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Sex Differences in the Prevalence of, and Trends in, Cardiovascular Risk Factors, Treatment, and Control in the United States, 2001 to 2016

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BACKGROUND: Improvements have been made in the treatment and control of some but not all major cardiovascular risk factors in the United States. It remains unclear whether women and men have benefited equally.

METHODS: Data from the 2001 to 2002 through the 2015 to 2016 US National Health and Nutrition Examination Survey on adults aged 20 to 79 years were used. We assessed sex differences in temporal trends in the levels of systolic blood pressure, body mass index, smoking status, high-density lipoprotein and total cholesterol, and hemoglobin A_{1c}. Trends in treatment and control rates of hypertension, diabetes mellitus, and dyslipidemia were also assessed.

RESULTS: Overall, 35 416 participants (51% women) were included. Trends in systolic blood pressure, smoking status, high-density lipoprotein cholesterol, and hemoglobin A_{1c} were similar between the sexes. Body mass index increased more in women than men (P=0.006). Mean levels were 28.1 and 29.6 kg/m^2 in women and 27.9 and 29.0 kg/m^2 in men in 2001 to 2004 and 2013 to 2016, respectively. Total cholesterol decreased more in men than women (P=0.002): mean levels in 2001 to 2004 and 2013 to 2016, respectively, were 203 and 194 mg/dL in women and 201 and 188 mg/dL in men. Improvements in the control of hypertension, diabetes mellitus, and dyslipidemia were similar between the sexes; however, sex differences persisted. In 2013 to 2016, control rates in women versus men were 30% versus 22% for hypertension, 30% versus 20% for diabetes mellitus, and 51% versus 63% for dyslipidemia.

CONCLUSIONS: Temporal trends in cardiovascular risk factor levels were broadly similar between the sexes, except for total cholesterol and body mass index. Sex differences in the control of hypertension, diabetes mellitus, and dyslipidemia persist, and further efforts are required to reduce this differential.

Key Words: cardiovascular disease ■ prevention ■ risk factors ■ sex differences ■ treatment

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Clinical Perspective

What Is New?

- Between 2001 to 2004 and 2013 to 2016, trends in the reductions in systolic blood pressure and smoking prevalence and increasing prevalence of diabetes mellitus were similar between adult women and men in the United States.
- Reductions in total cholesterol were greater in men than women, and increases in body mass index were greater in women than men.
- The control of hypertension, diabetes mellitus, and dyslipidemia remained suboptimal in both sexes, with a lower prevalence of controlled hypertension and diabetes mellitus in men and a lower prevalence of controlled dyslipidemia in women.

What Are the Clinical Implications?

- The presence of clinically meaningful sex differences in the prevalence of and trends in cardiovascular risk factors, treatment, and control requires increased awareness to improve the prevention of cardiovascular disease in both women and men.
- Further efforts are particularly required to reduce the persistent sex differences in the control of hypertension, diabetes mellitus, and dyslipidemia.
- Sex-specific health promotion efforts may be needed to further reduce smoking rates and to curb the sharp increases in the prevalence of overweight and obesity and diabetes mellitus.

Cardiovascular disease (CVD) is the leading cause of death worldwide and accounts for ≈1 of every 3 deaths in US women and men.[1,2] Much of the burden of CVD can be avoided by keeping blood pressure, cholesterol, and glucose at healthy levels, avoiding tobacco, and maintaining a healthy weight.[1,3] Although the contribution of these risk factors to cardiovascular health is well established, underlying lifestyle factors are imperfect in many individuals, and differences exist between women and men. For example, tobacco use is generally more common in men than women, and women tend to have more favorable levels of blood pressure and cholesterol.[4–7] In contrast, the worldwide prevalence of obesity is higher in women than men.[8]

In addition to a healthy lifestyle, those with hypertension and dyslipidemia receive CVD risk reduction benefits from pharmacological treatment to control their blood pressure and cholesterol levels.[1] To reduce the risk of microvascular and macrovascular complications, those with diabetes mellitus benefit from pharmacological treatment to control glucose levels, regardless of sex. Although several studies have described the US trends in prevalence, treatment, and control rates for hypertension, diabetes mellitus, and dyslipidemia, sex-specific results have not been reported consistently.[9–12]

CVD has long been seen as a condition primarily affecting men. Although the age-specific rates of CVD are higher in men than women in most age groups, the actual lifetime risk of CVD is similar for women and men.[13,14] Furthermore, evidence suggests that CVD rates not only differ between the sexes but can also differ between age and racial groups within the same sex.[1] In the past several decades, the American Heart Association's Go Red for Women campaign and women-specific guidelines for the prevention of CVD in the United States were initiated to increase awareness of sex differences in CVD and the importance of CVD in women.[15–19] However, it is unknown whether these initiatives have had an impact on sex differences in cardiovascular risk factor levels and treatment and control patterns. Moreover, where sex-specific trends have been reported, these were generally not presented for different age and racial groups, nor separately for those with and without a history of CVD.[9–12] If such differences exist, health promotion efforts should be reformulated to take this into account.

To address these evidence gaps, we used data from the National Health and Nutrition Examination Survey (NHANES) to quantify sex differences in trends in cardiovascular risk factors (blood pressure, cholesterol, hemoglobin A_{1c} [HbA_{1c}], weight, and smoking) and the prevalence, treatment, and control of hypertension, diabetes mellitus, and dyslipidemia in the United States from 2001 to 2016, overall and by age group, by race, and among those with or without a history of CVD.

