Articles

Lifetime risk of developing coronary heart disease

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Summary

Background The lifetime risk of developing coronary heart disease has not been estimated in a general population. We investigated the lifetime risks of initial coronary events at different ages.

Methods We assessed data for 7733 participants in the Framingham Heart Study, who had been examined at least once at age 40–94 years between 1971 and 1975, found to be free of coronary heart disease, and then followed up. We estimated the lifetime risks of coronary heart disease (angina pectoris, coronary insufficiency, myocardial infarction, or death from coronary heart disease) by multiple-decrement life-table methods.

Findings The 7733 patients were followed up for a total of 109 948 person-years. Overall, 1157 participants developed coronary heart disease. 1312 died from non-coronary heart disease causes. Lifetime risk of coronary heart disease at age 40 years was 48·6% (95% CI 45·8–51·3) for men and 31·7% (29·2–34·2) for women. At age 70 years, lifetime risk was 34·9% (31·2–38·7) for men and 24·2% (21·4–27·0) for women. After we excluded isolated angina pectoris as an initial event, the lifetime risk of coronary artery disease events at age 40 years was 42·4% for men and 24·9% for women.

Interpretation Lifetime risk at age 40 years is one in two for men and one in three for women. Even at age 70 years it is one in three for men and one in four for women. This knowledge may promote efforts in education, screening, and treatment for prevention of coronary heart disease in younger and older patients.

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Introduction

The calculation of lifetime risk is useful for the estimation of cumulative risk of developing a disease during an individual's remaining lifespan. Estimates of lifetime risk assist clinicians, researchers, and policy-makers in the assessment of the burden of a disease in a population. The risks of developing two or more diseases can be compared and clinical and public health measures can be taken commensurate with the burden of disease.

The lifetime risks of developing several diseases, including cancer,[1,2] osteoporotic fractures,[3] dementia,[4] and Alzheimer's disease,[4] have been calculated. The most widely publicised example is the lifetime risk of breast cancer, which was estimated to be 12·6% (one in eight) for women in the USA.[5] This value has been widely cited in the media and has increased public awareness of, and interest in, prevention, screening, and treatment of breast cancer.

Although mortality from coronary heart disease has fallen substantially in the past three decades,[6] it remains the single leading cause of death for adults worldwide,[7] and is expected to remain the leading cause of death and disability in the western world well into the 21st century.[8] Despite this projection, no estimates of lifetime risk of coronary heart disease have been made in a general population. Previous estimates of the lifetime risk[3,9,10] have been limited by reliance on death-certificate data or short duration of follow-up. The Framingham Heart Study, with its well-described population, careful documentation of events due to coronary heart disease and causes of death, and long-term follow-up, provides an opportunity to describe the lifetime risk of developing coronary heart disease in a community-based sample. We estimated the lifetime risk of coronary heart disease for men and women free from coronary heart disease events at different ages.

Methods

Participants

The Framingham Heart Study is a continuing study that started in 1948, when 5209 residents of Framingham, Massachusetts, USA, aged 28–62 years, were enrolled in a prospective epidemiological cohort study.[11,12] Participants are assessed every 2 years by medical histories, physical examinations, and selected laboratory tests. In 1971, 5124 of the original participants' offspring and offsprings' spouses were enrolled and followed up every 4 years.[13]

For the analysis of lifetime risks of coronary heart disease, to reflect contemporary experience, we assessed data from all 7733 participants who had attended at least one examination in 1971–75 at age 40–94 years. Participants who had no history, symptoms, or signs of coronary heart disease before or at the index examination were included.

	Age 35–44 years		Age 45–54 years		Age 55–64 years		Age 65–74 years	
	Men (n=738)	Women (n=749)	Men (n=676)	Women (n=717)	Men (n=640)	Women (n=898)	Men (n=366)	Women (n=531)
Diabetes*	19 (3%)	9 (1%)	29 (4%)	13 (2%)	38 (6%)	35 (4%)	36 (10%)	33 (6%)
Current smoker†	316 (43%)	312 (42%)	311 (46%)	303 (42%)	314 (49%)	336 (37%)	158 (43%)	98 (19%)
Hypertension‡	204 (28%)	112 (15%)	258 (38%)	223 (31%)	313 (49%)	409 (46%)	222 (61%)	364 (69%)
Mean total cholesterol (mmol/L)	5·4	5·0	5·6	5·6	5·7	6·2	5·7	6·3

*Defined as previous history of diabetes, non-fasting blood glucose >11·1 mmol/L for original cohort participants, fasting plasma glucose ⩾7·8 mmol/L for offspring, or receiving medical therapy. †Defined as regular smoking during year before index examination. ‡Defined as systolic blood pressure ⩾140 mm Hg, diastolic blood pressure ⩾90 mm Hg, or receiving medical therapy.

