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Incidence, Etiology, and Survival Trends from Cardiovascular-related Sudden Cardiac Arrest in Children and Young Adults Ages 0-35: A 30-Year Review

Running title: *Meyer et al.; Sudden Cardiac Arrest in Children and Young Adults*

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Abstract:

Background - Sudden cardiac arrest is a leading cause of death in children and young adults. This study determined the incidence, etiology, and outcomes of cardiovascular-related out-of-hospital cardiac arrest (OHCA) in individuals less than age 35.

Methods and Results - A retrospective cohort of OHCA in children and young adults from 1980 through 2009 was identified from the King County (Washington) Division of Emergency Medical Services' Cardiac Arrest Database. Incidence was calculated using population census data and etiologies determined by review of autopsy reports and all available medical records. A total of 361 cases (26 cases ages 0-2, 30 cases ages 3-13, 60 cases ages 14-24, and 245 cases ages 25-35) of OHCA were treated by EMS responders, for an overall incidence of 2.28 per 100,000 person-years (2.1 in ages 0-2, 0.61 in ages 3-13, 1.44 in ages 14-24, and 4.40 in ages 25-35). The most common etiologies of OHCA were congenital abnormalities (84.0%) in ages 0-2 and (21%) in ages 3-13, presumed primary arrhythmia (23.5%) in ages 14-24, and coronary artery disease (42.9%) in ages 25-35. The overall survival rate was 26.9% (3.8% in ages 0-2, 40.0% in ages 3-13, 36.7% in ages 14-24, and 27.8% in ages 25-35). Survival increased throughout the study period from 13.0% in 1980-1989 to 40.2% in 2000-2009 ($p<0.001$).

Conclusions - The incidence of OHCA in children and young adults is higher than previously reported, and a more specific understanding of etiology should guide future prevention programs. Survival trends support contemporary resuscitation protocols for OHCA in the young.

Key words: death, sudden; exercise; heart arrest; pediatrics; resuscitation

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Introduction

Sudden cardiac arrest (SCA) in children and young adults is a devastating event and a leading cause of death in this population.[1, 2] Sudden death from cardiovascular disease is also the principal cause of death in young athletes during exercise and represents 75% of all fatalities during sport.[2, 3] The incidence of SCA in the young is widely debated, ranging from 0.5 – 20 per 100,000 person-years.[3-11] Prior estimates have utilized highly variable methodology for case ascertainment, from search of public media reports to hospital reporting systems, making comparison across studies and age ranges difficult. Many studies also include all causes of SCA, such as trauma, respiratory failure, drowning, and overdose.[5, 6, 10] Limited data is available characterizing only cardiovascular causes of SCA which may be preventable through targeted screening programs.

The etiology of cardiovascular-related SCA in the young is broad, involving congenital cardiac disorders, inheritable cardiomyopathies, primary electrical diseases, and premature atherosclerosis. The leading cause of SCA in young athletes in the U.S. is reported to be hypertrophic cardiomyopathy (HCM),[3, 12] yet few studies have detailed the etiology of SCA in the general pediatric population or compared cardiovascular abnormalities in athletes versus non-athletes. SCA in the young has a low survival rate, with survival to hospital discharge less than 15% in many communities.[5, 6, 10, 13-17] Uncertainty regarding the frequency of SCA in the young, variable etiology, and poor outcomes have raised several issues concerning the indication, feasibility, and cost-effectiveness of primary and secondary prevention strategies.[18-23] An accurate estimate of the frequency of SCA in the young combined with a precise determination of the specific causes will assist the development of more effective prevention strategies. This study examines the incidence, specific cardiac etiologies, and outcomes of cardiovascular-related

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out-of-hospital cardiac arrest (OHCA) in the pediatric and young adult population in King County, Washington, over a 30 year period.

Methods

Study Setting and Population

The study area was King County, Washington, excluding Seattle, which covers 2,000 square miles, has a population of 1.23 million, and includes urban, suburban, and rural areas. Approximately 50% (620,000) of the population is age 35 and under. The emergency medical services (EMS) system in the study community is a 2-tiered response system and has maintained an ongoing registry of each cardiac arrest treated since 1976.

The study population consisted of patients ages 0-35 with treated OHCA between 1980 and 2009. All EMS reported cases were reviewed to determine the likely cause of cardiac arrest. Only cases with confirmed or likely cardiovascular etiologies were included in this study to calculate incidence and survival rates. Non-cardiac etiologies, such as trauma, respiratory failure, drowning, and overdose, were excluded. Cases due to sudden infant death syndrome (SIDS) were also excluded as a cardiac etiology could not be confirmed.

Data Collection and Classification

The EMS medical incident reports, the electronic defibrillator recording when available, and the dispatch tape are reviewed to determine patient demographics (age and gender), event circumstances (witness status, location, citizen CPR status, and arrest before EMS arrival), EMS response intervals, presenting rhythm, and immediate outcome (admission to hospital versus death). In cases where the EMS response interval could not be determined, the average EMS response time across all cases was assumed.

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Etiology was determined using all available information, including EMS incident reports, autopsy reports, death certificates, and hospital records when available, and a specific cause of SCA was determined for each case. Etiologies were categorized into subgroups of like cardiac disorders to compare survival and etiology based on age of occurrence: 1) all primary electrical diseases, 2) all cardiomyopathies, 3) atherosclerotic coronary artery disease (CAD), 4) congenital anomalies, 5) other cardiac causes, and 6) cardiac etiology unspecified. Primary electrical diseases included long QT syndrome, Wolff-Parkinson White syndrome, and presumed primary arrhythmia. Cases thought to be cardiac in origin based on the details of the event and resuscitation but in which a specific cause could not be determined by autopsy (autopsy-negative sudden unexplained death) were classified as a presumed primary arrhythmia. Cases of survival in which medical records identified no structural cardiac disease or other specific disorder were also classified as a presumed primary arrhythmia. The cardiomyopathic group included HCM, arrythmogenic right ventricular cardiomyopathy, dilated cardiomyopathy, and left ventricular non-compaction. Congenital anomalies included complex heart anomalies such as tetralogy of Fallot, hypoplastic left heart, transposition of the great vessels, chromosomal alterations, and ventricular septal defects. Various other etiologies that could not be classified as primary electrical disease, cardiomyopathy, CAD, or congenital anomaly included aortic dissection/Marfan syndrome, commotio cordis, bicuspid aortic valve/stenosis, pericarditis, coronary arteritis, and mitral valve prolapse. It is possible some of these findings were incidental and not causal; however, no other etiology could be confirmed. Cases due to multiple abnormalities in which a single cause could not be determined and cases that expired without autopsy were considered to be of unspecified cardiac etiology.

