

# Association Between Socioeconomic Determinants and the Metabolic Syndrome in the German Health Interview and Examination Survey for Adults (DEGS1) – A Mediation Analysis

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Manuscript submitted March 28, 2017; resubmitted June 23, 2017; accepted August 1, 2017


## ■ Abstract

**BACKGROUND:** Metabolic syndrome and different socio-economic characteristics including education and occupational status have been found to be associated in previous research. Nonetheless, theoretical models defining core variables and causal processes accounting for these associations are lacking. **OBJECTIVES:** The main objectives of the present investigation are (1) to present a theoretical model integrating physiological, biochemical, and psychosocial factors determining metabolic syndrome prevalence and (2) to corroborate the hypothesis that socioeconomic determinants are (partially) mediated by health-related behaviors, health risks, and dietary habits. **METHODS:** The research hypothesis is tested with cross-sectional data from the German Health Interview and Examination Survey for Adults (DEGS1) conducted from 2008 to 2011 (n = 7,987) by means of multivariate regression models which appropriately take into account the stochastic dependence of metabolic syndrome components. **RESULTS:** The results suggest that the metabolic syndrome is less frequent among individuals with a higher educational level and those who have a partner.

These associations may point to protective effects of social support, self-efficacy, and other socio-psychological constructs in relation to metabolic syndrome incidence. Furthermore, frequent consumption of wine, muesli, fruits, and raw vegetables are associated with lower prevalence rates of metabolic syndrome components. The associations of occupational status, income, and employment are partially mediated by health-related behavior, physiological and psychosocial factors, and dietary habits. Sensitivity analyses have suggested that even small changes in the distribution of potential risk and protective factors may reduce the prevalence of metabolic syndrome components. **CONCLUSIONS** Health-related behavior (smoking, physical activity) and physiological and psychosocial factors mediate the association between socioeconomic characteristics and metabolic syndrome prevalence. However, metabolic syndrome components were much less frequent among individuals with a higher educational level, higher income and occupational status, and those having a life partner.

**Keywords:** metabolic syndrome · social epidemiology · diabetes · hypertension · obesity · multivariate regression

## 1. Introduction

lthough different attempts to define the metabolic syndrome have been proposed for clinical practice and research, the most general working definition consists of the co-occurrence of glucose intolerance (or type 2 diabetes) in combination with obesity, hypertension, and/or dyslipidemia [1]. More recently, a classifica-

tion procedure has been recommended by the International Diabetes Federation (IDF) and other health organizations (AHA/NHLBI), whereby the metabolic syndrome was diagnosed if any 3 out of the following 5 risk factors are present:

1. Elevated waist circumference (cut-off values depend on population- and country-specific definitions)

2. Elevated triglycerides (or corresponding drug treatment) ( $\geq 150$  mg/dl)
3. Reduced high-density lipoprotein cholesterol (HDL-C) (or corresponding drug treatment) ( $< 40$  mg/dl males,  $< 50$  mg/dl females)
4. Elevated blood pressure (or corresponding drug treatment) (systolic  $\geq 130$  and/or diastolic  $\geq 85$  mmHg)
5. Elevated fasting glucose (or corresponding drug treatment) ( $\geq 100$  mg/dl) [2].

Previous epidemiological studies with data from the general population in Europe, the USA, China, and South Korea have reported similarly high prevalence rates of 24.3%, 22.9%, 24.5%, and 16.3%, respectively [3-6], despite the use of different diagnostic criteria for each specific population. Also, estimates of all-cause and cardiovascular mortality rates based on 11 prospective European cohort studies are higher among persons diagnosed with the metabolic syndrome than among persons without it [7]. The presence of hyperinsulinemia plus 2 or more other components, including obesity, hypertension, dyslipidemia, and impaired glucose regulation, has been associated with increased risk of mortality, especially among men [7].

Yet, several scholars have criticized the metabolic syndrome concept for its lack of clinical usefulness [8]. Important limitations concern the loss of information due to dichotomization of the metabolic syndrome and/or its components, omission of established risk factors such as age and sex, heterogeneity of syndrome definitions leading to identification of different sub-populations at risk, and difficulties regarding the appropriate weighting of metabolic syndrome components [9]. In face of these limitations, it has been argued that the metabolic syndrome should not be applied as a clinical diagnosis or management tool [9, 10].

#### Abbreviations:

AHA	American Heart Association
BMI	body mass index
DEGS1	German Health Interview and Examination Survey for Adults
HDL	high-density lipoprotein cholesterol
IDF	International Diabetes Federation
NHLBI	National Heart, Lung, and Blood Institute
ISEI	International Socio-Economic Index of Occupational Status
MAD	median absolute deviation
MHB	multivariate hierarchical Bayesian
PSU	primary sampling unit

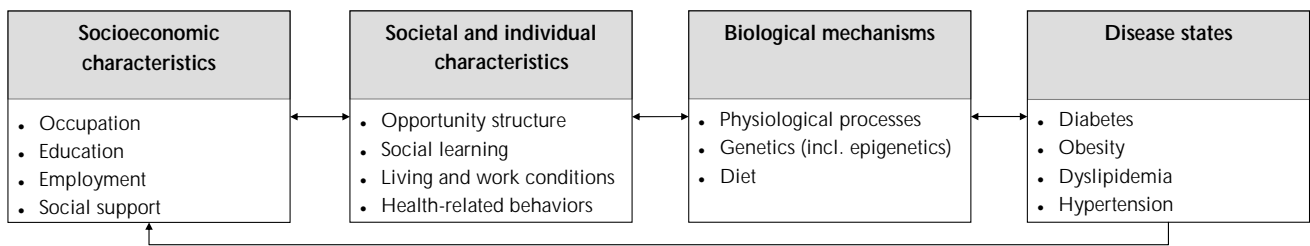
### 1.1 Socioeconomic determinants

In spite of the fact that the pathogenesis of the metabolic syndrome has not been fully understood so far, one of the most accepted pathophysiological mechanisms is insulin resistance. Previous findings have suggested an association between insulin resistance and reduction in HDL cholesterol, increased risk of hypertriglyceridemia, hypertension, higher rates of proinflammatory cytokines, and impaired glucose tolerance [1, 11, 12]. In general, these conditions lead to increased cardiovascular disease and risk of type 2 diabetes, and are often co-determined by socioeconomic and psychosocial factors. For instance, depending on the country's socioeconomic development, the prevalence of major risk factors such as blood pressure, smoking, fasting plasma glucose, and total cholesterol are associated with education [13]. Health risks and health-adverse outcomes are usually more frequent among groups with lower education and socioeconomic status [14]. Moreover, lifestyle-related factors playing a key role in the clinical management of the metabolic syndrome [15], such as physical activity, diet characteristics, and smoking behavior, are largely determined by social learning processes and social experiences during an individual's lifetime [16, 17].

