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Association between diabetes, metabolic syndrome and heart attack in U.S. adults, BRFSS 2015

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-022990
Article Type:	Research
Date Submitted by the Author:	25-Mar-2018
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Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, metabolic syndrome, heart attack

Association between diabetes, metabolic syndrome and heart attack in U.S. adults, BRFSS 2015

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Abstract:

Objectives: Evidence regarding which condition - MS or DM - is a better predictor for heart attack risk, however, is limited. This study aimed to compare the magnitude of the effects of DM and MS on heart attack using the 2015 Behavioral Risk Factor Surveillance System (BRFSS) database. **Design:** Observational study. **Methods:** A total of 332,008 subjects aged over 18 years were included in the analysis. All subjects were classified into four groups based on their DM and MS status: neither DM nor MS, DM alone, MS alone, and both DM and MS. Odds ratios and their 95% confidence intervals from hierarchical logistic regressions were used to examine the effect of DM and MS on heart attack after adjusting other covariates using the neither DM nor MS group as the reference. **Results**: Differences in weighted frequency distributions of gender, age category (over 45 years or not), smoking status, education, race, physical activity, and daily vegetables and fruits consumption were significantly different across the four groups (p<0.05). The weighted prevalence of heart attack was 5.2% for neither DM nor MS group, 8.5% for DM only group, 11.0% for MS only group and 16.1% for both DM and MS group. The weighted prevalence of heart attack in MS only group was significantly higher than that in the DM only group (p<0.01). After adjusting for confounding variables, DM only and MS only were both found to be independently associated with heart attack compared with those with neither DM nor MS (DM alone, OR =2.09, 95% CIs =1.72-2.54, MS alone, OR =2.58, 95% CIs =2.36-2.81). **Conclusion:** The BRFSS 2015 data indicated that MS alone and DM alone had comparable effects on risk of heart attack in US adults, and the odds of risk are doubled than US adults with neither DM nor

MS.

Key Words: Metabolic syndrome, Diabetes, Heart attack

Strengths and limitations of this study

► BRFSS is a routine health-related telephone survey assessing a range of conditions.

►Weighted frequency distributions and summary statistics were used to describe the sample characteristics in each group.

►Limitation: chronic diseases were self-reported by answers.

Background

Coronary heart disease (CHD) is the leading cause of morbidity and mortality worldwide. CHD alone caused approximately 1 of every 7 deaths in the U.S. with 370,213 deaths due to CHD in 2013. [1] Each year, around 660,000 Americans are estimated to have a new heart attack (defined as first hospitalized heart attack or CHD death) and around 305,000 Americans have a recurrent attack. Furthermore, an additional 160,000 silent heart attacks are estimated to occur each year. [1]

Diabetes mellitus (DM), especially type 2 diabetes, is associated with clustered risk factors for CHD. Among adults with DM, the prevalence of hypertension, hypercholesterolemia, and obesity is ranged 75% to 85%, 70% to 80%, and 60% to 70%, respectively.[1-3] Patients with DM had higher morbidity and mortality of CHD, including heart attack. In a subgroup analysis of the FRISC II trial, diabetic patients with unstable coronary artery disease had a significantly higher rate of heart attack than non-diabetic patients.[4]

Metabolic syndrome (MS) is a multi-component risk factor for CHD that includes a cluster of individual cardiometabolic risk factors related to abdominal obesity and insulin resistance. Clinically, MS is a useful entity for communicating the nature of lifestyle-related cardiometabolic risk for both patients and clinicians.[1] MS is a risk factor for heart attack in both women and men, from all regions and ethnic groups worldwide.[5]

DM and MS are both associated with heart attack. Evidence regarding whether MS alone has stronger association with heart attack than DM alone, however, are limited. The ongoing Behavioral Risk Factor Surveillance System (BRFSS) assesses chronic conditions, such as DM, hypertension, hypercholesterolemia, and heart attack.[6] The objective of the present study was to determine whether risk of heart attack differs in people with DM alone and MS alone using the 2015 BRFSS database.

Methods

Participants

BRFSS is the nation's premier system of health-related telephone surveys that collect state data about U.S. residents regarding their health-related risk behaviors, chronic health conditions, and use of preventive services. BRFSS completes more than 400,000 adult interviews each year, making it the largest continuously conducted health survey system in the world.[7] In 2015, 50 states, the District of Columbia, Guam, and Puerto Rico collected data from interviews conducted both by landline telephone and cellular telephone. Questions used in this study in 2015 BRFSS survey include heart attack history, diabetes history, physical activity, dyslipidemia, hypertension awareness, chronic health conditions, alcohol consumption, fruits and vegetables, and currently smoking.[8]

There were 441,456 subjects in the 2015 BRFSS survey. The response rate from cellular telephone is 47.2%, which is slightly lower than that from landline telephone (48.2%).[9] Unknown responses or non-responses were coded as missing in questions included in the study, and there were 332,008 subjects included in the analysis after removing missing values.

Measures

Socio-demographic variables, such as age (18-44 year or 45+ year), race,

ethnicity (Hispanic, Latino/a, or Spanish origin or no), education, smoking status (current smoker or not) and annual household income were categorized according to the original variables.

Respondents' lifestyles were assessed by questions on their physical activity, fruits, and vegetables consumption. Fruit consumption was categorized as "consumed fruit one or more times per day" or "consumed fruit less than one time per day". Vegetable consumption was categorized as "consumed vegetables one or more times per day" or "consumed vegetables one or more times per day". Physical activity index was categorized as whether "meet aerobic recommendations" or not.

In the 2015 BRFSS, chronic diseases were self-reported by answers to questions on chronic diseases history. Heart attack was defined as yes to the question "ever told you had a heart attack, also called a myocardial infarction". Diabetes was defined by a yes answer to the question "ever told you have diabetes". Respondents with pre-diabetes, borderline diabetes, or gestational diabetes were excluded. Body mass index (BMI) was calculated by self-reported height and weight. Similarly, hypertension was defined as a yes answer to the question "have you ever been told by a doctor, nurse or other health professional that you have high blood pressure". Borderline hypertension, pre-hypertension, and gestational hypertension were all excluded from the study. Dyslipidemia was defined as a yes answer to the question "have you ever been told by a doctor, nurse or other health professional that your blood cholesterol is high". Stroke was defined as yes to the question of "ever told you had a stroke". Depression was a yes answer to the question of "ever told you that you have a depressive disorder, including depression, major depression, dysthymia, or minor".

MS was diagnosed based on the ATP-III definition.[10] The components of MS were diabetes, hypertension, central obesity, and dyslipidemia. Respondents who had more than three components were regarded as having MS. In this study, the "MS alone" group means that respondents had the other three components of MS excluding diabetes. Central obesity was diagnosed according to the MS definition issued by the American College of Endocrinology with BMI ≥ 25.0 kg/m^2 regarded as central obesity.[11]

Statistical analysis

Each record in the 2015 BRFSS data was weighted using raking weighting methodology [12]. Final weight was assigned to each respondent. Weighted percentages of respondents who ever had heart attack were calculated.

Weighted Chi-square tests was performed to determine respondents' characteristic differences across groups. Weighted hierarchical logistic regression analysis was applied to investigate in greater depth. Odds ratios (OR) and corresponding 95% confidence intervals (CIs) were derived from weighted hierarchical logistic regression analysis. Survey related procedures in SAS v9.4 (SAS Institute Inc., Cary, NC) were used for all data analysis. The significance level was set at $p < 0.05$, and all tests were two-sided.

Patient and public involvement

This study was an analysis of the 2015 BRFSS database. The database was downloaded via the U.S. Centers for Disease Control and Prevention website.

Results

Demographic Characteristics

There were 332,008 respondents involved in this study. All respondents were categorized into four groups as follows: neither DM nor MS, DM alone (having DM without MS), MS alone (having MS without DM), and DM plus MS. There were 237,334 respondents with neither DM nor MS, 45,191 respondents with DM alone, 8,416 respondents with MS alone and 41,067 respondents with both DM and MS (Table 1). Differences in the weighted percentages of gender, age category, smoking status, education level, race, ethnicity, and annual household income were statistically significant among the four groups (p<0.01). In addition, the above characteristics were significantly different between DM alone and MS alone group (p<0.001). In both MS and DM group, 91% were aged over 45 years, and 21.5% did not graduate high school, which were higher than the other three groups. Moreover, 17.6% of respondents in the MS and DM group had annual household incomes lower than $15,000 and the low income percentage is much higher than the other three groups. Less people were white in the DM alone group (71.4%) compared with that in the MS alone group (80.4%). However, More respondents were Latino in the DM alone group (19.3%) than in the MS alone group (10.3%, p<0.001), and more respondents were current smokers in the DM alone group (16.0%) compared with the MS alone group (15.3%, p<0.001, Table 1).

Lifestyle

Lifestyle measurements were also compared in the four groups (Table 1). The weighted percentage of physical activity index, daily fruit consumption and vegetables consumption were all significantly different across the four groups. The physical activity index was statistically significant between the DM alone and MS alone groups (48.2% vs 47.6%, p<0.001). The DM and MS group had the least weighted percentage of respondents whose physical activity met the aerobic recommendations. The weighted percentage of respondents who consumed fruit one or more times per day was higher in the DM alone group, compared to that in the MS alone group (58.8% vs 56.8%, p<0.001). However, daily vegetables consumption was similar between the DM alone and the MS alone groups (76.9% vs 76.8%, p=0.019). In the DM and MS group, the weighted percentage of daily vegetable consumption is the least among the four groups (73.4%)

MS components and chronic diseases

Among the 332,008 respondents, 21,896 respondents had heart attack, accounting for the weighted prevalence of 5.2%. MS alone had higher weighted prevalence of heart attack than that in DM alone (11.0%, 8.5%, respectively, p<0.001). The weighted prevalence of heart attack in the DM plus MS group was the highest (16.1%, Table 2). The overall weighted prevalence of dyslipidemia, hypertension, diabetes, and central obesity was 36.6%, 37.5%, 13.2%, and 67.2%, respectively (Table 2). In the DM alone group, 83% respondents had one component of MS other than DM, with 17% people having no other components of MS besides DM.

The overall weighted prevalence of stroke was 3.6%. The weighted prevalence of stroke were significantly different between the DM alone and MS alone groups (4.8% vs. 6.6%, p<0.001). The weighted prevalence of stroke in the DM plus MS group was the highest among the four groups (9.7%). The overall weighted prevalence of depression was 18.2%. Compared with DM alone, MS alone had significantly higher weighted prevalence of depression (16.4% vs 24.1%, p<0.001). The highest weighted prevalence of depression was observed in the DM plus MS group (27.7%).

Logistic regression

Logistic regression was conducted to compare the difference among the four groups in their association with heart attack, using the neither DM nor MS group as the reference (Table 3). Results from unadjusted logistic regression analysis showed that both DM alone (OR=3.275, 95% CI =2.812-3.815) and MS alone (OR =4.366, 95% CI = 4.055-4.700) groups had significantly elevated odds of heart attack than neither DM nor MS group. The DM plus MS group had the highest odds of heart attack among the three groups (OR =6.787, 95% CI =6.331-7.275)

To identify an independent relationship between DM, MS and heart attack, hierarchical logistic regression analysis was performed. After adjusting for confounders (gender, age, education, smoking, race, physical activity index, daily fruit consumption, daily vegetable consumption, stroke, and depression) DM alone and MS alone were found to have independently increased odds of heart attack compared with the neither DM nor MS group (DM alone, AOR =2.089, 95% CI =1.716-2.543, MS alone, AOR =2.575, 95% CI =2.363-2.806). The DM plus MS group had the highest odds of heart attack (AOR = 3.451, 95% CI = 3.156-3.772, p all < 0.001, Table 3).

Predictive probability values

After adjusting for confounders such as gender, age, education, smoking, race, physical activity index, daily fruit consumption, daily vegetable consumption, stroke, and depression, the predictive probability value of each respondent from the logistic regression analysis was calculated. Receivers operating characteristic (ROC) curve analyses were performed to determine the predictive probability value of different DM and MS groups in predicting heart attack. ROC analysis showed that the area under curve (AUC) for the predictive probability of heart attack was 0.788 (95% CI: 0.784-0.791, p<0.01) in the whole population. In the DM alone, MS alone, and DM plus MS group, the AUC were 0.705 (95% CI: 0.685 - 0.726, p< 0.01), 0.678 (95% CI: 0.670 - 0.687, p< 0.01) and 0.678 (95% CI: 0.670 - 0.685, p <0.01). There were no statistically significant differences among these three groups.

The sensitivity and the specificity of the predictive probability in predicting heart attack were also calculated. If the predictive probability value was over 0.5, the predictive probability was set as positive, otherwise as negative. The sensitivity and the specificity of the predictive probability in predicting heart attack in the whole population were 2.9% and 99.8%. In the DM alone group, the sensitivity was 0.5% (0-1.0%) and the specificity was 100%. In the MS alone group, the sensitivity was 2.5% (2.0%-2.96%) and the specificity was 99.6% (99.4%-99.8%). In the DM plus MS group, the sensitivity was 7.3% (6.62%-7.98%) and the specificity was 98.6% (98.3%-98.9%).

Discussion

In the 2015 BRFSS data, respondents with MS alone and DM alone were both associated with elevated risk of heart attack and the amount of increase is doubled compare to respondents with neither DM nor MS. MS did not appear to be a greater hazard for heart attack than DM from our analysis results. MS combined with DM increased more risk of heart attack by over 3.4 fold compared with respondents with neither DM nor MS.