Table 1: **Age-specific and sex-specific baseline characteristics of participants**

Methods

All deaths or possible coronary heart disease events were assessed by three physicians who reviewed all available medical information. Deaths were assigned to one of six mutually exclusive causes: coronary heart disease, stroke, other cardiovascular disease, cancer, other, or unknown. We were able to ascertain the vital status of all but 20 participants.

We diagnosed participants as having developed coronary heart disease after review of study data, outside medical records, and electrocardiograms.[14] Coronary heart disease events were: angina pectoris (brief recurrent chest discomfort for up to 15 min, brought on by exertion and relieved by rest or glyceryl trinitrate); coronary insufficiency (prolonged chest discomfort associated with transient repolarisation abnormality, without criteria for myocardial infarction); myocardial infarction (serial electrocardiographic changes leading to development of new pathological Q waves, characteristic rise and fall of serum myocardial markers with a suggestive clinical history, or evidence at necropsy of new or recent infarction); and death due to coronary heart disease (available information that implied coronary heart disease as the probable cause).

Statistical analysis

All statistical analyses were done with SAS (version 6.1). For calculation of lifetime risk, we used a modified technique of survival analysis.[4] (A detailed description of the calculation of lifetime risk is available from *The Lancet* and *The Lancet* website at www.thelancet.com)

Because few participants survived after age 94 years, we calculated lifetime risk only up to age 94 years. Each participant was followed up from entry until July, 1996, the year of first coronary heart disease event, death, age 95 years, or the last follow-up examination. We calculated hazard ratios, age-specific incidence, cumulative incidence, and Kaplan-Meier curves for survival probabilities. We adjusted for the competing risk of death from non-coronary heart disease causes to give a true remaining lifetime risk.[4,15] We calculated risks separately for men and women at index ages 40 years, 50 years, 60 years, and 70 years.

Results

7733 participants were followed up for 109 948 person-years. The baseline characteristics are shown in table 1.

	Men	Women
Manifestation of coronary heart disease		
Total number	684	473
Angina pectoris	233 (34%)	197 (42%)
Coronary insufficiency	24 (4%)	26 (5%)
Myocardial infarction	346 (51%)	210 (44%)
Coronary death	81 (12%)	40 (8%)
Cause of non-coronary death		
Total number	589	723
Cerebrovascular accident	37 (6%)	66 (9%)
Other cardiovascular disease	37 (6%)	51 (7%)
Cancer	248 (42%)	245 (34%)
Other identified cause	176 (30%)	232 (32%)
Unknown	91 (15%)	129 (18%)

Table 2: **First manifestations of coronary heart disease for cases, and causes of death for people who died free of coronary heart disease**

During follow-up, 1157 participants developed coronary heart disease and 1312 died from non-coronary causes (table 2).

The risk of developing coronary heart disease before age 40 years was low (1·2% in men, 0·2% in women, data not shown). At age 40 years, the lifetime risk of coronary heart disease was 48·6% (about one in two) for men, and 31·7% (about one in three) for women (table 3). As age free of coronary heart disease increased, the lifetime risk of a first coronary heart disease event decreased. At age 70 years, however, the lifetime risk was still high, at about one in three for men and about one in four for women.

We estimated cumulative risks of coronary heart disease adjusted for non-coronary heart disease deaths for each of the index ages (figure 1). In men and women, the cumulative risk rose with age, and especially steeply after age 60 years until about age 90 years, after which cumulative risk seemed to flatten out. The curves rise more steeply for men than women for all index ages, which shows higher short-term risks of coronary heart disease in men. At all ages men had a higher lifetime risk of coronary heart disease than women.

At ages 40–60 years the lifetime risk of hard coronary heart disease events, excluding angina pectoris (ie, coronary insufficiency, myocardial infarction and coronary death, table 4) was 6–7% lower than that for all coronary heart disease (table 3). At age 70 years, the difference was 2–3%, which suggests that new-onset isolated angina pectoris contributed little to incident coronary heart disease after age 70 years.