Cases were also classified based on their relationship to exercise. Exercise-related SCA

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was defined as cardiac arrest during or within one hour of physical activity. Differences in etiology and survival were compared between exercise-related and non-exercise related SCA. Survival was measured as survival to hospital discharge.

Incident reports and hospital records from cases occurring between 1986-1989 were not available for review. Therefore, cases from this time period were not included in the analysis of outcome by type of cardiac etiology or the relation of SCA to exercise. The event and resuscitation characteristics for these cases were available in the cardiac arrest registry so calculations related to incidence, resuscitation details, and survival rates included data from these years.

Statistical Analysis

Population-based incidence rates per 100,000 person-years were calculated using census data broken into three 10-year intervals (1980-1989, 1990-1999, and 2000-2009). Population data was determined at the mid-way point in each interval, and this number used as the average population over the 10-year time period to determine incidence rates across each interval. Overall and age specific incidence rates across the 30-year study were calculated by finding the mean of the three 10-year periods, and 95% confidence intervals were calculated using the Newcombe-Wilson method. Incidence, survival rates, and etiologies were analyzed based on the age ranges 0-2, 3-13, 14-24, and 25-35 years.

SPSS 14.0 (Chicago, Illinois, USA) was used for statistical analysis. Descriptive statistics are reported as means and standard deviation, or medians and interquartile range. Continuous variables were analyzed using analysis of variance (ANOVA). Categorical variables were analyzed using Mantel-Haenszel Chi-square. A univariate logistic regression was used to determine the odds ratio of survival by age, gender, etiology, witnessed arrest, location (public

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versus private), bystander CPR, arrest before EMS arrival, EMS response time, and first rhythm of ventricular fibrillation or ventricular tachycardia (VF/VT). A multivariate logistic regression was used to model survival and potential predictors of outcome.

An analysis of survival from 2000-2004 versus 2005-2009 was completed to evaluate the effect of the CPR protocol change that occurred in January 2005.[24] A multivariate logistic regression was used to model survival and potential predictors of outcome to determine the effect of the protocol change on survival.

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Results

Overall, a total of 361 cases of cardiovascular-related OHCA in individuals ages 0-35 across the 30-year interval were included in the study (**Figure 1**). EMS incident reports and hospital records were not available in 47 cases between 1986-1989. Arrest and resuscitation details were available for all 361 cases and used for calculation of incidence and event characterization.

Incidence and Event Characteristics

Table 1 shows subject and event characteristics. Cases were divided into three time intervals to compare event characteristics and survival across the 30-year time period. The average annual incidence rate of OHCA for the overall study population was 2.28 (95% CI 2.06-2.52) per 100,000 persons. Age stratified incidence rates were 2.1 (95% CI 1.44-3.06) in ages 0-2, 0.61 (95% CI 0.43-0.88) in ages 3-13, 1.44 (95% CI 1.12-1.85) in ages 14-24, and 4.40 (95% CI 3.90-4.99) in ages 25-35.

The mean age of OHCA victims was 25.1 (SD±10.1) and was not statistically different across the period. The majority of arrests occurred in males (70.6%), before EMS arrival (92.2%), and were witnessed (66.7%). The mean EMS response time (from 9-1-1 call to arrival

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on scene) was 4.9 (±2.5) minutes after the call was received.

Survival Outcomes

The overall survival rate to hospital discharge was 26.9% (97/361) for the 30-year period, with a significant increase from 1980-1989 (13.0%) to 2000-2009 (40.2%) (p <0.001) (**Table 2**). In a univariate logistic regression analysis, the main factors associated with survival were witnessed arrest (OR 13.42; 95% CI 5.48-32.88), initial rhythm of VF/VT (OR 9.37; 95% CI 4.91-17.88), bystander CPR (OR 3.15; 95% CI 1.82-5.44), and public location of arrest (OR 1.97; 95% CI 1.2-3.24). In a multivariate logistic regression analysis, independent predictors for survival were witnessed arrest (adjusted OR 6.29; 95% CI 4.68-30.81), first rhythm of VF/VT (6.50; 95% CI 3.09-13.66), and bystander CPR (2.28; 95% CI 1.18-4.41).

When analyzed based on etiology subgroups, there was no difference in survival over the 30 year time period among primary electrical and cardiomyopathic causes, although both groups had higher survival rates compared to CAD and congenital abnormalities. In the 302 cases in which the relation of OHCA to exercise could be determined, a total of 77 cases (25%) occurred during or within one hour of exercise with a 37.7% survival, although exercise was not statistically associated with survival.

Analysis of survival rates between 2000-2004 and 2005-2009 was also conducted given the CPR protocol change in January of 2005 in which minimizing interruptions in chest compressions was emphasized. The overall survival rate in the first five-year period was 25.4% compared to 58.2% in the second five-year period (p<0.01). Univariate and multivariate logistic regression analysis showed no significant difference in EMS response time, witnessed arrest, bystander CPR, first rhythm, or location of arrest between the two five-year periods.

