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SPECIAL ARTICLE

Regional differences in incidence of sudden cardiac death in the young

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ABSTRACT

Background: Observational data on sudden cardiac death (SCD) in the young are scarce, but the SCD incidence seems to differ among regions and races. The objective of this study is to examine regional differences in SCD incidence within a population among young individuals (<40 years) and to assess whether regional incidences are associated with socio-economic status (SES).

Methods: SCD cases aged <40 years were identified in 12 provinces of the Netherlands by using death certificates recorded by Statistics Netherlands during 1996-2006. Regional incidence estimates were standardised for age to the Dutch population and assessed for two age categories; 1-29 years and 30-39 years. Regional SCD incidence was related to regional SES with a Spearman correlation coefficient.

Results: The nationwide incidence of SCD at ages 1 to 40 years was 1.6 (95% CI 1.5 to 1.7) per 100,000 person-years and the incidence increased substantially after 30 years of age. Significant differences in regional incidences were assessed for both age categories (1-29 and 30-39 years). Although in the population aged 1-29 years significant differences were found in the SCD incidence between regions, no relation could be found with SES. In men aged 30-39 years, the incidence of SCD was inversely related to SES; a low socio-economic status was associated with a relatively high incidence of SCD.

Conclusion: Between regions, statistically significant differences in SCD incidence exist in young individuals. The nationwide incidence of SCD increased substantially after 30 years of age and was inversely related to SES in men aged 30-39 years.

KEYWORDS

Epidemiology, socio-economic status, sudden cardiac death

INTRODUCTION

The incidence of sudden cardiac death (SCD) in the young is estimated to be 0.9 to 1.6 per 100,000 person-years.[1] Often, cardiac diseases such as cardiomyopathies, primary arrhythmia syndromes, myocarditis or coronary artery disease are the underlying causes of SCD in the young.[1-3] In the SCD victims aged 30-40 years, coronary artery disease accounts for a relatively high percentage of deaths in comparison with younger SCD victims in whom monogenetic inherited diseases and congenital diseases prevail.[1,4] Coronary artery disease is attributed to both genetic factors (for example the presence of familial hypercholesterolaemia) and lifestyle factors such as smoking or inactivity. In the general population, (all ages) a low socio-economic status (SES) is positively associated with the presence of cardiovascular risk factors and the occurrence of premature cardiac death.[5-11]

Observational population-based data on SCD in the young are scarce, but it seems that the incidence of SCD (over all ages) differs among races and between regions.[11-16] However, the comparability of studies on incidence is poor as most former studies were restricted to only a single regional observation without focusing on differences across or within regions.[17,18] Multiple factors might be responsible for differences in the regional SCD incidence, among which the regional age and gender distribution and the regional prevalence of inherited cardiac diseases and coronary artery disease.[19-25] In addition, regional

differences in accessibility of care may also explain differences in out-of-hospital SCD among regions.[26,27]
The primary objective of the current study is to examine regional differences in SCD at young age (1-40 years) and to assess whether regional incidences in SCD differ between age categories (<30 years and 30-39 years) and are associated with differences in regional SES.

MATERIALS AND METHODS

Definitions

SCD is defined as sudden unexpected death due to a cardiac cause within 24 hours after the onset of symptoms.[1]

Incidence of sudden death

To estimate the regional incidence of SCD we used nationwide data on the primary cause of death recorded by Statistics Netherlands[28] over the period 1996-2006. Death certificates do not include information on the duration of preceding symptoms and the actual time of cardiac arrest, which makes it difficult to identify the 'sudden' deaths. To solve this problem, we defined sudden death as death taking place out of hospital, assuming that these deaths occurred unexpectedly and within a few hours after the onset of severe symptoms.[29,30] Because no dedicated ICD code exists for 'SCD', we reviewed the literature to define the most common causes of SCD and selected corresponding ICD-10 codes to compose a proxy for SCD as we have described earlier (*table 1*).[1]

Study regions

The study regions were defined by the boundaries of the 12 provinces of the Netherlands. Information on the regional age and gender distribution was derived from the National Cause of Death Register. For every region, scores for socio-economic status (SES) were derived from the Netherlands Institute for Social Research (SCP) over 2006. This SES score is based on information on income, unemployment and level of education per postal (zip) code. Scores were converted into factor scores by a principal component analysis as described before.[31] For the purpose of this study, the factor scores of each postal code were aggregated to the study regions weighted by the number of inhabitants.

