Predictors of Incident Heart Failure in a Large Insured Population
A One Million Person-Year Follow-Up Study

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Background—Studies on the incidence and predictors of heart failure (HF) are often restricted to elderly persons or identify only inpatient cases.

Methods and Results—We determined the incidence and predictors of new HF diagnosed in either outpatient or inpatient settings, among 359,947 women and men (age ≥18 years) insured by Kaiser Permanente Georgia at any time during calendar years 2000 to 2005. Subjects were free of HF at baseline, and incident HF was identified with ICD-9 codes (1 inpatient or 2 outpatient HF visits). We developed multivariable Cox models to assess the association of antecedent factors (coronary heart disease, hypertension, diabetes mellitus, atrial fibrillation, and valvular heart disease) with incident HF. Separate models were created for each sex and for newly diagnosed HF in outpatient or inpatient settings. There were 4001 incident HF cases (50% women and 48% in subjects <65 years old), during 1 015 794 person-years of follow-up. The incidence rate of HF was greater in men than in women (4.24 versus 3.68 per 1000 person-years) but was stable across the study interval in both sexes. Two thirds of incident HF cases from this population occurred in outpatients. These 5 antecedent factors and age yielded excellent discrimination for incident HF in both outpatients and inpatients and in both sexes (C <0.85 in all models).

Conclusions—Common modifiable risk factors accurately discriminate women and men at risk for HF diagnosed in either outpatient or inpatient settings. Approximately two thirds of new HF cases in our insured population were diagnosed in outpatients; more research is needed to characterize these subjects and their prognosis. (Circ Heart Fail. 2010;3:698-705.)

Key Words: heart failure ■ epidemiology ■ risk factors

The epidemic of heart failure (HF) imposes a tremendous health and economic burden on society.1 Heart failure is the most common cause of hospitalization in the elderly, and its prevalence continues to rise as the result of the aging population, improved care of acute cardiovascular diseases, and burgeoning rates of HF risk factors such as hypertension and diabetes mellitus.1 Although an increasing prevalence of HF is consistently reported, published trends of HF incidence vary,2–15 with some studies reporting declining trends,2,3 others suggesting more stable rates,4 and still others showing actual increases in incidence over time.15 Prior studies on the incidence and predictors of HF are often restricted to the elderly population (age ≥65 years)2,5,7,8,15 or to incident HF events diagnosed in the inpatient setting.5,7,8,10,12,13 Few studies from real-world practice have reported HF incidence in populations including both elderly and nonelderly adults or new HF cases diagnosed in outpatient as well as inpatient settings. The inclusion of these populations in HF epidemiological studies is critical so that HF risk factors can be detected and managed in all at-risk groups to mitigate the burden of HF on society.1

Clinical Perspective on p 705

Kaiser Permanente Georgia is a large, managed-care organization that provides comprehensive medical care to more than 300,000 members in the greater metropolitan Atlanta, Georgia, area. We analyzed the medical records of Kaiser enrollees from 2000 to 2005 to identify incident HF cases and their antecedent risk factors. Specifically, our objectives were (1) to report the sex-specific incidence rate and prevalence of HF across a 6-year period from 2000 to 2005 in adults ages ≥18 years; (2) to determine the predictors of incident HF in women and men; and (3) to compare the incidence rates and predictors of HF diagnosed in outpatient compared with inpatient settings.
Methods

Kaiser Permanente Georgia Data
We analyzed data from the electronic medical record system of Kaiser Permanente Georgia. This data base includes claims data for both inpatient and outpatient diagnoses using the International Classification of Diseases, Ninth Revision (ICD-9) codes, beneficiary identifiers, admission and discharge dates for inpatient visits, encounter dates for outpatient visits, patient date of birth, and sex. The study was approved by the Institutional Review Board of Kaiser Permanente Georgia.

