Out-of-Hospital Cardiac Deaths in Adolescents and Young Adults in the United States, 1989 to 1998

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Background: Out-of-hospital cardiac death (OHCD), often occurring suddenly and unexpectedly, is a major public health problem. The purpose of this study is to assess the epidemiologic pattern and secular trend of OHCD in adolescents and young adults aged 15–34 years in the United States.

Methods: United States national vital statistics mortality data from 1989 to 1998 were analyzed. OHCD was defined as death that occurred either at a pre-transport location, or in the emergency room, or was classified as "dead on arrival" in the emergency room, with an underlying cause of death as a cardiac disease (ICD-9 codes 390–398, 402, 404–429, 745, or 746).

Results: Of the 48,573 cardiac deaths occurring during 1989 to 1998, 31,827 (66%) were out of hospital. Of all OHCD victims from 1989 to 1998, 70% were men, and 76% were aged 25–34 years. The leading underlying causes of OHCD were coronary heart disease (29%), cardiomyopathy (18%), and arrhythmias (14%). The OHCD rates (per million population) were twice as high in men as in women (57.0 vs. 26.7 in 1997 and 1998), in African Americans as in whites (84.9 vs. 35.9 in 1997 and 1998), and increased with age. From 1989–1990 to 1997–1998, the age-adjusted OHCD death rates increased in both men (11%) and women (33%), and in African Americans (11%) and whites (19%).

Conclusions: Although cardiac death remains rare in U.S. adolescents and young adults, the increased trend in OHCD rates in this age group warrants further investigation of etiology and prevention strategies.

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Introduction

Out-of-hospital death from cardiac disease, often occurring suddenly and unexpectedly, is a major challenge in clinical cardiology and emergency medicine, and it remains a significant public health problem in the United States.[1–4] Although considerable attention has been paid to recent trends in out-of-hospital "sudden" cardiac death among middle-aged and older adults,[4] few studies beyond anecdotal evidence or case reports are available in the literature on this event in young people.[5–20] Epidemiologic investigation of cardiac disease in young people is of particular clinical and public health importance for several reasons: (1) premature cardiac death in a young person is catastrophic; (2) subsets of young patients who are at high risk for cardiac death could be identifiable; and (3) recent advances in evaluation and therapy have significantly improved the prognosis for patients at high risk of cardiac death.[5–9]

Clinically, sudden cardiac death (SCD) is the sudden, unexpected natural death from a cardiac cause a short time (often within one hour) after the onset of symptoms in a person without any prior condition that would appear fatal.[2,3] Unfortunately, such a definition is difficult to apply in public health surveillance because information on time of onset is often not available from death certificate datasets.[4,21] The purpose of this current report is to characterize the epidemiologic features of out-of-hospital cardiac death (OHCD), the majority of which could be sudden cardiac death, in U.S. adolescents and young adults aged 15–34 years, and to describe the secular trend of OHCD in this age group from 1989 to 1998.

Methods

These analyses used the U.S. vital statistics mortality data compiled by the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention. Death certificates are processed in state vital statistics offices, and then sent to the NCHS for entry into a detailed national

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Table 1. Distribution (%) of place of death among all cardiac disease victims aged 15–34 years, by selected characteristics during 1989 to 1998 and trend from 1989 to 1998

		Place of death (%)				
		Out of hospital				
	Total cardiac deaths,[a] *n*	Pre-transport	"Dead on arrival"	Emergency room	In hospital	Missing
Gender						
Male	31,659	26.0	9.6	34.8	27.4	2.3
Female	16,914	19.7	7.1	29.7	41.3	2.2
Age groups (years)						
15–19	4,915	15.3	8.8	37.5	36.3	2.1
20–24	7,408	20.6	8.1	33.3	35.9	2.2
25–29	12,230	24.1	8.9	31.9	33.0	2.1
30–34	24,020	26.4	8.8	32.6	29.8	2.4
Race/ethnicity						
White	32,941	25.5	8.3	33.4	30.7	2.1
African American	14,269	20.0	9.9	32.3	35.4	2.4
American Indian or Alaska Native	396	22.2	7.3	27.3	33.3	9.9
Asian or Pacific Islander	967	21.6	6.0	34.4	36.4	1.6
Year of death						
1989	4,881	20.9	11.4	28.7	34.3	4.7
1990	4,694	22.4	10.6	30.1	34.9	2.0
1991	4,875	21.4	10.1	32.0	33.9	2.6
1992	4,852	22.2	9.2	33.7	32.8	2.1
1993	5,024	23.5	8.7	33.6	31.9	2.3
1994	4,983	24.1	8.9	33.6	31.1	2.3
1995	5,000	24.7	8.0	33.5	31.4	2.2
1996	4,718	25.2	7.3	35.8	29.5	2.2
1997	4,838	27.2	6.6	35.0	30.3	0.9
1998	4,708	26.3	6.3	34.4	32.2	0.8

