

# THE METABOLIC SYNDROME AND ALL-CAUSE MORTALITY IN AN INSURED LIVES POPULATION

C. Allen Pinkham,\* Marianne E. Cumming,<sup>†</sup> and Howard Minuk<sup>‡</sup>

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## ABSTRACT

Metabolic syndrome and its association with mortality have not been studied in insured lives populations. The Swiss Re Study evaluated metabolic syndrome prevalence and associated mortality from all causes and circulatory disease in a cohort of 35,470 predominantly healthy individuals, aged 18–83 years, who were issued life insurance policies between 1986 and 1997. Metabolic syndrome was defined using the National Cholesterol Education Program (NCEP) Expert Panel Adult Treatment Panel (ATP) III guidelines. The NCEP obesity criteria were modified with a prediction equation using body mass index, gender, and age substituted for waist circumference. Adjustments also were made for nonfasting triglyceride and blood glucose values. Risk ratios for policyholders identified with metabolic syndrome were 1.16 ( $P = .156$ ) for mortality from all causes and 1.45 ( $P = .080$ ) for mortality from circulatory disease compared with individuals without the syndrome. Risk was proportional to the number of components, or score, of the metabolic syndrome present. Risk ratios for metabolic syndrome score were 1.14 ( $P < .001$ ) for mortality from all causes and 1.38 ( $P < .001$ ) for mortality from circulatory disease compared with individuals without metabolic syndrome factors. In both all-cause and circulatory death models, relative risk was highest for the blood pressure risk factor. Based on a modified NCEP definition, increased mortality risk is associated with metabolic syndrome in an insured lives cohort and has life insurance mortality pricing implications.

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## 1. INTRODUCTION

Metabolic syndrome is a cluster of related cardiovascular risk factors that increase the risk for heart disease, stroke, diabetes mellitus, and chronic kidney disease. Various definitions have been used to identify metabolic syndrome (Reaven 1988; NCEP 2002; Alberti and Zimmet 1998). Presently, the criteria that have been most widely accepted and used in the United States are based on those proposed by the National Cholesterol Education Program Expert Panel (NCEP) on

the Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (NCEP 2002). The NCEP defines metabolic syndrome as the presence of three or more of the following: (1) increased waist circumference ( $>40$  inches [102 cm] for men,  $>35$  inches [88 cm] for women); (2) elevated triglycerides ( $\geq 150$  mg/dL [1.7 mmol/L]); (3) low HDL ( $<40$  mg/dL [1 mmol/L] in men,  $<50$  mg/dL [1.3 mmol/L] in women); (4) hypertension ( $\geq 130/\geq 85$  mmHg); and (5) impaired fasting glucose ( $\geq 110$  mg/dL [6.1 mmol/L]). Recently the International Diabetes Federation proposed what they hope will be a global consensus definition with a universally applied definition allowing for easier comparison of different studies (IDF 2005).

Further understanding of the combined risk factors in metabolic syndrome is important for the prediction of risk related to subsequent development of type 2 diabetes mellitus, cardiovascular disease, and cardiovascular and all-cause mortality. Prevalence of metabolic syndrome is

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\* C. Allen Pinkham, ASA, MAAA, MA, is an Assistant Vice President for Applied Research and Development at Swiss Re Life and Health America, 1700 Magnavox Way, Fort Wayne, IN 46804, allen\_pinkham@swissre.com.

<sup>†</sup> Marianne E. Cumming, MSc, MD, is a Vice President and Medical Director at Swiss Re Life and Health America, 1700 Magnavox Way, Fort Wayne, IN 46804, marianne\_cumming@swissre.com.

<sup>‡</sup> Howard Minuk MD, FRCPC, is the Chief Medical Officer (Canada) at Swiss Re Life and Health America, Suite 3000, 161 Bay Street, Toronto, ON, M5J 2T6, howard\_minuk@swissre.com.

growing largely because of increases in obesity. Overall prevalence of metabolic syndrome in adults over 20 years of age was estimated to be 22% in the Third National Health and Nutrition Examination Survey (NHANES III), based on the NCEP criteria. Prevalence generally increases with age, with an estimate of 6.7% in 20- to 39-year-olds compared with over 40% for participants over 60 (Ford, Giles, and Dietz 2002).

