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Trends of risk profile among middle-aged adults hospitalized for acute ischemic stroke in United States 2006–2017

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Abstract

Background: Recent studies reported increasing trends in hospitalization of stroke patients aged 35–64 years.

Aim: To examine changes in risk factor profiles among patients aged 35–64 years hospitalized with acute ischemic stroke between 2006 and 2017 in the United States.

Methods: We used data from the National Inpatient Sample of the Healthcare Cost and Utilization Project from 2006 through 2017. Principal ICD-9-CM/ICD-10-CM codes were used to identify acute ischemic stroke hospitalizations, and secondary codes were used to identify the presence of four major stroke risk factors: hypertension, diabetes, lipid disorders, and tobacco use. We used the relative percent change to assess the changes in the prevalence of risk profile between 2006–2007 and 2016–2017 and linear regression models to obtain the p values for the overall trends across six time periods.

Results: Approximately 1.5 million acute ischemic stroke hospitalizations occurred during 2006–2017. The prevalence of having all four risk factors increased from 4.1% in 2006–2007 to 9.1% in 2016–2017 (relative percent change 122.0%, $p < 0.001$ for trend), prevalence of any three risk factors increased from 24.5% to 33.8% (relative percent change 38.0%, $p < 0.001$). Prevalence of only two risk factors decreased from 36.1% to 32.7% ($p < 0.001$), only one risk factor decreased from 25.2% to 18.1% ($p < 0.001$), and absence of risk factors decreased from 10.1% to 6.2% ($p < 0.001$). The most prevalent triad of risk factors was hypertension, diabetes, and lipid disorders (14.3% in 2006–2007 and 19.8% in 2016–2017), and the most common dyad risk factors was hypertension and lipid disorders (12.6% in 2006–2007 and 11.9% in 2016–2017).

Conclusions: The prevalence of hospitalized acute ischemic stroke patients aged 35–64 years with all four or any three of four major stroke risk factors increased by 122% and 38%, while those with only one risk factor or no risk factor has declined by 28% and 39%, respectively,

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Authors' contributions

Study conception and design: Tong, Yang, George, Gillespie and Merritt; Analysis and interpretation of data: Tong, Yang; Drafting of manuscript: Tong, Yang; Critical revision: Tong, Yang, George, Gillespie and Merritt.

Declaration of conflicting interests

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Supplemental material

Supplemental material for this article is available online.

from 2006 to 2017. Younger adults are increasingly at higher risk for stroke from preventable and treatable risk factors. This growing public health problem will require clinicians, healthcare systems, and public health efforts to implement more effective prevention strategies among this population.

Keywords

Acute ischemic stroke; hospitalizations; risk factors; disparity

Introduction

Stroke is the third leading cause of death among women and the fifth leading cause of death among men and a leading cause of serious long-term disability in the United States (US).[1] Recent studies have reported that younger adults have experienced a stalled stroke mortality decline and significant increases in stroke hospitalizations and prevalence of multiple stroke risk factors (RFs).[2–4]

Stroke prevention is a major goal of the Million Hearts® initiative, which is co-led by the Centers for Disease Control and Prevention and the Centers for Medicare and Medicaid Services.[5] Despite the public health concern of increasing stroke hospitalizations among younger adults, limited studies have examined the co-existing RFs among younger stroke patients in the United States. The present study examined the trends and changes in the RF profiles among patients aged 35–64 years old hospitalized with acute ischemic stroke (AIS) between 2006 and 2017. The findings may help stimulating efforts for improving the management of long-term risk reduction for incident and recurrent stroke.

Methods

Data sources and study sample

We used the National (Nationwide) Inpatient Sample (NIS) to examine hospitalizations among adults aged 35–64 years from 2006 to 2017. National Inpatient Sample is part of the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality (AHRQ). The NIS is a database of hospital inpatient stays derived from billing data submitted by hospitals to statewide data organizations across the United States.[6] We excluded hospitalizations if they were designated as elective.

