

Supplementary Online Content

Panwar B, Judd SE, Wadley VG, et al. Association of fibroblast growth factor 23 with risk of incident coronary heart disease in community-living adults. *JAMA Cardiol*. Published online March 7, 2018. doi:10.1001/jamacardio.2018.0139

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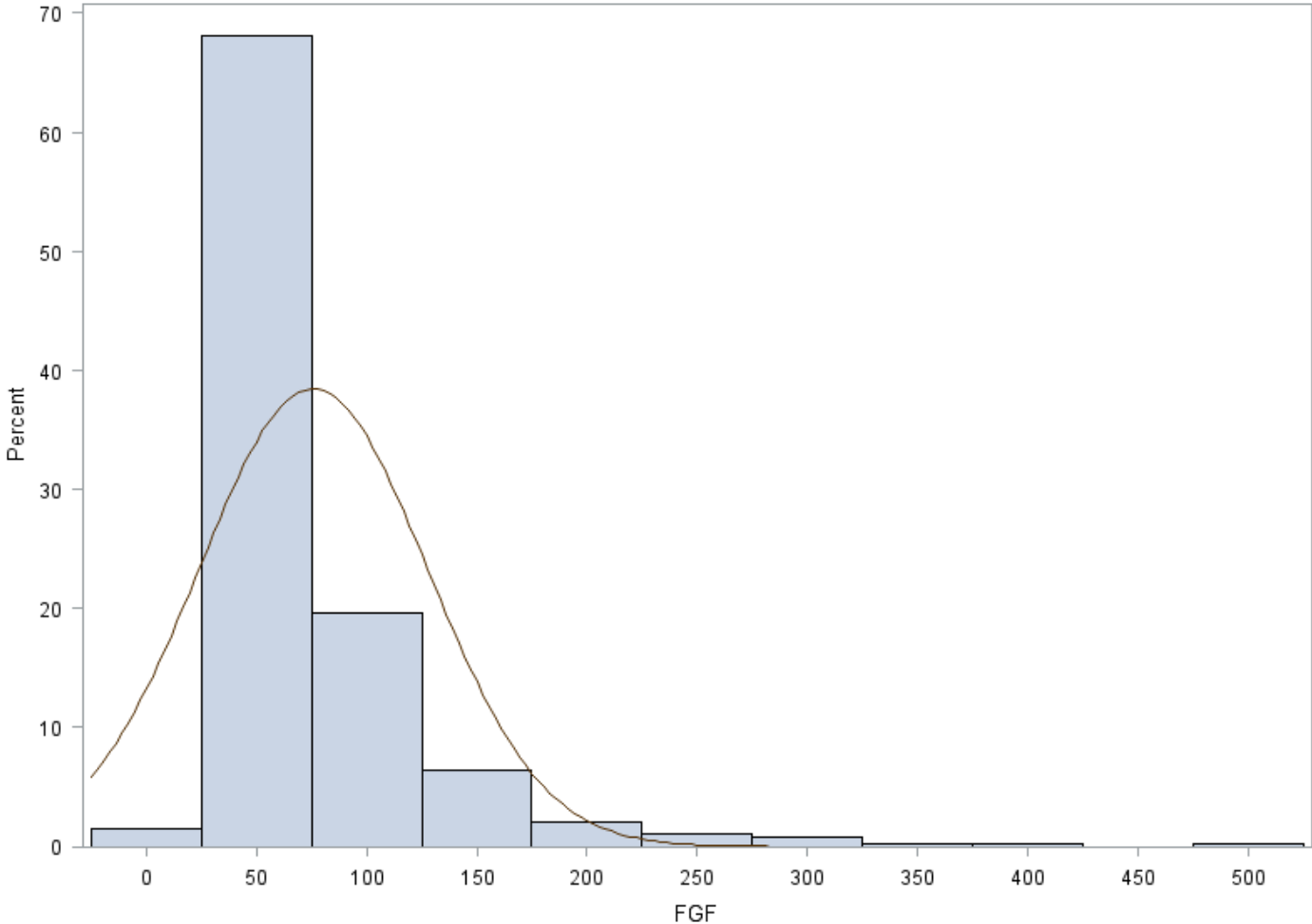
eTable 4. Hazard ratio (95% CI) of fatal coronary heart disease as a function of baseline fibroblast growth factor 23 concentrations overall and stratified by sex

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This supplementary material has been provided by the authors to give readers additional information about their work.

