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Review Article

Global burden of Sudden Cardiac Death and insights from India

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ABSTRACT

Sudden Cardiac death (SCD) is a major clinical event causing adverse impact on global economy. This review summarizes the available epidemiological data on SCD from different parts of the world. It contrasts the Indian and global perception on the issues influencing data collection, burden of SCD and sudden deaths occurring following Myocardial Infarction. The differences in data from India and rest of the world are highlighted.

1. Introduction

Sudden Cardiac Death (SCD) is a catastrophic event, which has a huge adverse impact on the health care system. The ubiquitous distribution of this clinical syndrome mandates it being recognized as a worldwide phenomenon with the realization that a rising incidence negatively affects global economy. There is an evident geographical imbalance in the currently available statistical figures on the global burden of SCD as practically almost entire published literature in this area is from North America, Western Europe and few countries of the Asia pacific. This fact assumes significance as the perception of the practicing clinician towards this problem and prioritizing of health care resources in the community are invariably influenced by this data. In this review, I would like to present an overview of data collection tools, the global burden of sudden death, the epidemiology of post Myocardial Infarction (MI) SCD and would make an attempt to contrast the global and Indian perception on issues related to these areas.

2. Data collection tools

Compiling accurate data of SCD even when a standard definition is used is a challenging task as categorizing a death as sudden is mostly retrospective and clarity of the circumstances leading to the terminal event is often lacking. Ideally long-term population based prospective mortality surveillance methods should be employed to obtain reliable statistical data, however these are difficult to conduct and hence different methodologies have been used to obtain the currently available epidemiological figures. Death certificates are commonly used for SCD surveillance as they provide objective documented mortality information. They are

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particularly useful in generating uniform data when standard disease codes are used. The accuracy of information however depends on the physician completing the document. The time interval between onset of symptoms and death is not recorded and often deaths occurring after prolonged chronic pathologies are misclassified as SCD. They thus suffer from several flaws and hence SCD statistics relying solely on retrospective death certificates are likely to be an overestimate.[1] To improve reliability of data, information from other sources like hospital records, forensic documents and questionnaires are used to supplement facts obtained from death certificates.[2,3] Data obtained from first responders is useful as onsite information can be obtained, but unwitnessed deaths are missed and in absence of detailed clinical records, non-cardiac deaths are sometimes counted amongst SCD cases. Autopsy data is a meager resource of information as in general autopsy rates are low and moreover it alone cannot conclusively diagnose an arrhythmic death. To overcome the limitations of each of these methodologies, a multiple source method of ascertainment has been used in a few studies in order to capture all the SCD cases.[4,5] While initial recruitment of cases was achieved by emergency medical personnel, medical examiner, or hospitals, information obtained from medical records, death certificates and autopsy was also used for analyzing data. It is increasingly realized that these proven conventional tools used in developing countries may not be feasible or reliable in collecting mortality data from developing countries. Verbal autopsy has evolved as a new tool to circumvent the epidemiological constraints prevalent in these countries. Though initially developed as a tool to be used in acquiring data on child and maternal deaths, it has subsequently been validated as a reliable mortality surveillance system in other age groups too.[6,7] Using a questionnaire based approach many large studies have successfully employed this methodology to gather data on mortality and SCD.[8–10]

3. Burden of SCD in the population

True incidence of SCD in the community is difficult to ascertain in view of varied definitions and methodologies employed in different studies. The population included in each of these studies is dissimilar, making generalized inferences difficult. Further, in many of the studies the figures available are an estimate rather than exact data obtained from a prospective population based assessment. Table 1 highlights these facts and gives a summary of data obtained from different parts of the world. One of the earliest long-term systematic studies on SCD was the Paris Prospective Study.[3] The factors influencing sudden death in a cohort of about 7000 middle aged working male population followed up for 23 years were analyzed in this study. SCD constituted 5.6% of total mortality and about 1/5th of all the cardiovascular deaths. The analysis of the United States vital statistics mortality data from 1989 to 1998 showed that 63% of the 7 lakh cardiac deaths in the country were sudden.[11] This surveillance report from the US center for disease control and prevention is the basis for the estimated annual SCD figures of about 4.5–5 lakhs in the United States.

Table 1 – The figures of Sudden Cardiac Death obtained from studies conducted in various countries are summarized. These are variously expressed as incidence, prevalence or proportion of total mortality.