We used the International Classification of Diseases, Ninth/Tenth Revision, Clinical Modification (ICD-9-CM/ICD-10-CM), or Clinical Classification Software (CCS) codes created by AHRQ to identify the hospitalizations. AIS was identified using the principal diagnosis of ICD-9 codes of 433.01, 433.10, 433.11, 433.21, 433.31, 433.81, 433.91, 434.00, 434.01, 434.11, 434.91,and 436 for the NIS between 2006 and third quarter of 2015 and ICD-10 codes I63 for the NIS fourth quarter of 2015–2017. Our analyses did not include any transient ischemic attacks (TIA) events.

Statistical methods

The unit of analysis was hospital discharge. Because of changes implemented in the redesign beginning with 2012 data, we used trend weights developed by AHRQ to make estimates comparable for data prior to 2012.[7]

We calculated the hospitalization rate by using intercensal population estimates as the denominators. We assessed the prevalence of four major stroke RFs (hypertension, diabetes, lipid disorders, and tobacco use) and their combinations (16 mutually exclusive sub-groups) using secondary codes for each hospitalization (the list of ICD9/ICD10 codes for the four RFs were presented in Supplemental Table I). We combined NIS annual data to create six consecutive two-year time periods to obtain statistically stable estimates between 2006 and 2017. We calculated the relative percent changes (RPCs) in the prevalence of RFs between 2006–2007 and 2016–2017, and we conducted linear trend analyses across six time periods using linear regression models.

We used SAS 9.4-callable SUDAAN (Research Triangle Institute, Research Triangle Park, NC) to account for the multistage, disproportionate stratified sampling design for NIS. Due to the large sample size, a more conservative two-sided p value <0.01 was considered statistically significant. Because the data are publicly available and do not contain direct personal identifiers, this study was exempt from review by the institutional review board of the Centers for Diseases Control and Prevention.

Results

During 2006–2017, we identified approximately 1.5 million AIS hospitalizations among adults aged 35–64 years. The absolute number of AIS hospitalizations increased significantly from 169,484 (rate of 71.1/100,000 population) in 2006–2007 to 312,485 (125.0/100,000 populations) in 2016–2017 (Table 1). Among all AIS hospitalizations, 9.8% were aged 35–44 years, 31.6% were 45–54 years, and 58.6% were 55–64 years. More than half (58.2%) were men, and 25.7% were non-Hispanic Black (Table 1). Overall, the prevalence of hypertension, diabetes, lipid disorders, and tobacco use all increased significantly from 2006 to 2017. The prevalence of hypertension, lipid disorders, diabetes, and tobacco use was 81.8%, 56.5%, 45.4%, and 37.6%, respectively, in 2016–2017 (Supplemental Table II). AIS patients with none, only one RF, or only two RFs decreased significantly from 2006–2007 to 2016–2017: 10.1% vs. 6.2% for none (RPC −38.6%), 25.2% vs. 18.1% for only 1 RF (RPC −28.2%), and 36.1% vs. 32.7% for only two RFs (RPC −9.4%) (Table 2). The prevalence of any three or all four RFs increased significantly from 2006–2007 to 2016–2017: 24.5% vs. 33.8% for any three RFs (RPC 38.0%) and 4.1% vs. 9.1% for all four RFs (RPC 122.0%). In general, the most common dyad of RFs was hypertension and lipid disorders with no significant change observed across the study period (12.6% vs. 11.9% in 2006–2007 and 2016–2017, RPC −5.6%). The most prevalent triad was hypertension, diabetes, and lipid disorders, which increased significantly from 14.3% to 19.8% (RPC 38.5%). All other RFs triad groups also increased significantly between 2006–2007 and 2016–2017, with RPCs ranging from 16.7% to 38.8%. The prevalence of having all four RFs, while low, more than doubled from 2006–2007 to 2016–2017.