Data analysis

The crude incidence rates (with corresponding 95% CI) of out-of-hospital SCD were reported by age, gender and study region. Age was categorised into two subgroups (1-29 years and 30-39 years). These subgroups were chosen because the percentage of deaths due to coronary artery disease increases with age (especially after 30 years of age) and a low SES is related to a high prevalence of vascular risk factors and coronary artery disease.[5-8]
Person-years were based on the number of subjects in the relevant age categories per study region from 1996-2006. In addition, comparability of the study regions was obtained by standardising the overall incidence rates to the Dutch population for age and gender.
Because aggregated data were used, a Spearman ranking correlation coefficient was chosen to describe the relation of SCD incidence and SES. Two-tailed significance levels of $p<0.05$ were used. All analyses were performed in agreement with privacy legislation in the Netherlands.[32]

RESULTS

Nationwide incidence estimates

During the study period 1996-2006, 1458 cases of SCD were reported coming from 92,374,043 person-years of follow-up. This yielded a nationwide crude incidence of SCD of 1.6 (95% CI 1.5 to 1.7) per 100,000 person-years. The incidence of SCD increased with age and was higher in men than in women (*figures 1* and *2*). A substantial increase in SCD incidence was seen especially in men after

Table 1. *Overview of selected ICD codes that were used as a proxy for SCD*

Selected causes of cardiac death	Corresponding ICD codes
Coronary artery disease (ischaemic)	E78.4, I21, I24
Conduction disorders	I45.6, I45.8, I45.9, I49.0, I49.9
Myocarditis	I40, I41
Cardiomyopathy	I42.0-I42.9
Coronary pathology (nonischaemic)	I25.4
Congenital cardiac diseases	Q20-Q24, Q87.4
Valve abnormalities	I34.1, I35.0
Other cardiovascular diseases	I46
Sudden death with unknown cause	R96

Figure 1. *Nationwide incidence (per 100,000 person-years) of SCD in persons aged 1-39 years, for men and women for the period 1996-2006*

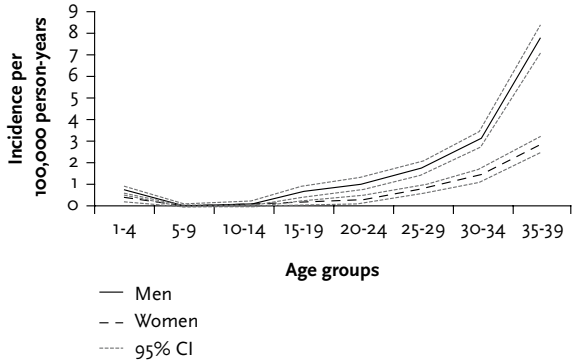


Figure 2A. *Regional incidence (per 100,000 person-years) of SCD in persons aged 1-29 years, standardised for age to the Dutch population. The regions presented at the X-axis are arranged from the north to the south of Holland*

