

Epidemiology of Sudden Cardiac Death: Global and Regional Perspectives



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Despite advancements in prevention and treatment, sudden cardiac death (SCD) remains a leading cause of mortality and is responsible for approximately half of all deaths from cardiovascular disease. Outcomes continue to remain poor following a sudden cardiac arrest, with most individuals not surviving. Although coronary heart disease remains the dominant underlying condition, our understanding of SCD is improving through greater knowledge of clinical risk factors, cardiomyopathies, and primary arrhythmic disorders. However, despite a growing wealth of information from studies in North America, Europe, and Japan, data from other global regions (and particularly from low- and middle-income countries) remains scarce.

Keywords

Sudden cardiac death • Sudden death • Epidemiology • Ventricular arrhythmia

Introduction

Sudden cardiac death (SCD) is a leading cause of mortality and responsible for approximately half of all deaths from cardiovascular disease [1]. It is generally accepted that SCD refers to an unexpected death or arrest from a cardiovascular cause. Most studies refer to SCD as a sudden death from a cardiovascular cause which occurs within one hour of symptom onset when witnessed, or if not witnessed, an unexpected death from a cardiovascular cause where the individual was observed to be alive within the previous 24 hours. However, non-cardiac causes such as pulmonary embolism, stroke, and aortic syndromes can also lead to rapid death and should be considered as alternate pathologies.

Despite its importance and societal burden, our understanding of SCD epidemiology is limited. The epidemiological study of SCD has been particularly hampered by definitional and methodological challenges. Although much progress has been made through implantable cardioverter

defibrillators, community-based cardiopulmonary resuscitation, and coronary heart disease (CHD) management, SCD still remains the cause of 15–20% of deaths in Western societies [2]. Furthermore, there is a comparative dearth of information on SCD from other global regions, particularly low and middle income countries. In this manuscript, we review the epidemiology of SCD focussing on both global and available regional data, with detail on specific conditions, risk prediction, and intervention included elsewhere in this Special Issue on Ventricular Arrhythmias and SCD.

Regional and Global Incidence of SCD

The following sections summarise the available data on the global and regional incidence of SCD (Figure 1). However, estimates of SCD need to be interpreted in the context of several limitations. First, utilised definitions vary from study

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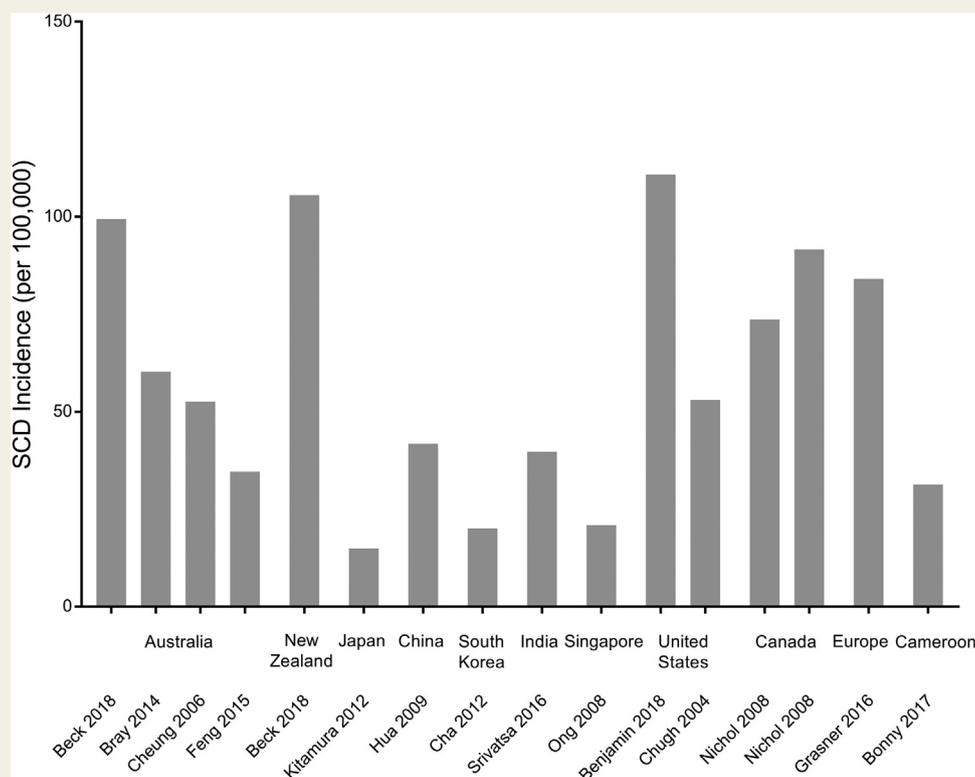


