Supplementary Online Content


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eFigure 2. Distribution of fibroblast growth factor 23 concentrations among women
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This supplementary material has been provided by the authors to give readers additional information about their work.
**eFigure 1.** Distribution of fibroblast growth factor 23 concentrations among men
eFigure 2. Distribution of fibroblast growth factor 23 concentrations among women
**eTable 1.** Hazard ratio (95% CI) of incident coronary heart disease as a function of baseline fibroblast growth factor 23 concentrations stratified by race

<table>
<thead>
<tr>
<th></th>
<th>FGF23 Quartile 1 (≤ 53 RU/ml)</th>
<th>FGF23 Quartile 2 (53 - 70 RU/ml)</th>
<th>FGF23 Quartile 3 (70.5-100 RU/ml)</th>
<th>FGF23 Quartile 4 (&gt; 100 RU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Black</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>66</td>
<td>71</td>
<td>76</td>
<td>143</td>
</tr>
<tr>
<td>Model 1*</td>
<td>ref</td>
<td>1.61 (1.00, 2.59)</td>
<td>1.52 (0.96, 2.39)</td>
<td>4.07 (2.55, 6.48)</td>
</tr>
<tr>
<td>Model 2†</td>
<td>ref</td>
<td>1.56 (0.87, 2.79)</td>
<td>1.28 (0.70, 2.33)</td>
<td>4.37 (2.43, 7.88)</td>
</tr>
<tr>
<td>Model 3‡</td>
<td>ref</td>
<td>1.29 (0.66, 2.52)</td>
<td>0.99 (0.47, 2.09)</td>
<td>3.15 (1.53, 6.49)</td>
</tr>
<tr>
<td><strong>White</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>56</td>
<td>112</td>
<td>132</td>
<td>173</td>
</tr>
<tr>
<td>Model 1*</td>
<td>ref</td>
<td>1.67 (1.02, 2.71)</td>
<td>2.11 (1.27, 3.51)</td>
<td>3.62 (2.13, 6.14)</td>
</tr>
<tr>
<td>Model 2†</td>
<td>ref</td>
<td>2.25 (1.26, 4.02)</td>
<td>1.97 (1.06, 3.68)</td>
<td>2.47 (1.27, 4.79)</td>
</tr>
<tr>
<td>Model 3‡</td>
<td>ref</td>
<td>2.18 (1.13, 4.21)</td>
<td>1.83 (0.93, 3.59)</td>
<td>2.11 (1.02, 4.35)</td>
</tr>
</tbody>
</table>

* Adjusted for age and sex
† Adjusted for age, sex, body mass index, systolic blood pressure, diastolic blood pressure, diabetes, income, education, neighborhood socioeconomic characteristics, physical activity, cigarette smoking, left ventricular hypertrophy, and use of aspirin, statins, and renin-angiotensin-aldosterone system inhibitors.
‡ Adjusted for age, sex, body mass index, systolic blood pressure, diastolic blood pressure, diabetes, income, education, neighborhood socioeconomic characteristics, physical activity, cigarette smoking, left ventricular hypertrophy, and use of aspirin, statins, and renin-angiotensin-aldosterone system inhibitors, estimated glomerular filtration rate, natural log-transformed albumin to creatinine ratio, natural log-transformed C-reactive protein, intact parathyroid hormone, triglycerides, high density lipoprotein-cholesterol, and total cholesterol.
### eTable 2. Hazard ratio (95% CI) of incident coronary heart disease as a function of baseline fibroblast growth factor 23 concentrations stratified by chronic kidney disease status