In life insurance risk assessment, metabolic syndrome criteria frequently are considered as part of the cardiovascular risk evaluation. Preferred risk classification most commonly includes the parameters build, blood pressure, total cholesterol, and blood glucose. These parameters are either part of or closely associated with metabolic syndrome criteria. Different companies have various exclusion criteria for their preferred products. In general, determinants center on numbers associated with these parameters and do not focus on combination risk. Applying the metabolic syndrome definition enables assessment of the importance of both the individual and combined risks associated with the cluster of risk factors known as metabolic syndrome. The goal of this study is to identify the prevalence of metabolic syndrome and to assess the association of metabolic syndrome with cardiovascular and all-cause mortality in a large predominantly healthy insured lives population during 15 years of follow-up. Mortality associated with metabolic syndrome is assessed using various models.

## 2. METHODS

### 2.1 Data Issues

The Swiss Re Metabolic Syndrome Study is a retrospective study of 35,470 individuals issued insurance policies between 1986 and 1997 and followed until policy lapse, death, or policy anniversary in 2001. Policies were selected based on availability of laboratory values and physical measurements that are components of the metabolic syndrome. Using a modified NCEP definition, positive metabolic syndrome status was assigned with the presence of three or more risk factors. Status was considered negative with the presence of fewer than three risk factors. Metabolic syndrome score, or the total number of positive risk factors, was also determined.

Metabolic syndrome was defined by modified NCEP criteria. Waist circumference measurements, which are not routinely collected in life insurance risk assessment, were not available for our population. A prediction equation with body mass index ( $\text{kg}/\text{m}^2$ ), age, smoking status, and gender was substituted for waist circumference and gender using the NHANES 1999–2000 data set, which provides waist circumference and height and weight information (NHANES 2004). A number of logistic regression models were considered, including those with gender-specific or single-BMI thresholds. The model with BMI, age, gender, smoking status, and all their two-way-interaction terms provided the best fit (specificity 0.909, sensitivity 0.857). Prior to BMI calculation, one inch was subtracted from the recorded height for insurance policyholders to correct for differences in how height is commonly measured in insurance applicants (with shoes on) as compared to how it was measured in the NHANES study (without shoes). The equivalent BMI thresholds for some representative age/gender/smoking status combinations are shown in Table 1. A number of other studies (Ford 2004; Malik et al. 2004; Hu et al. 2004) used BMI equivalents of 30  $\text{kg}/\text{m}^2$ , which would appear to be a less effective choice based on the NHANES data. The prediction equation from this model was used to assign the abdominal obesity status of the metabolic syndrome definition.

Thresholds were applied to nonfasting glucose levels based on time since last meal. Higher thresholds were used for shorter fasting times. Blood glucose levels at or above 140  $\text{mg}/\text{dL}$  (7.8  $\text{mmol}/\text{L}$ ), 120  $\text{mg}/\text{dL}$  (6.7  $\text{mmol}/\text{L}$ ), and 110  $\text{mg}/\text{dL}$  (6.1  $\text{mmol}/\text{L}$ ) for fasting times of one hour or less, two hours, and three hours or more,

Table 1  
Equivalent BMI ( $\text{kg}/\text{m}^2$ ) Thresholds for the Obesity Factor

Age	Female Nonsmoker	Female Smoker	Male Nonsmoker	Male Smoker
25	28.1	27.1	30.2	29.8
35	27.6	26.6	29.6	29.2
45	27.1	26.0	29.0	28.7
55	26.5	25.4	28.4	28.0
65	25.8	24.7	27.7	27.4
75	25.1	24.0	27.1	26.7

respectively, were considered positive for the glucose risk factor (ECDCDM 2003). Positive glucose status was assigned to the 250 policies identified at underwriting as having diabetes mellitus or hyperglycemia, regardless of their recorded blood glucose level.