Detailed Etiology

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The most specific cause of cardiac arrest was determined for each case after review of all available information including autopsy reports, death certificates, EMS incident reports, and hospital or emergency room records. Records were available for 314 of the 361 cases (records from 1986-1989 could not be located to conduct this review). Of the 314 cases, there were 221 deaths. The etiology in cases of death was determined by review of the EMS Medical Incident Report Form and death certificate in all cases, and the autopsy report if performed (161/221). In cases of survival, etiology was determined by review of the EMS Medical Incident Report Form, emergency room and hospital records. Etiologies were placed into subgroups to compare like cardiac etiologies including: 1) primary electrical diseases, 2) cardiomyopathies, 3) CAD, 4) congenital anomalies, 5) other cardiac causes, and 6) cardiac etiology unspecified (**Table 3**).

The etiology subgroups were examined based on survival, gender, age and association with exercise (**Table 4**). Primary electrical disease, cardiomyopathy, and CAD all occurred most frequently in the 25-35 age group. Congenital abnormalities were the predominant cause of arrest in ages 0-2. Coronary artery disease was found only in the oldest age range (25-35) and 89% occurred in males. The highest survival rates were in the primary electrical (51.4%) and cardiomyopathic subgroups (41.7%), and the lowest survival was in the congenital anomalies (6.4%).

Figure 2 shows the specific etiologies that were most prevalent in each age group. The main cause of SCA in ages 0-2 (84.0%) and in ages 3-13 (21.0%) were congenital anomalies. The leading cause of OHCA in ages 14-24 was presumed primary arrhythmia (23.5%). All cases of coronary artery disease occurred in the 25-35 population and accounted for nearly half (42.9%) of the cardiac events in this age group.

A comparison of the specific etiologies for exercise-related versus non-exercise related

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OHCA in ages 14-35 showed no significant differences (**Figure 3**). The leading cause of cardiac arrest in both the exercise and non-exercise related events was CAD at 39% and 33% respectively. Hypertrophic cardiomyopathy represented less than 4% of cases in persons 14-35 years old in both groups.

Discussion

The incidence of OHCA in children and young adults is widely debated and largely unknown. In the U.S., there is no mandatory reporting system for juvenile sudden death making accurate estimation of the magnitude of this problem difficult. This study provides a unique 30-year perspective in which all cases of OHCA in King County, Washington, with EMS response were entered into a single cardiac arrest database.

This study provides a unique estimate of the risk of OHCA for persons 0-35 years old. Other studies of pediatric OHCA have included all causes of non-traumatic cardiac arrest, such as drowning, respiratory failure, and drug poisoning, making estimates of cardiovascular-related SCA challenging, and thus difficult to draw conclusions which impact primary prevention.[10] Many cardiac screening programs, especially those in young athletes, have focused on adolescents and young adults. Our study identified the risk of OHCA to be 1:69,000 persons per year for ages 14-24 and 1:23,000 persons per year in ages 25-35. These results are comparable to a 3-year prospective population-based study in Oregon which utilized similar methodology and reported an incidence of 1:59,000 for OHCA in children ages 10-14.[25] Eckart et al. also reported a high incidence of cardiovascular-related sudden death in military personnel ages 18-35 in which the incidence of sudden cardiac death (SCD) was approximately 1 in 25,000.[11]

The incidence of OHCA in adolescents and young adults in this study is substantially

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higher than initial estimates of SCD in young competitive athletes ranging from 1:160,000 to 1:300,000 deaths per year in athletes ages 12-35.[3, 8, 9] However, these studies underestimate the incidence of SCD in athletes due to the lack of a systematic reporting system, incomplete identification of all cases, and heavy reliance of case ascertainment through search of public media reports, catastrophic insurance claims, and other electronic databases. In contrast, a recent study on the incidence of SCD in National Collegiate Athletic Association (NCAA) athletes demonstrates the incidence of SCD in college-aged athletes is 4-5 times higher than traditional estimates.[2] The overall risk of SCD in NCAA athletes was 1:43,000, with higher risks found in male athletes (1:33,000), black male athletes (1:13,000), and male basketball players (1:7,000).[2] The NCAA study utilized an internal reporting system and demonstrated that reliance on media reports, even in this high profile population, missed 44% of cases.[2]

Questions exist regarding the relative risk of SCA in competitive athletes versus the general population, and if this risk justifies a separate, more advanced cardiovascular screening program in athletes. It is generally accepted that exercise and intense physical exertion through athletic participation increase the likelihood of sudden death for many disorders predisposing to SCA. An Italian study identified a 2.5 times relative risk for SCD in adolescents and young adults engaged in competitive sports versus an age-matched non-athletic population.[26] Marijon et al. also reported the relative risk of sports-related sudden death was 4.5 times higher in competitive young athletes ages 10-35 compared to noncompetitive sports participants of the same age in France.[27] While this study could not determine a rate of OHCA in young athletes, it is unlikely to be significantly less than what was found for the overall adolescent and young adult population. In addition, the high rate of such events determined in this study may justify the development of more aggressive screening programs for the general adolescent and young

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adult population, and not just competitive athletes.

Accurate characterization of the etiology of pediatric OHCA allows more targeted screening programs towards the causes posing the greatest risk. This study details the various cardiac disorders leading to OHCA in the young stratified by age. A comprehensive evaluation of each case was performed by review of all available medical records to determine the circumstances and specific cause of death. This is necessary as a previous report found that determination of SCA based on death certificates alone was inaccurate.[2]

Several studies have reported HCM as the leading cause of SCD in young competitive athletes ages 12-35 in the U.S., representing up to 36% of cases.[3, 12] In this study, HCM represented only 18% of cases for ages 3-13, with just one case of HCM occurring in a child less than 10 years old. In addition, this study found less than 3% of OHCA in the general population ages 14-35 was due to HCM.

