

Current Burden of Sudden Cardiac Death: Multiple Source Surveillance Versus Retrospective Death Certificate-Based Review in a Large U.S. Community

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OBJECTIVES	We sought to determine the annual incidence of sudden cardiac death (SCD) in the general population using a prospective approach. To assess the validity of retrospective surveillance, a simultaneous comparison was made with a death certificate-based method of determining SCD incidence.
BACKGROUND	Accurate surveillance and characterization of SCD in the general population is likely to significantly facilitate current and future community-based preventive and therapeutic interventions.
METHODS	We performed a prospective evaluation of SCD among all residents of Multnomah County, Oregon (population 660,486) using multiple sources of surveillance. A comprehensive analysis of circumstances of death, medical records, and available autopsy data was performed. Comparisons were made with a retrospective, death certificate-based determination of SCD incidence using International Classification of Diseases-Version 10 codes and location of death.
RESULTS	Between February 1, 2002, and January 31, 2003, 353 residents suffered SCD (incidence 53 of 100,000; median age 69 years, 57% male) accounting for 5.6% of overall mortality. Of these, 75 cases (21%) were identified using sources other than first responders. Resuscitation was attempted in 237 cases (67%) and successful (survival to hospital discharge) in 28 (8%). The retrospective death certificate-based review yielded 1,007 cases (incidence 153 of 100,000; median age 81 years, 51% male), and the positive predictive value of this methodology was 19%.
CONCLUSIONS	Sudden cardiac death accounts for 5.6% of annual mortality, and prospective evaluation in the general population appears to be feasible. The use of multiple sources of ascertainment and information significantly enhances phenotyping of SCD cases. Retrospective death certificate-based surveillance results in significant overestimation of SCD incidence. (J Am Coll Cardiol 2004;44:1268–75) © 2004 by the American College of Cardiology Foundation

Despite recent advances in resuscitation science, survival from cardiac arrest remains low, and sudden cardiac death (SCD) is a major public health issue. However, the magnitude of SCD in the general population still remains unknown. Estimates of the annual incidence of SCD in the U.S. range from 184,000 to >400,000 (1–4). There may be two reasons for these diverse assessments. First, prospective community-based studies of SCD have not been performed. Existing studies have focused on the incidence of primary cardiac arrest as ascertained from first responder agencies (3,5,6). To reflect occurrence in the general population, multiple sources of case ascertainment should be employed, but such studies are not available. Secondly, death certificate data have been used as a surrogate for national surveillance

of SCD, but the accuracy of this methodology may be limited (1,7,8). The absence of prospective evaluations of SCD involving a direct count in the general population, with evaluation at the time of the event or shortly thereafter, has been identified as a prominent “scientific gap” in our knowledge regarding SCD (1).

Prospective assessments of SCD in the general population are likely to facilitate investigative and preventive approaches to this significant public health problem. Specifically, these approaches will likely enhance the accuracy of phenotyping for this complex condition—an essential prerequisite for the application of new genomic strategies for the advancement of SCD mechanisms (9). Finally, such an approach would also furnish the prospective gold standard against which the validity of death certificate-based surveillance could be tested. We therefore performed a prospective evaluation of annual SCD incidence in a large U.S. community, using multiple sources of case ascertainment. Comparisons were made with death certificate-based determination of SCD, based on the hypothesis that this retrospective technique was likely to overestimate the incidence of SCD in the general population.

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Abbreviations and Acronyms

- ACLS = advanced cardiac life support
- CAD = coronary artery disease
- CI = confidence interval
- ICD-10 = International Classification of Diseases-
Version 10
- OR = odds ratio
- SCD = sudden cardiac death
- VF = ventricular fibrillation
- VT = ventricular tachycardia

METHODS

All aspects of this investigation were approved by the Institutional Review Board, Oregon Health and Science University. **Prospective evaluation. CASE ASCERTAINMENT SOURCES.** The study population included all residents of Multnomah County, Oregon (population: 660,486), irrespective of age. Residents who suffered sudden unexpected death between February 1, 2002, and January 31, 2003, were identified from several sources—the emergency medical response system, the county medical examiner’s office, and 16 area hospitals. The county has a two-tiered advanced cardiac life support (ACLS) emergency medical response system. Advanced cardiac life support staffed fire engine companies provide the first response with backup by ACLS transporting ambulances. Investigators were alerted to cases either by physicians of record from the emergency medical services or by the office of the county medical examiner. Identified cases were screened to identify subjects with presumed cardiac arrest and eventually those that met the criteria for SCD (Fig. 1).

