

# Association of Cardiorespiratory Fitness With Coronary Heart Disease in Asymptomatic Men

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## Abstract

**Objective:** To examine the association of cardiorespiratory fitness (CRF) with risk of coronary heart disease (CHD) while controlling for an individual's Framingham Risk Score (FRS)—predicted CHD risk.

**Patients and Methods:** The study included 29,854 men from the Aerobics Center Longitudinal Study, who received a baseline examination from January 1, 1979, to December 31, 2002. Coronary heart disease events included self-reported myocardial infarction or revascularization or CHD death. Multivariable survival analysis investigated the association between CRF, FRS, and CHD. Cardiorespiratory fitness was analyzed as both a continuous and a categorical variable. The population was stratified by “low” and “moderate or high” risk of CHD to test for differences in the FRS stratified by CRF.

**Results:** Compared with men without incident CHD, men with incident CHD were older (mean age, 51.6 years vs 44.6 years), had lower average maximally achieved fitness (10.9 metabolic equivalent of tasks vs 12.0 metabolic equivalent of tasks [METs]), and were more likely to have moderate or high 10-year CHD risk ( $P < .001$ ). Cardiorespiratory fitness, defined as maximal METs, exhibited a 20% lower risk of CHD (hazard ratio, 0.80; 95% CI, 0.77-0.83) for each 1-unit MET increase. Among men in the low CRF strata, individuals with moderate or high 10-year CHD risk, according to the FRS, had a higher CHD risk (hazard ratio, 6.55; 95% CI, 3.64-11.82) than men with low CHD risk according to the FRS.

**Conclusion:** Clinicians should promote physical activity to improve CRF so as to reduce CHD risk, even to patients with otherwise low CHD risk.

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The American Heart Association<sup>1</sup> stated that one of its 2020 Impact Goals was to reduce deaths from cardiovascular disease (CVD) by 20%. Most CVD deaths in 2006 and 2007 were caused by coronary heart disease (CHD), which is defined as plaque accumulation in the arteries of the heart, decreasing the supply of oxygen-rich blood.<sup>2</sup> Several risk factors have been shown to predict CHD, including smoking,<sup>3</sup> diabetes,<sup>4</sup> hypertension,<sup>5</sup> and hypercholesterolemia.<sup>6</sup>

Coronary heart disease risk equations, such as the Framingham Risk Score (FRS), have been developed and used to account for these and other risk factors.<sup>7</sup> The FRS provides a sex-specific risk score that accounts for age, systolic and diastolic blood pressure, total cholesterol level, high-density lipoprotein cholesterol (HDL-C) level, diabetes diagnosis, and smoking status.<sup>8</sup> Previous studies<sup>9-11</sup> have modified the FRS with the addition of C-reactive protein,<sup>10</sup> deletion of diabetes diagnosis,<sup>11</sup> and alterations

to blood pressure definitions<sup>12</sup>; yet none of these modifications involved assessing the association between cardiorespiratory fitness (CRF), FRS, and CHD.

Previous research reports CRF's significant protective effects on all-cause mortality,<sup>13,14</sup> cancer-related mortality,<sup>15</sup> diabetes incidence,<sup>16</sup> CHD incidence,<sup>17</sup> and CHD mortality.<sup>8,18,19</sup> Barlow et al<sup>20</sup> reported that a 1-unit metabolic equivalent of task (MET) increase in baseline CRF resulted in an 18% decrease in CVD mortality in FRS-classified “low-risk” adults over a 30-year follow-up period. However, this result reflects control for additional factors besides CRF, such as body mass index (calculated as the weight in kilograms divided by the height in meters squared) and family history of early CHD, which are not included in the FRS.

The aim of this study was to examine the association of CRF with 10-year risk of CHD while controlling for an individual's FRS—predicted CHD risk. Our secondary aim was to

investigate whether the relationship between CRF and 10-year risk of CHD differs in “moderate- or high-risk” men.

