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Prevalence and Trends of Metabolic Syndrome in the Adult U.S. Population, 1999–2010

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Objectives This study sought to characterize the prevalence of metabolic syndrome (MetS), its 5 components, and their pharmacological treatment in U.S. adults by sex and race/ethnicity over time.

Background MetS is a constellation of clinical risk factors for cardiovascular disease, stroke, kidney disease, and type 2 diabetes mellitus.

Methods Prevalence estimates were estimated in adults (≥20 years) from the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2010 (in 2-year survey waves). The biological thresholds, defined by the 2009 Joint Scientific Statement, were: 1) waist circumference ≥102 cm (males adults) and ≥88 cm (female adults); 2) fasting plasma glucose ≥100 mg/dl; 3) blood pressure of ≧130/85 mm Hg; 4) triglycerides ≥150 mg/dl; and 5) high-density lipoprotein-cholesterol (HDL-C) <40 mg/dl (male adults) and <50 mg/dl (female adults). Prescription drug use was estimated for lipid-modifying agents, anti-hypertensives, and anti-hyperglycemic medications.

Results From 1999 and 2000 to 2009 and 2010, the age-adjusted prevalence of MetS (based on biologic thresholds) decreased from 25.5% (95% confidence interval [CI]: 22.5 to 28.6) to 22.9% (95% CI: 20.3 to 25.5). During this period, hypertriglyceridemia prevalence decreased (33.5% to 24.3%), as did elevated blood pressure (32.3% to 24.0%). The prevalence of hyperglycemia increased (12.9% to 19.9%), as did elevated waist circumference (45.4% to 56.1%). These trends varied considerably by sex and race/ethnicity. Decreases in elevated blood pressure, suboptimal triglycerides, and high-density lipoprotein-cholesterol prevalence have corresponded with increases in anti-hypertensive and lipid-modifying drugs, respectively.

Conclusions The increasing prevalence of abdominal obesity, particularly among female adults, highlights the urgency of addressing abdominal obesity as a healthcare priority. The use of therapies for MetS components aligns with favorable trends in their prevalence. (J Am Coll Cardiol 2013;62:697–703) © 2013 by the American College of Cardiology Foundation

In this paper, we examine trends in the prevalence of metabolic syndrome (MetS), its 5 components, and their pharmacological treatment in U.S. adults by sex and race/ethnicity from 1999 to 2010. The metabolic syndrome (MetS), defined by a constellation of clinical criteria, is used to identify patients at increased risk for cardiovascular disease (CVD), type II diabetes mellitus (T2DM), and all-cause mortality (1–4). The integrated epidemiological concept of MetS originated from the observation that several metabolic risk factors often co-occur in patients at high risk of CVD, namely abdominal obesity, dyslipidemia, elevated blood pressure, impaired fasting glucose, and insulin resistance (5). The risk factors that comprise MetS are independently associated with CVD and T2DM and have become the therapeutic targets of lifestyle modification, medications, and surgical interventions (6). Furthermore, there is evidence that MetS is an effective and simple clinical tool for identifying high-risk subjects predisposed to CVD and T2DM (7). Although these targets have been in place for more than a decade, U.S. trends of MetS prevalence in the overall population and across sex and race/ethnicity groups have not been characterized. The primary objectives of this paper are to: 1) examine trends in the prevalence of MetS, its

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Abbreviations and Acronyms

CI = confidence interval

CVD = cardiovascular disease

HDL-C = high-density lipoprotein cholesterol

MA = Mexican-American

MetS = metabolic syndrome

NHANES = National Health and Nutrition Examination Survey

T2DM = type II diabetes mellitus

components, and the pharmacological treatments used to control these components in the adult U.S. population between 1999 and 2010; and 2) compare time trends in these risk factors by race/ethnicity and sex.