DEFINITION OF SCD. World Health Organization criteria were employed, and SCD was defined as sudden unexpected death either within 1 h of symptom onset (event witnessed), or within 24 h of having been observed alive and symptom free (unwitnessed). Subjects with non-cardiac chronic and terminal illness (e.g., terminal cancer) were excluded on the basis that such deaths were not unexpected. Additionally, all patients with an identifiable non-cardiac etiology of sudden death were excluded. Cases of sudden cardiac arrest associated with trauma, violent death, overdose, drowning, and suicide were also excluded. If they met the criteria, survivors of cardiac arrest were included under SCD cases.

POSTMORTEM EXAMINATION. Detailed information, including results of cardiac pathologic examination and toxicology screen, was obtained in all cases in which an autopsy was conducted. Autopsies were performed at the discretion of the medical examiner or attending physician. Patients with >50% stenosis in one or more coronary arteries were considered to have significant coronary artery disease (CAD). Detailed criteria for cardiac pathologic diagnosis have been published previously (10).

IDENTIFICATION OF SCD CASES. All available medical records were obtained. A comprehensive evaluation was performed for each case of unexpected death, including analysis of the circumstances of death, medical records, and available autopsy data. All collected information was assembled in a relational database. A process of in-house adjudication was employed to determine cases meeting criteria for SCD. Independent assessments were made by three cardiologists, followed by a consensus review. In the event of a disagreement regarding a specific case, the determination was based on the majority opinion.