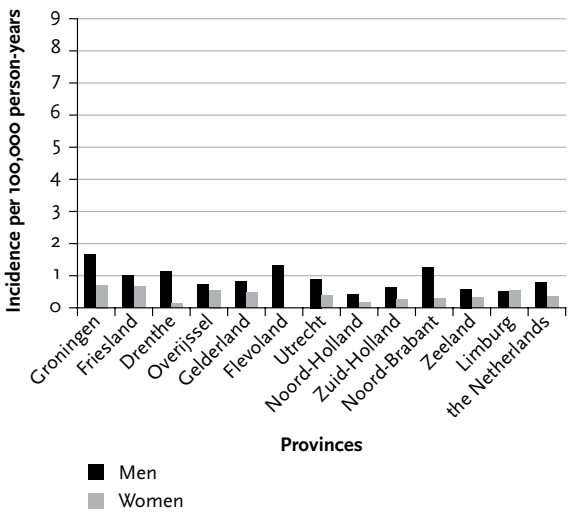
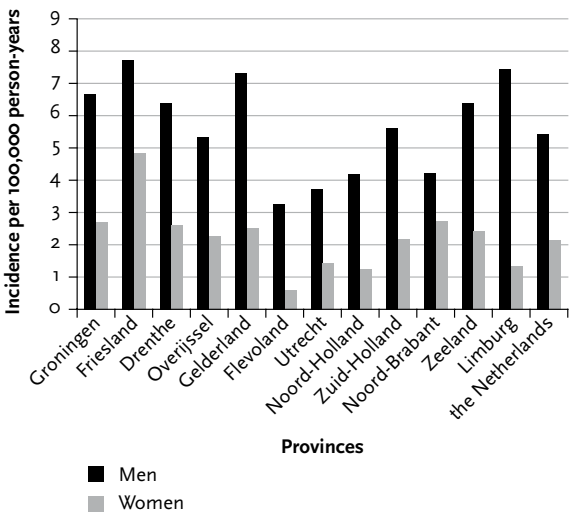


Figure 2B. *Regional incidence (per 100,000 person-years) of SCD in persons aged 30-39 years, standardised for age to the Dutch population. The regions presented at the X-axis are arranged from the north to the south of Holland*



30 years of age. The nationwide incidence of SCD in 1-29 year old men was 0.77 (95% CI 0.67 to 0.87) per 100,000 person-years and in women 0.34 (95% CI 0.28 to 0.40) per 100,000 person-years. The nationwide incidence of SCD in 30-39 year old men was 5.52 (95% CI 5.14 to 5.90) per 100,000 person-years and in women 2.17 (95% CI 1.93 to 2.41) per 100,000 person-years (*table 2*).

Regional incidence estimates

Regional incidence estimates with corresponding 95% confidence intervals are presented in *table 2*. Statistically significant differences in incidence estimates of regional SCD incidences compared with the nationwide SCD incidence were found in both age categories for both men and women. However, no clear north-south or east-west patterns emerged.

Regional incidence estimates standardised to the Dutch population are presented in *figures 2A* and *2B*. In both age categories (1-29 years and 30-39 years) the incidence varies between regions for both men and women.

Regional SES

A low factor score represents a high socio-economic status. The relations between regional incidence estimates for SCD (standardised to the Dutch population) in the young and SES are presented in *figures 3A to 3C*. In younger victims (1-29 years) no significant association could be established between the incidence of SCD and SES (in men 1-29 years, the Spearman' s rho is -0.03 (p=0.93), while in women 1-29 years, the Spearman' s rho is 0.55 p=0.07). In 30-39 year old men, an inverse relation was found between the SCD incidence and SES; a low SES was associated with a higher incidence of SCD in this age category. In women no statistically significant correlation could be established (in men >30 years, the Spearman's rho is 0.76 (p<0.01), in women >30 years, the Spearman's rho is 0.53 (p=0.08).

DISCUSSION

Disparities in SCD incidence in the young were found among study regions and age categories (1-29 and 30-39 years). In 30-39 year old men, the incidence of SCD was inversely related to SES. In men and women aged 1-29 years and in women aged 30-39 years, no significant association with SES and SCD incidence could be observed. In the young, cardiomyopathies, primary arrhythmia syndromes and congenital heart diseases are common causes of SCD.[1,4] Clustering of (inherited) cardiac diseases in populations (and regions) can be responsible for differences in SCD incidence, as is previously described by others.[23,25,33] An example is the high prevalence of a primary arrhythmia syndrome similar to the Brugada syndrome in the southeast of Asia that is responsible for a high number of SCDs in that region.[23,33] In the Netherlands, a founder mutation that causes hypertrophic cardiomyopathy in the majority of cases is predominantly detected in the north-western part of the country.[25] Furthermore, a haplotype (associated with familiar idiopathic ventricular fibrillation) was recently identified, which originates from the centre of the Netherlands.[20] In the current study, no clear patterns in SCD incidence in

Table 2. *Incidence (per 100,000 person-years) of SCD in young persons (1-39 years) in the Netherlands, by age (1-29 and 30-39 years), sex and province. Period 1996-2006*