Methods

We used data from the National Health and Nutrition Examination Survey (NHANES) representative of the civilian, noninstitutionalized U.S. population (8). The NHANES is a series of cross-sectional, national, stratified, multistage probability surveys of the civilian, noninstitutionalized U.S. population conducted by the Centers for Disease Control and Prevention. Beginning in 1999, NHANES became a continuous program with 2-year cycles meant to provide national estimates of the U.S. population. Participants were recruited using a multistage, stratified sampling design consisting of 4 stages of selection: 1) counties or small groups of contiguous counties; 2) a block or group of blocks containing a cluster of households; 3) households; and 4) 1 or more participants from households. Because of the differential probabilities of selection, sampling weights were created to reflect the base probabilities of selection, adjustment for nonresponse, and post-stratification. All adults provided written informed consent; the study was approved by the National Center for Health Statistics Institutional/Ethics Review Board. This analysis was reviewed by the University of Pennsylvania Institutional Review Board and was considered exempt from full review.

Our study data were collected in 6 of the 2-year cycles from 1999 to 2000 and from 2009 to 2010. We included individuals aged 20 or older who self-reported as Mexican-American (MA), non-MA white (hereinafter white), or non-MA black (hereinafter black) who fasted for 8 h or more and had complete information on the relevant variables of interest (e.g., glucose, HDL-C, triglycerides, blood pressure, and waist circumference). We excluded individuals who did not fulfill the fasting criteria and those whose fasting status was unknown leading to a final analytic sample with the following individuals: 1,613 in 1999 to 2000; 1,908 in 2001 to 2002; 1,687 in 2003 to 2004; 1,703 in 2005 to 2006; 1,869 in 2007 to 2008; and 2,034 in 2009 to 2010 (Online Tables 1 and 2). The Online Appendix describes the data, sample selection, and methods used to estimate all components of the syndrome and other aspects of the analysis (see the expanded Methods section in the Online Appendix).

Briefly, MetS was estimated using criteria consistent with the most recent harmonized definition of MetS published in 2009 (Table 1) (3,9). Patients who met 3 or more of the criteria were defined as having MetS. Waist circumference was measured at the high point of the iliac crest at minimal respiration to the nearest 0.1 cm. Serum triglyceride concentrations were enzymatically measured after hydrolyzation to glycerol, and HDL-C was measured after the precipitation of other lipoproteins with a heparin–manganese chloride mixture. Plasma glucose concentrations were determined using an enzymatic reaction. Up to 4 attempts were made to collect 3 blood pressure readings in the mobile examination center; the average of all available measures was used. Race/ethnicity was determined by self-reported survey responses, and categorized as non-MA white, non-MA black, and MA.

Table 1 Components of the Metabolic Syndrome

Components*	Term	Defined Cutoff
Elevated waist circumference	Abdominal obesity	≥102 cm for male adults, and ≥88 cm for female adults in the United States (11)
Elevated blood pressure	Hypertension	Systolic BP ≥ 130 mm Hg, diastolic BP ≥ 85 mm Hg or antihypertensive drug treatment in a patient with history of hypertension (3)
Elevated triglycerides	Dyslipidemia	Triglycerides ≥ 150 mg/dl or drug treatment for elevated triglycerides
Low HDL-C	Dyslipidemia	HDL-C <40 mg/dl in men or <50 mg/dl in women or drug treatment for reduced HDL-C (3)
Elevated fasting plasma glucose	Hyperglycemia	≥100 mg/dl or drug treatment for elevated glucose (3)

*The presence of any 3 of 5 components results in a diagnosis of the metabolic syndrome. Source: 2009 Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity (3)

BP = blood pressure; HDL-C = high-density lipoprotein cholesterol.

To complement the trends analysis in the clinical (biological) thresholds of the MetS, we also estimated the age-adjusted prevalence of the use of each of the following prescription drug classes: 1) lipid-modifying agents; 2) anti-hypertensive; and 3) anti-hyperglycemic medications. Although the Joint Scientific Statement (3) classifies use of these agents as an equal criterion for meeting the definition of specific components (e.g., using anti-hypertensive medication is equal to being hypertensive), medication use in NHANES is coded based on the therapeutic indication of the attendant generic drug code, thus the true indication is unknown. Although NHANES collects information on self-reported use of medication for high blood pressure and glucose, such information is not available for lipid medication. As lipid-modifying agents (e.g., statins or fibric acids derivatives) can both increase HDL-C and lower triglyceride levels (10,11), we chose to focus on trends in classes of drugs rather than make assumptions on therapeutic indication that might lead to overestimates of MetS. The interview weight was used for trends in medications. A list of the medications used and their therapeutic indicators are provided in the Online Appendix.