[a]Cardiac disease defined as ICD-9 codes of 390–398, 402, 404–429, or 745–746.

mortality database file.[22] Causes of death on the death certificate are reported by physicians in clinical practice, coroners, or medical examiners. Demographic data such as race/ethnicity, gender, and age are reported by funeral directors, usually from their own observation or information provided by family members. We defined a cardiac disease death as one for which the underlying cause was classified by the International Classification of Diseases, Ninth Revision (ICD-9) as codes 390–398, 402, 404–429, 745, or 746. The OHCD was defined as a cardiac disease death that was reported as occurring in a pre-transport location such as home, or in the emergency room, or was classified as "dead on arrival" in the emergency room.[4]

All analyses were limited to deaths among U.S. residents aged 15–34 years from 1989 to 1998 because in this 10-year period there was consistency in the coding of place of death on death certificates and the use of ICD-9 classifications. We assessed the proportions of cardiac deaths by location of death for groups defined by gender; race (white, African-American, American Indian/Alaska Native, and Asian/Pacific Islander); age group (15–19, 20–24, 25–29, and 30–34 years); and year. We also assessed differences in the distributions of underlying cause for OHCDs for groups defined by age group (15–24 and 25–34 years), gender, and race. The OHCD rates were calculated for groups defined by age group, gender, and race (white, African American). We were not able to calculate death rates for American Indians/Alaska Natives and Asian/Pacific Islanders because of the small numbers of deaths. Because of the large amount of missing data in earlier years and small numbers, we did not report results for persons of Hispanic ethnicity. Denominators were obtained from the U.S. Bureau of the Census mid-year estimates of the resident population for each group.[23] Age-adjusted mortality rates were standardized by the direct method to the 2000 projected U.S. population.[24] Trends in OHCD rates were smoothed using a 2-year moving average. Relative change in OHCD rate, from 1989–1990 to 1997–1998 was calculated as the average of the death rates in 1997 and 1998 minus the average of the death rates in 1989 and 1990, divided by the average of the death rates in 1989 and 1990, then multiplied by 100.

Results

Of the 48,573 cardiac disease deaths among U.S. adolescents and young adults aged 15–34 years during 1989–1998, 31,827 (65.5%) occurred out of hospital. The proportion of OHCDs among all cardiac deaths was greater among men (70.4%) than women (56.5%). The OHCDs accounted for 61.6% of all cardiac deaths for those aged 15–19 years, 62.0% for 20–24 years, 64.9% for 25–29, and 67.8% for 30–34. During this 10-year period, the proportion of cardiac deaths that occurred in a pre-transport location increased with age; conversely, the proportion that occurred in the emergency room or in the hospital decreased with age (Table 1). The OHCDs accounted for 67.2% of all

Table 2. Distribution (%) of underlying cause among out-of-hospital cardiac death victims, by age and gender, United States, 1989–1998

	15–24 Years		25–34 Years		
Type of cardiac disease (ICD-9 codes)	**Men (*n*=5203)**	**Women (*n*=2414)**	**Men (*n*=17,073)**	**Women (*n*=7137)**	**Total (N=31,827)**
Coronary heart disease (410–414)	12.1	9.5	37.6	26.0	28.7
Cardiomyopathy (425)	23.7	14.6	17.8	14.0	17.7
Conduction disorder and dysrhythmias (426–427)	19.9	19.6	10.8	13.9	13.6
Congenital heart disease (745–746)	16.9	16.9	4.6	6.5	8.0
Carditis and non-rheumatic valvular heart disease (420–424, 429.0)	9.7	10.9	5.5	8.4	7.2
Pulmonary heart disease (415–417)	4.3	14.9	3.9	10.7	6.3
Hypertensive heart disease (402, 404)	2.6	1.7	6.2	6.7	5.4
Heart failure (428)	1.5	2.7	1.5	2.4	1.8
Rheumatic heart disease (390–398)	1.7	4.8	1.4	4.7	2.5
Heart disease, ill-defined (429.1–429.9)	7.7	4.5	10.7	6.8	8.9
Total	100.0	100.0	100.0	100.0	100.0