Figure 1 Global incidence of SCD.

Incidence demonstrated is from selected studies reporting SCD in all age groups, with the exception of India (Srivatsa 2016; ≥ 35 years old) and Cameroon (Bonny 2017; ≥ 18 years old).

Abbreviation: SCD, sudden cardiac death.

to study, despite attempts at standardisation. Second, it can be challenging to exclude non-cardiac causes of death, particularly when complete documentation of event and background history is unavailable, and autopsies are not routinely performed. Third, data sources and methodology for case ascertainment differ widely. In particular, as SCD is often identified through emergency medical systems (EMS), regional variation in the use of EMS systems affects results. Nevertheless, interrogation of the available data still provides useful insights into SCD epidemiology despite these issues.

Australia and New Zealand

There have been a few studies of SCD incidence in Australia and New Zealand (Table 1). The most comprehensive data is from the Aus-Roc Epistry (the epidemiology registry of the Australian Resuscitation Outcomes Consortium), which included 19,722 out-of-hospital cardiac arrest (OOHCA) cases in 2015 from seven EMS services in Australia and New Zealand. The overall incidence rate in Australia was 99.4 per 100,000 [3]. Another large study included 12,421 EMS-attended OOHCA in Perth, Western Australia, estimating an incidence of 60.2 per 100,000 across all age groups. Other reports in Australia have estimated an incidence of all SCD ranging from 34.6 to 89.1 per 100,000 [5–9]. Sudden cardiac death figures in younger age groups vary from 1.1

to 8.7 per 100,000 [10–12], with corresponding estimates in adults over 18 years of age ranging from 102.0 to 147.8 per 100,000 [13,14]. A few studies [15–17] have suggested that the incidence of EMS-treated OOHCA is not dissimilar in New Zealand to Australia [15], and the AusROC Epistry demonstrated a similar incidence of all EMS-attended OOHCA of 105.5 per 100,000 [3].

East Asia

Although there is limited data from China, the most populous country within this region, one report assessed SCD from death certificates supplemented by medical records and interviews with family, hospital personnel, or other witnesses to the death. In four distinct regional populations, these investigators found an overall incidence of 41.8 per 100,000 [18]. In Japan, a prospective, nationwide registry included all EMS-treated OOHCA (only 1.3% of all OOHCA had no resuscitation) and described a very low incidence of 14.9 per 100,000 [19]. Another report from Osaka, Japan, included OOHCA of presumed cardiac origin in those ≥ 18 years of age, estimating an incidence of 36 per 100,000 [20]. The incidence of SCD was similarly low in South Korea, where a national database reported an incidence of 20.1 per 100,000 [21]. Data from 10 hospitals in Taipei City, Taiwan, suggested an incidence of EMS-treated OOHCA of 28.4 per 100,000 [21].

