RESEARCH ARTICLE

SUDDEN DEATH IN 15-64 YEARS-OLD TAIWANESE POPULATION: A DATA-BASED RETROSPECTIVE COHORT STUDY

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ABSTRACT

Background: Sudden death (SD) among working-aged population is rare but devastating. Understanding the incidence and causes of SD is essential in the development of preventive strategies.

Aims & Objective: To investigate the incidence, risk factors and comorbidities in 15-64 years old population in Taiwan.

Materials and Methods: Incidence rates and causes of death were determined using the Taiwanese National Health Insurance Research Database (NHIRD) recorded between 2000 and 2009. Deaths were identified using the International Classification of Disease (ICD) codes. Poisson regression models were used to assess the relative risks (RRs) associated with the gender, age, seasonal and day-of-the-week variables.

Results: A total of 1269 males (73.8%) and 451 females (26.2%) SD cases were identified from a cohort of 1 million beneficiaries. The annual incidence of SD increased by10.3% from 2000 (14.5 per 100000 person-years) to 2009 (24.8 per 100000 person-years). The 10-year cumulative SD incidence was highest among people aged 55-64 years (794.3) and lowest among people aged 15-24 years (92.4). In all year and age groups, incidence rates were significantly higher among males than females (P<0.01). After adjusting for gender and age, increased risk of SD were noted 55-64 years (RR: 1.3, 95% CI: 0.1 to 1.5, p=0.000), in winter (RR: 0.10, 95% CI: 0.0 to 0.3, p=0.006) and on Mondays (RR: 0.19, 95% CI: 0.0 to 0.2, p=0.04). Cardiovascular causes accounted for the majority of medical comorbidities for SD (73.9%), mostly due to hypertension (incidence rates: 26.1%).

Conclusion: Male, 55-64 years-old, winter and Monday were major determinants of SD in Taiwan. Cardiovascular disease prevention and health promotion programs may help reduce the risk of SD.

Key Words: Sudden Death (SD); Incidence; Risk Factors; Age Distribution; Retrospective Cohort Study

Introduction

It is estimated that Sudden death (SD) occurs once every minute in the United States, ranging between 180000 and 450000 cases annually. Most SD cases appear to have been in good health, never had a prior coronary attack.[1] Sudden death (SD) in the young and middle-aged individuals have impact on the community as apparently healthy persons are affected. According to some definitions of SD, the time interval between the onset of symptoms and death is 24 hour; however, it has subsequently been reduced to 1 hour.[2-4] In recent prospective studies using multiple sources from the United States, the Netherlands, Ireland, and China, SD rates ranged from 50 to 100 per 100000 people in the general population.[5-9] Applying the age-specific incidence rates to the Dutch population would result in an overall incidence rate for the population of 0.19 to 1.92 per 1000 person-years.[10-12]

The incidence of SD is related to age, gender, seasonal variation, day of the week, and associated disease. In general, the SD risk is higher in males than in females, and increases with age. Incidence for SD is highest in winter and lowest in summer.[13,14] Most SD cases are observed on Monday.[12] The most common cause of sudden deaths is previously undetected cardiovascular disease. The incidence of coronary SD widely from 12.0% to 72.7%, partly due to the population studied.[15-19] According to studies in Japan and China, the incidence of SD in the general population is lower in Asia when compared with the West.[6-11], although this is likely due to the limited data available in Asia. So far, no study has been done to identify the risk of SD in Taiwan. Although SD is rare, it is usually fatal and is rising in incidence. Therefore, this population-based retrospective cohort study was conducted to understand the incidence and contributing factors of SD in Taiwan. The National Health Insurance (NHI) program which covers 99.7% of the population in Taiwan was used. To accurately identify the high-risk population, we examined the 15-64 years old population and explored the influence of gender, age, day-of-the-week and seasonal patterns.

Materials and Methods

Data Collection

The Taiwanese National Health Insurance Bureau (NHIB) provided electronic data with patients' gender, date of birth, the classification codes of the diagnosed diseases, data on health services received, and the clinic or hospital code. The NHIB collects data from the NHI program and sorts it into data files each year, including registration files and original claims data for reimbursement. These data files were de-identified by scrambling the identification codes of both patients and medical facilities, and the files were then sent to the National Health Research Institutes (NHRI) to form the original files of the NHIRD. Using the NHIRD claims data, we analyzed a cohort of 100,000 beneficiary's age between 15-64 diagnosed of SD from 2000 to 2009. The members of the general population included in this study were 1269 men and 451 women.

