Absolute and Attributable Risks of Heart Failure Incidence in Relation to Optimal Risk Factors

Aaron R. Folsom, MD; Kazumasa Yamagishi, MD, PhD; Atsushi Hozawa, MD, PhD; Lloyd E. Chambless, PhD; for the Atherosclerosis Risk in Communities Study Investigators

Background—Epidemiological studies have shown that a large proportion of coronary heart disease and stroke events are explained by borderline or elevated risk factors and that adults with optimal risk factors greatly avoid these events. The degree to which this applies to heart failure incidence is not well documented.

Methods and Results—We categorized baseline (1987–1989) risk factors in the Atherosclerosis Risk in Communities Study cohort (n=13 460, aged 45 to 64 years) into optimal, borderline, and elevated groups based on national guidelines, using a 4-factor score (blood pressure, plasma cholesterol, diabetes, and smoking) and a 5-factor score (which included body mass). Incidence of hospitalized heart failure (n=1344) was identified over a 16-year period. Only 4.9% of the cohort at baseline had all optimal risk factors based on the 4-factor score and 2.6% using the 5-factor score. Compared with participants with any elevated risk factor using the 4-factor score, the age-, sex-, and race-adjusted relative hazard for heart failure events was 0.18 (95% CI, 0.10 to 0.32) for those with all optimal risk factors and 0.35 (95% CI, 0.30 to 0.41) for those with only borderline risk factors. A population-attributable fraction estimate suggested that having at least 1 of the 4 risk factors, elevated or borderline, accounted for 77.1% of heart failure events. For the 5-factor score, that percentage was 88.8%.

Conclusion—Middle-aged adults with optimal (low) risk factors have low incidence rates of heart failure, which supports redoubled efforts to prevent risk factor development in the first place. (Circ Heart Fail. 2009;2:11-17.)

Key Words: epidemiology ■ heart failure ■ risk factors

Much of the United States adult population is at risk of cardiovascular disease (CVD) by virtue of having ≥1 traditional CVD risk factors, including high blood pressure (BP), high blood cholesterol, cigarette smoking, diabetes, and excess body weight. However, recent epidemiological studies by Stamler et al and others have emphasized the potential of primary prevention by showing that adults with no risk factors have a low incidence of CVD.1–6 We recently showed that this was true for CVD among blacks and whites in the Atherosclerosis Risk in Communities (ARIC) study.7 Maintaining a life without developing a CVD risk factor therefore should be a universal goal.

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Prior studies of optimal CVD risk have generally focused on rates of coronary heart disease (CHD), stroke, or total CVD. Heart failure is a growing public health problem and eventually affects 1 in 5 US adults.9 Although heart failure has several risk factors in common with CHD and is often a result of CHD, no study has documented the degree to which adults with optimal risk factors avoid heart failure. To examine this issue, we calculated the absolute and attributable risks of heart failure incidence in relation to optimal risk factor levels in the ARIC study. In addition, we performed risk estimates for CHD and stroke separately, as our previous article pooled these outcomes.

Methods

Study Design and Subjects

The ARIC Study is a prospective cohort study of atherosclerotic diseases in 4 US communities: Forsyth County, NC; Jackson, Miss; Washington County, Md; and the northwest suburbs of Minneapolis, Minn.10 The cohort comprised, at baseline in 1987 to 1989, 15 792 men and women aged 45 to 64 years who were selected by list or area probability sampling. Only blacks were recruited in the Jackson study center. The baseline home interview and clinic examination measured various risk factors and cardiovascular conditions. The ARIC Study protocol was approved by the institutional review board of each participating university.

Baseline Examination

Sitting BP was measured 3 times using a random-zero sphygmomanometer after 5 minutes of rest.11 The mean of the last 2 measure-
ments was used for analysis. Use of antihypertensive medications within the past 2 weeks of baseline interview was self-reported. Fasting plasma total cholesterol was measured by enzymatic methods. Serum glucose was measured by a hexokinase/glucose-6-phosphate dehydrogenase method. Smoking status (current, former, or never smokers) was derived from interviews. Body mass index (kg/m²) was computed from weight in a scrub suit and standing height. Preexisting heart failure at baseline was defined as the first occurrence of either a hospitalization that included an International Classification of Diseases, 9th Revision (ICD-9) discharge code of 428 (428.0 to 428.9) among the primary causes of death during the prior year, and by surveying discharge lists from local hospitals and death certificates from state vital statistics offices otherwise through December 31, 2005 (heart failure and CHD) or December 31, 2004 (stroke). CVD events in ARIC were ascertained by contacting participants annually, identifying hospitalizations and deaths during the prior year, and by surveying discharge lists from local hospitals and death certificates from state vital statistics offices for potential CVD events. Incident heart failure in ARIC was defined as the first occurrence of either a hospitalization that included an International Classification of Diseases, 9th Revision (ICD-9) discharge code of 428 (428.0 to 428.9) among the primary or secondary diagnoses or else a death certificate with an ICD-9 code of 428 or an ICD-10 code of I50 among the listed or underlying causes of death.