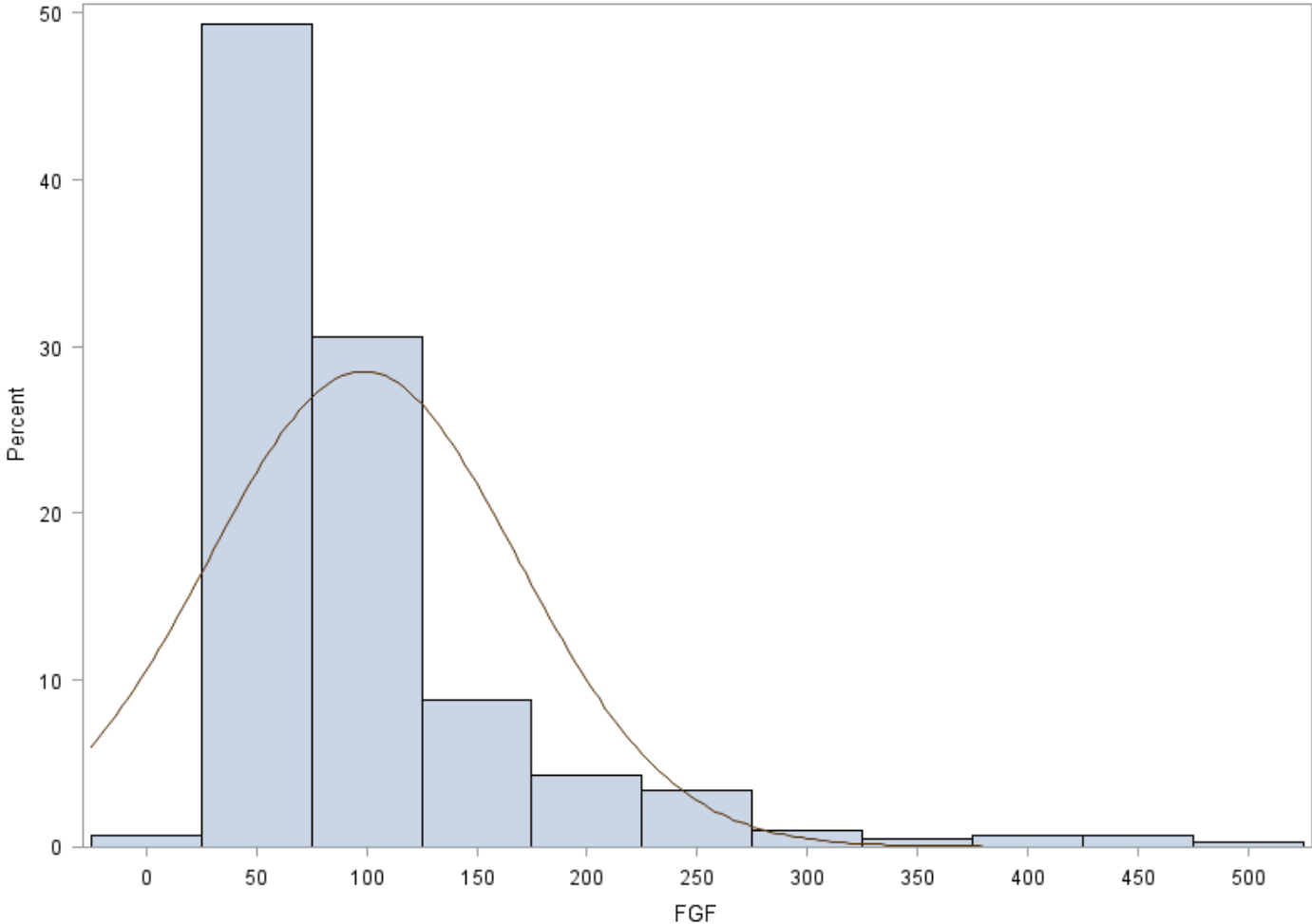
eFigure 1. Distribution of fibroblast growth factor 23 concentrations among men

histogram



eFigure 2. Distribution of fibroblast growth factor 23 concentrations among women

histogram



eTable 1. Hazard ratio (95% CI) of incident coronary heart disease as a function of baseline fibroblast growth factor 23 concentrations stratified by race

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

* 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

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

* 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

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

* 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.

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

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

* 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.

^l 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

	FGF23 < 69 RU/ml	FGF23 ≥ 69 RU/ml	Per doubling of FGF23
N	12	43	55
Model 1*	ref	3.46 (1.76,6.79)	1.65 (1.35,2.03)
Model 2†	ref	2.18 (1.07,4.44)	1.35 (0.95,1.91)
Men			
N	5	25	30
Model 1*	ref	6.64 (2.47,17.87)	2.21 (1.59,3.09)
Model 2†	ref	4.30 (1.36,13.57)	1.79 (1.17,2.74)
Women			
N	7	18	25
Model 1*	ref	1.48 (0.65,3.39)	1.41 (1.04,1.92)
Model 2†	ref	0.95 (0.39,2.29)	1.32 (0.90,1.93)
Model 3‡	ref	0.97 (0.42,2.27)	1.23 (0.74,2.03)

*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