Access of the NHIRD has been approved by the NHRI Review Committee. Cases of SD were identified from the NHIRD from 2000 to 2009 by using the ninth revision of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). The codes were converted into ICD-9-CM for data analysis.

Definitions

We have excluded cases involving acute respiratory failure (ICD-9-CM codes518.81) or trauma (injury or poisoning, ICD-9-CM codes 800 to 999.9). An SD case was defined as a diagnosis of s, instantaneous death (ICD-9-CM 798.1), death occurring in less than 24 h from onset of symptoms, not otherwise explained (ICD-9-CM 798.2) , and Unattended death (ICD-9-CM 798.9).[20]

Statistical Analysis

Annual incidence of SD was calculated by dividing the number of new cases during a period by the number of people at risk in the population at the beginning of the study. The 10-year cumulative incidence refers to the number of new cases divided by the size of the population at risk from 2000 to 2009. Poisson regression models were used to assess the relative risks (RRs) and 95% confidence intervals (CIs) of SD incidence associated with the gender, age, seasonal and day-of-the-week variables. P-values <0.05 were considered statistically significant.

Results

Demographic Characteristics of Sudden Death by Gender, Age, Season and Day-of-the Week

Table 1 showed that during the 10-years period (2000–2009), 1720 people from the general population were diagnosed with SD. The majority of cases (73.8%, n: 1269) involved men, and 26.2% (n: 451) involved women. The ratio of male to female incidence was 2.9:1. The 55–64-years-old group accounted for 35.0% (n: 602) of the cases, followed by the 45–54-years-old group (29.5%, n: 508), and the 35–44-years-old group (17.5%, n: 301). The ≥45 years-old group constituted 64.5% of the cases. A seasonal of SD, the percentage were highest in the winter (27.5%, n: 474) and lowest in the summer (23.6%, n: 406), the day-of-the-week was highest on Mondays (15.9%, n: 275) and lowest on Thursday (13.3%, n: 227) [Table1].

The Annual Incidences and 10-year Cumulative Incidence of SD in the Study Cohort

The annual incidence of SD increased by10.3% from 14.5 in 2000 to 24.8 per 100000 person-years in 2009. In the patients, the 10-year cumulative incidence of SD was 273.7 per 100000 person-years. In the 10-year cumulative incidence, the age group with the highest incidence was the 55-64 years-old group (794.3 per 100000 person-years), and that with lowest was the 15-24 years-old group (92.4 per 100000 person-years) [Table 2]. The incidence of SD in 2000-2009 years was higher for males than for females (all p<0.01) [Table 3].

Association of SD with Age Group and Gender

A seasonal pattern was observed in SD, as the standardized rates were highest in the 55-64 years-old group and lowest in the 15-24 years-old group. Correspondingly, the gender- adjusted RR were 0.2 (95% CI 0.1 to 0.3, p<0.000) in the 55-64 years-old group, -0.5 (95% CI -0.7 to -0.4, p<0.000) in the 45-54 years-old group, and -0.9 (95% CI -1.2 to -0.8, p<0.000) in the 35-44 years-old group,-1.4 (95% CI -1.6 to 1. 2, p<0.005) in the 25-34 years-old group, compared with the 15-24 years-old group [Table 4]. The incidence of SD in all age group was higher for males than for females (all p<0.01) [Table 5].

Association of SD with Months & Seasonal Variation

The incidence of SD in the winter months (December to

February) was 64.7per 100000 person-years, followed by 56.0 per 100000 person-years in the spring (March to May), 53.9 per 100000 person-years in autumn (September to November), and 52.3 per 100000 person-years in the summer (June to August). Correspondingly, the age- adjusted RR were 0.10 (95% CI 0.0 to 0.3, p<0.006) in the winter, 0.03 (95% CI -0.1 to -0.2) in the spring, and -0.02 (95% CI -0.2 to -0.1) in the autumn, compared with the summer [Table 6].