Incident and Fatal Events

We followed all participants from the baseline examination in 1987 to 1989 to the date of CVD event, death, loss to follow-up, or otherwise through December 31, 2005 (heart failure and CHD) or December 31, 2004 (stroke). CVD events in ARIC were ascertained by contacting participants annually, identifying hospitalizations and deaths during the prior year, and by surveying discharge lists from local hospitals and death certificates from state vital statistics offices for potential CVD events. Incident heart failure in ARIC was defined as the first occurrence of either a hospitalization that included an International Classification of Diseases, 9th Revision (ICD-9) discharge code of 428 (428.0 to 428.9) among the primary or secondary diagnoses or else a death certificate with an ICD-9 code of 428 or an ICD-10 code of I50 among the listed or underlying causes of death.

For patients hospitalized with a potential MI, trained abstractors recorded the presenting symptoms and related clinical information, including cardiac enzymes, and photocopied up to 3 12-lead ECGs for Minnesota coding. Out-of-hospital deaths were investigated by means of death certificates and, in most cases, by an interview with one or more next of kin and a questionnaire filled out by the
patient’s physician. Coroner reports or autopsy reports, when available, were abstracted for use in validation. A CHD event was defined as a validated definite or probable hospitalized MI or a definite CHD death. The criteria for definite or probable MI were based on combinations of chest pain symptoms, ECG changes, and cardiac enzyme levels.21,22 The criteria for definite fatal CHD were based on chest pain symptoms, history of CHD, underlying cause of death from the death certificate, and any other associated hospital information or medical history, including that from an ARIC clinic visit.21,22

The diagnostic classification of stroke was described previously.24 In brief, for potential hospitalized strokes, the abstractors recorded signs and symptoms and photocopied neuroimaging (CT or MRI) and other diagnostic reports. Using criteria adopted from the National Survey of Stroke,25 strokes were classified by computer algorithm and separate review by a physician, with disagreements resolved by a second physician.

Statistical Analyses
Of 15 792 ARIC participants at baseline, we excluded, due to small numbers, participants who were neither white nor black subjects (n=48). We further excluded 1971 participants who had a history of heart failure, CHD or stroke, or could not be classified on history. Subjects (n=313) who did not have complete information on plasma cholesterol, cigarette smoking, BP value, or serum glucose were also excluded. In all, 13 460 participants were included in the analysis for the 4-factor score and slightly fewer (n=13 453) for the 5-factor score.

Crude incidence rates were calculated separately for each end point (heart failure, CHD, or stroke) according to risk factor groups. Persons with multiple end points were included with all individual end points. Follow-up time went from baseline until the first of (1) incident end point, (2) lost to follow-up, (3) death, or (4) cessation of follow-up. The relative hazards (RH) of incident of heart failure (or CHD or stroke) in relation to risk factor groups were estimated from Cox proportional hazard models adjusted for age, sex, and some other diagnostic reports. Using criteria adopted from the National Survey of Stroke,25 strokes were classified by computer algorithm and separate review by a physician, with disagreements resolved by a second physician.

Results
Prevalence of Risk Categories
As shown in Table 1, the ARIC Study cohort in 1987 to 1989 had a baseline mean age of 53.9 years. Higher proportions of blacks than of whites had hypertension (53.8% versus 27.9%), diabetes (17.5% versus 8.0%), and obesity (39.3% versus 21.6%). However, more blacks than whites had an optimal cholesterol level (40.4% versus 36.8%) and had never smoked (47.3% versus 41.4%). As shown in Table 2, based on the 4-factor score involving BP, cholesterol, diabetes, and smoking, only 4.9% of the cohort had all optimal risk factors (3.0% in blacks and 5.6% in whites). On the other hand, 78.5% of blacks had at least 1 of the 4 risk factors elevated, compared with 60.6% of whites. When we instead used the 5-factor score that included body mass index, only 2.6% of the cohort had all optimal risk factors (1.0% in blacks and 3.2% in whites), and 85.5% of blacks and 67.1% of whites had at least one elevated risk factor.

