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ORIGINAL RESEARCH ARTICLE

Declining Trend of Sudden Cardiac Death in Younger Individuals: A 20-Year Nationwide Study

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BACKGROUND: Declining cardiovascular mortality rates have been well-documented, yet temporal trends of sudden cardiac death (SCD) in young individuals remain unclear. We provide contemporary nationwide estimates of the temporal trends of SCD in young individuals (1–35 years of age) from 2000 through 2019 and correlate these trends to changes in out-of-hospital cardiac arrest (OHCA) patterns, rates of inherited cardiac diseases, and implantations of implantable cardioverter defibrillators (ICD).

METHODS: All individuals between 1 and 35 years of age living in Denmark from 2000 through 2019 were included, with annual re-evaluation of the at-risk population in regard to age. Adjudication of SCD cases relied on multiple sources, including death certificates, medical files, and autopsy reports. Information on OHCA, diagnostic rates, and ICD implantations were captured from nationwide administrative registries. Annual incidence rates of SCD were calculated, and temporal trends in SCD incidence were computed as percentage change annualized. Trends in OHCA survival and characteristics, diagnostic rates of inherited cardiac diseases, and ICD implantations were assessed.

RESULTS: During the 20-year study period (47.5 million person-years), 1057 SCDs were identified (median age, 29 years; 69% male). The overall incidence of SCD was 2.2 per 100 000 person-years and declined by 3.31% (95% CI, 2.42–4.20) annually, corresponding to a 49% (95% CI, 38.7–57.6) reduction during the study. Rates of witnessed SCD declined markedly (percentage change annualized −7.03% [95% CI, −8.57 to −5.48]), but we observed no changes in the rate of unwitnessed SCD (percentage change annualized −0.09% [95% CI, −1.48 to 1.31]). Therefore, the proportion of unwitnessed SCD increased by 79% (P<0.001). Survival after OHCA in young individuals (1 to 35 years of age) increased from 3.9% to 28%, mainly because of increased bystander cardiopulmonary resuscitation and defibrillation rates. Diagnostic rates of inherited cardiac diseases increased 10-fold (incidence rate ratio, 10.4 [95% CI, 8.46–12.90]) and the ICD implantation rate increased 2-fold (incidence rate ratio, 1.97 [95% CI, 1.51–2.60]).

CONCLUSIONS: SCD incidence rates in young individuals declined by 49% over the past 2 decades. The decline was paralleled by improved survival of OHCA, higher diagnostic rates of inherited cardiac diseases, and higher ICD implantation rates. However, rates of unwitnessed SCD were unchanged, which calls for new perspectives in preventive strategies.

Key Words: death, sudden, cardiac ■ epidemiology ■ heart arrest ■ resuscitation

Overall and cardiovascular disease mortality rates in Western countries have declined in recent decades,[1,2] but sudden cardiac death (SCD) among young individuals (≤35 years of age) continues to pose a substantial public health challenge associated with vast psychological consequences and a substantial loss of productive years.[3,4]

The incidence rates (IRs) of SCD among young individuals in Western countries range from 1 to 3 per 100 000 person-years (PR), yet there is limited research

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Clinical Perspective

What Is New?

- Over the past 20 years, the incidence of sudden cardiac death in young individuals (1–35 years of age) declined by 49%.
- During the same period, 30-day survival after out-of-hospital cardiac arrest increased from 4% to 28%, driven by: improved bystander cardiopulmonary resuscitation rates, reaching +80%; diagnostic rates of inherited cardiac diseases increasing 10-fold; and implantable cardioverter defibrillator implantations in young adults increasing markedly.
- We observed no decline in the incidence of unwitnessed sudden cardiac death during the study period.

What Are the Clinical Implications?

- Because the majority (73%) of sudden cardiac deaths in the most recent years were unwitnessed, preventive strategies targeting unwitnessed cardiac arrests need further attention. Incorporating connected devices (eg, smart watches) in prevention could potentially help identify ventricular arrhythmias and thus improve survival of unwitnessed cardiac arrest.
- Low bystander automated external defibrillation rates (8%) call for further improvement in early automated external defibrillator deployment.

Nonstandard Abbreviations and Acronyms

AED	automated external defibrillator
CPR	cardiopulmonary resuscitation
ICD	implantable cardioverter defibrillator
IR	incidence rate
IRR	incidence rate ratio
OHCA	out-of-hospital cardiac arrest
PCA	percentage change annualized
PY	person-years
SCD	sudden cardiac death
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology

on contemporary data, and previous studies on temporal trends have had conflicting results.[5–9] Because the causes and circumstances of cardiac arrest are strongly age-dependent,[10] temporal trends in the elderly population cannot be extrapolated reliably to young individuals. Given the decline in mortality rates over the past decades, contemporary estimates of SCD incidence are crucial for evaluating and implementing specific preventive health initiatives targeting young individuals.

We provide contemporary nationwide estimates of the incidence of SCD among young individuals (1–35 years of age) in Denmark. We evaluated the temporal trends from 2000 through 2019 in relation to changes in out-of-hospital cardiac arrest (OHCA) patterns, diagnostic rates of inherited cardiac diseases, and implantable cardioverter defibrillator (ICD) implantations. We aimed to identify subgroups of the SCD population in which preventive strategies have had less impact and where targeted preventive initiatives could be beneficial.

METHODS

This nationwide observational study complies with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for observational cohort studies.

Data Availability

Data are owned by a third party, and the authors do not have the right to share data; however, upon request, the authors will help in applying to the third party for approval of data sharing.