Table 1 Global Incidence of Sudden Cardiac Death

Region	Country	Region	Study year(s)	Incidence per 100,000	Reference
Australia & New Zealand	Australia	National	2015	All: 99.4	Beck 2018 [3]
Australia & New Zealand	Australia	Ipswich, Queensland	1985–1999	All: 50.6	Scott 1993 [8]
Australia & New Zealand	Australia	Perth, Western Australia	1996–1999	All: 89.1	Finn 2001 [7]
Australia & New Zealand	Australia	Perth, Western Australia	1997–2010	All: 60.2	Bray 2014 [4]
Australia & New Zealand	Australia	Sydney, New South Wales	2004–2005	All: 52.6	Cheung 2006 [5]
Australia & New Zealand	Australia	Western Australia	1997–2010	All: 34.6	Feng 2015 [6,9]
Australia & New Zealand	Australia	Western Australia	1997–2014	< 18yo: 8.7	Inoue 2017 [1]
Australia & New Zealand	Australia	Sydney, New South Wales	1994–2002	≤ 35yo: 1.1	Doolan 2004 [12]
Australia & New Zealand	Australia	Victoria	2002–2003	≥ 17yo: 147.8	Jennings 2006 [14]
Australia & New Zealand	Australia	Queensland	2000–2002	≥ 18yo: 102.0	Woodall 2007 [13]
Australia & New Zealand	New Zealand	National	2015	All: 105.5	Beck 2018 [3]
Australia & New Zealand	New Zealand	National	2006–2009	≤ 40yo: 2.0	Wilms 2012 [10]
East Asia	Japan	Osaka	1998–2003	≥ 18yo: 36	Iwami 2007 [20]
East Asia	Japan	National	2005–2009	All: 14.9	Kitamura 2012 [9]
East Asia	China	Regional	2005–2006	All: 41.8	Hua 2009 [18]
East Asia	China	Beijing	2008–2009	All: 38.4	Zhang 2014 [76]
East Asia	South Korea	National	2006–2008	All: 20.1	Cha 2012 [21]
South Asia	India	Tirunelveli, South India	2010–2011	≥ 35yo: 39.7	Srivatsa 2016 [22]
South East Asia	Singapore	Singapore	2001–2004	20.9	Ong 2008 [25]
North America	United States	Multiple regions	2005–2015	All: 110.8	Benjamin 2018 [28]
North America	United States	Oregon	2002–2003	All: 53	Chugh 2004 [29]
North America	Canada	Ottawa, Canada	2006–2007	All: 73.6	Nichol 2008 [30]
North America	Canada	Toronto, Canada	2006–2007	All: 91.6	Nichol 2008 [30]
Europe	27 countries	–	2014	All: 84.0	Grasner 2016 [31]
Europe	France	Saint-Etienne, France	1991–1992	All: 94.1	Giraud 1996 [77]
Europe	Denmark	Copenhagen, Denmark	2004–2007	All: 73.8	Steinmetz 2008 [78]
Africa	Cameroon	Douala, Cameroon	2013	≥ 18yo: 31.3	Bonny 2017 [32]

South Asia

There is minimal available data from the South Asian region. A few studies of variable methodological quality have estimated the burden of SCD in India. One using single-centre autopsy data calculated a SCD incidence in those >35 years of 39.7 per 100,000, although the degree to which this accurately reflects the community prevalence of SCD is not certain [22]. Other studies have calculated SCD prevalence in India with verbal autopsies or questionnaire approaches; however, incidence was not estimated [23,24]. We are not aware of incidence data from other countries in South Asia, such as Pakistan, Bangladesh, Nepal, Sri Lanka and Bhutan.

South East Asia

There is a similar scarcity of community-based data on SCD incidence in South East Asia. One report from Singapore found an EMS-attended SCD incidence of 20.9 per 100,000 [25]. Other reports in this region have estimated the incidence of sudden unexplained death syndrome in Thailand and the Philippines using questionnaires and interviews, but whether these accurately reflect community SCD across all ages is uncertain [26,27]. We are not aware of incidence data

from other countries in South East Asia, such as Malaysia and Indonesia.

Other Global Regions

Considerably more data on SCD is available from North American and European populations. Overall, the annual incidence of SCD appears to approximate 50 to 100 per 100,000 in the general population in these regions. The Resuscitation Outcomes Consortium (ROC) maintained a registry of OOHCA in multiple regions throughout the United States (US) from 2005 to 2015; the incidence of all EMS-assessed cardiac arrests was 110.8 per 100,000 [28]. In another prospective evaluation of a large population in Oregon, United States, the incidence of sudden cardiac arrest was 53 per 100,000 between 2002 and 2003; retrospective death certificate review over the same time period over-estimated this by three-fold [29]. In Canada, the incidence has been reported to vary from 73.6 to 91.7 per 100,000 [30]. Other studies from Europe report similar figures; the EuReCa ONE Study included data from 27 countries in October 2014 and estimated an overall annual incidence of 84.0 per 100,000 [31]. We are aware of one prospective report from sub-Saharan Africa; in Douala, Cameroon, it was estimated that SCD

incidence was 33.6 per 100,000 through a three-level case reporting and ascertainment system [32]. There is a paucity of data from other less developed regions of the world; although there are some reports on SCD using autopsy, in-hospital, and defibrillator information, these are insufficient to estimate the true incidence of SCD in these regions [33,34].