MS is a cluster of risk factors contributing to the pathogenesis of atherosclerosis.[13] There are several definitions of MS and different definitions of MS had different components.[14-16] Many large-scale clinical trials and meta-analyses have reported that the presence of MS is a strong predictor for heart attack in many different populations.[5, 17-19] In the INTERHEART case-control study involving 26,903 subjects from 52 countries, MS was associated with an increased risk of heart attack, both using the WHO definition (OR=2.69) and the IDF definition (OR=2.20) .The direction of associations were similar across all regions and ethnic groups.[5] A large family study in Finland and Sweden of 4,483 subjects also identified the association between MS and an increased risk of heart attack in all subjects using the WHO definition.[19] Similar results were observed when the 2001 NCEP and 2004 revised NCEP definitions were used.[17, 18]

DM is one of the components in most definitions of MS. The risk for cardiovascular disease (CVD) is 2-8 fold higher in the diabetic population than that in the non-diabetic population of a similar age, sex and ethnicity and CVD is the leading cause of morbidity and mortality among patients with type 2 diabetes.[20-22]

Previous researchers have investigated the effects of DM on heart attack. Consistent with our findings, it has been reported that DM was associated with an increased heart attack risk in both men and women.[23] A cohort study using the UK General Practice Research Database showed a much larger relative risk of heart attack in DM.[24]

Both DM and MS were associated with an increased risk of heart attack. However, evidence regarding whether MS alone is better than DM alone for evaluating heart attack are limited. There were studies to evaluate the relationship between MS and DM on CVD events. Results from different studies regarding differences in CVD events between DM and MS were conflicting. The Ansung-Ansan cohort study showed that there was no difference in the risk of incident CVD between individuals with DM alone and MS alone.[25] Yet, in the REACH registry, presence of newly detected DM but not MS was associated with an increased risk of CVD events.[26] Besides the difference in population characteristics in these studies, the sample size and the definitions of CVD maybe affect the results.

In the logistic analysis of this study, MS alone and DM alone were found to have similar odds of heart attack. MS and DM have similar ROC, specificity and sensitivity when each group used independently to predict the odds of heart attack after adjusting all other covariates in the logistic regression model. All these indicated that MS and DM may have similar effects on heart attack in the US adults.

The diagnosis of MS in this study was different from the original definition of MS. However, the association between MS and heart attack was consistent. MS, regardless of its definition, was associated with heart attack.

DM typically co-presents with at least one metabolic abnormality. In our analysis, the weighted prevalence of hypertension, dyslipidemia and overweight in DM alone group was 13.9%, 12.2% and 56.8%, respectively. Of the respondents with DM, 83% had at least one or more components of MS other than DM. As shown in a population-based cohort study, DM with only one component of MS had more than twofold higher CVD risk than those with DM only.[27] These associations may be helpful to explain in this study why DM and MS had similar effects on heart attack. Further studies were needed to evaluate the association between MS alone, DM alone with heart attack. Our results indicated that to prevent heart attack or CVD, even a diabetic person does not meet the criteria of MS, much more attention should be paid to control metabolic abnormalities.

There were some limitations in our study. First, the definition of MS is revised according to the contents of 2015 BRFSS. MS was diagnosed based on the ATP-III definition.[10] The components of MS were diabetes, hypertension, central obesity, and dyslipidemia. Respondents who had more than three components were regarded as having MS. According to the ATP-III definition, central obesity was diagnosed basing on waist circumference. We used BMI to classify individuals as central obesity because waist circumference was not available. The MS definition from the American College of Endocrinology recommends that BMI >25kg/m^2 or a waist circumference >40 inches for men, >35 inches for women was regarded as obesity.[11] Therefore in the present study, we used BMI ≥25 kg/m^2 as the cut-off point for obesity. Secondly, in the 2015 BRFSS, there were no data on triglyceride and high-density lipoprotein. Dyslipidemia was assessed by whether respondents had ever been told their blood cholesterol was high. Thirdly, the self-reported nature of the cross-sectional study may lead to underestimate the actual prevalence of heart attack. In this study, 13.2% respondents had diabetes. However, some diabetic respondents may have silent heart attack without any symptoms. Fourthly, gestational diabetes and pre-diabetes were excluded. These two conditions are both important risk factors for DM that has been excluded from the study.

In conclusion, even though the weighted percentage of heart attack in MS alone was higher than that in DM alone, MS and DM had similar effects on heart attack, which could double the risk of heart attack. Furthermore, when MS is combined with DM, the risk of heart attack will be increased by over 3.5 fold. Considering the nature of the cross-sectional study in the 2015 BRFSS data, prospective studies are needed to confirm the association between MS alone, DM alone with heart attack.

Contributors GRY and DL designed the study and analyzed the data. GRY draft the manuscript. DL and TD revised the manuscript. All authors read and approved the final manuscript.

Funding This work was supported by Beijing Municipal Training Foundation for Highly-qualified and Technological Talents of Health System [2014-3-013] and Capital's Funds for Health Improvement and Research [2016-2-2054]. Dr. Li's and Dr. Dye's time is partly supported by the University of Rochester's Clinical and Translational Science Award (CTSA) number UL1 TR000042 and UL1 TR002001 from the National Center for Advancing Translational Sciences of the National Institutes of Health.

Competing interests None declared.

Ethics approval Not applicable.

Data sharing statement No additional data are available..

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Table 1. Demographic and lifestyle characteristics among the four groups according to the presence of metabolic syndrome and diabetes

	Total	Neither DM nor MS	DM alone	MS alone	DM plus MS	p value
Number	332,008	237334	8416	45191	41067	
Gender						<0.01
Male, n (weighted %)	144458 (49.9%)	98983 (48.4%)	4049 (56.4%)	22377 (57.1%)	19049 (51.8%)	
Female, n (weighted %)	187550 (50.1%)	138351 (51.6%)	4367 (43.6%)	22814 (42.9%)*	22018 (48.2%)	
Age						<0.01
<45 years, n (weighted %)	67420 (36.9%)	61527 (44.7%)	944 (20.4%)	3054 (14.6%)	1895 (9.0%)	
≥45 years, n (weighted %)	264588 (63.1%)	175807 (55.3%)	7472 (79.6%)	42137 (85.4%)*	39172 (91.0%)	
Annual household income						<0.01
<15000, n (weighted %)	26368 (9.8%)	15248 (8.3%)	1009 (15.2%)	4100 (10.9%)	6011 (17.6%)	
15000-25000, n (weighted %)	42954 (15.2%)	27083 (13.6%)	1459 (21.8%)	6503 (17.3%)	7909 (22.9%)	
25000-35000, n (weighted %)	29733 (9.9%)	19853 (9.4%)	877 (11.5%)	4533 (11.0%)	4470 (12.0%)	
35000-50000, n (weighted %)	40705 (13.6%)	28453 (13.5%)	1039 (13.3%)	6103 (14.7%)	5110 (13.7%)	
>50000, n (weighted %)	144082 (51.5%)	112776 (55.2%)	2616 (38.2%)	17422 (46.1%)*	11268 (33.8%)	

Latino						<0.01
Yes, n (weighted %)	22487 (13.8%)	16018 (14.0%)	853 (19.3%)	2257 (10.3%)*	3359 (15.0%)	
No, n (weighted %)	307115 (86.2%)	219670 (86.0%)	7490 (80.7%)	42626 (89.7%)	37329 (85.0%)	
Race						<0.01
White, n (weighted %)	279446 (77.8%)	202115 (78.4%)	6730 (71.4%)	38756 (80.4%)*	31845 (72.7%)	
African America, n (weighted %)	26653 (12.4%)	16453 (11.4%)	740 (13.9%)	3815 (12.9%)	5645 (18.1%)	
America Indian, n (weighted %)	5718 (1.7%)	3673 (1.6%)	263 (3.3%)	670 (1.5%)	1112 (2.5%)	
Asian, n (weighted %)	7092 (4.8%)	5688 (5.2%)	243 (7.3%)	535 (2.5%)	626 (3.5%)	
Native Hawaiian, n (weighted %)	1872 (0.4%)	1338 (0.4%)	49 (0.5%)	213 (0.3%)	272 (0.3%)	
Other race, n (weighted %)	4058 (2.7%)	4058 (2.7%)	215 (3.5%)	647 (2.2%)	839 (2.6%)	
No preferred race, n (weighted %)	745 (0.3%)	577 (0.3%)	14 (0.1%)	60 (0.2%)	94 (0.2%)	
Multiracial but preferred race not answered, n (weighted %)	6 (0.0%)	4 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.0%)	
Education						<0.01
Did not	21989	12296	917	3607	5169	

graduate high school, n (weighted %)	(11.8%)	(9.7%)	(20.3%)	(14.9%)	(21.5%)	
Graduated high school, n (weighted %)	88636 (26.9%)	58399 (25.6%)	2672 (29.4%)	14028 (31.2%)	13537 (31.1%)	
Attended college or technical school, n (weighted %)	90001 (31.5%)	63868 (32.0%)	2238 (28.1%)	12302 (30.3%)	11593 (30.2%)	
Graduated from college or technical school, n (weighted %)	130722 (29.8%)	102289 (32.7%)	2561 (22.3%)	15185 (23.6%)*	10687 (17.2%)	
Currently smoking						<0.01
No, n (weighted %)	280808 (84.5%)	200158 (84.4%)	6944 (84.0%)	38788 (84.7%)	34918 (85.4%)	
Yes, n (weighted %)	43947 (15.5%)	31827 (15.6%)	1230 (16.0%)	5547 (15.3%)*	5343 (14.6%)	
Physical activity index						<0.01
Meet aerobic recommendations, n (weighted %)	164390 (52.8%)	124593 (55.4%)	3712 (48.2%)	20530 (47.6%)	15555 (40.8%)	
Did not meet aerobic recommendations, n	136791 (47.2%)	90370 (44.6%)	3735 (51.8%)	20831 (52.4%)*	21855 (59.2%)	

(weighted %)						
Fruit						<0.01
Consumed fruit one or more times per day, n (weighted %)	195725 (61.4%)	143690 (62.9%)	4795 (58.8%)	25173 (56.8%)	22067 (56.0%)	
Consumed fruit less than one time per day, n (weighted %)	111948 (38.6%)	76183 (37.1%)	2854 (41.2%)	16897 (43.2%)*	16014 (44.0%)	
Vegetable						<0.01
Vegetables one or more times per day, n (weighted %)	243504 (79.7%)	177711 (81.0%)	5766 (76.9%)	32262 (76.8%)	27765 (73.4%)	
Vegetables less than one time per day, n (weighted %)	58881 (20.3%)	38567 (19.0%)	1691 (23.1%)	9081 (23.2%)	9542 (26.6%)	

* Compared with DM alone group, p<0.05

Abbreviation: DM: diabetes mellitus, MS: metabolic syndrome

Table 2. Chronic diseases among the four groups according to the presence of metabolic syndrome and diabetes

Chronic diseases	Total	Neither DM nor MS	DM alone	MS alone	DM plus MS	P value
Heart attack, n (weighted %)	21896 (5.2%)	8863 (2.7%)	851 (8.5%)	5310 (11.0%)*	6872 (16.1%)	<0.01
Hypertension, n (weighted %)	147655 (37.5%)	64705 (21.9%)	1411 (13.9%)	45191 (100.0%)*	36348 (87.6%)	<0.01
Dyslipidemia, n (weighted %)	140653 (36.6%)	62526 (22.2%)	1102 (12.2%)	45191 (100.0%)*	31834 (77.6%)	<0.01
Central obesity, n (weighted %)	223112 (67.2%)	135589 (59.1%)	4551 (56.8%)	45191 (100.0%)*	37781 (92.3%)	<0.01
Stroke, n (weighted %)	15013 (3.6%)	6910 (2.2%)	544 (4.8%)	3228 (6.6%)*	4331 (9.7%)	<0.01
Depression, n (weighted %)	64290 (18.3%)	40520 (16.1%)	1574 (16.4%)	10687 (24.1%)*	11509 (27.7%)	<0.01

* Compared with DM alone group, p<0.05

Abbreviation: DM: diabetes mellitus, MS: metabolic syndrome

Table 3. The odds ratio and 95% confidence intervals of DM and MS related to heart attack in the hierarchy logistic regression analysis

	Odds Ratio	95% confidence intervals	p value
Model 1			
DM alone	3.275	2.812-3.815	<0.01
MS alone	4.366	4.055-4.700	<0.01
DM plus MS	6.787	6.331-7.275	<0.01
Model 2			
DM alone	2.097	1.768-2.486	<0.01
MS alone	2.852	2.637-3.084	<0.01
DM plus MS	4.058	3.756-4.384	<0.01
Model 3			
DM alone	2.116	1.748-2.562	<0.01
MS alone	2.820	2.594-3.067	<0.01
DM plus MS	3.987	3.660-4.344	<0.01
Model 4			
DM alone	2.089	1.716-2.543	<0.01
MS alone	2.575	2.363-2.806	<0.01
DM plus MS	3.451	3.156-3.772	<0.01

Model 1: unadjusted

Model 2: adjusted for gender, age (45 years or not), education, current smoking, race

Model 3: adjusted for gender, age (45 years or not), education, current smoking, race, physical activity index, fruits consumed one or more times per day, vegetable consumed one or more times per day

Model 4 adjusted for gender, age (45 years or not), education, current smoking, race, physical activity index, fruits consumed one or more times per day, vegetable consumed one or more times per day, stroke, and depression

Abbreviation: DM: diabetes mellitus, MS: metabolic syndrome

BMJ Open

Association between diabetes, metabolic syndrome and heart attack in U.S. adults: a cross-sectional analysis using the Behavioral Risk Factor Surveillance System 2015

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-022990.R1
Article Type:	Original research
Date Submitted by the Author:	03-Dec-2018
Complete List of Authors:	Yang, Guang-Ran; Beijing Tongren Hospital, Capital Medical University, Department of Endocrinology; School of Medicine and Dentistry, University of Rochester, Clinical and Translational Science Institute Dye, Timothy ; School of Medicine and Dentistry, University of Rochester, Clinical and Translational Science Institute Li, Dongmei; School of Medicine and Dentistry, University of Rochester, Clinical and Translational Science Institute
Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Diabetes and endocrinology
Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, metabolic syndrome, heart attack

Association between diabetes, metabolic syndrome and heart attack in U.S. adults: a cross-sectional analysis using the Behavioral Risk Factor Surveillance System 2015

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Abstract:

Objectives: Diabetes mellitus (DM) and metabolic syndrome (MS) are both associated with heart attack. Evidence regarding which condition - MS or DM - is better associated with heart attack, however, is limited. The purpose of this study is to examine DM and MS, and their comparative associations with heart attack, using the 2015 Behavioral Risk Factor Surveillance System (BRFSS). **Design:** Cross-sectional study. **Methods:** A total of 332,008 subjects aged over 18-year were included in the analysis. All subjects were classified into four groups based on their DM and MS status: neither DM nor MS, DM without MS, MS without DM, and both DM and MS. Hierarchical logistic regressions were used to examine the effect of DM and MS on heart attack using the neither DM nor MS group as the reference. **Results**: Differences in weighted frequency distributions of gender, age category (over 45 years or not), smoking status, education, race, physical activity, and daily vegetables and fruits consumption were significantly different across the four groups ($p<0.05$). The weighted prevalence of heart attack was 5.2% for neither DM nor MS group, 8.5% for DM only group, 11.0% for MS only group and 16.1% for both DM and MS group. The weighted prevalence of heart attack in MS only group was significantly higher than that in the DM only group ($p<0.01$). After adjusting for confounding variables, DM only and MS only were both found to be independently associated with heart attack compared with those with neither DM nor MS (DM without MS, odds ratio=2.09, MS without DM, odds ratio=2.58, p all <0.01). **Conclusion:** The BRFSS 2015 data indicated that MS without DM and DM without MS had comparable effects on heart attack in U.S adults, and the odds of risk are doubled than U.S. adults with neither DM nor MS.