Patients With Incident and Prevalent HF
We analyzed electronic medical records from 191,396 women and 168,551 men, ages ≥18 years, who were enrolled in Kaiser Permanente Georgia at any time during the calendar years 2000 to 2005. We included subjects who were Kaiser members for at least 1 year before study entry and were free of HF (ie, no ICD-9 code for HF) during this prestudy period to avoid misclassifying patients with prior HF as an incident HF case. A new diagnosis of HF was assigned as occurring in either the inpatient setting (1 new inpatient claim for HF using ICD-9 codes 402.1X, 402.4X, 402.5X, and 428.XX) or the outpatient setting (2 outpatient claims for HF using the same ICD-9 codes, with the date of diagnosis occurring on the date of the first outpatient claim). The validity of a diagnosis of incident HF in the hospital (inpatient) setting has been reported in a different Kaiser division (Kaiser Permanente Northern California), with a positive predictive value of 97% for ICD-9 coded HF when compared with the gold standard of chart review against Framingham clinical criteria for HF.16 Outpatient diagnosis of incident HF has not been similarly validated and may be less accurate than an in-hospital HF diagnosis, prompting us to require 2 separate claims (and not just 1) to diagnose incident HF in the outpatient setting. New HF cases were considered as being diagnosed first in either the inpatient or outpatient setting, but not both. Prevalent HF cases were identified as having a diagnosis code for HF at any period during that particular observation year. Once patients were identified as having incident HF, they were censored from analyses calculating incident HF for subsequent observation years but were included in subsequent years’ analyses for prevalent HF.

Antecedent Risk Factors
ICD-9 codes, ICD-9-Clinical Modification (ICD-9-CM) codes, and Current Procedural Terminology version 4 (CPT-4) codes were also used to document the presence of the following risk factors before an incident HF case: hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation, and valvular heart disease. These antecedent factors had to be coded during 1 or more patient encounters before the encounter during which incident HF was diagnosed and could be identified in either inpatient or outpatient settings. These factors were chosen because they were found to predict incident HF in prior studies.1,5–13 Other factors including self-reported race and obesity were not considered because these data were not systematically collected in Kaiser Georgia health records during the study period. Hypertension was identified by ICD-9 codes 401.X, 402.XX, 403.XX, 404.XX, 405.XX, and 437.2. Diabetes mellitus was identified by ICD-9 code 250.xx or at least 1 pharmacy claim for an antihyperglycemic medication, defined by Generic Product Identifier (GPI) codes (Medi-Span, Master Drug Database; 2003). GPI codes for antidiabetic drugs were insulins (GPI code 2710), sulfonylureas (2720), antidiabetic amino acid derivatives (2723), biguanides (2725), meglitinide analogues (2728), α-glucosidase inhibitors (2750), insulin-sensitizing agents (2760), and antidiabetic combinations (2799). Coronary heart disease was diagnosed for any of the following codes: myocardial infarction (ICD-9-CM 410.XX); angina or ischemic heart disease (ICD-9-CM 411.xx); and total number of study participants within each observation year. Both the incidence rate and prevalence of HF were determined separately in women and men in 4 specific age groups: 18 to 54 years, 55 to 64 years, 65 to 74 years, and ≥75 years. Age at the time of study entry and the proportions of patients with antecedent HF risk factors among both incident HF cases and noncases were documented separately by sex and also separately in patients who were diagnosed with HF in outpatient compared with inpatient settings. Comparisons of these descriptive statistics were conducted using χ² tests and t tests between subjects with and without incident HF.

Cox proportional hazards regression models were created separately in men and women to assess the hazard of incident HF associated with each antecedent risk factor: age, hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation, and valvular heart disease. Cox models were chosen to account for differential follow-up times (censoring) of patients who may have disenrolled from the Kaiser Permanente health plan or died before the development of incident HF. For each sex, 3 Cox models were constructed to assess the association between risk factors and incident HF: (1) unadjusted, in which the univariable odds ratio and 95% confidence limits for each risk factor were determined; (2) each risk factor adjusted for age only; and (3) each risk factor adjusted for age as well as all other risk factors. Separate Cox models were similarly constructed for new inpatient and outpatient HF cases (sex was also included as a covariate in the fully adjusted models). For all Cox models, hazard ratios with 95% confidence limits and probability values were presented for each cofactor. C-statistics were generated to assess how well the fully adjusted models discriminated a new HF case from a noncase. A probability value of 0.05 was used to designate statistical significance. SAS statistical software, version 9.1, was used for all analyses (SAS Institute Inc, Cary, NC).