Outcomes Following SCD

Outcomes following OOHCA remain poor despite efforts to progress cardiopulmonary resuscitation (CPR) and post-resuscitation care. In the AusROC Epistry in Australia and New Zealand, immediate post-event survival was 28% (range 21–36%) in cases of attempted resuscitation, but only 12% (range 9–17%) survived to hospital discharge or to 30 days [3]. Survival rates appear to be significantly lower in other Asia Pacific countries, with the PAROS (Pan-Asian Resuscitation Outcomes Study) reporting survival to hospital discharge rates of non-traumatic arrests as being 5.6% in Japan, 9.9% in Korea, 1.0% in Malaysia, 2.5% in Singapore, 2.7% in Thailand, and 4.8% in Taiwan [35]. This study also included the United Arab Emirates, who reported a survival to hospital discharge rate of 2.8% [35]. In the United States, survival to hospital discharge after EMS-treated OOHCA in 2015 was 12.4% in the ROC registry [28]. Similar survival rates appear to exist in Europe; the EuReCa ONE Study reported an overall survival rate of 10.3% to hospital discharge or 30 days [31].

Trends in Incidence, Rhythm and Survival

Most of the available data seem to support a declining incidence of SCD in recent years. For example, several studies from Western Australia have reported that age-standardised rates of SCD decreased in the late 1990s and early 2000s. However, more contemporary data now raise the possibility of a potential increase in recent years [4,6,36]. Similarly, the incidence of OOHCA <18 years of age has been reported to have decreased from 14.1 (1997–2000) to 8.7 (2011–2014) per 100,000 in Perth, Western Australia [11]. Sudden cardiac death rates have also been observed to have declined elsewhere, including in Sweden, Netherlands, and Japan [37–39]. The Framingham Investigators have also described a 49% decrease in SCD from 1950–1959 to 1990–1999 in the United States [40]. Although the US ROC registry has reported an increase in the rate of EMS-treated OOHCA from 47.1 per 100,000 in 2008 to 66.0 per 100,000 in 2015, this may reflect greater treatment of OOHCA rather than a true increase in overall incidence [28]. Trends in the incidence rates in other regions of the world, particularly low and middle income countries, is less certain.

In addition to quality CPR, the rhythm on first assessment has a significant influence on outcome. For example, in the ROC registry, survival rates were significantly higher if the

first rhythm was shockable (30.2%) or layperson-initiated CPR occurred (43.6%) [28]. In the Cardiac Arrest Registry to Enhance Survival (CARES) in the US, automated external defibrillator (AED) use and bystander CPR explained as much as 50.4% of survival variation across 132 counties [3]. Thus, trends in the first detected rhythm are of great importance to understanding and subsequently attempting to reduce SCD. Data from North America and Europe suggest that ventricular fibrillation (VF) as the first rhythm has declined between 1980 and 2000 [41–43]. These trends may have plateaued in recent years, with the ROC registry describing the proportion of shockable rhythms ranging from 20.2 to 21.9% between 2007 and 2015 [28]. A variety of explanations has been proffered for the initial increase and subsequent maintenance of a majority of cases where asystole or pulseless electrical activity (PEA) is the first rhythm, including a greater proportion of unwitnessed arrests at home, increasing use of beta blockers and implantable defibrillators in high risk patients, and older patients who may have other non-cardiac precipitants leading to PEA [44]. There is less data on temporal trends in first rhythm from other regions; however, reports suggest that geographic variation in the proportion of shockable rhythms exist. For example, the AusROC registry has described that 28% of arrest demonstrated a shockable rhythm in Australia and New Zealand [3]. However, the PAROS study reported a much lower proportion of shockable rhythms of between 4.1% and 18.7% of arrests in the Asia Pacific [35].