There can be variability in the timing of blood collection for underwriting relative to when an applicant finished their last meal, which can affect the interpretation of the baseline level of serum triglycerides. Fasting equivalent estimates were developed for serum triglyceride levels using an insurance laboratory data set of approximately 3.5 million recorded triglyceride values and the corresponding duration between last meal and blood draw. Age- and gender-specific factors were developed using distributions of mean triglyceride levels by fasting duration in hours. Triglyceride values were found to level off at a fasting duration of nine hours. Triglyceride levels of nine hours or greater were selected as the fasting equivalents. Adjustment factors were calculated by dividing mean triglyceride level at nine or more hours by mean triglyceride level at each hourly interval up to nine hours. Factors for males ages 40–49 are shown in Table 2. Factors for other age and gender combinations were found to have similar patterns. These ratios were applied to the insured lives data set nonfasting triglyceride values and compared to the NCEP threshold triglyceride level of 150 mg/dL (1.7 mmol/L) to determine the triglyceride status for metabolic syndrome.

## 2.2 Statistical Analysis

Cox proportional hazard models (Cox models) were used to analyze the mortality impact of metabolic syndrome. A brief review of Cox models may be beneficial for interpreting the results of this and the other cited studies. Cox models are well-known and widely used survival models, generally regarded as the gold standard test for statistical significance in clinical and pharmacological studies. They allow multivariate exploration, handle censored data (lapses and active policies) well, yield tests of statistical significance, and allow survival projections of specific combinations of variables.

Cox models are regarded as semiparametric models. They do not require a choice for the form of the survival times, only that the hazards are

Table 2  
Triglyceride Distribution for Males 40–49

Fasting Time (hr)	Mean Triglyceride (mg/dL)	Ratio to Fasting
0	206.2	0.801
1	223.5	0.739
2	224.3	0.737
3	225.1	0.734
4	223.9	0.738
5	222.9	0.741
6	210.5	0.785
7	198.1	0.834
8	181.1	0.912
9+	165.2	1.000

proportional. The validity of the proportional hazards assumption can be checked using various graphical and analytical methods. The results presented in this paper were checked for consistency with the proportional hazards assumption.

An important feature of the Cox model is the calculation of risk ratios (also referred to as hazards ratios). Risk ratios (RRs) represent the proportional change in survival for any increase of one unit for that variable across its entire range of values. A RR greater than 1.00 means reduced survival (i.e., higher mortality). The RR is basically analogous to a mortality ratio or actual-to-expected ratio in an actuarial study.

Another important feature is the determination of the statistical significance of the RR. This is represented by the *P*-value or its related confidence interval (CI). The *P*-value can be considered an estimate of the probability of obtaining a value as extreme as the observed value when there is actually no difference in survival at different values of the covariate. The smaller the *P*-value, the more likely there is a true difference in survival for that covariate. Standard practice is to consider a *P*-value less than or equal to .05 as significant. Equivalently, a 95% CI that does not include 1.00 would be significant.

Cox models were fitted to this data set using all-cause mortality as the dependent variable. Different models were fitted for metabolic syndrome status (positive with three or more risk factors), metabolic syndrome score (total number of positive risk factors), and individual metabolic syndrome definition components. Issue age, issue year, gender, and smoking status were included in all models to avoid potential confounding by

Table 3  
**Baseline Characteristics of Entire Cohort and Those Who Died of Any Cause and Known Circulatory Causes**

