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Trends in incidence of disability in activities of daily living among Chinese older adults, 1993-2006

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Abstract

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Employment or Affiliation		X		X		X		X		X		X				
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Honoraria		X		X		X		X		X		X				
Speaker Forum		X		X		X		X		X		X				
Consultant		X		X		X		X		X		X				
Stocks		X		X		X		X		X		X				
Royalties		X		X		X		X		X		X				
Expert Testimony		X		X		X		X		X		X				
Board Member		X		X		X		X		X		X				
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* Authors can be listed by abbreviations of their names.

For all "Yes" responses, provide a brief explanation here:

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BACKGROUND—A decline in prevalence of disability in activities of daily living (ADL) among Chinese elderly people has been reported, but data on secular trends of incidence of ADL disability are sparse.

OBJECTIVES—We seek to investigate the time trends in incidence of ADL disability among Chinese older adults, and further, to explore factors potentially contributing to the trends.

DESIGN—A population-based prospective study.

SETTING—Participants were selected from nine provinces of China through a multistage, randomized, cluster sampling process.

PARTICIPANTS—We identified three consecutive cohorts of people aged ≥60 years within China Health and Nutrition Survey: cohort 1993-2000 (n=831), cohort 1997-2004 (n=1,091), and cohort 2000-2006 (n=1,152).

MEASUREMENTS—Disability in ADL was defined as inability to perform at least one of the five self-care activities, i.e., transferring, dressing, toileting, bathing, and feeding. Data were analyzed with Cox and generalized estimating equation models.

RESULTS—The incidence (per 1,000 person-years) of ADL disability significantly decreased from 35.3 in 1993-2000 and 28.9 in 1997-2004 to 24.3 in 2000-2006 in Chinese older adults ($P_{\text{trend}} < .001$). The incidence of ADL disability significantly decreased in both men and women, in young-old adults (aged 60-74 years), and in those living in rural area ($P_{\text{trend}} < .02$) after controlling for multiple potential influential factors. Of the five ADL items, the decline in incidence of disability was significant in transferring ($P_{\text{trend}} < .001$) and bathing ($P_{\text{trend}} = .002$) and marginally significant in toileting ($P_{\text{trend}} = .061$), but the incidence was stable in dressing ($P_{\text{trend}} = .384$) and feeding ($P_{\text{trend}} = .258$).

CONCLUSION—The incidence of ADL disability decreased from 1993 to 2006 among older adults in China, especially in transferring and bathing, independent of socio-demographics, lifestyles, and chronic health conditions.

Keywords

incidence; trend; activities of daily living; elderly; China

A decline in both prevalence and incidence of disability in activities of daily living (ADL) in the past 2-3 decades has been reported among older adults in high-income countries.¹⁻³ In China, several studies have also shown a downward trend in prevalence of ADL disability in older adults.⁴⁻⁶ The favorable trend in prevalence of ADL disability is likely due partly to a declining incidence of disability. However, no population-based studies have so far investigated the secular trends in incidence of ADL disability in China. Moreover, the time trends in disability by specific ADL tasks have not been reported in Chinese older adults.

Late-life functional disability has been associated with unhealthy lifestyles (e.g., smoking) and chronic health conditions or multimorbidity, e.g., diabetes, cardiovascular diseases (CVDs), and dementia.⁷⁻¹¹ Therefore, changes in prevalence of these factors may affect the time trends of late-life ADL disability. It has been estimated that the decrease in cardiovascular risk contributes to around 22% reduction in disability in the United States.¹²

Stroke is a leading contributor to physical disability and disability-adjusted life-years in China.¹³ Physical functioning deteriorates following a clinical stroke, and a considerable proportion of patients with stroke become dependent in ADL, especially among older patients.¹⁴ Previously, cross-sectional studies have shown that the association between CVDs (e.g., stroke) and disability becomes weaker over time.^{4,15} However, the time trends in the strength of longitudinal association between chronic conditions and risk of disability has not yet been investigated. Given the significant impacts of functional dependence on quality of life and social care system,¹⁶ clarifying the time trend of disabling effects of modifiable risk factors will have important implications for public health.

