Cardiorespiratory Fitness and Coronary Heart Disease Risk Factors
The LDS Hospital Fitness Institute Cohort

Michael J. LaMonte, PhD; Patricia A. Eisenman, PhD; Ted D. Adams, PhD, MPH; Barry B. Shultz, PhD; Barbara E. Ainsworth, PhD, MPH; Frank G. Yanowitz, MD

Background—Cardiorespiratory fitness is favorably associated with most modifiable coronary heart disease (CHD) risk factors. Findings are limited, however, by few data for women, persons with existing CHD, and low-risk populations. In the present study, we described cross-sectional associations between cardiorespiratory fitness and CHD risk factors in a large cohort of middle-aged men and women, of whom the majority were LDS Church members (Mormons), with and without existing CHD.

Methods and Results—Comprehensive health examinations were performed on 3232 men (age 45.9 ± 10.8 years) and 1128 women (age 43.8 ± 12.8 years) between 1975 and 1997. Maximal treadmill exercise testing was used to categorize those with (12% of the men and 10% of the women) and those without CHD into age- and sex-specific cardiorespiratory fitness quintiles. After adjustments for age, body fat, smoking status, and family history of CHD, favorable associations were observed between fitness and most CHD risk factors among men and women, regardless of CHD status.

Conclusions—These data indicate that enhanced levels of cardiorespiratory fitness may confer resistance to elevations in CHD risk factors even in a low-risk sample of middle-aged men and women. Furthermore, these findings reinforce current public health recommendations that advocate increased national levels of physical activity and cardiorespiratory fitness for primary and secondary CHD prevention. (Circulation. 2000;102:1623-1628.)

Key Words: cardiovascular disease ■ risk factors ■ exercise ■ women

Recent reports document a large national health burden of chronic disease with significant proportions due to behavioral dimensions such as physical inactivity and low levels of cardiorespiratory fitness.1,2 Physical inactivity confers a relative3 and attributable4 risk for death due to coronary heart disease (CHD) that is similar to that of other major modifiable risk factors. With the high prevalence of physical inactivity,1 increasing population physical activity levels may confer substantial reductions in incident CHD.

A current understanding of the relationship between sedentary lifestyles and CHD has emerged from pioneering works that used self-reported physical activity to represent the degree of exposure.1 Cardiorespiratory fitness assessed with maximal exercise testing is a more precise and reliable measure than self-reported physical activity. This may in part explain the larger risk estimates for death due to CHD associated with low levels of measured fitness compared with self-reported physical inactivity.1 Correlations between carefully aggregated habitual activity levels and cardiorespiratory fitness measured with maximal exercise testing have been large (r = 0.50 to 0.83).5 The objective measure of cardiorespiratory fitness might therefore more accurately reflect the consequences of a sedentary or irregularly active lifestyle.

Compared with physical activity,1,3 fewer reports are available on the association between cardiorespiratory fitness and CHD.6–10 Existing studies have often had modest sample sizes with relatively small percentages of women. Cardiorespiratory fitness has frequently been extrapolated from submaximal exercise, few reports have included participants with existing CHD, and there is a paucity of data from low-risk populations. In the present investigation, we described the association between measured cardiorespiratory fitness and coronary risk factors in a large low-risk sample of middle-aged men and women with and without CHD.

Methods
Study Design and Participants
Cross-sectional analyses were performed on 3232 men and 1128 women who underwent a comprehensive health assessment at the LDS Hospital Fitness Institute (Salt Lake City, Utah) between 1975 and 1997. Participants were mostly white-collar executives who had the health evaluation performed for employment reasons or for personal interest. The majority of participants were residents of Utah.
Exercise intolerance was defined as (1) failure to achieve \( \geq 85\% \) of age-predicted maximal heart rate or (2) premature termination of the exercise stress test for reasons other than exhaustion.