Key Words: Metabolic syndrome, Diabetes, Heart attack

Strengths and limitations of this study

► BRFSS is a routine health-related telephone survey assessing a range of conditions.

►Weighted frequency distributions and summary statistics were used to describe the sample characteristics in each group.

►Limitation: chronic diseases were self-reported by answers.

Background

Coronary heart disease (CHD) is the leading cause of morbidity and mortality worldwide. CHD alone caused approximately 1 of every 7 deaths in the U.S. with 366,801 deaths due to CHD in 2015. [1] Each year, around 660,000 Americans are estimated to have a new heart attack (defined as first hospitalized heart attack or CHD death) and around 305,000 Americans have a recurrent attack. Furthermore, an additional 160,000 silent heart attacks are estimated to occur each year. [2]

Diabetes mellitus (DM), especially type 2 diabetes, is associated with clustered risk factors for CHD. Among adults with DM, the prevalence of hypertension, hypercholesterolemia, and obesity is ranged 75% to 85%, 70% to 80%, and 60% to 70%, respectively.[2-4] Patients with DM had higher morbidity and mortality of CHD, including heart attack. In a subgroup analysis of the FRISC II trial, diabetic patients with unstable coronary artery disease had a significantly higher rate of heart attack than non-diabetic patients.[5]

Metabolic syndrome (MS) is a multi-component risk factor for CHD that includes a cluster of individual cardiometabolic risk factors related to abdominal obesity and insulin resistance. Clinically, MS is a useful entity for communicating the nature of lifestyle-related cardiometabolic risk for both patients and clinicians.[2] MS is a risk factor for heart attack in both women and men, from all regions and ethnic groups worldwide.[6]

DM and MS are both associated with heart attack. Evidence regarding whether MS without DM has stronger association with heart attack than DM without MS, however, are limited. The ongoing Behavioral Risk Factor Surveillance System (BRFSS) assesses chronic conditions, such as DM, hypertension, hypercholesterolemia, and heart attack.[7] The objective of the present study was to determine whether risk of heart attack differs in people with DM without MS and MS without DM using the 2015 BRFSS database.

Methods

Participants

BRFSS is the nation's premier system of health-related telephone surveys that collect state data about U.S. residents regarding their health-related risk behaviors, chronic health conditions, and use of preventive services. BRFSS completes more than 400,000 adult interviews each year, making it the largest continuously conducted health survey system in the world.[8] In 2015, 50 states, the District of Columbia, Guam, and Puerto Rico collected data from interviews conducted both by landline telephone and cellular telephone. Questions used in this study in 2015 BRFSS survey include heart attack history, diabetes history, physical activity, dyslipidemia, hypertension awareness, chronic health conditions, alcohol consumption, fruits and vegetables, and currently smoking.[9]

There were 441,456 subjects in the 2015 BRFSS survey. The response rate from cellular telephone is 47.2%, which is slightly lower than that from landline telephone (48.2%).[10] Unknown responses or non-responses were coded as missing in questions included in the study, and there were 332,008 subjects included in the analysis after removing missing values.

Measures

Socio-demographic variables, such as age (18-44 year or 45+ year), race,

ethnicity (Hispanic, Latino/a, or Spanish origin or no), education, smoking status (current smoker or not) and annual household income were categorized according to the original variables.

Respondents' lifestyles were assessed by questions on their physical activity, fruits, and vegetables consumption. Fruit consumption was categorized as “consumed fruit one or more times per day” or “consumed fruit less than one time per day”. Vegetable consumption was categorized as “consumed vegetables one or more times per day” or “consumed vegetables one or more times per day”. Physical activity index was categorized as whether “meet aerobic recommendations” or not.

In the 2015 BRFSS, chronic diseases were self-reported by answers to questions on chronic diseases history. Heart attack was defined as yes to the question “has a doctor, nurse, or other health professional ever told you had a heart attack, also called a myocardial infarction”. Diabetes was defined by a yes answer to the question “has a doctor, nurse, or other health professional ever told you have diabetes”. Respondents with pre-diabetes, borderline diabetes, or gestational diabetes were excluded. Body mass index (BMI) was calculated by self-reported height and weight. Similarly, hypertension was defined as a yes answer to the question “have you ever been told by a doctor, nurse or other health professional that you have high blood pressure”. Borderline hypertension, pre-hypertension, and gestational hypertension were all excluded from the study. Dyslipidemia was defined as a yes answer to the question “have you ever been told by a doctor, nurse or other health professional that your blood cholesterol is high”. Stroke was defined as yes to the question of “ever told you had a stroke”. Depression was a yes answer to the question of “ever told you that you have a depressive disorder, including depression, major depression, dysthymia, or minor”.

MS was diagnosed based on the ATP-III definition.[11] The components of MS were abdominal obesity (waist circumference >40 inches in men or >35 inches in women), triglycerides ≥150 mg/dl, high density lipoprotein cholesterol <40 mg/dl in men or <50mg/dl in women, blood pressure ≥130/85 mmHg, and fasting glucose ≥110 mg/dl. As these were no data of waist circumference, blood pressure, fasting glucose and lipid profile. The diagnose of MS was revised based on the questions in the BRFSS. The revised components of MS included diabetes, hypertension, BMI ≥25.0 kg/m^2, and dyslipidemia. Respondents who had at least three components were regarded as having MS. In this study, the “MS without DM” group means that respondents had the other three components of MS excluding diabetes.

Statistical analysis

Each record in the 2015 BRFSS data was weighted using raking weighting methodology [12]. Final weight was assigned to each respondent. Weighted percentages of respondents who ever had heart attack were calculated.

Weighted Chi-square tests was performed to determine respondents' characteristic differences across groups. Weighted hierarchical logistic regression analysis was applied to investigate in greater depth. Odds ratios (OR) and corresponding 95% confidence intervals (CIs) were derived from weighted hierarchical logistic regression analysis. The predictive probability value of each respondent from the logistic regression analysis was calculated. Receivers operating characteristic (ROC) curve analyses, the sensitivity and the specificity of the predictive probability were performed to compare the association of different DM and MS groups with heart attack. Survey related procedures in SAS v9.4 (SAS Institute Inc., Cary, NC) were used for all data analysis. The significance level was set at $p<0.05$, and all tests were two-sided.

Patient and public involvement

This study was an analysis of the 2015 BRFSS database. The database was downloaded via the U.S. Centers for Disease Control and Prevention website.

Results

Demographic Characteristics

There were 332,008 respondents involved in this study. All respondents were categorized into four groups as follows: neither DM nor MS, DM without MS (having DM without MS), MS without DM (having MS without DM), and DM plus MS. There were 237,334 respondents with neither DM nor MS, 45,191 respondents with DM without MS, 8,416 respondents with MS without DM and 41,067 respondents with both DM and MS (Table 1). Differences in the weighted percentages of gender, age category, smoking status, education level, race, ethnicity, and annual household income were statistically significant among the four groups (p<0.01). In addition, the above characteristics were significantly different between DM without MS and MS without DM group (p<0.001). In both MS and DM group, 91% were aged over 45 years, and 21.5% did not graduate high school, which were higher than the other three groups. Moreover, 17.6% of respondents in the MS and DM group had annual household incomes lower than $15,000 and the low income percentage is much higher than the other three groups. Less people were white in the DM without MS group (71.4%) compared with that in the MS without DM group (80.4%). However, More respondents were Latino in the DM without MS group (19.3%) than in the MS without DM group (10.3%, p<0.001), and more respondents were current smokers in the DM without MS group (16.0%) compared with the MS without DM group (15.3%, p<0.001, Table 1).

Lifestyle

Lifestyle measurements were also compared in the four groups (Table 1). The weighted percentage of physical activity index, daily fruit consumption and vegetables consumption were all significantly different across the four groups. The physical activity index was statistically significant between the DM without MS and MS without DM groups (48.2% vs 47.6%, p<0.001). The DM and MS group had the least weighted percentage of respondents whose physical activity met the aerobic recommendations. The weighted percentage of respondents who consumed fruit one or more times per day was higher in the DM without MS group, compared to that in the MS without DM group (58.8% vs 56.8%, p<0.001). However, daily vegetables consumption was similar between the DM without MS and the MS without DM groups (76.9% vs 76.8%, p=0.019). In the DM and MS group, the weighted percentage of daily vegetable consumption is the least among the four groups (73.4%) .

MS components and chronic diseases

Among the 332,008 respondents, 21,896 respondents had heart attack, accounting for the weighted prevalence of 5.2%. MS without DM had higher weighted prevalence of heart attack than that in DM without MS (11.0%, 8.5%, respectively, p<0.001). The weighted prevalence of heart attack in the DM plus MS group was the highest (16.1%, Table 2). The overall weighted prevalence of dyslipidemia, hypertension, diabetes, and BMI ≥25.0 kg/m^2 was 36.6%, 37.5%, 13.2%, and 67.2%, respectively (Table 2). In the DM without MS group, 83% respondents had one component of MS other than DM, with 17% people having no other components of MS besides DM.

The overall weighted prevalence of stroke was 3.6%. The weighted prevalence of stroke were significantly different between the DM without MS and MS without DM groups (4.8% vs 6.6%, p<0.001). The weighted prevalence of stroke in the DM plus MS group was the highest among the four groups (9.7%). The overall weighted prevalence of depression was 18.2%. Compared with DM without MS, MS without DM had significantly higher weighted prevalence of depression (16.4% vs 24.1%, p<0.001). The highest weighted prevalence of depression was observed in the DM plus MS group (27.7%).

Logistic regression

Logistic regression was conducted to compare the difference among the four groups in their association with heart attack, using the neither DM nor MS group as the reference (Table 3). Results from unadjusted logistic regression analysis showed that both DM without MS (OR=3.275, 95% CI=2.812-3.815) and MS without DM (OR=4.366, 95% CI=4.055-4.700) groups had significantly elevated odds of heart attack than neither DM nor MS group. The DM plus MS group had the highest odds of heart attack among the three groups (OR=6.787, 95% CI=6.331-7.275)

To identify an independent relationship between DM, MS and heart attack, hierarchical logistic regression analysis was performed. After adjusting for confounders (gender, age, education, smoking, race, physical activity index, daily fruit consumption, daily vegetable consumption, stroke, and depression) DM without MS and MS without DM were found to have independently increased odds of heart attack compared with the neither DM nor MS group (DM without MS, adjusted OR=2.089, 95% CI =1.716-2.543, MS without DM, adjusted OR =2.575, 95% CI =2.363-2.806). The DM plus MS group had the highest odds of heart attack (adjusted OR=3.451, 95% CI =3.156-3.772, p all < 0.001, Table 3).

Predictive probability values

After adjusting for confounders such as gender, age, education, smoking, race, physical activity index, daily fruit consumption, daily vegetable consumption, stroke, and depression, the predictive probability value of each respondent from the logistic regression analysis was calculated. Receivers operating characteristic (ROC) curve analyses were performed to determine the predictive probability value of different DM and MS groups in predicting heart attack. ROC analysis showed that the area under curve (AUC) for the predictive probability of heart attack was 0.788 (95% CI: 0.784-0.791, p<0.01) in the whole population. In the DM without MS, MS without DM, and DM plus MS group, the AUC were 0.705 (95% CI: 0.685-0.726, p<0.01), 0.678 (95% CI: 0.670-0.687, p<0.01) and 0.678 (95% CI: 0.670-0.685, p<0.01). There were no statistically significant differences among these three groups.

The sensitivity and the specificity of the predictive probability in predicting heart attack were also calculated. If the predictive probability value was over 0.5, the predictive probability was set as positive, otherwise as negative. The sensitivity and the specificity of the predictive probability in predicting heart attack in the whole population were 2.9% and 99.8%. In the DM without MS group, the sensitivity was 0.5% (0-1.0%) and the specificity was 100%. In the MS without DM group, the sensitivity was 2.5% (2.0%-2.96%) and the specificity was 99.6% (99.4%-99.8%). In the DM plus MS group, the sensitivity was 7.3% (6.62%-7.98%) and the specificity was 98.6% (98.3%-98.9%).

Discussion

In the 2015 BRFSS data, respondents with MS without DM and DM without MS were both associated with elevated risk of heart attack and the amount of increase is doubled compare to respondents with neither DM nor MS. MS did not appear to be a greater odds for heart attack than DM from our analysis results. MS combined with DM increased more risk of heart attack by over 3.4 fold compared with respondents with neither DM nor MS.

MS is a cluster of risk factors contributing to the pathogenesis of atherosclerosis.[13] There are several definitions of MS and different definitions of MS had different components.[14-16] Many large-scale clinical trials and meta-analyses have reported that the presence of MS is a strong predictor for heart attack in many different populations.[6, 17-19] In the INTERHEART case-control study involving 26,903 subjects from 52 countries, MS was associated with an increased risk of heart attack, both using the WHO definition (OR=2.69) and the IDF definition (OR=2.20) .The direction of associations were similar across all regions and ethnic groups.[6] A large family study in Finland and Sweden of 4,483 subjects also identified the association between MS and an increased risk of heart attack in all subjects using the WHO definition.[19] Similar results were observed when the 2001 NCEP and 2004 revised NCEP definitions were used.[17, 18] In our analysis, the association between MS and heart attack was consistent. MS, regardless of its definition, was associated with heart attack.

