all medical care for the population of Olmsted County. All incident cases of overt coronary heart disease (myocardial infarction, sudden death, angiographically documented coronary heart disease, and unstable angina) that occurred in this population between 1979 and 1998 were assessed. The investigators reported a 17% decrease in myocardial infarction and sudden deaths between 1979 and 1998. The total incidence of coronary heart disease decreased by 9% from 1988 until 1998.<sup>25</sup>

## EFFECTIVE SECONDARY PREVENTION IN PATIENTS WITH CORONARY HEART DISEASE

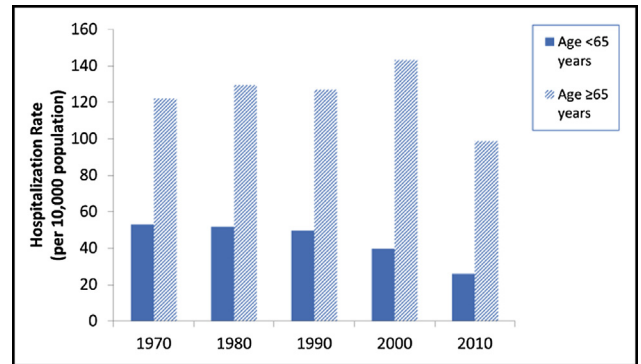
If secondary prevention in patients with symptomatic or asymptomatic coronary heart disease has been effective, it would cause a decrease in the frequency of myocardial infarction and sudden cardiac death.

## DECLINES IN HOSPITALIZATIONS FOR ACUTE MYOCARDIAL INFARCTION

Based on US hospital discharge diagnoses, there has been a striking reduction in the frequency of patients hospitalized with acute myocardial infarction, as shown in [Figure 3](#).

The hospitalization rate for acute myocardial infarction decreased from 175/10,000 in 1970 to 125/10,000 in 2010; a 29% relative decrease. Most of the decrease (32%) occurred between 2000 and 2010.<sup>8</sup>

The universal definition of acute myocardial infarction changed in 2000 from one based on creatine kinase-MB levels to one based on the more sensitive cardiac troponin levels.<sup>26</sup> The decrease in hospitalizations for acute myocardial infarction during the period 2000 to 2010 becomes even more striking in that many patients previously diagnosed with unstable angina were now diagnosed with acute myocardial infarction by the new definition after 2000.<sup>26</sup>



**Figure 3** Hospitalization rate/10,000 for acute myocardial infarction, US 1970-2010.<sup>8</sup>

The largest decrease in acute myocardial infarction hospitalizations was in patients younger than 65 years. The rate decreased from 53 per 10,000 in 1970 to 26 in 2010: a 51% decrease. In patients 65 years and older, this rate decreased from 122 in 1970 to 99 in 2010: a 19% relative decrease.<sup>8</sup>

The proportion of all hospitalizations for acute myocardial infarction (initial and recurrent) in patients younger than 65 years has decreased from 34% in 1965 to 21% in 2010. In patients over 65 years of age it increased from 66% in 1965 to 79% in 2010.<sup>8</sup>

The median age of patients with an initial acute myocardial infarction in the Worcester Heart Attack Study increased from 63 years in 1975 to 73 in 2005, reflecting the decrease in acute myocardial infarction in younger patients.<sup>24</sup>

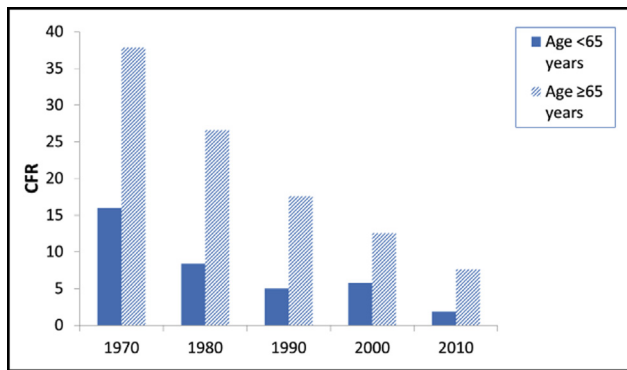
The decrease in acute myocardial infarction in younger individuals may be due to decreased exposure to risk factors such as smoking and higher cholesterol levels when they were young; on the other hand, individuals aged 65 years and older were more likely to have been exposed to these risk factors when they were young.

This suggests that younger Americans may have a lower prevalence of obstructive coronary heart disease because of a lower exposure to smoking and higher cholesterol levels when they were in the first few decades of their life.