Results
Incidence and Prevalence of HF
Overall, there were 4001 incident HF cases during 1,015,794 person-years of follow-up. In women, there were 2018 incident HF cases during 548,634 person-years of follow-up, for an overall incidence rate of 3.68 (95% confidence interval, 3.52 to 3.84) per 1000 person-years of follow-up. In men, there were 1983 incident HF cases during 467,161 person-years of follow-up, for an overall incidence rate of 4.24 (95% confidence interval, 4.05 to 4.43) per 1000 person-years of follow-up. The incidence rate of HF did not change in either women or men across the study interval (Table 1), although the incidence rate of HF was higher in men compared with women in any given observation year. As expected, the incidence rate of HF increased markedly with increasing age (Table 1). For the first 3 age groups (18 to 54 years, 55 to 64 years, and 65 to 74 years), men had a higher rate of incident HF than women for most observation years (Table 1). However, for the ≥75-year age group, women had a similar or even slightly higher HF incidence rate than men for observation years 2000 to 2002 and 2004, whereas men had higher incidence rates in years 2003 and 2005, with overall incidence rates being similar between sexes for the age group.
Of the total 4001 incident HF cases in the Kaiser Georgia population, 1925 (48%) occurred in subjects who were ≥65 years old.

Although HF incidence did not increase across observation years, there was a steady increase in the prevalence of HF across observation years for both women and men (Table 2). In most of the observation years, the actual number of prevalent HF cases was similar or slightly higher in women compared with men (due to the greater number of women in the overall Kaiser Georgia population). However, thecalcul-

<table>
<thead>
<tr>
<th>Observation Year</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>P for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of incident cases</td>
<td>273</td>
<td>344</td>
<td>390</td>
<td>350</td>
<td>338</td>
<td>323</td>
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</tr>
<tr>
<td>Person-years of follow-up</td>
<td>83 930</td>
<td>88 819</td>
<td>93 462</td>
<td>93 360</td>
<td>93 807</td>
<td>95 256</td>
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<tr>
<td>Incidence rate*</td>
<td>3.25</td>
<td>3.87</td>
<td>4.17</td>
<td>3.75</td>
<td>3.60</td>
<td>3.39</td>
<td>0.87</td>
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<tr>
<td>Incident rate by age group*</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>18–54 years</td>
<td>0.97</td>
<td>1.18</td>
<td>1.33</td>
<td>1.32</td>
<td>1.11</td>
<td>0.91</td>
<td></td>
</tr>
<tr>
<td>55–64 years</td>
<td>7.29</td>
<td>7.53</td>
<td>6.91</td>
<td>5.86</td>
<td>6.54</td>
<td>5.48</td>
<td></td>
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<tr>
<td>65–74 years</td>
<td>22.23</td>
<td>20.14</td>
<td>22.98</td>
<td>18.21</td>
<td>16.36</td>
<td>15.57</td>
<td></td>
</tr>
<tr>
<td>≥75 years</td>
<td>56.40</td>
<td>56.34</td>
<td>52.81</td>
<td>44.19</td>
<td>42.14</td>
<td>41.39</td>
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<tr>
<td><strong>Men</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>No. of incident cases</td>
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<td>322</td>
<td>359</td>
<td>352</td>
<td>355</td>
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</tr>
<tr>
<td>Person-years of follow-up</td>
<td>72 114</td>
<td>75 732</td>
<td>79 512</td>
<td>79 862</td>
<td>79 862</td>
<td>80 079</td>
<td></td>
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<tr>
<td>Incidence rate*</td>
<td>3.45</td>
<td>4.25</td>
<td>4.52</td>
<td>4.41</td>
<td>4.45</td>
<td>4.32</td>
<td>0.16</td>
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<td>Incident rate by age group*</td>
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<td></td>
</tr>
<tr>
<td>18–54 years</td>
<td>1.36</td>
<td>1.48</td>
<td>1.56</td>
<td>1.34</td>
<td>1.55</td>
<td>1.22</td>
<td></td>
</tr>
<tr>
<td>55–64 years</td>
<td>6.76</td>
<td>10.47</td>
<td>11.83</td>
<td>9.21</td>
<td>8.78</td>
<td>8.95</td>
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</tr>
<tr>
<td>65–74 years</td>
<td>27.24</td>
<td>24.56</td>
<td>24.79</td>
<td>25.15</td>
<td>26.09</td>
<td>18.49</td>
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</tr>
<tr>
<td>≥75 years</td>
<td>55.25</td>
<td>56.07</td>
<td>49.01</td>
<td>57.13</td>
<td>40.40</td>
<td>57.83</td>
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</tr>
</tbody>
</table>

*Incident rate is presented per 1000 person-years of follow-up.