Characteristic	Entire Cohort ( <i>n</i> = 35,470)	All-Cause Deaths ( <i>n</i> = 503)	Known Circulatory Deaths ( <i>n</i> = 107)
Age, mean (SD), yr	40.8 (11.0)	55.3 (12.7)	59.1 (12.0)
Male, no. (%)	26,703 (75)	384 (76)	90 (84)
Issue year, median (range)	1991 (1986–97)	1990 (1986–97)	1989 (1986–97)
Smokers, no. (%)	3,902 (11)	88 (17)	14 (13)
Body Mass Index, mean (SD), kg/m <sup>2</sup>	26.4 (4.0)	27.1 (4.1)	27.9 (3.9)
Systolic BP, mean (SD), mm Hg	119.0 (12.7)	127.8 (14.5)	133.5 (13.7)
Diastolic BP, mean (SD), mm Hg	75.4 (8.7)	78.6 (8.3)	80.5 (7.7)
HDL cholesterol, mean (SD), mg/dL	51.8 (15.6)	50.0 (16.0)	46.7 (14.4)
LDL cholesterol, mean (SD), mg/dL	121.6 (35.9)	136.4 (40.4)	137.6 (39.1)
Fasting triglycerides, mean (SD), mg/dL	134.2 (95.1)	147.8 (97.2)	160.2 (99.0)
Blood glucose, mean (SD), mg/dL	84.6 (19.4)	92.6 (27.5)	93.9 (32.5)
Metabolic syndrome, no. (%)	4,843 (14)	123 (24)	34 (32)
Metabolic syndrome score, mean (SD)	1.1 (1.2)	1.7 (1.3)	2.1 (1.2)
Obesity definition, no. (%)	8,641 (24)	193 (38)	50 (47)
HDL definition, no. (%)	10,002 (28)	179 (36)	46 (43)
Blood pressure definition, no. (%)	8,960 (25)	257 (51)	71 (66)
Triglyceride definition, no. (%)	10,715 (30)	171 (34)	47 (44)
Glucose definition, no. (%)	1,560 (4)	59 (12)	14 (13)

these variables. Additional models were also fitted for known circulatory deaths. All statistical calculations were done using SAS version 9.1. Additional background on Cox models can be found in a variety of survival model texts (Allison 1995; Collett 2003).

### 3. RESULTS

Mean follow-up time was 7.3 years (range 1–15 years) with 503 deaths. Known circulatory causes accounted for 107 deaths, with the cause not identified in 131 of the deaths. Baseline characteristics of the entire cohort and of the death groups are shown in Table 3.

#### 3.1 All-Cause Mortality

Table 4 summarizes the Cox proportional hazards model results. Relative risk of metabolic syndrome based on status (model 1) is 1.16 but not significant ( $P = .156$ ). In contrast, relative risk for the metabolic syndrome score (model 2) is highly significant ( $P < .001$ ), with a relative risk of 1.14. Results for individual components of the definition (model 3) are significant ( $P \leq .020$ ), with the exception of obesity ( $P = .165$ ). However, relative risk associated with triglyceride status was found to be less than one. The implication that fasting triglyceride values below the

150 mg/dL threshold have worse mortality than those above prompted further analysis. Mortality was poorest at triglyceride values above 400 mg/dL. Triglyceride values between 150 and 400 mg/dL yielded better mortality than triglyceride values below 150 mg/dL when controlling for all other metabolic syndrome factors. Consequently, in this particular cohort of insurance policyholders, the triglyceride factor result would have been optimized with a model using an alternative triglyceride threshold of 400 mg/dL and would have resulted in a greater risk ratio (1.71) and higher significance ( $P < .001$ ) for the overall metabolic syndrome status result.