Data Sources

All Danish citizens are assigned a unique civil registration number, which allows data linkage at the individual level across the administrative registries in Denmark. These registries are government-maintained and comprise longitudinally collected administrative and health care data.[11]

Information from several registries was included. The Danish Civil Registration System holds information on sex, migration, and vital status, and was used to identify the study population.[11] The Danish Register of Causes of Death holds information on the causes and circumstances of all deaths in Denmark.[12] The National Patient Registry holds information on all hospital encounters and procedures and was used to identify comorbidities.[13] The Danish National Prescription Registry holds information on prescriptions redeemed at Danish pharmacies since 1995 and was used to identify comorbidities and comedication.[14]

Additional data sources were: a clinical database containing detailed information on all SCD among young individuals (1–35 years of age) in Denmark from 2000 through 2019[15]; the Danish Cardiac Arrest Registry, which comprises information on all OHCA in Denmark since 2001 with attempted resuscitation[16]; and the Danish Pacemaker and ICD Registry, which comprises clinical information on all pacemakers and ICDs implanted since 1982.[17]

Study Population and Characteristics

All individuals between 1 and 35 years of age living in Denmark from 2000 through 2019 were included. The annual at-risk population was identified on January 1 of each year (index date) and followed until the date of death, the date of the 36th birthday, or January 1 of the following year, whichever came first. SCD cases were identified through a multisource approach, which has been described previously.[15,18] Adjudication was based on a manual examination of all death certificates, autopsy reports, and discharge summaries from the 14 days preceding death.

SCD was defined as sudden, unexpected death of presumed cardiac origin that occurred within 1 hour of symptom onset in witnessed cases and within 24 hours of last seen alive and well in unwitnessed cases.[19] Resuscitated cardiac arrest in people who survived to hospital discharge was not considered SCD.

To contextualize the trends in SCD, we examined trends in: (1) survival and bystander interventions in all OHCA in individuals between 1 and 35 years of age registered in the Danish Cardiac Arrest Registry from 2001 through 2019, (2) diagnostic rates of inherited cardiac diseases, and (3) all ICD implantations registered during the study period in individuals between 1 and 35 years of age. All ICD implantations were identified from the Danish Pacemaker and ICD Registry, which also contained information about the indication for ICD implantation.

Comorbidities were identified from the Danish National Patient Registry as any hospital contact with a given diagnosis in the 10 years preceding the index date; hypertension, diabetes, and psychiatric disease were also identified by recent comedication.[20,21] Any comorbidity was defined as the presence of hypertension, cardiovascular disease, chronic kidney disease, diabetes, chronic obstructive pulmonary disease, epilepsy, or psychiatric disease (see Table S1 for definitions of comorbidity). Information on comorbidities was available until 2018.

Statistical Analyses

For descriptive statistics, categorical variables were presented as count and percentage, and continuous variables were presented as median and interquartile range. Temporal trends in continuous variables were assessed with linear regression and presented as 20-year absolute change, and in categorial variables with logistic regression with year as a covariate and presented as 20-year relative risk.

IRs were calculated as the ratio between mortality counts and the appropriate background population, with CIs calculated by the Poisson exact method. Annual IRs were standardized on age and sex by direct standardization, using 5-year age groups and the average Danish population throughout the study period as the standard population. CIs for directly standardized IRs were calculated based on the gamma distribution.[22] Temporal trends in directly standardized IRs were calculated as the percentage change annualized (PCA) by fitting log-linear models to the directly standardized IRs, using weighted least square regression.[23] PCA values were compared by a Wald test of the log-linear models.

Temporal trends in the incidence of OHCA were evaluated for the first 15 years (2001–2015) because of changes in registration practice in the OHCA registry in 2016.[16]

A 2-sided P value of 5% was considered significant. All calculations were performed in R v 4.2.1 (R Foundation for Statistical Computing) using the following packages: data.table, targets, tidyverse, heaven, epiR, and gtsummary.

Ethics

This study complies with the Helsinki Declaration and was approved by the Regional Data Committee (P-2019-813 and P-2019-523). Registry-based studies on deidentified data are exempt from ethical approvals in Denmark. Because of data regulations, counts <4 have been masked (≤3) throughout the article.

RESULTS

During the 20-year study period, 4 274 630 unique individuals were observed for 47.5 million PY. In total, 15 186 deaths occurred, of which 1057 (7%) were categorized as SCD.

Trends in Population Characteristics

The average population in Denmark between the 1 and 35 years of age was 2.38 million (median age, 18 years [interquartile range, 10–27]; 51% male), and population size, age, and sex distribution remained stable throughout the study (Table S2). Whereas the overall comorbidity burden was low, the prevalence of most comorbidities increased annually. The prevalence of individuals with a previous cardiac arrest or an ICD increased significantly during the study period (estimated 20-year RR, 8.05 [P<0.001] and 11.03 [P<0.001], respectively). The diagnostic rates of potentially inherited cardiac diseases (ie, primary arrhythmias and cardiomyopathies) increased from 3.98 per 100 000 PY (95% CI, 3.23–4.82) to 41.22 per 100 000 PY (95% CI, 38.70–43.83), corresponding to an incidence rate ratio (IRR) of 10.4 (95% CI, 8.46–12.90; P<0.001) throughout the study period (primary arrhythmias, IRR 29.9 [95% CI, 14.5–76.1; P<0.001]; cardiomyopathies, 8.61 [95% CI, 7.0–10.7; P<0.001]; Figure 1).

Clinical characteristics of the 1057 patients experiencing SCD (median age, 29 years [interquartile range, 22–33]; 69% male) stratified by time period are shown in Table 1. Throughout the study period, there was a trend toward a higher proportion of male sex (estimated 20-year RR, 1.13; P=0.085). The prevalence of cardiovascular disease remained constant (15%; P_{trend}=0.55). The autopsy rate was stable at 67% (P_{trend}=0.64). Sudden unexplained death was the most frequent cause of death (53%), followed by coronary artery disease (13%) and cardiomyopathies (8%). No substantial changes in causes of death were observed (P=0.60; Table S3).The proportion of unwitnessed SCD increased by 79% during the study period (estimated 20-year RR, 1.79; P<0.001).

SCD IRs and Temporal Trends

SCD IRs are presented in Table 2. The overall SCD IR throughout the study period was 2.2 per 100 000 PY (95% CI, 2.1–2.4). Crude SCD rates decreased from 2.89 per 100 000 PY (95% CI, 2.56–3.24) in 2000 through 2003 to 1.67 (95% CI, 1.42–1.94) per 100 000 PY in 2016 through 2019. After sex and age adjustment, the annual decline (PCA) was −3.31% (95% CI, −4.20 to −2.42), accumulating to a 49.0% (95% CI, 38.7–57.6) reduction in SCD incidence over the 20-year period (Figure 2).