The pattern of changes in risk profiles from 2006–2007 to 2016–2017 were consistent across age, sex, and racial and ethnic groups (Supplemental Table III, Figures 1 and 2). Patients aged 35–44 years had the highest prevalence of zero RFs while 55–64 years had the lowest. Men had a higher prevalence of having two or more RFs compared to women, and non-Hispanic Blacks had the highest prevalence of only two RFs and all four RFs compared to other racial and ethnic groups. All sex-racial and ethnic groups had significant increases in the prevalence of having any three RFs. Hispanic women experienced the largest increase in having any three RFs (24.9% in 2006–2007 to 37.7% in 2016–2017, RPC 51.4%), followed by non-Hispanic Black men with RPC of 43.4%. Hispanic men had the highest prevalence of having any three RFs in 2016–2017. The prevalence of all four RFs more than doubled across all sex-racial and ethnic groups, except Hispanic men and women of other racial group. While non-Hispanic White women had the largest RPC in having all four RFs of 148.6%, men of other racial groups had highest prevalence of all four RFs (Figures 1 and 2).

Discussion

Our data provide the latest trends in RFs among AIS patients aged 35–64 years in the United States. The total number and rate of AIS hospitalizations among this age group increased substantially from 2006 to 2017. Among AIS hospitalizations, the prevalence of all four RFs more than doubled between 2006–2007 and 2016–2017, and the prevalence of having any three RFs increased 38%. Those younger AIS patients with none of the four RFs decreased 38.6% from 2006 to 2017.

The findings of increasing trends in AIS hospitalizations and multiple co-existing stroke RFs among younger adults (35–64 years) are consistent with several studies.[3,4,8,9] George et al.[3] reported significant increases in ischemic stroke hospitalizations and associated traditional stroke RFs from 2003 to 2012 among individuals aged 18–54 years. Towfighi et al.[8] identified significant increases in ischemic stroke hospitalizations among those aged 35–44 years between 1997 and 2006. The extensive 27-year population study from the Dijon Stroke Registry showed a significant increase in ischemic stroke incidence in individuals aged <55 years as well as a rising prevalence of cardiovascular disease RFs, especially smoking.[9]

Increasing trends in the prevalence of multiple co-existing RFs among younger AIS patients is concerning. Our study suggested that nearly 1-in-11 younger AIS patients had four RFs and 1-in-3 had three RFs in 2016–2017. A review study indicated that the rising incidence of stroke among younger adults coincided with an increasing prevalence of traditional RFs and discussed the long-term risk of cardiovascular disease, functional outcome, and psychosocial consequence.[10] Other studies reported an increased prevalence of individual RFs in the United States.[11–14] The prevalence of diagnosed diabetes increased significantly with an annual percentage change of 4.4% from 1990 to 2008 among those aged 45–64 years in the United States.[11] The latest National Diabetes Statistic Report reported that the prevalence of diabetes among adults aged 18 years or older in the US increased from 9.5% in 1999–2002 to 12.0% in 2013–2016, estimating 34.1 million adults aged 18 years and older had either diagnosed or undiagnosed diabetes in 2018.[12] Studies from the National Health and

Nutrition Examination Survey reported that the prevalence of obesity has more than doubled since the late 1980s, preceding the increase in diabetes, and 42.4% of American adults had obesity in 2017–2018.[13,14] Diabetes and obesity are associated with a significantly increased risk of cardiovascular disease and stroke,[15] and the prevalence of obesity increased from 30.7% in 2007–2008 to 40.0% in 2017–2018 among adults aged 20–39 years and from 36.2% in 2007–2008 to 44.8% in 2017–2018 among adults aged 40–59 years.[13,14] Significant increases of stroke RFs among younger adults present a growing challenge for stroke prevention, as secondary stroke prevention is a much-longer life-long commitment for younger adults who experience a stroke. These findings should prompt a sense of urgency toward awareness, detection, and management of co-existing RFs for stroke among younger adults.