Previous research focusing on the associations between socioeconomic determinants and the metabolic syndrome has provided evidence of increased metabolic syndrome risk among individuals with lower education or low socioeconomic status [18-22]. However, these results are limited in two major aspects:

1. They lack a theoretical model accounting for the specific mechanisms linking socioeconomic determinants and the metabolic syndrome. Consequently, variable selection remains arbitrary to some extent, and does not enable a systematic understanding of causal processes.
2. The statistical methods used in previous research do not take into account the stochastic dependence between the different metabolic syndrome components, and therefore fail to synthesize the strength of associations between dependent variables and metabolic syndrome components.

In order to advance the understanding of these phenomena, a theoretical model explaining how different socioeconomic characteristics of individuals are associated with the probability of the met-



**Figure 1.** Theoretical model of potential causal pathways between socioeconomic determinants and metabolic syndrome onset.

abolic syndrome is proposed in the present investigation. In addition, multivariate regression methods which appropriately take into account the stochastic dependence of metabolic syndrome components will be utilized to investigate the validity of the research hypothesis.

### 1.2 Theoretical model and research hypothesis

The interplay of physiological, biochemical, and psychosocial factors influencing metabolic syndrome prevalence can be theoretically explained in the bio-psycho-social model depicted in **Figure 1**. The model states that the socioeconomic characteristics of individuals interact with the opportunity structure of society (e.g. job and income opportunities). At the same time, these characteristics code-determine social learning processes and experiences increasing the probability of particular health-related behaviors (e.g. smoking) as well as living and work conditions (e.g. neighborhoods and occupational class). Therefore, these processes imply that socioeconomic characteristics may indirectly affect the biological mechanisms responsible for the occurrence of particular health states. It is thus expected that these characteristics have only a mediated effect on the probability of observing certain health states such as the metabolic syndrome.

Within this theory, for instance, education and occupational status would have an indirect effect on health by determining the quality of living conditions, exposure levels to noxious chemical or physical agents at work and home, particular dietary habits via social learning processes with family, friends and peer groups, and consequently by triggering biological mechanisms leading to the co-occurrence of metabolic syndrome components. Finally, since health state, physiological processes, and genetic predisposition obviously have an impact on the socioeconomic characteristics of individuals (e.g. loss of income due to impairment of

bodily structures and/or functions), the theoretical model considers reverse causation effects or feedback processes.

On the basis of these theoretical considerations, the present investigation aims to evaluate data from the German Health Interview and Examination Survey for Adults (DEGS1) under the following research hypothesis:

H1: The associations between the socioeconomic characteristics of individuals and the metabolic syndrome are (partially) mediated by:

1. Health-related behavior associated with social learning processes (smoking and physical activity)
2. Physiological and psychosocial risk and/or protective factors linked to specific biological mechanisms (mental health states)
3. The specific profile of dietary habits directly determining several states of metabolic dysfunction and cardiovascular disease such as insulin resistance and type 2 diabetes (consumption frequency of fruits, vegetables, dietary fibers, sweets, and alcoholic beverages).

As mentioned above, the metabolic syndrome concept has low utility as a clinical diagnosis or disease management tool. Hence, in the present study, the metabolic syndrome denotes the observed increased probability of the co-occurrence of specific symptoms and/or diseases associated with higher mortality risk. More importantly, the research hypothesis will be tested by considering simultaneously the prevalence of metabolic syndrome components by the multivariate methods described below, and by assessing the extent to which relevant health-adverse factors and socioeconomic characteristics are associated with the co-occurrence of two or more metabolic syndrome components. By adopting a multivariate approach,

all permissible combinations of metabolic syndrome and the actual values of the single components are being taken into account. Therefore, potential biases arising from misclassification of the syndrome and/or dichotomization of the metabolic syndrome and its single components are reduced.

## 2. Methods

### 2.1 Sample

The German Health Interview and Examination Survey for Adults (DEGS1) conducted by the Robert Koch Institute between 2008 and 2011 is a large random sample of the German adult population 18-79 years of age [23, 24]. The DEGS1 is a two-stage stratified cluster sample, with subdivisions called primary sampling units (PSUs) which are based on the German administrative districts. The sampling probabilities are proportional to the PSU sizes. Within each PSU, local population registers were stratified by 10-year age groups, from which simple random samples of individuals were drawn. Eligible persons in the PSUs were invited to participate in the survey. Data collection in the PSUs was performed by a team composed of a study physician and three technicians. Information contained in the DEGS1 survey and utilized in the present study consists of:

1. A semiquantitative, self-administered food frequency questionnaire
2. An assessment of currently used medications (prescription and over-the-counter)
3. A standardized physician-administered, computer-assisted personal interview
4. A standardized questionnaire completed by the survey participants
5. Standardized measurements and physical performance tests

The full sample size (including missing data) considered in the present study comprised 7,987 participants. Depending on the type of analyses, as presented below, the effective sample size of the complete-case dataset varied from 5,854 to 6,866 records. According to the Robert Koch Institute [25], the DEGS1 data included in the public use file available to the author did not contain information on ethnicity or migratory background of participants since the sample is not satisfactorily representative of Germany's immigrant population. Therefore, specific factors associated with the migratory background of individuals could not be considered. Because of this, combined with the fact

that the response rates in the DEGS1 were only about 42% [23], inferences made in the present investigation were not intended to be representative of the entire German population.

According to the Robert Koch Institute (RKI), "the implementation of DEGS1 conforms to the principles outlined in the Declaration of Helsinki and to the German Federal Data Protection Act." The RKI also stated: "The DEGS1 study protocol was consented with the Federal and State Commissioners for Data Protection and approved by the Charité-Universitätsmedizin Berlin ethics committee in September 2008 (No. EA2/047/08). Participants provided written informed consent prior to the interview and examination" [23].

The data analyzed for this investigation were obtained from the DEGS1 public use file made available by the RKI on request [24].