We observed marked differences in SCD incidence according to sex and witnessed status. Male individuals

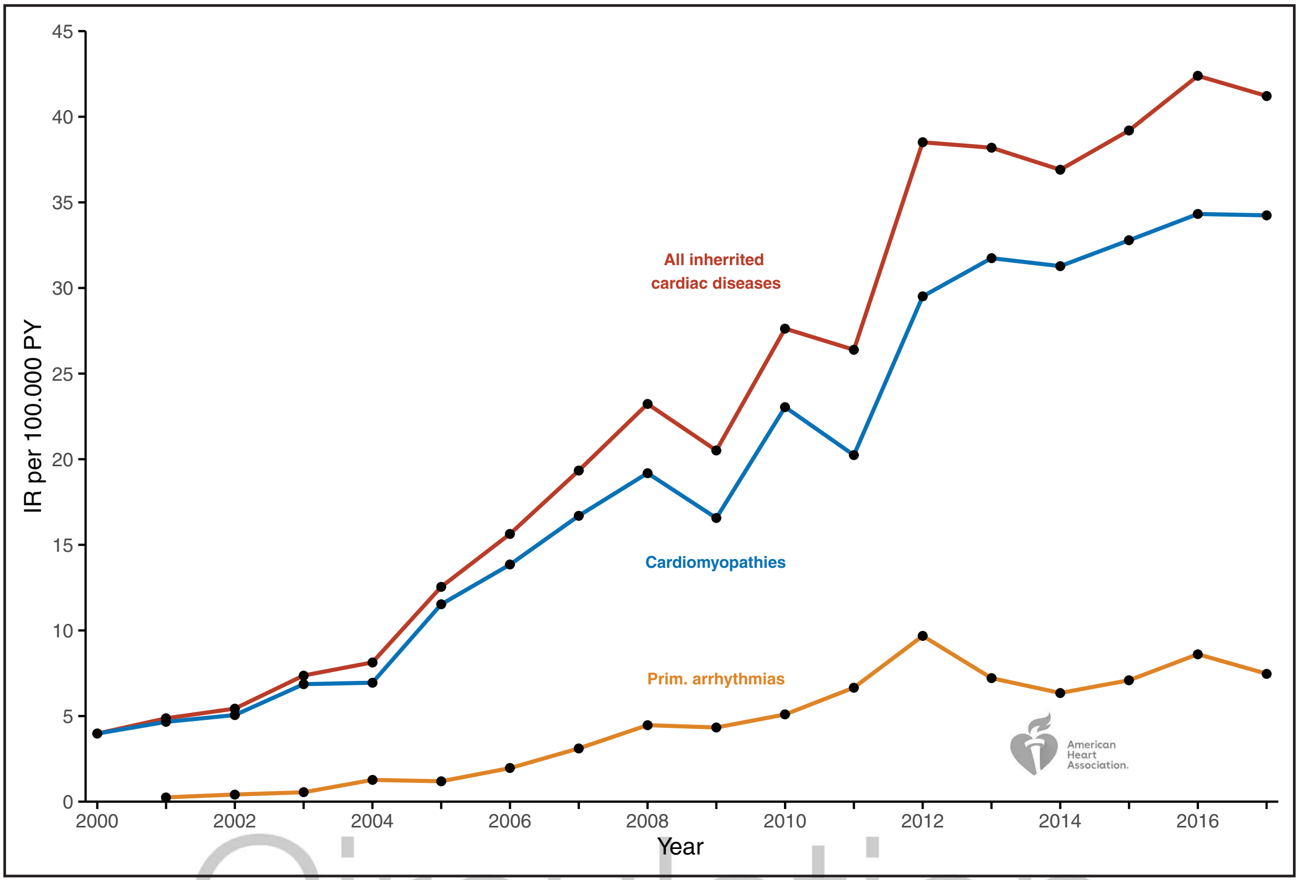

Figure 1. Diagnostic rates of inherited cardiac diseases from 2000 to 2017.
IR indicates incidence rate.

were at considerably higher risk of SCD (IRR, 2.2 [95% CI, 1.9–2.5; $P<0.001$]), and there was a trend toward an increasing discrepancy between the sexes throughout the study period, illustrated by a 1.9% lower PCA in male compared with female individuals ($P_{difference}=0.052$; Figure 3A). The incidence of witnessed SCD decreased significantly, with a PCA of −7.03% (95% CI, −8.57 to −5.48). However, we observed no difference in the incidence of unwitnessed SCD (PCA, −0.09% [95% CI, −1.48 to 1.31]; Figure 3B).

Out-of-Hospital Cardiac Arrest

From 2001 to 2019, 2562 OHCAs in individuals between 1 and 35 years of age were registered (median age, 25 years [interquartile range, 19–31]; 70% male). The overall incidence of OHCA from 2001 to 2015 was 5.79 OHCAs per 100 000 PY (95% CI, 5.57–6.02) and did not change significantly (annual change, −0.027 [95% CI, −0.11 to 0.05]); however, the incidence of resuscitated OHCAs increased from 0.21 per 100 000 PY (95% CI, 0.05–0.55) to 0.89 per 100 000 PY (95% CI, 0.56–1.32), corresponding to an IRR of 4.14 (95% CI, 1.43–17.5; $P=0.021$; Figure 4). Comparing the first with the last time periods, we observed increasing proportions of witnessed OHCAs (28% versus 39%; $P<0.001$), bystander cardiopulmonary resuscitation (CPR; 30% versus 79%; $P<0.001$), and bystander defibrillation (1.8% versus 7.7%; $P<0.001$). Furthermore, 30-day survival increased significantly (3.9% versus 28%; $P<0.001$; Figure 5). Overall, OHCA characteristics were similar between the sexes, except for female individuals being younger (24 versus 26 years of age; $P=0.014$) and OHCAs in women more often occurring in private residences (67% versus 56%; $P<0.001$). The 30-day survival was significantly better among female individuals (22% versus 16%; $P<0.001$). When temporal changes in OHCA characteristics were assessed, bystander CPR and defibrillation rates improved markedly more among female individuals, and surpassed the rates among male individuals (Table S4).