We used age standardized prevalence estimates through the direct method using the 2000 U.S. population as the standard

(see the expanded Methods section in the Online Appendix for detailed summary of the statistical methods). This allows examination of the prevalence of MetS and its components over time. For time–trend analysis, our primary outcome was the prevalence rate of change per year from survey wave 1 (1999 to 2000) to survey wave 6 (2009 to 2010). We used 2 modeling strategies, both age-adjusted, by fitting separate models for each sex and race/ethnicity group for MetS and its individual components. First, we modeled the likelihood that an individual had MetS or had met each of the MetS components using logistic regression. Second, we estimated MetS prevalence as the ratio of the number of cases in comparison with the total population using a Poisson model. All models were age-adjusted and the direction and significance level for both model specifications were qualitatively equivalent. Statistical analyses accounted for the complex sampling design, nonresponse, differential sampling, and noncoverage, as recommended by the NHANES statistical documentation. The NHANES morning fasting sample weight was used for all MetS and its component-specific prevalence estimates.

Results

Approximately one-fifth of the adult U.S. population remains at high cardiometabolic risk (Table 2). From 1999 to 2010, the age-adjusted prevalence of MetS (based on biological thresholds) decreased from 25.5% (95% CI: 22.5 to 28.6) to 22.9% (95% CI: 20.3 to 25.5) ($p^{trend} = 0.024$). The MA race, particularly female adults, have a higher MetS prevalence than the other subgroups.

Although the prevalence of MetS has declined in the total population when measuring clinical targets, there is a divergence in trends for its individual components, mainly in high waist circumference for the total population and among the sex and race/ethnicity groups (Fig. 1). For example, the prevalence of abdominal obesity for the total population increased from 45.4% (95% CI: 40.7 to 50.0) in 1999 to 56.1% (CI: 52.8 to 59.4) in 2010. Of note, baseline rates of abdominal obesity were much higher among female adults than male adults, particularly among MAs (Online Tables 4, 5, and 6). Estimates of elevated blood pressure for the total population declined over time from 32.3% (29.0 to 35.6) in 1999 to 24.0% (20.9 to 27.1) ($p^{trend} < 0.001$) in 2010 (Table 2). Among male adults, only whites experienced a decline in elevated blood pressure, whereas among female adults, both whites and MAs showed a decline. This reduction aligns with increased awareness and pharmacological treatment of elevated blood pressure (Fig. 2). The prevalence of hypertriglyceridemia also declined in the total population over the study period, from 33.5% (29.8 to 37.3) to 24.3% (21.6 to 26.9) ($p^{trend} < 0.001$). Similar to elevated blood pressure, all racial groups experienced a decline in elevated triglycerides except for blacks (Online Tables 4, 5, and 6), although the latter group showed the lowest baseline prevalence of hypertriglyceridemia (Fig. 1). During the same time period the use of lipid-modifying agents rose from 8% (7.3 to 8.7%) to 15.6% (14.6 to 16.5) in the total NHANES sample (Fig. 2). A similar trend in greater use of lipid-modifying agents was observed among all of the population subgroups. Although some of the variability in HDL-C trends between 2001 and 2006 is likely attributable to a change in the laboratory assay during this time period (12), there was an overall decline in suboptimal HDL-C in the total population from 38.5% (33.6 to 43.5) in 1999 to 30.1% (29.9 to 33.2) in 2010 ($p^{trend} < 0.001$). All racial groups experienced a decline in the prevalence of suboptimal HDL-C over time (Online Table 4), except for black males (Online Table 5). In contrast to the reduced prevalence of other MetS components, the prevalence of hyperglycemia rose in the total population from 12.9% (95% CI: 9.8 to 16.0%) in 1999 to 19.9% (95% CI: 16.4 to 23.5%) in 2010 ($p^{trend} < 0.001$) (Table 2), with the MA male adults group having the fastest increase among all subgroups of the population.