Association of SD with Weekly Variation

A weekly variation pattern was observed in SD, as the standardized rates were highest in the Monday (42.5 per 100000 person-years) and lowest in the Thursday (35.1 per 100000 person-years). Correspondingly, the age-adjusted RR were 0.19 (95% CI 0.0 to 0.2, p<0.04) in the Monday, 0.17 (95% CI -0.0 to 0.4) in the Sunday, 0.08(95% CI -0.1 to 0.3) in the Saturday, 0.06 (95% CI -0.1 to 0.2) in the Tuesday,0.03 (95% CI -0.2 to 0.2) in the Wednesday and 0.01 (95% CI -0.24 to 0.2) in Friday, compared with the Thursday[Table 7].

Medical Comorbidities for Sudden Death

Cardiovascular System: Table 8 shows that the most common cause of SD was related to the cardiovascular system (73.9%, n: 1271). In the majority of cases, SD was caused by essential hypertension (incidence rates: 26.1%, n: 448). In particular, other and unspecified hyperlipidaemia constituted most of the related to the SD (incidence rates: 17.9%, n: 309) in the cardiovascular disease subgroup, followed by mixed hyperlipidaemia (incidence rates: 10.1%, n: 173). The fourth, fifth and sixth leading causes of death involving the cardiovascular system were congestive heart failure (incidence rates: 8.1%, n: 139), other and unspecified angina pectoris (incidence rates: 6.1%, n:105) and chronic ischemic heart disease, unspecified (incidence rates:5.6%, n: 97), In addition to congestive heart failure, the other cardiovascular diseases of the percentage related SD was higher for males than for females [Table 8].

Respiratory System: The second cause of SD was related to the respiratory system which constituted 47.8% of the cases (n: 822). In this group, acute nasopharyngitis caused most of the disease (incidence rates: 14.0%, n: 241), acute upper respiratory infections of unspecified site (incidence rates: 9.3%, n:159) and acute pharyngitis (incidence rates: 9.1%, n:156). In addition to Malignant neoplasm of bronchus and lung, unspecified, the other respiratory diseases of the percentage related SD was higher for females than for males [Table 8].

Diabetes Mellitus: The third cause of SD was related to the diabetes mellitus and constituted 22.0% (n: 379) of all cases. The percentage of diabetes mellitus and constituted was higher for males than for females of SD [Table 8].

The fourth medical comorbidities of SD was related to gastrointestinal system 289 (16.8%), medical comorbidities in accordance with the ranking of gouty arthropathy 231(13.4%), contact dermatitis and other eczema, unspecified cause 151 (8.8%), liver system 73 (4.2%), dizziness and giddiness 53(3.1%), anxiety 27 (1.6%), and chronic renal failure 15 (0.9%). The percentage of dizziness and giddiness and anxiety were higher for females than for males of SD [Table 8].

Table-1: Demographic characteristics of Sudden Death (n=1720), 2000–2009, by Gender, Age, Season and Day-of-the week

Variable		Male N (%)	Female N (%)	Total N (%)
Age	15-24	97 (7.6)	24 (5.3)	121 (7.0)
	25-34	139 (11.0)	49 (10.9)	188 (10.9)
	35-44	234 (18.4)	67 (14.9)	301 (17.5)
	45-54	388 (30.6)	120 (26.6)	508 (29.5)
	55-64	411 (32.4)	191 (42.4)	602 (35.0)
Season	Winter	347 (27.3)	127 (28.2)	474 (27.5)
	Spring	312 (24.6)	114 (25.3)	426 (24.8)
	summer	294 (23.2)	112 (24.8)	406 (23.6)
	autumn	316 (24.9)	98 (21.7)	414 (24.1)
Day-of-the week	Mon	211 (16.6)	64 (14.2)	275 (15.9)
	Tue	174 (13.7)	66 (14.6)	240 (13.9)
	Wed	177 (13.9)	57 (12.6)	234 (13.7)
	Thu	170 (13.4)	57 (12.6)	227 (13.3)
	Fri	164 (12.9)	65 (14.4)	229 (13.3)
	Sat	177 (13.9)	69 (15.3)	246 (14.3)
	Sun	196 (15.4)	73 (16.2)	269 (15.6)
Total		1269 (73.8)	451 (26.2)	1720 (100.0)

Table-2: Incidence Rate* and 10-year Cumulative Incidence‡ of Sudden Death, 2000–2009, by Year and Age Group