Heart Failure Incidence
The mean duration of follow-up was 15.7 years (maximum, 19 years) during which 1344 incident heart failure events occurred. Compared to participants with any elevated risk factor using the 4-factor score, the age-, sex-, and race-adjusted RH for heart failure events was 0.18 (95% CI, 0.10 to 0.32) for those with all optimal risk factors (n=12 events among 665 participants) and 0.35 (95% CI, 0.30 to 0.41) for those with borderline risk factors only (Table 3). These RHs were 0.28 and 0.31, respectively, in blacks and 0.16 and 0.36 in whites. The PAF estimate suggested that having at least one elevated risk factor in the 4-factor score accounted for 70.6% of heart failure events; borderline risk factors accounted for just 6.5% more. Thus, elevated and borderline
levels of the 4 risk factors, together, seemed to account for a majority heart failure events in blacks (67.5%) and whites (79.1%).

When we instead computed risks using the 5-factor score (also with body mass index), the low prevalence of having only optimal risk factors meant that only 3 heart failure events occurred in whites with optimal risk factors, and 0 in blacks. The PAF estimates suggested that elevated and borderline levels of the 5 factors accounted for 88.8% of heart failure events overall—100% in blacks and 85.8% in whites.

Overall, 30% of participants who developed clear “ischemic” heart failure, that is, they had a definite or probable MI or coronary revascularization between ARIC baseline and the first heart failure event. This percentage with an interim CHD event was 8% in those with all optimal risk factors, 27% in those with only borderline risk factors, and 31% in those having any elevated risk factor, based on the 4-factor score. The PAF of having nonoptimal levels of the 4 factors was 94.2% for “ischemic” heart failure (ie, after interim CHD) and 69.6% for “nonischemic” heart failure (ie, no interim CHD).

### CHD and Stroke Incidence

We previously reported the PAF of CVD (CHD plus stroke) for elevated or borderline risk factors using the 4-factor score was 76.4% in ARIC over 13 years. We have now recalculated these PAFs for CHD and stroke, separately, over 15 to 16 years. Among blacks, the PAFs were 100% for CHD events (Table 4) and 85.8% for strokes (Table 5). Among whites, these values were 75.0% and 59.9%, respectively.

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**Table 3. Incidence Rate, RH, and PAF for Heart Failure Among Risk Groups in the ARIC Study, 1987–2005**

<table>
<thead>
<tr>
<th>Risk Profile Based on 4-Factor Score*</th>
<th>No. of Subjects at Risk</th>
<th>No. of Subjects Developing Heart Failure</th>
<th>Incidence Rate†</th>
<th>Adjusted RH (95% CI)‡</th>
<th>PAF, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total sample</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All optimal risk factors</td>
<td>665</td>
<td>12</td>
<td>1.1</td>
<td>0.18 (0.10–0.32)</td>
<td>0.0</td>
</tr>
<tr>
<td>Borderline risk factors only</td>
<td>4028</td>
<td>177</td>
<td>2.7</td>
<td>0.35 (0.30–0.41)</td>
<td>6.5</td>
</tr>
<tr>
<td>Having any elevated risk factors</td>
<td>8767</td>
<td>1155</td>
<td>8.6</td>
<td>1.0§</td>
<td>70.6</td>
</tr>
<tr>
<td><strong>Blacks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All optimal risk factors</td>
<td>103</td>
<td>4</td>
<td>2.4</td>
<td>0.28 (0.10–0.74)</td>
<td>0.0</td>
</tr>
<tr>
<td>Borderline risk factors only</td>
<td>638</td>
<td>33</td>
<td>3.2</td>
<td>0.31 (0.22–0.44)</td>
<td>0.8</td>
</tr>
<tr>
<td>Having any elevated risk factors</td>
<td>2700</td>
<td>444</td>
<td>11.2</td>
<td>1.0§</td>
<td>66.7</td>
</tr>
<tr>
<td><strong>Whites</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All optimal risk factors</td>
<td>562</td>
<td>8</td>
<td>0.8</td>
<td>0.16 (0.08–0.31)</td>
<td>0.0</td>
</tr>
<tr>
<td>Borderline risk factors only</td>
<td>3390</td>
<td>144</td>
<td>2.6</td>
<td>0.36 (0.30–0.43)</td>
<td>9.5</td>
</tr>
<tr>
<td>Having any elevated risk factors</td>
<td>6067</td>
<td>711</td>
<td>7.6</td>
<td>1.0§</td>
<td>69.6</td>
</tr>
</tbody>
</table>

*This 4-factor score included blood pressure, plasma cholesterol, diabetes, and smoking as categorized in Table 1.
†Crude incidence rate per 1000 person-years.
‡RH adjusted for age and sex, plus race for the total sample.
§The reference group for the RH is those having any elevated risk factor.