This study found a higher proportion of autopsy-negative SUD in the general population than prior reports of sudden death in same-aged competitive athletes. Autopsy-negative SUD is reported in only 3% of sudden death cases in young competitive athletes ages 12-35 in the U.S.,[3] while it accounted for 10% of OHCA in persons ages 14-35 in this study. Autopsy-negative SUD also represents a substantially larger proportion of SCD in the young in other study populations. Autopsy-negative SUD represents approximately 30% of SCD in Australia[28, 29] and 36% of SCD in Denmark[30] in individuals less than 35 years old. In U.S. military personnel ages 18-35, autopsy-negative SUD accounts for 41% of cardiovascular-related sudden death.[11] Autopsy-negative SUD may be due to inherited arrhythmia syndromes and ion channel disorders such as long QT syndrome, short QT syndrome, Brugada syndrome, and familial catecholaminergic polymorphic ventricular tachycardia, or other primary electrical diseases such

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as Wolff-Parkinson-White syndrome.[12] The accurate diagnosis of ion channelopathies postmortem is still limited; however, post-mortem genetic testing (so called "molecular autopsy"), if performed, identifies a pathogenic cardiac ion channel mutation in over one-third of cases.[13, 31, 32] A better understanding of etiology in survivors with a negative evaluation after SCA is also needed.

We analyzed those cases of OHCA that occurred during or within one hour of exercise to determine if causation was different in exercise-related events. While this group is not a direct surrogate for competitive athletes, there were no significant differences in etiology between exercise and non-exercise related events. HCM represented only 4% of cases of exercise-related OHCA in this study, compared to one-third of cases reported in competitive athletes.[3] Presumed primary arrhythmia was the leading cause of exercise-related OHCA (23%) in adolescents and young adults ages 14-25 found in this study. More research is needed to understand these differences, if they are real or influenced by methodology, ascertainment bias, or study demographics.

The reason for the difference in etiologies of SCA found in this study compared to prior reports in young competitive athletes is uncertain. Disparities may be due to differences in methodology and case identification, differences in the demographics and ethnicity of young competitive athletes versus the general population, or perhaps variability in the likelihood of SCA with vigorous exercise depending on the specific etiology. More research is needed to understand the specific etiologies that cause SCA in the young general population and in competitive athletes to guide the development of appropriate screening procedures.

As expected, coronary artery disease becomes the main risk factor for SCA in young adults ages 25-35. In children ages 0-13, congenital anomalies were the most common cause of

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OHCA, suggesting that enhanced postnatal diagnosis and management of congenital cardiac disorders may provide the largest impact for prevention of young pediatric SCD.

This study found an important increase in survival from 13% in the 1980's to 40% in the past decade. Outcomes from pediatric OHCA are generally poor as reported in past studies.[5, 6, 10, 13-17] This study demonstrates that improved survival rates are possible using a robust community-based EMS system and modern resuscitation protocols. It also suggests the CPR protocol change on January 1, 2005 was associated with a significant increase in survival The 2005 guidelines called for a single shock without rhythm reanalysis, stacked shocks, or post-shock pulse check, and extended the period of CPR between shocks to 2 minutes.[24, 33] A 2006 report suggested the new resuscitation guidelines may improve outcomes for adults with out-of-hospital ventricular fibrillation arrest.[33] To our knowledge, this is the first study comparing outcomes of pediatric OHCA before and after implementation of the new guidelines. In this study, survival in the five years prior to this protocol change was 25.4%, which is consistent with a survival of 25.4% in the 1990's. In the five years after the protocol change and controlling for covariates that impact outcomes, survival increased dramatically to 58.2%.

This study is limited by its retrospective design and lack of a mandatory reporting system for OHCA. It is possible cases of OHCA were not captured by the EMS system and the actual incidence of OHCA in this population could be higher. However, we believe this to be unlikely since all EMS run reports flow to the King County EMS and thus all EMS-treated cardiac arrests are captured. To further verify capture of all cardiac arrests, redundant sources of information such as dispatch codes are also screened. Census data can also be imprecise although is the only means of calculating incidence in population-based studies. In addition, although a comprehensive review of all available medical reports was performed, inherent limitations to

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current autopsy protocols, coroner diagnoses, and the lack of post-mortem genetic testing in cases of a negative autopsy complicate the determination of a specific disorder as the cause of cardiac arrest.

Conclusion

This study indicates that cardiovascular-related OHCA in children and young adults is more common than reported in prior estimates. The favorable survival trends identified over the last three decades provide compelling support of contemporary resuscitation protocols for OHCA in the young. A detailed characterization of the etiologies affecting different age groups should guide the development of targeted screening programs and more effective strategies for prevention.

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References:

1. Heron M, Hoyert D, Murphy S, Xy J, Kochanek K, Tejada-Vera B. Deaths: Final Data for 2006. *Natl Vital Stat Rep.* 2009;57:1-136.

2. Harmon KG, Asif IM, Klossner D, Drezner JA. Incidence of sudden cardiac death in national collegiate athletic association athletes. *Circulation.* 2011;123:1594-1600.

3. Maron BJ, Doerer JJ, Haas TS, Tierney DM, Mueller FO. Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980-2006. *Circulation.* 2009;119:1085-

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1092.

4. Gerein RB, Osmond MH, Stiell IG, Nesbitt LP, Burns S. What are the etiology and epidemiology of out-of-hospital pediatric cardiopulmonary arrest in Ontario, Canada? *Acad Emerg Med.* 2006;13:653-658.

5. Donohoe RT, Innes J, Gadd S, Whitbread M, Moore F. Out-of-hospital cardiac arrest in patients aged 35 years and under: a 4-year study of frequency and survival in London. *Resuscitation.* 2010;81:36-41.

6. Park CB, Shin SD, Suh GJ, Ahn KO, Cha WC, Song KJ, Kim SJ, Lee EJ, Ong ME. Pediatric out-of-hospital cardiac arrest in Korea: A nationwide population-based study. *Resuscitation.* 2010;81:512-517.

7. Eckart RE, Scoville SL, Campbell CL, Shry EA, Stajduhar KC, Potter RN, Pearse LA, Virmani R.. Sudden death in young adults: a 25-year review of autopsies in military recruits. *Ann Intern Med*. 2004;141:829-834.