Country	Year	Population studied (n =)	Population characteristics	Method of assessment	SCD statistics
USA[11]	2001	719,456	Deceased US residents aged ≥35 years, with underlying cardiac disease	Death certificates	456,076 (63% of cardiac deaths)
USA[1]	2004	6, 60,486	Multnomah county residents	Multiple sources ascertainment	53/100,000
France[3]	1999	7079	Male workers aged 43–52 years followed up for a mean of 23 years	Medical examination, blood reports, hospital records, death certificates	5.6% of total mortality
Netherlands[12]	1997	133000	SCD cases in the age group 20–75 years over a period of 3 years (1991–1994)	GPs, ambulance personnel, and hospital records	97/100,000
Ireland[5]	2008	414,277	Population in 3 counties in west of Ireland in the year 2005	Multiple sources ascertainment	51.5/100,000
Japan[14]	2013	1934	Subjects in Hisayama town aged >25 years from 1962 –2009	Autopsy	Prevalence in the four, 12 year periods was 4%, 6.2%, 8.6% and 9.7% respectively
China[15]	2009	678,718	Prospective study of 4 regions for 1 year	Death certificates, hospital records, Interview of relatives and witnesses	41.8/100,000
India[19]	2012	22,724	Kindreds of medical students in the state of Andhra Pradesh who died due to any cause	Verbal autopsy	10% of total mortality
Thailand[33]	1993	316,931	20–49 years from 401 villages in 4 districts who died suddenly in the year 1990	Mailed questionnaires and direct interview of relatives	38/100,000

All deaths occurring out of hospital, in the emergency room or "dead on arrival" associated with underlying heart diseases as per ICD codes were presumed to be sudden without further adjudication. The Maastricht study from the Netherlands collected data from a defined geographical area having 1.3-lakh inhabitants between ages 20 and 75 years.[12] There were 515 witnessed and unwitnessed victims of sudden cardiac arrest included in the period from 1991 to 1994 resulting in an annual incidence of respectively 9.8–9.0/10,000 population. The Oregon sudden unexpected death study is a comprehensive assessment of incidence of SCD obtained from the Multnomah County with a population of 6 lakhs using multiple sources of surveillance initially from 2002 to 2003 and continued thereafter.[13] Cases were identified by the first responders, medical examiner's office and area hospitals. A total of 353 cases met the criteria for SCD, based on the circumstances of death, hospital records and autopsy data, which were available in 12% of the cases. This study found the annual incidence of SCD to be 53 per 1 lakh residents constituting 5.6% of total mortality. Using the same methodology of multiple source surveillance, a study of 4-lakh residents from west of Ireland involving predominantly rural population in the year 2005 recorded 212 cases of sudden cardiac arrest, resulting in an incidence of 51.5/1-lakh population.[5] This study had an autopsy rate of 96.6%. Data from Asia has been relatively sparse and the impact of SCD is being increasingly perceived with the progressively increasing incidence of Coronary Artery Disease (CAD). A study in the Okinawa island of Japan showed that SCD constituted 10% of total deaths and the crude incidence rate was 0.37/1000 population.[2] The Hisayama study was an autopsy-based study involving adult population in a town in Japan from 1962 to 2009 illustrating trends of Sudden Unexpected Deaths (SUD) over this period. Deaths due to strokes, heart disease, aortic aneurysm and dissection were included in this study. It showed that SUD and deaths due to strokes declined over time but prevalence of SCD doubled from 4% to 9.7% in the four, 12-year study periods and this paralleled the increase in ischemic heart disease during this time.[14] A 3-level surveillance and case ascertainment system during a period of 1 year in 4 regions of mainland China with a population of about 6 lakhs, found SCD prevalence to be 41.8/1 lakh population accounting for 9.5% of total mortality. An autopsy series of 14,000 from across China found that 12.5% of these deaths could be categorized as sudden.[15,16] India presents unique challenges in employing conventional epidemiological tools to collect mortality data and possibly due to these factors until recently there was no contribution to global SCD data. Registration of deaths is not universal and only a proportion of them are medically certified. Lack of uniform codes and inconsistent physician attribution of causes contributes to the unreliability of death certificates. The coverage of emergency services with first responders is limited to select areas and they do not collect data on out-of-hospital deaths. Autopsies are almost entirely confined to medico legal cases conducted in government run hospitals. To overcome these impediments, verbal autopsy using questionnaires administered by trained health workers was used to collect mortality data in 45 villages in the state of Andhra Pradesh. Analysis of this data revealed that cardiovascular diseases were the leading causes of mortality in rural population. Though the questionnaires of this study were not specifically designed to obtain SCD information, retrospectively data was analyzed to estimate the prevalence of sudden deaths in this rural population.[17,18] The first data of SCD in Indian population was obtained by applying the verbal autopsy methodology to medical students across the state of Andhra Pradesh.[19] In this study a 2-level questionnaire was administered to the respondents with the objective of ascertaining the details of deaths in their kindreds. By using this novel strategy, fairly reliable mortality data of a large general population was obtained from about 500 medical students. Each of these deaths was categorized by a 3 member adjudication system as SCD or otherwise. Of the 22,000 population there were 1691 recallable deaths and finally 173 out of these (10.3%) were adjudicated as SCD. A major difference compared to the data from developed countries was that the SCD population was younger (mean age 60.8 ± 14 years), with 21% younger than 50 years. The study highlighted the fact that unevaluated ischemic heart disease was the predominant cause of SCD in the general population. It was found that in the SCD cohort there was a large prevalence of coronary risk factors without traditional risk factors known to be associated with sudden death. Extrapolating the data to national mortality figures, it can be roughly estimated that annually about 7-lakh SCD cases occur in India.