Our study showed substantial disparities in the prevalence of RFs by age, sex, race, and ethnicity, suggesting persistent disparities consistent with the findings of earlier studies. Patients with AIS aged 35–44 years had the highest prevalence of zero RF, and men had a higher prevalence of having two or more RFs compared to women. The findings were consistent with the results showing that the traditional stroke RFs were more frequent among men and those over 44 in Helsinki Young Stroke Registry.[16] A large multi-national European cohort study of patients aged 18–55 years with cerebrovascular event also found that dyslipidemia, smoking, hypertension, and diabetes were more prevalent among men, and dyslipidemia and cardiovascular disease were most prevalent among aged 35 and older.[17] In US, a recent publication from the REGARDS study reported that among both White and Black races aged 45–64 years, women had lower stroke risk than men.[18] In our study, non-Hispanic Blacks had the highest prevalence of only two RFs and all four RFs compared to other racial and ethnic groups. The finding was consistent with the high prevalence of hypertension and diabetes identified in the general US adult population.[19] The cross-sectional study among US adults reported that the age-adjusted prevalence of obesity, hypertension, and diabetes was highest among non-Hispanic Blacks as compared to other racial and ethnic groups.[19] A 2011 REGARDS study suggested that approximately half of the racial disparity in stroke risk was attributable to traditional RFs and socioeconomic factors among participants aged 45–65 years.[20]

The significant changes in RFs identified during AIS hospitalizations may also have implications in predicting the recurrence of stroke among younger stroke survivors. The traditional stroke RFs included in our study are associated with the increased risk of stroke recurrence.[21] A cohort study developed a nomogram to predict the risk of stroke recurrence among young adults aged 18–49 years after first ischemic stroke.[22] Hypertension, diabetes, and smoking status were significant predictors of stroke recurrence in the nomogram. In our study, we found that the overall prevalence of hypertension, diabetes, and tobacco use increased from 75.2% to 81.8%, 39.1% to 45.4%, and 27.9% to 37.6%, respectively, from 2006–2007 to 2016–2017 as well as the significantly increased trends in multiple co-existing RFs among younger AIS patients. In addition, the trends in stroke mortality of county-level data showed that roughly three times as many counties experienced increases in stroke death rates for middle-aged adults (35–64 years) compared with counties that experienced increases in stroke death rates for older adults for 2010–2016.[23] Our findings suggested a

critical need to improve stroke prevention among the younger population, reinforcing the effective efforts to reduce the recurrent stroke and stroke mortality.

The findings of the present study represent hospitalizations throughout the United States. However, our study has limitations. First, the NIS is an event-level database, and we were not able to identify the patients who may have had repeat hospitalizations in any calendar year at the national level. Second, coding changes from ICD-9 to ICD-10 in 2015 might impact the trends in identifying the AIS hospitalizations. However, studies suggested that the changes from ICD-9 to ICD-10 had minor impact on the stroke hospitalizations.[24] Third, due to the nature of administrative data, there was a lack of clinical information, especially stroke severity, which is associated with the stroke outcomes and the underlying cause of stroke. Fourth, the increased use of magnetic resonance imaging and enhanced computed tomography of the brain may lead to an increase in diagnosed ischemic stroke. Finally, the RFs might be underestimated since they were obtained from the secondary diagnosis codes. It was possible that some comorbidities may not be recorded during admissions.

Conclusions

Our findings suggest a significant shift in the prevalence of RFs toward multiple co-existing RFs among hospitalized AIS patients aged 35–64 years from 2006 to 2017. Stroke can be substantially prevented through public health and clinical strategies to promote awareness of and interventions to prevent and manage multiple co-existing RFs as identified by the Million Hearts initiative's efforts of optimizing care and keeping people healthy by controlling hypertension, managing cholesterol, and implementing tobacco cessation protocols. The increased trend of multiple co-existing RFs among younger stroke patients requires clinicians, healthcare system, and public health efforts to implement more effective prevention and control strategies among this population to achieve long-term stroke risk reduction.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Disclaimer