cardiac deaths in the young (aged 15–34 years) white population; 62.2% among African Americans; 56.8% among American Indians/Alaska Natives, and 62.0% among Asian/Pacific Islanders. Proportions of missing information on place of death ranged from 1.6% (Asians or Pacific Islanders) to 9.9% (American Indians or Alaska Natives). From 1989 to 1998, the overall proportion of OHCDs in young adults increased from 61.0% to 66.9%: the proportion of cardiac deaths that occurred in a pre-transport location increased from 20.9% to 26.3% and the proportion of emergency room OHCDs increased from 28.7% to 34.4%, while the proportion of "dead on arrival" decreased from 11.4% to 6.3% (Table 1).

Of the 31,827 OHCD cases among young people during 1989–1998, 70% were men and 76% were aged 25–34 years. The leading underlying causes of OHCDs were coronary heart disease (CHD, 28.7%), cardiomyopathy (17.7%), and conduction disorders or dysrhythmias (13.6%) (Table 2). The distribution of underlying causes for OHCDs varied by age, gender, and race. In general, cardiomyopathy, conduction disorders or dysrhythmias, and congenital heart disease were more common in the younger group (aged 15–24); CHD was more frequent in the older group (aged 25–34). In each age subgroup, men had higher proportions of CHD, cardiomyopathy, and ill-defined heart disease, but lower proportions of pulmonary heart disease and rheumatic heart disease (Table 2). African Americans had notable higher proportions of cardiomyopathy and hypertensive heart disease, but lower proportions of CHD and congenital heart disease (data not shown).

Age-specific OHCD rates increased with age in 1997 and 1998 (Table 3). Among adults aged 30–34 years, the rates were 4.6 times in men and 4.0 times in women as high as among those aged 15–19 years. Within each age group, the OHCD rate was higher among men than women. The male-to-female ratio for age-specific OHCD rate was 2.0 at 15–19 years, 1.8 at 20–24 years, 2.1 at 25–29, and 2.3 at 30–34. The overall age-adjusted OHCD rate was twice as high in men as in women (57.0 vs. 26.7 per million population) in 1997 and 1998. African Americans had higher age-adjusted rates than whites, with a black-to-white mortality ratio of 2.2 in men and 2.5 in women in 1997 and 1998. Both age-specific and age-adjusted rates in 1997 and 1998 were higher than those in 1989 and 1990. The magnitude of increase in OHCD rates was consistently higher in women than in men (Table 3). The overall increase in age-adjusted SCD rates was 11% in men, 33% in women, 11% in African Americans, and 19% in whites. From 1989 and 1990 to 1997 and 1998, age-adjusted OHCD rates increased among both whites and African Americans in analyses by gender (Figure 1).

Discussion

This is the first national surveillance report on trends in OHCD in U.S. adolescents and young adults aged 15–34 years. Although cardiac death remains rare in this age group,[25] the age-adjusted rates for OHCD increased in both whites and African Americans and among both men and women from 1989 to 1998, with women experiencing larger relative increases in rates. These trends need to be closely monitored, especially as total cardiovascular disease (CVD) mortality has declined dramatically in the general U.S. population over the last three decades.[26]

We found no evidence that the increases were due to any inconsistency in reporting and coding of "place of death" or the "underlying cause of death" on death certificates. In addition, there was no increase in overall mortality from cardiac diseases in this age group during the study period. Thus, several other issues should be considered when attempting to explain the trends reported: (1) Did the incidence of underlying cardiac