Table 2. Prevalence of Heart Failure From 2000 to 2005 by Sex and by Age Group

<table>
<thead>
<tr>
<th>Observation Year</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>P for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of prevalent HF cases*</td>
<td>947</td>
<td>1265</td>
<td>1540</td>
<td>1680</td>
<td>1826</td>
<td>1898</td>
<td></td>
</tr>
<tr>
<td>Total No. of study participants</td>
<td>93 879</td>
<td>99 068</td>
<td>103 903</td>
<td>104 176</td>
<td>105 126</td>
<td>106 129</td>
<td></td>
</tr>
<tr>
<td>Prevalence, %</td>
<td>1.01</td>
<td>1.28</td>
<td>1.48</td>
<td>1.61</td>
<td>1.74</td>
<td>1.79</td>
<td>0.0006</td>
</tr>
<tr>
<td>Prevalence by age group, %</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>18–54 years</td>
<td>0.34</td>
<td>0.41</td>
<td>0.47</td>
<td>0.51</td>
<td>0.54</td>
<td>0.52</td>
<td></td>
</tr>
<tr>
<td>55–64 years</td>
<td>2.41</td>
<td>2.67</td>
<td>2.89</td>
<td>3.07</td>
<td>3.22</td>
<td>3.17</td>
<td></td>
</tr>
<tr>
<td>65–74 years</td>
<td>5.87</td>
<td>6.07</td>
<td>7.11</td>
<td>7.29</td>
<td>7.63</td>
<td>7.68</td>
<td></td>
</tr>
<tr>
<td>≥75 years</td>
<td>15.68</td>
<td>15.78</td>
<td>17.19</td>
<td>17.17</td>
<td>17.74</td>
<td>17.67</td>
<td></td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of prevalent HF cases*</td>
<td>956</td>
<td>1193</td>
<td>1420</td>
<td>1633</td>
<td>1782</td>
<td>1916</td>
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<tr>
<td>Total No. of study participants</td>
<td>81 214</td>
<td>84 997</td>
<td>88 928</td>
<td>89 726</td>
<td>90 154</td>
<td>90 167</td>
<td></td>
</tr>
<tr>
<td>Prevalence, %</td>
<td>1.18</td>
<td>1.40</td>
<td>1.60</td>
<td>1.82</td>
<td>1.98</td>
<td>2.12</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Prevalence by age group, %</td>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>18–54 years</td>
<td>0.41</td>
<td>0.47</td>
<td>0.53</td>
<td>0.57</td>
<td>0.60</td>
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</tr>
<tr>
<td>55–64 years</td>
<td>3.35</td>
<td>3.53</td>
<td>4.13</td>
<td>4.25</td>
<td>4.42</td>
<td>4.64</td>
<td></td>
</tr>
<tr>
<td>65–74 years</td>
<td>8.05</td>
<td>8.03</td>
<td>8.54</td>
<td>9.68</td>
<td>10.48</td>
<td>10.14</td>
<td></td>
</tr>
<tr>
<td>≥75 years</td>
<td>17.00</td>
<td>15.62</td>
<td>17.01</td>
<td>18.61</td>
<td>18.37</td>
<td>19.75</td>
<td></td>
</tr>
</tbody>
</table>

*The number of prevalent cases in each year does not necessarily equal the number of incident cases from that year plus the number of prevalent cases from the prior year because patients with prevalent HF may become lost to follow-up as the result of either death or discontinuation of their insurance plan.
Predictors of Incident HF in Women and Men

The mean age in the year before diagnosis in patients who had incident HF was 65.6 ± 15.3 years in women and 62.6 ± 13.3 years in men (Table 3). In patients with incident HF, there was a high prevalence of risk factors in both sexes: >75% of women and men had hypertension; >30% of women and men had diabetes; nearly 18% of women and 27% of men had coronary artery disease; 8% of women and 10% of men had atrial fibrillation; and 9% of both women and men had valvular heart disease. More than 80% of women and men with incident HF had at least 1 diagnosed HF risk factor, and 14% of women and 19% of men with incident HF had 3 or more antecedent HF risk factors.