8. Maron BJ, Gohman TE, Aeppli D. Prevalence of sudden cardiac death during competitive sports activities in Minnesota high school athletes. *J Am Coll Cardiol*. 1998;32:1881-1884.

9. Van Camp SP, Bloor CM, Mueller FO, Cantu RC, Olson HG. Nontraumatic sports death in high school and college athletes. *Med Sci Sports Exerc.* 1995;27:641-647.

10. Atkins DL, Everson-Stewart S, Sears GK, Daya M, Osmond MH, Warden CR, Berg RA. Epidemiology and outcomes from out-of-hospital cardiac arrest in children: the Resuscitation Outcomes Consortium Epistry-Cardiac Arrest. *Circulation*. 2009;119:1484-1491.

11. Eckart RE, Shry EA, Burke AP, McNear JA, Appel DA, Castillo-Rojas LM, Avedissian L, Pearse LA, Potter RN, Tremaine L, Gentlesk PJ, Huffer L, Reich SS, Stevenson WG. Sudden death in young adults an autopsy-based series of a population undergoing active surveillance. J *Am Coll Cardio.l* 2011;58:1254-1261.

12. Maron BJ. Sudden death in young athletes. *N Engl J Med*. 2003;349:1064-1075.

13. Donoghue AJ, Nadkarni V, Berg RA, Osmond MH, Wells G, Nesbitt L, Stiell IG. Out-of-hospital pediatric cardiac arrest: an epidemiologic review and assessment of current knowledge. *Ann Emerg Med.* 2005;46:512-522.

14. Mogayzel C, Quan L, Graves JR, Tiedeman D, Fahrenbruch C, Herndon P. Out-of-hospital ventricular fibrillation in children and adolescents: causes and outcomes. *Ann Emerg Med*. 1995;25:484-491.

15. Pitetti R, Glustein JZ, Bhende MS. Prehospital care and outcome of pediatric out-of-hospital cardiac arrest. *Prehosp Emerg Care.* 2002;6:283-290.

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16. Tham LP, Chan I. Paediatric out-of-hospital cardiac arrests: epidemiology and outcome. *Singapore Med J*. 2005;46:289-296.

17. Young KD, Gausche-Hill M, McClung CD, Lewis RJ. A prospective, population-based study of the epidemiology and outcome of out-of-hospital pediatric cardiopulmonary arrest. *Pediatrics*. 2004;114:157-164.

18. Drezner J, Corrado D. Is there evidence for recommending electrocardiogram as part of the pre-participation examination? *Clin J Sport Med*. 2011;21:18-24.

19. Drezner JA, Courson RW, Roberts WO, Mosesso VN, Jr., Link MS, Maron BJ. Inter-association task force recommendations on emergency preparedness and management of sudden cardiac arrest in high school and college athletic programs: a consensus statement. *Heart Rhythm*. 2007;4:549-565.

20. Drezner JA, Rao AL, Heistand J, Bloomingdale MK, Harmon KG. Effectiveness of emergency response planning for sudden cardiac arrest in United States high schools with automated external defibrillators. *Circulation*. 2009;120:518-525.

21. Wheeler MT, Heidenreich PA, Froelicher VF, Hlatky MA, Ashley EA. Cost-effectiveness of preparticipation screening for prevention of sudden cardiac death in young athletes. *Ann Intern Med*. 2010;152:276-286.

22. Maron BJ, Thompson PD, Ackerman MJ, Balady G, Berger S, Cohen D, Dimeff R, Douglas PS, Glover DW, Hutter AM, Krauss MD, Maron MS, Mitten MJ, Roberts WO, Puffer JC. Recommendations and considerations related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007 update: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation. *Circulation*. 2007;115:1643-1655.

23. Ronco R, King W, Donley DK, Tilden SJ. Outcome and cost at a children's hospital following resuscitation for out-of-hospital cardiopulmonary arrest. *Arch Pediatr Adolesc Med*. 1995;149:210-214.

24. ECC Committee, Subcommittees and Task Forces of the American Heart Association. 2005 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2005;112:IV1-203.

25. Chugh SS, Reinier K, Balaji S, Uy-Evanado A, Vickers C, Mariani R, Gunson K, Jui J. Population-based analysis of sudden death in children: The Oregon Sudden Unexpected Death Study. *Heart Rhythm*. 2009;6:1618-1622.

26. Corrado D, Basso C, Rizzoli G, Schiavon M, Thiene G. Does sports activity enhance the risk of sudden death in adolescents and young adults? *J Am Coll Cardiol.* 2003;42:1959-1963.

27. Marijon E, Tafflet M, Celermajer DS, Dumas F, Perier MC, Mustafic H, Toussaint JF,

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Desnos M, Rieu M, Benameur N, Le Heuzey JY, Empana JP, Jouven X. Sports-related sudden death in the general population. *Circulation.* 2011;124:672-681.

28. Doolan A, Langlois N, Semsarian C. Causes of sudden cardiac death in young Australians. *Med J Aust.* 2004;180:110-112.

29. Puranik R, Chow CK, Duflou JA, Kilborn MJ, McGuire MA. Sudden death in the young. *Heart Rhythm*. 2005;2:1277-1282.

30. Winkel BG, Holst AG, Theilade J, Kristensen IB, Thomsen JL, Ottesen GL, Bundgaard H, Svendsen JH, Haunso S, Tfelt-Hansen J. Nationwide study of sudden cardiac death in persons aged 1-35 years. *Eur Heart J*. 2010;32:983-990.

31. Tester DJ, Ackerman MJ. The role of molecular autopsy in unexplained sudden cardiac death. *Curr Opin Cardiol.* 2006;21:166-172.

32. Tester DJ, Spoon DB, Valdivia HH, Makielski JC, Ackerman MJ. Targeted mutational analysis of the RyR2-encoded cardiac ryanodine receptor in sudden unexplained death: a molecular autopsy of 49 medical examiner/coroner's cases. *Mayo Clin Proc*. 2004;79:1380-1384.