		Men		Women	
	Age (years)	**Incidence**	**95% CI***	**Incidence**	**95% CI***
Groningen	1-29	1.77[2]	1.63-191	0.71[2]	0.62-0.80
	30-39	6.56[2]	6.14-6.98	2.80[2]	2.52-3.08
Friesland	1-29	0.98[2]	0.88-1.09	0.65[2]	0.56-0.74
	30-39	7.70[2]	7.25-8.15	4.93[2]	4.56-5.30
Drenthe	1-29	0.98	0.87-1.09	0.12[1]	0.08-0.16
	30-39	6.57[2]	6.15-6.99	2.84[2]	2.56-3.12
Overijssel	1-29	0.72	0.63-0.81	0.54[2]	0.46-0.62
	30-39	5.44	5.06-5.82	2.34	2.09-2.59
Gelderland	1-29	0.81	0.71-0.91	0.47	0.39-0.55
	30-39	7.37[2]	6.93-7.81	2.62	2.35-2.89
Flevoland	1-29	1.18[2]	1.06-1.30	0.00[1]	0.00-0.00
	30-39	3.45[1]	3.15-3.75	0.62[1]	0.49-0.75
Utrecht	1-29	0.89	0.79-0.99	0.38	0.31-0.45
	30-39	3.69[1]	3.38-4.00	1.53[1]	1.32-1.74
Noord-Holland	1-29	0.40[1]	0.33-0.47	0.16[1]	0.12-0.20
	30-39	4.12[1]	3.79-4.45	1.26[1]	1.07-1.45
Zuid-Holland	1-29	0.65	0.56-0.74	0.25	0.19-0.31
	30-39	5.59	5.20-5.98	2.17	1.93-2.41
Noord-Brabant	1-29	1.25[2]	1.13-1.37	0.33	0.27-0.39
	30-39	4.27[1]	3.93-4.61	2.72[2]	2.45-2.99
Zeeland	1-29	0.54[1]	0.46-0.62	0.29	0.23-0.35
	30-39	6.28	5.87-6.69	2.37	2.11-2.63
Limburg	1-29	0.97	0.86-1.08	0.49[2]	0.41-0.57
	30-39	7.75[2]	7.30-8.20	1.47[1]	1.27-1.67
The Netherlands	1-29	0.77	0.67-0.87	0.34	0.28-0.40
	30-39	5.52	5.14-5.90	2.17	1.93-2.41

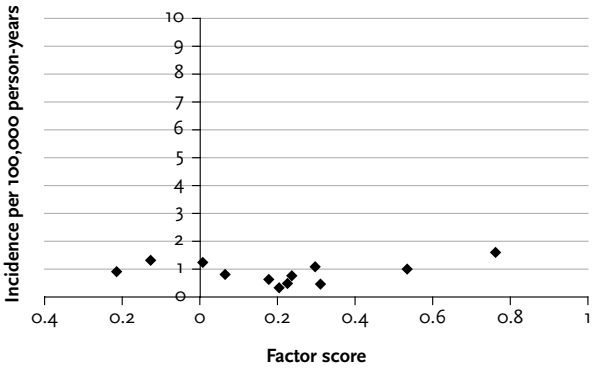
*** CI = confidence interval; [1]Incidence statistically significantly lower than nationwide incidence, [2]Incidence statistically significantly higher than the nationwide incidence.**

the young (1-29 years) were found that might be explained by this regional clustering of inherited diseases. However, the low incidence rates of SCD and the presence of other factors that are associated with the occurrence of SCD might have obscured such an association.

Little is known about the relation between SES and SCD in the young. In the older age categories (>30 years), coronary artery disease is responsible for a high proportion of SCD, especially in men.[4,34,35] Because a low SES is related to a high prevalence of vascular risk factors and prevalence of coronary artery disease, this might explain the increased incidence of SCD at older age in regions with a relatively low SES.[5-8] Our findings correspond with the findings from other studies. Huff and coworkers reported that SES (by deprivation index which was based on unemployment, household, overcrowding, car ownership and home ownership) was inversely associated with all-cause mortality in 0-74 year olds and cardiovascular disease mortality.[7] In people aged 25 to 64 years a low SES is associated with a higher rate of myocardial infarction and death due to coronary artery disease.[6] We investigated the association between SES and SCD in the young. Yet, below 30 years of age, no significant association could be established between SES and SCD incidence.