Table 3. Numbers of cases[a] and rates[b] (per million population) for out-of-hospital cardiac death and relative change[c] since 1989 and 1990 among U.S. residents aged 15 to 34 years, by selected characteristics, United States, 1997 and 1998

	Men			Women		
		Death rate			Death rate	
Population characteristics	**Number of deaths[a]**	**Per million[b]**	**Change[c]**	**Number of deaths[a]**	**Per million[b]**	**Change[c]**
Age-specific rate						
15–19 years	236	23.8	+13.3%	112	12.0	+34.8%
20–24 years	323	36.0	+23.3%	170	19.7	+37.8%
25–29 years	543	58.0	+16.7%	256	27.3	+31.3%
30–34 years	1114	109.4	+5.5%	487	47.4	+30.6%
Age-adjusted rate[d]						
Total (15–34 years)	2216	57.0	+11.3%	1025	26.7	+32.8%
White	1561	49.3	+12.0%	685	22.4	+39.1%
African American	578	110.9	+2.8%	317	56.2	+16.8%
American Indian/Alaska Native	23	—	—	10	—	—
Asian/Pacific Islander	54	—	—	13	—	—

[a]Average of the annual cases in 1997 and 1998.
[b]Average of death rates in 1997 and 1998.
[c]Relative change (%) since 1989–1990 is calculated as the average of the rates in 1997 and 1998 minus the average of the rate in 1989 and 1990, divided by the average of the rates in 1989 and 1990, and multiplied times 100.
[d]Age-standardized to the 2000 projected U.S. population.

diseases increase among young adults? (2) Did the prevalence of CVD risk factors and of factors that trigger sudden cardiac arrest increase? and (3) Has either the utilization or practice of emergency medical care services changed over time.

Among older OHCD victims (≥35 years) during the study period, CHD accounted for over 70% of the underlying causes.[4] The current study, in contrast, suggests a more diverse etiology of cardiac deaths in young people. An OHCD is most commonly associated with cardiomyopathy and dysrhythmias among victims aged 15–24 years, and with CHD among those dying at aged 25–34 years. The majority of cardiomyopathies or dysrhythmias in the young are likely to be familial and related to genetics.[5–8,27] National surveillance data suggest a decline between 1979 and 1997 in deaths among persons with congenital heart defects,[28] but there is no available surveillance data to assess whether the prevalence and incidence of cardiomyopathy, dysrhythmia, congenital heart defects, and other attributable conditions have increased in the young U.S. population during this time period.

Our in-depth analyses of trend in death rates from the specific underlying causes of OHCD in young persons indicate that the rates (per million population) increased between 1989–1990 and 1997–1998 for cardiomyopathy (3.6 to 4.8 for those aged 15–24 years; and 8.0 to 10.8 for those aged 25–34); dysrhythmia (3.5 to 4.4 for those aged 15–24; 6.5 to 7.1 for those aged 25–34); pulmonary heart disease (2.5 to 3.9 for those aged 24–35 years); and hypertensive heart disease (3.0 to 4.6 for those aged 25–34 years). Death rates did not change between 1989–1990 and 1997–1998 for CHD (2.3 for those aged 15–24 years; 19.6 for 25–34) or congenital heart disease (3.6 for those aged 15–24 years and 3.0 for 25–34).

Overall, ischemic coronary heart disease accounted for 29% of SCDs in the 15 to 34 age group. Increasing evidence supports the hypothesis that atherosclerosis begins in early childhood as deposits of fatty streaks in the intima of large muscular arteries.[29] For those in the 15 to 34 age group, fatty streaks and clinically significant raised lesions increase rapidly in prevalence and extent.[29] The degree of atherosclerosis on vulnerable sites of arteries is significantly associated with the common CVD risk factors in adolescents and young adults.[30,31] National surveillance data have shown upward trends in the prevalence of CVD risk factors, such as cigarette smoking, obesity, and diabetes, among