DM is one of the components in most definitions of MS. The risk for cardiovascular disease (CVD) is 2-8 fold higher in the diabetic population than that in the non-diabetic population of a similar age, sex and ethnicity and CVD is the leading cause of morbidity and mortality among patients with type 2 diabetes.[20-22]

Previous researchers have investigated the effects of DM on heart attack. Consistent with our findings, it has been reported that DM was associated with an increased heart attack risk in both men and women.[23] A cohort study using the UK General Practice Research Database showed a much larger relative risk of heart attack in DM.[24]

Both DM and MS were associated with an increased risk of heart attack. However, evidence regarding whether MS without DM is better than DM without MS for evaluating heart attack are limited. There were studies to evaluate the relationship between MS and DM on CVD events. Results from different studies regarding differences in CVD events between DM and MS were conflicting. The Ansung-Ansan cohort study showed that there was no difference in the risk of incident CVD between individuals with DM without MS and MS without DM.[25] Yet, in the REACH registry, presence of newly detected DM but not MS was associated with an increased risk of CVD events.[26] Besides the difference in population characteristics in these studies, the sample size and the definitions of CVD maybe affect the results.

There were fewer studies conducted in U.S. adults to compare the effects of MS and DM on heart attack. In the logistic analysis of this study, MS without DM and DM without MS were found to have similar odds of heart attack. MS and DM have similar ROC, specificity and sensitivity when each group used independently to predict the odds of heart attack after adjusting all other covariates in the logistic regression model. All these showed that MS and DM may have similar effects on heart attack in the U.S. adults, which was different from the results of previous study in U.S. population. [27] Our results indicated that to prevent heart attack or CVD, even a diabetic person does not meet the criteria of MS, much more attention should be paid to control metabolic abnormalities.

DM typically co-presents with at least one metabolic abnormality. In our analysis, the weighted prevalence of hypertension, dyslipidemia and overweight in DM without MS group was 13.9%, 12.2% and 56.8%, respectively. Of the respondents with DM, 83% had at least one or more components of MS other than DM. As shown in a population-based cohort study, DM with only one component of MS had more than twofold higher CVD risk than those with DM only.[28] These associations may be helpful to explain in this study why DM and MS had similar effects on heart attack. Further studies were needed to evaluate the association between MS without DM, DM without MS with heart attack.

There were some limitations in our study. First, the definition of MS is revised according to the contents of 2015 BRFSS. MS was diagnosed based on the ATP-III definition.[11] The components of MS were diabetes, hypertension, BMI ≥25.0 kg/m^2, and dyslipidemia. Respondents who had at least three components were regarded as having MS. According to the ATP-III definition, central obesity was diagnosed basing on waist circumference. We used BMI ≥25.0 kg/m^2 to classify individuals because waist circumference was not available. The MS definition from the American College of Endocrinology recommends that BMI >25kg/m^2 or a waist circumference >40 inches for men, >35 inches for women was regarded as obesity. [29] Therefore in the present study, we used BMI ≥25 kg/m^2 as a component of MS. Secondly, in the 2015 BRFSS, there were no data on triglyceride and high-density lipoprotein. Dyslipidemia was assessed by whether respondents had ever been told their blood cholesterol was high. Thirdly, the self-reported nature of the cross-sectional study may lead to underestimate the actual prevalence of heart attack. In this study, 13.2% respondents had diabetes. However, some diabetic respondents may have silent heart attack without any symptoms. In the BRFSS survey the data of fatal heart attack are not included, which may also underestimate the actual prevalence of heart attack. Fourthly, gestational diabetes and pre-diabetes were excluded. These two conditions are both important risk factors for DM that has been excluded from the study. In this study, 24.8% subjects in the 2015 BRFSS data with unknown responses or non-responses in questions included in the study were excluded from the analysis under the assumption of missing completely at random, which might result in some bias of the results when the assumption is not valid.

In conclusion, even though the weighted percentage of heart attack in MS without DM was higher than that in DM without MS, MS and DM had similar effects on heart attack, which could double the risk of heart attack. Furthermore, when MS is combined with DM, the risk of heart attack will be increased by over 3.4 fold. Considering the nature of the cross-sectional study in the 2015 BRFSS data, prospective studies are needed to confirm the association between MS without DM, DM without MS with heart attack.

Contributors GRY and DL designed the study and analyzed the data. GRY draft the manuscript. DL and TD revised the manuscript. All authors read and approved the final manuscript.

Funding This work was supported by Beijing Municipal Training Foundation for Highly-qualified and Technological Talents of Health System [2014-3-013] and Capital's Funds for Health Improvement and Research [2016-2-2054]. Dr. Li's and Dr. Dye's time is partly supported by the University of Rochester's Clinical and Translational Science Award (CTSA) number UL1 TR000042 and UL1 TR002001 from the National Center for Advancing Translational Sciences of the National Institutes of Health.

Competing interests None declared.

Ethics approval The 2015 BRFSS annual survey data does not include any identifiable information and is publically available from the Centers for Disease Control and Prevention website (https://www.cdc.gov/brfss/annual_data/annual_2015.html).

Data sharing statement All the data is publically available from the Centers for Disease Control and Prevention website (https://www.cdc.gov/brfss/annual_data/annual_2015.html).

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Table 1. Demographic and lifestyle characteristics among the four groups according to the presence of metabolic syndrome and diabetes

	Total	Neither DM nor MS	DM without MS	MS without DM	DM plus MS	p value
Number	332,008	237334	8416	45191	41067	
Gender						<0.01
Male, n (weighted %)	144458 (49.9%)	98983 (48.4%)	4049 (56.4%)	22377 (57.1%)	19049 (51.8%)	
Female, n (weighted %)	187550 (50.1%)	138351 (51.6%)	4367 (43.6%)	22814 (42.9%)*	22018 (48.2%)	
Age						<0.01
<45 years, n (weighted %)	67420 (36.9%)	61527 (44.7%)	944 (20.4%)	3054 (14.6%)	1895 (9.0%)	
≥45 years, n (weighted %)	264588 (63.1%)	175807 (55.3%)	7472 (79.6%)	42137 (85.4%)*	39172 (91.0%)	
Annual household income						<0.01
<15000, n (weighted %)	26368 (9.8%)	15248 (8.3%)	1009 (15.2%)	4100 (10.9%)	6011 (17.6%)	
15000-25000, n (weighted %)	42954 (15.2%)	27083 (13.6%)	1459 (21.8%)	6503 (17.3%)	7909 (22.9%)	

25000-35000, n (weighted %)	29733 (9.9%)	19853 (9.4%)	877 (11.5%)	4533 (11.0%)	4470 (12.0%)	
35000-50000, n (weighted %)	40705 (13.6%)	28453 (13.5%)	1039 (13.3%)	6103 (14.7%)	5110 (13.7%)	
>50000, n (weighted %)	144082 (51.5%)	112776 (55.2%)	2616 (38.2%)	17422 (46.1%)*	11268 (33.8%)	
Latino						<0.01
Yes, n (weighted %)	22487 (13.8%)	16018 (14.0%)	853 (19.3%)	2257 (10.3%)*	3359 (15.0%)	
No, n (weighted %)	307115 (86.2%)	219670 (86.0%)	7490 (80.7%)	42626 (89.7%)	37329 (85.0%)	
Race						<0.01
White, n (weighted %)	279446 (77.8%)	202115 (78.4%)	6730 (71.4%)	38756 (80.4%)*	31845 (72.7%)	
African America, n (weighted %)	26653 (12.4%)	16453 (11.4%)	740 (13.9%)	3815 (12.9%)	5645 (18.1%)	
America Indian, n (weighted %)	5718 (1.7%)	3673 (1.6%)	263 (3.3%)	670 (1.5%)	1112 (2.5%)	
Asian, n (weighted %)	7092 (4.8%)	5688 (5.2%)	243 (7.3%)	535 (2.5%)	626 (3.5%)	

Native Hawaiian, n (weighted %)	1872 (0.4%)	1338 (0.4%)	49 (0.5%)	213 (0.3%)	272 (0.3%)	
Other race, n (weighted %)	4058 (2.7%)	4058 (2.7%)	215 (3.5%)	647 (2.2%)	839 (2.6%)	
No preferred race, n (weighted %)	745 (0.3%)	577 (0.3%)	14 (0.1%)	60 (0.2%)	94 (0.2%)	
Multiracial but preferred race not answered, n (weighted %)	6 (0.0%)	4 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.0%)	
Education						<0.01
Did not graduate high school, n (weighted %)	21989 (11.8%)	12296 (9.7%)	917 (20.3%)	3607 (14.9%)	5169 (21.5%)	
Graduated high school, n (weighted %)	88636 (26.9%)	58399 (25.6%)	2672 (29.4%)	14028 (31.2%)	13537 (31.1%)	
Attended college or technical	90001 (31.5%)	63868 (32.0%)	2238 (28.1%)	12302 (30.3%)	11593 (30.2%)	

school, n (weighted %)						
Graduated from college or technical school, n (weighted %)	130722 (29.8%)	102289 (32.7%)	2561 (22.3%)	15185 (23.6%)*	10687 (17.2%)	
Currently smoking						<0.01
No, n (weighted %)	280808 (84.5%)	200158 (84.4%)	6944 (84.0%)	38788 (84.7%)	34918 (85.4%)	
Yes, n (weighted %)	43947 (15.5%)	31827 (15.6%)	1230 (16.0%)	5547 (15.3%)*	5343 (14.6%)	
Physical activity index						<0.01
Meet aerobic recommendations, n (weighted %)	164390 (52.8%)	124593 (55.4%)	3712 (48.2%)	20530 (47.6%)	15555 (40.8%)	
Did not meet aerobic recommendations, n (weighted	136791 (47.2%)	90370 (44.6%)	3735 (51.8%)	20831 (52.4%)*	21855 (59.2%)	

%)						
Fruit						<0.01
Consumed fruit one or more times per day, n (weighted %)	195725 (61.4%)	143690 (62.9%)	4795 (58.8%)	25173 (56.8%)	22067 (56.0%)	
Consumed fruit less than one time per day, n (weighted %)	111948 (38.6%)	76183 (37.1%)	2854 (41.2%)	16897 (43.2%)*	16014 (44.0%)	
Vegetable						<0.01
Vegetables one or more times per day, n (weighted %)	243504 (79.7%)	177711 (81.0%)	5766 (76.9%)	32262 (76.8%)	27765 (73.4%)	
Vegetables less than one time per day, n (weighted %)	58881 (20.3%)	38567 (19.0%)	1691 (23.1%)	9081 (23.2%)	9542 (26.6%)	

* Compared with DM without MS group, p<0.05

Abbreviation: DM: diabetes mellitus, MS: metabolic syndrome

Table 2. Chronic diseases among the four groups according to the presence of metabolic syndrome and diabetes

Chronic diseases	Total	Neither DM nor MS	DM without MS	MS without DM	DM plus MS	P value
Heart attack, n (weighted %)	21896 (5.2%)	8863 (2.7%)	851 (8.5%)	5310 (11.0%)*	6872 (16.1%)	<0.01
Hypertension, n (weighted %)	147655 (37.5%)	64705 (21.9%)	1411 (13.9%)	45191 (100.0%)*	36348 (87.6%)	<0.01
Dyslipidemia, n (weighted %)	140653 (36.6%)	62526 (22.2%)	1102 (12.2%)	45191 (100.0%)*	31834 (77.6%)	<0.01
BMI ≥ 25.0 kg/m^2, n (weighted %)	223112 (67.2%)	135589 (59.1%)	4551 (56.8%)	45191 (100.0%)*	37781 (92.3%)	<0.01
Stroke, n (weighted %)	15013 (3.6%)	6910 (2.2%)	544 (4.8%)	3228 (6.6%)*	4331 (9.7%)	<0.01
Depression, n (weighted %)	64290 (18.3%)	40520 (16.1%)	1574 (16.4%)	10687 (24.1%)*	11509 (27.7%)	<0.01

* Compared with DM without MS group, p<0.05

Abbreviation: DM: diabetes mellitus, MS: metabolic syndrome

Table 3. The odds ratio and 95% confidence intervals of DM and MS related to heart attack in the hierarchy logistic regression analysis

	Odds Ratio	95% confidence intervals	p value
Model 1 (n=332,008)			
DM without MS	3.275	2.812-3.815	<0.01
MS without DM	4.366	4.055-4.700	<0.01
DM plus MS	6.787	6.331-7.275	<0.01
Model 2 (n=319,712)			
DM without MS	2.097	1.768-2.486	<0.01
MS without DM	2.852	2.637-3.084	<0.01
DM plus MS	4.058	3.756-4.384	<0.01
Model 3 (n=282,332)			
DM without MS	2.116	1.748-2.562	<0.01
MS without DM	2.820	2.594-3.067	<0.01
DM plus MS	3.987	3.660-4.344	<0.01
Model 4 (n=280,977)			
DM without MS	2.089	1.716-2.543	<0.01
MS without DM	2.575	2.363-2.806	<0.01
DM plus MS	3.451	3.156-3.772	<0.01

Model 1: unadjusted

Model 2: adjusted for gender, age (45 years or not), education, current smoking, race

Model 3: adjusted for gender, age (45 years or not), education, current smoking, race, physical activity index, fruits consumed one or more times per day, vegetable consumed one or more times per day

Model 4 adjusted for gender, age (45 years or not), education, current smoking, race, physical activity index, fruits consumed one or more times per day, vegetable consumed one or more times per day, stroke, and depression

Abbreviation: DM: diabetes mellitus, MS: metabolic syndrome

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-7*
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	NA
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	7-8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	7-8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8-11
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-10
		(b) Indicate number of participants with missing data for each variable of interest	8-10
Outcome data	15*	Report numbers of outcome events or summary measures	9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-11