Comment

We found that the prevalence of MetS has slightly declined when measured on the basis of clinical targets using the biological thresholds outlined in Adult Treatment Panel-3 (10,11) and the Joint Scientific Statement (3). However, even with this decline, approximately one-fifth of the adult U.S. population would be classified as having MetS, living with suboptimal measures for at least 3 of 5 MetS components. These results indicate a limited decline in the prevalence of MetS in the past decade. Our results are consistent with an earlier analysis of NHANES III (1988 to 1994) that used similar ATP III criteria to define MetS and found that approximately 22% of U.S. adults (24% after age adjustment) had MetS, with similar sex and race/ethnicity patterning (13).

The MetS is an epidemiological construct of different permutations of risk factors, each with unique clinical implications and treatment strategies (14). Understanding the trends in the population's burden of MetS is valuable given the recognition that certain cardiometabolic risk factors tend to co-exist. There is evidence suggesting that specific clusters of 3 or more MetS factors are not necessarily associated with greater risk for CVD outcomes and that fasting glucose is the main predictor of T2DM (15). However, it is important to identify the population with MetS because these individuals have a particularly adverse metabolic state that warrants aggressive intervention for specific traits. For example, results from the Framingham Study indicate that trait combinations that did not include fasting glucose also imparted an increased risk for incident T2DM (15). Increasing awareness of MetS may also account for some of the declines in its component risk factors. For instance, in our analysis and in previous evidence of time trends in MetS components, there has been a decline in average lipid levels among U.S. adults from 1960 to 2006,

Table 2 Age-Standardized Prevalence of the Metabolic Syndrome in the United States, 1999 to 2010