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**Table 4. Incidence Rate, RH, and PAF for CHD Among Risk Groups in the ARIC Study, 1987–2005**

<table>
<thead>
<tr>
<th>Risk Profile Based on 4-Factor Score*</th>
<th>No. of Subjects at Risk</th>
<th>No. of Subjects Developing CHD</th>
<th>Incidence Rate†</th>
<th>Adjusted RH (95% CI)‡</th>
<th>PAF, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total sample</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All optimal risk factors</td>
<td>665</td>
<td>10</td>
<td>0.9</td>
<td>0.15 (0.08–0.28)</td>
<td>0.0</td>
</tr>
<tr>
<td>Borderline risk factors only</td>
<td>4028</td>
<td>160</td>
<td>2.4</td>
<td>0.33 (0.28–0.39)</td>
<td>7.5</td>
</tr>
<tr>
<td>Having any elevated risk factors</td>
<td>8767</td>
<td>995</td>
<td>7.5</td>
<td>1.0§</td>
<td>72.5</td>
</tr>
<tr>
<td><strong>Blacks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All optimal risk factors</td>
<td>103</td>
<td>0</td>
<td>0.0</td>
<td>0.00</td>
<td>0.0</td>
</tr>
<tr>
<td>Borderline risk factors only</td>
<td>638</td>
<td>11</td>
<td>1.1</td>
<td>0.14 (0.08–0.25)</td>
<td>3.3</td>
</tr>
<tr>
<td>Having any elevated risk factors</td>
<td>2700</td>
<td>327</td>
<td>8.2</td>
<td>1.0§</td>
<td>96.7</td>
</tr>
<tr>
<td><strong>Whites</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All optimal risk factors</td>
<td>562</td>
<td>10</td>
<td>1.1</td>
<td>0.18 (0.10–0.34)</td>
<td>0.0</td>
</tr>
<tr>
<td>Borderline risk factors only</td>
<td>3390</td>
<td>149</td>
<td>2.7</td>
<td>0.37 (0.31–0.45)</td>
<td>9.1</td>
</tr>
<tr>
<td>Having any elevated risk factors</td>
<td>6067</td>
<td>668</td>
<td>7.2</td>
<td>1.0§</td>
<td>65.9</td>
</tr>
</tbody>
</table>

*This 4-factor score included blood pressure, plasma cholesterol, diabetes, and smoking as categorized in Table 1.
†Crude incidence rate per 1000 person-years.
‡RH adjusted for age and sex, plus race for the total sample.
§The reference group for the RH is those having any elevated risk factor.
If instead we used the 5-factor score, among blacks the PAFs were 100% for CHD and 55.5% for strokes, and among whites were 76.9% for CHD and 75.9% for strokes.

Discussion

The main findings of this study of middle-aged adults recruited in the late 1980s and followed an average of 15 years were that (1) incidence of heart failure, especially “ischemic” heart failure, seemed explained to large degree (77% or more) by traditional CVD risk factors and (2) the few subjects with optimal risk factors rarely developed heart failure. This was true for both blacks and whites. Previous studies (eg, the Framingham Heart Study8,9,27) have documented the absolute and relative risks of heart failure in relation to traditional risk factors. Lifetime risk of heart failure in Framingham was 20%.9 Hypertension was a key risk factor; PAFs suggested it accounted for 39% of heart failure events in Framingham men and 59% in women.28 Previous studies have also demonstrated that subjects with a favorable CVD risk profile rarely develop CHD and/or stroke.1–7 Others have reported that those with CVD-healthy behaviors are also at low CVD risk.29,30 However, our report seems to be the first to show that ≈77% of heart failure events in middle-aged adults might also be prevented with the avoidance of risk factors. It, therefore, further emphasizes the need for preventing the development of risk factors in the first place, in addition to other recommended strategies for the primary and secondary prevention of heart failure.31

The prevalence of an optimal risk factor profile in this sample, and in previous reports, was low. Only 3.0% of these middle-aged blacks and 5.6% of whites had optimal levels of BP, plasma cholesterol, and serum glucose, and had never smoked. Only 1.0% and 3.2%, respectively, had optimal risk factors if body mass index was also included in the profile. The lower prevalence of optimal risk factors in blacks than whites was also reported by the Multiple Risk Factor Intervention Study4 and Third National Health and Nutrition Examination Survey.32 Although the prevalences of several risk factors have declined in recent years in the United States, prevalences of diabetes and obesity are rising, and the ethnic pattern remains. Meanwhile, CHD and stroke mortality are declining in the United States, but heart failure hospitalizations and health care costs are increasing. Clearly, population and individual approaches to CVD risk factor prevention need to remain a priority.