Emergency Medical Services

Medical Examiner

Hospital or Provider

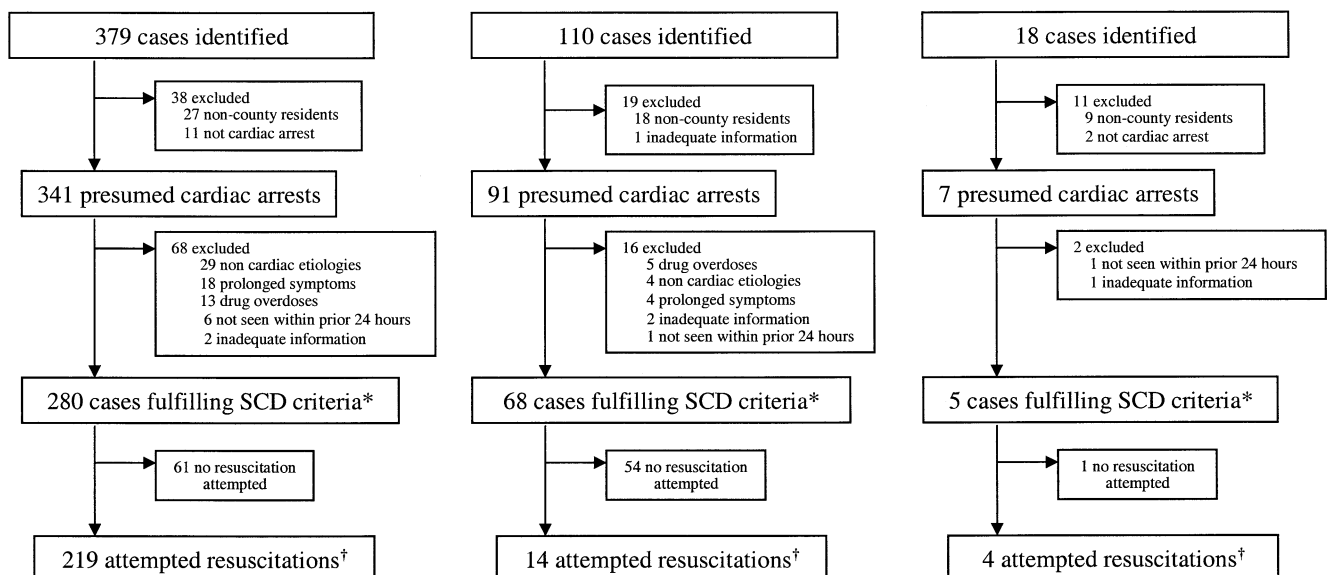


Figure 1. Details of case ascertainment and prospective identification of sudden cardiac death (SCD) cases. *353 total SCD cases in Multnomah County. †237 total attempted resuscitations.

Table 1. Subject Characteristics and Survival Outcome

	Presumed Cardiac Arrest	Prospectively Defined SCD	Death Certificate-Based SCD
Annual incidence/100,000	67*	53*	153*
Total number	439*	353*	1,007*
Female	178 (41%)	151 (43%)†	495 (49%)†
Median age (yrs)	67	69‡	81†
Witnessed	208 (47%)	184 (52%)	N/A
Attempted resuscitation	286 (65%)	237 (67%)	N/A
Return of spontaneous circulation	43 (10%)	39 (11%)	N/A
Survival to hospital discharge	29 (7%)	28 (8%)	N/A

*p < 0.05 for differences between the three groups (chi-square test); †p = 0.05 for prospective versus death certificate SCD (chi-square test for nominal variables, Wilcoxon-Mann-Whitney for medians).
N/A = not applicable; SCD = sudden cardiac death.

Retrospective evaluation using death certificates. The U.S. Centers for Disease Control and Prevention have published an estimate of the annual incidence of SCD in the U.S. based on death certificate data, and this previously described methodology was employed (2). Death certificate data were reviewed at the Oregon State Health Division on a quarterly basis. Subjects met criteria for death certificate-based SCD if they were classified under one or more specific International Classification of Diseases-Version 10 (ICD-10) codes and also died out-of-hospital or in an emergency room. The following ICD-10 codes were used: disease of heart (I00 to I09, I11, I20 to I51); congenital heart disease (Q20 to Q24); and ill-defined cause of death (R95 to R99) (2).

Statistical methods. All calculations were performed using SPSS 11.5 for Windows. Categorized nominal data were compared using the chi-square test. If any cell values were <5, the Fisher exact test was used. Categorized rates were compared using the chi-square test of equality of multinomial proportions. Medians were compared using the Wilcoxon-Mann-Whitney test. The influence of individual variables on survival to hospital discharge was estimated using odds ratios (ORs) obtained from logistic regression models. All variables were first entered individually to obtain unadjusted ORs. Variables with statistically significant coefficients were tested for predictive significance using the forward likelihood ratio method. Adjusted ORs were determined for all variables that were significantly predictive of outcome. Validity of death certificate-based SCD was assessed by determining the sensitivity, specificity, and predictive value of the technique using prospectively determined SCD as the standard. Sensitivity was the proportion of prospectively determined SCDs identified correctly, and specificity was the proportion of non-SCD cases (from overall annual mortality in the county) identified correctly. Positive predictive value was the proportion of death certificate cases that were correctly designated as SCDs.

RESULTS

Annual incidence of SCD. PROSPECTIVE EVALUATION. Between February 1, 2002, and January 31, 2003, 439 cases of presumed cardiac arrest were identified (incidence 67 of

100,000; Table 1). Of these, 353 cases met the criteria for SCD (incidence 53 of 100,000; Table 1). Details of case ascertainment as well as the process of determining cases that met the criteria for SCD are provided in Figure 1. Overall, 78% of all SCD cases were identified through the emergency medical response system, 20% through the county medical examiner’s office, and 2% through local hospitals. Death certificate records for Multnomah County residents over the same time period showed that prospectively identified SCD accounted for 5.6% of all deaths among county residents (total deaths in Multnomah County, n = 6,255).