Total Population	1999–2000	2001–2002	2003–2004	2005–2006	2007–2008	2009–2010	p^{trend}
Metabolic Syndrome							
Total population	25.54% (22.49–28.58)	27.37% (25.25–29.50)	25.76% (22.98–28.53)	23.18% (20.22–26.15)	24.94% (21.46–28.42)	22.90% (20.28–25.53)	0.024
Male adults	23.35% (18.04–28.65)	27.45% (23.96–30.94)	25.26% (20.50–30.02)	24.57% (20.78–28.35)	26.54% (23.57–29.50)	23.69% (18.79–28.58)	0.54
Female adults	27.50% (24.49–30.50)	26.98% (24.54–29.42)	26.20% (22.05–30.35)	22.10% (18.19–26.01)	23.54% (18.69–28.38)	21.80% (19.04–24.56)	0.005
Waist Circumference							
Total population	45.35% (40.66–50.04)	48.96% (46.18–51.74)	55.35% (52.29–58.41)	54.24% (50.64–57.84)	53.78% (50.60–56.95)	56.07% (52.79–59.35)	< 0.001
Male adults	36.48% (30.55–42.41)	39.82% (35.30–44.33)	46.02% (41.52–50.51)	46.41% (42.17–50.64)	45.44% (41.88–49.01)	46.44% (41.22–51.66)	0.011
Female adults	53.53% (48.55–58.51)	57.67% (53.59–61.75)	64.41% (60.03–68.79)	61.70% (56.80–66.60)	61.93% (56.82–67.04)	65.38% (62.36–68.39)	< 0.001
Blood Pressure							
Total population	32.30% (29.00–35.61)	34.69% (31.60–37.77)	30.56% (27.35–33.78)	30.44% (27.80–33.08)	24.25% (22.28–26.21)	24.04% (20.91–27.18)	< 0.001
Male adults	35.22% (30.66–39.78)	37.21% (31.93–42.50)	34.64% (29.74–39.54)	33.95% (30.75–37.16)	25.18% (22.21–28.15)	27.84% (23.99–31.69)	< 0.001
Female adults	29.28% (25.99–32.56)	32.15% (29.33–34.98)	26.42% (23.24–29.59)	27.27% (23.39–31.15)	22.80% (20.15–25.45)	20.19% (17.02–23.36)	< 0.001
Triglycerides							
Total population	33.53% (29.76–37.30)	33.32% (31.22–35.41)	32.37% (28.97–35.77)	30.20% (26.84–33.56)	28.84% (26.12–31.56)	24.25% (21.57–26.93)	< 0.001
Male adults	35.04% (28.17–41.91)	37.85% (33.50–42.21)	36.06% (31.01–41.10)	35.45% (31.24–39.67)	34.71% (30.88–38.55)	26.26% (21.89–30.62)	0.004
Female adults	32.03% (28.17–35.90)	28.54% (26.78–30.30)	28.50% (24.74–32.25)	25.24% (21.83–28.66)	23.56% (19.84–27.28)	21.74% (17.76–25.71)	< 0.001
HDL-C							
Total population	38.51% (33.56–43.46)	33.86% (31.13–36.59)	27.50% (24.60–30.39)	21.33% (19.05–23.62)	28.30% (24.21–32.40)	30.05% (26.93–33.16)	< 0.001
Male adults	35.56% (29.59–41.53)	31.57% (27.72–35.43)	22.49% (16.86–28.12)	20.61% (17.52–23.70)	27.28% (23.72–30.85)	27.91% (23.81–32.01)	0.004
Female adults	41.04% (35.14–46.93)	35.97% (32.99–38.96)	32.48% (27.09–37.87)	22.16% (18.89–25.43)	29.30% (23.83–34.78)	32.00% (28.69–35.30)	< 0.001
Glucose							
Total population	12.94% (9.84–16.04)	15.62% (13.58–17.66)	14.15% (12.53–15.76)	17.89% (15.34–20.44)	22.82% (19.71–25.94)	19.92% (16.38–23.47)	< 0.001
Male adults	16.44% (12.17–20.70)	18.77% (15.26–22.27)	17.76% (15.22–20.30)	20.54% (16.45–24.62)	28.64% (24.31–32.97)	25.01% (20.10–29.92)	< 0.001
Female adults	10.05% (7.85–12.25)	12.58% (11.12–14.05)	10.41% (8.17–12.66)	15.60% (12.45–18.75)	17.46% (13.51–21.40)	15.14% (11.98–18.30)	< 0.001

HDL-C = high-density lipoprotein cholesterol.

