The 5-Year Incidence of New Onset Diabetes for All Possible Combinations of NCEP ATP III Metabolic Syndrome Criteria

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Background

Metabolic syndrome (MetS) is a cluster of risk factors including obesity, impaired fasting glucose, hypertension, and dyslipidemia (low HDL cholesterol and/or hypertriglyceridemia) that is known to predict the development of diabetes.

Because individuals can qualify for MetS by meeting any 3 of the 5 criteria, not all persons with MetS have the same cluster of risk factors. Whether the possible combinations of criteria are equal in terms of conferring diabetes risk is not known. Furthermore, it is possible that combinations of criteria insufficient to qualify an individual for MetS, or even a single criterion, confer greater risk of incident diabetes than some clusters of criteria that meet the MetS definition.

Objective

We sought to simultaneously evaluate the 5-year risk of incident diabetes associated with all possible combinations of MetS criteria.

Study Design and Methods

We used an observational study design that capitalizes on the comprehensive medical utilization data maintained by Kaiser Permanente Northwest (KPNW), including an electronic medical record of all patient encounters, laboratory results that are analyzed by a single regional laboratory using standardized methods, and dispenses from pharmacies located in all clinics.

We identified 58,056 non-pregnant adults age 30 or older who had no prior evidence of diabetes and had all MetS components measured in 2003 or 2004, and who remained KPNW members for at least five years following the date that the last of the MetS components was measured (index date).

The five components of the MetS are:

1. Elevated fasting glucose (> 100 mg/dl)
2. Elevated blood pressure (systolic > 130 mmHg or diastolic > 85 mmHg or on anti-hypertensive drug treatment)
3. Reduced HDL cholesterol (< 40 mg/dl in men or < 50 mg/dl in women or on drug treatment)
4. Elevated triglycerides (>150 mg/dl or on drug treatment)
5. Elevated waist circumference. Because waist circumference is rarely measured or recorded in the medical record, we substituted body mass index for the waist circumference criterion, using the cut-point of > 28.8 kg/m^2 as was done in other published studies.

MetS was defined as presence of three or more of the above criteria. Subjects were followed for up to 5 years from the index date for new onset of diabetes, defined as an inpatient or outpatient diagnosis (ICD-9-CM codes 250.xx), a dispensing of an anti-hyperglycemic medication, or a fasting plasma glucose result > 125mg/dl. We estimated the age and sex-adjusted incidence of diabetes for each of the five components of MetS and by number of MetS components.

We then estimated age and sex-adjusted diabetes incidence for all possible combinations of components of MetS.

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Results

Table 1. Characteristics of patients who did and did not develop diabetes within 5 years.

	Developed Diabetes	Did Not Develop Diabetes	p value
n (%)	3,527 (6.1%)	54,529 (93.9%)	--
Mean Age	58.7 (11.3)	56.8 (12.0)	<0.0001
Age Group			<0.0001
30-44	11.4%	16.8%	
45-54	26.1%	28.7%	
55-64	33.7%	29.3%	
65-74	20.5%	17.2%	
75+	8.4%	8.1%	
% Men	51.5%	44.1%	<0.0001
% non-white	10.1%	8.2%	<0.0001
Current smoker	14.5%	12.4%	<0.0001
Mean BMI	34.3 (7.2)	29.6 (6.2)	<0.0001
% BMI > 28.8 kg/m^2	78.2%	48.4%	<0.0001
Mean Systolic BP	137 (18)	130 (18)	<0.0001
Mean Diastolic BP	81 (11)	79 (11)	<0.0001
% > 135/85 mmHg	58.8%	43.4%	<0.0001
Mean LDL-C	117 (33)	122 (33)	<0.0001
LDL > 100 mg/dl	69.2%	74.3%	<0.0001
Mean HDL-C	47 (12)	55 (16)	<0.0001
HDL < 40/50 mg/dl	43.2%	24.6%	<0.0001
Mean Triglycerides	208 (164)	143 (104)	<0.0001
Triglycerides > 150 mg/dl	59.3%	34.0%	<0.0001
Mean Fasting Glucose	108 (14)	94 (9)	<0.0001
FPG > 100 mg/dl	77.4%	24.2%	<0.0001

Table 2. Diabetes Incidence by age, sex, race/ethnicity, smoking and history of cardiovascular disease.