		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Association between diabetes, metabolic syndrome and heart attack in U.S. adults: a cross-sectional analysis using the Behavioral Risk Factor Surveillance System 2015

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-022990.R2
Article Type:	Original research
Date Submitted by the Author:	18-Apr-2019
Complete List of Authors:	Yang, Guang-Ran; Beijing Tongren Hospital, Capital Medical University, Department of Endocrinology; School of Medicine and Dentistry, University of Rochester, Clinical and Translational Science Institute Dye, Timothy ; School of Medicine and Dentistry, University of Rochester, Clinical and Translational Science Institute Li, Dongmei; School of Medicine and Dentistry, University of Rochester, Clinical and Translational Science Institute
Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Diabetes and endocrinology
Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, metabolic syndrome, heart attack

Association between diabetes, metabolic syndrome and heart attack in U.S. adults: a cross-sectional analysis using the Behavioral Risk Factor Surveillance System 2015

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Abstract:

Objectives: Diabetes mellitus (DM) and metabolic syndrome (MS) are both associated with heart attack. Evidence regarding which condition - MS or DM - is better associated with heart attack, however, is limited. The purpose of this study is to examine DM and MS, and their comparative associations with heart attack, using the 2015 Behavioral Risk Factor Surveillance System (BRFSS). **Design:** Cross-sectional study. **Methods:** A total of 332,008 subjects aged over 18-year were included in the analysis. All subjects were classified into four groups based on their DM and MS status: neither DM nor MS, DM without MS, MS without DM, and both DM and MS. Hierarchical logistic regressions were used to examine the effect of DM and MS on heart attack using the neither DM nor MS group as the reference. **Results**: Differences in weighted frequency distributions of gender, age category (over 45 years or not), smoking status, education, race, physical activity, and daily vegetables and fruits consumption were significantly different across the four groups ($p<0.05$). The weighted prevalence of heart attack was 5.2% for neither DM nor MS group, 8.5% for DM without MS group, 11.0% for MS without DM group and 16.1% for both DM and MS group. The weighted prevalence of heart attack in MS without DM group was significantly higher than that in the DM without MS group ($p<0.01$). After adjusting for confounding variables, DM without MS and MS without DM were both found to be independently associated with heart attack compared with those without DM nor MS (DM without MS, odds ratio=2.09, MS without DM, odds ratio=2.58, p all <0.01). **Conclusion:** The BRFSS 2015 data indicated that MS without DM and DM without MS had comparable effects on heart attack, and the odds of risk are doubled than U.S.

adults with neither DM nor MS.

Key Words: Metabolic syndrome, Diabetes, Heart attack

Strengths and limitations of this study

► BRFSS is a routine health-related telephone survey assessing a range of conditions.

►Weighted frequency distributions and summary statistics were used to describe the sample characteristics in each group.

►Limitation: chronic diseases were self-reported by answers.

Background

Coronary heart disease (CHD) is the leading cause of morbidity and mortality worldwide. CHD alone caused approximately 1 of every 7 deaths in the U.S. with 366,801 deaths due to CHD in 2015. [1] Each year, around 660,000 Americans are estimated to have a new heart attack (defined as first hospitalized heart attack or CHD death) and around 305,000 Americans have a recurrent attack. Furthermore, an additional 160,000 silent heart attacks are estimated to occur each year. [2]

Diabetes mellitus (DM), especially type 2 diabetes, is associated with clustered risk factors for CHD. Among adults with DM, the prevalence of hypertension, hypercholesterolemia, and obesity is ranged 75% to 85%, 70% to 80%, and 60% to 70%, respectively.[2-4] Patients with DM had higher morbidity and mortality of CHD, including heart attack. In a subgroup analysis of the FRISC II trial, diabetic patients with unstable coronary artery disease had a significantly higher rate of heart attack than non-diabetic patients.[5]

Metabolic syndrome (MS) is a multi-component risk factor for CHD that includes a cluster of individual cardiometabolic risk factors related to abdominal obesity and insulin resistance. Clinically, MS is a useful entity for communicating the nature of lifestyle-related cardiometabolic risk for both patients and clinicians.[2] MS is a risk factor for heart attack in both women and men, from all regions and ethnic groups worldwide.[6]

DM and MS are both associated with heart attack. Evidence regarding whether MS without DM has stronger association with heart attack than DM without MS, however, are limited. The ongoing Behavioral Risk Factor Surveillance System (BRFSS) assesses chronic conditions, such as DM, hypertension, hypercholesterolemia, and heart attack.[7] The objective of the present study was to determine whether risk of heart attack differs in people with DM without MS and MS without DM using the 2015 BRFSS database.

Methods

Participants

BRFSS is the nation's premier system of health-related telephone surveys that collect state data about U.S. residents regarding their health-related risk behaviors, chronic health conditions, and use of preventive services. BRFSS completes more than 400,000 adult interviews each year, making it the largest continuously conducted health survey system in the world.[8] In 2015, 50 states, the District of Columbia, Guam, and Puerto Rico collected data from interviews conducted both by landline telephone and cellular telephone. Questions used in this study in 2015 BRFSS survey include heart attack history, diabetes history, physical activity, dyslipidemia, hypertension awareness, chronic health conditions, alcohol consumption, fruits and vegetables, and currently smoking.[9]

There were 441,456 subjects in the 2015 BRFSS survey. The response rate from cellular telephone is 47.2%, which is slightly lower than that from landline telephone (48.2%).[10] Unknown responses or non-responses were coded as missing in questions included in the study, and there were 332,008 subjects included in the analysis after removing missing values.

Measures

Socio-demographic variables, such as age (18-44 year or 45+ year), race,

ethnicity (Hispanic, Latino/a, or Spanish origin or no), education, smoking status (current smoker or not) and annual household income were categorized according to the original variables.

Respondents' lifestyles were assessed by questions on their physical activity, fruits, and vegetables consumption. Fruit consumption was categorized as "consumed fruit one or more times per day" or "consumed fruit less than one time per day". Vegetable consumption was categorized as "consumed vegetables one or more times per day" or "consumed vegetables one or more times per day". Physical activity index was categorized as whether "meet aerobic recommendations" or not.

In the 2015 BRFSS, chronic diseases were self-reported by answers to questions on chronic diseases history. Heart attack was defined as yes to the question "has a doctor, nurse, or other health professional ever told you had a heart attack, also called a myocardial infarction". Diabetes was defined by a yes answer to the question "has a doctor, nurse, or other health professional ever told you have diabetes". Respondents with pre-diabetes, borderline diabetes, or gestational diabetes were excluded. Body mass index (BMI) was calculated by self-reported height and weight. Similarly, hypertension was defined as a yes answer to the question "have you ever been told by a doctor, nurse or other health professional that you have high blood pressure". Borderline hypertension, pre-hypertension, and gestational hypertension were all excluded from the study. Dyslipidemia was defined as a yes answer to the question "have you ever been told by a doctor, nurse or other health professional that your blood cholesterol is high". Stroke was defined as yes to the question of "ever told you had a stroke". Depression was a yes answer to the question of “ever told you that you have a depressive disorder, including depression, major depression, dysthymia, or minor”.

MS was diagnosed based on the ATP-III definition.[11] The components of MS were abdominal obesity (waist circumference >40 inches in men or >35 inches in women), triglycerides ≥150 mg/dl, high density lipoprotein cholesterol <40 mg/dl in men or <50mg/dl in women, blood pressure ≥130/85 mmHg, and fasting glucose ≥110 mg/dl. As these were no data of waist circumference, blood pressure, fasting glucose and lipid profile. The diagnose of MS was revised based on the questions in the BRFSS. The revised components of MS included diabetes, hypertension, BMI ≥25.0 kg/m^2, and dyslipidemia. Respondents who had at least three components were regarded as having MS. In this study, the “MS without DM” group means that respondents had the other three components of MS excluding diabetes.

Statistical analysis

Each record in the 2015 BRFSS data was weighted using raking weighting methodology [12]. Raking adjusted the BRFSS data to allow underrepresented groups in the sample to be more accurately represented in the final data set. Final weight was assigned to each respondent. All statistical analysis take the complex sampling design into account through incorporate the final weight in the data analysis. Weighted percentages of respondents who ever had heart attack were calculated.

Weighted Chi-square tests was performed to determine respondents' characteristic differences across groups. Weighted hierarchical logistic regression analysis was applied to investigate in greater depth. Odds ratios

(OR) and corresponding 95% confidence intervals (CIs) were derived from weighted hierarchical logistic regression analysis. Survey related procedures in SAS v9.4 (SAS Institute Inc., Cary, NC) were used for all data analysis. The significance level was set at *p*<0.05, and all tests were two-sided.

Patient and public involvement

This study was an analysis of the 2015 BRFSS database. The database was downloaded via the U.S. Centers for Disease Control and Prevention website.

Results

Demographic Characteristics

There were 332,008 respondents involved in this study. All respondents were categorized into four groups as follows: neither DM nor MS, DM without MS (having DM without MS), MS without DM (having MS without DM), and DM plus MS. There were 237,334 respondents with neither DM nor MS, 45,191 respondents with DM without MS, 8,416 respondents with MS without DM and 41,067 respondents with both DM and MS (Table 1). Differences in the weighted percentages of gender, age category, smoking status, education level, race, ethnicity, and annual household income were statistically significant among the four groups (p<0.01). In addition, the above characteristics were significantly different between DM without MS and MS without DM group (p<0.001). In both MS and DM group, 91% were aged over 45 years, and 21.5% did not graduate high school, which were higher than the other three groups. Moreover, 17.6% of respondents in the MS and DM group had annual household incomes lower than $15,000 and the low income percentage is much higher than the other three groups. Less people were white in the DM without MS group (71.4%) compared with that in the MS without DM group (80.4%). However, more respondents were Hispanic, Latino, or Spanish origin in the DM without MS group (19.3%) than in the MS without DM group (10.3%, $p<0.001$), and more respondents were current smokers in the DM without MS group (16.0%) compared with the MS without DM group (15.3%, $p<0.001$, Table 1).

Lifestyle

Lifestyle measurements were also compared in the four groups (Table 1). The weighted percentage of physical activity index, daily fruit consumption and vegetable consumption were all significantly different across the four groups. The physical activity index in the DM without MS and MS without DM groups was 48.2%, 47.6%, respectively ($p<0.001$). The DM and MS group had the least weighted percentage of respondents whose physical activity met the aerobic recommendations. The weighted percentage of respondents who consumed fruit one or more times per day was higher in the DM without MS group, compared to that in the MS without DM group (58.8% vs 56.8%, $p<0.001$). However, daily vegetable consumption was similar between the DM without MS and the MS without DM groups (76.9% vs 76.8%, $p=0.019$). In the DM and MS group, the weighted percentage of daily vegetable consumption is the least among the four groups (73.4%).

MS components and chronic diseases

Among the 332,008 respondents, 21,896 respondents had heart attack, accounting for the weighted prevalence of 5.2%. MS without DM had higher weighted prevalence of heart attack than that in DM without MS (11.0%, 8.5%, respectively, p<0.001). The weighted prevalence of heart attack in the DM plus MS group was the highest (16.1%, Table 2). The overall weighted prevalence of dyslipidemia, hypertension, diabetes, and BMI ≥25.0 kg/m^2 was 36.6%, 37.5%, 13.2%, and 67.2%, respectively (Table 2). In the DM without MS group, 83% respondents had one component of MS other than DM, with 17% people having no other components of MS besides DM.

The overall weighted prevalence of stroke was 3.6%. The weighted prevalence of stroke were significantly different between the DM without MS and MS without DM groups (4.8% vs 6.6%, p<0.001). The weighted prevalence of stroke in the DM plus MS group was the highest among the four groups (9.7%). The overall weighted prevalence of depression was 18.2%. Compared with DM without MS, MS without DM had significantly higher weighted prevalence of depression (16.4% vs 24.1%, p<0.001). The highest weighted prevalence of depression was observed in the DM plus MS group (27.7%).

Logistic regression

Logistic regression was conducted to compare the difference among the four groups in their association with heart attack, using the neither DM nor MS group as the reference (Table 3). Results from unadjusted logistic regression analysis showed that both DM without MS (OR=3.28, 95% CI=2.81-3.82) and MS without DM (OR=4.37, 95% CI=4.06-4.70) groups had significantly elevated odds of heart attack than neither DM nor MS group. The DM plus MS group had the highest odds of heart attack among the three groups (OR=6.79, 95% CI=6.33-7.28)

To identify an independent relationship between DM, MS and heart attack, hierarchical logistic regression analysis was performed. After adjusting for confounders (gender, age, education, smoking, race, physical activity index, daily fruit consumption, daily vegetable consumption, stroke, and depression) DM without MS and MS without DM were found to have independently increased odds of heart attack compared with the neither DM nor MS group (DM without MS, adjusted OR=2.09, 95% CI =1.72-2.54, MS without DM, adjusted OR =2.58, 95% CI =2.36-2.81). The DM plus MS group had the highest odds of heart attack (adjusted OR=3.45, 95% CI =3.16-3.77, p all <0.001, Table 3).

Discussion

In the 2015 BRFSS data, respondents with MS without DM and DM without MS were both associated with elevated risk of heart attack and the amount of increase is doubled compare to respondents with neither DM nor MS. MS did not appear to be a greater odds for heart attack than DM from our analysis results. MS combined with DM increased more risk of heart attack by over 3.4 fold compared with respondents with neither DM nor MS.

MS is a cluster of risk factors contributing to the pathogenesis of atherosclerosis.[13] There are several definitions of MS and different definitions of MS had different components.[14-16] Many large-scale clinical trials and meta-analyses have reported that the presence of MS is a strong predictor for heart attack in many different populations.[6, 17-19] In the INTERHEART case-control study involving 26,903 subjects from 52 countries, MS was associated with an increased risk of heart attack, both using the WHO definition (OR=2.69) and the IDF definition (OR=2.20) .The direction of associations were similar across all regions and ethnic groups.[6] A large family study in Finland and Sweden of 4,483 subjects also identified the association between MS and an increased risk of heart attack in all subjects using the WHO definition.[19] Similar results were observed when the 2001 NCEP and 2004 revised NCEP definitions were used.[17, 18] In our analysis, the association between MS and heart attack was consistent. MS, regardless of its definition, was associated with heart attack.