<table>
<thead>
<tr>
<th></th>
<th>FGF23 Quartile 1 (≤ 53 RU/ml)</th>
<th>FGF23 Quartile 2 (53 - 70 RU/ml)</th>
<th>FGF23 Quartile 3 (70.5-100 RU/ml)</th>
<th>FGF23 Quartile 4 (&gt; 100 RU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CKD</strong></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>N</td>
<td>22</td>
<td>39</td>
<td>63</td>
<td>158</td>
</tr>
<tr>
<td>Model 1*</td>
<td>ref</td>
<td>1.67 (0.69,4.07)</td>
<td>1.84 (0.82,4.14)</td>
<td>3.61 (1.62,8.04)</td>
</tr>
<tr>
<td>Model 2†</td>
<td>ref</td>
<td>1.85 (0.52,6.63)</td>
<td>1.84 (0.57,5.94)</td>
<td>4.29 (1.31,14.08)</td>
</tr>
<tr>
<td>Model 3‡</td>
<td>ref</td>
<td>4.51 (0.99,20.39)</td>
<td>2.53 (0.62,10.27)</td>
<td>2.91 (1.08,32.49)</td>
</tr>
<tr>
<td><strong>No CKD</strong></td>
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<tr>
<td>N</td>
<td>95</td>
<td>140</td>
<td>140</td>
<td>134</td>
</tr>
<tr>
<td>Model 1*</td>
<td>ref</td>
<td>1.53 (1.05,2.25)</td>
<td>1.73 (1.16,2.57)</td>
<td>2.54 (1.65,3.92)</td>
</tr>
<tr>
<td>Model 2†</td>
<td>ref</td>
<td>1.74 (1.12,2.70)</td>
<td>1.42 (0.89,2.27)</td>
<td>1.85 (1.11,3.10)</td>
</tr>
<tr>
<td>Model 3‡</td>
<td>ref</td>
<td>1.62 (1.02,2.57)</td>
<td>1.24 (0.74,2.08)</td>
<td>1.68 (0.99,2.93)</td>
</tr>
</tbody>
</table>

* Adjusted for age and sex
† Adjusted for age, race, sex, body mass index, systolic blood pressure, diastolic blood pressure, diabetes, income, education, neighborhood socioeconomic characteristics, physical activity, cigarette smoking, left ventricular hypertrophy, and use of aspirin, statins, and renin-angiotensin-aldosterone system inhibitors.
‡ Adjusted for age, race, sex, body mass index, systolic blood pressure, diastolic blood pressure, diabetes, income, education, neighborhood socioeconomic characteristics, physical activity, cigarette smoking, left ventricular hypertrophy, and use of aspirin, statins, and renin-angiotensin-aldosterone system inhibitors, estimated glomerular filtration rate, natural log-transformed albumin to creatinine ratio, natural log-transformed C-reactive protein, intact parathyroid hormone, triglycerides, high density lipoprotein-cholesterol, and total cholesterol.
**eTable 3.** Hazard ratio (95% CI) of incident coronary heart disease as a function of baseline fibroblast growth factor 23 concentrations stratified by hormone-replacement therapy use in the subset of women with available data

<table>
<thead>
<tr>
<th></th>
<th>FGF23 Quartile 1 (53 RU/ml)</th>
<th>FGF23 Quartile 2 (53 - 70 RU/ml)</th>
<th>FGF23 Quartile 3 (70.5-100 RU/ml)</th>
<th>FGF23 Quartile 4 (&gt; 100 RU/ml)</th>
<th>Per doubling of FGF23</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Women not reporting hormone replacement therapy use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events, N</td>
<td>20</td>
<td>29</td>
<td>38</td>
<td>78</td>
<td>165</td>
</tr>
<tr>
<td></td>
<td>ref</td>
<td>1.21 (0.57,2.57)</td>
<td>1.50 (0.74,3.05)</td>
<td>2.83 (1.42,5.62)</td>
<td>1.37 (1.11,1.68)</td>
</tr>
<tr>
<td>Model 1</td>
<td>ref</td>
<td>3.33 (0.65,16.97)</td>
<td>4.22 (0.88,20.24)</td>
<td>6.69 (1.53,29.20)</td>
<td>1.41 (1.07,1.85)</td>
</tr>
<tr>
<td>Model 2</td>
<td>ref</td>
<td>2.71 (0.42,17.56)</td>
<td>4.12 (0.72,23.42)</td>
<td>7.37 (1.07,50.67)</td>
<td>2.57 (1.49,4.43)</td>
</tr>
<tr>
<td>Model 3</td>
<td>ref</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Women reporting hormone replacement therapy use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events, N</td>
<td>21</td>
<td>21</td>
<td>41</td>
<td>75</td>
<td>158</td>
</tr>
<tr>
<td></td>
<td>ref</td>
<td>0.81 (0.36,1.78)</td>
<td>1.31 (0.62,2.79)</td>
<td>1.89 (0.92,3.89)</td>
<td>1.38 (1.06,1.80)</td>
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<td>Model 1</td>
<td>ref</td>
<td>0.85 (0.28,2.61)</td>
<td>0.96 (0.28,3.35)</td>
<td>1.46 (0.51,4.21)</td>
<td>1.47 (1.06,2.04)</td>
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<tr>
<td>Model 2</td>
<td>ref</td>
<td>0.94 (0.17,5.12)</td>
<td>1.24 (0.20,7.59)</td>
<td>2.07 (0.47,9.18)</td>
<td>1.48 (0.96,2.28)</td>
</tr>
</tbody>
</table>