METHODS

In 2-year cycles, NHANES enrolls civilian, noninstitutionalized people living in the United States. Participants are selected with a multistage probability sampling approach such that nationally representative estimates can be generated. Data were used from the eight 2-year NHANES cycles conducted between 2001 to 2002 and 2015 to 2016. NHANES cycles were combined into four 4-year periods (2001–2004, 2005–2008, 2009–2012, and 2013–2016) to produce sex-specific estimates with greater statistical reliability.[20] The present study included 35 416 adults (51% women) 20 to 79 years of age at study assessment. The full protocols and methods for data collection are reported elsewhere.[21] All participants provided written informed consent, and the research ethics boards of the National Center for Health Statistics approved all protocols; the data are publicly available. The analytic methods and study materials used for this analysis will be made available to other researchers for purposes of reproducing the results or replicating the procedure on request.

Risk Factors, Treatment, and Definitions

Information on age, sex, and race were solicited at a screening interview. Participants with a self-reported history of heart disease, stroke, or heart failure were categorized as having a history of CVD. The use of antihypertensive, lipid-lowering, and antidiabetic medication was self-reported.

Systolic blood pressure (SBP) was calculated as the mean of 3 readings obtained according to a standardized protocol. Current smoking was self-reported. Body mass index (BMI) was calculated from measured weight (in kilograms) divided by measured height (in meters) squared. Healthy weight, overweight, and obesity were defined as a BMI ≥18.5 to <25 kg/m^2, ≥25 to <30 kg/m^2, and ≥30 kg/m^2, respectively. High-density lipoprotein cholesterol, total cholesterol (TC), and HbA_{1c} were measured using blood collected during the study visit according to standardized procedures. Hypertension was defined as an SBP ≥130 mm Hg or diastolic blood pressure ≥80 mm Hg or the use of antihypertensive medication.[22] Diabetes mellitus was defined as HbA_{1c} ≥6.5% or the use of antidiabetic medication. Dyslipidemia was defined as TC ≥240 mg/dL or the use of lipid-lowering medication. The control of hypertension, diabetes mellitus, and dyslipidemia was defined as SBP/diastolic blood pressure <130/80 mm Hg, HbA_{1c} <6.5%, and TC <240 mg/dL, respectively. The proportion of US adults receiving treatment was calculated among those with the condition. Risk factor control was calculated among those with the condition, stratified by those with and without treatment. In supplementary analyses, individuals with diabetes mellitus were categorized according to HbA_{1c} levels of <6.5% (strict control), ≥6.5% to <7% (intermediate control), ≥7% and <7.5% (lenient control), and ≥7.5% (not controlled). We created a summary score (range 0–4) based on the presence or absence of 4 risk factors: current smoking, hypertension, diabetes mellitus, and dyslipidemia. Overweight/obesity was not included because it is causally related to the other risk factors.

Statistical Analyses

Age-standardized summary statistics, with 95% CIs, were computed separately for women and men using the age distribution for the US adult population in 2015 to 2016 as the standard. Means were estimated for risk factors measured on a continuous scale, and prevalence was estimated for categorical variables. Women-to-men differences, with 95% CIs, were computed on the absolute scale using linear regression analyses. *P* values for sex differences in linear trends across calendar periods were derived by adding an interaction term between sex and calendar period to the model. For each risk factor, participants with missing data were excluded from the analyses. Subgroup analyses were conducted by age group (20–34, 35–49, 50–64, and 65–79 years), history of CVD, and race (Hispanic, non-Hispanic white, non-Hispanic black, and other). Three-way interaction terms were added to the model, which also included the constituent 2-way interaction terms, to assess whether sex differences in linear trends differed by age group, history of CVD, or race. To obtain nationally representative values, all analyses were weighted using the NHANES sample weights, thus taking account of the complex sampling design.[23,24] Analyses were performed in R version 3.3.0 using the "Survey" package.

RESULTS

Data from 35 416 participants (51% women) were analyzed (Table I in the online-only Data Supplement). The Table shows the age-standardized risk factor levels and treatment and control rates for women and men in 2013 to 2016. Results for 2001 to 2004, 2005 to 2008, and 2009 to 2012 are provided in Tables II, III, and IV in the online-only Data Supplement, respectively.

Blood Pressure and Hypertension

Changes in SBP over time were similar in women and men: mean levels in 2001 to 2004 and 2013 to 2016 were 122 mm Hg and 120 mm Hg, respectively, in women and 124 mm Hg in both calendar periods in men (*P* for interaction by sex=0.113) (Figure 1 and Table V in the online-only Data Supplement). However, sex differences in SBP trends were present among those aged 50 years or older (*P* for interaction by sex and age <0.001; Figure 2 and Table VI in the online-only Data Supplement [for 2013–2016 levels]) but did not differ by CVD status or race (Figures I and II in the online-only Data Supplement).

Between 2001 to 2004 and 2013 to 2016, the prevalence of hypertension decreased from 43% to 42% in women and from 51% to 49% in men (*P* for interaction by sex=0.085; Figure III and Table V in the online-only Data Supplement). Over this calendar period, the percentage of those with hypertension taking antihypertensive medication increased from 52% to 64% in women and from 40% to 53% in men. Similarly, the percentage with controlled blood pressure increased from 16% to 30% in women and from 14% to 22% in men (Figure 3). In 2013 to 2016, sex differences in the prevalence of hypertension were greater in younger than older adults (Table VII in the online-only Data Supplement), and treatment and control rates for hypertension were higher among women than men at younger age but not at older age (Figure IV in the online-only Data Supplement and Table VIII in the online-only Data Supplement). Also in 2013 to 2016, treatment rates were higher among those with than without a history of CVD in both sexes (Figure 4), and sex differences in the treatment and control of hypertension were similar across race/ethnicity groups (Figure V in the online-only Data Supplement).