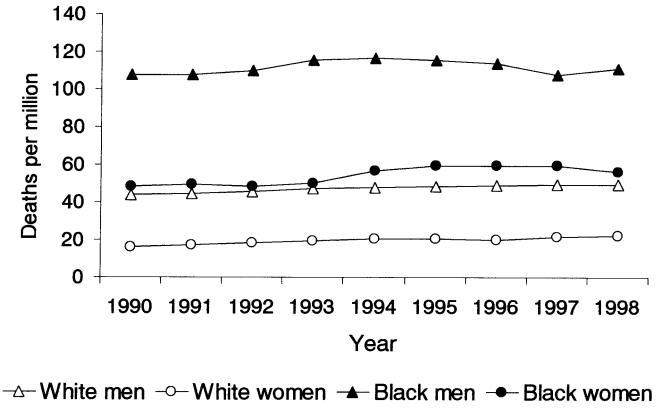

Figure 1. Age-adjusted rates for out-of-hospital cardiac death (per million population) in U.S. residents aged 15–34 years, by race and gender, United States, 1989–1998. Rates were standardized to 2000 U.S. population and smoothed based on the 2-year moving average.

young people during this decade.[32,33] Such increase in the prevalence of CVD risk factors may contribute to the increasing trend in OHCD, as these factors could act as either promoters of the formation of atherosclerosis or as potential precipitators or triggers of the onset of fatal arrhythmias among those with underlying conditions such as CHD, cardiomyopathies, or dysrhythmias. Additional precipitating factors may include physical exertion,[34] anorexia,[35] illicit drug use,[36] and antipsychotic drug use,[37] but it is unlikely that these factors would contribute greatly to the observed trends in this study.

The declines in the proportions of cardiac deaths that were classified as dead on arrival and the increases in the proportion of cardiac death that occurred in pre-transport locations may reflect changes in emergency medical system practices. For example, in many communities, the current practice may be to transport persons declared dead on the site directly to the medical examiner's office for autopsy, rather than to a hospital emergency room. However, the proportion of overall OHCDs would not be affected.

The observation of a larger relative increase in the SCD rate among young women during the 10-year period is a surprising finding that warrants further investigation. The International Long QT Syndrome Registry indicates that congenital long QT syndrome (LQTS) occurs predominantly in women (over 70% of all LQTS cases); female patients with the LQTS have a higher risk of cardiac events after the age of 15 years than their male counterparts.[38] Unfortunately, information on the LQTS is not available on death certificate or hospital discharge charts, and it is thus difficult to determine whether the incidence of this syndrome or its death rate has increased over time. Women may also have a higher predisposition for pro-arrhythmia[39,40] and greater vulnerability to bradycardia-related torsade de pointes.[41] Further investigation is thus needed to examine trends among women in the use of potential cardiac repolarization-prolonging agents, including antipsychotics and recreational drugs.

Surveillance reports utilizing death certificate data have several limitations. First, the accuracy of the underlying cause of death depends on the certifier of each death and the state and national nosologists who determine the ICD-9 codes and the underlying cause. The cause-of-death information on the death certificate is not always validated by medical record or autopsy verification. Thus, misclassification of cases may occur; however, the direction of misclassification that may result in either under-reporting or over-reporting the incidence cannot be determined. In addition, the time of onset of disease symptoms and time of death are not available for analyses. Studies involving retrospective physician review have reported, however, that the validity of the underlying cause of death on the death certificate for both out-of-hospital CHD deaths and sudden cardiac death is reasonably high.[42–45]

The increased trend in mortality from OHCD in U.S. adolescents and young adults indicates an urgent need for public health initiatives to promote heart-healthy lifestyle choices in childhood and to support heart-healthy policies and environments for the community. Young children should be taught about the necessity for avoiding tobacco, alcohol, and drugs, and the importance of weight management, regular physical activity, and a diet low in saturated fats and cholesterol but rich in fruits and vegetables. Additional public health initiatives are needed to improve early awareness and recognition of a family history of premature sudden death, coronary heart disease, cardiomyopathies, and dysrhythmias, as well as prodromal symptoms and signs, such as chest pain, syncope, or an abnormal electrocardiogram. Such educational and media efforts should specifically target primary care physicians, parents, teachers, and younger persons, who may dismiss heart attack or cardiac arrest as a problem of the elderly. National efforts are needed to increase the proportion of the general public, including young adults, who are trained to recognize symptoms of heart attack and cardiac arrest and are willing to participate in the "chain of survival," which includes dialing 9-1-1, attempting cardiac resuscitation, and using automated external defibrillators[46] until emergency personnel arrive.