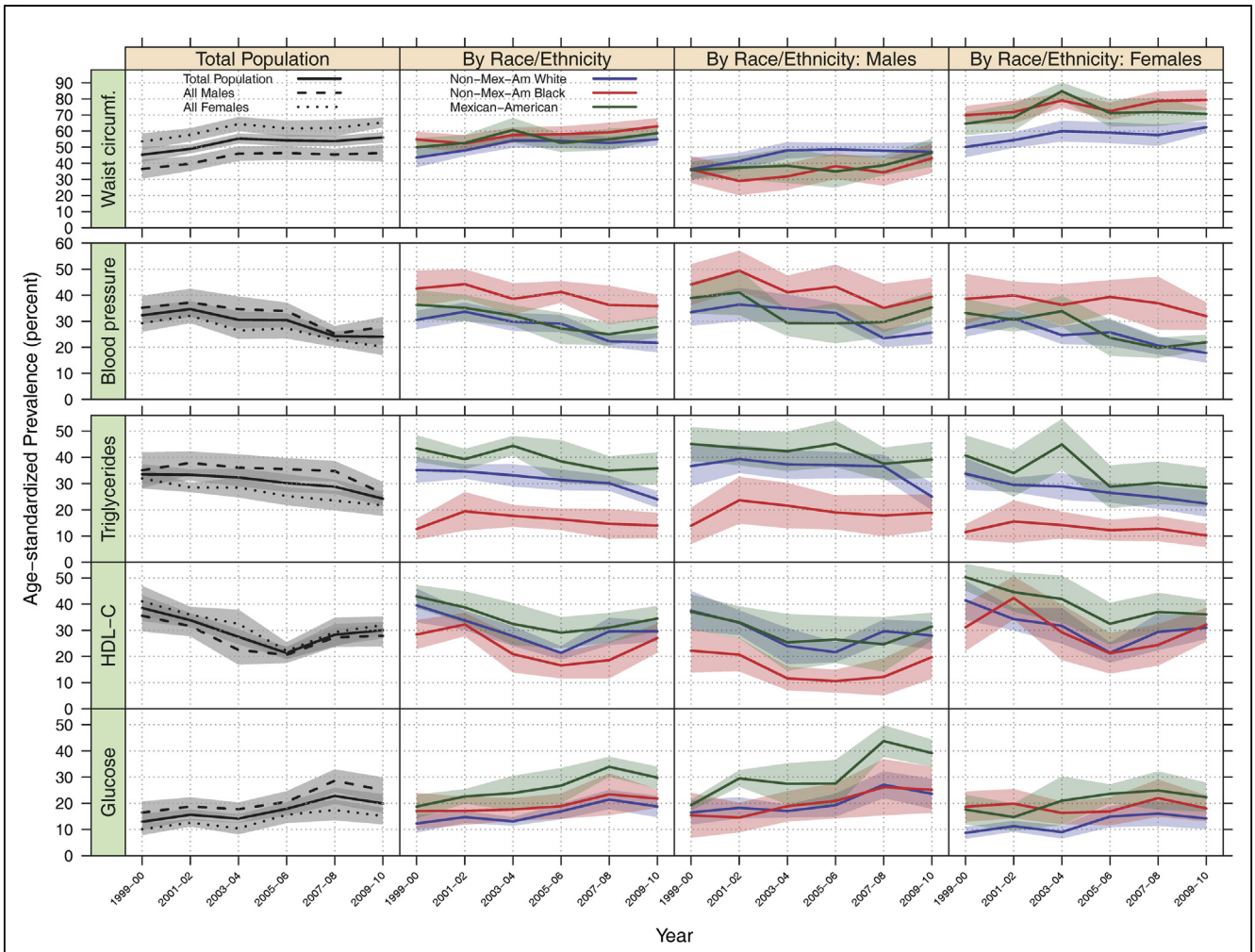

Figure 1 **Prevalence and Trends of the 5 Components of Metabolic Syndrome in the Adult U.S. Population, 1999 to 2010**

Prevalence and trends of the components of MetS for U.S. adults aged 20 or older for the total population by sex (first column), by race/ethnicity (second column), and by race/ethnicity and sex (third and fourth columns). Waist circumf. = waist circumference; HDL-C = high-density lipoprotein cholesterol; Non-Mex-Am = non-Mexican American. Table 1 shows the cut-offs defined as high risk for each indicator. Shaded areas represent 95% confidence intervals.

which has largely been attributed to the growing proportion of the population receiving lipid-lowering medication (16,17). Perhaps the successes we have observed in lipid management are partly due to increasing clinical recognition of the importance of screening for this variable in the presence of abdominal obesity (e.g., as both are components of MetS). In the current analysis, MetS components had divergent trends. We observed pronounced declines in dyslipidemia, specifically in hypertriglyceridemia, results that align with previous studies (18). Concurrent with improvements in dyslipidemia, we observed higher use of drugs over time that target suboptimal lipid profiles such as statins, fibrates, and niacin derivatives (Fig. 2). Indeed, favorable trends in blood pressure and dyslipidemia may reflect increasing availability and use of pharmacological interventions. This is in contrast to our observations on the increasing trend of abdominal obesity, most pronounced in female adults, which may identify a population at a potentially high cardiometabolic risk. Particularly important are the sex and racial differences in the prevalence of increased waist circumference. White male adults are more likely to have abdominal obesity than their counterparts of other race/ethnicity, but the opposite is true among white female adults.