### Statistical Analyses

Glucose and triglyceride values were log (base 10) transformed to better approach normality. Other variables demonstrated small amounts of skewness due to outlying values, but these outliers were retained in the analyses because of their possible association with fitness. Linear regression was used to adjust mean risk factor values for age, percent body fat, smoking status, and family history of CHD to better assess the independent effect of fitness. Polynomial trend modeling was used to describe the shape of the association between risk factors and cardiorespiratory fitness. The highest-order polynomial term that was significant and the percent linear variation are reported. Logistic regression models were constructed to evaluate the clinical relevance of the association between fitness and CHD risk factors. Sample size limited logistic analyses to men and women without CHD. Fitness tertiles were formed according to MET levels of maximal exercise performance to enable a comparison with existing data. CHD risk factors associated with the insulin-resistance metabolic syndrome were dichotomized as Systolic blood pressure (SBP; \( \geq 140 \) mm Hg or not), glucose (\( \geq 6.1 \) mmol/L or not), triglycerides (\( \geq 1.7 \) mmol/L or not), and LDL (\( \geq 3.4 \) mmol/L or not). Statistical significance was evaluated with point estimates and the reported 2-tailed probability or the 95% CI. All analyses were performed with SPSS-PC+ (Version 6.1).

### Results

The majority of participants in the present study were whites from middle and upper socioeconomic levels and members of the LDS Church. Participants were middle aged and marginally overweight and displayed average levels of cardiorespiratory fitness (Table 1). The prevalence of smoking, CHD, and family history of heart disease was low. Except for marginally elevated LDL levels, the cohort risk factor profile was clinically acceptable (Table 2).

### Table 1. Participant Characteristics

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Weight, kg</th>
<th>Body mass index, kg/m²</th>
<th>Body fat, %</th>
<th>VO₂max, ml ⋅ kg⁻¹ ⋅ min⁻¹</th>
<th>SBP, mm Hg</th>
<th>HDL cholesterol, mmol/L</th>
<th>Triglycerides, mmol/L</th>
<th>Glucose, mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (n=4360)</td>
<td>Men (n=3232)</td>
<td>Women (n=1128)</td>
<td>All (n=4360)</td>
<td>Men (n=3232)</td>
<td>All (n=3232)</td>
<td>Women (n=1128)</td>
<td>All (n=3232)</td>
<td>Men (n=3232)</td>
</tr>
<tr>
<td>-------</td>
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<td>---------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>45.4±11.4</td>
<td>45.9±10.8</td>
<td>43.8±12.8</td>
<td>45.1±47.5</td>
<td>45.5±46.3</td>
<td>43.1±44.6</td>
<td>81.0±16.6</td>
<td>85.9±14.4</td>
<td>66.7±14.1</td>
</tr>
</tbody>
</table>

| Fitness level, % | CHD, % | Family history of CHD, % | Values are mean±SD (95% CI). | *Known or suspected CHD.

### Table 2. CHD Risk Factor Profiles

<table>
<thead>
<tr>
<th>SBP, mm Hg</th>
<th>Glucose, mmol/L</th>
<th>Triglycerides, mmol/L</th>
<th>HDL cholesterol, mmol/L</th>
<th>Total cholesterol, mmol/L</th>
<th>LDL cholesterol, mmol/L</th>
<th>TC/HDL*</th>
</tr>
</thead>
<tbody>
<tr>
<td>122.9±16.3</td>
<td>5.34±1.04</td>
<td>3.39±0.98</td>
<td>5.81±1.10</td>
<td>5.33±1.07</td>
<td>3.33±0.97</td>
<td>4.8±1.9</td>
</tr>
<tr>
<td>124.7±15.8</td>
<td>5.44±1.0</td>
<td>3.49±0.97</td>
<td>5.19±1.10</td>
<td>5.37±1.05</td>
<td>3.49±0.97</td>
<td>5.2±1.9</td>
</tr>
<tr>
<td>118.2±17.1</td>
<td>5.07±1.11</td>
<td>3.11±0.98</td>
<td>5.19±1.10</td>
<td>5.15±1.05</td>
<td>3.15±0.98</td>
<td>3.7±1.3</td>
</tr>
<tr>
<td>(122.5–123.5)</td>
<td>(5.29–5.36)</td>
<td>(5.32–5.38)</td>
<td>(5.02–5.13)</td>
<td>(5.08–5.48)</td>
<td>(5.02–5.48)</td>
<td>(3.6–3.8)</td>
</tr>
</tbody>
</table>

Values are mean±SD (95% CI). *TC/HDL, ratio of total to HDL cholesterol, is calculated from mg/dL values. Approximate conversions: total, LDL, and HDL cholesterol are 38.6 mg/dL per mmol/L; triglycerides, 88.5 mg/dL per mmol/L; and glucose, 18 mg/dL per mmol/L.
The prevalence of clinically relevant risk factor values was higher among men than women: SBP (15.4% versus 10.9%), glucose (8.6% versus 3.1%), triglycerides (35.2% versus 20.3%), and LDL (50.4% versus 33.9%). After adjustment for potential confounders, significant inverse associations persisted between fitness and all risk factors except glucose among men (Figure 1) and between fitness and SBP and triglycerides among women (Figure 2).