Each of the 5 risk factors (hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation, and valvular heart disease) conferred a substantial risk for incident HF in both women and men in unadjusted models (Table 4). The hazard ratios associated with these factors became somewhat attenuated but remained significant after adjusting for age alone. In the fully adjusted models, all risk factors independently predicted incident HF in men, and all factors except for valvular heart disease predicted incident HF in women (Table 4). In both women and men, hypertension was the most common HF risk factor and was also associated with the greatest hazard for development of HF after multivariable adjustment (hazard ratio, 3.18; 95% CI, 2.80 to 3.60; *P* < 0.0001 in women; hazard ratio, 3.00; 95% CI, 2.66 to 3.39; *P* < 0.0001 in men). These 5 factors in addition to age had excellent ability to discriminate HF cases from noncases in both women (C = 0.886) and men (C = 0.877).

Predictors of Incident HF in Outpatients Compared With Inpatients

Of the 4001 incident HF cases, 1362 (34%) were diagnosed on an inpatient basis and 2639 (66%) were diagnosed on an outpatient basis. The mean age at inpatient diagnosis was slightly higher compared with outpatient diagnosis (65.1 ± 14.5 years versus 63.3 ± 14.3 years), and women comprised 52% of incident inpatient HF cases and 50% of outpatient HF cases. The prevalence of antecedent HF risk factors was about 10% higher for new inpatient HF cases compared with new outpatient cases for each of the 5 factors: hypertension, diabetes, coronary artery disease, atrial fibrillation, and valvular heart disease (Table 5). Nearly 90% of inpatient cases and 78% of outpatient cases were associated with 1 or more antecedent factors, and 27% of inpatient cases and 11% of outpatient cases were associated with 3 or more of these factors.

Hypertension, diabetes, coronary artery disease, atrial fibrillation, and valvular heart disease were all strong incident

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**Table 3. Characteristics of Patients With and Without Incident Heart Failure by Sex (All Observation Years Combined)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Women</th>
<th>Men</th>
<th><em>P</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>2018</td>
<td>1893</td>
<td>...</td>
</tr>
<tr>
<td>Age, years, mean ± SD</td>
<td>65.2 ± 15.3</td>
<td>62.6 ± 13.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Comorbidities, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>1623 (80.4)</td>
<td>1513 (76.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>616 (30.5)</td>
<td>629 (31.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>362 (17.9)</td>
<td>540 (27.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>163 (8.1)</td>
<td>192 (9.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>184 (9.1)</td>
<td>169 (8.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>No. of comorbidities, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>349 (17.3)</td>
<td>397 (20.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>1</td>
<td>737 (36.5)</td>
<td>592 (29.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>2</td>
<td>649 (32.2)</td>
<td>615 (31.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3</td>
<td>223 (11.1)</td>
<td>302 (15.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>4</td>
<td>56 (2.8)</td>
<td>70 (3.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>5</td>
<td>4 (0.2)</td>
<td>7 (0.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>No. in each age group, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–54 years</td>
<td>512 (25.4)</td>
<td>544 (27.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>55–64 years</td>
<td>376 (18.6)</td>
<td>493 (24.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>65–74 years</td>
<td>530 (26.3)</td>
<td>571 (28.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>≥ 75 years</td>
<td>600 (29.7)</td>
<td>375 (18.9)</td>
<td>&lt;0.0001</td>
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</table>
HF predictors in the inpatient setting (Table 6). Age was also a predictor of inpatient HF, but sex was not. In comparison, in the outpatient setting, female sex was associated with a slightly lower hazard of incident HF compared with male sex (Table 6). Hypertension, diabetes, coronary artery disease, and atrial fibrillation (but not valvular heart disease) were also significant predictors of new outpatient HF but were not associated with as large of a hazard ratio for HF as compared with the inpatient setting. In both the outpatient and inpatient settings, models consisting of these 5 factors along with sex and age had