RETROSPECTIVE SURVEILLANCE. During the same time period, the retrospective death certificate-based review yielded 1,007 cases (incidence 153 of 100,000) (Table 1). Subjects identified as having SCD by retrospective death certificate review were older and more often female than subjects identified by prospective, community-based methods (Table 1). For the purpose of validating the death certificate method, survivors were not included in the comparison. Of the 325 SCD non-survivors identified by prospective methods, 193 were correctly identified by retrospective review, resulting in a sensitivity of 59%. The remainder (41%), were missed by the death certificate review for several reasons, specifically inpatient location of death (25%), diabetes as cause of death (15%), and miscellaneous other non-cardiac causes of death (60%). A total of 6,255 residents of the county died during the same time period. The death certificate method identified 5,116 non-SCDs correctly, resulting in a specificity of 86%. Of the cases designated as SCD by the death certificate method, only 193 were identified correctly, resulting in a positive predictive value of 19%.

Detailed description of prospectively defined SCD cases. AGE AND GENDER. In residents age <35 years, the highest incidence was observed in the 0- to 5-year age group (Fig. 2). Over 35 years of age, the highest incidence was observed in the 75- to 84-year age group. Approximately 25% of all SCD cases occurred at age <65 years. The gender- and age-based composition of prospectively deter-

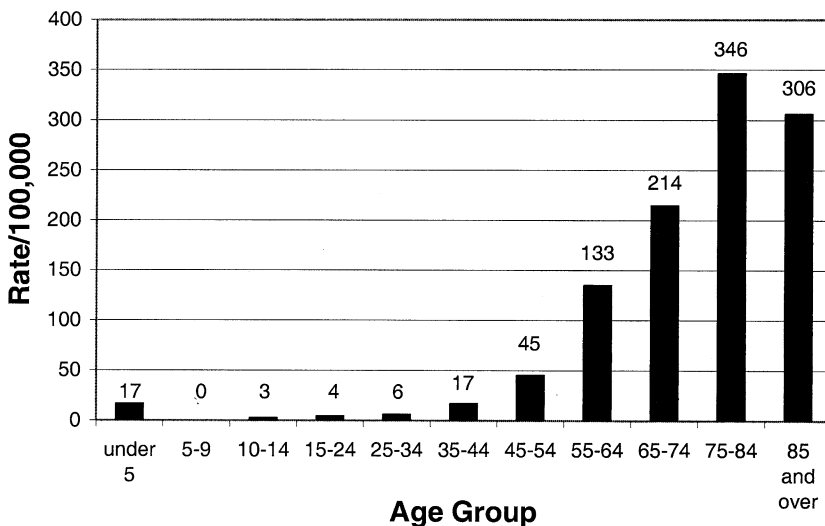


Figure 2. Age-based annual incidence of sudden cardiac death among residents of Multnomah County, Oregon (population 660,486).

mined SCD cases is shown in **Figure 3**. Overall, 43% of SCD cases were female.

ETIOLOGY OF SCD. Previous medical records were obtained in 53% of cases, and a further 4% were confirmed as not having seen a physician before death. Overall, 50% of cases over age 35 years had CAD that had been identified (**Table 2**). Nine patients had aortic stenosis with varying degrees of severity (severe, n = 1; moderate, n = 3; mild to moderate, n = 3; mild n = 2). Four patients had congenital heart disease. The two cases in the <35 years age group (non-autopsy) were Ebstein's anomaly with Wolff-Parkinson-White syndrome and congenital aortic valve disease with two prosthetic valve replacements. Autopsies were conducted in 12% of all cases (n = 41) (**Table 3**). Associated CAD was observed exclusively in subjects age 35 years or older and was observed in 76% of this age group. Significant stenosis of the coronary arteries was observed in the majority of cases, but plaque rupture with thrombus was uncommon

and was identified in only one subject with CAD. In the >35 years age group, one patient had severe pulmonic stenosis (previously repaired ventricular septal defect) and a second had a bicuspid aortic valve.