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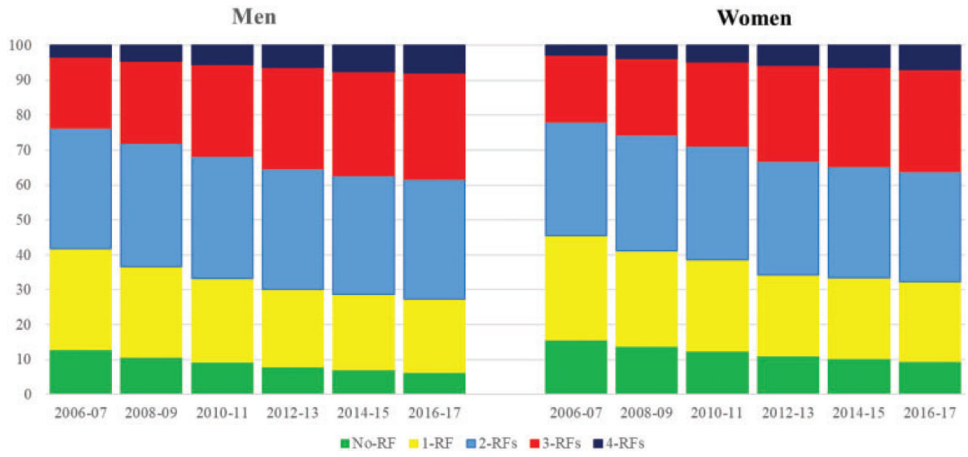

Figure 1.
Prevalence of risk factors by sex and year, United States 2006–2017.

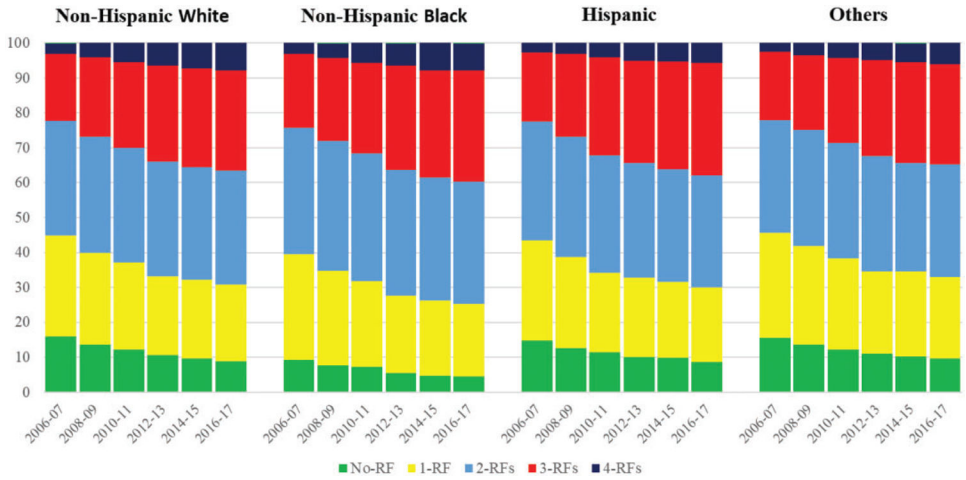

Figure 2.
Prevalence of risk factors by race and ethnicity and year, United States 2006–2017.

Table 1.

Descriptive information (% with 95% confidence interval) on AIS hospitalizations among 35–64 years, 2006–2017