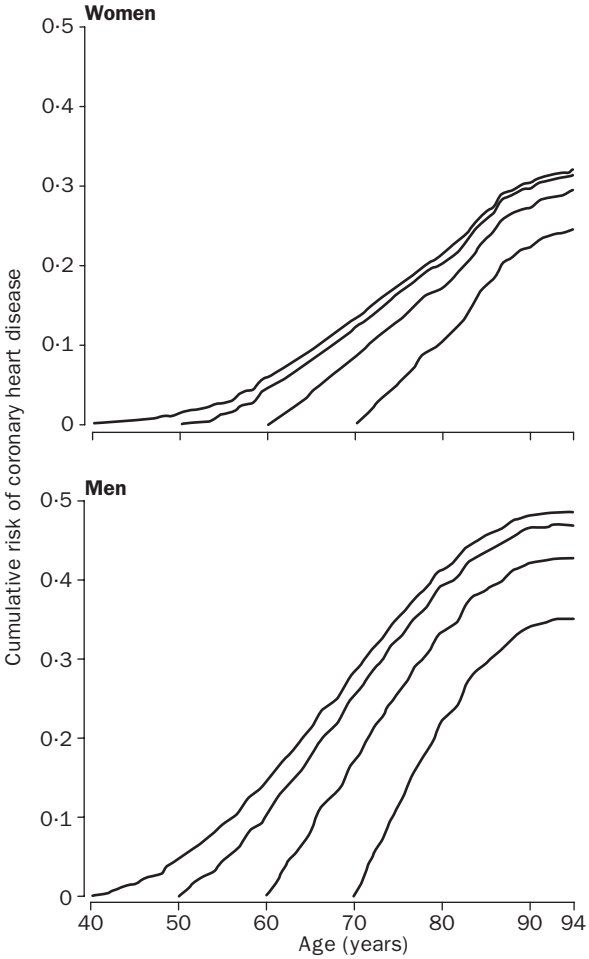
Discussion

Lifetime risk of coronary heart disease was one in two for men and one in three for women. The risk lessened with age, but remained high at older ages. We estimated lifetime risk rather than unadjusted cumulative incidence. Although unadjusted cumulative incidence is more easily calculated, it generally overestimates the risk of diseases if the prevalence in the population is more than 10%, or if competing risks of mortality are high.[2] Calculation of unadjusted cumulative incidence assumes that people who do not live to the upper age limit of observation would have developed the disease at the same rate as those who survived. By contrast, lifetime risk estimates reflect the measured risk of disease for actual lifespan and

Age (years)	Lifetime risk* (95% CI)	
	Men	Women
40	48·6% (45·8–51·3)	31·7% (29·2–34·2)
50	46·9% (44·0–49·8)	31·1% (28·6–33·7)
60	42·7% (39·5–45·8)	29·0% (26·3–31·6)
70	34·9% (31·2–38·7)	24·2% (21·4–27·0)

*Angina pectoris, coronary insufficiency, myocardial infarction, or coronary death.

Table 3: **Lifetime risk of first coronary heart disease event at different ages reached free of coronary heart disease**



Cumulative risk and lifetime risk of coronary heart disease for men and women

Individual curves are shown for baseline ages of 40 years, 50 years, 60 years, and 70 years reached free of coronary heart disease. Cumulative risk up to age 94 years represents lifetime risk for that baseline age.

represent more accurately the individual risk and the population burden of a disease.

The fall in lifetime risk of coronary heart disease with age reached free of events reflected the shorter life expectancy and period at risk for older participants. Also, at older ages, competing causes of death may increase in importance because people highly susceptible to coronary heart disease would have developed it at younger ages. At older ages, men continued to have higher lifetime risks of coronary heart disease than women. The differences in lifetime risk between men and women diminished slightly with each decade, but were still substantial at age 70 years.

Our results can be compared with lifetime risk estimates for other diseases to assess the absolute population-wide risks. Such data are more easily understood by the general population than relative risk estimates, which do not give meaningful measures of absolute risk. With estimates of lifetime risk of coronary artery disease, policymakers may be better able to promote public interest in prevention, screening, and treatment of coronary heart disease and related cardiovascular diseases in younger people, who have high long-term risks, and in older people, who remain at high risk. Lifetime risk data can guide the allocation of resources to improve public-health and preventive services for coronary heart disease. Our results may also be useful in the design of epidemiological studies.