LOCATION OF SCD. Eighty-two percent of arrests took place at home, of which 46% were witnessed. The location did not vary significantly when stratified by age or gender (range, 79% to 86% at home). Thirty-four arrests (9.6%, 21 witnessed) took place in care facilities (nursing care, rehabilitation, adult foster care, assisted living, and the like) or doctors' offices. Eight arrests (2.2%), all witnessed, took place in non-residential "community units" (schools, sports centers, malls, churches) (11). Overall, 52% of SCDs were witnessed.

SURVIVAL OUTCOME. Among SCD, resuscitation was attempted in 237 cases (**Table 1**). A multiple regression analysis showed that only the ratio of ventricular fibrillation (VF) to ventricular tachycardia (VT) and arrest location

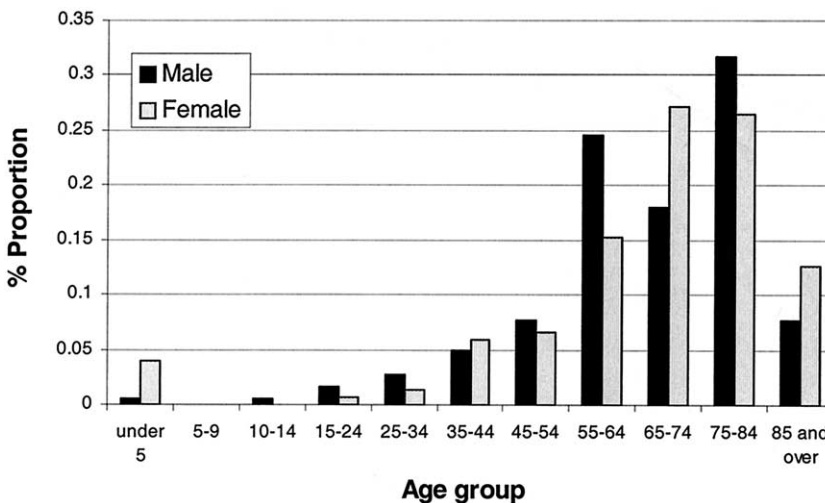


Figure 3. Gender- and age-based composition of prospectively determined sudden cardiac death cohort.

Table 2. Conditions Associated With Sudden Cardiac Death*

Associated Conditions	Age <35 Yrs	Age ≥35 Yrs	All Ages
Number of cases	19	169	188
Coronary artery disease	0†	84 (50%)†	84 (45%)
CHF/cardiomyopathy	0†	46 (27%)†	46 (25%)
Aortic stenosis	0	9 (5.3%)	9 (4.8%)
Congenital heart disease	2 (10%)	2 (1.1%)	4 (2.1%)
Seizure disorder	1 (5.2%)	12 (7.1%)	13 (6.9%)
No significant associated conditions	14 (74%)	55 (32%)	69 (37%)

*Analysis is limited to subjects with availability of previous clinical records/autopsy results (n = 188). †Age groups <35 yrs versus ≥35 yrs, p < 0.05 (Fisher exact test).

CHF = congestive heart failure.

were significant predictors of survival. If the presenting arrhythmia was VF/VT, the adjusted OR for survival was 10.2 (95% confidence interval [CI] 2.9 to 36). If the arrest took place outside the home, the adjusted OR was 3.1 (95% CI 1.3 to 76). The frequency of each variable among survivors and non-survivors is listed in Table 4. The overall survival rate when patients presented with VF or pulseless VT was 24%, compared with 2% when patients presented with pulseless electrical activity or asystole (p < 0.001, Fisher exact test) (Fig. 4). For SCD cases who presented with VF/VT and had a witnessed cardiac arrest, survival to hospital discharge was 29%. Females had a lower rate of VF compared with males (35.3 vs. 50%, p = 0.019, Fisher exact test). Survival in VF cases was not significantly different between genders (females 25.7% vs. males 23.7%, p = 0.51, chi-square test), but survival in pulseless electrical activity/asystole cases occurred only among women (4.7%). Overall survival to hospital discharge among the subgroup of SCD subjects who underwent resuscitation was identical in men and women (11.8%).