We previously reported a decline in prevalence of ADL disability from 1997 to 2006 among older adults in China.⁴ In current analysis, we seek to investigate the secular trends in incidence of ADL disability among Chinese older adults, and further, to explore factors that potentially contribute to the time trends.

METHODS

Study Design and Population

Study participants were derived from China Health and Nutrition Survey (CHNS). CHNS is a nationwide longitudinal survey on health risk factors, nutritional status, and health outcomes in Chinese populations (age ≥ 2 years). The study sample for CHNS was drawn from nine provinces (Liaoning, Heilongjiang, Jiangsu, Shandong, Henan, Hubei, Hunan, Guangxi, and Guizhou) through a multistage, randomized, cluster sampling process, as fully described elsewhere.¹⁷ The CHNS survey was conducted in 1989, 1991, 1993, 1997, 2000, 2004, 2006, 2009, and 2011. ADL were assessed only in surveys of 1993 to 2006 for people aged ≥ 55 years. In this study, we only included older adults who were aged ≥ 60 years.

To explore the trends in incidence of ADL disability over time, we identified three consecutive cohorts within CHNS that covered three time periods: cohort 1 (1993-2000), cohort 2 (1997-2004), and cohort 3 (2000-2006). Each cohort (time period) covered three waves of survey: the first wave was considered as baseline survey, and the two successive waves were considered as follow-up surveys. Because we aimed to determine incidence of ADL disability, individuals with ADL disability at baseline of each of the three cohorts were excluded from the analytical sample. Figure 1 shows the flowchart of study participants. Of all eligible subjects who were free of ADL disability at baseline of each of the three cohorts (n=4,119), 831 out of 1,209 (68.7%) in cohort 1, 1,091 out of 1,447 (75.4%) in cohort 2, and 1,152 out of 1,463 (78.7%) in cohort 3 underwent at least one follow-up assessment. Of the total number of 1,045 (25.4%) subjects who had no follow-up data, 678 (64.9%) were due to dropouts and 367 (35.1%) died. Compared to participants, non-participants were older, more likely to be unmarried, more likely to go to a hospital for health care, and have more chronic diseases.

Of all the 3,074 participants, 920 (29.9%) were included in at least 2 of the three cohorts: 306 were included in all three cohorts, 205 were included in cohorts 1 and 2, 359 were included in cohorts 2 and 3, and 50 were included in cohorts 1 and 3 (Figure 1).

Data Collection and Definitions

Data were collected by trained and certified health professionals through interviews and physical examinations.¹⁷ Smoking status was categorized into never, former, and current smoking. Alcohol intake was categorized into no regular, light-to-moderate (1-14 drinks per week for men or 1-7 drinks per week for women), and heavy (>14 drinks per week for men or >7 drinks per week for women) drinking.¹⁸ Physically active (data available from 1997 onward) was defined as participation in 150 minutes of moderate-intensity aerobic physical activity throughout the week or participation in 75 minutes of vigorous-intensity aerobic physical activity throughout the week or an equivalent combination of moderate- and vigorous-intensity activity.¹⁹ Dietary reference intake was defined according to the recommendation that of the total energy, acceptable macronutrient distribution range should be 45-65% for carbohydrate, 20-35% for fat, and 10-35% for protein.²⁰

Body mass index (BMI) was calculated as measured weight (kg) divided by height (meters) squared. Obesity was defined as a BMI ≥ 28 kg/m², a cut-off proposed specifically for Chinese adults.²¹ Hypertension was defined as systolic pressure ≥ 140 mmHg, or diastolic pressure ≥ 90 mmHg, or currently using antihypertensive medications.²² Multimorbidity was defined as concurrently having two or more chronic health conditions that included obesity and hypertension; self-reported physician diagnosis of diabetes, heart disease or myocardial infarction, and stroke; self-reported joint or muscle pain, eye/hearing problems, urinating or defecating problems, anxiety, exhaustion, unexplained weight loss, memory complaint, and other chronic noncommunicable conditions.