ICD Implantation

During the 20-year study period, 687 ICDs were implanted in individuals between 1 and 35 years of age (Figure 6). The ICD implantation rate increased from 0.81 per 100 000 PY in 2000 to 2003 (95% CI, 0.65–1.01) to 1.61 per 100 000 PY (95% CI, 1.37–1.87) in 2016 to 2019, corresponding to an IRR of 1.97 (95% CI, 1.51–2.60). The most prevalent cardiac diagnoses leading to

Table 1. Characteristics of All Sudden Cardiac Death Cases Stratified by Time Period

Characteristics	Overall (n=1057)	2000 to 2003 (n=277)	2004 to 2007 (n=247)	2008 to 2011 (n=203)	2012 to 2015 (n=169)	2016 to 2019 (n=161)	Estimated 20-year RR	95% CI, for RR
Male sex	733 (69)	173 (62)	183 (74)	144 (71)	113 (67)	120 (75)	1.13	0.99 to 1.29
Age, y	29 (22–33)	29 (23–33)	29 (22–33)	29 (22–34)	28 (22–33)	29 (22–32)	−0.18	−1.90 to 1.54
Comorbidity								
Any of the following	414 (39)	75 (27)	92 (37)	87 (43)	89 (53)	71 (44)	1.62	1.28 to 2.02
HT	51 (5)	14 (5)	12 (5)	9 (4)	5 (3)	11 (7)	1.12	0.44 to 2.82
CVD	167 (16)	44 (16)	45 (18)	29 (14)	24 (14)	25 (16)	0.86	0.53 to 1.39
IHD	22 (2)	7 (3)	8 (3)	≤3	≤3	5 (3)	0.63	0.14 to 2.66
Previous MI	14 (1)	4 (1)	5 (2)	≤3	≤3	5 (3)	1.34	0.21 to 8.04
Previous CA	9 (1)	≤3	4 (2)	≤3	≤3	≤3	0.44	0.033 to 4.32
AF	19 (2)	6 (2)	≤3	≤3	5 (3)	≤3	0.98	0.20 to 4.55
CM	32 (3)	11 (4)	8 (3)	7 (3)	≤3	≤3	0.41	0.11 to 1.37
Conduction disease	44 (4)	10 (4)	11 (5)	6 (3)	9 (5)	8 (5)	1.33	0.48 to 3.58
Congenital HD	66 (6)	17 (6)	17 (7)	13 (6)	11 (7)	8 (5)	0.80	0.35 to 1.81
ICD	8 (1)	≤3	≤3	≤3	≤3	4 (3)	39.50	2.91 to 1030
Epilepsy	143 (14)	15 (5)	23 (9)	36 (18)	38 (22)	31 (19)	4.48	2.69 to 7.50
Psychiatric disease	193 (18)	25 (9)	37 (15)	42 (20)	53 (31)	36 (22)	2.70	2.01 to 4.69
Diabetes	44 (4)	11 (4)	15 (6)	9 (4)	4 (2Q)	5 (3)	0.64	0.22 to 1.75
Death-related circumstances								
Unwitnessed SCD	577 (59)	120 (47)	112 (51)	112 (58)	123 (74)	110 (73)	1.79	1.51 to 2.12
Died during sleep	322 (36)	78 (33)	75 (36)	60 (35)	47 (35)	62 (44)	1.32	0.97 to 1.77
Sports-related	58 (5.6)	16 (5.8)	15 (6.1)	14 (6.9)	6 (3.6)	7 (4.7)	0.80	0.33 to 1.92
Autopsy performed	707 (67)	182 (66)	166 (67)	148 (73)	107 (63)	104 (65)	0.96	0.83 to 1.12

Data are n (%) or median (Q1–Q3). AF indicates atrial fibrillation; CA, cardiac arrest; CM, cardiomyopathy; CVD, cardiovascular disease; HD, heart disease; HT, hypertension; ICD, implantable cardioverter defibrillator; IHD, ischemic heart disease; MI, myocardial infarction; RR, relative risk; and SCD, sudden cardiac death.

ICD implantation were nonischemic cardiomyopathies (n=243 [35%]) and primary arrhythmias (n=182 [26%]). The majority of ICDs were secondary preventive ICDs (n=187 [74.2%]).

DISCUSSION

This longitudinal study provides contemporary nationwide incidence estimates for SCD based on a large cohort of individuals between 1 and 35 years of age with SCD in Denmark. The principal findings of the study include a significant decrease in the incidence of SCD (49% over the past 20 years), 7-fold improved survival after OHCA in young individuals, and higher rates of ICD implantation. This study is among the first to contextualize the trends in SCD to OHCA survival and ICD implantations in young individuals. The study provides an up-to-date overview of the epidemiology of SCD with potential implications for future preventive initiatives to reduce SCD.

IRs of SCD

The reported IR of 1.67 per 100 000 PY in the most recent time period (2016–2019) is comparable to the IR reported in the literature. Direct cross-study comparison of IRs is difficult because of wide-ranging differences in methodology and study populations. Our multisource identification of SCD, based on all deaths in Denmark from 2000 to 2019, reduces the risk of selection bias typically associated with epidemiological studies on selected populations (autopsy cohorts) or ICD codes from death certificates, and offers the most accurate estimate of the true burden of SCD.