### 2.2 Multiple imputation

In order to deal with potential bias resulting from item non-response, the whole dataset was imputed by the method of chained equations [26]. Categorical and metrical variables were imputed by multinomial log-linear models via neural networks and predictive mean matching, respectively. Ten imputed datasets containing the 31 variables considered in the present study were generated by massive imputation using a total of 301 different predictor variables, including 174 health-related, 11 dietary, and 16 sociodemographic variables. The distribution of the 31 imputed variables in each of the ten imputed datasets was compared with the original distribution of the complete-case dataset (i.e. the dataset obtained by listwise deletion of cases with missing data). These distributions along with a more detailed description of the imputation methods are fully reported in the supplemental material.

### 2.3 Variables

Definition of the metabolic syndrome in the DEGS1. The definition of the metabolic syndrome on the basis of all cut points and criteria recommended in the IDF and AHA/NHLBI joint statement (see introduction section) cannot be applied with the information supplied in the DEGS1 dataset available to the author. Therefore, variables which could serve as proxy measures of the IDF-AHA/NHLBI diagnostic criteria were selected from the DEGS1 public use file. An overview of the proxy measures used to define the metabolic syndrome and their measurement protocol are pro-

**Table 1.** Definition of the metabolic syndrome using data from the DEGS1 public use file

Variable	Name of variable in data base	Measurement protocol [23]
Obesity (BMI $\geq 30$ kg/m <sup>2</sup> )	USadipos	Standardized weight and height measurements. Portable electronic scales (SECE, Germany), stadiometer (Holtain, UK); accuracy 0.1 kg and 0.1 cm, respectively. Both measurements done in underwear and with shoes removed.
Dyslipidemia	KHlipB	Information on medical history obtained in physician-administered computer-assisted interviews. Question: "Have you suffered or do you suffer from lipid metabolism disorders (high lipid levels such as cholesterol or triglycerides)? If yes, were these conditions diagnosed by a physician?"
Hypertension (stage 1: systolic blood pressure $\geq 140$ mmHg [27])	USSys23	Standardized blood pressure measurements. Automated blood pressure device (Datascop Accutor Plus, The Netherlands). 3 measurements were made following a standardized protocol. The average of the second and third measurement was reported, and the corresponding grade I hypertension cut point was used to classify individual participants. Diastolic blood pressure was not taken into account to reduce the number of missing values which were produced if both values were considered simultaneously.
Diabetes mellitus	KHdiab	Information on medical history obtained in physician-administered, computer-assisted interviews. Question: "Have you suffered or do you suffer from glucose-disorder or diabetes? If yes, were these conditions diagnosed by a physician?"

vided in **Table 1**. All dependent variables are dichotomous variables (0 = absence of disease or disorder, 1 = presence of disease or disorder).

**Sociodemographic variables.** The educational levels are reported in the CASMIN Educational Classification scheme [28]. They are distinguished:

1. Primary education (not completed general education, general elementary education, and basic vocational training)
2. Intermediate education (from intermediate general education to vocational maturity education)
3. Tertiary education (lower and higher tertiary education)

Occupational status is operationalized on the basis of the International Socio-Economic Index of Occupational Status (ISEI) [29]. The ISEI measures the attributes of occupations that convert the respondent's educational level into income levels and thus operationalizes social prestige on the basis of power resources available to individuals [30]. Income status is assessed by the equalized net household income which takes into account both household size and composition [29]. Occupational and income status were assessed by ordinal variables ranging from 1.0 to 7.0 using intervals of 0.5. Information on life partner is reported as a categorical variable with the following three levels:

1. Respondent is not married and does not have a life partner
2. Respondent is married and lives with spouse
3. Respondent has a life partner (i.e. not married, separated, divorced or widowed but with life partner)

Employment status is reported by assessing whether the respondent:

1. Has never been employed
2. Was formerly employed (retired or unemployed)
3. Is currently employed

**Health-related behaviors.** Smoking status was assessed by the question "Do you currently smoke, even if occasionally?" The response format was: 1 = yes, daily, 2 = yes, occasionally, 3 = no, formerly smoker, 4 = no, never smoked. Physical activity was measured by the question "How frequently do you do sports?" The response format was: 1 = no sport, 2 = less than 1 hour per week, 3 = often, between 1 and 2 hours per week, 4 = often, between 2 and 4 hours per week, 5 = often, more than 4 hours per week.

**Potentially health-adverse factors and/or risks.** The DEGS1 public use file contains several mental health-related variables, including data from screening instruments of affective or stress symp-

toms and information on diagnosed mental disorders. Even though mental disorders or psychosocial hazards are likely to be associated with metabolic syndrome prevalence, in the present study, only depression and anxiety, two of the most frequently diagnosed mental disorders, were included in the analysis. It is thus intended to focus on mental health states which may have a stronger association with the prevalence of metabolic syndrome components.

**Medication.** Given the cross-sectional design of the DEGS1 datasets, it is necessary to take into account in the regression models whether the respondent is currently under treatment for metabolic syndrome components since some interventions may have direct consequences on the status of these components. Therefore, the fully adjusted models described below include four additional variables on whether the respondent is currently taking anti-hypertensives, beta blockers, dyslipidemic medication, or antidiabetic agents (response format: 0 = no, 1 = yes). No further medications or interventions such as weight loss or lifestyle were included in the analysis.

**Dietary habits.** Dietary habits related to the major food types discussed in the introduction section were assessed by the general question: "How often do you eat/drink ...?" The response format was: 1 = never, 2 = once per month, 3 = 2-3 times per month, 4 = 1-2 times per week, 5 = 3-4 times per week, 6 = 5-6 times per week, 7 = once per day, 8 = 2 times per day, 9 = 3 times per day, 10 = 4-5 times per day, 11 = more than 5 times per day). The variables included in the present study cover the following four major food types:

- Beverages (sweet drinks, beer, wine, liquors)
- Dietary fiber (muesli, whole-grain bread)
- Animal products (hard cheese, sausages, meat, fish)
- Fruits and vegetables (raw and cooked)

