

## Supplemental Files

**Table 1: Characteristics of IGF Proteins Amongst Normoglycemics and Pre-diabetics in the Cardiovascular Health Study**

	<b>Non-diabetic (1320)</b>	<b>Prediabetics (559)</b>	<b>p-value</b>
<b>Female</b>	Mean (sd)	Mean (sd)	
IGF-I	91.2 (30.5)	96.2 (30.8)	0.001
IGFBP-3	3672 (801)	3883 (917)	<0.0001
	<b>Non-diabetic (800)</b>	<b>Prediabetics (454)</b>	<b>p-value</b>
<b>Male</b>	Mean (sd)	Mean (sd)	
IGF-I	105.7 (33.9)	108 (34.5)	0.28
IGFBP-3	3353 (789)	3476 (826)	0.01

**Table 2: Tabulation of Normoglycemics Versus Prediabetic Adults by Tertiles of IGFBP-3 levels in Men and Women.**

<b>Female</b>	<b>Tertile 1</b>	<b>Tertile 2</b>	<b>Tertile 3</b>
	<b>n(%)</b>	<b>n(%)</b>	<b>n(%)</b>
Non-diabetic	455 (73)	472 (75)	393 (63)
Pre-diabetic	172 (27)	154 (25)	233 (37)
Total	627	626	626
<b>Male</b>	<b>Tertile 1</b>	<b>Tertile 2</b>	<b>Tertile 3</b>
	<b>n(%)</b>	<b>n(%)</b>	<b>n(%)</b>
Non-diabetic	288 (69)	261 (62)	251 (60)
Pre-diabetic	130 (31)	159 (38)	165 (40)
Total	418	420	416

**Table 3: HRs (95 % CI) for Incident Diabetes by tertiles of IGF proteins in Normoglycemic Women (n=1320)**

	<b>Hazard Ratios (95% CI)</b>			p-value (trend)
	Tertile 1 (n=440)	Tertile 2 (n=440)	Tertile 3 (n=458)	
<b>Total IGF-I, (µg/l)</b>	<b>26.5 – 75.6</b>	<b>75.7 – 100</b>	<b>100.1 – 215.6</b>	
Subjects, cases/total	36/440	39/440	51/440	
Adjusted for age, race and BMI	ref	1.00 (0.64 - 1.58)	1.35 (0.88 – 2.08)	0.135
Multivariate adjusted	ref	0.88 (0.54 - 1.45)	1.03 (0.59 – 1.79)	0.787
<b>IGFBP-3, (µg/l)</b>	<b>1425 – 3330</b>	<b>3337 – 3990</b>	<b>3991 – 6580</b>	
Subjects, cases/total	29/440	48/440	49/440	
Adjusted for age, race and BMI	ref	1.58 (0.99 – 2.5)	1.61 (1.01 - 2.56)	0.053
Multivariate adjusted	ref	1.67 (1.02 - 2.74)	1.70 (0.97 – 3.0)	0.084

Multivariate adjusted: age, race, BMI, smoking, alcohol, cholesterol, hypertension, C-reactive protein, adiponectin, physical activity and fasting insulin. For IGF-I, Multivariate adjusted models adjusted additionally for IGFBP-3 levels; for IGFBP-3, Multivariate adjusted models adjusted additionally for IGF-I levels.

**Table 4: HRs (95 % CI) for Incident Diabetes by Tertiles of IGF Proteins in Normoglycemic Men (n=800)**

	<b>Hazard Ratios (95% CI)</b>			p-value (trend)
	Tertile 1 (n=267)	Tertile 2 (n=267)	Tertile 3 (n=266)	
<b>Total IGF-I, (µg/l)</b>	<b>24.9 – 90.6</b>	<b>90.7 – 115.6</b>	<b>115.7 – 412.4</b>	
Subjects, cases/total	24/267	19/267	21/266	
Adjusted for age, race and BMI	ref	0.68 (0.37 - 1.25)	0.73 (0.40 - 1.32)	0.325
Multivariate adjusted	ref	0.58 (0.30 - 1.14)	0.65 (0.31 - 1.34)	0.318
<b>IGFBP-3, (µg/l)</b>	<b>1235 – 3002.5</b>	<b>3003 – 3679.5</b>	<b>3680 – 6734.5</b>	
Subjects, cases/total	22/267	19/267	24/266	
Adjusted for age, race and BMI	ref	0.72 (0.38 - 1.36)	0.98 (0.53 - 1.79)	0.991
Multivariate adjusted	ref	0.86 (0.44 - 1.70)	1.29 (0.60 – 2.76)	0.483

Multivariate adjusted: age, race, BMI, smoking, alcohol, cholesterol, hypertension, C-reactive protein, adiponectin, physical activity and fasting insulin. For IGF-I, Multivariate adjusted adjusts additionally for IGFBP-3 levels; for IGFBP-3, Multivariate adjusted adjusts additionally for IGF-I level.