In response to efforts to improve CPR and post resuscitation care, survival rates are increasing, but overall remain low. In Perth, Western Australia, survival to hospital discharge appeared to increase from 7.3% in 1997 to 12.0% in 2010 [4]. Data from the ROC registry in the United States show that survival to hospital discharge increased from 10.2% to 12.4% between 2006 and 2015 [28]. In Denmark, 30-day survival similarly increased from 3.5% to 10.8% between 2001 and 2010 [45]. In Japan, survival also appears to be increasing to some extent. In one study, 30-day survival with favourable neurological outcome increased from 1.6% in 2005 to 2.8% in 2009 [19]. In South Korea, survival to discharge increased in metropolitan areas (3.6% in 2006 to 5.3% in 2010) but interestingly remained low in rural areas (0.5% in 2006 to 0.8% in 2010) [46]. However, data on survival trends from other regions, again particularly from low and middle income countries, remains scarce.

SCD Risk Factors

Age, Sex and Ethnicity

The majority of SCD occurs in the adult population in whom the incidence of SCD rises with increasing age (Figure 2 and Table 2) [2,29]. Amongst individuals under 35 years of age, the highest incidence is observed in the 0–5 year age group [29]. Data suggest that men have a three- to four-fold higher risk for SCD compared to women, although recent studies suggest this disparity may be declining [29]. It is well-

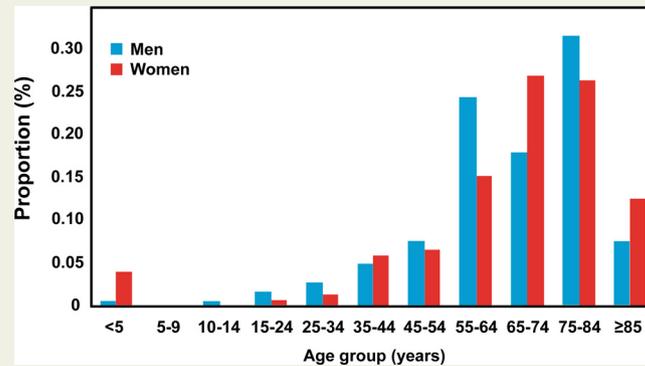


Figure 2 Age and Gender Distribution of Sudden Cardiac Death.

Adapted with permission from Chugh et al., *Journal of the American College of Cardiology*, 2004 [24].

established that individuals of African-American descent appear to have a higher rates of SCD and poorer outcomes compared to those of Caucasian or Hispanic descent [47]. Although there are few multi-ethnic studies, some data suggest that the incidence of SCD is lower in Asian individuals which is consistent with population estimates from Asian regions discussed above [48].

Clinical Risk Factors

Several other clinical risk factors have been associated with SCD in epidemiologic studies. Coronary heart disease risk factors including hypertension, diabetes, dyslipidaemia, cigarette smoking, and obesity are predictive of SCD in men and in women [2,49]. Somewhat unexpectedly, this is also the case amongst the young; 58% of subjects aged 5 to 34 years of age who experienced SCD in the Oregon Sudden Cardiac Death Study had at least one cardiovascular risk factor [50]. Moreover, there was a 39% prevalence of obesity in these young individuals [50]. Family history of SCD may also represent a risk factor for SCD [51]. More recent data suggest other clinical comorbidities may be associated with subsequent SCD, including atrial fibrillation, chronic kidney disease, and obstructive sleep apnoea [52–54]. Serious mental illnesses, such as depression, anxiety, and psychosis, have also been linked to SCD [44]. Lifestyle factors may also play a role in predisposing to SCD. Dietary patterns including greater fish, n-3 polyunsaturated fatty acids, magnesium and a Mediterranean-style diet appear to be protective [55,56]. Heavy alcohol use appears to be harmful, with some data suggesting small-to-moderate alcohol intake potentially conferring a reduced risk [57]. Other studies point to the role of potential triggers such as emotional stress, air pollution, and diurnal/seasonal variation [44,58]. Finally, despite vigorous exercise being a possible trigger, most studies support regular physical activity lowering the risk of SCD [59].