Body Mass Index

Between 2001 to 2004 and 2013 to 2016, mean BMI increased from 28.1 kg/m^2 to 29.6 kg/m^2 in women and from 27.9 kg/m^2 to 29.0 kg/m^2 in men (*P* for interaction by sex=0.006; Figure 1 and Table V in the online-only Data Supplement). In 2013 to 2016, the percentage of women who were overweight was 11 percentage points lower than in men, but women were more often obese (Table). There were minimal differences in trends across age groups and by CVD status (Figure 2 and Figure I in the online-only Data Supplement). Even though there was no statistical evidence for interaction

Table. Age-Standardized Prevalence of Risk Factors, Treatment, and Control in 2013 to 2016, by Sex

	Women	Men	Women vs Men
Age, y	47.2 (16.1)	47.5 (16.3)	…
Race, %			
Hispanic	28.8	26.4	…
Non-Hispanic white	35.8	37.4	…
Non-Hispanic black	20.7	20.7	…
Other	14.7	15.6	…
Risk factors			
Systolic BP, mm Hg	119.8 (119.3 to 120.3)	124.1 (123.4 to 124.8)	−4.3 (−5.0 to −3.5)
Current smoking, %	18.4 (16.6 to 20.3)	21.7 (19.8 to 23.6)	−3.3 (−5.0 to −1.5)
BMI, kg/m^2	29.6 (29.3 to 30.0)	29.0 (28.7 to 29.3)	0.6 (0.3 to 0.9)
Healthy weight, %	29.9 (28.2 to 31.6)	24.2 (22.5 to 26.0)	5.7 (3.5 to 7.9)
Overweight, %	26.9 (25.6 to 28.2)	37.8 (35.7 to 39.8)	−10.9 (−13.6 to −8.2)
Obese, %	41.6 (39.8 to 43.4)	36.8 (34.4 to 39.2)	4.8 (2.1 to 7.5)
Total cholesterol, mg/dL	193.9 (192.4 to 195.4)	188.3 (186.3 to 190.4)	5.5 (3.5 to 7.5)
HDL cholesterol, mg/dL	59.8 (58.9 to 60.6)	48.2 (47.5 to 48.9)	11.6 (10.8 to 12.3)
HbA_{1c}, %	5.6 (5.6 to 5.6)	5.7 (5.6 to 5.7)	−0.1 (−0.1 to 0.0)
History of CVD, %	5.8 (4.9 to 6.7)	8.1 (7.0 to 9.1)	−2.3 (−3.7 to −0.8)
Treatment and control			
Hypertension, %	42.1 (40.8 to 43.5)	49.1 (46.8 to 51.5)	−7.0 (−9.6 to −4.4)
Treated, %	64.1 (61.3 to 66.9)	53.6 (51.1 to 56.1)	10.5 (7.5 to 13.5)
Controlled among treated, %	46.8 (43.1 to 50.5)	41.3 (37.3 to 45.3)	5.6 (0.8 to 10.3)
Controlled among overall population, %	30.0 (26.8 to 33.2)	22.1 (19.4 to 24.9)	7.9 (4.5 to 11.3)
Diabetes mellitus, %	10.8 (9.7 to 11.8)	13.0 (11.7 to 14.2)	−2.2 (−3.6 to −0.7)
Treated, %	80.8 (77.8 to 83.9)	80.2 (75.6 to 84.8)	0.6 (−3.9 to 5.2)
Controlled among treated, %	36.5 (30.5 to 42.4)	24.7 (19.2 to 30.2)	11.8 (4.3 to 19.2)
Controlled among overall population, %	29.5 (24.5 to 34.5)	19.8 (14.9 to 24.7)	9.7 (3.5 to 15.8)
Dyslipidemia, %	25.9 (24.2 to 27.5)	29.5 (28.0 to 31.1)	−3.7 (−5.9 to −1.4)
Treated, %	56.1 (52.3 to 59.8)	67.5 (64.0 to 71.0)	−11.5 (−15.5 to −7.5)
Controlled among treated, %	90.1 (87.4 to 92.7)	93.7 (91.8 to 95.7)	−3.7 (−6.5 to −0.8)
Controlled among overall population, %	50.5 (46.6 to 54.3)	63.3 (60.0 to 66.6)	−12.8 (−17.2 to −8.5)
Number of risk factors*			
None	40.0 (38.3 to 41.6)	31.0 (28.5 to 33.5)	9.0 (6.7 to 11.2)
1 risk factor	31.5 (29.9 to 33.0)	34.9 (32.8 to 36.9)	−3.4 (−5.7 to −1.1)
2 risk factors	19.5 (18.6 to 20.4)	23.8 (22.3 to 25.2)	−4.2 (−5.7 to −2.7)
3 or 4 risk factors	9.0 (8.0 to 10.1)	10.4 (9.1 to 11.7)	−1.4 (−3.1 to 0.3)

Age and race are sample means (SD) and percentages, respectively. Other values are means for continuous variables and percentages for categorical variables, age-standardized to the US standard population in 2015 to 2016. Values between brackets indicate 95% CI. BMI indicates body mass index; BP, indicates blood pressure; CVD, cardiovascular disease; HbA_{1c}, hemoglobin A_{1c}; and HDL, high-density lipoprotein.

*Risk factors were current smoking, hypertension, dyslipidemia, and diabetes mellitus. Participants with a self-reported Asian background were included in the "other" group.

in trends by race, sex differences in BMI were greatest among non-Hispanic black individuals (Figure II and Tables V and VI in the online-only Data Supplement).