#### 2.4 Regression models

The research hypothesis is investigated by means of multivariate hierarchical Bayesian (MHB) models, as described in detail elsewhere [31]. In general, these models are defined by considering the left-hand side of the regression equation as a matrix of dependent variables and estimating individual-specific random effects. Since the metabolic syndrome is defined in terms of the increased co-occurrence of different disorders

and/or dysfunctional states, it is necessary to account for the statistical dependence among those health states defining the syndrome. The research hypothesis was thus examined by estimating two MHB regression models. The first model was called the socioeconomic model and included socioeconomic variables only at the right-hand side of the regression model. In the second model (the fully adjusted model) in contrast, health-related behaviors, potential health risks, and dietary habits were included as mediators. In both models, the matrix of dependent variables comprises the four variables defining the metabolic syndrome, namely diabetes mellitus, obesity, dyslipidemia, and stage 1 hypertension. The results obtained from the MHB regression models represent odds ratios averaged over all four dependent variables. For instance, an odds ratio of 1 for a certain independent variable means that the average association across all four metabolic syndrome components is 1. The socioeconomic and the fully adjusted model were estimated:

1. Using the complete-case dataset ( $n = 6,589$  and  $n = 5,854$ , respectively)
2. Using each one of the ten imputed datasets ( $n = 7,987$ )

The results obtained using the ten imputed datasets were summarized by taking the mean of the odds ratios and corresponding standard errors from the estimated models. A detailed description of the MHB regression models and their mixing properties are provided in the supplemental material.

The regression models described above and the number and type of variables were determined *before* performing the estimation of the MHB models to reduce the risk of false positive results arising from the large sample size and number of potential combinations of data [32]. The reported confidence intervals were estimated at the 99% level to reduce the probability of false positives for small effects [33]. P-values are not supplied since they give poor information about the likely result of a future replication [34].

#### 2.5 Predictive power and sensitivity analyses

Predictive power analyses were performed to examine the adequacy of model specification and robustness of results. Predictive power analysis was based on 1000 observations randomly sampled from the complete-case dataset, and plugged into the fully adjusted regression models as new obser-

**Table 2.** Descriptive statistics: proportions for categorical variables (%), mean (continuous variables), median (ordinal variables), median absolute deviation (MAD), and number of missing data per variable (n = 7,987)

Variable	Statistic	Missing
Diabetes mellitus <sup>a</sup>	No = 7,260 (91.5%), yes = 671 (8.5%), with type 1 = 12, type 2 = 665.	56
Obesity	No = 5,363 (75.9%), yes = 1,702 (24.1%)	922
Dyslipidemia	No = 5,399 (69.3%), yes = 2,389 (30.7%)	199
Hypertension	No = 5,918 (83.4%), yes = 1,177 (16.6%)	892
Smoking	Smoker = 1,651 (20.9%), occasional smoker = 464 (5.9%), former smoker = 2,395 (30.3%), never smoker = 3,388 (42.9%)	89
Sport	No sports = 2,524 (32.6%), Sport < 1h = 1,264 (16.3%), Sport 1-2h = 2,022 (26.1%), Sport 2-4h = 1,203 (15.5%), Sport > 4h = 727 (9.4%)	247
Depression	Never diagnosed = 6,987 (88.3%), diagnosed = 924 (11.7%)	76
Anxiety	Never diagnosed = 7,500 (94.9%), diagnosed = 403 (5.1%)	84
Antihypertensives	No medication = 6,996 (98.7%), medication = 95 (1.3%)	896
Beta blockers	No medication = 5,870 (82.8%), medication = 1,221 (17.2%)	896
Dyslipidemic medication	No medication = 6,231 (87.9%), medication = 860 (12.1%)	896
Antidiabetic agents	No medication = 6,687 (94.3%), medication = 404 (5.7%)	896
Gender	Male = 3,789 (47.4%), female = 4,198 (52.6%)	0
Education	Primary = 2,551 (32.3%), intermediate = 3,844 (48.7%), tertiary = 1,502 (19.0%)	90
Employment	Not employed = 211 (2.7%), formerly employed = 2,775 (35.9%), employed = 4,736 (61.3%)	265
Partner	No partner = 1,480 (19.0%), married = 5,052 (64.8%), with partner = 1,262 (16.2%)	193
BMI	Mean = 26.47, SD = 4.84	167
Sweet drinks	Median = 2, MAD = 1.48	1,014
Beer	Median = 3, MAD = 2.97	1,059
Wine	Median = 2, MAD = 1.48	1,049
Liquors	Median = 1, MAD = 0	1,014
Muesli	Median = 1, MAD = 0	1,123
Whole-grain bread	Median = 5, MAD = 2.97	1,013
Hard cheese	Median = 5, MAD = 1.48	997
Sausages	Median = 2, MAD = 1.48	1,045
Meat	Median = 4, MAD = 1.48	1,001
Fish	Median = 3, MAD = 1.48	1,007
Fruit	Median = 7, MAD = 1.48	1,006
Raw vegetables	Median = 4, MAD = 1.48	1,065
Cooked vegetables	Median = 4, MAD = 1.48	1,072
Sweets	Median = 3, MAD = 2.97	1,043
Age	Mean = 52.22, SD = 16.39	0
Occupational status	Median = 3, MAD = 1.48	225
Income status	Median = 4, MAD = 2.97	0

**Legend:** <sup>a</sup> Information on diabetes type is supplied by the variable KHdiabtyp from the public use file. Note that the frequencies supplied in the variable KHdiab (yes = 671) differ from those of the KHdiabtyp variable (type I + type II diabetes = 677). In the present investigation, the variable KHdiab only is used in the regression analysis, as described in **Table 1**.

vations. Subsequently, 1000 estimates from the posterior distribution of the estimated model were sampled to obtain the matrix of predicted prevalence rates for single metabolic syndrome components. Sensitivity analyses were performed by randomly sampling again 1000 observations from the original dataset, but with the following conditions:

1. The sampling probability of an observation was reduced by one-third if smoking behavior = "current smoker", physical activity = "never", diagnosed depression = "yes", anxiety = "yes", being treated for metabolic syndrome components, and if income status = 1 to 3.
2. The sampling probability of an observation was increased by two for more frequent muesli and fruit consumption, and by three for more frequent physical activity, having a partner, and not being treated for metabolic syndrome components.

This modified dataset was used again to predict new prevalence rates from the posterior distribution of the estimated regression model, as explained before.

It should be noted that the parameter values used in the sensitivity analysis are chosen arbitrarily (e.g. doubling the sampling probability for certain variable categories). Nonetheless, the aim of the sensitivity analysis was to quantify the extent to which small changes in the sample distribution of important variables such as smoking behavior, BMI, and some dietary habits may have affected the prevalence of metabolic syndrome components. Therefore, these values actually represent a set of possible sample characteristics by means of which plausible changes in the distribution of metabolic syndrome components can be estimated.