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No Incident HF</th>
<th>Incident HF as an Inpatient</th>
<th>Incident HF as an Outpatient</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>355 946</td>
<td>1362</td>
<td>2639</td>
</tr>
<tr>
<td>Age, years</td>
<td>37.8±13.9</td>
<td>65.1±14.5</td>
<td>63.3±14.3</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>189 378 (53.2)</td>
<td>709 (52.1)</td>
<td>1309 (49.6)</td>
</tr>
</tbody>
</table>

Comorbidities, n (%):

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No Incident HF</th>
<th>Incident HF as an Inpatient</th>
<th>Incident HF as an Outpatient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>41 670 (11.7)</td>
<td>1179 (86.6)</td>
<td>1957 (74.2)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>11 099 (3.1)</td>
<td>534 (39.2)</td>
<td>711 (26.9)</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>2808 (0.8)</td>
<td>410 (30.1)</td>
<td>492 (18.6)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>646 (0.2)</td>
<td>207 (15.2)</td>
<td>148 (5.6)</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>1323 (0.4)</td>
<td>201 (14.8)</td>
<td>152 (5.8)</td>
</tr>
</tbody>
</table>

No. of comorbidities, n (%):

<table>
<thead>
<tr>
<th>No. of comorbidities, n (%)</th>
<th>Incidence HF as an Inpatient</th>
<th>&lt;0.0001</th>
<th>Incidence HF as an Outpatient</th>
<th>&lt;0.0001</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>309 393 (86.9)</td>
<td>155 (11.4)</td>
<td>591 (22.4)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>37 607 (10.6)</td>
<td>353 (25.9)</td>
<td>976 (37.0)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>8246 (2.3)</td>
<td>486 (35.7)</td>
<td>778 (29.5)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>676 (0.2)</td>
<td>272 (20.0)</td>
<td>253 (9.6)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>24 (0.0)</td>
<td>90 (6.6)</td>
<td>36 (1.4)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>6 (0.4)</td>
<td>5 (0.2)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

No. in each age group, n (%):

<table>
<thead>
<tr>
<th>No. in each age group, n (%)</th>
<th>Incidence HF as an Inpatient</th>
<th>&lt;0.0001</th>
<th>Incidence HF as an Outpatient</th>
<th>&lt;0.0001</th>
</tr>
</thead>
<tbody>
<tr>
<td>18–54 years</td>
<td>312 218 (87.7)</td>
<td>335 (24.6)</td>
<td>721 (27.3)</td>
<td></td>
</tr>
<tr>
<td>55–64 years</td>
<td>25 875 (7.3)</td>
<td>296 (21.9)</td>
<td>571 (21.6)</td>
<td></td>
</tr>
<tr>
<td>65–74 years</td>
<td>13 261 (3.7)</td>
<td>344 (25.3)</td>
<td>757 (28.7)</td>
<td></td>
</tr>
<tr>
<td>≥75 years</td>
<td>4592 (1.3)</td>
<td>385 (28.3)</td>
<td>590 (22.4)</td>
<td></td>
</tr>
</tbody>
</table>

Patients diagnosed with incident HF as inpatients and outpatients are shown separately.

*Compared with the “no incident HF” group.
excellent discrimination for incident HF (C=0.869 in the inpatient setting; C=0.859 in the outpatient setting).

### Discussion

In this study of medically insured adults in the Southeastern United States, the annual incidence of HF was stable in both sexes from 2000 to 2005, but the prevalence steadily increased. Both the incidence rate and prevalence of HF were higher in men than in women for all observation years. Importantly, we found that a substantial number of incident cases occurred in subjects \( \geq 65 \) years old; more than half were in women; and two thirds of incident cases from our population were diagnosed on an outpatient basis. In addition to age, we determined that 5 HF risk factors (hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation, and valvular heart disease) were highly prevalent before the diagnosis of incident HF, and more than 80% of subjects with incident HF had 1 or more of these antecedent risk factors. These 5 factors, along with age and sex, had excellent ability to discriminate an HF case from a noncase in women and men and in patients diagnosed with new HF on either an outpatient or inpatient basis.