Smoking

Smoking rates decreased from 22% in women and 29% in men in 2001 to 2004 to 18% in women and 22% in men in 2013 to 2016 (*P* for interaction by sex=0.114) (Figure 1 and Table V in the online-only Data Supplement). In both sexes, smoking rates were highest among the youngest adults (Figure 2 and Table VI in the online-only Data Supplement). For Hispanics, non-Hispanic blacks, and people of other races or ethnicities, smoking rates were 8 to 10 percentage points lower in women than in men (Figure II and Table VI in the online-only Data).

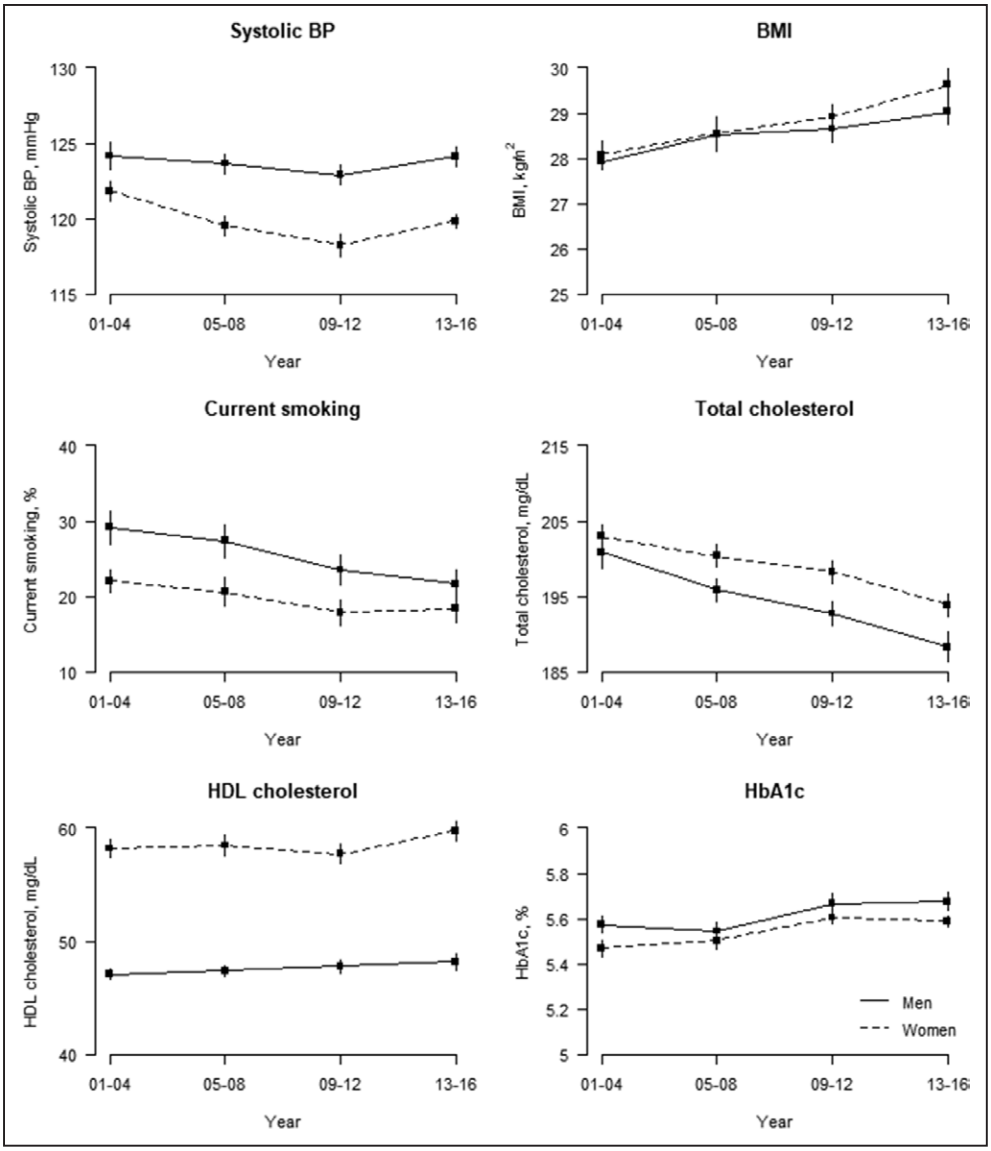

Figure 1. Trends in systolic BP, BMI, current smoking, total cholesterol, HDL cholesterol, and HbA_{1c}, by sex.
Solid lines are for men, and dashed lines are for women. All estimates are age-standardized to the US standard population in 2015 to 2016. Error bars indicate 95% CIs. BMI indicates body mass index; BP, blood pressure; HbA_{1c}, hemoglobin A_{1c}; and HDL, high-density lipoprotein.

TC, High-Density Lipoprotein Cholesterol, and Dyslipidemia

Mean high-density lipoprotein cholesterol levels were 58 mg/dL in women and 47 mg/dL in men in 2001 to 2004 and 60 mg/dL in women and 48 mg/dL in men in 2013 to 2016 (*P* for interaction by sex=0.872) (Figure 1 and Table V in the online-only Data Supplement). Reductions in TC were greater in men than women; mean levels were 203 mg/dL in women and 201 mg/dL in men in 2001 to 2004 and 194 mg/dL in women and 188 mg/dL in men in 2013 to 2016 (*P* for interaction by sex=0.002) (Figure 1 and Table V in the online-only Data Supplement). In each calendar period, TC was similar for women and men aged <35 years, lower among women than men in the 35- to 49-year age range, and then higher in women than men in the 2 older age groups (Figure 2).