### 3. Results

#### 3.1 Descriptive statistics

Descriptive statistics of the sample are provided in **Table 2**. Regarding the prevalence of single components of the metabolic syndrome, it can be observed that dyslipidemia and obesity were the most common symptoms in the sample in comparison to hypertension and diabetes. However, these single prevalence rates can more appropriately be interpreted by taking into account that the metabolic syndrome is defined in terms of co-

occurrence of components. Although in the present investigation the definitional criteria of the IDF and AHA/NHLBI joint statement could not be applied (see methods section), it is still possible for descriptive purposes to define the metabolic syndrome as the presence of two out of four criteria considered in this investigation (diabetes, obesity, dyslipidemia, and hypertension). Thereby, comorbidity rates for each metabolic syndrome component can be estimated and compared.

In **Table 3**, comorbidity rates of diabetes, obesity, dyslipidemia, and hypertension are reported. Among participants with dyslipidemia the ratio of cases with and without co-occurrence of other metabolic syndrome components is about 1:1, whereas the corresponding ratio among participants with diabetes is almost 1:5, even though the prevalence rate of dyslipidemia alone is the highest among all diagnostic criteria (compare **Tables 2** and **3**). This result suggests that comorbidity rates among diabetics are much greater than among individuals suffering from other metabolic syndrome components.

#### 3.2 Regression models

The results of the regression analysis described in the methods section are presented in **Table 4**. The odds ratios of the socioeconomic models reveal that higher educational level, higher income, and occupational status were associated with lower prevalence rates of the metabolic syndrome. On the other hand, married and retired respondents had increased odds for each metabolic syndrome component in comparison with unemployed and respondents without a life partner.

In relation to the research hypothesis, the following can be observed in the results obtained from the fully adjusted models: the odds ratio estimates of the socioeconomic variables are subject to large mediation effects resulting from the consideration of health-related behaviors, potential health risks, and dietary habits. For instance, if the odds ratio estimates of the socioeconomic models and the fully adjusted models in **Table 4** are compared, it can be seen that the strength of association for education, income status, and life partner are reduced or reversed in the complete-case and imputed dataset. At the same time, the large odds differences seen among formerly employed in comparison to unemployed respondents seem to be partially mediated by the whole set of mediators (e.g. from 4.73 to 1.37, see **Table 4**).

Whereas increased physical activity (at least more than 2 hours per week) was associated with a



substantial decrease in odds, the estimates obtained for smoking behavior were contradictory, and depended on whether the complete-case or the imputed dataset was considered. Estimates obtained with the complete-case dataset suggested that former smokers had a higher metabolic syndrome prevalence than current smokers. In contrast, the odds ratios calculated from the imputed datasets revealed that both former smokers and never-smokers were associated with greater health-adverse odds than current smokers.

Regarding the odds ratio estimates of dietary habits, the results obtained with the complete-case and imputed dataset also differed to some extent. However, a more frequent consumption of wine, muesli, hard cheese, and fruits was generally associated with decreased prevalence of metabolic syndrome components in both models. In contrast, increases in odds were consistently observed for liquors, whole-grain bread, sausages, and meat.

Even though the effect sizes in all food groups may seem to be quite small, it should be recalled that the original responses to dietary habits were given on an ordinal 11-point scale. In fact, these associations had a similar order of magnitude as the odds ratios corresponding to age (OR 1.04 99% CI 1.04-1.04, imputed model in **Table 4**), and may have had a large impact on the overall odds. For instance, the median frequency of muesli consumption in the sample corresponded to the category 1 = "never" (see **Table 2**). According to **Table 4**, the odds ratio of muesli consumption is 0.97, with 99% CI 0.96-0.97. Thus, *ceteris paribus*, by increasing the frequency of muesli consumption to 1-2 times per week (i.e. category 4), an odds ratio of about 0.88 can be expected.

### 3.3 Predictive power and sensitivity analysis

The predictive power of the fully adjusted regression models with complete-case and imputed

**Table 3.** Prevalence rates of the metabolic syndrome by diagnostic criteria in the complete-case dataset (n = 6,866)

Metabolic syndrome criteria	Metabolic syndrome <sup>a</sup>	
	No (%)	Yes (%)
<i>Diagnostic criteria</i>		
No risk	3,248 (47.31)	N/A
Dyslipidemia	1,065 (15.51)	N/A
Dyslipidemia, hypertension	N/A	249 (3.63)
Hypertension	417 (6.07)	N/A
Obesity	657 (9.57)	N/A
Obesity, dyslipidemia	N/A	367 (5.35)
Obesity, dyslipidemia, hypertension	N/A	127 (1.85)
Obesity, hypertension	N/A	189 (2.75)
Diabetes,	97 (1.41)	N/A
Diabetes, dyslipidemia	N/A	103 (1.5)
Diabetes, dyslipidemia, hypertension	N/A	36 (0.52)
Diabetes, hypertension	N/A	28 (0.41)
Diabetes, obesity	N/A	81 (1.18)
Diabetes, obesity, dyslipidemia	N/A	112 (1.63)
Diabetes, obesity, dyslipidemia, hypertension	N/A	51 (0.74)
Diabetes, obesity, hypertension	N/A	39 (0.57)
<i>Cases with metabolic syndrome given the presence of:</i>		
Diabetes	97 (1.41)	450 (6.55)
Obesity	657 (9.57)	966 (14.07)
Dyslipidemia	1,065 (15.51)	1,045 (15.22)
Hypertension	417 (6.07)	719 (10.47)
<b>Total prevalence of metabolic syndrome</b>	<b>5,484 (79.87)</b>	<b>1,382 (20.13)</b>

**Legend:** Frequencies and proportions (%) reported. <sup>a</sup> Metabolic syndrome means the presence of two or more metabolic syndrome components, as described in **Table 1**. N/A = not applicable by definition.

datasets is reported in **Table 5**. Point estimates of the imputed datasets are closer to the original prevalence rates, albeit with some efficiency loss in comparison with the complete-case dataset. Predicted prevalence rates obtained for diabetes from the regression models tend to be higher than the observed ones (8% against 14% of the complete-case and imputed datasets, respectively).