Table 4  
**Relative Risk of Death from Any Cause**

Model Variable(s)	Relative Risk	P-Value
Model 1		
Metabolic syndrome status	1.16	.156
Model 2		
Metabolic syndrome score	1.14	<.001
Model 3		
Obesity status	1.14	.165
HDL status	1.27	.020
Blood pressure status	1.53	<.001
Triglyceride status	0.76	.006
Glucose status	1.41	.015

Table 5  
Relative Risk of Death from Circulatory Causes

Model Variable(s)	Relative Risk	P-Value
Model 4 Metabolic syndrome status	1.45	.080
Model 5 Metabolic syndrome score	1.38	<.001
Model 6 Obesity status	1.31	.178
HDL status	1.44	.087
Blood pressure status	2.30	<.001
Triglyceride status	0.97	.869
Glucose status	1.30	.373

### 3.2 Circulatory Cause of Death Mortality

Metabolic syndrome appears to be more predictive of death from circulatory causes than of all-cause mortality (Table 5). Relative risk for metabolic syndrome status (model 4) for known circulatory deaths is 1.45 ( $P = .080$ ) but not quite significant. Relative risk for metabolic syndrome score (model 5) is 1.38 and is highly significant ( $P < .001$ ). Results for individual components of the definition (model 6) demonstrate significance for hypertension only.

### 3.3 Metabolic Syndrome Prevalence

Prevalence of NCEP-defined metabolic syndrome in our insured lives cohort is 13.7%. Based on our

analysis, prevalence of metabolic syndrome in the NHANES 1999–2000 data set is 24.8% and is 14.3% in a 2002 insurance laboratory data set. Prevalence of metabolic syndrome status and score, component risk factors in the cohort, the insurance laboratory data set, and NHANES 1999–2000 are summarized in Table 6.

## 4. DISCUSSION

### 4.1 Mortality

The present study reports increased mortality associated with metabolic syndrome score, based on a modified NCEP definition in a predominantly healthy insured lives population with about 94% of cases classified as standard risk. In this large insured lives population, both increased all-cause (RR 1.14,  $P < .001$ ) and circulatory (RR 1.38,  $P < .001$ ) mortality are statistically significant for metabolic syndrome score. This means that all-cause and circulatory mortality increases proportionally to the number of positive risk factors. Relative risk for metabolic syndrome score is higher for circulatory deaths. Consideration of the number of factors is a better description of risk than the use of a threshold of three or more positive factors.

All-cause mortality risk associated with metabolic syndrome status is moderately elevated but not statistically significant (RR 1.16,  $P = .156$ ).

Table 6  
Metabolic Syndrome Prevalence

Variable	Value	NHANES 1999–2000 Frequency	Contemporary Lab Data (2002) Frequency	Study Cohort (1986–97) Frequency
Metabolic syndrome status	Yes	24.8%	14.3%	13.7%
	No	75.2	85.7	86.3
Metabolic syndrome score	0	22.0	36.2	38.5
	1	28.8	29.1	28.6
	2	24.4	20.4	19.3
	3	17.0	10.6	9.7
	4	6.1	3.4	3.6
	5	1.8	0.4	0.3
Obesity	Yes	44.9	36.8	24.4
	No	55.1	63.2	75.6
HDL	Yes	45.2	23.0	28.2
	No	54.8	77.0	71.8
Blood pressure	Yes	32.7	21.5	25.3
	No	67.3	78.5	74.7
Triglycerides	Yes	31.3	31.4	30.2
	No	68.7	68.6	69.8
Glucose	Yes	7.6	4.2	4.4
	No	92.4	95.8	95.6

Circulatory mortality risk for metabolic syndrome status (RR 1.45,  $P = .080$ ) was elevated but not quite statistically significant. Actual risk associated with circulatory deaths may be even higher than stated as cause is unknown for 26% (131/503) of the deaths. The risk is likely higher because a portion of the unknowns will be circulatory deaths, and they are more likely to have metabolic syndrome based on this result. This contaminates the noncirculatory death group with a higher proportion of metabolic syndrome than would be the case if all the circulatory deaths were known and probably has dampened the relative risk slightly.

Given that the majority of insured lives in this study are standard risks, the risk assigned to individual metabolic syndrome components is sufficiently small to remain in the standard risk pool and to contribute to the nonsignificant result over the average 7.3-year follow-up period. However, the significant metabolic syndrome score RRs for both all-cause and circulatory mortality highlight the impact of subtle, increasing cardiovascular risk factors on mortality. The most significant of the individual metabolic syndrome components is blood pressure (RR 1.53,  $P < .001$  for all causes and RR 2.30,  $P < .001$  for circulatory deaths).