Year	Age Groups (Year)					
	15-24	25-34	35-44	45-54	55-64	Total
2000	6.0	6.2	13.7	25.3	51.9	14.5
2001	6.9	8.6	12.9	32.3	76.7	18.7
2002	7.2	10.9	13.7	29.4	81.5	19.6
2003	9.6	10.3	17.2	32.3	79.2	21.3
2004	12.2	11.7	25.4	41.4	72.9	25.4
2005	11.7	14.3	28.2	42.4	89.1	28.5
2006	15.2	14.8	22.1	43.0	73.0	27.0
2007	4.1	9.4	19.6	43.7	63.4	22.8
2008	7.4	14.0	19.8	33.5	74.0	24.2
2009	8.3	16.1	20.0	38.2	62.0	24.8
10-year Cumulative	92.4	126.4	208.0	396.5	794.3	273.7

* Annual incidence (per 100,000 person-years) is the number of new cases of SD divided by the size of the population at risk in each year.
‡ 10-year cumulative incidence is the number of new cases of SD divided by the size of the population at risk from 2000 to 2009.

Table-3: Annual incidence of Sudden Death in sex group, 2000–2009

Year	Annual incidence*			RR (95%CI)	P-value
	Male	Female	Total		
2000	4.19	1.69	5.87	2.60 (2.17–3.12)	0.000
2001	5.41	1.92	7.33	2.79 (2.33–3.35)	0.000
2002	7.80	1.92	7.67	4.01 (3.32–4.84)	0.000
2003	6.16	2.21	8.37	4.10 (3.40–4.95)	0.000
2004	7.27	2.73	10.00	4.12 (3.41–4.99)	0.000
2005	8.78	2.56	11.34	11.36 (8.88–14.53)	0.000
2006	8.14	2.67	10.81	5.42 (4.43–6.62)	0.007
2007	7.15	2.03	9.19	4.46 (3.67–5.42)	0.000
2008	7.15	2.67	9.83	6.05 (4.94–7.41)	0.000
2009	7.09	3.02	10.12	3.55 (2.95–4.28)	0.000

*Annual incidence is the number of new cases of SD divided by the size of the population at risk in each year.

Table-4: Incidence Rate of Sudden Death (n=1720), 2000–2009, by Age Group

Age	Incidence Rate	RR (95 %CI)*	P-value
15-24	7.7	1 (reference)	—
25-34	10.5	-1.4 (-1.6~-1.2)	0.005
35-44	17.3	-0.9 (-1.2~-0.8)	0.000
45-54	33.1	-0.5 (-0.7~-0.4)	0.000
55-64	66.2	0.2 (0.1~0.3)	0.000

* The relative risks (95% Confidence Intervals, CI) are derived from Poisson regression model adjusted for gender.

Table 5. Incidence Rate* of Sudden Death (n=1720), 2000–2009, by Age and Gender

Age (Years)	Number/ Incidence rates		RR (95%CI)	P-value
	Male	Female		
15-24	97 (5.6)	24 (1.4)	0.6 (0.3~2.3)	0.005
25-34	139 (12.4)	49 (2.9)	1.0 (0.7~1.4)	0.000
35-44	234 (13.6)	67 (3.9)	1.1 (0.9~1.7)	0.000
45-54	388 (22.6)	120 (6.9)	1.2 (0.9~1.4)	0.000
55-64	411 (23.9)	191 (11.1)	1.3 (0.1~1.5)	0.000

*Incidence rates are per 100,000 person-years.

Table 6. Incidence Rate* of Sudden Death (n=1720), 2000–2009, by Months and Season

Months	Season	Total/Months	Incidence Rate	RR (95%CI)‡	P-value
3	Spring	22.4	56.0	0.03 (-0.1~-0.2)	0.27
4		20.5			
5		24.8			
6	Summer	23.4	52.3	1 (reference)	—
7		20.2			
8		22.3			
9	Autumn	23.4	53.9	-0.02 (-0.2~-0.1)	0.83
10		21.2			
11		20.1			
12	Winter	21.2	64.7	0.10 (0.0~0.3)	0.006
1		29.8			
2		24.5			

* Incidence rates are per 100,000 person-years.
‡ The relative risks (95% Confidence Intervals, CI) are derived from Poisson regression model adjusted for gender and age.