**Table 5: HRs (95 % CI) for Incident Diabetes by tertiles of IGF proteins in women with prediabetes (n=559)**

	<b>Hazard Ratios (95% CI)</b>			p-value (trend)
	Tertile 1 (n=187)	Tertile 2 (n=186)	Tertile 3 (n=186)	
<b>Total IGF-I, (µg/l)</b>	<b>31.8 – 80</b>	<b>80 – 107.4</b>	<b>107.4 – 281</b>	
Subjects, cases/total	42/187	52/186	48/186	
Adjusted for age, race and BMI	ref	1.17 (0.78 - 1.76)	1.10 (0.73 – 1.67)	0.705
Multivariate adjusted	ref	0.93 (0.59 - 1.46)	0.75 (0.42 – 1.33)	0.301
<b>IGFBP-3, (µg/l)</b>	<b>1757 – 3437</b>	<b>3441 – 4251</b>	<b>4258 – 6841</b>	
Subjects, cases/total	37/188	49/185	56/186	
Adjusted for age, race and BMI	ref	1.37 (0.89 – 2.1)	1.52 (1.00 - 2.32)	0.056
Multivariate adjusted	ref	1.54 (0.96 - 2.46)	1.93 (1.08 – 3.45)	0.03

Multivariate adjusted: age, race, BMI, smoking, alcohol, cholesterol, hypertension, C-reactive protein, physical activity and fasting insulin. For IGF-I, Multivariate adjusted models adjusted additionally for IGFBP-3 levels; for IGFBP-3, Multivariate adjusted models adjusted additionally for IGF-I levels.

**Table 6: HRs (95 % CI) for Incident Diabetes by Tertiles of IGF Proteins in Men with prediabetes (n=454)**

	<b>Hazard Ratios (95% CI)</b>			p-value (trend)
	Tertile 1 (n=152)	Tertile 2 (n=151)	Tertile 3 (n=151)	
<b>Total IGF-I, (µg/l)</b>	<b>29.6 – 88.3</b>	<b>88.5 – 119.1</b>	<b>119.2 – 257.7</b>	
Subjects, cases/total	38/152	38/151	37/151	
Adjusted for age, race and BMI	ref	0.86 (0.55 - 1.36)	0.88 (0.55 - 1.39)	0.595
Multivariate adjusted	ref	0.92 (0.56 - 1.5)	0.94 (0.52 - 1.71)	0.842
<b>IGFBP-3, (µg/l)</b>	<b>1350 – 3103</b>	<b>3111 – 3801</b>	<b>3802 – 7633</b>	
Subjects, cases/total	38/152	40/151	35/151	
Adjusted for age, race and BMI	ref	1.04 (0.67 - 1.63)	0.74 (0.46 - 1.18)	0.201
Multivariate adjusted	ref	1.08 (0.66 - 1.77)	0.83 (0.46 - 1.50)	0.526

Multivariate adjusted: age, race, BMI, smoking, alcohol, cholesterol, hypertension, C-reactive protein, physical activity adiponectin, and fasting insulin. For IGF-I, Multivariate adjusted adjusts additionally for IGFBP-3 levels; for IGFBP-3, Multivariate adjusted adjusts additionally for IGF-I level.

**Table 7: HRs (95 % CI) for Incident Diabetes by tertiles of IGF proteins in women who were not on hormone replacement therapy (n=1580)**

	Hazard Ratios (95% CI)			p-value (trend)
	Tertile 1	Tertile 2	Tertile 3	
<b>Total IGF-I, (µg/l)</b>	<b>27.8 – 80.6</b>	<b>80.6 – 105.8</b>	<b>106 – 215.6</b>	
Adjusted for age, race and BMI	ref	1.16 (0.83 - 1.61)	1.32 (0.95 - 1.83)	0.10
Multivariate adjusted	ref	0.93 (0.65 - 1.33)	0.85 (0.56 - 1.30)	0.46
<b>IGFBP-3, (µg/l)</b>	<b>1425 – 3399</b>	<b>3400 – 4115</b>	<b>4116 – 6841</b>	
Adjusted for age, race and BMI	ref	1.15 (0.81 - 1.64)	1.66 (1.19 - 2.30)	0.002
Multivariate adjusted	ref	1.25 (0.86 – 1.83)	1.87 (1.22 – 2.87)	0.003

Multivariate adjusted: age, race, BMI, smoking, alcohol, cholesterol, hypertension, C-reactive protein, adiponectin, physical activity and fasting insulin. For IGF-I, Multivariate adjusted models adjusted additionally for IGFBP-3 levels; for IGFBP-3, Multivariate adjusted models adjusted additionally for IGF-I levels.