Basic ADL were measured according to self-reported responses to questions (i.e., do you have any difficulty in doing this activity?), which involved five activities of self-care tasks, i.e., transferring (standing up from long-term sitting), dressing, toileting, bathing, and feeding. The answers to these questions included five options: “1 no difficulty”, “2 have some difficulty, but can still do it”, “3 need help to do it”, “4 cannot do it at all”, and “9 unknown”. Persons who gave answer “yes” to “3 need help to do it” or “4 cannot do it at all” in at least one of the five self-care activities were defined as having disability in basic ADL.²³

Statistical Analysis

The time trends in baseline characteristics across the three time periods were assessed using the generalized estimating equation (GEE) models, with an identity link and a normal distribution for continuous variables, and a logit link and a binomial distribution for categorical variables. The GEE models could address the correlation of repeat participation of the same individuals over time (e.g., persons included in two or three cohorts in this study).

We calculated incidence of ADL disability according to person-years of follow-up. For persons who did not develop ADL disability at last contact, the follow-up time was calculated from baseline survey to last contact. For those who developed ADL disability, the onset time of ADL disability was assumed to be in the midpoint between the two surveys owing to its insidious onset.²⁴ Thus, the follow-up time was estimated as full time during

which subjects remained free of ADL disability plus half of follow-up time during which ADL disability developed. GEE models were employed to assess the trends in incidence of ADL disability over time after controlling for age, sex, race, marital status, education, living region, access to health care facility, smoking, alcohol intake, physical activity, diet, chronic multimorbidity, and follow time. We assessed the time trends of ADL disability by age (60-74 vs. 75 years), sex, and living region (urban vs. rural area).²⁵ Cox proportional hazards models were used to examine the association of various factors with ADL disability in each of the three cohorts. The time trends in associations between various factors and ADL disability across the three cohorts were examined with multiple GEE models, in which the interaction term between survey time and individual factors or related disorders was included into the model together with covariates.

We conducted multiple-imputation analysis to assess impact of missing data at baseline and dropouts (but not deceased) during follow-ups on the trends of ADL disability.²⁶

IBM SPSS Statistics 22 for Windows (IBM SPSS Inc., Chicago, Illinois, USA) was used for all analyses.

RESULTS

Characteristics of Study Participants

Participants received more years of education ($P_{\text{trend}} < .001$) and less likely to go to hospitals (vs. local or village clinics) for health care ($P_{\text{trend}} = .041$) over time. After controlling for age, sex, education, and living region, people were more likely to have chronic multimorbidity ($P_{\text{trend}} < .001$) over time. The mean age and the proportions of sex, race, marital status, rural residents, smoking, alcohol intake, and unfavorable diet did not differ significantly across cohorts over time ($P_{\text{trend}} > .05$) (Table 1).

Trend in Incidence of ADL Disability

Overall, the incidence of ADL disability (per 1,000 person-years) significantly decreased from 35.3 in 1993-2000 and 28.9 in 1997-2004 to 24.3 in 2000-2006 ($P_{\text{trend}} < .001$). The decline in incidence of ADL disability was significant in both men ($P_{\text{trend}} = .018$) and women ($P_{\text{trend}} = .003$), in young-old adults (aged 60-74 years) ($P_{\text{trend}} = .001$), and in those living in rural area ($P_{\text{trend}} < .001$), and was statistically marginal in old-old adults ($P_{\text{trend}} = .066$) (Table 2).

After controlling for multiple covariates, the incidence of ADL disability was higher in old-old adults than in young-old adults within each of the three cohorts (all $P < .001$), and in men than in women for cohort 1997-2004 ($P = .041$). There was no significant difference in incidence of ADL disability by living regions within any of the three cohorts (all $P > .05$).