CHRONOBIOLOGICAL ASSOCIATIONS. A strong diurnal trend for the occurrence of SCD was observed. The 4-h period with the greatest event rate was between 8 AM and noon, with 27% of cases, whereas the lowest event rate was between midnight and 4 AM, with 8% of cases (p < 0.001, chi-square test). Significant daily or seasonal variations in occurrence of SCD were not observed.

DISCUSSION

Summary of main findings. In this prospective evaluation of a large U.S. community, the annual incidence of SCD was 53 per 100,000 residents and accounted for 5.6% of overall deaths. Eighty-two percent of SCDs took place at

Table 3. Cardiac Abnormalities Identified in the Autopsy Subgroup (n = 41)

	Age <35 Yrs	Age ≥35 Yrs	All Ages
Number of subjects	12	29	41
Coronary artery disease	0*	22 (76%)*	22 (54%)
Cardiac rupture	0	1 (4%)	1 (3%)
Myocarditis	0	1 (3%)	1 (2%)
Congenital heart disease	0	2 (7%)	2 (4%)
Aortic dissection	0	1 (3%)	1 (2%)

*Age groups <35 yrs versus ≥35 yrs, p < 0.05 (Fisher exact test).

home, and 43% of cases were female. Among patients over age 35 years who underwent autopsy, significant CAD was observed in 76%. Overall survival to hospital discharge was 8%. In a multivariate model, survival was dependent on VT/VF being the presenting arrhythmia (OR 10.2, CI 2.9 to 36.0) and location of SCD occurrence outside the home (OR 3.1, CI 1.3 to 7.6). The retrospective, death certificate-based method of surveillance resulted in an almost threefold overestimation of annual SCD incidence.

Although there is a lack of studies of SCD that use multiple sources, there are several studies that have prospectively examined the community incidence of primary cardiac arrest using data collected by first responders. The incidence of primary cardiac arrest and SCD in the present study is lower than some published studies, but it is also higher than others. From several studies, the annual incidence of treated primary cardiac arrest has ranged between 41 and 89 of 100,000 (3,12-15). If we use presumed cardiac arrest cases to calculate the annual incidence in the present study (n = 439), this figure is 67 of 100,000 residents (Table 1). A prospective study in the Maastricht area of the Netherlands reported an annual incidence of sudden out-of-hospital cardiac arrests of 90 to 100 of 100,000 residents age 20 to 75 years (16). On the other hand, a retrospective study of SCD among residents of southern Okinawa, Japan that employed multiple sources reported a

Table 4. Comparison Between Cardiac Arrest Survivors and Non-Survivors Among SCD Cases That Underwent Resuscitation (n = 237)

	Survivors	Non-Survivors
Total	28	209
Mean age (yrs)	65	67
Median age (yrs)	68	70
Males	16 (57%)	118 (56%)
Witnessed arrest	28 (100%)*	141 (68%)*
Location of arrest		
Home	13 (46%)*	170 (81%)*
Work	2 (7%)	4 (2%)
Emergency department	3 (11%)*	2 (1%)*
Terminal arrhythmia reported	27 (96%)	198 (95%)
VF/VT	24 (86%)*	74 (34%)*
PEA/asystole	3 (11%)*	124 (63%)*

*p < 0.05 for survivors versus non-survivors (chi-square test for location-home, Fisher exact test for all others).

PEA = pulseless electrical activity; SCD = sudden cardiac death; VF = ventricular fibrillation; VT = ventricular tachycardia.