### Discussion

CHD, the leading cause of death among US adults, is a multifactorial process with cultural and behavioral origins. Recent reports have described the cardiovascular benefits of physical activity and cardiorespiratory fitness. The current study showed significant favorable associations between fitness and most CHD risk factors among men and women, regardless of CHD status. Higher fitness significantly reduced the odds of clinically relevant risk factor values among men and women without CHD.

Cardiorespiratory fitness was favorably associated with CHD risk factors despite a relatively homogeneous cohort and after statistical adjustment for age, percent body fat, smoking status, and family history of heart disease. Our findings are consistent with cross-sectional reports on Aerobics Center Longitudinal Study (ACLS) men and women, as well as other observational data. Furthermore, associations between fitness and CHD risk factors similar to those seen in the current data have been reported at baseline in prospective studies that have subsequently demonstrated reduced coronary mortality rates in fit versus unfit men and women.

Extensive reviews have summarized observational and experimental data that show desirable effects of exercise on glyce-
A surprising that enhanced fitness appears to protect against many chronic diseases that is not regulated by the Food and Drug Administration.32 Because risk factors synergistically multiply the individual risk of CHD,28 even small risk factor reductions associated with increased fitness could substantially lower the probability of incident CHD.

The homogeneity of the cohort may have resulted in underestimation of the influence of body fat.34 Nonetheless, the current observations support previous data6–10,24,34 that show enhanced cardiorespiratory fitness profile; therefore, we looked at the relationship from a clinical perspective. Recent ACLS reports have shown fitness to be inversely associated with the prevalence26 and associated mortality risk33 of CHD risk factor clustering. By applying the criteria used by ACLS investigators, we observed that low-fit men (Figure 1) and women (Figure 2) were 3 to 6 times more likely to have clinically relevant risk factor levels than their high-fit counterparts. The associations remained significant even after adjustment for body fat. Our hydrostatic estimate of total body fat does not precisely quantify the more atherogenic central fat depot.34 Nonetheless, the current observations support previous data6–10,24,34 that show enhanced cardiorespiratory fitness levels confer protection against elevated CHD risk independent of the influence of body fat.

Recommendations that promote the cardiovascular benefits of physical activity and cardiorespiratory fitness1,2 are potentially limited by little data from low-risk populations.35 Significant inverse associations were reported between baseline self-reported physical activity and fatal coronary events among 27 658 adults after a 6-year follow-up in the Adventist Health Study.35 Potential misclassification on exposure and selection bias reduces the generalizability of these data until other studies confirm the health benefits of physical activity in low-risk populations. Low coronary mortality rates have been reported among Mormons,36,37 including men with lethal genetic predisposition.38 Between 1993 and 1995, Utah ranked first and third nationally for the lowest cardiovascular and CHD death rates, respectively.21 Our cross-sectional findings showed that a large cohort of middle-aged men and women, the majority of whom are Mormon, demonstrated (1) average levels of cardiorespiratory fitness, (2) clinically acceptable values for most CHD risk factors, and (3) inverse associations between fitness and CHD risk factors, regardless

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### Table 4. CHD Risk Factors According to Cardiorespiratory Fitness Level Among Women Without CHD (n=1019)