Electrocardiographic Parameters

Electrocardiogram (ECG) parameters may represent intermediate phenotypes related to clinical risk factors and/or reflect the presence of structural heart disease or an arrhythmic syndrome. Several ECG parameters, including greater

resting heart rate and markers of abnormal cardiac depolarisation and repolarisation, have been previously associated with a risk of SCD, as have specific abnormalities associated with primary arrhythmic disorders (e.g. long and short QT syndromes, Brugada syndrome, arrhythmogenic right ventricular cardiomyopathy (ARVC), and Wolff-Parkinson-White syndrome) [49]. More recently, combinations of ECG parameters reflecting different aspects of cardiac electrophysiology have been utilised to predict SCD risk. Using data from the Oregon Sudden Cardiac Death Study, ECG parameters which remained predictive of SCD in the final model included heart rate, left ventricular (LV) hypertrophy, QRS transition zone, QRS-T angle QTc and T-peak-to-T-end [60].

Coronary Heart Disease

Sudden cardiac death accounts for approximately half of all CHD-related deaths in the United States, and CHD is thought to be the structural basis for approximately 70% of all SCD, however the latter proportion is known to vary by age, gender, race, and ethnicity (Figure 3) [1]. Even amongst the young, CHD is a relatively common cause of SCD. In the Oregon Sudden Cardiac Death Study, CHD was the second most common condition (22%) underlying SCD among subjects aged 5 to 34 years [50]. The spectrum of substrates underlying CHD-related SCD include transient ischaemia, acute coronary syndromes, scar-related pathophysiology, and ischaemic cardiomyopathies [61]. The risk of SCD is greatest in the first month following a myocardial infarction and decreases over time, although those who develop ventricular remodelling and heart failure have a subsequent increase in risk [62]. However, two-thirds of CHD-related SCD occurs as either the first clinical manifestation of CHD or in supposedly low-risk individuals based on current risk prediction methods, thwarting efforts to reduce the burden of CHD-related SCD [61]. Although data is limited from other regions of the world, it may be reasonable to predict that the proportion of CHD-related SCD may parallel the incidence of CHD mortality as it has in Western countries [62]. Supporting this fact is data demonstrating that CHD is the basis for only 25–50% of SCD in Japan,

Table 2 Selected risk factors for Sudden Cardiac Death

Demographics
– Increasing age
– Male gender
– African-American or non-Asian ethnicity
Coronary heart disease risk factors
– Hypertension
– Diabetes
– Dyslipidaemia
– Cigarette smoking
– Obesity
Electrocardiographic parameters
– Heart rate
– QRS duration or fragmentation
– Q waves or dynamic ST segment changes
– QTc interval
– QRS-T angle
– QRS transition zone
– T-peak-to-T-end interval
– Increased R wave voltage
– Specific abnormalities associated with primary arrhythmic disorders
Lifestyle/psychosocial factors
– Depression and anxiety
– Diet (greater fish, n-3 fatty polyunsaturated acids, Mediterranean diet protective)
– Heavy alcohol use
– Limited physical activity
Genetics
– Family history of sudden cardiac death
– Specific mutations/polymorphisms
Specific conditions
– Coronary heart disease
– Atrial fibrillation
– Chronic kidney disease
– Obstructive sleep apnoea
– Dilated cardiomyopathies
– Hypertrophic cardiomyopathy
– Arrhythmogenic right ventricular dysplasia
– Infiltrative diseases (e.g. sarcoidosis, amyloidosis)
– Valvular heart disease
– Congenital abnormalities
Inherited arrhythmic syndromes
– Long and short QT syndromes
– Brugada syndrome
– Catecholaminergic polymorphic ventricular tachycardia
– Early repolarisation syndrome

commensurate with known lower CHD incidence and mortality [39,63]. It is therefore likely that wide variation in CHD-related SCD exists, as it does with CHD, with possibly high rates in regions such as Central Asia, Oceania and Eastern Europe [64].