Also notable are the sex and racial differences in the prevalence of individual MetS components. We found that white male adults are more likely to have abdominal obesity than their counterparts of other race/ethnicity, but the opposite is true among white female adults. We also found that black male adults and black female adults consistently had a higher prevalence of elevated blood pressure than other groups, but they showed the lowest dyslipidemia prevalence levels. Additionally, MAs, both overall and by sex, consistently had a higher prevalence of low HDL-C,

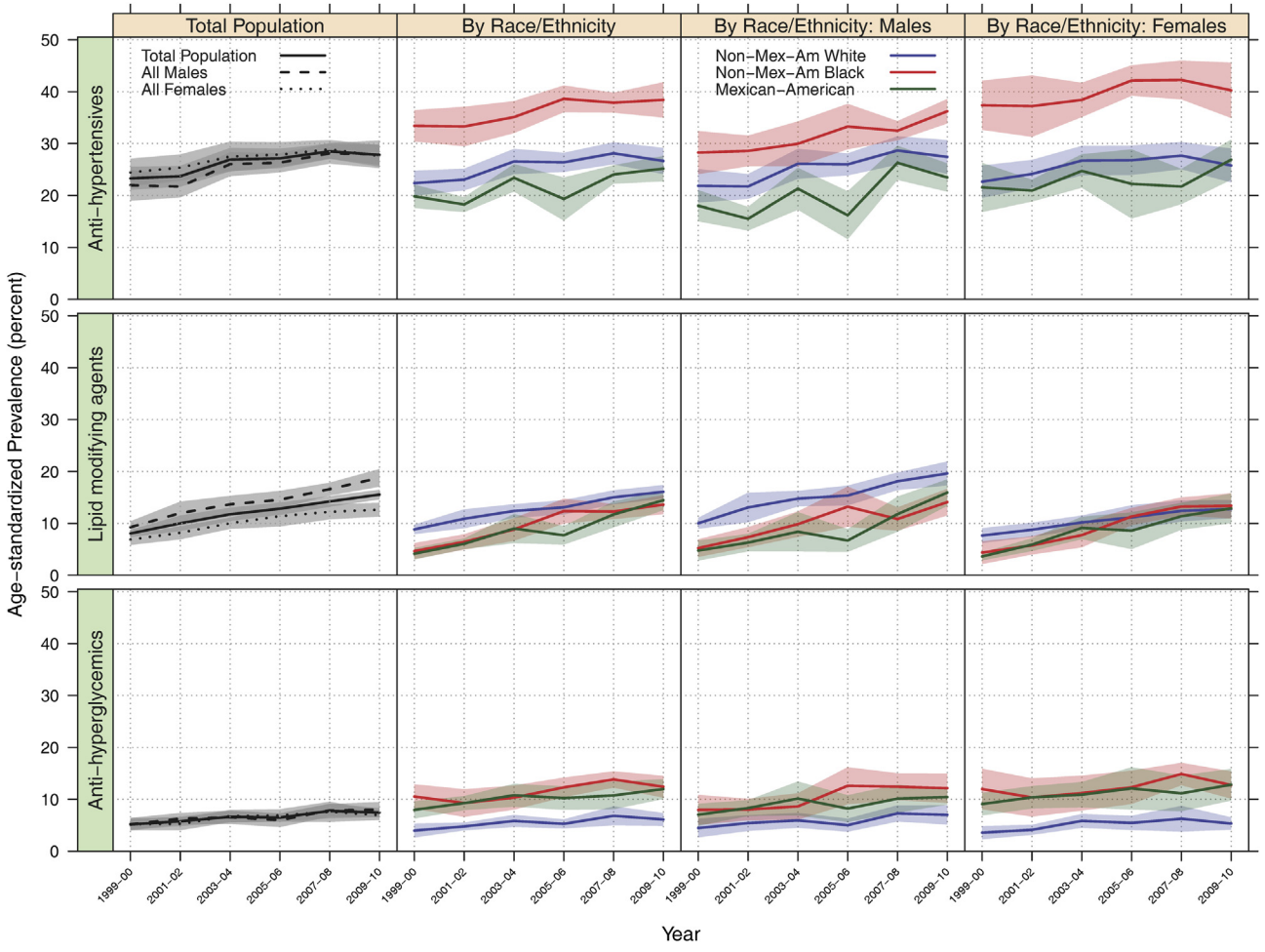

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Figure 2 **Prevalence and Trends of Prescription Drug Use Related to Components of Metabolic Syndrome in the Adult U.S. Population, 1999 to 2010**