33. Rea TD, Helbock M, Perry S, Garcia M, Cloyd, Becker L, Eisenberg M. Increasing use of cardiopulmonary resuscitation during out-of-hospital ventricular fibrillation arrest: survival implications of guideline changes. *Circulation*. 2006;114:2760-2765.

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Table 1. Subject and event characteristics.

Characteristic	1980-1989	1990-1999	2000-2009	TOTAL	p-value*
Total Arrests Ages 0-35	108	126	127	361	
Incidence Rate (95% CI)	2.44 (2.02-2.94)	2.35 (1.98-2.80)	2.06 (1.73-2.45)	2.28 (2.06-2.52)	
Gender					
Male (n, %)	68 (63.0)	92 (73.0)	95 (74.8)	255 (70.6)	0.107
Age					
Mean Age	24.8	26.4	23.9	25.1	0.161
95% CI	22.8-26.7	24.7-28.1	22.1-25.8	24.0-26.1	
Median Age (25%, 75%)	27.5 (21.25, 33)	30 (23.5, 33.25)	28 (16, 32)	29 (20, 33)	
Age Categories					
0 thru 2	9 (8.3)	7 (5.6)	10 (7.9)	26 (7.2)	0.722
3 thru 13	7 (6.5)	9 (7.1)	14 (11.0)	30 (8.3)	
14 thru 24	18 (16.7)	19 (15.1)	23 (18.1)	60 (16.6)	
25 thru 35	74 (68.5)	91 (72.2)	80 (63.0)	245 (67.9)	
Response Time[†]					
Mean	4.8	4.6	5.2	4.9	0.116
95% CI	4.3-5.2	4.2-5.0	4.8-5.3	4.6-5.1	
Witnessed Arrest[‡]	66 (61.1)	83 (65.9)	87 (68.5)	236 (66.7)	0.721
Bystander CPR	62 (57.4)	67 (53.2)	75 (59.1)	204 (56.5)	0.675
Initial Rhythm V-Fib	50 (46.3)	70 (55.6)	70 (55.1)	190 (52.6)	0.289
Arrest in Public Location	27 (25)	44 (34.9)	47 (37.0)	118 (32.7)	0.119
Arrest Before EMS Arrival	100 (92.6)	113 (89.7)	120 (94.5)	333 (92.2)	0.356
Etiology[§]					
Primary Electrical	13 (21.3)	32 (25.4)	25 (19.7)	70 (22.3)	0.007
Cardiomyopathic	10 (16.4)	12 (9.5)	38 (29.9)	60 (19.1)	
Coronary Artery Disease	13 (21.3)	42 (33.3)	35 (27.6)	90 (28.7)	
Congenital	13 (21.3)	18 (14.3)	16 (12.6)	47 (15.0)	
Other	8 (13.1)	19 (7.9)	7 (5.5)	25 (8.0)	
Cardiac Unspecified	4 (6.6)	12 (9.5)	6 (4.7)	22 (7.0)	

* P-value corresponds to statistical differences between the three time periods.

[†]Mean response time was used for 33 cases.

[‡]Six cases had a missing witness variable (n=354).

[§]Etiologies in 1980-1989 time period excludes data from 1986-1989 due to lack of records (total cases= 61).

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Table 2. Survival outcomes for cardiac arrest in patients ages 0-35.

Characteristic	1980-1989	1990-1999	2000-2009	Total 1980-2009
Survivors- % survival (n/total)	13.0% (14/108)	25.4% (32/126)	40.2% (51/127)	26.9% (97/361)
p value				<0.001
Gender				
Male	13.2% (9/68)	25.0% (23/92)	37.9% (36/95)	26.8% (67/255)
Female	12.5% (5/40)	26.5% (9/34)	46.9% (15/32)	26.9% (28/106)
p value	0.913	0.866	0.37	0.523
Odds Ratio (95% CI)*				0.84 (0.49-1.43)
Age				
0 thru 2	0.0% (0/9)	14.3% (1/7)	0.0% (0/10)	3.8% (1/26)
3 thru 13	0.0% (0/7)	22.2% (2/9)	71.4% (10/14)	40.0% (12/33)
14 thru 24	0.0% (0/18)	31.6% (6/19)	43.5% (10/23)	26.7% (16/60)
25 thru 35	18.9% (14/74)	25.3% (23/91)	38.8% (31/80)	27.8% (68/245)
Odds Ratio (95% CI)	1.08 (0.99-1.18)	1.02 (0.97-1.06)	1.00 (0.97-1.03)	1.01 (0.10-1.04)
p-value	0.083	0.457	0.989	0.331
Response Time[†]				
0 - 3 min	14.8% (4/27)	33.3% (11/33)	52.6% (10/19)	31.6% (25/79)
4 - 7 min	14.3% (10/70)	25.3% (21/83)	40.2% (39/97)	28.0% (70/250
> 8 min	0.0% (0/11)	0.0% (0/10)	18.2% (2/11)	6.3% (2/32)
Odds Ratio (95% CI)	0.71 (0.54-0.93)	0.80 (0.67-0.97)	0.79 (0.65-0.95)	0.81 (0.72-0.90)
Witness[‡]				
yes	21.2% (14/66)	36.1% (30/83)	54.0% (47/87)	39.1% (91/233)
no	0.0% (0/38)	4.7% (2/43)	10.0% (4/40)	5.0% (6/121)
p-value	0.002	<0.001	<0.001	<0.001
Odds Ratio (95% CI)				13.42 (5.48-32.88)
CPR				
Bystander CPR provided	15.9% (7/44)	33.3% (26/78)	51.2% (42/82)	36.8% (75/204)
No Bystander CPR provided	10.9% (7/64)	12.5% (6/48)	20.0% (9/45)	14.0% (22/157)
p-value	0.450	0.009	0.001	<0.001
Odds Ratio (95% CI)				3.15 (1.82-5.44)
First Rhythm				
V-FIB	26.0% (13/50)	40.0% (28/70)	60.0% (42/70)	43.7% (83/190)
Non-VF	1.7% (1/58)	7.1% (4/56)	15.8% (9/57)	8.2% (14/171)
p-value	<0.001	<0.001	<0.001	<0.001
Odds Ratio (95% CI)				9.37 (4.91-17.88)
Location				
Public	18.5% (5/27)	36.6% (17/44)	46.8% (22/47)	37.3% (44/118)
Private	11.1% (9/81)	18.3% (15/82)	36.3% (29/80)	21.8% (53/243)
p-value	0.333	0.018	0.265	0.007
Odds Ratio (95% CI)				1.97 (1.20-3.24)