We observed a 3.3% annual decline in SCD incidence, accumulating to a 49% reduction in SCD over the 20-year study period. All observed subgroups exhibited declining rates, apart from unwitnessed SCD, where the IR remained stable. Our group has previously reported temporal trends in young SCD from 2000 through 2009,[7] and the trend has continued to decline at a comparable

Table 2. Incidence Rates and Temporal Trends of Sudden Cardiac Death in Young Individuals (1–35 Years of Age)

Variables	SCD cases	Person-years, in millions	Crude incidence estimates				Adjusted annual changes	
			Crude IR	IR, 95% CI	IRR	IRR, 95% CI	PCA, %	PCA, 95% CI
All SCD	1 057	47.5	2.2	2.1 to 2.4	–	–	−3.31	−4.2 to −2.42
By groups								
Time period								
2000 to 2003*	277*	9.6*	2.89*	2.56 to 3.24*	–	–	–	–
2004 to 2007	247	9.4	2.6	2.3 to 3.0	0.91	0.77 to 1.1	–	–
2008 to 2011	203	9.4	2.2	1.9 to 2.5	0.75	0.62 to 0.89	–	–
2012 to 2015	169	9.4	1.8	1.5 to 2.1	0.62	0.51 to 0.75	–	–
2016 to 2019	161	9.7	1.67	1.42 to 1.94	0.58	0.47 to 0.7	–	–
Sex								
Female	324	23.3	1.4	1.2 to 1.5	–	–	−4.66*	−6.17 to −3.14*
Male	733	24.2	3.0	2.8 to 3.3	2.2	1.9 to 2.5	−2.73	−3.95 to −1.50
Age, y								
1 to 18*	175*	23.8*	0.74*	0.63 to 0.85*	–	–	−4.7*	−7.5 to −1.9*
19 to 35*	882*	23.7*	3.70*	3.50 to 4.00*	5.1*	4.3 to 6.0*	−2.8*	−3.9 to −1.8*
Witnessed status								
Witnessed	406*	47.5*	0.85*		–	–	−7.03	−5.46 to −2.71
Unwitnessed	651	47.5	1.37*		1.6	–	−0.09	−1.48 to 1.31

IR indicates incidence rate; IRR, incidence rate ratio; PCA, percentage change annualized; and SCD, sudden cardiac death.
*Xxx.

rate over the past decade. Similar findings have been reported in young SCD,[5,24] SCD in all ages,[2,9] and cardiovascular mortality,[2] supporting an overall trend of declining SCD mortality rates.

Improved Survival After OHCA

The reduction in SCD mortality rates is multifactorial, but improved survival after OHCA is among the most important contributors. Several strategies to improve OHCA survival have been implemented in Denmark in the past decades, including widespread CPR training, layperson activation (heart runner program), and increased public automated external defibrillator (AED) availability,[25,26] and the effects of these community-based interventions on survival are well documented.[27,28] During the study period, survival after OHCA in individuals between the ages of 1 and 35 years increased from 4% to 28%, concomitant with an increase in bystander CPR and defibrillation to ≈80% and 8%, respectively. Although a considerable proportion of OHCAs in young individuals are noncardiac,[29] this improved survival translates directly into a lower SCD incidence. Although the rate of bystander defibrillation increased significantly during the study period, AEDs were only used in 8% of young people with OHCA. The low rate was likely because most arrests occurred in private homes, where rates of bystander defibrillation remain low.[30] Early bystander defibrillation is a key prognostic factor for survival,[27] and further improvement in the rate of bystander AED use is critical in improving survival rates.

The proportion of female individuals with SCD decreased during the study period, although just missing statistical significance (*P*=0.058), likely an issue of statistical power. Similar findings have been described in studies of both younger[8] and older[9] SCD cohorts, and higher OHCA survival rates have been reported in female individuals.[31,32] In the current study, bystander CPR and defibrillation rates, key prognostic markers for improved survival, increased in both sexes, but the increase was markedly higher among females, for whom the rates surpassed those among males. This difference likely contributed to the observed discrepancy between sexes in OHCA survival and SCD incidence. The equal CPR and defibrillation rates in recent years contrast previous reports of OHCA in female individuals[32,33] and could reflect differences in study populations and characteristics (younger age in the current study) or cultural differences toward resuscitation attempts in girls and young women.

Prevention of SCD and Identification of High-Risk Individuals

Prevention of SCD in the general population has proven difficult because of the sudden nature of the event and the confluence of risk factors for sudden cardiac arrest and SCD and all-cause mortality.[34] Thus, preventive strategies are primarily aimed toward high-risk individuals with known cardiac diseases.