Prescription drug use related to components of MetS for U.S. adults aged 20 or older for the total population by sex (first column), by race/ethnicity (second column), and by race/ethnicity and sex (third and fourth columns). Online Appendix Table 7 shows the specific medications included as anti-hypertensive, lipid-modifying agents, and anti-hyperglycemic. Shaded areas represent 95% confidence intervals. Abbreviations as in Figure 1.

high triglycerides, and high blood glucose than other subgroups.

Study limitations. It is likely that multitudes of factors, in addition to known risk factors, affect cardiometabolic risk. These may include socioeconomic status and regional differences in access to care, which we did not measure in our analysis. Also, trends in HDL-C may be underestimated due to variations in the assay during the study period (12). NHANES provides adjusted estimates for effected survey waves that exceed the maximum allowable bias, but these changes are known to be responsible for secondary variation in point estimates across the 6 waves (12). A more detailed examination of these changes and their impact on the measurement of HDL-C has been previously published (16,17). In addition, conclusions that are based on strict cutoffs limit our understanding of individuals who are near the cutoff points and may have risks similar to subjects with MetS, but do not classify as meeting a certain risk factor (19,20). The cutpoints for elevated waist circumference are not well-defined, particularly for subjects of non-European race. It remains unclear whether the same criteria for abdominal obesity should be applied to individuals of a particular ethnic group, regardless of their country of residence or origin (3). The most recent harmonized definition of MetS has consistent cutoffs for all risk factors, but recommends that the cutoff values for abdominal obesity be selected based on the study or population being examined (3). In the current analyses, we imposed the U.S. cutoffs (11) on all NHANES respondents, consistent with the methods of previous studies (13). Given that the U.S. cutoffs are the most generous for defining abdominal obesity ($\geq$102 cm for male adults and $\geq$88 cm for female adults), as compared with potentially choosing the lower Latin American or African cutoffs based on ancestry for racial subgroups, our

estimates of the burden of abdominal obesity may, in fact, be conservative. Also, as the use of self-reported race/ethnicity is susceptible to misclassification bias, the NHANES sampling strategy might be responsible for fluctuations and variation between the prevalence estimates in survey waves. A final limitation of this work is that while it demonstrates MetS trends, it does not show how these trends correlate with trends in clinically significant outcomes, such as cardiovascular morbidity and mortality. However, our observation of divergent trends in MetS components is important evidence of the ongoing burdens of risk for CVD in the U.S., and suggests that priority should be placed in addressing those risk factors that have increased in prevalence over the past decade (i.e., obesity and hyperglycemia) (4,5,9,10).

Conclusions

Our analysis examined the patterns of MetS across 6 waves of NHANES between 1999 and 2010 and showed that although the prevalence of MetS (as it is currently defined) has declined slightly over time, there have been population-level changes in its components. Most striking is the upward trend in abdominal obesity across the entire U.S. population since the first survey wave in 1999 and 2000. Insulin resistance also appears to be on the rise. However, there is a downward trend in elevated triglycerides with a current overall prevalence near 25% likely corresponding with increased use of statins and other lipid-modifying agents. Our results demonstrate potential targets for interventions to reduce the future burden of CVD and T2DM, and confirm the urgent need for multifaceted and coordinated treatment programs to address the increasing prevalence of obesity in the United States.

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Key Words: hypertension ■ hypertriglyceridemia ■ metabolic syndrome ■ waist circumference.

APPENDIX

For an expanded Methods section, and supplemental tables, please see the online version of this article.