* Adjusted for age, race
†Adjusted for variables in Model 1 plus body mass index, systolic blood pressure, diastolic blood pressure, diabetes, income, education, physical activity, neighborhood socioeconomic characteristics, cigarette smoking, left ventricular hypertrophy, and use of aspirin, statins, and renin-angiotensin-aldosterone system inhibitors.
‡Adjusted for variables in Model 2 plus estimated glomerular filtration rate, natural log-transformed albumin to creatinine ratio, natural log-transformed C-reactive protein, intact parathyroid hormone, triglycerides, high density lipoprotein-cholesterol, and total cholesterol.

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**eTable 4.** Hazard ratio (95% CI) of fatal coronary heart disease as a function of baseline fibroblast growth factor 23 concentrations overall and stratified by sex

<table>
<thead>
<tr>
<th></th>
<th>FGF23 Quartile 1 (≤ 53 RU/ml)</th>
<th>FGF23 Quartile 2 (53 - 70 RU/ml)</th>
<th>FGF23 Quartile 3 (70.5-100 RU/ml)</th>
<th>FGF23 Quartile 4 (&gt; 100 RU/ml)</th>
<th>Per doubling of FGF23</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>38</td>
<td>60</td>
<td>73</td>
<td>129</td>
<td>300</td>
</tr>
<tr>
<td><strong>Model 1</strong></td>
<td>ref</td>
<td>1.93 (1.19, 3.12)</td>
<td>2.20 (1.38, 3.50)</td>
<td>5.12 (3.19, 8.21)</td>
<td>1.76 (1.49, 2.09)</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td>ref</td>
<td>2.03 (1.19, 3.46)</td>
<td>1.74 (1.01, 3.01)</td>
<td>3.85 (2.23, 6.62)</td>
<td>1.62 (1.33, 1.96)</td>
</tr>
<tr>
<td><strong>Model 3</strong></td>
<td>ref</td>
<td>1.95 (1.10, 3.43)</td>
<td>1.40 (0.76, 2.59)</td>
<td>2.15 (1.15, 4.03)</td>
<td>1.49 (1.16, 1.92)</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>N</strong></td>
<td>23</td>
<td>42</td>
<td>47</td>
<td>67</td>
<td>179</td>
</tr>
<tr>
<td><strong>Model 1</strong></td>
<td>ref</td>
<td>2.57 (1.41, 4.69)</td>
<td>2.95 (1.64, 5.29)</td>
<td>7.27 (3.96, 13.35)</td>
<td>2.72 (2.07, 3.57)</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td>ref</td>
<td>2.75 (1.41, 5.34)</td>
<td>2.42 (1.22, 4.78)</td>
<td>5.27 (2.59, 10.72)</td>
<td>2.61 (1.99, 3.43)</td>
</tr>
<tr>
<td><strong>Model 3</strong></td>
<td>ref</td>
<td>2.89 (1.41, 5.96)</td>
<td>2.29 (1.07, 4.89)</td>
<td>2.79 (1.23, 6.32)</td>
<td>1.82 (1.24, 2.69)</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>N</strong></td>
<td>15</td>
<td>18</td>
<td>26</td>
<td>62</td>
<td>121</td>
</tr>
<tr>
<td><strong>Model 1</strong></td>
<td>ref</td>
<td>0.97 (0.45, 2.09)</td>
<td>1.11 (0.54, 2.29)</td>
<td>2.49 (1.29, 4.79)</td>
<td>1.55 (1.27, 1.90)</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td>ref</td>
<td>1.04 (0.42, 2.61)</td>
<td>0.89 (0.36, 2.82)</td>
<td>2.12 (0.96, 4.62)</td>
<td>1.49 (1.18, 1.89)</td>
</tr>
<tr>
<td><strong>Model 3</strong></td>
<td>ref</td>
<td>0.79 (0.31, 1.96)</td>
<td>0.47 (0.16, 1.35)</td>
<td>1.04 (0.47, 2.34)</td>
<td>1.39 (0.97, 1.99)</td>
</tr>
<tr>
<td><strong>Model 4</strong></td>
<td>ref</td>
<td>0.96 (0.27, 3.35)</td>
<td>1.02 (0.26, 3.94)</td>
<td>2.05 (0.66, 6.33)</td>
<td>1.71 (1.09, 2.68)</td>
</tr>
</tbody>
</table>