The prevalence, treatment, and control of dyslipidemia increased over calendar periods for women and men (Figure 3). Compared with women, men were more likely to be treated and to have controlled dyslipidemia, especially at older age (Table IX in the online-only Data Supplement for 2013–2016 rates). Treatment rates in women versus men were 40% versus 48% in 2001 to 2004 and 56% versus 67% in 2013 to 2016. Control rates in women versus men in the overall population were 33% versus 40% in 2001 to 2004 and 51% versus 63% in 2013 to 2016. A higher percentage of men than women with CVD had dyslipidemia, whereas rates were similar for those without CVD (Table VII in the online-only Data Supplement for 2013–2016 rates]). Sex differences in treatment and control rates differed minimally by CVD status (Figure 4 and Table IX in the online-only Data Supplement).

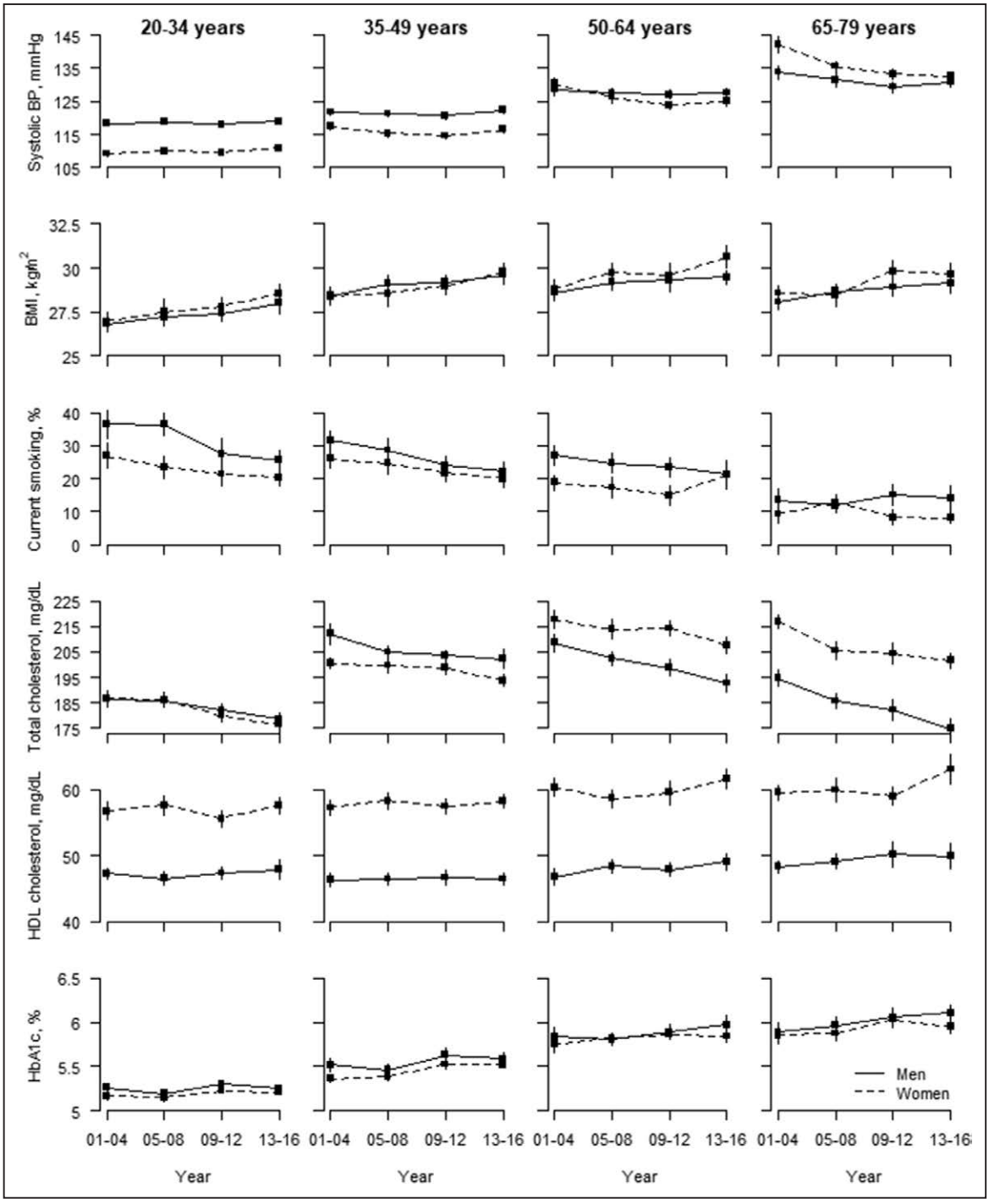

Figure 2. Trends in systolic BP, BMI, current smoking, total cholesterol, HDL cholesterol, and HbA_{1c}, by sex and age group.
Solid lines are for men, and dashed lines are for women. All estimates are age-standardized to the US standard population in 2015 to 2016. Error bars indicate 95% CIs. BMI indicates body mass index; BP, blood pressure; HbA_{1c}, hemoglobin A_{1c}; and HDL, high-density lipoprotein.

HbA_{1c} and Diabetes Mellitus

Mean levels of HbA_{1c} increased over calendar periods for both women and men (*P* for interaction by sex=0.835) (Figure 1 and Table V in the online-only Data Supplement). The prevalence of diabetes mellitus was lower among women than men (11% versus 13% in 2013–2016). The prevalence of diabetes mellitus increased across calendar periods equally for women and men (*P* for interaction by sex=0.285) (Figure III in the online-only Data Supplement). Between 2001 to 2004 and 2013 to 2016, treatment rates among those with diabetes mellitus increased from 76% to 81% in women and from 72% to 80% in men. Control rates were 21% in women and 20% in men in 2001 to 2004 and 30% versus 20% in 2013 to 2016 (*P* for interaction by sex=0.159) (Figure 3 and Table V in the online-