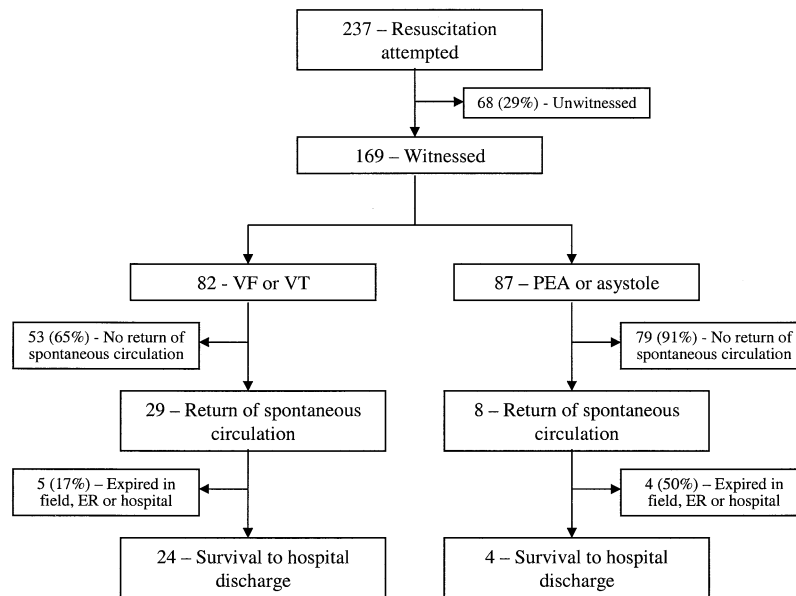


Figure 4. Outcome of attempted resuscitations. A modified Utstein-style template has been used for witnessed arrests. ER = emergency room; PEA = pulseless electrical activity; VF = ventricular fibrillation; VT = ventricular tachycardia.

crude annual incidence rate of 37 per 100,000 residents—lower than the rate observed in the present study (17).

Because the present study examined the incidence of SCD (not primary cardiac arrest) among all age groups, the overall objective as well as the definition employed were different from previous studies. Also, multiple sources of case ascertainment were employed. In addition to first responders, the medical examiner and area hospitals and physicians reported cases. In addition to data from first responders, access to hospital records, circumstances of death, and autopsy information likely enabled a broader and more efficient exclusion of non-cardiac etiologies of sudden death. For instance, on the grounds that such deaths are not unexpected, patients who died after a non-cardiac terminal illness such as cancer were excluded. As a result, although the incidence is lower, the results are likely to be a more accurate assessment of the occurrence of sudden death directly related to a cardiac etiology in the general population. As shown in Figure 1, 99 of 379 cases (26%) initially ascertained via the emergency medical services eventually did not meet the criteria for SCD. If the present study had limited case ascertainment to first responders, only 280 (80%) of total SCD cases would have been identified, resulting in a significant underestimation. However, it is possible that we were unable to track some cases of SCD, which may have contributed to a likely modest underestimation of incidence. The first category may be patients with unwitnessed SCD who were discovered more than 24 h after their death. Also, county residents who suffered SCD while traveling out of state may also not have been ascertained. The major source of case ascertainment were the first responders (single company with 33 ambulances and 150 paramedics), and we tracked every sudden cardiac arrest on a daily basis. The

second major source was the county medical examiner. In the state of Oregon, all deaths that do not occur in a hospital have to, by law, be reported to the medical examiner. We reviewed every death reported to the medical examiner on a daily basis to identify cases of SCD among these. Because all cases of SCD have to be unexpected, as reported universally in previous studies, hospitals are an unlikely source of SCDs—hence the small number from area hospitals. Hence it is very likely that we captured the vast majority of SCDs that occurred in Multnomah County.

The gender distribution of SCD in the general population was significantly different from that previously reported among treated cases of primary cardiac arrest. In the present study, the gender difference in SCD occurrence was low (57% male vs. 43% female), whereas most studies of primary cardiac arrest have reported a threefold higher incidence in men compared with women (18). This probably reflects the differences in the way cases were ascertained and defined in the two types of populations. In the present study, among patients with primary cardiac arrest who underwent resuscitation, women had a lower prevalence of VF and a higher rate of pulseless electrical activity as the presenting arrhythmia. This trend is similar to previously reported findings (18). There were no differences between genders with respect to the overall survival rate.