Characteristics	Overall	2006–2007	2008–2009	2010–2011	2012–2013	2014–2015	2016–2017
Total number	1,509,203	169,484	207,518	248,501	275,740	295,475	312,485
Rates per 100,000 population	102.5	71.1	85.5	101.0	111.7	118.9	125.0
Age in groups							
35–44 years	9.8 (9.7, 9.9)	10.6 (10.2, 10.9)	10.1 (9.8, 10.5)	9.7 (9.4, 10.0)	9.5 (9.2, 9.7)	9.5 (9.3, 9.8)	9.7 (9.5, 10.0)
45–54 years	31.6 (31.4, 31.8)	33.0 (32.4, 33.6)	33.0 (32.5, 33.5)	32.8 (32.2, 33.2)	31.6 (31.2, 32.0)	30.7 (30.3, 31.1)	30.0 (29.7, 30.4)
55–64 years	58.6 (58.3, 58.9)	56.5 (55.8, 57.1)	56.9 (56.2, 57.5)	57.6 (57.0, 58.1)	58.9 (58.5, 59.4)	59.7 (59.3, 60.2)	60.2 (59.8, 60.6)
Men	58.2 (58.0, 58.4)	56.5 (55.8, 57.2)	57.6 (57.0, 58.2)	58.1 (57.6, 58.6)	58.3 (57.9, 58.7)	58.7 (58.3, 59.1)	59.1 (58.7, 60.0)
Race/ethnicity							
Non-Hispanic White	58.2 (57.4, 59.0)	58.0 (55.2, 60.7)	60.0 (57.7, 62.3)	57.3 (55.0, 59.5)	58.7 (57.5, 59.8)	58.4 (57.3, 59.4)	57.3 (56.3, 58.4)
Non-Hispanic Black	25.7 (25.0, 26.4)	25.3 (23.0, 27.8)	24.1 (22.1, 26.2)	27.2 (25.1, 29.3)	25.3 (24.4, 26.2)	25.7 (24.8, 26.6)	26.0 (25.1, 27.0)
Hispanic	9.7 (9.3, 10.1)	10.5 (9.0, 12.2)	9.0 (7.8, 10.2)	9.4 (8.2, 10.7)	9.5 (8.8, 10.1)	9.6 (9.0, 10.2)	10.2 (9.6, 10.9)
Others	6.4 (6.2, 6.7)	6.2 (5.4, 7.1)	6.9 (6.0, 8.0)	6.1 (5.4, 7.0)	6.6 (6.1, 7.1)	6.3 (5.9, 6.7)	6.4 (6.0, 6.8)
Discharged to home	54.4 (54.0, 54.7)	56.3 (55.2, 57.4)	56.7 (55.8, 57.7)	54.6 (53.8, 55.5)	54.7 (54.2, 55.3)	53.5 (53.0, 54.0)	52.1 (51.6, 52.6)
In-hospital death	2.5 (2.4, 2.6)	3.0 (2.8, 3.2)	2.6 (2.4, 2.8)	2.6 (2.5, 2.8)	2.4 (2.2, 2.5)	2.3 (2.2, 2.5)	2.4 (2.2, 2.5)

Table 2.

The prevalence of risk factors by year among AIS hospitalizations aged 35–64 years, 2006–2017