4. SCD following Myocardial Infarction

SCD is a devastating clinical event, which is temporally associated with MI throughout its natural and intervened course. In the early phase, it is related to electrical instability of the myocardium, recurrent ischemia and cardiac rupture while in the later phases it is related to myocardial remodeling leading to macro reentrant VT. It has been observed that the first month following MI is a period of increased vulnerability to overall mortality and sudden death.[20,21] It was demonstrated in the DANAMI trial that half of all deaths and 63% of cardiac deaths occurred in the first month following MI. However the difficulty in adjudicating all sudden deaths as arrhythmic was shown by the limited autopsy data of the VALIANT trial where 12% of the presumed sudden deaths were due to cardiac rupture.[22]

Over the years, there has been in general an improvement in post-MI outcomes, which can be attributed to improved ICU care, timely reperfusion, appropriate revascularization and increased usage of evidence based medications. These measures have contributed to reduction in overall mortality and in the incidence of sudden death, a fact which is evident not only in the controlled clinical trials but also in the community based studies. The Framingham heart study is a follow up data of 333 patients predominantly with QMI, over a 17-year period beginning 1968, when cardiac enzymes became available. The first year incidence of SCD in this report was 3.6% while the cumulative 5-year incidence was 7%.[23] Subsequent studies, where routine incorporation of evidence based modern therapies was increasingly being practiced, documented a progressive decrement in these figures. CAMI was a 1 year follow up study for 3178 patients admitted with MI from 1990 to 92, in nine Canadian hospitals where 1.9% of the mortality was due