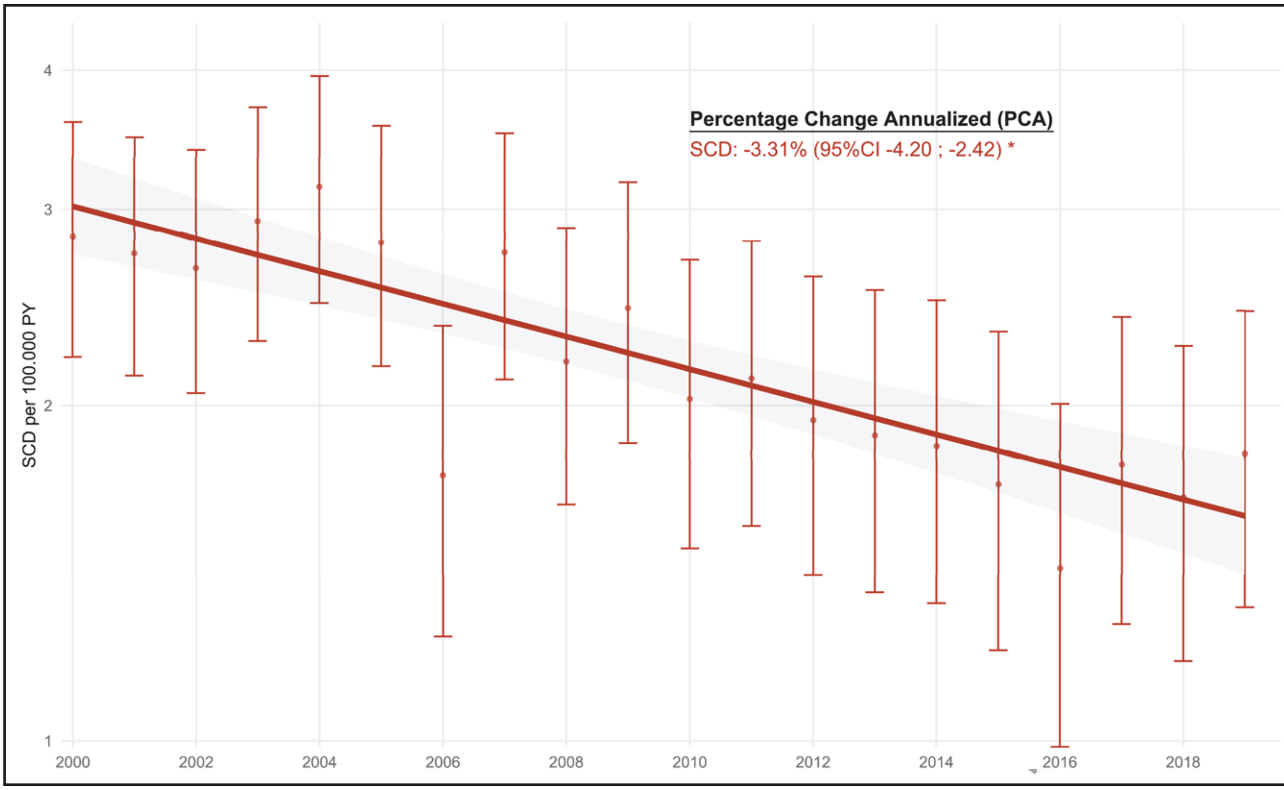

Figure 2. Incidence of sudden cardiac death from 2000 to 2019.
SCD indicates sudden cardiac death.

Over the past decades, our understanding of the pathophysiology and genetics underlying inherited cardiac diseases has advanced substantially, and diagnostic criteria for inherited cardiac diseases have improved. Combined with systematic family evaluation of relatives of people who experienced sudden cardiac arrest or SCD, in whom the risk of inherited cardiac diseases is significantly higher,[35,36] we likely identify more individuals at risk of SCD, in whom preventive measures can reduce the risk of cardiac events. In the current study, the diagnostic rates of potentially inherited cardiac diseases increased 10-fold, which is an important contributing factor to the decreasing rates of SCD.

ICD implantation is a key component in preventing SCD in high-risk patients, as it significantly reduces the risk of arrhythmic death.[19,37] During the study period, the implantation rate of ICD doubled, and the prevalence of

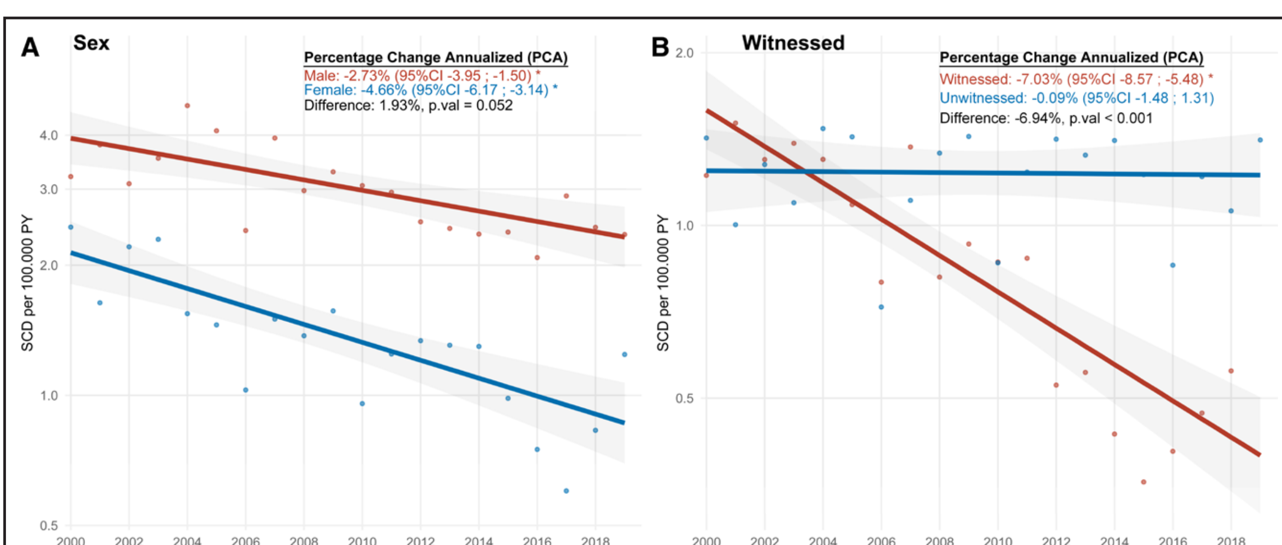

Figure 3. Temporal trends in sudden cardiac death incidence by sex and witnessed status.
A, Sex. **B**, Witnessed status. SCD indicates sudden cardiac death.