<table>
<thead>
<tr>
<th>Fitness Level</th>
<th>SBP, mm Hg</th>
<th>Glucose, mmol/L</th>
<th>Triglycerides, mmol/L</th>
<th>Total Cholesterol, mmol/L</th>
<th>LDL Cholesterol, mmol/L</th>
<th>HDL Cholesterol, mmol/L</th>
<th>TC/HDL*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>123.2±5.2</td>
<td>5.34±0.21</td>
<td>2.05±0.15</td>
<td>5.36±0.28</td>
<td>3.11±0.25</td>
<td>1.17±0.01</td>
<td>5.1±0.27</td>
</tr>
<tr>
<td>(120.9–125.5)</td>
<td>(5.25–5.43)</td>
<td>(1.99–2.12)</td>
<td>(5.24–5.49)</td>
<td>(3.19–3.42)</td>
<td>(1.16–1.18)</td>
<td>(4.9–5.2)</td>
<td></td>
</tr>
<tr>
<td>n=23</td>
<td>n=15</td>
<td>n=21</td>
<td>n=21</td>
<td>n=21</td>
<td>n=21</td>
<td>n=21</td>
<td></td>
</tr>
<tr>
<td>Fair</td>
<td>122.3±5.9</td>
<td>5.31±0.25</td>
<td>1.86±0.29</td>
<td>5.31±0.34</td>
<td>3.31±0.27</td>
<td>1.18±0.03</td>
<td>4.9±0.38</td>
</tr>
<tr>
<td>(121.2–123.3)</td>
<td>(5.27–5.36)</td>
<td>(1.80–1.91)</td>
<td>(5.24–5.37)</td>
<td>(3.26–3.36)</td>
<td>(1.17–1.19)</td>
<td>(4.8–4.99)</td>
<td></td>
</tr>
<tr>
<td>n=130</td>
<td>n=111</td>
<td>n=124</td>
<td>n=126</td>
<td>n=121</td>
<td>n=124</td>
<td>n=124</td>
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</tr>
<tr>
<td>Average</td>
<td>124.1±6.1</td>
<td>5.38±0.26</td>
<td>1.83±0.26</td>
<td>5.39±0.35</td>
<td>3.41±0.28</td>
<td>1.19±0.02</td>
<td>4.98±0.39</td>
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<tr>
<td>(123.4–124.7)</td>
<td>(5.36–5.41)</td>
<td>(1.80–1.85)</td>
<td>(5.36–5.34)</td>
<td>(3.38–3.44)</td>
<td>(1.18–1.194)</td>
<td>(4.95–5.0)</td>
<td></td>
</tr>
<tr>
<td>n=403</td>
<td>n=391</td>
<td>n=402</td>
<td>n=401</td>
<td>n=399</td>
<td>n=401</td>
<td>n=399</td>
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</tr>
<tr>
<td>Good</td>
<td>122.4±5.9</td>
<td>5.32±0.25</td>
<td>1.65±0.25</td>
<td>5.29±0.34</td>
<td>3.35±0.27</td>
<td>1.21±0.02</td>
<td>4.8±0.38</td>
</tr>
<tr>
<td>(113.6–116.8)</td>
<td>(5.29–5.34)</td>
<td>(1.62–1.68)</td>
<td>(5.26–5.32)</td>
<td>(3.33–3.38)</td>
<td>(1.20–1.218)</td>
<td>(4.7–4.86)</td>
<td></td>
</tr>
<tr>
<td>n=384</td>
<td>n=371</td>
<td>n=376</td>
<td>n=380</td>
<td>n=374</td>
<td>n=375</td>
<td>n=375</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>120.0±5.9</td>
<td>5.22±0.24</td>
<td>1.52±0.24</td>
<td>5.15±0.34</td>
<td>3.26±0.27</td>
<td>1.22±0.02</td>
<td>4.6±0.40</td>
</tr>
<tr>
<td>(118.5–121.5)</td>
<td>(5.16–5.28)</td>
<td>(1.46–1.58)</td>
<td>(5.06–5.24)</td>
<td>(3.19–3.32)</td>
<td>(1.21–1.23)</td>
<td>(4.5–4.7)</td>
<td></td>
</tr>
<tr>
<td>n=67</td>
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<td>n=63</td>
<td></td>
</tr>
<tr>
<td>Trend†</td>
<td>Quadratic</td>
<td>Quadratic</td>
<td>Quadratic</td>
<td>Quadratic</td>
<td>Quadratic</td>
<td>Linear</td>
<td>Quadratic</td>
</tr>
<tr>
<td>P</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.04</td>
<td>0.0001</td>
<td>0.001</td>
<td>0.001</td>
<td>0.0003</td>
</tr>
<tr>
<td>Linear, %‡</td>
<td>27</td>
<td>30</td>
<td>90</td>
<td>37</td>
<td>4</td>
<td>94</td>
<td>67</td>
</tr>
</tbody>
</table>

See Table 3 for legend.