DM is one of the components in most definitions of MS. The risk for cardiovascular disease (CVD) is 2-8 fold higher in the diabetic population than that in the non-diabetic population of a similar age, sex and ethnicity and CVD is the leading cause of morbidity and mortality among patients with type 2 diabetes.[20-22]

Previous researchers have investigated the effects of DM on heart attack. Consistent with our findings, it has been reported that DM was associated with an increased heart attack risk in both men and women.[23] A cohort study using the UK General Practice Research Database showed a much larger relative risk of heart attack in DM.[24]

Both DM and MS were associated with an increased risk of heart attack. However, evidence regarding whether MS without DM is better than DM without MS for evaluating heart attack are limited. There were studies to evaluate the relationship between MS and DM on CVD events. Results from different studies regarding differences in CVD events between DM and MS were conflicting. The Ansung-Ansan cohort study showed that there was no difference in the risk of incident CVD between individuals with DM without MS and MS without DM.[25] Yet, in the REACH registry, presence of newly detected DM but not MS was associated with an increased risk of CVD events.[26] Besides the difference in population characteristics in these studies, the sample size and the definitions of CVD maybe affect the results.

There were fewer studies conducted in U.S. adults to compare the effects of MS and DM on heart attack. In the logistic analysis of this study, MS without DM and DM without MS were found to have similar odds of heart attack. This showed that MS and DM may have similar effects on heart attack in the U.S. adults, which was different from the results of previous study in U.S. population.[27] Our results indicated that to prevent heart attack or CVD, even a diabetic person does not meet the criteria of MS, much more attention should be paid to control metabolic abnormalities.

DM typically co-presents with at least one metabolic abnormality. In our analysis, the weighted prevalence of hypertension, dyslipidemia and overweight in DM without MS group was 13.9%, 12.2% and 56.8%, respectively. Of the respondents with DM, 83% had at least one or more components of MS other than DM. As shown in a population-based cohort study, DM with only one component of MS had more than twofold higher CVD risk than those with DM only.[28] These associations may be helpful to explain in this study why DM and MS had similar effects on heart attack. Further studies were needed to evaluate the association between MS without DM, DM without MS with heart attack.

There were some limitations in our study. First, the definition of MS was revised according to the contents of 2015 BRFSS. MS was diagnosed based on the ATP-III definition.[11] The components of MS were diabetes, hypertension, BMI ≥25.0 kg/m^2, and dyslipidemia. Respondents who had at least three components were regarded as having MS. According to the ATP-III definition, central obesity was diagnosed basing on waist circumference. We used BMI ≥25.0 kg/m^2 to classify individuals because waist circumference was not available. The MS definition from the American College of Endocrinology recommends that BMI >25kg/m^2 or a waist circumference >40 inches for men, >35 inches for women was regarded as obesity. [29] Therefore in the present study, we used BMI ≥25 kg/m^2 as a component of MS. Secondly, in the 2015 BRFSS, there were no data on triglyceride and high-density lipoprotein. Dyslipidemia was assessed by whether respondents had ever been told their blood cholesterol was high. Thirdly, the self-reported nature of the cross-sectional study may lead to underestimate the actual prevalence of heart attack. In this study, 13.2% respondents had diabetes. However, some diabetic respondents may have silent heart attack without any symptoms. In the BRFSS survey the data of fatal heart attack are not included, which may also underestimate the actual prevalence of heart attack. Fourthly, gestational diabetes and pre-diabetes were excluded. These two conditions are both important risk factors for DM that has been excluded from the study. In this study, 24.8% subjects in the 2015 BRFSS data with unknown responses or non-responses in questions included in the study were excluded from the analysis under the assumption of missing completely at random, which might result in some bias of the results when the assumption is not valid.

In conclusion, even though the weighted percentage of heart attack in MS without DM was higher than that in DM without MS, MS and DM had similar effects on heart attack, which could double the risk of heart attack. Furthermore, when MS is combined with DM, the risk of heart attack will be increased by over 3.4 fold. Considering the nature of the cross-sectional study in the 2015 BRFSS data, prospective studies are needed to confirm the association between MS without DM, DM without MS with heart attack.

Contributors GRY and DL designed the study and analyzed the data. GRY draft the manuscript. DL and TD revised the manuscript. All authors read and approved the final manuscript.

Funding This work was supported by Beijing Municipal Training Foundation for Highly-qualified and Technological Talents of Health System [2014-3-013] and Capital's Funds for Health Improvement and Research [2016-2-2054]. Dr. Li's and Dr. Dye's time is partly supported by the University of Rochester's Clinical and Translational Science Award (CTSA) number UL1 TR000042 and UL1 TR002001 from the National Center for Advancing Translational Sciences of the National Institutes of Health.

Competing interests None declared.

Ethics approval The 2015 BRFSS annual survey data does not include any identifiable information and is publically available from the Centers for Disease Control and Prevention website (https://www.cdc.gov/brfss/annual_data/annual_2015.html).

Data sharing statement All the data is publically available from the Centers for Disease Control and Prevention website (https://www.cdc.gov/brfss/annual_data/annual_2015.html).

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Table 1. Demographic and lifestyle characteristics among the four groups according to the presence of metabolic syndrome and diabetes

	Total	Neither DM nor MS	DM without MS	MS without DM	DM plus MS	p value
Number	332,008	237,334	8,416	45,191	41,067	
Gender						<0.01
Male, n (weighted %)	144,458 (49.9%)	98,983 (48.4%)	4,049 (56.4%)	22,377 (57.1%)	19,049 (51.8%)	
Female, n (weighted %)	187,550 (50.1%)	138,351 (51.6%)	4,367 (43.6%)	22,814 (42.9%)*	22,018 (48.2%)	
Age						<0.01
<45 years, n (weighted %)	67,420 (36.9%)	61,527 (44.7%)	944 (20.4%)	3,054 (14.6%)	1,895 (9.0%)	
≥45 years, n (weighted %)	264,588 (63.1%)	175,807 (55.3%)	7,472 (79.6%)	42,137 (85.4%)*	39,172 (91.0%)	
Annual household income						<0.01
<15000, n (weighted %)	26,368 (9.8%)	15,248 (8.3%)	1,009 (15.2%)	4,100 (10.9%)	6,011 (17.6%)	
15000-25000, n (weighted %)	42,954 (15.2%)	27,083 (13.6%)	1,459 (21.8%)	6,503 (17.3%)	7,909 (22.9%)	
25000-35000, n (weighted %)	29,733 (9.9%)	19,853 (9.4%)	877 (11.5%)	4,533 (11.0%)	4,470 (12.0%)	

35000-50000, n (weighted %)	40,705 (13.6%)	28,453 (13.5%)	1,039 (13.3%)	6,103 (14.7%)	5,110 (13.7%)	
>50000, n (weighted %)	144,082 (51.5%)	112,776 (55.2%)	2,616 (38.2%)	17,422 (46.1%)*	11,268 (33.8%)	
Ethnicity (Hispanic, Latino/a, or Spanish origin or no),						<0.01
Yes, n (weighted %)	22,487 (13.8%)	16,018 (14.0%)	853 (19.3%)	2,257 (10.3%)*	3,359 (15.0%)	
No, n (weighted %)	307,115 (86.2%)	219,670 (86.0%)	7,490 (80.7%)	42,626 (89.7%)	37,329 (85.0%)	
Race						<0.01
White, n (weighted %)	279,446 (77.8%)	202,115 (78.4%)	6,730 (71.4%)	38,756 (80.4%)*	31,845 (72.7%)	
African America, n (weighted %)	26,653 (12.4%)	16,453 (11.4%)	740 (13.9%)	3,815 (12.9%)	5,645 (18.1%)	
America Indian, n (weighted %)	5,718 (1.7%)	3,673 (1.6%)	263 (3.3%)	670 (1.5%)	1,112 (2.5%)	
Asian, n (weighted %)	7,092 (4.8%)	5,688 (5.2%)	243 (7.3%)	535 (2.5%)	626 (3.5%)	
Native Hawaiian, n (weighted %)	1,872 (0.4%)	1,338 (0.4%)	49 (0.5%)	213 (0.3%)	272 (0.3%)	
Other race, n (weighted %)	4,058 (2.7%)	4,058 (2.7%)	215 (3.5%)	647 (2.2%)	839 (2.6%)	
No preferred race, n	745 (0.3%)	577 (0.3%)	14 (0.1%)	60 (0.2%)	94 (0.2%)	

(weighted %)						
Multiracial but preferred race not answered, n (weighted %)	6 (0.0%)	4 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.0%)	
Education						<0.01
Did not graduate high school, n (weighted %)	21,989 (11.8%)	12,296 (9.7%)	917 (20.3%)	3,607 (14.9%)	5,169 (21.5%)	
Graduated high school, n (weighted %)	88,636 (26.9%)	58,399 (25.6%)	2,672 (29.4%)	14,028 (31.2%)	13,537 (31.1%)	
Attended college or technical school, n (weighted %)	90,001 (31.5%)	63,868 (32.0%)	2,238 (28.1%)	12,302 (30.3%)	11,593 (30.2%)	
Graduated from college or technical school, n (weighted %)	130,722 (29.8%)	102,289 (32.7%)	2,561 (22.3%)	15,185 (23.6%)*	10,687 (17.2%)	
Currently smoking						<0.01
No, n (weighted %)	280,808 (84.5%)	200,158 (84.4%)	6,944 (84.0%)	38,788 (84.7%)	34,918 (85.4%)	
Yes, n (weighted %)	43,947 (15.5%)	31,827 (15.6%)	1,230 (16.0%)	5,547 (15.3%)*	5,343 (14.6%)	
Physical activity index						<0.01
Meet aerobic	164,390 (52.8%)	124,593 (55.4%)	3,712 (48.2%)	20,530 (47.6%)	15,555 (40.8%)	

recommendations, n (weighted %)						
Did not meet aerobic recommendations, n (weighted %)	136,791 (47.2%)	90,370 (44.6%)	3,735 (51.8%)	20,831 (52.4%)*	21,855 (59.2%)	
Fruit						<0.01
Consumed fruit one or more times per day, n (weighted %)	195,725 (61.4%)	143,690 (62.9%)	4,795 (58.8%)	25,173 (56.8%)	22,067 (56.0%)	
Consumed fruit less than one time per day, n (weighted %)	111,948 (38.6%)	76,183 (37.1%)	2,854 (41.2%)	16,897 (43.2%)*	16,014 (44.0%)	
Vegetable						<0.01
Vegetables one or more times per day, n (weighted %)	243,504 (79.7%)	177,711 (81.0%)	5,766 (76.9%)	32,262 (76.8%)	27,765 (73.4%)	
Vegetables less than one time per day, n (weighted %)	58,881 (20.3%)	38,567 (19.0%)	1,691 (23.1%)	9,081 (23.2%)	9,542 (26.6%)	

* Compared with DM without MS group, $p<0.05$

Abbreviation: DM: diabetes mellitus, MS: metabolic syndrome

Table 2. Chronic diseases among the four groups according to the presence of metabolic syndrome and diabetes

Chronic diseases	Total	Neither DM nor MS	DM without MS	MS without DM	DM plus MS	P value
Heart attack, n (weighted %)	21,896 (5.2%)	8,863 (2.7%)	851 (8.5%)	5,310 (11.0%)*	6,872 (16.1%)	<0.01
Hypertension, n (weighted %)	147,655 (37.5%)	64,705 (21.9%)	1,411 (13.9%)	45,191 (100.0%)*	36,348 (87.6%)	<0.01
Dyslipidemia, n (weighted %)	140,653 (36.6%)	62,526 (22.2%)	1,102 (12.2%)	45,191 (100.0%)*	31,834 (77.6%)	<0.01
BMI ≥ 25.0 kg/m², n (weighted %)	223,112 (67.2%)	135,589 (59.1%)	4,551 (56.8%)	45,191 (100.0%)*	37,781 (92.3%)	<0.01
Stroke, n (weighted %)	15,013 (3.6%)	6,910 (2.2%)	544 (4.8%)	3,228 (6.6%)*	4,331 (9.7%)	<0.01
Depression, n (weighted %)	64,290 (18.3%)	40,520 (16.1%)	1,574 (16.4%)	10,687 (24.1%)*	11,509 (27.7%)	<0.01

* Compared with DM without MS group, p<0.05

Abbreviation: DM: diabetes mellitus, MS: metabolic syndrome

Table 3. The odds ratio and 95% confidence intervals of DM and MS related to heart attack in the hierarchy logistic regression analysis

	Odds Ratio	95% confidence intervals	p value
Model 1 (n=332,008)			
DM without MS	3.28	2.81-3.82	<0.01
MS without DM	4.37	4.06-4.70	<0.01
DM plus MS	6.79	6.33-7.28	<0.01
Model 2 (n=319,712)			
DM without MS	2.10	1.77-2.49	<0.01
MS without DM	2.85	2.64-3.09	<0.01
DM plus MS	4.06	3.76-4.38	<0.01
Model 3 (n=282,332)			
DM without MS	2.12	1.75-2.56	<0.01
MS without DM	2.82	2.59-3.07	<0.01
DM plus MS	3.99	3.66-4.34	<0.01
Model 4 (n=280,977)			
DM without MS	2.09	1.72-2.54	<0.01
MS without DM	2.58	2.36-2.81	<0.01
DM plus MS	3.45	3.16-3.77	<0.01

Model 1: unadjusted
Model 2: adjusted for gender, age (45 years or not), education, current smoking, race
Model 3: adjusted for gender, age (45 years or not), education, current smoking, race, physical activity index, fruits consumed one or more times per day, vegetable consumed one or more times per day
Model 4 adjusted for gender, age (45 years or not), education, current smoking, race, physical activity index, fruits consumed one or more times per day, vegetable consumed one or more times per day, stroke, and depression
Abbreviation: DM: diabetes mellitus, MS: metabolic syndrome

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-7*
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	NA
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	7-8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8-11
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-10
		(b) Indicate number of participants with missing data for each variable of interest	8-10
Outcome data	15*	Report numbers of outcome events or summary measures	9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-11