Results of other population-based studies that demonstrate a relationship between NCEP-defined metabolic syndrome and increased mortality are summarized in Table 7. Compared with the present study, evaluation of the National Health and Nutrition Examination Survey

(NHANES) II Mortality Study data demonstrated nearly identical relative risk of all-cause mortality with moderately elevated risk without statistical significance (Ford 2004). The RRs for cardiovascular disease (significant) and circulatory disease (not significant) were somewhat higher. Similar to our study, Ford also found an increased risk as the number of metabolic syndrome criteria increased. He found that a linear trend for the cardiovascular disease result was significant, but not significant for all-cause or circulatory results.

A separate analysis of the NHANES II data reported higher coronary, cardiovascular, and total mortality that is explained by inclusion of a higher number of individuals with preexisting diseases (Malik et al. 2004). Mortality was more strongly predicted with metabolic syndrome than with the individual components.

The Kuopio Ischaemic Heart Disease Risk Factor Study was directly compared to the present study. Models controlling for conventional risk factors as well as LDL cholesterol, smoking, family history of CHD, and examination year were compared in males. Relative risk for all-cause mortality (2.02) was higher and significant in the Kuopio study, whereas the same model yielded a nonsignificant relative risk for all-cause mortality (1.16) in the present study. Their other models, adjusting for other variables, yielded lower, nonsignificant RRs (1.67). Population differences may explain the higher relative risk in the Kuopio study. The present study consists of a large U.S. insured lives population who all qualified for and purchased life insurance policies after extensive

Table 7  
**Published Metabolic Syndrome Study Summary**

Reference	Study Population	Number of Participants	All-Cause Mortality, RR	Cardiovascular/Circulatory Mortality, RR
Lakka et al. 2002	Kuopio Ischaemic Heart Disease Study	1,209 men	Status 1.67	CVD status 2.27
Ford 2004	NHANES II	2,431	Status 1.15	CVD status 1.37 <sup>a</sup> Circ status 1.23
Malik et al. 2004	NHANES II	6,255	Status 1.40 <sup>a</sup>	CVD status 1.82 <sup>a</sup>
Hunt et al. 2004	San Antonio Heart Study	2,372	Status 1.06	CVD status 2.01 <sup>a</sup>
Katzmarzyk et al. 2005	Aerobics Center Longitudinal Study	19,173 men	Status 1.11–1.55 (by build groups)	CVD status 1.80–2.83 (by build groups)
Current study	Swiss Re 2004 Insured Lives Study	35,470	Status 1.16, score 1.14 <sup>a</sup>	Circ. status 1.45, circ. score 1.38 <sup>a</sup>

Note: Selected studies include primarily healthy middle-aged individuals.

The average follow-up intervals are between 7.3 and 13.5 years.

<sup>a</sup>Result was statistically significant at the .05 level.

underwriting evaluation. The Kuopio study is smaller, limited to Finnish males, and excludes only those with histories of coronary heart disease, cancer, and diabetes mellitus. Longer average follow-up (11.6 years) compared with the present study (7.3 years) may contribute to the higher relative risk in the Kuopio study given that adverse risk related to metabolic syndrome, including diabetes and cardiovascular disease, develops over time. Metabolic syndrome may be more predictive of adverse risk farther into the future.

Several other studies have demonstrated statistically significant increased all-cause and cardiovascular mortality risk using various definitions for metabolic syndrome. Additionally, these studies have demonstrated the relative importance of the number of components, compared with a threshold approach for diagnosis. Studies have also demonstrated the high significance for cardiovascular or circulatory deaths (Hunt et al. 2004; Katzmarzyk et al. 2005; Hu et al. 2004; Wilson et al. 1999; Isomaa et al. 2001; Trevisan et al. 1998; Ridker et al. 2003; Marroquin et al. 2004; Kip et al. 2004).