	Number of Subjects	Developed Diabetes Within 5 Years	Crude Incidence per 1,000 person-years	Age/Sex Adjusted Incidece per 1,000 person- years
Total Sample	58,056	6.1%	12.5 (12.1-12.9)	5.3 (4.5-6.3)
Age				
30-44	9,575	4.2%	8.6 (7.8-9.4)	8.5 (7.7-9.4)
45-54	16,548	5.6%	11.4 (10.7-12.2)	11.3 (10.6-12.1)
55-64	17,147	6.9%	14.3 (13.5-15.2)	14.1 (13.3-15.0)
65-74	10,088	7.2%	14.8 (13.8-15.9)	14.6 (13.6-15.7)
75+	4,698	6.3%	13.0 (11.6-14.5)	12.9 (11.5-14.5)
Sex				
Men	25,872	7.0%	14.5 (13.9-15.2)	14.4 (13.7-15.0)
Women	32,184	5.3%	10.9 (10.3-11.4)	10.8 (10.3-11.3)
Race/Ethnicity				
White	42,928	6.1%	12.6 (12.2-13.1)	12.1 (11.6-12.6)
African-American	853	9.1%	19.2 (15.4-24.0)	19.8 (15.8-24.7)
Hispanic	1,074	7.5%	15.5 (12.4-19.3)	16.3 (13.1-20.4)
Native-American	346	8.4%	17.4 (12.1-25.0)	17.1 (11.9-24.6)
Asian-American	1,570	6.9%	14.2 (11.8-17.2)	14.9 (12.4-18.0)
Unknown	11,285	5.3%	10.8 (10.0-11.7)	11.3 (10.4-12.3)
Current Smoker	7,265	7.0%	14.6 (13.3-15.9)	14.6 (13.4-16.0)
Non-Smoker	50,791	5.9%	12.2 (11.8-13.6)	11.9 (11.5-12.4)
Cardiovascular Disease	7,835	9.7%	20.4 (19.0-21.9)	18.1 (16.7-19.6)
No Cardiovascular Disease	50,221	5.5%	11.3 (10.9-11.7)	11.4 (11.0-11.8)

Figure 1. Diabetes Incidence for Individual Metabolic Syndrome Components

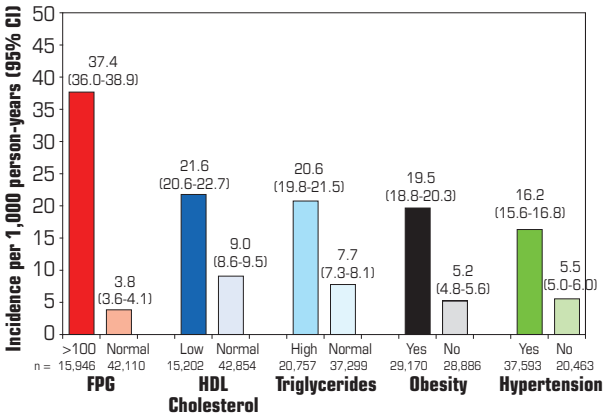

Figure 2. Population Proportion and Diabetes Risk by Metabolic Syndrome Factor Count

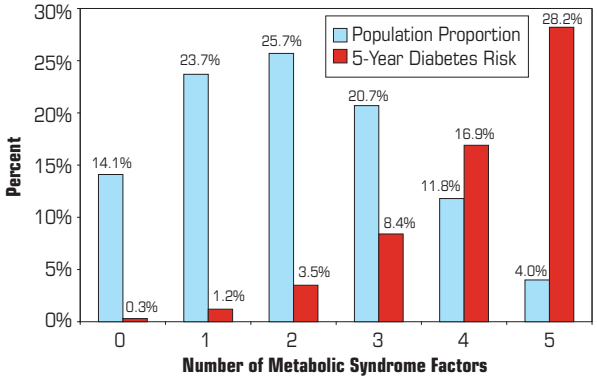

Figure 3. Age/sex Adjusted Incidence of Diabetes by Number of Metabolic Syndrome Components