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Arrest Before EMS Arrival				
Yes	11.0% (11/100)	22.1% (25/113)	37.5% (45/120)	24.3% (81/333)
No	37.5% (3/8)	53.8% (7/13)	85.7% (6/7)	57.1% (16/28)
p-value	0.066	0.02	0.017	<0.001
Odds Ratio (95% CI)				0.19 (0.08-0.44)
Etiology Subgroup[§]				
Primary Electrical	53.8% (7/13)	43.8% (14/32)	60.0% (15/25)	51.4% (36/70)
Cardiomyopathic	0.0% (0/10)	16.7% (2/12)	60.5% (23/38)	41.7% (25/60)
Coronary Artery Disease	0.0% (0/13)	14.3% (6/42)	22.9% (8/35)	15.6% (14/90)
Congenital	0.0% (0/13)	11.1% (2/18)	6.3% (1/16)	6.4% (3/47)
Other	0.0% (0/8)	20.0% (2/10)	28.6% (2/7)	16.0% (4/25)
Cardiac-Unspecified	50.0% (2/4)	50.0% (6/12)	33.3% (2/6)	45.5% (10/22)
p-value	<0.001	0.011	<0.001	<0.001
Exercise[‖]				
yes	6.7% (1/15)	39.3% (11/28)	50.0% (17/34)	37.7% (29/77)
no	14.3% (6/42)	22.1% (21/95)	35.2% (31/88)	25.8% (58/225)
p-value	0.662	0.087	0.152	0.053
Odds Ratio (95% CI)				1.75 (0.99-3.08)

*Odds ratio of survival for univariate analysis. The relation of categorical variables to survival was analyzed by Mantel-Haentzel Chi-square, with the odds ratio and 95% CI shown from the combined categories.
[†]Mean response time was used for 33 cases.
[‡]Six cases had a missing witness variable (n=354).
[§]Excludes data from 1986-1989 due to lack of records (total cases= 314).
[‖]Excludes data from 1986-1989 and cases in which exercise prior to arrest could not be determined (total cases= 302).

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Table 3. Specific etiologies of OHCA in persons ages 0-35.

Etiology	# of Cases	Survival n (%)
Primary Electrical	70	36 (51.4)
Arrhythmia Other[†]	5	5 (100.0)
Commotio Cordis	1	1 (100.0)
Long QT	13	9 (69.2)
Presumed Primary Arrhythmia	46	18 (39.1)
WPW*	5	3 (60.0)
Cardiomyopathic	60	25 (41.7)
ARVC	5	0 (0.0)
Dilated Cardiomyopathy	30	17 (56.7)
HCM	14	7 (50.0)
LV Noncompaction	1	1 (100.0)
Myocarditis	10	0 (0.0)
Other (25)	25	4 (16.0)
Anomalous Origin of Coronary Arteries	2	0 (0.0)
Aortic Dissection/Marfans	2	0 (0.0)
Cardiomegaly	5	0 (0.0)
Coronary Arteritis	1	0 (0.0)
Dysrhythmia Other Structural Disease[‡]	2	0 (0.0)
LV Rupture	1	0 (0.0)
Mitral Valve Prolapse	8	2 (25.0)
Pericarditis	1	0 (0.0)
Valvular Disease[§]	3	2 (66.6)
Coronary Artery Disease	90	14 (15.6)
Congenital[‖]	47	3 (6.4)
Cardiac- Unspecified	22	10 (45.5)
Total	314	92 (29.3)

*ARVC=Arrhythmogenic Right Ventricular Cardiomyopathy, HCM=Hypertrophic Cardiomyopathy, LV Rupture= Left Ventricular Rupture, WPW=Wolff-Parkinson-White.

[†]Arrhythmia Other included cases with a history of: supraventricular tachycardia, paroxysmal ventricular tachycardia, anomalous AV excitation, and recurrent ventricular fibrillation of unknown etiology.

[‡]Dysrhythmia Other Structural Disease included: focal hemorrhage of conducting system, and dysrhythmia with myocardial scar.

[§]Valvular disease included: aortic stenosis and endocarditis.

[‖]Congenital conditions included: tetralogy of Fallot, hypoplastic left heart, ventricular septal defects, valvular defects, congenital chromosomal alterations, transposition of the great vessels, endocardial fibroelastosis, mitochondrial encephalomyopathy, and charge syndrome.

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Table 4. Characteristics of etiology subgroups.