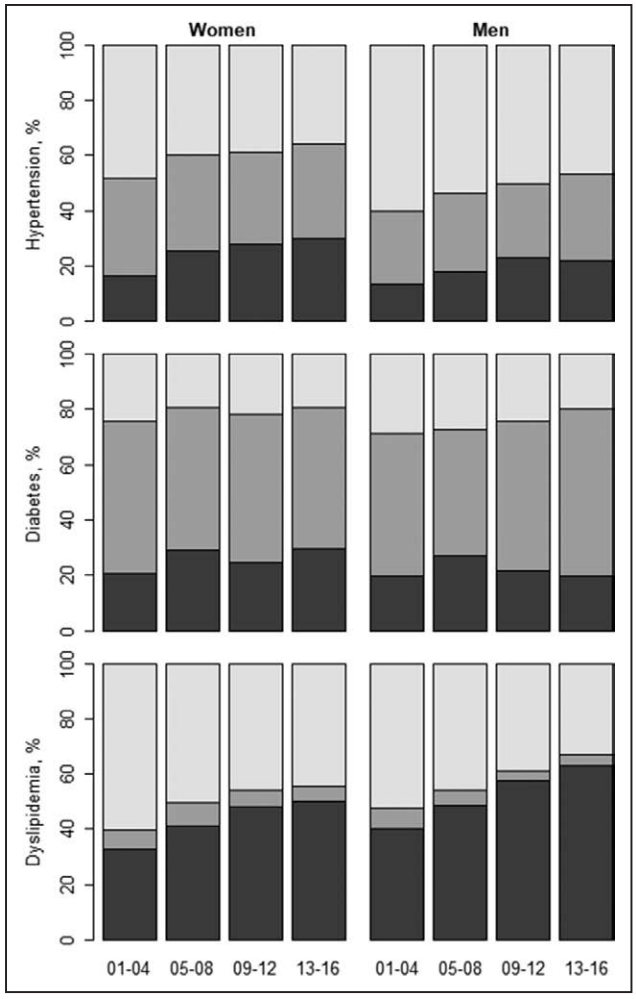

Figure 3. Treatment and control of hypertension, diabetes mellitus, and dyslipidemia, by sex and calendar period.
Black areas represent treated and controlled cases; gray areas, treated but uncontrolled cases; and light gray areas, untreated and uncontrolled cases. Hypertension was defined as a systolic/diastolic blood pressure ≥130/80 mm Hg or the use of antihypertensive medication. Diabetes mellitus was defined as hemoglobin A_{1c} ≥6.5% or the use of antidiabetic medication. Dyslipidemia was defined as total cholesterol ≥240 mg/dL or the use of lipid-lowering medication. The control of hypertension, diabetes mellitus, and dyslipidemia, respectively, was defined as systolic/diastolic blood pressure <130/80 mm Hg, hemoglobin A_{1c} <6.5%, and total cholesterol <240 mg/dL.

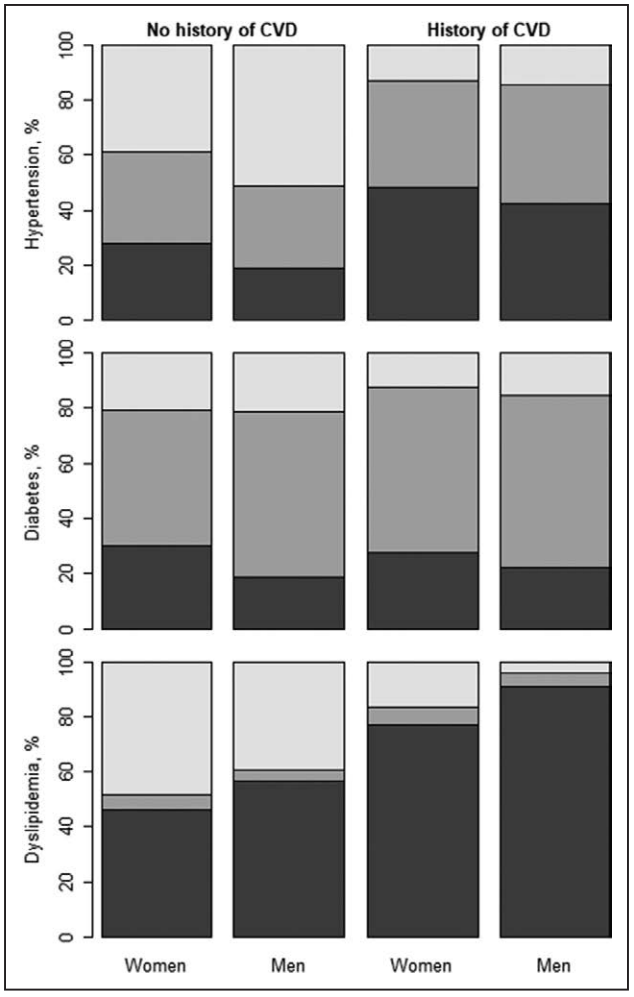

Figure 4. Treatment and control of hypertension, diabetes mellitus, and dyslipidemia in 2013 to 2016, by sex and history of CVD.
Black areas represent treated and controlled cases. Gray areas represent treated but uncontrolled cases; light gray areas, untreated and uncontrolled cases. Hypertension was defined as a systolic/diastolic blood pressure ≥130/80 mm Hg or the use of antihypertensive medication. Diabetes mellitus was defined as hemoglobin A_{1c} ≥6.5% or the use of antidiabetic medication. Dyslipidemia was defined as total cholesterol ≥240 mg/dL or the use of lipid-lowering medication. The control of hypertension, diabetes mellitus, and dyslipidemia, respectively, was defined as systolic/diastolic blood pressure <130/80 mm Hg, hemoglobin A_{1c} <6.5%, and total cholesterol <240 mg/dL. CVD indicates cardiovascular disease.

only Data Supplement). In 2013 to 2016, there was no evidence of variations in sex differences in treatment and control rates by age, CVD status, or race (Figure 4 and Figures IV and V and Table X in the online-only Data Supplement). Control rates were similar or higher in women than men in all calendar periods and subgroups, regardless of HbA_{1c} target value (Figure VI and Table XI in the online-only Data Supplement for trends and Figures VII through IX and Tables XII through XIV in the online-only Data Supplement for 2013–2016 rates).