to presumed arrhythmic death.[24] A linear assessment of SCD incidence in the MI population ($n = 3296$) was conducted in Olmsted county of Minnesota from 1979 to 2005 with a median follow up of 4.7 years.[25] In this period the documented reduction in SCD was 20% and 38% in the 2nd and 3rd octets compared to the first 8 years of the study. This progressive decline in SCD mortality was not just a part of decrease in overall MI mortality but there was also a reduction in absolute numbers as seen by the fact that SCD in this study constituted 20–30% of all deaths compared to about 50% in the previous studies. The risk of SCD in the 30-day survivors post-MI declined to 1.2%/year, which is lower than that expected in the general population. A similar linear study from Japan over 14 years period from 1986 documented a progressive decrease in the first year post MI SCD from 1.1% to 0.2%.[26] These trends emphatically demonstrate correlation of improved in-hospital and post-discharge care of these patients with the reduction in mortality. This fact was reiterated in a study conducted in 2 European centers where optimal evidence based therapy achieved an annual SCD incidence of 0.4%. This study was conducted in a closely supervised setting where 84% of the patients were revascularized, 94% received beta blockers and aspirin, 74% received ACE inhibitors and 64% received statins.[27] Unfortunately data from India does not seem to reflect these encouraging positive global trends in the outcomes of MI. A comprehensive data on the acute coronary syndromes in India was obtained by the CREATE registry which is a prospective database of over 20,000 patients from 89 hospitals in 50 cities.[28] This report gave the first insight into the epidemic of CAD from this part of the globe. A striking difference evident in this study was in the constitution of patient population where, in contrast to previous literature, it was shown that about 60% of the patients with Acute Coronary Syndrome (ACS) had STEMI. The patients were younger (mean age 57.5 years) and had delayed presentation to the hospital (mean time of presentation = 6 h) after the clinical event. Only 58% of STEMI patients received thrombolytic therapy and 8% had PCI. By design the follow up was only for 30 days and the overall mortality at that point was 9% in STEMI and 3.6% in NSTEMI population. The study additionally revealed the significant influence of socio economic factors on the treatment and demonstrated a clear gradient of mortality across different classes, with highest mortality in patients among lower socio economic strata. The only focused report on the incidence of SCD in post STEMI population in India is a single center study, which collected data prospectively in 939 patients who were followed up for a mean period of 41 months.[29] This study replicated the facts noted in the CREATE study that distinguished the STEMI population of India from those in the published literature and they included younger age group, lesser number of patients receiving reperfusion therapy, and delayed presentation to hospital. This study further showed that the cumulative incidence of SCD at 1 month, and first 3 years was 4.9%, 6.5%, 8%and 8.9% respectively. SCD constituted about 50% of mortality in hospital and throughout the follow up period. Importantly, over half of all the SCD occurred in the first month while about 3/4^{ths} were seen in the first year after the index STEMI. It follows that there is a rapid attrition of ICD eligible patients as a significant number of SCD occur even before these devices can be considered. This pattern is in sharp contrast to the temporal profile of sudden deaths observed in the VALIANT study where approximately only 25% of SCD occurred in the first month while 65% occurred after 90 days (Fig. 1).

In this study, the factors that were shown to predict SCD by multivariate analysis were female gender, severe LV Dysfunction, absence of reperfusion & revascularization and poor adherence to medications. The issue of global variability in adherence to evidence based medications in patients with cardiovascular disease was addressed by the PURE study which prospectively recruited about 1.5 lakh patients from 17 countries.[30] This report highlighted the fact that proven evidence based medications are globally underused and the compliance to these medications is worse in low-income countries. Patients with CAD of south Asian subset, which included India revealed strikingly low usage of preventive medications – beta-blockers 11.9%, Antiplatelets 11.6%, ACEI/ARB 26.2% and statins 4.8%.

5. Inferences and strategies for SCD prevention

Many important facts emerge from the data available. Firstly the issue of defining epidemiology of the problem of SCD is far from complete as the global data is not universally represented. There is a need to design innovative strategies to acquire data from underdeveloped areas of the world.[31] As this data is becoming available, it is clearly apparent that there exists a wide geographical heterogeneity in the burden of SCD and the factors influencing it. Secondly, the rising incidence of clinical and sub clinical CAD in the developing countries predicts the nurturing of a large population with a vulnerable substrate for SCD and an explosion in SCD numbers. The immediate focus in these communities should be on primary and secondary prevention programs, wider reach of first

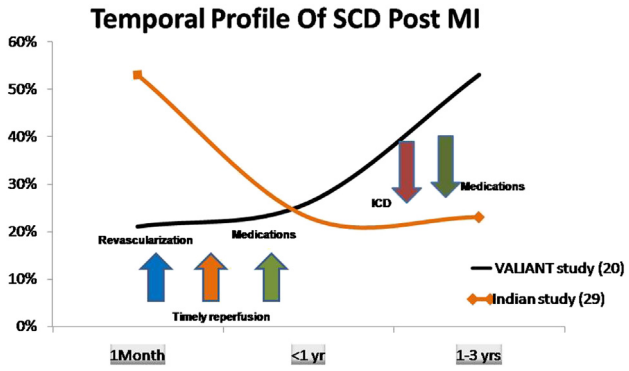

Fig. 1 – The distribution of sudden deaths over 3 years in the VALIANT and the Indian study are contrasted in this figure. Most of the SCD in the Indian study occurred in the first year. In the early period, the reduction in SCD is achieved by reperfusion, revascularization and compliance with medications. Beyond this period, use of defibrillators in addition to medications has shown to decrease incidence of SCD. The figure highlights the areas where SCD prevention measures need to be focused in India.