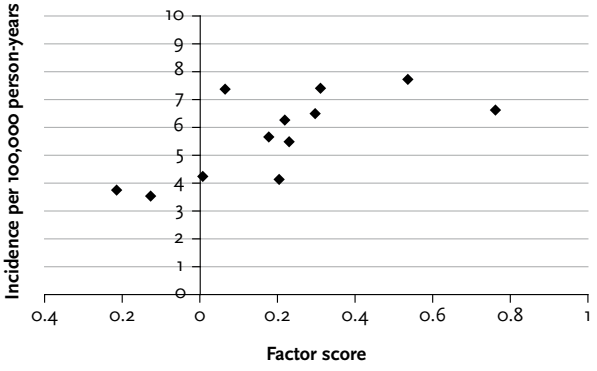
The strength of the current study is the nationwide approach leading to large number of cases of sudden cardiac death. The study also has some limitations that need to be addressed. First, ecological fallacy might have weakened the associations of SCD incidence and SES. No individual information on SES was available; scores assessed for each postal code were aggregated to regions which might have lead to an underestimation of the reported associations. Secondly, racial dispersion was not taken into account in the current study, although this might be partly incorporated in SES. Racial differences are associated with the prevalence of hypertension and obesity, and the development of coronary artery disease.[5] As mentioned before, also inherited cardiac diseases that underlie SCD in the young may cluster among races.[23,25,33] Thirdly, we were not able to collect information on the survival rates of cardiac arrest in the young in the Netherlands, while survival rates might be influenced

Figure 3A. *Regional incidence of SCD (per 100,000 person-years) and regional SES (factor score), in men aged 1-29 years*



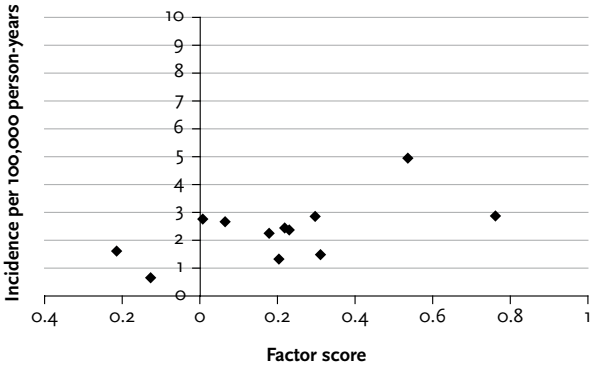
*** A low factor score represents a high SES, and a high factor score indicates a low SES. Zero represents a mean SES.**

Figure 3B. *Regional incidence SCD (per 100,000 person-years) and regional SES (factor score), in men aged 30-39 years*



*** A low factor score represents a high SES, and a high factor score indicates a low SES. Zero represents a mean SES.**

Figure 3C. *Regional incidence SCD (per 100,000 person-years) and regional SES (factor score), in women 30-39 years*



*** A low factor score represents a high SES, and a high factor score indicates a low SES. Zero represents a mean SES.**

by the presence of a witness or by the mean response times of emergency services.[26,27] However, in contrast to other countries, the differences in mean response times of emergency services are relatively small in the Netherlands.[36,37] We do not expect that this affected the observed difference in SCD rate across study regions.

The current study was primarily designed to investigate differences in incidence of SCD in the young across regions. More studies are needed to investigate the underlying mechanisms that are responsible for disparity in regional SCD incidences. A nationwide disease-specific registry of all SCD cases at young age might be helpful to identify predictors or causal factors that are related to the occurrence of SCD. This information may be of value for the future development of preventive strategies directed to high-risk populations or regions.

In conclusion, significant differences in the SCD incidence in young individuals across study regions were observed. The nationwide incidence of SCD substantially increases after 30 years of age, especially in men. The SCD incidence in men aged >30 years seems to be inversely related to SES. This might be due to the increasing percentage of deaths due to coronary artery disease with age.

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