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References

1. Lown B. Sudden cardiac death: the major challenge confronting contemporary cardiology. Am J Cardiol 1979;43:313–28.
2. Myerburg RJ. Sudden cardiac death: exploring the limits of our knowledge. J Cardiovasc Electrophysiol 2001;12:369–81.
3. Zipes DP, Wellens HJ. Sudden cardiac death. Circulation 1998;98:2334–51.
4. Zheng ZJ, Croft JB, Giles WH, Mensah GA. Sudden cardiac death in the United States, 1989 to1998. Circulation 2001;104:2158–63.
5. Denfield SW, Garson A Jr. Sudden death in children and young adults. Pediatr Clin North Am 1990;37:215–31.
6. Silka MJ. Sudden death due to cardiovascular disease during childhood. Pediatr Ann 1991;20:360,362-7.
7. Gillette PC, Garson A Jr. Sudden cardiac death in the pediatric population. Circulation 1992;85(suppl 1):I64–9.
8. Liberthson RR. Sudden death from cardiac causes in children and young adults. N Engl J Med 1996;334:1039–44.
9. Molander N. Sudden natural death in later childhood and adolescence. Arch Dis Child 1982;57:572–6.
10. Kennedy HL, Whitlock JA, Buckingham TA. Cardiovascular sudden death in young persons. J Am Coll Cardiol 1984;3:485.
11. Driscoll DJ, Edwards WD. Sudden unexpected death in children and adolescents. J Am Coll Cardiol 1985;5:(suppl 6):118B–21B.
12. Garson A Jr, McNamara DG. Sudden death in a pediatric cardiology population, 1958 to 1983: relation to prior arrhythmias. J Am Coll Cardiol 1985; 5:(suppl 6):134B–7B.
13. Topaz O, Edwards JE. Pathologic features of sudden death in children, adolescents, and young adults. Chest 1985;87:476–82.
14. Neuspiel DR, Kuller LH. Sudden and unexpected natural death in childhood and adolescence. JAMA 1985;254:1321–5.