Trends in Incidence of Disability in ADL Items

Of the five specific ADL items, the incidence of disability was the highest for transferring, followed by bathing, toileting or dressing, and the lowest for feeding within each cohort. The decrease in incidence of disability from 1993-2000 to 2000-2006 was statistically significant for transferring ($P_{\text{trend}} < .001$) and bathing ($P_{\text{trend}} = .002$), and marginally significant for

toileting ($P_{\text{trend}}=.061$), but the incidence of disability was stable over time for dressing ($P_{\text{trend}}=.384$) and feeding ($P_{\text{trend}}=.258$) (Figure 2).

Trends in Associations of Various Factors with Disability

The hazard ratio of ADL disability was significantly associated with older age across three cohorts, and there was no significant change in the disabling effect of age (Table 3). Being a female, having received more years of education, current smoking, and alcohol intake tended to be negatively associated with ADL disability in the early cohorts, but the associations disappeared in the cohort 2000-2006, and the trends of associations with ADL disability were significant for primary school (vs. no formal school, $P_{\text{trend}}=.031$) and for current smoking ($P_{\text{trend}}=.008$), and marginally significant for heavy alcohol consumption ($P_{\text{trend}}=.078$). Having chronic multimorbidity was associated with an elevated risk of ADL disability, but the trend of the association was not statistically significant. The strength of associations of ADL disability with other factors (e.g., race, marital status, living region, access to health care, and diets) did not alter significantly over time (Table 3).

Sensitivity Analysis

The multiple-imputation analysis on the missing data owing to dropouts (not deceased) showed similar results in terms of the time trends of ADL disability, but the incidence rates of ADL disability from the imputation analysis were higher than those from the sample without imputation (Supplementary table 1). The imputation analysis showed a decreasing trend of disability in all ADL items except for feeding (Supplementary figure).

Furthermore, we repeated the analyses by excluding individuals from subsequent cohorts who were already included in the previous cohort, which yielded results similar to those from the main analyses (data not shown).

DISCUSSION

This study of a nationwide sample in China showed that the incidence of ADL disability among people aged 60 years decreased from 1993 to 2006, and the decline was evident in both men and women, in young-old adults (60-74 years), and in rural residents, even when a broad range of factors (e.g., socio-demographics, lifestyles, and chronic health conditions) were taken into consideration. We also found that of the five self-care activities, the incidence of disability decreased mainly in transferring and bathing.

Our study supports the potential that the decreasing prevalence of ADL disability among Chinese older adults, as previously reported,^{4,5} might be partly attributed to the declining incidence of disability. Furthermore, previous research has revealed a pattern of functional decline and recovery in ADL in older adults,²⁷ and that the transition from ADL-disabled condition to active status is nontrivial.²⁸ Thus, the increase in recovery rate of ADL disability (or decrease in duration of disability) over time may also contribute to decline in prevalence of ADL disability. In support of this view, we did find an increasing recovery rate of ADL disability over time in additional analyses (Supplementary table 2).

Previous studies have reported different prevalence of ADL disability between urban and rural areas in China, but the rural-urban difference tends to diminish over time.^{4,25} Similarly, we found that the incidence of ADL disability was generally comparable between rural and urban residents across the three cohorts, although the decline in incident disability was more evident in rural residents. In the past three decades, China has experienced quick industrialization and urbanization, and rural areas have acquired certain characteristics of urban environments.²⁶ This may partly reflect the fact that the urban-rural gap in lifestyles and socioeconomic status had gradually diminished in China.