		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	13-15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Association between diabetes, metabolic syndrome and heart attack in U.S. adults: a cross-sectional analysis using the Behavioral Risk Factor Surveillance System 2015

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-022990.R3
Article Type:	Original research
Date Submitted by the Author:	15-Jul-2019
Complete List of Authors:	Yang, Guang-Ran; Beijing Tongren Hospital, Capital Medical University, Department of Endocrinology; School of Medicine and Dentistry, University of Rochester, Clinical and Translational Science Institute Dye, Timothy ; School of Medicine and Dentistry, University of Rochester, Clinical and Translational Science Institute Li, Dongmei; School of Medicine and Dentistry, University of Rochester, Clinical and Translational Science Institute
Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Diabetes and endocrinology
Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, metabolic syndrome, heart attack

Association between diabetes, metabolic syndrome and heart attack in U.S. adults: a cross-sectional analysis using the Behavioral Risk Factor Surveillance System 2015

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Abstract:

Objectives: Diabetes mellitus (DM) and metabolic syndrome (MS) are both associated with heart attack. Evidence regarding which condition - MS or DM - is better associated with heart attack, however, is limited. The purpose of this study is to examine DM and MS, and their comparative associations with heart attack, using the 2015 Behavioral Risk Factor Surveillance System (BRFSS). **Design:** Cross-sectional study. **Methods:** A total of 332,008 subjects aged over 18-year were included in the analysis. All subjects were classified into four groups based on their DM and MS status: neither DM nor MS, DM without MS, MS without DM, and both DM and MS. A weighted hierarchical logistic regression was used to examine the difference between the four groups in their association with the risk of a heart attack. **Results**: Differences in weighted frequency distributions of gender, age category (over 45 years or not), smoking status, education, race, physical activity, and daily vegetable and fruit consumption were significantly different across the four groups ($p<0.05$). The weighted prevalence of heart attack was 5.2% for neither DM nor MS group, 8.5% for DM without MS group, 11.0% for MS without DM group and 16.1% for both DM and MS group. The weighted prevalence of heart attack in MS without DM group was significantly higher than that in the DM without MS group ($p<0.01$). After adjusting for confounding variables, DM without MS and MS without DM were both found to be independently associated with heart attack compared with those without DM nor MS (DM without MS, odds ratio=2.09, MS without DM, odds ratio=2.58, p all <0.01). **Conclusion:** The BRFSS 2015 data indicated that MS without DM and DM without MS had comparable effects on heart attack, and the odds of risk are

doubled than U.S. adults with neither DM nor MS.

Key Words: Metabolic syndrome, Diabetes, Heart attack

Strengths and limitations of this study

► BRFSS is a routine health-related telephone survey assessing a range of conditions.

►Weighted frequency distributions and summary statistics were used to describe the sample characteristics in each group.

►Limitation: chronic diseases were self-reported by answers.

Background

Coronary heart disease (CHD) is the leading cause of morbidity and mortality worldwide. CHD alone caused approximately 1 of every 7 deaths in the U.S. with 366,801 deaths due to CHD in 2015. [1] Each year, around 660,000 Americans are estimated to have a new heart attack (defined as first hospitalized heart attack or CHD death) and around 305,000 Americans have a recurrent attack. Furthermore, an additional 160,000 silent heart attacks are estimated to occur each year. [2]

Diabetes mellitus (DM), especially type 2 diabetes, is associated with clustered risk factors for CHD. Among adults with DM, the prevalence of hypertension, hypercholesterolemia, and obesity is ranged 75% to 85%, 70% to 80%, and 60% to 70%, respectively.[2-4] Patients with DM had higher morbidity and mortality of CHD, including heart attack. In a subgroup analysis of the FRISC II trial, diabetic patients with unstable coronary artery disease had a significantly higher rate of heart attack than non-diabetic patients.[5]

Metabolic syndrome (MS) is a multi-component risk factor for CHD that includes a cluster of individual cardiometabolic risk factors related to abdominal obesity and insulin resistance. Clinically, MS is a useful entity for communicating the nature of lifestyle-related cardiometabolic risk for both patients and clinicians.[2] MS is a risk factor for heart attack in both women and men, from all regions and ethnic groups worldwide.[6]

DM and MS are both associated with heart attack. Evidence regarding whether MS without DM has stronger association with heart attack than DM without MS, however, is limited. The ongoing Behavioral Risk Factor Surveillance System (BRFSS) assesses chronic conditions, such as DM, hypertension, hypercholesterolemia, and heart attack.[7] The objective of the present study was to determine whether the risk of heart attack differs in people with DM without MS and MS without DM using the 2015 BRFSS database.

Methods

Participants

BRFSS is the nation's premier system of health-related telephone surveys that collect state data about U.S. residents regarding their health-related risk behaviors, chronic health conditions, and use of preventive services. BRFSS completes more than 400,000 adult interviews each year, making it the largest continuously conducted health survey system in the world.[8] In 2015, 50 states, the District of Columbia, Guam, and Puerto Rico collected data from interviews conducted both by landline telephone and cellular telephone. Questions used in this study in 2015 BRFSS survey include heart attack history, diabetes history, physical activity, dyslipidemia, hypertension awareness, chronic health conditions, alcohol consumption, fruits and vegetables, and currently smoking.[9]

There were 441,456 subjects in the 2015 BRFSS survey. The response rate from cellular telephone is 47.2%, which is slightly lower than that from landline telephone (48.2%).[10] Unknown responses or non-responses were coded as missing in questions included in the study, and there were 332,008 subjects included in the analysis after removing missing values.

Measures

Socio-demographic variables, such as age (18-44 year or 45+ year), race, ethnicity (Hispanic, Latino/a, or Spanish origin or no), education, smoking status (current smoker or not) and annual household income were categorized according to the original variables.

Respondents' lifestyles were assessed by questions on their physical activity, fruit, and vegetable consumption. Fruit consumption was categorized as "consumed fruit one or more times per day" or "consumed fruit less than one time per day". Vegetable consumption was categorized as "consumed vegetables one or more times per day" or "consumed vegetables one or more times per day". Physical activity index was categorized as whether "meet aerobic recommendations" or not.

In the 2015 BRFSS, chronic diseases were self-reported by answers to questions on chronic diseases history. Heart attack was defined as yes to the question "has a doctor, nurse, or other health professional ever told you had a heart attack, also called a myocardial infarction". Diabetes was defined by a yes answer to the question "has a doctor, nurse, or other health professional ever told you have diabetes". Respondents with pre-diabetes, borderline diabetes, or gestational diabetes were excluded. Body mass index (BMI) was calculated by self-reported height and weight. Similarly, hypertension was defined as a yes answer to the question "have you ever been told by a doctor, nurse or other health professional that you have high blood pressure". Borderline hypertension, pre-hypertension, and gestational hypertension were all excluded from the study. Dyslipidemia was defined as a yes answer to the question "have you ever been told by a doctor, nurse or other health professional that your blood cholesterol is high". Stroke was defined as yes to the question of “ever told you had a stroke”. Depression was a yes answer to the question of “ever told you that you have a depressive disorder, including depression, major depression, dysthymia, or minor”.

MS was diagnosed based on the ATP-III definition.[11] The components of MS were abdominal obesity (waist circumference >40 inches in men or >35 inches in women), triglycerides ≥150 mg/dl, high density lipoprotein cholesterol <40 mg/dl in men or <50mg/dl in women, blood pressure ≥130/85 mmHg, and fasting glucose ≥110 mg/dl. As these was no available data on waist circumference, blood pressure, fasting glucose and lipid profile. The diagnose of MS was revised based on the questions in the BRFSS. The revised components of MS included diabetes, hypertension, BMI ≥25.0 kg/m^2, and dyslipidemia. Respondents who had at least three components were regarded as having MS. In this study, the “MS without DM” group means that respondents had the other three components of MS excluding diabetes.

Statistical analysis

Each record in the 2015 BRFSS data was weighted using raking weighting methodology [12]. Raking adjusted the BRFSS data to allow underrepresented groups in the sample to be more accurately represented in the final data set. Final weights were assigned to each respondent. All statistical analyses and prevalence estimates have been weighted. Weighted percentages of respondents who ever had heart attack were calculated.

Weighted Chi-square tests was performed to determine respondents’ characteristic differences across groups. A weighted hierarchical logistic regression was used to examine the difference between the four groups in their association with the risk of a heart attack. Odds ratios (OR) and corresponding 95% confidence intervals (CIs) were derived from weighted hierarchical logistic regression analysis. Survey related procedures in SAS v9.4 (SAS Institute Inc., Cary, NC) were used for all data analyses. The significance level was set at $p<0.05$, and all tests were two-sided.

Patient and public involvement

This study was an analysis of the 2015 BRFSS database. The database was downloaded via the U.S. Centers for Disease Control and Prevention website.

Results

Demographic Characteristics

There were 332,008 respondents involved in this study. All respondents were categorized into four groups as follows: neither DM nor MS, DM without MS (having DM without MS), MS without DM (having MS without DM), and DM plus MS. There were 237,334 respondents with neither DM nor MS, 45,191 respondents with DM without MS, 8,416 respondents with MS without DM and 41,067 respondents with both DM and MS (Table 1). Differences in the percentages of gender, age category, smoking status, education level, race, ethnicity, and annual household income were statistically significant among the four groups (p<0.01). In addition, the above characteristics were significantly different between DM without MS and MS without DM group (p<0.001). In both MS and DM group, 91% were aged over 45 years, and 21.5% did not graduate high school, which were higher than the other three groups. Moreover, 17.6% of respondents in the MS and DM group had annual household incomes lower than $15,000 and the low income percentage is much higher than the other three groups. Less people were white in the DM without MS group (71.4%) compared with that in the MS without DM group (80.4%). However, more respondents were Hispanic, Latino, or Spanish origin in the DM without MS group (19.3%) than in the MS without DM group (10.3%, p<0.001), and more respondents were current smokers in the DM without MS group (16.0%) compared with the MS without DM group (15.3%, p<0.001, Table 1).

Lifestyle

Lifestyle measurements were also compared in the four groups (Table 1). The percentage of physical activity index, daily fruit consumption and vegetable consumption were all significantly different across the four groups. The physical activity index in the DM without MS and MS without DM groups was 48.2%, 47.6%, respectively (p<0.001). The DM and MS group had the least percentage of respondents whose physical activity met the aerobic recommendations. The percentage of respondents who consumed fruit one or more times per day was higher in the DM without MS group, compared to that in the MS without DM group (58.8% vs 56.8%, p<0.001). However, daily vegetable consumption was similar between the DM without MS and the MS without DM groups (76.9% vs 76.8%, p=0.019). In the DM and MS group, the percentage of daily vegetable consumption is the least among the four groups (73.4%).

MS components and chronic diseases

Among the 332,008 respondents, 21,896 respondents had heart attack, accounting for the prevalence of 5.2%. MS without DM had higher prevalence of heart attack than that in DM without MS (11.0%, 8.5%, respectively, p<0.001). The prevalence of heart attack in the DM plus MS group was the highest (16.1%, Table 2). The overall prevalence of dyslipidemia, hypertension, diabetes, and BMI ≥25.0 kg/m^2 was 36.6%, 37.5%, 13.2%, and 67.2%, respectively (Table 2). In the DM without MS group, 83% respondents had one component of MS other than DM, with 17% people having no other components of MS besides DM.

The overall prevalence of stroke was 3.6%. The prevalence of stroke was significantly different between the DM without MS and MS without DM groups (4.8% vs 6.6%, p<0.001). The prevalence of stroke in the DM plus MS group was the highest among the four groups (9.7%). The overall prevalence of depression was 18.2%. Compared with DM without MS, MS without DM had significantly higher prevalence of depression (16.4% vs 24.1%, p<0.001). The highest prevalence of depression was observed in the DM plus MS group (27.7%).

Logistic regression

Logistic regression was conducted to compare the difference among the four groups in their association with heart attack, using the neither DM nor MS group as the reference (Table 3). Results from unadjusted logistic regression analysis showed that both DM without MS (OR=3.28, 95% CI=2.81-3.82) and MS without DM (OR=4.37, 95% CI=4.06-4.70) groups had significantly elevated odds of heart attack than neither DM nor MS group. The DM plus MS group had the highest odds of heart attack among the three groups (OR=6.79, 95% CI=6.33-7.28)

To identify an independent relationship between DM, MS and heart attack, hierarchical logistic regression analysis was performed. After adjusting for confounders (gender, age, education, smoking, race, physical activity index, daily fruit consumption, daily vegetable consumption, stroke, and depression) DM without MS and MS without DM were found to have independently increased odds of heart attack compared with the neither DM nor MS group (DM without MS, adjusted OR=2.09, 95% CI =1.72-2.54, MS without DM, adjusted OR =2.58, 95% CI =2.36-2.81). The DM plus MS group had the highest odds of heart attack (adjusted OR=3.45, 95% CI =3.16-3.77, p all <0.001, Table 3).

Discussion

In the 2015 BRFSS data, respondents with MS without DM and DM without MS were both associated with elevated risk of heart attack and the amount of increase is doubled compare to respondents with neither DM nor MS. MS did not appear to be a greater odds for heart attack than DM from our analysis results. MS combined with DM increased more risk of heart attack by over 3.4 fold compared with respondents with neither DM nor MS.

MS is a cluster of risk factors contributing to the pathogenesis of atherosclerosis.[13] There are several definitions of MS and different definitions of MS had different components.[14-16] Many large-scale clinical trials and meta-analyses have reported that the presence of MS is a strong predictor for heart attack in many different populations.[6, 17-19] In the INTERHEART case-control study involving 26,903 subjects from 52 countries, MS was associated with an increased risk of heart attack, both using the WHO definition (OR=2.69) and the IDF definition (OR=2.20) .The direction of associations were similar across all regions and ethnic groups.[6] A large family study in Finland and Sweden of 4,483 subjects also identified the association between MS and an increased risk of heart attack in all subjects using the WHO definition.[19] Similar results were observed when the 2001 NCEP and 2004 revised NCEP definitions were used.[17, 18] In our analysis, the association between MS and heart attack was consistent. MS, regardless of its definition, was associated with heart attack.