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mia24 and resting blood pressure.25 We observed fitness to be strongly and inversely associated with fasting glucose and resting SBP levels even after adjustment for influential variables. This observation has clinical significance because elevated fasting glucose and resting SBP have been suggested as markers for insulin resistance,26 which is known to increase CHD risk by clustering adverse conditions of hyperglycemia, hypertension, and dyslipidemia.27,28 Because skeletal muscle is a large and robust substrate depot for active and fit persons,24 it is not surprising that enhanced fitness appears to protect against elevated blood pressure, glucose, and lipid values.

The extent to which blood lipids were associated with cardiorespiratory fitness among the current cohort is contrary to some studies29,30 but similar to others.6–10 We observed significant inverse linear trends for TC and LDL across fitness levels among men regardless of CHD status. Fitness was favorably and significantly associated with HDL and TC/HDL among women even after adjustment for age and body fat and despite no association between fitness and TC. Among men and women with CHD (data not shown), percent differences in lipid levels between the lowest and highest fitness groups (eg, triglycerides 25% decrease, LDL 12% decrease) were similar to the expected effect of low-dose fibrinolytic acid derivatives and HMG-CoA reductase inhibitors.31 Exercise, which is essentially an anabolic agent, is one of few dose-response agents with proven therapeutic effects for many chronic diseases that is not regulated by the Food and Drug Administration.32 Because risk factors synergistically multiply the individual risk of CHD,28 even small risk factor reductions associated with increased fitness could substantially lower the probability of incident CHD.
of CHD status. These observations are consistent with cross-sectional data from other cohorts, among whom prospective studies subsequently showed that fitness independently protected against coronary mortality. It is therefore plausible that fitness contributes to the low CHD incidence and mortality rates previously described for Utah Mormons. Our findings and those from the Adventist Health Study suggest that physical activity and cardiorespiratory fitness confer substantial cardiovascular benefits, even in low-risk populations of men and women.

The present study has potential limitations that deserve consideration. Although cardiorespiratory fitness (VO2 max) was predicted from time during a maximal treadmill test as opposed to measured aerobic power, correlations between predicted and measured VO2 max are large. Recent evidence of only modest genetic contributions to cardiorespiratory fitness, reported training gains of up to 30%, and rapid detraining-related losses illustrate the plasticity of cardiorespiratory fitness and should temper genetic arguments against targeting fitness enhancement for CHD prevention. A recent randomized trial showed that sedentary or irregularly active individuals can achieve health-related levels of cardiorespiratory fitness through regular moderate-intensity lifestyle activities such as brisk walking. Our data lack more precise indices of coronary risk (e.g., regional adiposity, insulin, lipoprotein subfractions) that may have resulted in stronger associations with fitness. Attempts to control for medications and diet were not made. Our analyses lacked an index of habitual physical activity. With some of the variation in cardiorespiratory fitness not accounted for by genetic or environmental transmission, the level of habitual physical activity may indeed account for the remainder. Furthermore, differences in risk estimates for CHD mortality between fitness and physical activity may reflect different mechanisms through which fitness and activity confer cardiovascular health benefits. Last, we see a large need for data on ethnic minorities and persons with lower socioeconomic status for whom different levels of physical activity and CHD rates have been described.

We conclude that cardiorespiratory fitness was significantly and favorably associated with CHD risk factors independent of age, percent body fat, and family history of CHD, and regardless of CHD status, in a low-risk population of middle-aged men and women. These findings support public health recommendations for increased physical activity and

Figure 1. Unadjusted (A) and adjusted (B) odds ratios of clinical threshold values for risk factors across low, moderate, and high levels of cardiorespiratory fitness (CRF) in 2715 LDS Hospital Fitness Institute men. Number on columns indicates cases at or above clinical threshold value; High CRF, referent. Adjusted odds ratios were controlled for age, percent body fat, smoking, and family history of heart disease.

Figure 2. Unadjusted (A) and adjusted (B) odds ratios for clinical threshold values for risk factors common to insulin-resistant metabolic syndrome across low, moderate, and high levels of cardiorespiratory fitness (CRF) in 980 LDS Hospital Fitness Institute women. Number on columns indicates cases at or above clinical threshold value; High CRF, referent.
cardiorespiratory fitness to prevent the morbidity and mortality associated with CHD.

Acknowledgments
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