The results of the sensitivity analysis are reported in **Table 6**. The prevalence rates of the dataset used in the sensitivity analyses are reported in detail in the supplemental material. As stated in the methods section, sensitivity analyses were based on a random sample of 1000 observations from the complete-case dataset in which the sampling probability was reduced or increased depending on selected potential risk and protective factors, respectively. The expected changes in the predicted prevalence rates of metabolic syndrome

**Table 4.** Results of the regression analysis

Variable	Complete-case dataset				Imputed datasets			
	Socioeconomic model		Adjusted model		Socioeconomic model		Adjusted model	
	OR	99% CI	OR	99% CI	OR	99% CI	OR	99% CI
Intercept	0.07	0.06-0.09	0.02	0.02-0.04	0.09	0.09-0.10	0.01	0.01-0.01
Intermediate education (ref.: primary education)	0.62	0.59-0.64	1.03	0.98-1.08	0.63	0.62-0.64	0.98	0.96-1.00
Tertiary education	0.68	0.63-0.73	0.86	0.82-0.90	0.62	0.61-0.64	0.82	0.80-0.85
Occupational status	0.90	0.87-0.92	0.95	0.94-0.97	0.95	0.94-0.96	0.96	0.95-0.97
Income status	0.99	0.97-1.00	0.97	0.97-0.98	0.99	0.99-1.00	0.99	0.98-0.99
Formerly employed (ref.: never employed)	4.73	3.85-5.60	1.37	1.18-1.49	3.22	3.00-3.47	1.19	1.13-1.25
Employed	1.75	1.45-2.30	1.33	1.22-1.55	1.25	1.16-1.34	1.19	1.13-1.25
Married (ref.: without partner)	1.37	1.29-1.45	1.00	0.96-1.04	1.16	1.14-1.18	0.96	0.95-0.98
With partner	0.45	0.41-0.49	0.72	0.67-0.78	0.47	0.46-0.48	0.74	0.71-0.76
Female (ref.: male)			0.96	0.91-1.01			0.91	0.89-0.92
Age			1.03	1.03-1.03			1.04	1.04-1.04
Occasional smoker (ref.: smoker)			0.93	0.81-1.05			0.99	0.95-1.03
Former smoker			1.20	1.13-1.25			1.31	1.29-1.33
Never smoker			1.04	0.98-1.14			1.11	1.09-1.14
Sport < 1h (ref. no sport)			0.98	0.93-1.02			0.96	0.93-0.99
Sport 1-2h			1.04	1.00-1.08			0.90	0.89-0.92
Sport 2-4h			0.77	0.72-0.84			0.75	0.74-0.77
Sport > 4h			0.81	0.76-0.87			0.73	0.71-0.76
Diagnosed depression (yes)			1.25	1.17-1.33			1.19	1.16-1.21
Diagnosed anxiety (yes)			1.29	1.20-1.41			1.17	1.15-1.19
Anti-hypertensives (yes)			1.29	1.15-1.46			1.47	1.40-1.54
Beta blockers (yes)			1.42	1.36-1.48			1.21	1.18-1.24
Dyslipidemic medication (yes)			1.98	1.87-2.09			1.73	1.66-1.79
Anti-diabetics (yes)			7.89	7.25-8.64			7.10	6.79-7.42
<i>Dietary habits</i>								
Sweet drinks			1.00	0.99-1.01			1.01	1.01-1.02
Beer			0.99	0.98-1.01			1.00	1.00-1.01
Wine			0.95	0.94-0.96			0.96	0.96-0.96
Liquors			1.05	1.03-1.06			1.02	1.01-1.03
Muesli			0.96	0.94-0.97			0.97	0.96-0.97
Whole-grain bread			1.02	1.01-1.03			1.01	1.01-1.02
Hard cheese			0.97	0.96-0.98			0.98	0.98-0.99
Sausages			1.03	1.01-1.06			1.04	1.04-1.05
Meat			1.06	1.04-1.08			1.04	1.03-1.05
Fish			1.00	0.98-1.01			0.99	0.98-1.00
Fruit			0.98	0.96-0.99			0.99	0.99-0.99
Raw vegetables			1.00	0.98-1.01			0.99	0.98-0.99
Cooked vegetables			1.00	0.98-1.02			1.02	1.01-1.03
Sweets			0.99	0.98-1.01			1.00	1.00-1.00

components reported in **Table 6** reveal that even small changes in the distribution of potential risk and protective factors can lead to reductions in prevalence rates. For example, muesli and fruit consumption, household income and percentage of respondents with a partner were only 1-2% higher than the correspondingly observed prevalence rates. The impact of these changes on the predicted prevalence rates suggest that about 2-3% average prevalence reduction could be attained for each one of the metabolic syndrome components (see **Table 6**).

#### 4. Discussion

In the present investigation, the research hypothesis stated that the associations between the socioeconomic characteristics of individuals and the metabolic syndrome are (partially) mediated by:

1. Health-related behaviors
2. Physiological and psychosocial risk and/or protective factors
3. The specific profile of dietary habits involving the frequency of fruit, vegetable, fiber, sweets, and alcoholic beverage consumption

Overall, the results of the regression analysis in the fully adjusted models confirmed this research hypothesis by the fact that almost all odds ratios corresponding to the socioeconomic variables were partially or fully mediated by consideration of appropriate covariates. In particular, having a life partner was an important factor leading to a substantial reduction in odds ratio estimates and providing evidence of the protective role social support might play regarding the syndrome. Furthermore, the associations between depression, anxiety, and metabolic syndrome (see **Table 4**) suggest that mental health states are important co-determinants in the etiology of the metabolic syndrome. The results concerning psychosocial factors such as having a life partner are thus in agreement with previous findings providing

evidence on the negative association between social support and cardiovascular reactivity in response to stressors [35], and on increased risk of the metabolic syndrome among individuals with lifetime history or current major depressive episodes in prospective studies [36, 37]. Potential mechanisms responsible for the potential risk and/or protective role of psychosocial factors may be emotion-related physiological responses via endocrine and immune functions (e.g. activation of the sympathetic-adrenal-medullary and hypothalamic-pituitary-adrenal axes) [35, 38, 39].