DM is one of the components in most definitions of MS. The risk for cardiovascular disease (CVD) is 2-8 fold higher in the diabetic population than that in the non-diabetic population of a similar age, sex and ethnicity and CVD is the leading cause of morbidity and mortality among patients with type 2 diabetes.[20-22]

Previous researchers have investigated the effects of DM on heart attack. Consistent with our findings, it has been reported that DM was associated with an increased heart attack risk in both men and women.[23] A cohort study using the UK General Practice Research Database showed a much larger relative risk of heart attack in DM.[24]

Both DM and MS were associated with an increased risk of heart attack. However, evidence regarding whether MS without DM is better than DM without MS for evaluating heart attack is limited. There were studies to evaluate the relationship between MS and DM on CVD events. Results from different studies regarding differences in CVD events between DM and MS were conflicting. The Ansung-Ansan cohort study showed that there was no difference in the risk of incident CVD between individuals with DM without MS and MS without DM.[25] Yet, in the REACH registry, presence of newly detected DM but not MS was associated with an increased risk of CVD events.[26] Besides the difference in population characteristics in these studies, the sample size and the definitions of CVD maybe affect the results.

There were fewer studies conducted in U.S. adults to compare the effects of MS and DM on heart attack. In the logistic analysis of this study, MS without DM and DM without MS were found to have similar odds of heart attack. This showed that MS and DM may have similar effects on heart attack in the U.S. adults, which was different from the results of previous study in U.S. population.[27] Our results indicated that to prevent heart attack or CVD, even a diabetic person does not meet the criteria of MS, much more attention should be paid to control metabolic abnormalities.

DM typically co-presents with at least one metabolic abnormality. In our analysis, the weighted prevalence of hypertension, dyslipidemia and overweight in DM without MS group was 13.9%, 12.2% and 56.8%, respectively. Of the respondents with DM, 83% had at least one or more components of MS other than DM. As shown in a population-based cohort study, DM with only one component of MS had more than twofold higher CVD risk than those with DM only.[28] These associations may be helpful to explain in this study why DM and MS had similar effects on heart attack. Further studies were needed to evaluate the association between MS without DM, DM without MS with heart attack.

There were some limitations in our study. First, the definition of MS was revised according to the contents of 2015 BRFSS. MS was diagnosed based on the ATP-III definition.[11] The components of MS were diabetes, hypertension, BMI ≥25.0 kg/m^2, and dyslipidemia. Respondents who had at least three components were regarded as having MS. According to the ATP-III definition, central obesity was diagnosed basing on waist circumference. We used BMI ≥25.0 kg/m^2 to classify individuals because waist circumference was not available. The MS definition from the American College of Endocrinology recommends that BMI >25kg/m^2 or a waist circumference >40 inches for men, >35 inches for women was regarded as obesity. [29] Therefore in the present study, we used BMI ≥25 kg/m^2 as a component of MS. Secondly, in the 2015 BRFSS, there were no data on triglyceride and high-density lipoprotein. Dyslipidemia was assessed by whether respondents had ever been told their blood cholesterol was high. Thirdly, the self-reported nature of the cross-sectional study may lead to underestimate the actual prevalence of heart attack. In this study, 13.2% respondents had diabetes. However, some diabetic respondents may have silent heart attack without any symptoms. In the BRFSS survey the data of fatal heart attack are not included, which may also underestimate the actual prevalence of heart attack. Fourthly, gestational diabetes and pre-diabetes were excluded. These two conditions are both important risk factors for DM that has been excluded from the study. In this study, 24.8% subjects in the 2015 BRFSS data with unknown responses or non-responses in questions included in the study were excluded from the analysis under the assumption of missing completely at random, which might result in some bias of the results when the assumption is not valid.

In conclusion, even though the weighted percentage of heart attack in MS without DM was higher than that in DM without MS, MS and DM had similar effects on heart attack, which could double the risk of heart attack.

Furthermore, when MS is combined with DM, the risk of heart attack will be increased by over 3.4 fold. Considering the nature of the cross-sectional study in the 2015 BRFSS data, prospective studies are needed to confirm the association between MS without DM, DM without MS with heart attack.

Contributors GRY and DL designed the study and analyzed the data. GRY draft the manuscript. DL and TD revised the manuscript. All authors read and approved the final manuscript.

Funding This work was supported by Beijing Municipal Training Foundation for Highly-qualified and Technological Talents of Health System [2014-3-013] and Capital's Funds for Health Improvement and Research [2016-2-2054]. Dr. Li's and Dr. Dye's time is partly supported by the University of Rochester's Clinical and Translational Science Award (CTSA) number UL1 TR000042 and UL1 TR002001 from the National Center for Advancing Translational Sciences of the National Institutes of Health.

Competing interests None declared.

Ethics approval The 2015 BRFSS annual survey data does not include any identifiable information and is publically available from the Centers for Disease Control and Prevention website (https://www.cdc.gov/brfss/annual_data/annual_2015.html).

Data sharing statement All the data is publically available from the Centers for Disease Control and Prevention website (https://www.cdc.gov/brfss/annual_data/annual_2015.html).

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Table 1. Demographic and lifestyle characteristics among the four groups according to the presence of metabolic syndrome and diabetes

	Total	Neither DM nor MS	DM without MS	MS without DM	DM plus MS	p value
Number	332,008	237,334	8,416	45,191	41,067	
Gender						<0.01
Male, n (weighted %)	144,458 (49.9%)	98,983 (48.4%)	4,049 (56.4%)	22,377 (57.1%)	19,049 (51.8%)	
Female, n (weighted %)	187,550 (50.1%)	138,351 (51.6%)	4,367 (43.6%)	22,814 (42.9%)*	22,018 (48.2%)	
Age						<0.01
<45 years, n (weighted %)	67,420 (36.9%)	61,527 (44.7%)	944 (20.4%)	3,054 (14.6%)	1,895 (9.0%)	
≥45 years, n (weighted %)	264,588 (63.1%)	175,807 (55.3%)	7,472 (79.6%)	42,137 (85.4%)*	39,172 (91.0%)	
Annual household income						<0.01
<15000, n (weighted %)	26,368 (9.8%)	15,248 (8.3%)	1,009 (15.2%)	4,100 (10.9%)	6,011 (17.6%)	
15000-25000, n (weighted %)	42,954 (15.2%)	27,083 (13.6%)	1,459 (21.8%)	6,503 (17.3%)	7,909 (22.9%)	
25000-35000, n (weighted %)	29,733 (9.9%)	19,853 (9.4%)	877 (11.5%)	4,533 (11.0%)	4,470 (12.0%)	

35000-50000, n (weighted %)	40,705 (13.6%)	28,453 (13.5%)	1,039 (13.3%)	6,103 (14.7%)	5,110 (13.7%)	
>50000, n (weighted %)	144,082 (51.5%)	112,776 (55.2%)	2,616 (38.2%)	17,422 (46.1%)*	11,268 (33.8%)	
Ethnicity (Hispanic, Latino/a, or Spanish origin or no),						<0.01
Yes, n (weighted %)	22,487 (13.8%)	16,018 (14.0%)	853 (19.3%)	2,257 (10.3%)*	3,359 (15.0%)	
No, n (weighted %)	307,115 (86.2%)	219,670 (86.0%)	7,490 (80.7%)	42,626 (89.7%)	37,329 (85.0%)	
Race						<0.01
White, n (weighted %)	279,446 (77.8%)	202,115 (78.4%)	6,730 (71.4%)	38,756 (80.4%)*	31,845 (72.7%)	
African America, n (weighted %)	26,653 (12.4%)	16,453 (11.4%)	740 (13.9%)	3,815 (12.9%)	5,645 (18.1%)	
America Indian, n (weighted %)	5,718 (1.7%)	3,673 (1.6%)	263 (3.3%)	670 (1.5%)	1,112 (2.5%)	
Asian, n (weighted %)	7,092 (4.8%)	5,688 (5.2%)	243 (7.3%)	535 (2.5%)	626 (3.5%)	
Native Hawaiian, n (weighted %)	1,872 (0.4%)	1,338 (0.4%)	49 (0.5%)	213 (0.3%)	272 (0.3%)	
Other race, n (weighted %)	4,058 (2.7%)	4,058 (2.7%)	215 (3.5%)	647 (2.2%)	839 (2.6%)	
No preferred race, n	745 (0.3%)	577 (0.3%)	14 (0.1%)	60 (0.2%)	94 (0.2%)	

(weighted %)						
Multiracial but preferred race not answered, n (weighted %)	6 (0.0%)	4 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.0%)	
Education						<0.01
Did not graduate high school, n (weighted %)	21,989 (11.8%)	12,296 (9.7%)	917 (20.3%)	3,607 (14.9%)	5,169 (21.5%)	
Graduated high school, n (weighted %)	88,636 (26.9%)	58,399 (25.6%)	2,672 (29.4%)	14,028 (31.2%)	13,537 (31.1%)	
Attended college or technical school, n (weighted %)	90,001 (31.5%)	63,868 (32.0%)	2,238 (28.1%)	12,302 (30.3%)	11,593 (30.2%)	
Graduated from college or technical school, n (weighted %)	130,722 (29.8%)	102,289 (32.7%)	2,561 (22.3%)	15,185 (23.6%)*	10,687 (17.2%)	
Currently smoking						<0.01
No, n (weighted %)	280,808 (84.5%)	200,158 (84.4%)	6,944 (84.0%)	38,788 (84.7%)	34,918 (85.4%)	
Yes, n (weighted %)	43,947 (15.5%)	31,827 (15.6%)	1,230 (16.0%)	5,547 (15.3%)*	5,343 (14.6%)	
Physical activity index						<0.01
Meet aerobic	164,390 (52.8%)	124,593 (55.4%)	3,712 (48.2%)	20,530 (47.6%)	15,555 (40.8%)	

recommendations, n (weighted %)						
Did not meet aerobic recommendations, n (weighted %)	136,791 (47.2%)	90,370 (44.6%)	3,735 (51.8%)	20,831 (52.4%)*	21,855 (59.2%)	
Fruit						<0.01
Consumed fruit one or more times per day, n (weighted %)	195,725 (61.4%)	143,690 (62.9%)	4,795 (58.8%)	25,173 (56.8%)	22,067 (56.0%)	
Consumed fruit less than one time per day, n (weighted %)	111,948 (38.6%)	76,183 (37.1%)	2,854 (41.2%)	16,897 (43.2%)*	16,014 (44.0%)	
Vegetable						<0.01
Vegetables one or more times per day, n (weighted %)	243,504 (79.7%)	177,711 (81.0%)	5,766 (76.9%)	32,262 (76.8%)	27,765 (73.4%)	
Vegetables less than one time per day, n (weighted %)	58,881 (20.3%)	38,567 (19.0%)	1,691 (23.1%)	9,081 (23.2%)	9,542 (26.6%)	

* Compared with DM without MS group, p<0.05

Abbreviation: DM: diabetes mellitus, MS: metabolic syndrome

Table 2. Chronic diseases among the four groups according to the presence of metabolic syndrome and diabetes

Chronic diseases	Total	Neither DM nor MS	DM without MS	MS without DM	DM plus MS	P value
Heart attack, n (weighted %)	21,896 (5.2%)	8,863 (2.7%)	851 (8.5%)	5,310 (11.0%)*	6,872 (16.1%)	<0.01
Hypertension, n (weighted %)	147,655 (37.5%)	64,705 (21.9%)	1,411 (13.9%)	45,191 (100.0%)*	36,348 (87.6%)	<0.01
Dyslipidemia, n (weighted %)	140,653 (36.6%)	62,526 (22.2%)	1,102 (12.2%)	45,191 (100.0%)*	31,834 (77.6%)	<0.01
BMI ≥ 25.0 kg/m^2, n (weighted %)	223,112 (67.2%)	135,589 (59.1%)	4,551 (56.8%)	45,191 (100.0%)*	37,781 (92.3%)	<0.01
Stroke, n (weighted %)	15,013 (3.6%)	6,910 (2.2%)	544 (4.8%)	3,228 (6.6%)*	4,331 (9.7%)	<0.01
Depression, n (weighted %)	64,290 (18.3%)	40,520 (16.1%)	1,574 (16.4%)	10,687 (24.1%)*	11,509 (27.7%)	<0.01

* Compared with DM without MS group, p<0.05

Abbreviation: DM: diabetes mellitus, MS: metabolic syndrome

Table 3. The odds ratio and 95% confidence intervals of DM and MS related to heart attack in the hierarchy logistic regression analysis

	Odds Ratio	95% confidence intervals	p value
Model 1 (n=332,008)			
DM without MS	3.28	2.81-3.82	<0.01
MS without DM	4.37	4.06-4.70	<0.01
DM plus MS	6.79	6.33-7.28	<0.01
Model 2 (n=319,712)			
DM without MS	2.10	1.77-2.49	<0.01
MS without DM	2.85	2.64-3.09	<0.01
DM plus MS	4.06	3.76-4.38	<0.01
Model 3 (n=282,332)			
DM without MS	2.12	1.75-2.56	<0.01
MS without DM	2.82	2.59-3.07	<0.01
DM plus MS	3.99	3.66-4.34	<0.01
Model 4 (n=280,977)			
DM without MS	2.09	1.72-2.54	<0.01
MS without DM	2.58	2.36-2.81	<0.01
DM plus MS	3.45	3.16-3.77	<0.01

Model 1: unadjusted

Model 2: adjusted for gender, age (45 years or not), education, current smoking, race

Model 3: adjusted for gender, age (45 years or not), education, current smoking, race, physical activity index, fruits consumed one or more times per day, vegetable consumed one or more times per day

Model 4 adjusted for gender, age (45 years or not), education, current smoking, race, physical activity index, fruits consumed one or more times per day, vegetable consumed one or more times per day, stroke, and depression

Abbreviation: DM: diabetes mellitus, MS: metabolic syndrome

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-7*
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	NA
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	7-8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8-11
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-10
		(b) Indicate number of participants with missing data for each variable of interest	8-10
Outcome data	15*	Report numbers of outcome events or summary measures	9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-11

		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	13-15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.