Earlier studies showed that the prevalence of disability decreased for transferring, bathing, toileting or dressing,^{2,30} but was stable for feeding.² To the best of our knowledge, the secular trends in incidence of disability by individual tasks of ADL have not yet been reported. Of the five self-care tasks in ADL, we found that the declining trend in incidence of disability was more evident in transferring and bathing, although the imputation analysis showed declining incidence of disability also for toileting and dressing, whereas the incidence of disability in feeding was stable. This might partly contribute to the declining prevalence of disability in transferring, bathing, toileting, and dressing as well as the stable prevalence of disability in feeding, as previously reported.^{2,30} The declining incidence of disability might be partly attributable to the improved contextual environmental factors and living conditions in the past 2-3 decades in China.³¹ For instance, functional capacity or the extent of disability depends on environmental support, use of technical aids (e.g., walkers), and modifications of the home environment (e.g., use of showers instead of bath-tubs),^{32,33} which might partly explain the declining trends in incident disability in transferring and bathing. Since these two tasks are most commonly affected in ADL disability in Chinese older adults,²⁸ the finding of decreasing incidence of disability in transferring and bathing has significant implication for public health and elderly care.

The potential factors contributing to the favorable trends in ADL disability over time are complex and remain poorly understood. Of those factors examined in our study, socio-demographic factors (e.g., age, sex, education, and living region) play a part in functional outcomes, which are in line with the literature.^{25,27} We found that people received more years of education over time that might contribute to the declining incidence of ADL disability, but the protective effect of higher educational attainments tended to decrease over time. Of note, smoking and heavy alcohol intake were associated with reduce risk of ADL disability in the cohorts 1993-2000 and 1997-2004, which is unexpected, but such an effect diminished over time and heavy alcohol consumption even became a potential risk factor for ADL disability in the cohort 2000-2006. In addition, chronic multimorbidity was associated with ADL disability, and the strength of association with ADL disability tended to decrease over time. Indeed, chronic health conditions might become less disabling over time owing to improvements in early diagnosis, medical treatment, and rehabilitation of these disorders.^{34,35} It was noteworthy that the favourable trends in ADL disability in China were accompanied by an increase in prevalence of obesity, hypertension, diabetes, and major CVDs.^{13,36-38} Thus, national strategic policies and intervention programs targeting major modifiable risk factors are imperative to tackle the increasing prevalence of CVDs, which may lead to a further decline in incidence of ADL disability.

The major strength of this study refers to the nationwide sample derived from a large and diverse population in China. Moreover, data were collected using consistent approaches over time, with the participation rate being rather high across cohorts (~70-80%). However, this study also has limitations. First, non-participants (or dropouts) were older and more likely to be unmarried and have multimorbidity than participants. However, multiple-imputation analysis could confirm the decreasing trend in incidence of ADL disability. Second, although the potential impacts of numerous chronic health conditions on the time trends of ADL disability were examined, we were not able to explore the effects of certain socio-cultural and environmental factors (e.g., improved medical techniques, social and family support, and public transportation) and additional chronic diseases (e.g., chronic obstructive pulmonary disease and dementia) due to lack of specific data. Finally, the use of self-reported information on lifestyle factors and chronic diseases might lead to underestimation of their true prevalence and associations with disability.

In summary, this study provided evidence that the incidence of ADL disability had decreased from 1993 to 2006 among Chinese elderly people, especially in the tasks of transferring and bathing. Given that a decline in incidence of ADL disability has significant implications for public health and health care policy in the aging society, our findings warrant independent confirmation in other populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Flowchart of the study population: China Health and Nutrition Survey, 1993-2006

Figure 2.

Trends in incidence of disability in activities of daily living by five items, 1993-2006