	2006–2007	2008–2009	2010–2011	2012–2013	2014–2015	2016–2017	RPC[a]
None of four RFs %	10.1 (9.7, 10.7)	9.0 (8.5, 9.5)	8.0 (7.5, 8.5)	6.8 (6.5, 7.1)	6.5 (6.3, 6.8)	6.2 (6.0, 6.5)[b]	−38.6%
One RF only %	25.2 (24.6, 25.8)	22.4 (21.8, 23.0)	20.7 (20.2, 21.3)	18.4 (18.0, 18.8)	18.3 (17.9, 18.6)	18.1 (17.8, 18.5)[b]	−28.2%
Hypertension (HTN)	15.3 (14.7, 15.9)	13.0 (12.5, 13.5)	12.0 (11.5, 12.4)	10.3 (10.0, 10.6)	10.1 (9.8, 10.4)	10.6 (10.3, 10.9)[b]	−30.7%
Tobacco	4.1 (3.8, 4.3)	3.9 (3.7, 4.1)	3.7 (3.5, 3.9)	3.3 (3.2, 3.5)	3.5 (3.4, 3.7)	3.6 (3.4, 3.7)[b]	−12.2%
Lipid disorder	3.2 (3.0, 3.5)	3.4 (3.2, 3.6)	3.4 (3.2, 3.6)	3.3 (3.1, 3.4)	3.1 (3.0, 3.2)	2.7 (2.5, 2.8)	−15.6%
Diabetes	2.6 (2.4, 2.8)	2.2 (2.0, 2.3)	1.7 (1.6, 1.9)	1.5 (1.4, 1.6)	1.5 (1.4, 1.6)	1.3 (1.2, 1.4)[b]	−50.0%
Any two of four RFs %	36.1 (35.5, 36.6)	36.0 (35.5, 36.6)	34.8 (34.3, 35.3)	34.0 (33.6, 34.4)	32.7 (32.3, 33.1)	32.7 (32.4, 33.1)[b]	−9.4%
HTN + lipid	12.6 (12.2, 13.0)	13.0 (12.5, 13.4)	13.5 (13.2, 13.9)	13.4 (13.2, 13.7)	12.3 (12.0, 12.6)	11.9 (11.6, 12.2)	−5.6%
HTN + diabetes	12.4 (11.9, 13.0)	11.1 (10.6, 11.5)	9.6 (9.2, 10.1)	9.1 (8.8, 9.4)	8.5 (8.3, 8.8)	8.7 (8.4, 8.9)[b]	−29.8%
HTN + tobacco	6.9 (6.5, 7.3)	7.3 (7.0, 7.7)	7.2 (6.9, 7.5)	7.2 (7.0, 7.4)	7.8 (7.5, 8.0)	8.5 (8.3, 8.8)[b]	23.2%
Lipid + tobacco	1.9 (1.8, 2.1)	2.3 (2.1, 2.5)	2.3 (2.1, 2.5)	2.2 (2.1, 2.3)	2.0 (1.9, 2.2)	1.7 (1.6, 1.8)	−10.5%
Diabetes + lipid	1.6 (1.4, 1.7)	1.6 (1.5, 1.8)	1.5 (1.4, 1.6)	1.5 (1.4, 1.6)	1.4 (1.3, 1.5)	1.3 (1.2, 1.4)	−18.8%
Diabetes + tobacco	0.7 (0.6, 0.8)	0.7 (0.7, 0.8)	0.6 (0.6, 0.7)	0.6 (0.6, 0.7)	0.6 (0.6, 0.7)	0.6 (0.6, 0.7)	−14.3%
Any three of four RFs %	24.5 (23.9, 25.1)	27.3 (26.6, 28.0)	29.9 (29.2, 30.5)	33.1 (32.6, 33.6)	33.8 (33.4, 34.2)	33.8 (33.4, 34.2)[b]	38.0%
HTN + diabetes + lipid	14.3 (13.8, 14.8)	15.5 (15.0, 16.0)	17.0 (16.5, 17.6)	19.0 (18.6, 19.4)	19.6 (19.2, 20.0)	19.8 (19.4, 20.2)[b]	38.5%
HTN + lipid + tobacco	6.7 (6.4, 7.1)	8.2 (7.8, 8.6)	9.0 (8.6, 9.3)	10.0 (9.6, 10.3)	9.7 (9.5, 10.0)	9.3 (9.1, 9.6)[b]	38.8%
HTN + diabetes + tobacco	2.9 (2.7, 3.1)	3.0 (2.8, 3.2)	3.1 (2.9, 3.3)	3.3 (3.2, 3.5)	3.7 (3.5, 3.8)	3.9 (3.8, 4.1)[b]	34.5%
Diabetes + lipid + tobacco	0.6 (0.5, 0.7)	0.7 (0.6, 0.8)	0.7 (0.7, 0.8)	0.8 (0.7, 0.9)	0.8 (0.7, 0.9)	0.7 (0.7, 0.8)[b]	16.7%
All four RFs %							
HTN + diabetes + lipid + tobacco	4.1 (3.8, 4.4)	5.3 (5.0, 5.6)	6.6 (6.3, 7.0)	7.7 (7.4, 7.9)	8.7 (8.5, 9.0)	9.1 (8.8, 9.3)[b]	122.0%

[a] RPC is calculated using the formula ((2016–2017) – (2006–2007))/(2006–2007))*100.

[b] Indicated the significant linear trends across six time periods ($p < 0.01$).