Number of Risk Factors

In both sexes, there was no major variation in the distribution of number of risk factors across calendar periods (Table, Figure 5, and Tables II through IV in the online-only Data Supplement). The percentage of women with no risk factors increased from 36% in 2001 to 2004 to 40% in 2013 to 2016. In the same period, the percentage of women with 3 or 4 risk factors increased from 7% to 9%. The percentage of men with no risk factors increased from 26% in 2001 to 2004 to 31% in 2013 to 2016, and the percentage with 3 or 4 risk factors increased from 9% in 2001 to 2004 to 10% in 2013 to 2016. In both sexes, the percentage with 1 or more risk factors increased with age and was higher among those with a history of CVD than among those with a history of CVD (Figures X and XI and Tables XV and XVI in the online-only Data Supplement, all for 2013–2016 rates). Of all racial and ethnic groups, non-Hispanic black women and men had the highest number of risk

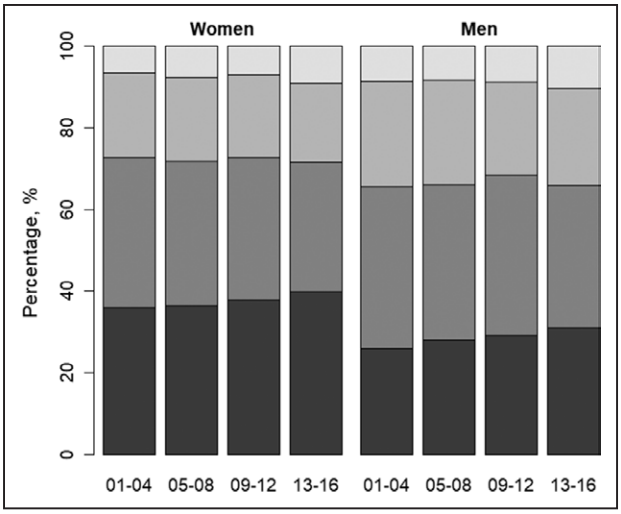

Figure 5. Trends in the number of risk factors, by sex and age group. Risk factors were current smoking, hypertension, dyslipidemia, and diabetes mellitus. Black areas represent individuals without risk factors; dark gray areas, individuals with 1 risk factor; gray areas, individuals with 2 risk factors; and light gray areas, individuals with 3 or 4 risk factors.

factors (Figure XII and Table XVII in the online-only Data Supplement, both for 2013–2016 rates).

DISCUSSION

In this study of nationally representative data for US adults between 2001 to 2004 and 2013 to 2016, trends in levels, prevalence, treatment, and control of several CVD risk factors were broadly similar between the sexes, but statistically significant sex differences were present in the trends in TC and BMI levels. Reductions in mean TC were lesser in women than men, and increases in BMI were greater in women than men. The control of hypertension, diabetes mellitus, and dyslipidemia remains suboptimal in both sexes, and a considerable number of women and men continue to smoke. Men were less likely to have control of hypertension and diabetes mellitus, whereas women were less likely than men to have adequate control of dyslipidemia. Sex differences in treatment rates might be responsible in part for the sex differences in control rates.

The trends in cardiovascular risk factors in the present study are consistent with the sex-specific US estimates from the noncommunicable disease risk factor collaboration (NCD-RisC) on global trends in SBP, BMI, diabetes mellitus, and TC.[8,25–27] Although NCD-RisC showed that major geographic variations in risk factor trends exist, sex differences within geographic regions were generally small. Smoking rates differ considerably across the world, and the ratio of women-to-men smoking prevalence rates is strongly related to a country's level of economic development.[7] In the United States and other high-income countries, the women-to-men smoking prevalence ratio is ≈0.8, but in many low- and middle-income countries, this ratio is typically <0.1. The present study demonstrates that the women-to-men smoking prevalence ratio in the United States differs by race and ethnicity; in 2013 to 2016, it was 1.0 among non-Hispanic whites but ranged between 0.48 and 0.66 for the other races/ethnicities. Although the prevalence of smoking has decreased in many countries, only one-fifth of countries are on track to reduce the prevalence of smoking by the voluntary global target of 30% in 2025 for men, and one-half are on track for women.[28]

In agreement with a previous NHANES report,[29] the present study indicates that there have been increases in the use of prescription medications to treat hypertension, diabetes mellitus, and dyslipidemia in both women and men in the United States over the past decades. In 2011 to 2012, 65% of women and 52% of men had at least 1 medication prescription, for any indication, and 16% of women and 13% of men used 5 or more medications.[29] Antihypertensive and lipid-lowering agents were the most commonly prescribed drugs in both sexes. Despite increases in treatment rates, a substantial proportion of adults are not treated according to current guidelines, and many of those treated do not achieve adequate control. Although the quality of risk factor management was suboptimal in both sexes, men were less likely to have control of hypertension and diabetes mellitus, whereas women were less likely than men to have adequate control of dyslipidemia. Because the sex difference in the percentage of individuals with controlled hypertension and dyslipidemia in the overall population was larger than among those treated, our study suggests that sex differences in treatment for hypertension and dyslipidemia underpin some of these differences in control rates.