15. Philips M, Robinowitz M, Higgins JR, Boran KJ, Reed T, Virmani R. Sudden cardiac death in Air Force recruits: a 20-year review. JAMA 1986;256:2696–9.
16. Thiene G, Nava A, Corrado D, Rossi L, Pennelli N. Right ventricular cardiomyopathy and sudden cardiac death in young people. N Engl J Med 1988;318:129–33.
17. Kramer MR, Drory Y, Lev B. Sudden death in young Israeli soldiers: analysis of 83 cases. Isr J Med Sci 1989;25:620–4.
18. Drory Y, Turetz Y, Hiss Y, et al. Sudden unexpected death in persons less than 40 years of age. Am J Cardiol 1991;68:1388–92.
19. Corrado D, Basso C, Poletti A, Angelini A, Valenti M, Thiene G. Sudden death in the young. Is acute coronary thrombosis the major precipitating factor? Circulation 1994;90:2315–23.
20. Steinberger J, Lucas RV Jr, Edwards JE, Titus JL. Causes of sudden unexpected cardiac death in the first two decades of life. Am J Cardiol 1996;77:992–5.
21. Gillum RF. Sudden coronary death in the United States: 1980–1985. Circulation 1989;79:756–65.
22. Murphy SL. Deaths: final data for 1998. Natl Vital Stat Rep 2000;48:1–105.
23. Deardorff K. US population estimates by age, sex, race and Hispanic origin: 1990 to 1997. U.S. Bureau of the Census, Current Population Report Series PPL-910. Washington DC: US Government Printing Office, 1998.
24. Klein RJ, Schoenborn CA. Age adjustment using the 2000 Projected U.S. population. Healthy People 2010 statistical notes, No. 20. Hyattsville MD: National Center for Health Statistics, 2001. DHHS Publication no. (PHS) 2001-1237.
25. Zheng ZJ, Croft JB, Giles WH, Mensah GA. State-specific mortality from sudden cardiac death—United States, 1999. MMWR Morb Mortal Wkly Rep 2002;51:123–6.
26. Centers for Disease Control and Prevention. Achievements in public health, 1900–1999: decline in deaths from heart disease and stroke—United States, 1900–1999. MMWR Morb Mortal Wkly Rep 1999;48:649–56.
27. Goodwin JF. Sudden cardiac death in the young. BMJ 1997;314:843.
28. Boneva RS, Botto LD, Moore CA, Yang Q, Correa A, Erickson D. Mortality associated with congenital heart defects in the United States: trends and racial disparities, 1979–1997. Circulation 2001;103:2376–81.
29. Strong JP, Malcom GT, McMahan CA, et al. Prevalence and extent of atherosclerosis in adolescents and young adults. Implications for prevention from the Pathobiological Determinants of Atherosclerosis in Youth Study. JAMA 1999;281:727–35.
30. McGill HC Jr, McMahan CA, Zieske AW, et al. Association of coronary heart disease risk factors with microscopic qualities of coronary atherosclerosis in youth. Circulation 2000;102:374–9.
31. McGill HC, McMahan CA, Zieske AW, et al. Association of coronary heart disease risk factors with the intermediate lesion of atherosclerosis in youth. Arterioscler Thromb Vasc Biol 2000;20:1998–2004.
32. Centers for Disease Control and Prevention. Trends in cigarette smoking among high school students—United States, 1991–1999. MMWR Morb Mortal Wkly Rep 2000;49;755–8.
33. Mokdad AH, Bowman BA, Ford ES, Vinicor F, Marks JS, Koplan JP. The continuing epidemics of obesity and diabetes in the United States. JAMA 2001;286:1195–1200.
34. Mittleman MA, Siscovick DS. Physical exertion as a trigger of myocardial infarction and sudden cardiac death. Cardiol Clin 1996;14:263–70.
35. Bauman JL, Grawe JJ, Winecoff AP, Hariman RJ. Cocaine-related sudden cardiac death: a hypothesis correlating basic science and clinical observations. J Clin Pharmacol 1994;34:902–11.
36. Isner JM, Roberts WC, Heymsfield SB, Yager J. Anorexia nervosa and sudden death. Ann Intern Med 1985;102:49–52.
37. Ray WA, Meredith S, Thapa PB, Meador KG, Hall K, Murray KT. Antipsychotics and the risk of sudden cardiac death. Arch Gen Psychiatry 2001;58:1161–7.
38. Locati EH, Zareba W, Moss AJ, et al. Age- and sex-related differences in clinical manifestations in patients with congenital long-QT syndrome: findings from the International LQTS Registry. Circulation 1998;97:2237–44.
39. Makkar RR, Fromm BS, Steinman RT, Meissner MD, Lehmann MH. Female gender as a risk factor for torsades de pointes associated with cardiovascular drugs. JAMA 1993;270:2590–7.
40. Pratt CM, Camm AJ, Cooper W, et al. Mortality in the Survival With ORal D-sotalol (SWORD) trial: why did patients die? Am J Cardiol 1998;81:869–76.
41. Kawasaki R, Machado C, Reinoehl J, et al. Increased propensity of women to develop torsades de pointes during complete heart block. J Cardiovasc Electrophysiol 1995;6:1032–8.
42. Folsom AR, Gomez-Marin O, Gillum RF, Kottke TE, Lohman W, Jacobs DR Jr. Out-of-hospital coronary death in an urban population—validation of death certificate diagnosis. The Minnesota Heart Survey. Am J Epidemiol 1987;125:1012–8.
43. Every NR, Parsons L, Hlatky MA, et al. Use and accuracy of state death certificates for classification of sudden cardiac deaths in high-risk populations. Am Heart J 1997;134:1129–32.
44. Iribarren C, Crow RS, Hannan PJ, Jacobs DR Jr, Luepker RV. Validation of death certificate diagnosis of out-of-hospital sudden cardiac death. Am J Cardiol 1998;82:50–3.
45. Coady SA, Sorlie PD, Cooper LS, Folsom AR, Rosamond WD, Conwill DE. Validation of death certificate diagnosis for coronary heart disease: The Atherosclerosis Risk in Community (ARIC) Study. J Clin Epidemiol 2001;54:40–50.
46. The Public Access Defibrillation Trial Investigators. Public-access defibrillation and survival after out-of-hospital cardiac arrest. N Engl J Med 2004;351:637–46.