## 4.2 Prevalence

The present study provides, to our knowledge, the first reported estimate of prevalence of metabolic syndrome in an insured lives population. Based on the NCEP definition, 13.7% of the insured lives population meet the criteria for metabolic syndrome. This prevalence rate is similar to the 14.3% found in a subset of life insurance applicants, based on our analysis of insurance laboratory data. We also analyzed the NHANES 1999–2000 data set and found that 24.8% of U.S. adults meet the NCEP criteria for metabolic syndrome (NHANES 2004). This is consistent with the prevalence estimates from NHANES III (22%) and from NHANES II (24% or 26%, using BMI) (Ford, Giles, and Dietz 2002; Ford 2004; Malik et al. 2004). Prevalence in the insured lives in the present study is substantially lower than prevalence reported for NHANES data. Explanations for this difference include socioeconomic and other factors since individuals in the present study were screened at time of underwriting for cardiovascular risk factors, including factors that are part of the NCEP metabolic syndrome definition. Screening determined eligibility for life insur-

ance, and all qualified for and purchased life insurance policies. Population prevalence of metabolic syndrome may have been lower during the policy issue years 1986–97 in the present study. Prevalence in published clinical studies has ranged from 8.8% to 25% depending on the population and the criteria used to define metabolic syndrome (Lakka et al. 2002; Hu et al. 2004; Isomaa et al. 2001; Ridker et al. 2003; Marroquin et al. 2004).

## 4.3 Study Limitations

The present study used a modified NCEP definition for metabolic syndrome based on available data. A prediction equation using BMI, age, smoking status, and gender was substituted for waist circumference, which is not generally collected on insurance applicants. Using the NHANES 1999–2000 data set, these measures are highly correlated. This type of adjustment was also used in other studies (Ford 2004; Malik et al. 2004; Hu et al. 2004; Ridker et al. 2003). However, the other studies used a gender-specific or single BMI threshold. Our study, which considered age and smoking status as well, more accurately imputed obesity status. Because our analysis included both fasting and nonfasting blood glucose samples, higher thresholds for nonfasting samples were used to identify abnormal glucose metabolism. These thresholds were selected for consistency with American Diabetes Association guidelines for random glucose and oral glucose tolerance testing for the identification of abnormal glucose metabolism (ECDCDM 2003). Similarly, fasting-equivalent estimates for triglycerides were used. Adjustment factors for triglycerides were developed using a large insurance applicant data set. The adjustments to nonfasting glucose and triglyceride levels are similar to those used in another study (Malik et al. 2004) and are thought to be reliable, although their impact is not known.

The average policy duration, until death, lapse, cancellation, or the end of the study, was 7.3 years. The accrual period represents a time of intensive pricing competition in the life insurance industry with the likely effect of increased lapse rates and shorter mean policy durations. The risk associated with metabolic syndrome may be underestimated because of the relatively young age of the cohort with low likelihood of preexisting

disease based on effective underwriting. Additionally, the deleterious effects of metabolic syndrome may not be fully realized given the shorter average policy duration. Likewise, risk for circulatory mortality associated with metabolic syndrome may be underestimated as cause is unknown for a number of deaths.

#### 4.4 Implications for Life Insurance

Metabolic syndrome has important implications for life insurance pricing and underwriting. Metabolic syndrome criteria are factored, either directly or indirectly, into cardiovascular risk classification. Parameters include build, blood pressure, total cholesterol, and blood glucose. Preferred risk classification includes these cardiovascular risk parameters that are part of or are closely related to metabolic syndrome. Mortality associated with cardiovascular risk factors that include some of the individual components of metabolic syndrome has been previously reported in insured lives populations (Niverthi and Ivanovic 2001; Ivanovic and Pinkham 2003; Pinkham, Ivanovic, and Cumming 2005). Exclusion criteria for preferred products focus on the risk of each individual parameter. Use of the metabolic syndrome definition allows for classification of combination risk associated with the cluster of cardiovascular risk factors.