Table 7. Incidence Rate* of Sudden Death (n=1720), 2000–2009, by Day-of-the week

Day-of-the-week	Incidence Rate	RR (95%CI)‡	P-value
Mon	42.5	0.19 (0.0~0.2)	0.04
Tue	37.1	0.06 (-0.1~0.2)	0.21
Wed	36.2	0.03 (-0.2~0.2)	0.31
Thu	35.1	1 (reference)	—
Fri	35.4	0.01 (-0.24~0.2)	0.80
Sat	38.0	0.08 (-0.1~0.3)	0.12
Sun	41.6	0.17 (-0.0~0.4)	0.06

* Incidence rates are per 100,000 person-years.
‡ The relative risks (95% Confidence Intervals, CI) are derived from Poisson regression model adjusted for gender and age.

Table-8: Medical Comorbidities in 1720 subjects with Sudden Death, 2000-2009

System & ICD-9 Code*		Outpatient			
		Male N (%)	Female N (%)	N (Rate)†	Total N (%)
Cardio-vascular	4019	290 (64.7)	158 (35.3)	448 (26.1)	1271 (73.9)
	2724	199 (64.4)	110 (35.6)	309 (17.9)	
	2722	104 (60.1)	69 (39.9)	173 (10.1)	
	4280	25 (17.9)	114 (82.0)	139 (8.1)	
	4139	63 (60.0)	42 (40.0)	105 (6.1)	
	4149	65 (67.0)	32 (32.9)	97 (5.6)	
Respiratory	460	62 (25.7)	179 (74.3)	241 (14.0)	822 (47.8)
	4659	55 (34.6)	104 (65.4)	159 (9.3)	
	462	68 (43.6)	88 (56.4)	156 (9.1)	
	4619	50 (40.3)	74 (59.7)	124 (7.2)	
	4660	41 (39.8)	62 (60.2)	103 (5.9)	
	49390	10 (33.3)	20 (66.7)	30 (1.8)	
	1629	6 (66.7)	3 (33.3)	9 (0.5)	
Diabetes mellitus	25000	128 (53.3)	112 (46.7)	240 (13.9)	379 (22.0)
	25060	69 (57.9)	50 (42.0)	119 (6.9)	
	25040	12 (60.0)	8 (40.0)	20 (1.2)	
GIT	53500	144 (73.9)	51 (26.2)	195 (11.3)	289 (16.8)
	5589	37 (39.4)	57 (60.7)	94 (5.5)	
Arthropathy	2740	172 (74.5)	59 (25.5)	231 (13.4)	23 (13.4)
Dermatology	6929	119 (78.8)	32 (21.2)	151 (8.8)	151 (8.8)
Liver	5715	29 (54.7)	24 (45.3)	53 (3.1)	73 (4.2)
	1550	12 (60.0)	8 (40.0)	20 (1.1)	
CNS	7804	20 (37.7)	33 (62.3)	53 (3.1)	53 (3.1)
Psychiatric	30000	10 (37.0)	17 (62.9)	27 (1.6)	27 (1.6)
Nephrology	585	10 (66.7)	5 (33.3)	15 (0.9)	15 (0.9)

* The ninth revision of the ICD-9-CM (The International Classification of Diseases, Clinical Modification) was used to code and classify morbidity data from the outpatient records. *4019: Essential hypertension; 2724: Other and unspecified hyperlipidaemia; 2722: Mixed hyperlipidemia; 4280: Congestive heart failure; 4139: Other and unspecified angina pectoris; 4149: Chronic ischemic heart disease, unspecified; 460: Acute nasopharyngitis [common cold]; 4659: Acute upper respiratory infections of unspecified site; 462: Acute pharyngitis; 4619: Acute sinusitis, unspecified; 4660: Acute bronchitis; 49390: Asthma, unspecified, without mention of status asthmatics; 1629: Malignant neoplasm of bronchus and lung, unspecified; 25000: Diabetes mellitus without mention of complication, Type II [non-insulin dependent type][NIDDM type]; 25060: Diabetes with neurological manifestations, Type II [non-insulin dependent type][NIDDM type][adult--onset type]; 25040: Diabetes with renal manifestations, Type II [non-insulin dependent type][NIDDM type][adult-onset type]; 53500: Acute gastritis, without mention of haemorrhage; 5589: Other and unspecified noninfectious gastroenteritis and colitis; 2740: Gouty arthropathy; 6929: Contact dermatitis and other eczema, unspecified cause; 5715: Cirrhosis of liver without mention of alcohol; 1550: Malignant neoplasm of liver, primary; 7804: Dizziness and giddiness; 30000: Anxiety state; 585: Chronic renal failure.*
† N (Rate): N, number of sudden deaths, with incidence rates in parentheses.