Several prior studies have reported sex-specific incidence rates and prevalence of HF in both community and insured populations.\(^1\)–\(^5\) Consistent with the findings from our study, these prior studies have reported a rising prevalence of HF over time in both sexes\(^2\)–\(^2\) as well as higher rates of both prevalence and incidence in men compared with women at any given point in time.\(^2\)–\(^5\) However, the actual trends in incident HF rates have varied in these studies. In a study of community-based participants from Olmstead County, HF incidence rates were stable from 1979 to 2000 in both men and women.\(^4\) However, in the Framingham Study, HF incidence rates were stable only in men from 1950 to 1999, whereas they declined by 31% to 40% in women during this same time period.\(^3\) In a Medicare population (all \( \geq 65 \) years old), HF incidence rates decreased overall in both men and women between 1994 and 2003,\(^2\) but, when separated into different age categories, HF incidence rates appeared to rise during this 10-year period for the youngest beneficiaries (age, 65 to 69 years), whereas it decreased in the oldest beneficiaries (\( \geq 85 \) years). In another study of elderly patients in the Northwestern United States, HF incidence rates actually increased in both men and women from the period 1970 to 1974 to 1990 to 1994.\(^15\) In the present study, the incidence rates of HF were stable from 2000 to 2005 in both insured men and women. Reasons for these disparate trends in sex-specific incidence rates are numerous, including different lengths of follow-up; different age mix of the study populations (with some restricted to patients ages \( \geq 65 \) years and others including younger subjects); inherent differences between community-based cohorts in some studies and medically insured (claims-based) populations in others; and regional differences in incidence rates within the United States. These variations highlight the need for ongoing surveillance of sex-specific HF incidence rates in different age groups and within different regions.

In both women and men, we found that age, hypertension, diabetes, coronary heart disease, and atrial fibrillation predicted incident HF. Valvular heart disease was also a predictor in men but not in women. These antecedent factors together performed very well at discriminating an incident

<table>
<thead>
<tr>
<th>Table 6. Cox Proportional Hazards Models: Predictors of Incident Heart Failure Diagnosed on an Inpatient or an Outpatient Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1*</td>
</tr>
<tr>
<td>Hazard Ratio</td>
</tr>
<tr>
<td>Inpatients</td>
</tr>
<tr>
<td>Age, per 10-year increase</td>
</tr>
<tr>
<td>Female sex</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>Coronary heart disease</td>
</tr>
<tr>
<td>Valvular heart disease</td>
</tr>
<tr>
<td>Outpatients</td>
</tr>
<tr>
<td>Age, per 10-year increase</td>
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<td>Coronary heart disease</td>
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<tr>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>Valvular heart disease</td>
</tr>
</tbody>
</table>

CI indicates confidence interval.

Predictors of incident HF are shown separately for inpatients and outpatients.

*Model 1 is unadjusted for any other risk factors. Model 2 is adjusted for age and sex. Model 3 is adjusted for age, sex, and all other risk factors.
HF case from a noncase. Prior studies have also focused on subjects’ risk profile for incident HF. These studies have often reported coronary heart disease as the major contributor to the development of incident HF. However, most of these studies were restricted to populations ≥65 years old. Our study included both elderly and nonelderly adults, and half of all incident HF cases occurred in patients <65 years old. We found hypertension to be the most prevalent antecedent risk factor and also the one most strongly associated with incident HF. Few other studies that have included younger subjects have similarly found hypertension to be the strongest contributor to incident HF in their study populations. Moreover, the prevalence of uncontrolled hypertension has been rising despite the availability of more pharmacological options to manage blood pressure.

Diabetes mellitus was also more prevalent than coronary heart disease in our population and was an important antecedent of incident HF. The inclusion of nonelderly patients in epidemiological studies of HF is essential to identify early risk factors that increase the lifetime risk of HF and to implement timely interventions to prevent the development or progression of HF.

An important aspect of our study is the inclusion of incident HF cases diagnosed on an outpatient basis. Most prior studies (even studies of community-based populations) have been restricted to new HF diagnoses identified through inpatient records or death certificates. Although outpatient diagnoses were not verified against standardized clinical criteria in this study, the relationship between antecedent factors and new HF was similar for both outpatient and inpatient HF diagnoses. Furthermore, the fact that two thirds of new HF cases from our population were diagnosed on an outpatient basis is eye-opening. A recent study from the Medicare population also included new HF cases diagnosed in outpatient settings but reported that outpatient diagnoses constituted only one third of incident HF cases. This difference may reflect the experience of older persons with Medicare: As the cumulative risk factor burden increases with age, there is an increased likelihood of having a more severe initial presentation of HF that requires hospitalization. The present study indicates that outpatient visits represent a key opportunity to identify patients with newly developed HF and suggests that early attention to and appropriate treatment of these patients might delay progression of HF and reduce HF hospitalization.