Age (years)	Lifetime risk* (95% CI)	
	Men	Women
40	42·4% (39·5–45·2)	24·9% (22·5–27·3)
50	40·8% (37·8–43·7)	24·6% (22·2–27·0)
60	37·9% (34·7–41·1)	23·7% (21·2–26·2)
70	32·4% (28·8–36·1)	21·1% (18·4–23·7)

*Coronary insufficiency, myocardial infarction, or coronary death.

Table 4: **Lifetime risk of a first coronary heart disease event, excluding angina pectoris**

Media and interest groups have publicised the lifetime risk of breast cancer of one in eight (derived from the National Cancer Institute's surveillance data) to good effect. In 1994, for example, nearly 60% of women aged older than 50 years reported having had a mammogram in the previous 2 years, compared with 25% in 1987.[16] Such effects may serve as a benchmark for those interested in prevention of coronary heart disease.

Screening and treatment of coronary heart disease risk factors is suboptimum. Data from phase two of the Third National Health and Nutrition Examination Survey (NHANES III)[17] show that among hypertensive adults in the USA, 68·4% were aware of their diagnosis, 53·6% were on antihypertensive treatment, and only 27·4% had controlled blood pressure. Even fewer patients with hypercholesterolaemia are identified, are on treatment, and reach target concentrations.[16,18] International health data show that inadequate screening, treatment, and control of cardiovascular disease risk factors contribute substantially to the morbidity and mortality of coronary heart disease.[19] Data such as ours may help to add impetus to local, national, and global efforts to promote awareness, treatment, and control of modifiable risk factors.

Lifetime risk estimates represent average values for populations and presence or absence of risk factors may raise or lower absolute lifetime risks for individuals. Our results may, however, still have important implications for individual patients. For example, there are no randomised trial results of hormone replacement in primary prevention of coronary heart disease, and its role is controversial. Observational data suggest that hormone-replacement therapy for postmenopausal women may effectively decrease the frequency of primary coronary heart disease events and mortality,[10,20,21] with a small excess risk of breast cancer. We estimate that the lifetime risk of coronary heart disease for a woman aged 50 years (31·1%) is nearly three times that for breast cancer (11·3%).[5] Such comparisons could be helpful to patients to explain the potential hazards and benefits of hormone-replacement therapy.

Treatment of isolated systolic hypertension and hypercholesterolaemia in older people decreases the frequency of coronary events.[22–25] Despite this finding, clinicians are more reluctant to treat older than younger patients,[26] perhaps because of perceived lower benefits of treatment or greater risk of side-effects. In addition, patients and clinicians may assume that reaching an older age free from coronary heart disease suggests that the patient is not susceptible. The high remaining lifetime risk of coronary heart disease among older men and women, however, provides a rationale for aggressive screening and treatment of hypertension and hypercholesterolaemia in older and younger patients.

Our study had several limitations. First, the Framingham Heart Study cohort consists almost

exclusively of white people from one area. Extrapolation of our data to different populations or ethnic groups may be inappropriate because of the differences in coronary heart disease seen around the world.[27] The risk factors present at baseline in our sample are, however, similar to those of the whole white population of the USA at the time of the study.[28] Second, because few participants survived past age 94 years, we did not calculate lifetime risk for the upper extreme of age. The cumulative risk curves, however, seemed to flatten out after age 90 years. Third, we were unable to identify the cause of death in about 17% of participants who died free from prevalent coronary heart disease. If some of these participants had died as a result of coronary heart disease, we may have underestimated the lifetime risk. Finally, because of their participation in periodic examinations, Framingham participants may have been motivated to modify risk factors, which would lessen their lifetime risk of coronary heart disease.

Further analyses of lifetime risk of coronary heart disease require novel statistical methods to account for changes in risk factor status over time. The results are not predictable since characteristics, such as smoking, that modify the risk of coronary heart disease also modify the risk of death from competing causes.

Contributors

Donald Lloyd-Jones and Daniel Levy were involved in the conception, design, interpretation of results, and writing and editing of the manuscript. Martin Larson and Alexa Beiser participated in the conception, design, statistical analysis, interpretation, and editing of the manuscript.

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