responders, timely management of ACS patients, and compliance with evidence based medications. The decline in the post MI mortality and SCD achieved in the developed countries in the last few decades predates the routine usage of ICD and can largely be attributed to adoption of these strategies.[32] Thirdly, a clearly visible distinction of the SCD cohort from India compared to the western world is the predominance of economically productive younger population, which is a matter of concern. Though intuitively this appears to result as a consequence of increasing prevalence of CAD in the young, it is prudent to investigate this problem further. It is apparent that the issues affecting post-MI mortality are neither uniform nor homogenous. Optimal implementation of primary and secondary prevention measures in some parts of the globe has resulted in decline in early post-MI mortality and SCD. In these communities prescription of defibrillators has further contributed to the reduction in the long-term mortality. India and possibly other countries with similar socio economic profile suffer from dual problems of a higher incidence of early post MI mortality and paucity of resources to fund ICDs. This warrants designing focused health care policies and evolving specific cost effective strategies.

Conflicts of interest

The author has none to declare.

REFERENCES

1. Chugh SS, Jui J, Gunson K, et al. Current burden of sudden cardiac death: multiple source surveillance versus retrospective death certificate-based review in a large U.S. community. *J Am Coll Cardiol*. 2004 Sep 15;44:1268–1275.
2. Tokashiki T, Muratani A, Kimura Y, et al. Sudden death in the general population in Okinawa: incidence and causes of death. *Jpn Circ J*. 1999;63:37–42.
3. Jouven X, Desnos M, Guerot C, et al. Predicting sudden death in the population: the Paris Prospective Study I. *Circulation*. 1999 Apr 20;99:1978–1983.
4. Chugh SS, Reinier K, Teodorescu C, et al. Epidemiology of sudden cardiac death: clinical and research implications. *Prog Cardiovasc Dis*. 2008;51:213–228.
5. Byrne R, Constant O, Smyth Y, et al. Multiple source surveillance incidence and aetiology of out-of-hospital sudden cardiac death in a rural population in the West of Ireland. *Eur Heart J*. 2008;29:1418–1423.
6. Chandramohan D, Maude GH, Rodrigues LC, et al. Verbal autopsies for adult deaths: issues in their development and validation. *Int J Epidemiol*. 1994;23:213–222.
7. Sibai AM, Fletcher A, Hills M, et al. Non-communicable disease mortality rates using the verbal autopsy in a cohort of middle aged and older populations in Beirut during wartime, 1983–1993. *J Epidemiol Commun Health*. 2001;55:271–276.
8. Jha P, Gajalakshmi V, Gupta PC, et al. RGI-CGHR Prospective Study Collaborators. Prospective Study of one million deaths in India: rationale, design, and validation results. *PLoS Med*. 2006;3:e18.
9. Mitra B. India's mortality measurement systems. In: Asma S, Jha P, Gupta PC, eds. *Counting the Dead in India in the 21st century*. Atlanta (Georgia): US Centers for Disease Control; 1999:B2–B8.
10. Gajalakshmi V, Peto R. Verbal autopsy of 80, 000 adult deaths in Tamil Nadu, South India. *BMC Public Health*. 2004;4:47.
11. Zheng ZJ, Croft JB, Giles WH, et al. Sudden cardiac death in the United States, 1989 to 1998. *Circulation*. 2001;104:2158–2163.
12. de Vreede-Swagemakers JJ, Gorgels AP, Dubois-Arbouw WI, et al. Out-of-hospital cardiac arrest in the 1990's: a population-based study in the Maastricht area on incidence, characteristics and survival. *J Am Coll Cardiol*. 1997;30:1500–1505.
13. Stecker EC, Vickers C, Waltz J, et al. Population-based analysis of sudden cardiac death with and without left ventricular systolic dysfunction: two-year findings from the Oregon Sudden Unexpected Death Study. *J Am Coll Cardiol*. 2006;47:1161–1166.
14. Nagata M, Ninomiya T, Doi Y, et al. Temporal trends in sudden unexpected death in a general population: the Hisayama study. *Am Heart J*. 2013;165:932–938.
15. Hua W, Zhang LF, Wu YF, et al. Incidence of sudden cardiac death in China: analysis of 4 regional populations. *J Am Coll Cardiol*. 2009;54:1110–1118.
16. Wang H, Yao Q, Zhu S, et al. The autopsy study of 553 cases of sudden cardiac death in Chinese adults. *Heart Vessels*. 2013 Jul 9 [Epub ahead of print].
17. Joshi R, Cardona M, Iyengar S, et al. Chronic diseases now a leading cause of death in rural India–mortality data from the Andhra Pradesh Rural Health Initiative. *Int J Epidemiol*. 2006;35:1522–1529.
18. Madhavan SR, Reddy S, Panuganti PK, et al. Epidemiology of sudden cardiac death in rural South India – insights from the Andhra Pradesh rural health initiative. *Indian Pacing Electrophysiol J*. 2011;11:93–102.
19. Rao BH, Sastry BK, Chugh SS, et al. Contribution of sudden cardiac death to total mortality in India - a population based study. *Int J Cardiol*. 2012;154:163–167.
20. Piccini JP, Zhang M, Pieper K, et al. Predictors of sudden cardiac death change with time after myocardial infarction: results from the VALIANT trial. *Eur Heart J*. 2010;31:211–221.
21. Busk M, Maeng M, Kristensen SD, et al. DANAMI-2 Investigators. Timing, causes, and predictors of death after three years' follow-up in the Danish Multicenter Randomized Study of Fibrinolysis versus Primary Angioplasty in Acute Myocardial Infarction (DANAMI-2) trial. *Am J Cardiol*. 2009;104:210–215.
22. Pouleur AC, Barkoudah E, Uno H, et al. VALIANT Investigators. Pathogenesis of sudden unexpected death in a clinical trial of patients with myocardial infarction and left ventricular dysfunction, heart failure, or both. *Circulation*. 2010;122:597–602.
23. Berger CJ, Murabito JM, Evans JC, et al. Prognosis after first myocardial infarction. Comparison of Q-wave and non-Q-wave myocardial infarction in the Framingham Heart Study. *JAMA*. 1992;268:1545–1551.
24. Rouleau JL, Talajic M, Sussex B, et al. Myocardial infarction patients in the 1990s–their risk factors, stratification and survival in Canada: the Canadian Assessment of Myocardial Infarction (CAMI) Study. *J Am Coll Cardiol*. 1996;27:1119–1127.
25. McGovern PG, Jacobs Jr DR, Shahar E, et al. Trends in acute coronary heart disease mortality, morbidity, and medical care from 1985 through 1997: the Minnesota heart survey. *Circulation*. 2001;104:19–24.
26. Ishikawa K, Kimura A, Taniwa T, et al. Secondary Prevention Group. Modification of treatment strategies over a period of 14 years has markedly reduced cardiac events among post-myocardial infarction patients. *Circ J*. 2002;66:881–885.
27. Mäkikallio TH, Barthel P, Schneider R, et al. Frequency of sudden cardiac death among acute myocardial infarction