## PATIENTS AND METHODS

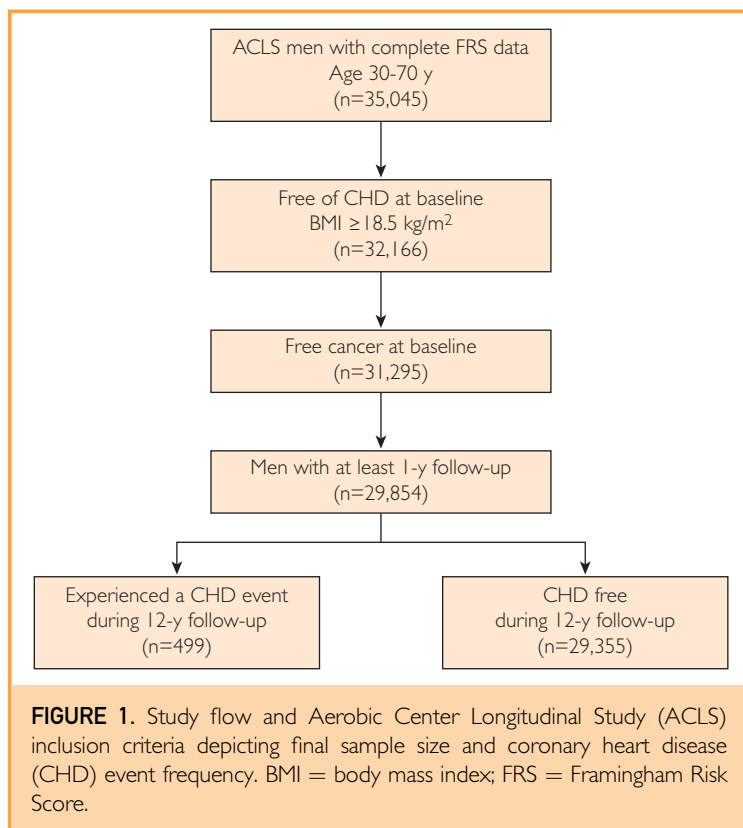
### Aerobics Center Longitudinal Study

The Aerobics Center Longitudinal Study (ACLS) is a prospective cohort study involving a large group of men and women. The participants were patients of the Cooper Clinic, in which they received a preventive medical examination and counseling on health behaviors during periodic visits. The participants were examined at least once from January 1, 1979, to December 31, 2002, at the Cooper Clinic, Dallas, Texas. The protocol for the ACLS was reviewed annually and approved by the institutional review board of the Cooper Institute. Women were excluded from these analyses because of a small number of CHD events ( $n=45$ ). Men were included on the basis of the following criteria: (1) age at baseline examination between 30 and 74 years; (2) complete data for outcome and predictor variables; and (3) free of CVD or cancer diagnosis at baseline. A flow diagram of the study population is depicted in Figure 1.

### Clinical Examination

The baseline clinical examination included an electrocardiogram, a 12-hour fasting blood chemistry analyses including cholesterol and glucose measurements, blood pressure assessment, and a maximal exercise test.<sup>21-23</sup> A standardized questionnaire was used to assess smoking status and other risk factors.

**Outcome Measure.** Coronary heart disease was defined through self-report of either revascularization (including bypass, coronary balloon, angioplasty, or stent) or myocardial infarction or CHD-specific mortality. A mail-back questionnaire was administered in 1982, 1986, 1990, 1995, 1999, and 2004, in which participants were asked to report their history of revascularization or myocardial infarction along with the incident date. The National Center for Health Statistic’s National Death Index was used to identify CHD deaths in the ACLS cohort; *International Classification of Disease* (Ninth and Tenth revisions) codes 410.0 to 414.0 were used to determine CHD as the primary cause of death.



In accordance with FRS’s follow-up time definition, the maximal follow-up time for the ACLS study population was 12 years.

**Application of the FRS.** The FRS was derived from the Framingham Heart Study,<sup>7</sup> which is an ongoing observational study initiated in 1948 and primarily recruits residents of Framingham, Massachusetts. In a study published in 1998,<sup>8</sup> the main outcome was a CHD event defined as a myocardial infarction, coronary insufficiency, or CHD death. This version of the FRS<sup>8</sup> incorporated categorical variables for age, hypertension, total cholesterol level, HDL-C level, smoking status, and diabetes to determine a point value that could be summed and interpreted as an overall 10-year risk of CHD. The definition of the risk factors was kept consistent with the 1998 FRS report,<sup>8</sup> and the risk factors were categorized on the basis of the score sheet. Diabetes was diagnosed if the fasting glucose level was higher than 140 mg/dL (to convert to mmol/L, multiply by 0.0259), and smoking status was self-reported.

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