Inherent sex differences in the biology and pathophysiology of CVD and its underlying mechanisms are likely to explain some of the sex differences present in the current study. Women of younger age tend to have more favorable lipid profiles than men, but cholesterol levels rise after the menopausal transition to levels higher than in men.[6] The lower rates of hypertension in women than men could be attributable to women's stronger anti-inflammatory immune profile, which might act as a compensatory mechanism to limit increases in blood pressure.[5] Furthermore, diabetes mellitus is a stronger risk factor for CVD in women than men.[30,31] It has been suggested that sex differences in body size and body size distribution might contribute to this sex difference,[32] because women are diagnosed with diabetes mellitus at a higher BMI than men, despite having similar levels of HbA_{1c}.[33] Age-specific CVD rates are lower in women than men, which has often been attributed to a protective effect of sex steroid hormones in women, especially estrogen. The exact role of sex steroid hormones in explaining women's lower age-specific

CVD rates, however, remains uncertain and warrants further investigation. Indeed, estrogen supplementation does not reduce the risk of CVD in postmenopausal women.[34] Also, although CVD rates in women increase with advanced age, there is no major acceleration of rates around the menopause.[35] Similarly, sex differences in established risk factors do not fully explain the sex difference in CVD risk.[36] For instance, the Tromsø study reported that the higher rate of myocardial infarction among men versus women persisted throughout life, largely independent of several major risk factors.[13] Further studies will be needed to assess the impact of sex-specific trends in risk factor levels on sex differences in CVD rates across the life span and within different sociodemographic and clinical subpopulations.

The lower rates of CVD in women than men until the age of 80 years might have contributed to a limited awareness of CVD risk among women themselves and their healthcare professionals.[1,19,37] Although awareness of the importance of CVD in women has increased over the past decades,[19] the present study suggests that it has not resulted in major changes in sex differences in the treatment and control of dyslipidemia. Nevertheless, the treatment and control of hypertension continued to be more favorable among women, although their advantage relative to men was smaller in older age. More frequent blood pressure measurements for women of childbearing age might contribute to the early detection and treatment of hypertension among younger women. Moreover, the lower blood pressure levels among women versus men and inherent biological differences might also lead to higher control rates.[5] Yet the lower TC levels among women versus men did not result in higher treatment and control rates of dyslipidemia, which suggests that biological factors alone do not fully explain the sex differences in risk factor control.

Although different treatment guidelines have been in use throughout the study period, differences in recommendations for the use of antihypertensive and lipid-lowering medications could contribute to the opposing patterns in the treatment and control of hypertension and dyslipidemia. The 2013 American College of Cardiology/American Heart Association guideline on the treatment of blood cholesterol recommends the use of moderate- to high-intensity statin therapy for patients with a 10-year risk of atherosclerotic CVD of ≥7.5%, with low-density lipoprotein cholesterol of 70 to 189 mg/dL and without diabetes mellitus or symptomatic CVD.[38] The 2017 American College of Cardiology/American Heart Association guideline for the prevention, detection, evaluation, and management of high blood pressure in adults only recommends antihypertensive medication in the presence of hypertension, with thresholds of systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg and systolic blood pressure 130 to 139 mm Hg or diastolic blood pressure 80 to 89 mm Hg, depending on CVD risk.[22] Because of a higher absolute risk of CVD in men, more men than women with a low-density lipoprotein cholesterol of 70 to 189 mg/dL could be eligible for treatment, whereas there is no scenario in which the use of antihypertensive medication is recommended based exclusively on 10-year risk of atherosclerotic CVD. Nonetheless, the sex difference in the prevalence of controlled dyslipidemia in favor of men was greatest in the older age groups, in which most women would also be eligible for treatment on the basis of a 10-year risk of atherosclerotic CVD of ≥7.5%. Thus, sex differences in CVD risk alone might not explain the age gradient in the risk factor control. Although a better understanding of these age-specific sex differences in the treatment and control of cardiovascular risk factors is required, the present study suggests that a life-course perspective is needed to reduce sex differences in the prevention and management of CVD.

The strengths of the study are the inclusion of a large, nationally representative sample of civilian, noninstitutionalized US women and men. Response rates were high for each calendar period, and data were collected using standardized procedures by trained study personnel, including extensive quality control. This study also has some limitations. First, treatment guidelines, diagnostic criteria, and screening practices have changed over time; however, we anticipate that such changes will have affected women and men in a similar way. Furthermore, we defined hypertension, diabetes mellitus, and dyslipidemia consistently over all NHANES periods, and hence, it is unlikely that these changes had major effects on our interpretation of sex differences in trends. Second, the NHANES are cross-sectional in design and do not enable direct assessment of the causes of changes in risk factor levels and management and control rates. In addition, we were not able to determine the impact of these sex-specific trends on changes in CVD morbidity and mortality. Third, because each survey includes data from a different sample, sampling error could affect comparisons over time; however, any bias from such issues is likely to be the same for both sexes. Fourth, a substantial number of comparisons were conducted in this study, and we cannot exclude the possibility that some of the reported trends were chance findings. In interpreting the findings, the effect size and its clinical implications should therefore be considered alongside the CIs. A further limitation is that some data were self-reported, and misreporting could be differential by sex.

In conclusion, trends in SBP, smoking, high-density lipoprotein cholesterol, and HbA_{1c} were broadly similar between the sexes in this nationally representative US sample. Reductions in TC between 2001 to 2004 and 2013 to 2016 were greater in men, and BMI increased to a greater extent in women. The control of hypertension, diabetes mellitus, and dyslipidemia remains sub-

optimal in both sexes, with a lower prevalence of controlled hypertension and diabetes mellitus in men and a lower prevalence of controlled dyslipidemia in women. Sex differences in treatment rates might underpin some of the differences in control rates.

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