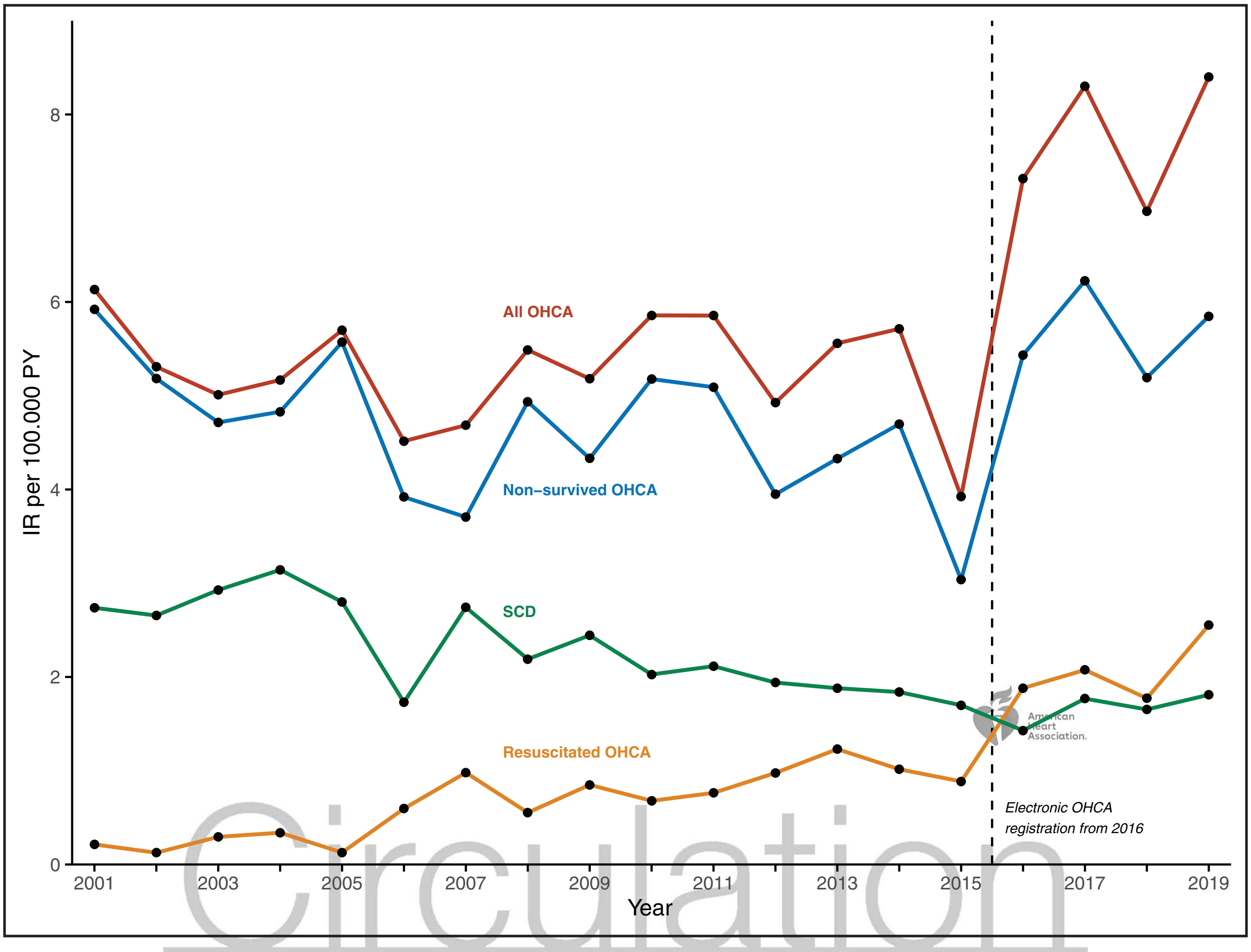

Figure 4. Incidence of out-of-hospital cardiac arrest in young individuals (1–35 years of age).
OHCA indicates out-of-hospital cardiac arrest; and SCD, sudden cardiac death.

ICDs in the young general population increased >10-fold. As the number of OHCA survivors increases, more patients will be evaluated for ICD implantation. Causes of OHCA among young individuals differ from those in the elderly, with more structural and inherited cardiac disease (ie, irreversible causes of cardiac arrest),[10,18] and among these individuals, secondary ICD implantation is more likely. In accordance, we found that the majority of implanted ICDs were for secondary prevention. Furthermore, the improved diagnostics of inherited cardiac diseases will identify more individuals with an indication for ICD implantation. Similar increasing trends in ICD rates have been reported in Western Australia, where ICD implantation rates increased 15-fold from 1995 to 2009,[9] paralleled by improved OHCA survival.

For both primary and secondary prevention ICDs, whether mortality reduction is attributable to the actual ICD, improved medical care and awareness in patients with an ICD (performance bias), or a combination remains speculative. However, a study by Hansen et al[26] found a significant decline in the delivery of appropriate shocks in patients with secondary ICDs during the past decade, and thus fewer who seem to benefit from their ICD. Because young individuals with an ICD have a high lifetime risk of device-related complications,[38] this finding highlights the need for better preimplantation risk stratification and identification of those who may benefit from an ICD, in order to reduce unnecessary implantations.

A surprising finding of this study was the discrepancy in SCD trends between witnessed and unwitnessed SCD. Because we only observed declining rates of SCD that were witnessed, the proportion of unwitnessed SCD increased by 79% to ≈3 in 4, which is markedly higher than previously reported.[39,40] Previous studies have identified key differences between witnessed and unwitnessed SCD (eg, more unexplained deaths, higher proportion of male individuals, different comorbidity profiles, more frequent death during sleep among unwitnessed SCD).[39,41] Therefore, this shift has substantial implications for the epidemiology of SCD, and future preventive measures must reflect this change, as strategies targeting OHCA may have a limited effect on preventing unwitnessed SCD.

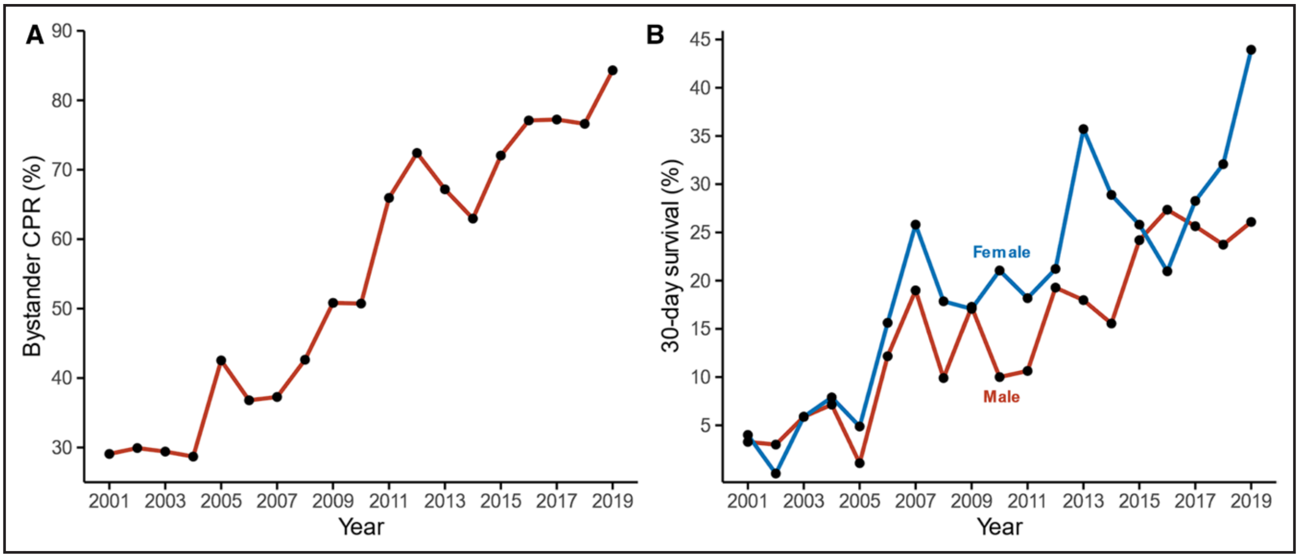

Figure 5. Temporal trends in bystander cardiopulmonary resuscitation and cardiac arrest survival in young individuals (1–35 years of age).
A, Cardiopulmonary resuscitation (CPR). **B**, Cardiac arrest survival.