**Strengths and Limitations of the Study**

Our study has several strengths. The study population was large, with more than one million person-years of follow-up, and had a substantial number of incident HF events. It included a broad range of patients, including both women and men, patients younger and older than 65 years, and patients whose HF diagnoses was first made in either outpatient or inpatient settings. We also included as predictors of incident HF certain risk factors that are not commonly considered in risk-prediction models for HF (eg, atrial fibrillation and valvular heart disease) but that are known contributors clinically to the development of HF. Our study also has limitations. Potential risk factors such as obesity, heavy alcohol use, and race or ethnicity were not systematically collected in Kaiser Georgia health records during the study period of 2000 to 2005 and hence were not included in our models. However, the 5 risk factors we analyzed, in addition to age, were able to discriminate incident HF cases from noncases. Diagnosis of incident HF was based on ICD-9 codes and not standardized clinical criteria. However, ICD-9 codes have been shown to accurately identify incident HF diagnoses in other studies, including within the Kaiser Permanente system. Moreover, the overall incidence of HF in our study was similar to that reported in community-based populations in which medical record adjudication was used to verify ICD-9 diagnoses. Our claims data identified HF diagnoses but did not document data on left ventricular function. Consequently, we are unable to determine the incidence and predictors of HF with reduced compared with preserved systolic function. Finally, the present study used data from adults who were medically insured by a health maintenance organization, and 94% of patients in our population were under 65 years of age. Our data may therefore not be representative of the incidence and predictors of HF in uninsured populations or in populations ages 65 years or older.

**Conclusion**

In a medically insured population from the Southeastern United States consisting of both elderly and nonelderly women and men, antecedent hypertension, diabetes, coronary artery disease, atrial fibrillation, and valvular heart disease were highly prevalent in individuals who had newly developed HF. Early recognition and treatment of these factors could potentially prevent or delay the development of HF in adults or reduce hospitalizations from HF. Two thirds of incident HF cases in our population were also diagnosed on an outpatient basis. Further research in outpatients diagnosed with new HF is essential to characterize these patients and their prognosis and may help mitigate the societal burden of HF.

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**Disclosures**

None.

**References**


Heart failure (HF) is a serious public health problem, and numerous studies document the rising prevalence of HF. However, published trends of HF incidence vary considerably. Moreover, most studies of HF incidence are restricted to persons ≥65 years old and include only those HF cases diagnosed in the inpatient setting. In Kaiser Permanente Georgia, a large health maintenance organization in the greater Atlanta, Georgia, region, 359,947 women and men ≥18 years old and free of HF at baseline were enrolled at any time during calendar years 2000 to 2005. These patients were followed for incident HF (identified by ICD-9 codes) in either the inpatient or outpatient setting, and the associations between antecedent factors (coronary heart disease, hypertension, diabetes mellitus, atrial fibrillation, and valvular heart disease) and incident HF were determined. After more than 1,000,000 person-years of follow-up, there were 4,001 incident HF cases, with 50% occurring in women and 48% in subjects <65 years old. Heart failure incidence rates were greater in men than in women and remained stable in both sexes throughout the study period. Two thirds of incident HF cases from this population occurred in outpatients. The 5 antecedent factors in addition to age were strong predictors of incident HF in both sexes and in both inpatient and outpatient settings. These data highlight the importance of including both elderly and nonelderly persons at risk, as well as outpatient and inpatient HF cases, in studies reporting sex-specific incidence rates of HF and its predictors.
Predictors of Incident Heart Failure in a Large Insured Population: A One Million Person-Year Follow-Up Study
Abhinav Goyal, Catherine R. Norton, Tracy N. Thomas, Robert L. Davis, Javed Butler, Varun Ashok, Liping Zhao, Viola Vaccarino and Peter W.F. Wilson

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