Moreover, the results reported in **Table 4** suggested that metabolic syndrome prevalence was lower in individuals with tertiary education, but not intermediate education, in comparison to those with primary education, even in the fully adjusted models. This fact may point to additional benefits of tertiary education in terms of increased knowledge of risk and/or protective factors or the relevance of several psychological processes affecting health outcomes (e.g. self-efficacy, emotion regulation, or problem-solving skills). For instance, self-efficacy has been related to increased physical activity and weight loss [40, 41], which are protective factors against the metabolic syndrome on their own. In a large Swedish prospective study, poor emotional control was not only associated with increased risk of coronary heart disease (hazard ratio 1.31 95% CI 1.18-1.45), but also more frequent among individuals with low education [42].

**Table 5.** Original vs. predicted prevalence rates (p) obtained from the fully adjusted models with complete case and imputed dataset

Dependent variable	Original prevalence		Prediction with complete-case model and dataset		Prediction with imputed models and datasets	
	p	99% CI	p	99% CI	p	99% CI
Diabetes	0.08	0.08-0.09	0.14	0.12-0.15	0.14	0.12-0.16
Obesity	0.24	0.23-0.25	0.20	0.19-0.21	0.25	0.24-0.27
Dyslipidemia	0.31	0.29-0.32	0.25	0.24-0.26	0.27	0.25-0.28
Hypertension	0.17	0.15-0.18	0.17	0.16-0.18	0.16	0.14-0.18

**Table 6.** Impact on predicted prevalence rates (p) of metabolic syndrome components obtained in the sensitivity analysis

Dependent variable	Prediction w. imputation models and datasets from Table 5		Impact on predicted prevalence rates in the sensitivity analysis	
	p	99% CI	p	99% CI
Diabetes	0.14	0.12-0.16	0.11	0.09-0.13
Obesity	0.25	0.24-0.27	0.23	0.21-0.24
Dyslipidemia	0.27	0.25-0.28	0.25	0.23-0.26
Hypertension	0.16	0.14-0.18	0.13	0.11-0.15

Since the odds ratio estimates regarding employment were given in relation to those respondents who have never been employed, the results suggested that the increased odds of metabolic syndrome among the employed population may have been related to factors concerning work conditions (e.g. work-related stressors, biomechanical, physical and/or chemical agents, etc.). For instance, previous findings in a South Korean sample indicated that shift work may be associated with increased metabolic syndrome prevalence [43].

Regarding the role of dietary habits on metabolic syndrome prevalence, the estimates reported in **Table 4** were slightly contradictory between the models calculated with the complete-case and the imputed models. A consistent direction of effect sizes were obtained for wine, fruit, meat, liquors, whole-grain bread, hard cheese, sausages, and muesli consumption. It seems that a more frequent intake of fruits and muesli and, at the same time, a decrease in liquors and meat consumption were associated with decreased prevalence of metabolic syndrome components. Since contradictory results between regression models with the complete-case and imputed datasets were also observed for smoking behavior (see **Table 4**), item non-response effects may have probably been responsible for the inconsistencies observed for food consumption profiles. Given that the imputed datasets took into account 301 different variables, it is likely that the estimates obtained with the imputed datasets controlled for health-related response tendencies, and were thus much more reliable estimates of the true associations. Hence, if the odds ratio estimates of the imputed datasets were to be preferred, frequent wine, muesli, fruit, and raw vegetable consumption were associated with lower prevalence rates of the metabolic syndrome.

The results of the imputed models also agree well with previous research indicating that a frequent consumption of red and processed meat increased the risk of the metabolic syndrome [5, 44]. In relation to alcohol consumption, previous results of a large prospective cohort study in Brazil suggested a positive association for frequent beer consumption (outside of meals) and a negative association for wine consumption during meals (1-4 drinks per week) with metabolic syndrome incidence, respectively [45]. Similar results were obtained in a study with a large sample in the USA suggesting a J-shaped alcohol-mortality association, whereby moderate wine consumption may have led to lower levels of cardiovascular disease [46]. Results from a recent meta-analysis of six

prospective studies found similar risk reductions for moderate drinkers (relative risk 0.86 95% CI 0.75-0.99) [47]. Several potential mechanisms accounting for the protective effect of moderate alcohol consumption included improved endothelial function [48], reduction of inflammatory reactions (e.g. interleukin 6 and 10, C-reactive protein) [49], reduced oxidative stress, and increased HDL levels [50].

Odds ratio estimates obtained for the role of smoking behavior differed substantially between the complete-case and imputed models. The results from the imputed models suggested that former and never-smokers had increased odds of metabolic syndrome. In contrast, odds ratio estimates of smoking behavior in the complete-case dataset suggested that only occasional smokers had increased syndrome prevalence, with no differences observed between current smokers and never-smokers. As stated above, the results of the imputed models were to be preferred given that they took into account potential confounding effects of item non-response tendencies. Even though smoking is a known risk factor for cardiovascular disease [51], its role in the incidence of the metabolic syndrome in terms of co-occurrence of several health-adverse outcomes seems to be more complex. For instance, Kim *et al.* (2009) reported a higher risk among former smokers than among sustained smokers in a longitudinal study in South Korea [52]. A lower risk of newly-diagnosed type 2 diabetes among current smokers has been reported in a large case-control study in China [53]. Similarly, Nagaya *et al.* (2007) report a moderate increase in risk among obese heavy smokers, but risk reductions among lean men in comparison to never smokers [54]. Therefore, the results of the imputed models of the present study suggested that the association between smoking and metabolic syndrome was not linear and may have been mediated by other factors. Even though smoking cessation among former smokers could have been due to the diagnosis of single metabolic syndrome components, the fact that odds ratio estimates were adjusted for medication suggested that this mechanism did not fully explain the observed variance. Unfortunately, the dataset available to the author did not allow a more detailed causal analysis of this association. Future studies with longitudinal data are necessary to confirm or reject these findings, and evaluate other potential mechanisms explaining the observed associations.

As stated in the introduction section, statistical inferences in the present investigation are related to the DEGS1 respondents and not to the whole

German population because of the low response rate of 42%. Prevalence rates of the metabolic syndrome obtained from other large studies conducted in Germany report to some extent similar results for diabetes mellitus [55], dyslipidemia ( $\geq 250$  mg/100 ml), obesity [56], depression, anxiety [57], and stage-1 hypertension [58]. Discrepancies between prevalence estimates are commonly related to sampling design, population, definition of variables, and year of data collection. Hypertension estimates may differ considerably depending on whether a history of hypertension is included and/or whether both systolic and diastolic blood pressure values are considered. In the present investigation, only systolic pressure was considered to reduce the higher number of missing values which arise by combining both blood pressure values (822 vs. 1,212 missing values and 16.7% vs. 13.7% prevalence rates, respectively). However, since the fully adjusted regression models took into account whether respondents received anti-hypertensive therapy or not, information on past or current hypertension was controlled for to some extent in the present study.