Study Strengths and Limitations

The strengths of this study include the careful assessment of CVD risk factors and cardiovascular incidence for an extended follow-up period. One limitation is that heart failure incidence, which was based on unvalidated hospital discharge and death certificate codes for heart failure, did not include outpatient events. However, heart failure hospital discharge codes have moderately good sensitivity and specificity.33,34 Moreover, surveillance of Rochester, Minn, indicates that 74% of heart failure cases identified in the outpatient setting are hospitalized within 1.7 years.33 A second limitation is that few events occurred in the optimal risk factor group, leading to imprecision in the heart failure incidence rate. However, this is the crux of our findings—that people with no risk factors rarely develop heart failure or other CVD events.

The use of PAF values also has strengths and limitations. The PAF offers an estimate on a population-wide basis of the proportion of cases that may be due to risk factors. It is best used when the risk factors being considered are causally related to the disease end point. This is believed to be the case for major cardiovascular risk factors. The PAF offers an estimate of the health potential of maintaining optimal risk

<table>
<thead>
<tr>
<th>Risk Profile Based on 4-Factor Score*</th>
<th>No. of Subjects at Risk</th>
<th>No. of Subjects Developing Stroke</th>
<th>Incidence Rate†</th>
<th>Adjusted RH (95% CI)‡</th>
<th>PAF, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sample</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All optimal risk factors</td>
<td>665</td>
<td>7</td>
<td>0.7</td>
<td>0.25 (0.12–0.53)</td>
<td>0.0</td>
</tr>
<tr>
<td>Borderline risk factors only</td>
<td>4028</td>
<td>87</td>
<td>1.4</td>
<td>0.42 (0.33–0.52)</td>
<td>5.7</td>
</tr>
<tr>
<td>Having any elevated risk factors</td>
<td>8767</td>
<td>517</td>
<td>4.0</td>
<td>1.0§</td>
<td>63.6</td>
</tr>
<tr>
<td>Blacks</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>All optimal risk factors</td>
<td>103</td>
<td>1</td>
<td>0.6</td>
<td>0.12 (0.02–0.86)</td>
<td>0.0</td>
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<tr>
<td>Borderline risk factors only</td>
<td>638</td>
<td>19</td>
<td>1.9</td>
<td>0.33 (0.21–0.52)</td>
<td>4.6</td>
</tr>
<tr>
<td>Having any elevated risk factors</td>
<td>2700</td>
<td>243</td>
<td>6.4</td>
<td>1.0§</td>
<td>81.2</td>
</tr>
<tr>
<td>Whites</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All optimal risk factors</td>
<td>562</td>
<td>6</td>
<td>0.7</td>
<td>0.31 (0.14–0.71)</td>
<td>0.0</td>
</tr>
<tr>
<td>Borderline risk factors only</td>
<td>3390</td>
<td>68</td>
<td>1.3</td>
<td>0.45 (0.35–0.59)</td>
<td>5.9</td>
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<tr>
<td>Having any elevated risk factors</td>
<td>6067</td>
<td>274</td>
<td>3.0</td>
<td>1.0§</td>
<td>54.0</td>
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</tbody>
</table>

*This 4-factor score included blood pressure, plasma cholesterol, diabetes, and smoking as categorized in Table 1.
†Crude incidence rate per 1000 person-years.
‡RH adjusted for age and sex, plus race for the total sample.
§The reference group for the RH is those having any elevated risk factor.
Factors life-long, but, of course, is idealistic because few Americans at present are able to do this.

**Conclusions**

Our data indicate that middle-aged adults with optimal (low) risk factor levels have low incidence rates of heart failure in addition to their low rates of CHD and stroke. Efforts need to continue not only for primary prevention of CVD but also for “primordial” prevention of CVD risk factors in the first place.

**Acknowledgments**

The authors thank the staff and participants of the ARIC study for their important contributions.

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**Disclosures**

None.

**References**


**CLINICAL PERSPECTIVE**

Using a large prospective cohort study of middle-aged adults, we categorized cardiovascular risk factors (blood pressure, plasma cholesterol, diabetes, and smoking) into optimal, borderline, and elevated categories at baseline (1987 to 1989) and then determined the incidence of hospitalized heart failure (n=1344) over 16 years. Only 4.9% of the cohort had all optimal risk factors. By calculating population-attributable fractions, we estimated that having at least 1 of the 4 risk factors, elevated or borderline, accounted for 77.1% of heart failure events. We conclude that middle-aged adults with optimal (low) risk factors have low incidence rates of heart failure, which supports redoubled efforts to prevent risk factor development in the first place.
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