Discussion

The high incidence of SD among the general population has been shown in numerous reports.[5-14] In the present study, the 10-year cumulative incidence of SD was 273.7 per 100000 person-years and the annual incidence rates of SD ranged increased by10.3% from 14.5 to 28.5 per 100000 person-years. We observed that the incidence of SD in the general population in Taiwan was slightly lower than that in the populations of the Netherlands, Ireland, China, Australia, and France[21], but higher than that in Japan[12]. In this study, the age group with the highest incidence was the 55-64 years-old group and that with lowest was the 15-24-years-old group. The highest incidence among middle-aged people.[22]

In this study, 1269 (73.8%) of the cases involved males, and 451 (26.2%) involved females. The male-to-female ratio was 2.9:1.[23] The incidence of SD in Taiwan is higher for males than for females.[24] The problem of SD is inexorably linked to coronary disease, and because the latter predominantly affects males, SD is perceived as a male problem.[25] In this study, the male predominance, which has also been observed in many SD studies, might be attributable to differences in the gender distribution across studies.[25,26]

Our study confirmed that the incidence was lowest in August, whereas the incidence peaked in January. The literature describes the relationship between winter temperatures and SD.[27] People should avoid exposure to severely cold temperatures because the associated cold weather could influence the cardiovascular diseases.[26]

Therefore we are in complete agreement with this advice that physicians should offer patients during the winter, particularly for patients with established ischemic heart disease or for those with known risk factors for cardiac disease.[28] The incidence of ischemic heart disease is higher in winter than in summer. Several biological mechanisms may be involved in the association between cold weather and SD. Low temperature has a hazardous effect on blood pressure, and may alter the ratio of myocardial oxygen supply to demand, increase ventricular wall stress, cardiac work and oxygen requirements, and reduce mechanical efficiency and coronary blood flow.[29,30]

We were able to determine the weekly variations in SD by using the population-based data. Further analysis revealed a highly varied incidence of SD, with the incidence rate peaking on Monday.[15,31,32] Ke[33] indicated that working long overtime hours and being on duty during holidays is harmful because work-related stress increases the secretion of people, which is associated with the increased risk of cardiovascular diseases. The cases of SD in the population were primarily caused by a high workload according to a survey conducted in Taiwan and Japan.[33-35] Other studies have reported that SD might be caused by excessive physical exertion, overeating, lack of sleep, mental or psychological stress, including episodes of anger, may also trigger sudden death, the "holiday heart syndrome", cardiovascular risk factors (e.g., hypertension, diabetes, smoking, and drinking) in several studies.[12,26, 35-37]

A winter increase in CHD events has been noted for many studies.[38-42]

We investigated clinical diagnoses of SD were principally cardiovascular diseases of hypertension (26.1%) in this study. The cardiac arrhythmias in hypertensive patients with left ventricular hypertrophy. Left ventricular hypertrophy has been shown to be an independent risk factor for SD. The patients with left ventricular hypertrophy allows identification of those who have the highest risk and, therefore, require the most antihypertensive therapeutic intervention.[43,44] Age and gender interactions among season, cold weather, day-of-week and SD have been reported in several studies.[5-7,20]

Conclusion

The annual incidence of SD increased from 14.5 in 2000 to 24.8 per 100 000 person-years in 2009 in Taiwan. The present analyses demonstrate marked variations in the occurrence of SD with peaks in 45-64-years-old people, in males (cardiovascular diseases), on Monday, and during the winter months. Our findings provide strong evidence of an ongoing epidemiological transition in Taiwan, where SD incidence rates increase mainly with cardiovascular diseases rates. Prevention strategies for cardiovascular diseases may be helpful in reducing the incidence of SD.[17,45,46]

LIMITIONS

There are some limitations in using the 2000 Longitudinal Health Insurance Database in this study. First, claims data were used that only those who visited a medical institution were enrolled. NHI database-registered SDs did not link to death certificate data; therefore, we could not confirm the SD by relevant data from medical records. We could only confirm the SD from the NHI database. Secondly, this database does not document disease severity, family status and lifestyle. The lack of these pieces of valuable information makes it difficult to evaluate the influence of these factors.

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