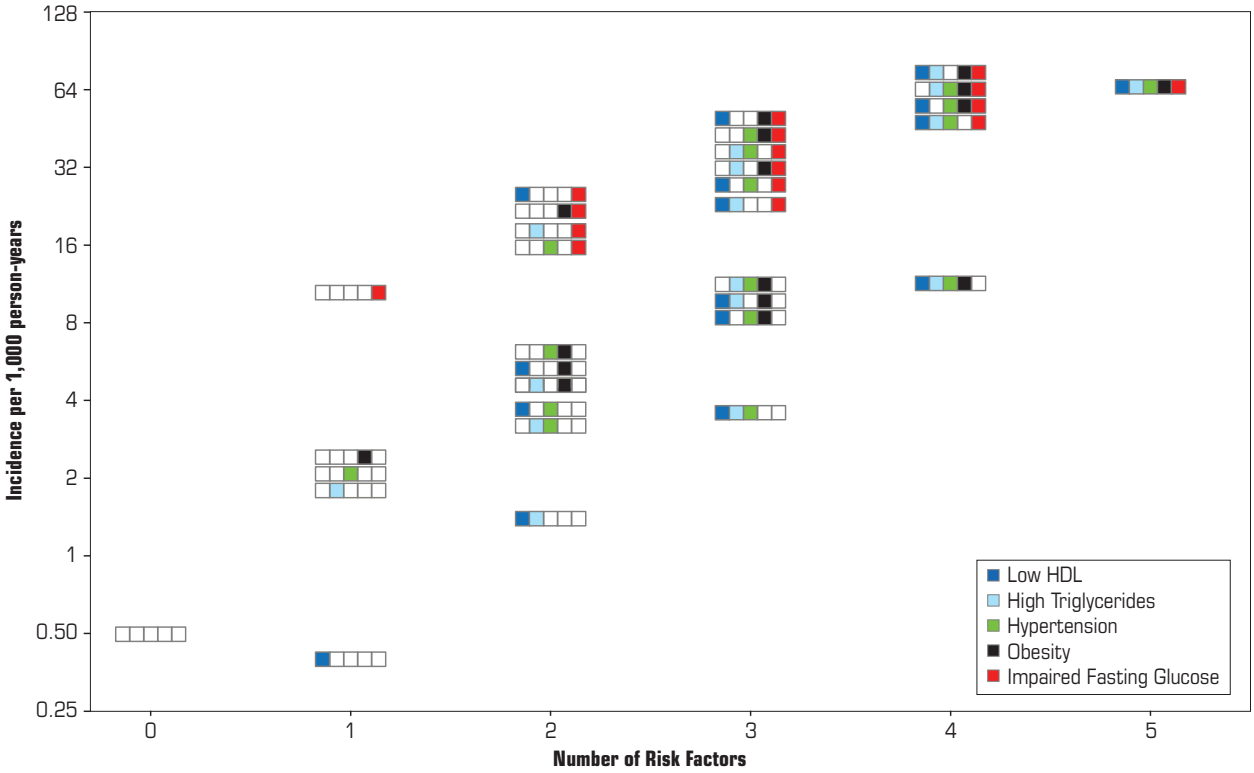

Table 3. Age and Sex Adjusted Diabetes incidence for all possible combinations of metabolic syndrome criteria.