Table 1

Baseline characteristics of participants in the three cohorts

Baseline characteristics ^a	Cohort 1, 1993-2000	Cohort 2, 1997-2004	Cohort 3, 2000-2006	<i>P</i> _{trend} ^b
No. of subjects	831	1,091	1,152	
Age (years)	67.5 (5.9)	67.8 (5.8)	67.8 (5.8)	.312
Women	441 (53.1)	582 (53.3)	605 (52.5)	.732
Race				
Han majority	736 (88.7)	973 (89.5)	1,013 (87.9)	
Minority	94 (11.3)	114 (10.5)	139 (12.1)	.430
Marital status				
Not married	218 (26.3)	302 (27.9)	293 (26.7)	
Married	610 (73.7)	782 (72.1)	805 (73.3)	.904
Education				
No formal school	625 (76.3)	709 (65.1)	609 (52.9)	
Primary school	109 (13.3)	192 (17.6)	275 (23.9)	
Middle school or above	85 (10.4)	188 (17.3)	268 (23.3)	<.001
Living region				
Urban	292 (35.1)	426 (39.0)	444 (38.5)	
Rural	539 (64.9)	665 (61.0)	708 (61.5)	.075
Access to health care facility				
Hospitals	181 (33.5)	257 (33.9)	228 (29.0)	
Local or village clinics	360 (66.5)	500 (66.1)	558 (71.0)	.041
Smoking				
Never	547 (66.2)	751 (69.0)	805 (70.1)	
Former	19 (2.3)	14 (1.3)	21 (1.8)	
Current	260 (31.5)	323 (29.7)	322 (28.0)	.147
Alcohol intake				
Never	607 (73.4)	815 (76.1)	845 (75.0)	
Light to moderate	165 (20.0)	182 (17.0)	171 (15.2)	
Heavy	55 (6.7)	74 (6.9)	111 (9.8)	.885
Physical activity				
Inactive	-	967 (88.6)	1,071 (93.0)	
Active	-	124 (11.4)	81 (7.0)	-
Diet				
Dietary reference intake diet	244 (29.6)	326 (30.3)	348 (30.5)	
Unfavorable diet	581 (70.4)	749 (69.7)	793 (69.5)	.595
Chronic multimorbidity				
No	785 (94.9)	976 (89.5)	988 (85.8)	
Yes	42 (5.1)	115 (10.5)	164 (14.2)	<.001

Values are mean (SD) for age and n (%) for others.

^aThe number of participants with missing value was 5 for race, 64 for marital status, 14 for education, 990 for access to health care facility, 12 for smoking, 49 for alcohol intake, 33 for diet, and 4 for chronic multimorbidity. A dummy variable was created for the missing value of all above variables in the subsequent multiple variable analysis.

^bGeneralized estimating equation models were employed to test the time trends, if applicable, controlling for age, sex, education, and living region.

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Table 2

Trends in incidence rate (per 1,000 person-years) of disability in activities of daily living by age, sex, and living region

Characteristics	Cohort 1, 1993-2000 (n=831)			Cohort 2, 1997-2004 (n=1,091)			Cohort 3, 2000-2006 (n=1,152)			<i>P</i> _{trend} ^a
	No. of cases	Person-years	Incidence rate	No. of cases	Person-years	Incidence rate	No. of cases	Person-years	Incidence rate	
Total	160	4,532	35.3	169	5,844	28.9	146	6,001	24.3	<.001
Age, years										
60-74	110	4,070	27.0	120	5,287	22.7	106	5,347	19.8	.001
75	50	461	108.5	49	557	88.0	40	654	61.2	.066
Sex										
Men	68	2,150	31.6	77	2,772	27.8	69	2,856	24.2	.018
Women	92	2,381	38.6	92	3,072	29.9	77	3,146	24.5	.003
Region										
Urban	52	1,612	32.3	57	2,293	24.9	58	2,325	24.9	.142
Rural	108	2,920	37.0	112	3,551	31.5	88	3,676	23.9	<.001

^a Generalized estimating equation models were employed to test the time trends after controlling for race, marital status, education, access to health care facility, smoking, alcohol intake, physical activity, diet, chronic multimorbidity, follow time, and if applicable, for age, sex, and living region.