Other Structural Heart Disease

Approximately 15% of overall SCD occurs in patients with other non-ischaemic structural heart disease in Western society [29,48]. This category encompasses dilated cardiomyopathies, hypertrophic cardiomyopathy, arrhythmogenic right ventricular dysplasia, infiltrative diseases (sarcoidosis, amyloidosis), valvular heart disease, and congenital abnormalities. The proportion of SCD caused by non-ischaemic cardiomyopathies is greater in younger age groups, and estimated to be 15–30% of SCD in those <35 years of age [44,65]. Moreover, in regions where CHD-related SCD is lower than in Western countries, other forms of structural heart disease may account for a greater proportion of SCD. For example, it has been estimated in Japan that cardiomyopathies account for 30–35% of SCD [63]. It should also be noted that, even in the absence of macroscopic structural heart disease, histologic examination can reveal the presence of concealed substrates such as focal myocarditis and regional ARVC [66]. Moreover, this category may expand as further research uncovers a structural basis for SCD of previously uncertain cause. As one example, recent evidence supports a high prevalence of mitral valve prolapse in unexplained SCD and stretch-induced fibrosis as a concealed substrate in these individuals following previously anecdotal associations [67,68].

Inherited Arrhythmic Disorders

In those with unexplained arrhythmic cardiac arrest not attributable to CHD or other disease, systematic testing reveals a potential cause in approximately 50%, of which two-thirds are primary arrhythmic disorders and the remaining have unrecognised structural disease [69]. Arrhythmic disorders include long and short QT syndromes, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, and early repolarisation syndrome. Overall, it is thought that arrhythmic disorders account for 1–2% of all SCD in Western countries [44]. However, there is data to suggest that geographic and possibly ethnic variation exists in these genetic disorders. For example, the prevalence of Brugada syndrome appears to be greater in Asian (9 per 1000) compared to European (3 per 1000) and North American (2 per 1000) populations [70]. Reports also suggest that early repolarisation is more common in African Americans than in individuals of Asian or Caucasian descent [71,72]. In contrast, the prevalence of long QT syndrome has been reported to be similar in Caucasian, Japanese, and Korean populations (0.5 per 1000) [73–75].

Conclusions

Although data from many regions of the world is limited, SCD remains a major public health burden worldwide. Improving our understanding of risk factors and underlying conditions, and how these vary across regional populations and ethnicities, may offer new opportunities

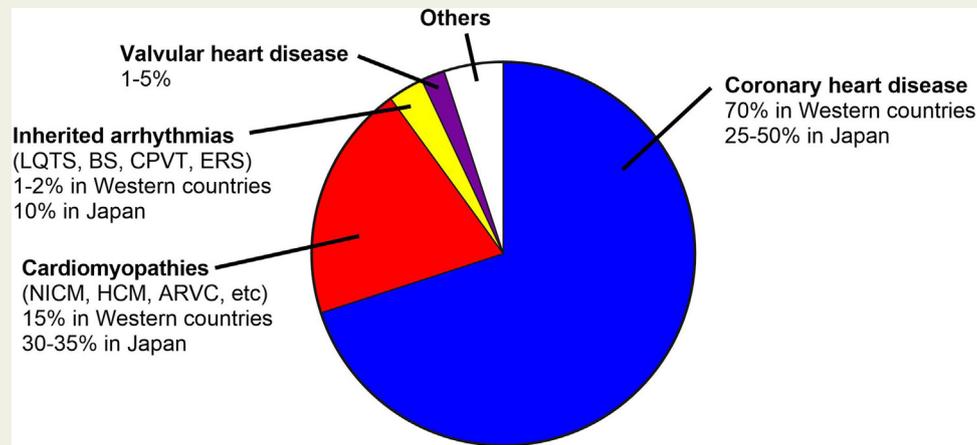


Figure 3 Causes of Sudden Cardiac Disease.

for prevention and treatment. Further study on the global and regional epidemiology of SCD is thus urgently required to reduce the societal burden of premature demise from SCD.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.hlc.2018.08.026>.

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