The present study identifies increased mortality risk with the presence of an increasing number of individual risk components that comprise metabolic syndrome. The risk associated with this cluster of risk factors is apparent without evidence of overt disease. Traditional underwriting risk assessment provides the opportunity to identify risk factors that are components of the metabolic syndrome before the subsequent development of clinically evident cardiovascular disease and/or type 2 diabetes. Given the additional risk identified, the present study supports the benefit of obtaining blood profiles and paramedical examinations for better classification of underwriting risk.

Clinical studies have identified relationships between coronary heart disease, myocardial infarction, stroke, and increased vascular thickness and stiffness with metabolic syndrome in men and women, and poorer short-term survival for women with metabolic syndrome combined with confirmed coronary heart disease (Ridker et al. 2003;

Marroquin et al. 2004; Hu et al. 2002; Alexander et al. 2003; Ninomiya et al. 2004; Girman et al. 2004; Sattar et al. 2003; Scuteri et al. 2004). These studies raise the possibility that the presence of metabolic syndrome could be indicative of worse outcome in cardiovascular disease and may have implications for underwriting substandard or rated cases. Further study to delineate the impact of metabolic syndrome on survival in preexisting disease is warranted.

Evaluation criteria for preferred pricing program eligibility include many of the risk factors included in the NCEP definition of metabolic syndrome. At the time of underwriting, metabolic syndrome may be identified on the basis of insurance laboratory and paramedical data. Most preferred pricing programs use threshold numbers associated with build, blood glucose, blood pressure, and cholesterol for exclusion criteria. The Society of Actuaries (SOA) 2002 preferred underwriting survey provided information on variations in preferred underwriting. Diabetes diagnosis, rather than blood glucose, was most often used for preferred exclusion. Ranges for build (BMI 24 to 32 kg/m<sup>2</sup>), blood pressure (120/80 to 150/90), total cholesterol (200 to 274 mg/dL), and cholesterol/HDL cholesterol ratio (4.0 to 6.5) were reported as the threshold numbers for preferred exclusion by the participating companies. Some of these threshold numbers are relatively high and are within higher cardiovascular risk levels. Within the survey ranges of build, blood pressure, and cholesterol, individuals who meet the diagnosis of metabolic syndrome may also qualify for preferred risk classification. That is, some preferred plans may include individuals who meet the criteria for diagnosis of metabolic syndrome (and its associated risks) if only values of single-risk components, rather than the cluster of risk factors, are considered. Additionally, the SOA 2002 preferred underwriting survey reported cholesterol, build, and blood pressure as the most common exceptions to preferred risk criteria. Eighteen percent of participating companies did not allow exceptions. For the rest of the companies making exceptions, higher-risk individuals may be classified in preferred groups based on cholesterol, build, and blood pressure. Thus, the number of individuals who meet metabolic syndrome criteria is very likely increased through exceptions. Considering the increased mortality asso-

ciated with metabolic syndrome in the present study, inclusion of individuals with multiple risk factors into preferred programs is not compatible with anticipated risk, given the narrow preferred market margins. Based on the magnitude of excess mortality identified in the present study, these individuals appear to belong in the standard residual class, rather than in a preferred class.

In conclusion, the modified NCEP-defined metabolic syndrome score is associated with increased risk of all-cause mortality and mortality from circulatory diseases in a large predominantly healthy insured lives population. Mortality risk increases proportionally with the number of positive risk factors that are components of the metabolic syndrome. In our study population, consideration of the number of factors is a better description of risk than the use of a threshold of three or more positive factors. As metabolic syndrome may be more predictive of future adverse risk, the presence of multiple risk factors in early durations may not influence early mortality results. However, as risk with metabolic syndrome develops over time, recognition of the presence of multiple risk factors and their long-term impact on mortality will be important for longer duration products. These findings have important implications in the assessment of risk in life insurance underwriting, particularly for preferred pricing programs.

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