Prevalence estimates of the metabolic syndrome and some odds ratio estimates among specific variables obtained in the present investigation (see **Table 3**) agreed well with previous findings. Neuhauser and Ellert (2008) using data from the German National Health Interview and Examination Survey (NHIES) 1998 ( $n = 7,124$ ) estimated a prevalence rate of the metabolic syndrome of about 13.3% on the basis of the classification scheme of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults [59]. Furthermore, by considering HbA1c cut-off values of  $>6.1\%$  and  $>6.0\%$ , the authors were able to classify ambiguous cases and perform sensitivity analysis leading to prevalence rates of the metabolic syndrome of 20.0% and 22.5%, respectively. Moreover, the odds ratio estimates corresponding to the variable age reported by Neuhauser and Ellert (2008) are similar to the estimates reported in the present investigation in spite of the differences in definitional criteria. For instance, Neuhauser and Ellert (2008) estimated the odds of metabolic syndrome among individuals in the age interval 70-79 to be 4.6 (95% CI 3.4-6.3). In the present investigation, the corresponding odds ratio would have been about 5.4 obtained by using the odds ratio estimate of 1.03, as reported in **Table 4**, and multiplying the logits by 57 years (i.e. the age range 75 years minus 18 years).

Predicted diabetes prevalence in **Table 5** was found to be almost twice the observed prevalence

rates (14% vs. 8%, respectively). This finding could be due to some underestimation of diabetes prevalence in the DEGS1 sample. For instance, prevalence rates of diabetes mellitus obtained in another study with a large sample of patients ( $n = 55,518$ ) in the primary care sector were 14.7% (type 2) and 0.5% (type 1) [60]. Finally, the sensitivity analysis provided evidence that prevention strategies for the metabolic syndrome should include primary prevention measures, involving dietary habits and health-related behaviors, and secondary prevention strategies targeting individuals suffering from the condition. The estimated impact of slight prevalence changes of risk and protective factors reported in **Table 6** (see also supplemental material) suggested that a coordinated prevention approach fostering small health-promoting modifications at different intervention levels (individual, societal, etc.) may have effected a measurable reduction in metabolic syndrome prevalence. Within this context, the present investigation provides further evidence that a Mediterranean-like diet characterized by frequent consumption of dietary fiber, fruits, vegetables, and moderate intake of wine may be an effective primary prevention factor for the reduction of metabolic syndrome, especially of (type 2) diabetes as the factor with highest comorbidity rates (see **Table 3**) [61-63].

## 5. Strengths and limitations

The first limitation of the present investigation is the cross-sectional design of the study. In particular, causal statements are limited regarding the specific patterns of temporal relationships of the associations, i.e. to what extent feedback or reverse causation processes affect the magnitude of associations and their interpretation [64]. However, it should be noted that the present investigation did not attempt to disentangle the temporal dynamics of reverse causality, but to test the mediation hypothesis of biologically plausible pathways responsible for the association between socioeconomic characteristics and the prevalence of metabolic syndrome components. Given the fact that the presence or absence of medical treatment for each metabolic syndrome component was taken into account in the regression models, the odds ratio can be interpreted as the marginal effects of socioeconomic characteristics, health-related behaviors, risk factors, and dietary habits on the frequency of metabolic syndrome components. The odds ratio estimates had taken into account the fact that some individuals may have already been diagnosed with the disease and, therefore, pro-

vided evidence of the direction of associations, i.e. whether the corresponding variable marginally increased or decreased the odds of metabolic syndrome prevalence.

The second major limitation is due to the fact that the DEGS1 public use file available to the author did not allow the definition of the metabolic syndrome according to the IDF-AHA/NHLBI joint statement. As a consequence, essential criteria such as HDL levels, triglycerides, fasting glucose levels, and elevated waist circumference could not be taken into account. Thus, a direct comparison of results obtained in the present investigation with those obtained on the basis of other diagnostic criteria of the metabolic syndrome is limited. However, previous findings based on different classifications of the metabolic syndrome agree to some extent with the present results. For example, Lindfeldt *et al.* (2003) used the following cut-off values for positive screening of the metabolic syndrome:

- Capillary blood glucose  $\geq 8.0$  mmol/l
- Serum triglycerides  $\geq 2.3$  mmol/l
- BMI  $\geq 30$  kg/m<sup>2</sup>
- Waist-to-hip ratio  $\geq 0.90$
- Blood pressure  $\geq 160$  and/or 95 mmHg

In agreement with the present investigation, the authors reported that low to moderate alcohol consumption and higher education were associated with lower odds ratios in relation to one or more metabolic syndrome components [19]. Finally, some recall bias due to self-reported information on diagnosed illnesses cannot be ruled out in spite of the fact that interviews in the DEGS1 study were conducted by physicians trained for the purposes of the survey.

On the other hand, the present study has several strengths. The efficiency and robustness of the regression analyses were enhanced by performing a comprehensive multiple imputation procedure

based on 301 additional variables. To the best of the author's knowledge, this is the first study to make use of a multivariate regression analysis which appropriately takes into account the statistical dependence of metabolic syndrome components. Therefore, the odds ratio estimates obtained capture the (marginal) associations of single covariates with the metabolic syndrome as a whole. Furthermore, both the formulation of the research hypothesis and the specification of the regression analysis were based on a theoretical causal model which defines plausible biological and psychosocial pathways linking socioeconomic characteristics and metabolic syndrome components. Given the fact that the regression models were not modified *a posteriori*, the results reported in the present study support the validity of the theoretical model presented in the introduction section since the likelihood of statistical artifacts deriving from the so-called multiple modeling can be considered low.

## 6. Conclusions

Metabolic syndrome components were much less frequent among individuals with a higher educational level, higher income and occupational status, and those having a life partner. These associations point to protective effects of social support, improved work conditions, and education related to the development of metabolic syndrome components. The associations of socioeconomic characteristics were partially or fully mediated by health-related behaviors, physiological and psychosocial risk and/or protective factors, and dietary habits. Sensitivity analyses suggested that even small changes in the distribution of risk and protective factors may have reduced the prevalence of metabolic syndrome components.

**Disclosures:** The author reported no conflict of interests.

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