Table 3
Trends in the associations between various factors and incident disability in activities of daily living, 1993-2006

Factors	Cohort 1, 1993-2000			Cohort 2, 1997-2004			Cohort 3, 2000-2006			P_{trend}^b
	No. of cases/Subjects	Hazard ratio (95% CI) ^a		No. of cases/Subjects	Hazard ratio (95% CI) ^a		No. of cases/Subjects	Hazard ratio (95% CI) ^a		
Age (years)										
60-74	110/721	Ref		120/950	Ref		106/1,010	Ref		
75	50/110	4.36 (2.96-6.43)		49/141	3.95 (2.73-5.72)		40/142	2.90 (1.95-4.30)		.918
Sex										
Men	68/390	Ref		77/509	Ref		69/547	Ref		
Women	92/441	0.63 (0.41-0.96)		92/582	0.60 (0.40-0.91)		77/605	0.82 (0.53-1.26)		.542
Race										
Han majority	148/736	Ref		156/973	Ref		127/1,013	Ref		
Minority	12/94	0.57 (0.32-1.04)		13/114	0.61 (0.35-1.09)		19/139	0.83 (0.51-1.36)		.182
Marital status										
Not married	55/218	Ref		58/302	Ref		52/293	Ref		
Married	105/610	0.99 (0.67-1.46)		111/782	0.94 (0.65-1.35)		87/805	0.70 (0.48-1.03)		.170
Education										
No formal school	136/625	Ref		115/709	Ref		85/609	Ref		
Primary school	10/109	0.42 (0.21-0.82)		31/192	0.92 (0.60-1.41)		36/275	1.02 (0.67-1.54)		.031
Middle school or above	12/85	0.55 (0.29-1.04)		23/188	0.67 (0.41-1.10)		25/268	0.75 (0.46-1.24)		.885
Living region										
Urban	52/292	Ref		57/426	Ref		58/444	Ref		
Rural	108/539	1.42 (0.95-2.13)		112/665	1.57 (1.08-2.28)		88/708	0.94 (0.64-1.37)		.394
Access to health care facility										
Hospital	39/181	Ref		33/257	Ref		21/228	Ref		
Local or village clinics	68/360	0.69 (0.43-1.11)		72/500	0.85 (0.52-1.39)		68/558	1.55 (0.90-2.67)		.119
Smoking										
Never	122/547	Ref		129/751	Ref		104/805	Ref		
Former	4/19	0.91 (0.33-2.53)		4/14	2.29 (0.81-6.42)		1/21	1.19 (0.03-1.44)		.484
Current	32/260	0.55 (0.35-0.86)		36/323	0.71 (0.46-1.09)		41/322	0.99 (0.64-1.52)		.008
Alcohol intake										

Factors	Cohort 1, 1993-2000			Cohort 2, 1997-2004			Cohort 3, 2000-2006			P_{trend}^b
	No. of cases/Subjects	Hazard ratio (95% CI) ^a		No. of cases/Subjects	Hazard ratio (95% CI) ^a		No. of cases/Subjects	Hazard ratio (95% CI) ^a		
Never	129/607	Ref		140/815	Ref		100/845	Ref		
Light to moderate	22/165	0.58 (0.35-0.96)		23/182	0.66 (0.41-1.06)		24/171	1.17 (0.73-1.87)		.170
Heavy	7/55	0.59 (0.26-1.34)		6/74	0.42 (0.18-0.99)		20/111	1.59 (0.95-2.66)		.078
Physically activity										
Inactive	-	-		152/967	Ref		138/1,071	Ref		
Active	-	-		17/124	1.05 (0.62-1.77)		8/81	0.82 (0.40-1.70)		.451
Diet										
Dietary reference intake diet	42/244	Ref		53/326	Ref		36/348	Ref		
Unfavorable diet	116/581	1.25 (0.87-1.81)		115/749	0.89 (0.64-1.24)		107/793	1.39 (0.95-2.04)		.977
Chronic multimorbidity										
No	146/785	Ref		149/976	Ref		116/988	Ref		
Yes	14/42	2.21 (1.25-3.90)		20/115	1.34 (0.83-2.16)		30/164	1.75 (1.15-2.66)		.931

^aHazard ratio and 95% confidence interval were derived from Cox models after controlling for all variables listed in the table.

^bGeneralized estimating equation models were used for the test of time trends after controlling for all variables listed in the table.