As reported by others, there was a strong association between the nature of the presenting arrhythmia and survival among the subjects who underwent resuscitation. Our rates of survival from VF and pulseless electrical activity/asystole (24% and 2%, respectively) show trends similar to the Seattle experience reported recently by Cobb *et al.* (32% and 3.5%) (3). In the present study, when the onset of SCD was witnessed and the presenting arrhythmia was VF/VT,

survival to hospital discharge was 29%. The overwhelming majority (82%) of SCDs occurred at home. These findings are identical to the observations made in the Maastricht study that evaluated primary cardiac arrest (16). The survival rate was better if the SCD occurred outside the home. This is likely related to a higher chance of the out-of-home SCD being a witnessed event (70% out-of-home SCDs were witnessed, compared with 46% of in-home SCDs, $p < 0.05$, chi-square test). As observed in the present study for SCD, previous investigations have found similar evidence of a circadian rhythm for occurrence of primary cardiac arrest (19,20). Among 1,019 primary cardiac arrests, Levine et al. observed that the frequency of cardiac arrests increased significantly from 6 AM until noon (20).

Because of the prospective nature of this investigation, community medical records could be obtained in a significant number of subjects (53%). Earlier autopsy series and studies of survivors have reported that approximately 50% of cases may present with SCD as the first and only manifestation of heart disease. Thus, it is likely that this subgroup constituted a significant number of cases for which medical records were not obtained. As expected, CAD dominated the conditions associated with SCD, and similar to previous observations, 76% of autopsied cases in the over 35 years age group had significant CAD (21,22). Heart failure, aortic stenosis, and congenital heart disease have also been previously associated with an increased risk of SCD. Among non-cardiac conditions, the association with seizure disorder is a recurring finding (10,23,24), but mechanisms and the pathophysiologic links between the two conditions remain unclear.

In the present study, death certificate-based retrospective surveillance resulted in a significant overestimation of SCD incidence. The annual incidence of 153 of 100,000 residents using this retrospective method is very similar to the rate observed nationally for the U.S. (162 of 100,000) using the same methodology (2). Although previous studies have pointed out the potential limitations of using death certificate data to determine SCD cases, comparisons with prospectively conducted incidence evaluation of SCD have not been available. Iribarren et al. (7) examined the validity of death certificate diagnosis of out-of-hospital SCD in a retrospective six-year mortality study. Compared with retrospectively obtained physician diagnosis of SCD, sensitivity was 87% and specificity 66%. Only 27% of the cases labeled SCD by death certificate agreed with the physician diagnosis. Every et al. (8) performed a retrospective comparison of death certificate-based SCD in high-risk patients with a paramedic-based classification system for cardiac arrest. They reported a sensitivity ranging from 78% to 85% and specificity 25% to 58% (8). In the present study, sensitivity and specificity were 59% and 86%, respectively. However, given the significant overestimation, the positive predictive value of death certificate-based determination of SCD was only 19%, that is, only 19% of death certificate-designated SCDs agreed with the prospectively defined

SCDs. Given the findings of the present study, death certificate-based surveillance, as presently employed, is unlikely to be a useful surveillance tool for SCD. For SCD, definitions and criteria should be employed prospectively among cases that occur in the general population, and based on our findings, such an evaluation should be feasible. Using this technique in a sample of representative U.S. communities could provide a more accurate assessment of the national incidence and the prevalence of SCD.

Conclusions. The SCD burden contributed to 5.6% of annual mortality in this large U.S. community, with an unexpectedly narrow difference between genders. Likelihood of successful resuscitation continues to be low but is strongly associated with VF/VT being the presenting arrhythmia. Retrospective, death certificate-based surveillance results in a significant overestimation. Prospective evaluation of SCD incidence using multiple sources appears to be feasible.

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