	Low HDL	High TG	Hyper-tension	Obesity	IFG	No. of Subjects	Developed Diabetes Within 5 Years	Proportion Relative to Overall Proportion	Diabetes Incidence per 1,000 person-hours
No Components						8,177	0.3%	0.05	0.5 (0.4 - 0.8)
Single Components Only									
	Yes					976	0.2%	0.03	0.4 (0.1 - 1.7)
		Yes				1,239	0.9%	0.15	1.8 (1.0 - 3.2)
			Yes			7,558	0.8%	0.13	1.6 (1.3 - 2.1)
				Yes		2,847	1.1%	0.18	2.3 (1.6 - 3.2)
					Yes	1,148	5.1%	0.84	10.5 (8.1 - 13.6)
Any One Component						13,768	1.2%	0.20	2.4 (2.1 - 2.8)
Two Components Only									
	Yes	Yes				697	0.7%	0.11	1.4 (0.6 - 3.5)
		Yes	Yes			2,368	1.6%	0.26	3.2 (2.3 - 4.4)
	Yes		Yes			850	1.7%	0.28	3.3 (2.0 - 5.6)
		Yes		Yes		970	2.3%	0.38	4.6 (3.0 - 7.0)
	Yes			Yes		933	1.9%	0.31	4.0 (2.5 - 6.3)
			Yes	Yes		5,725	2.5%	0.41	5.1 (4.3 - 6.0)
		Yes			Yes	310	7.1%	1.16	14.7 (9.7 - 22.3)
			Yes		Yes	2,160	7.6%	1.25	15.7 (13.4 - 18.3)
	Yes				Yes	144	9.0%	1.48	19.1 (11.1 - 33.0)
				Yes	Yes	768	10.3%	1.69	21.7 (17.4 - 27.1)
Any Two Components						14,925	3.5%	0.57	7.0 (6.4 - 7.6)
Three Components Only									
	Yes	Yes	Yes			1,166	1.8%	0.30	3.6 (2.4 - 5.5)
	Yes		Yes	Yes		1,637	4.1%	0.67	8.4 (6.6 - 10.6)
		Yes	Yes	Yes		3,257	4.3%	0.70	8.7 (7.4 - 10.3)
	Yes	Yes		Yes		965	4.7%	0.77	9.6 (7.2 - 12.9)
	Yes	Yes			Yes	199	11.1%	1.82	23.0 (15.1 - 34.9)
	Yes		Yes		Yes	322	13.0%	2.13	27.4 (20.2 - 37.1)
		Yes		Yes	Yes	383	13.6%	2.23	29.1 (22.1 - 38.2)
		Yes	Yes		Yes	980	14.4%	2.36	30.5 (25.8 - 36.1)
			Yes	Yes	Yes	2,832	15.4%	2.52	32.9 (29.9 - 36.2)
	Yes			Yes	Yes	268	15.7%	2.57	34.3 (25.4 - 46.5)
Any Three Components (Metabolic Syndrome)						12,009	8.4%	1.38	17.1 (16.1 - 18.2)
Four Components Only									
	Yes	Yes	Yes	Yes		2,745	5.6%	0.92	11.4 (9.8 - 13.4)
	Yes	Yes	Yes		Yes	592	21.8%	3.57	47.8 (40.2 - 57.0)
	Yes	Yes		Yes	Yes	439	23.2%	3.80	52.7 (43.4 - 64.0)
	Yes		Yes	Yes	Yes	954	23.9%	3.92	54.3 (47.7 - 61.9)
		Yes	Yes	Yes	Yes	2,132	25.6%	4.20	58.1 (53.4 - 63.3)
Any Four Components						6,862	16.9%	2.77	36.1 (34.1 - 38.3)
All Five Components	Yes	Yes	Yes	Yes	Yes	2,315	28.2%	4.62	65.7 (60.8 - 71.0)

Discussion

Although average diabetes risk increased exponentially with each additional MetS criterion, our results demonstrate that diabetes risk varied substantially depending upon which criteria were met.

Nearly half (46%) of patients who qualified for MetS did not have IFG, and these patients were at substantially lower risk of developing diabetes than those with IFG plus any other single criterion (and therefore did not qualify for MetS).

Patients with MetS comprised 36.5% and accounted for 80% of all incident diabetes. However, the heterogeneity of risk within the MetS combinations suggests that prevention strategies aimed at this relatively large proportion of the population would likely require more resources than the benefits would justify.

Conclusions

To our knowledge, this is the first study to simultaneously estimate diabetes incidence across all possible combinations of MetS components.

The presence of IFG, regardless of the presence of MetS, is more important in predicting incident diabetes than the presence of MetS without the IFG component.

The considerable variation in risk within MetS depending on the specific combination of factors suggests that improved tools for identifying more of the truly high-risk patients would likely enable more cost-effective and feasible prevention strategies.