## DECREASED MORTALITY IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

In addition to the decreasing frequency of acute myocardial infarction in the US population, there has been a striking decrease in the case fatality rate of patients hospitalized with acute myocardial infarction, as shown in [Figure 4](#). The hospital case fatality rate of patients younger than 65 years decreased from 16% in 1970 to <2% in 2010: an 88% relative decrease. In those aged 65 years and older, the decrease was from 38% in 1970 to 7% in 2010: an 82% relative decrease.<sup>8</sup>

The increased survival of patients with acute myocardial infarction could be due to more effective therapy (thrombolytics, percutaneous coronary intervention, beta-blockers,



**Figure 4** Case fatality rate (%), patients hospitalized with acute myocardial infarction US 1970-2010.<sup>8</sup>

aspirin and other antithrombotics, angiotensin-converting enzymes/angiotensin receptor blockers) and improved therapy in patients with heart failure secondary to acute myocardial infarction. The decrease in hospital case fatality rates in patients with acute myocardial infarction hospitalized after 2000 very likely was also due in part to changes in the diagnostic criteria for acute myocardial infarction. The more sensitive criteria for acute myocardial infarction led to the diagnosis in patients with less extensive infarction.<sup>26</sup>

## DECREASED DEATHS DUE TO MYOCARDIAL INFARCTION

The decreased incidence of acute myocardial infarction and the decreased case fatality rate of patients hospitalized with acute myocardial infarction have resulted in a very significant decrease in deaths from it in the US. Deaths from acute myocardial infarction decreased from 672,769 in 1970 to 412,364 in 2010: a 39% decrease.<sup>8</sup> These decreased deaths from acute myocardial infarction account for a significant portion of the decrease in deaths due to coronary heart disease.

## DECREASED INCIDENCE OF SUDDEN DEATH DUE TO CORONARY HEART DISEASE

More than half of the deaths from coronary heart disease in the US occur as cardiac arrest outside of hospitals or in emergency departments within 1 hour of the onset of symptoms<sup>27</sup> and are termed sudden cardiac deaths. Zheng et al<sup>28</sup> reported that 63% of all coronary heart disease deaths in 1998 were due to sudden cardiac death.

Sudden cardiac death is frequently the first evidence of the presence of coronary heart disease. Kuller et al<sup>23</sup> reported that only 50% of patients with sudden cardiac death in Baltimore had known coronary heart disease before their death.

The vast majority of sudden cardiac deaths is secondary to ventricular fibrillation in patients with coronary heart disease.<sup>29</sup>

**Table** Reasons for Decrease in Cardiac Deaths Mid-1960s Until 2012

	Prevention		Better RX
	Primary	Secondary	
Decreased incidence of coronary atherosclerosis	X		
Decreased progression of atherosclerosis to obstructive coronary artery disease	X	X	
Decreased incidence of AMI	X	X	
Decreased CFI of AMI			X
Decreased AMI deaths	X	X	X
Decreased incidence of sudden cardiac deaths	X	X	

AMI = acute myocardial infarction; CFI = collateral flow index; RX = treatment.

The incidence of out-of-hospital cardiac arrests with ventricular fibrillation has been followed very closely in Seattle, where all out-of-hospital cardiac arrests receive advanced life support from a single source: the Seattle Fire Department Medical services. Cobb et al<sup>29</sup> reported that the incidence of out-of-hospital cardiac arrests presenting with ventricular fibrillation decreased by 56% from 1980 to 2000.

The Worcester Heart Attack study reported a 60% decrease in the incidence of out-of-hospital sudden coronary deaths from 1975 to 1988 in men and a 69% decrease in women.<sup>24</sup>

The decrease in sudden cardiac deaths could be due in part, to a decrease in coronary atherosclerosis due to primary prevention, or secondary prevention (statins, aspirin, beta-blockers, and lifestyle changes) in patients with clinical evidence of coronary heart disease or in patients with asymptomatic coronary heart disease. The substantial decrease in sudden cardiac deaths over recent years is a major component of the decrease in coronary heart disease deaths in the US.

## CONCLUSIONS

Most of the decline in coronary heart disease deaths is due to a decrease in deaths due to acute myocardial infarction and to a reduction in sudden cardiac deaths. These deaths have been reduced by primary prevention, which has decreased the incidence of coronary atherosclerosis, and primary and secondary prevention, which have reduced the progression of coronary atherosclerosis to obstructive coronary heart disease.

In addition, the remarkable reduction in the case fatality rate of acute myocardial infarction is almost certainly due to more effective emergency treatment and transport of patients who then receive more rapid and effective in-hospital treatment.

The multiple factors that have led to the remarkable decline in coronary heart disease deaths in the US over the last 50 years are shown in the [Table](#).

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