Prevention of SCDs that occur unwitnessed or during sleep is particularly difficult, as timely recognition and intervention is hindered and survival chances thus dramatically lower. However, connected devices (eg, smart watches and speakers) are increasingly capable of identifying malignant arrhythmias and alerting first responders or family members.[42,43] In a recent study by Edgar et al,[44] wrist-derived photoplethysmography identified circulatory arrest in patients undergoing medically induced circulatory arrest (eg, during cardiac surgery), with a sensitivity of 95% and a positive predictive value of 90%. Although the trial was not based on real-life cardiac arrhythmic events (eg, OHCA), the results are intriguing. If these findings can be validated in larger trials, it would be an important step toward improved near-term prevention of cardiac arrest and SCD. These and similar solutions are in their infancy, but they present an exciting opportunity to monitor high-risk patients and lower mortality rates.[34,45]

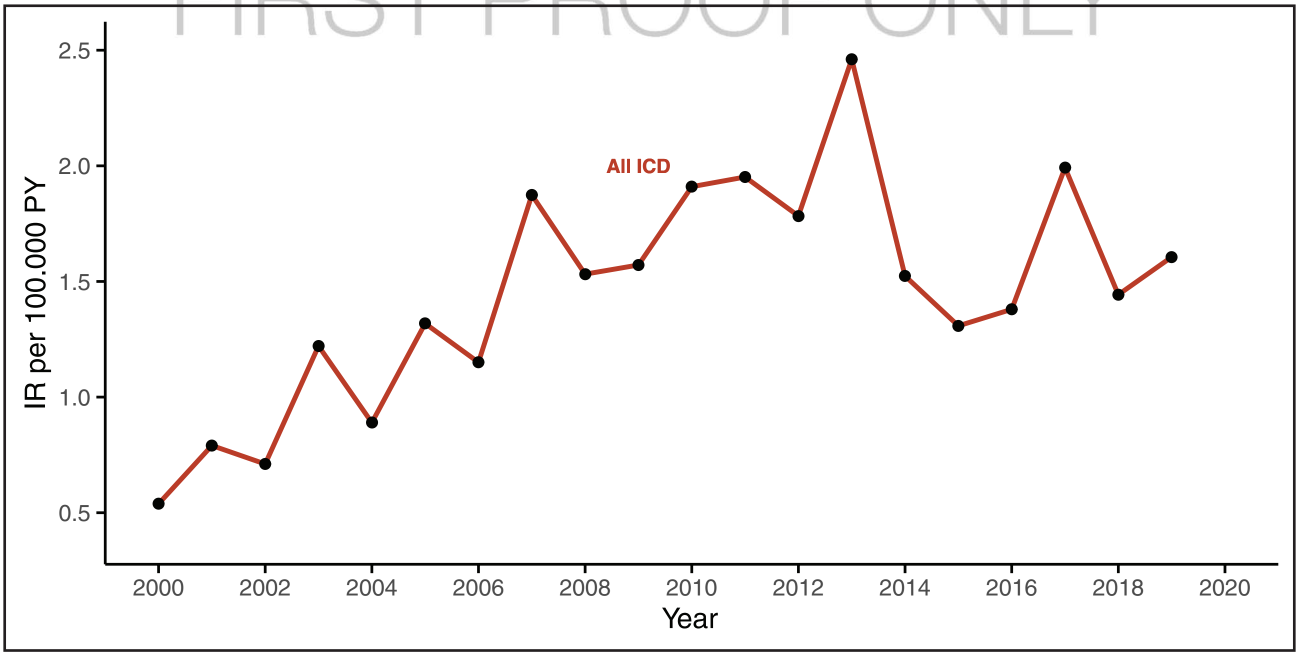

Figure 6. Implantable cardioverter defibrillator implantations in young individuals (age 1–35 years).
ICD indicates implantable cardioverter defibrillator; and IR, incidence rate.

Study Limitations

We acknowledge several limitations of our study. First, the observational nature imposes limitations on the assertions of causality, and interpretation should be made with caution. Second, changes in coding practices, diagnostic criteria, and procedural indications during the 20-year study period may have affected the observed trends. However, this would have less effect on SCD rates because of the multisource identification of SCD and primary effect estimates of comorbidity, diagnostic rates, and ICD implantation. In addition, the OHCA registry has undergone administrative changes during the study period, with the implementation of electronic registration of all OHCA cases since 2016.[16] This change has led to improved capture, which is evident from the increased incidence after 2016. However, the overall incidence of OHCA was stable both before and after 2016, and the improving trend in survival and bystander interventions was observed throughout the entire study period, indicating that the underreporting of OHCA cases was likely at random with limited effect on our estimates. We had no information about ICD therapies, which could have added further insight into the value of implanted ICDs. Third, information on modifiable risk factors (eg, body mass index, smoking, alcohol intake, and activity level) that may influence disease patterns was not available from the national registries.

Conclusions

Over the past 20 years, there has been a 49% decrease in the incidence of SCD in young individuals (1–35 years of age) in Denmark. Steep inclines in survival rates of cardiac arrest, diagnostic rates of inherited cardiac diseases, and ICD implantations parallelled the decline. However, we observed no change in the incidence of unwitnessed SCD, and preventive efforts are needed to address this issue (eg, by concentrating on near-term prevention).

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Disclosures

None.

Supplemental Material

Tables S1–S4

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