survivors with optimized medical and revascularization therapy. *Am J Cardiol.* 2006 Feb 15;97:480–484.
28. Xavier D, Pais P, Devereaux PJ, et al. CREATE Registry Investigators. Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. *Lancet.* 2008;371:1435–1442.
29. Rao BH, Sastry BKS, Korabathina R, et al. Sudden cardiac death after acute ST elevation myocardial infarction: insight from a developing country. *Heart Asia.* 2012;4:83–89.
30. Yusuf S, Islam S, Chow CK, et al. Prospective Urban Rural Epidemiology (PURE) Study Investigators. Use of secondary prevention drugs for cardiovascular disease in the community in high-income, middle-income, and low-income countries (the PURE Study): a prospective epidemiological survey. *Lancet.* 2011;378:1231–1243.
31. Rao BH. Epidemiological data heart rhythm disorders in India – a formidable but surmountable challenge. *Indian Pacing Electrophysiol J.* 2012;12:37–38.
32. Capewell S, Beaglehole R, Seddon M, et al. Explanation for the decline in coronary heart disease mortality rates in Auckland, New Zealand, between 1982 and 1993. *Circulation.* 2000;102:1511–1516.
33. Tungsanga K, Sriboonlue P. Sudden unexplained death syndrome in north-east Thailand. *Int J Epidemiol.* 1993;22:81–87.