* Adjusted for age, race, and sex (in models not stratified by sex)

† Adjusted for variables in Model 1 plus body mass index, systolic blood pressure, diastolic blood pressure, diabetes, income, education, neighborhood socioeconomic characteristics, physical activity, cigarette smoking, left ventricular hypertrophy, and use of aspirin, statins, and renin-angiotensin-aldosterone system inhibitors.

‡ Adjusted for variables in Model 2 plus estimated glomerular filtration rate, natural log-transformed albumin to creatinine ratio, natural log-transformed C-reactive protein, intact parathyroid hormone, triglycerides, high density lipoprotein-cholesterol, and total cholesterol.

¶ Adjusted for variables in Model 3 plus hormone replacement therapy in women with available data

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**eTable 5.** Hazard ratio (95% CI) of cardiovascular disease death as a function of baseline fibroblast growth factor 23 concentrations (categorized as above vs below the median concentration in the random cohort sample) overall and stratified by sex

<table>
<thead>
<tr>
<th></th>
<th>FGF23 &lt; 69 RU/ml</th>
<th>FGF23 ≥ 69 RU/ml</th>
<th>Per doubling of FGF23</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>12</td>
<td>43</td>
<td>55</td>
</tr>
<tr>
<td>Model 1*</td>
<td>ref</td>
<td>3.46 (1.76,6.79)</td>
<td>1.65 (1.35,2.03)</td>
</tr>
<tr>
<td>Model 2†</td>
<td>ref</td>
<td>2.18 (1.07,4.44)</td>
<td>1.35 (0.95,1.91)</td>
</tr>
</tbody>
</table>

**Men**

<table>
<thead>
<tr>
<th></th>
<th>FGF23 &lt; 69 RU/ml</th>
<th>FGF23 ≥ 69 RU/ml</th>
<th>Per doubling of FGF23</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>5</td>
<td>25</td>
<td>30</td>
</tr>
<tr>
<td>Model 1*</td>
<td>ref</td>
<td>6.64 (2.47,17.87)</td>
<td>2.21 (1.59,3.09)</td>
</tr>
<tr>
<td>Model 2†</td>
<td>ref</td>
<td>4.30 (1.36,13.57)</td>
<td>1.79 (1.17,2.74)</td>
</tr>
</tbody>
</table>

**Women**

<table>
<thead>
<tr>
<th></th>
<th>FGF23 &lt; 69 RU/ml</th>
<th>FGF23 ≥ 69 RU/ml</th>
<th>Per doubling of FGF23</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>7</td>
<td>18</td>
<td>25</td>
</tr>
<tr>
<td>Model 1*</td>
<td>ref</td>
<td>1.48 (0.65,3.39)</td>
<td>1.41 (1.04,1.92)</td>
</tr>
<tr>
<td>Model 2†</td>
<td>ref</td>
<td>0.95 (0.39,2.29)</td>
<td>1.32 (0.90,1.93)</td>
</tr>
<tr>
<td>Model 3‡</td>
<td>ref</td>
<td>0.97 (0.42,2.27)</td>
<td>1.23 (0.74,2.03)</td>
</tr>
</tbody>
</table>

*Adjusted for age, race and sex (in models not stratified by sex).

†Adjusted for variables in Model 1 plus systolic blood pressure, body mass index, current smoking, diabetes, dyslipidemia, estimated glomerular filtration rate, urine albumin to creatinine ratio, and intact parathyroid hormone concentrations.

‡Adjusted for variables in Model 2 plus hormone replacement therapy in women with available data