Characteristic	Primary Electrical	Cardiomyopathic	CAD*	Congenital	Other	Cardiac-Unspecified	Total	p-value
# of Cases	n=70	n=60	n=90	n=47	n=25	n=22		
Survival n (%)	36 (51.4)	25 (41.7)	14 (15.6)	3 (6.4)	4 (16.0)	10 (45.5)	92 (29.3)	<0.001
Gender								
Male	37 (52.9)	42 (70.0)	80 (88.9)	29 (61.7)	16 (64.0)	17 (77.3)	221 (70.4)	<0.001
Female	33 (52.9)	18 (30.0)	10 (11.1)	18 (38.3)	9 (36.0)	5 (22.7)	93 (29.6)	
Age								
0 thru 2	2 (2.9)	1 (1.7)	0 (0)	21 (44.7)	0 (0)	1 (4.5)	25 (8.0)	<0.001
3 thru 13	8 (11.4)	9 (15.0)	0 (0)	6 (12.8)	4 (16.0)	1 (4.5)	28 (8.9)	
14 thru 24	19 (27.1)	12 (20.0)	0 (0)	12 (25.5)	6 (24.0)	2 (9.1)	51 (16.2)	
25 thru 35	41 (58.6)	38 (63.3)	90 (100)	8 (17.0)	15 (60.0)	18 (81.8)	210 (66.9)	
Mean (st dev)	23.20 (9.26)	24.95 (9.30)	32.02 (2.96)	11.83 (11.95)	24.88 (8.34)	27.27 (9.43)	24.78 (10.55)	<0.001
95% CI	20.99-25.41	22.55-27.35	31.40-32.64	8.32-15.34	21.44-28.32	23.09-31.45	23.61-25.95	
Exercise[†]								
Yes	15 (21.4)	18 (30.0)	26 (28.9)	8 (17.0)	7 (28.0)	3 (13.6)	77 (24.5)	0.206
No	49 (70.0)	41 (68.3)	63 (70)	38 (80.9)	16 (64.0)	18 (81.8)	225 (71.7)	

*CAD=Coronary Artery Disease.
[†]Excludes data from 1986-1989 and cases in which exercise prior to arrest could not be determined (total cases= 302).

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Figure Legends:

Figure 1. Study population according to time period.

Figure 2. Detailed etiologies by age group. *CAD=Coronary Artery Disease, DCM=Dilated Cardiomyopathy, HCM= Hypertrophic Cardiomyopathy. †Other corresponds to all other etiologies.

Figure 3. Exercise and non-exercise related etiologies in ages 14-35. *CAD=Coronary Artery Disease, DCM=Dilated Cardiomyopathy, HCM= Hypertrophic Cardiomyopathy †Other corresponds to all other possible etiologies.

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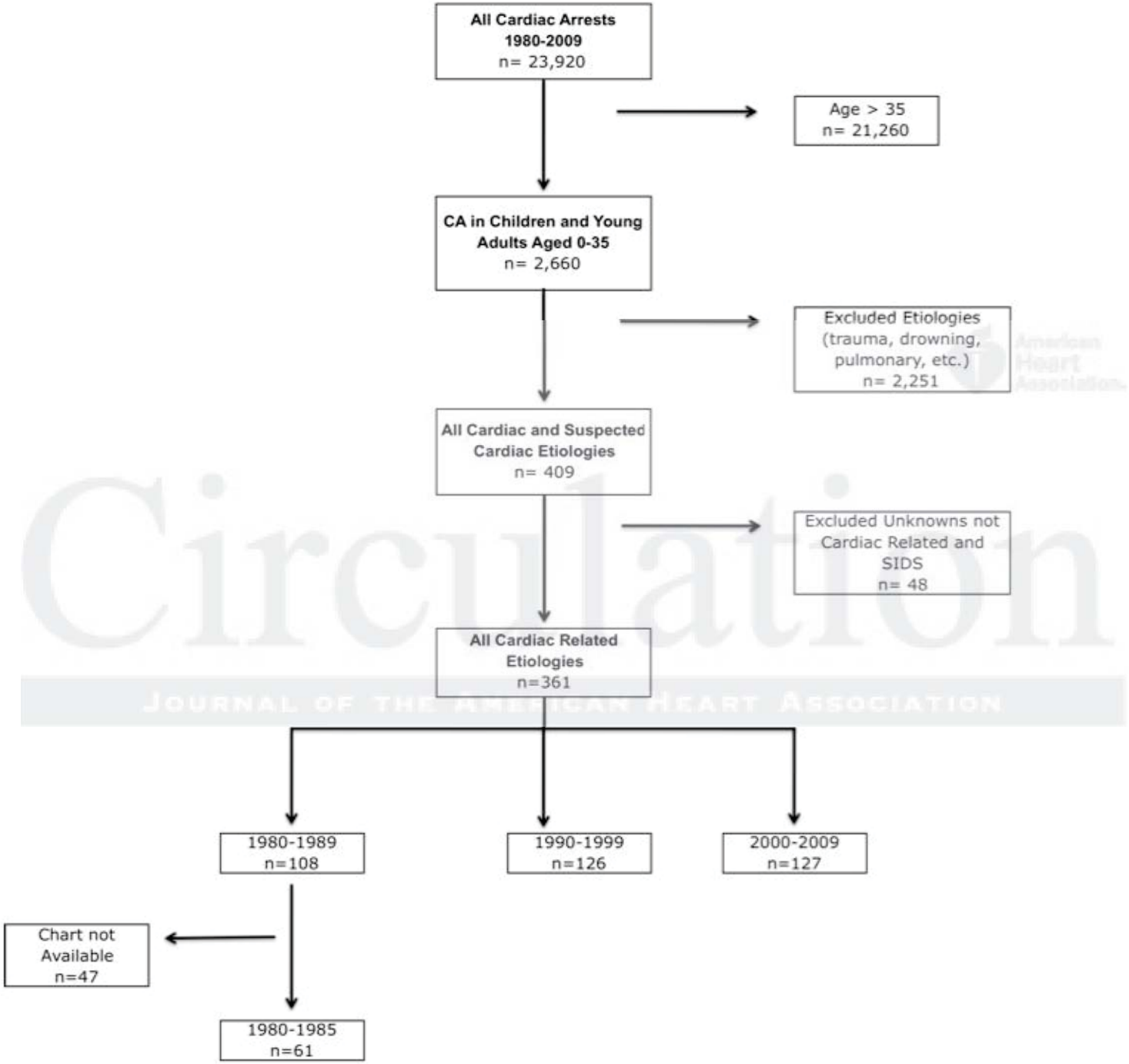

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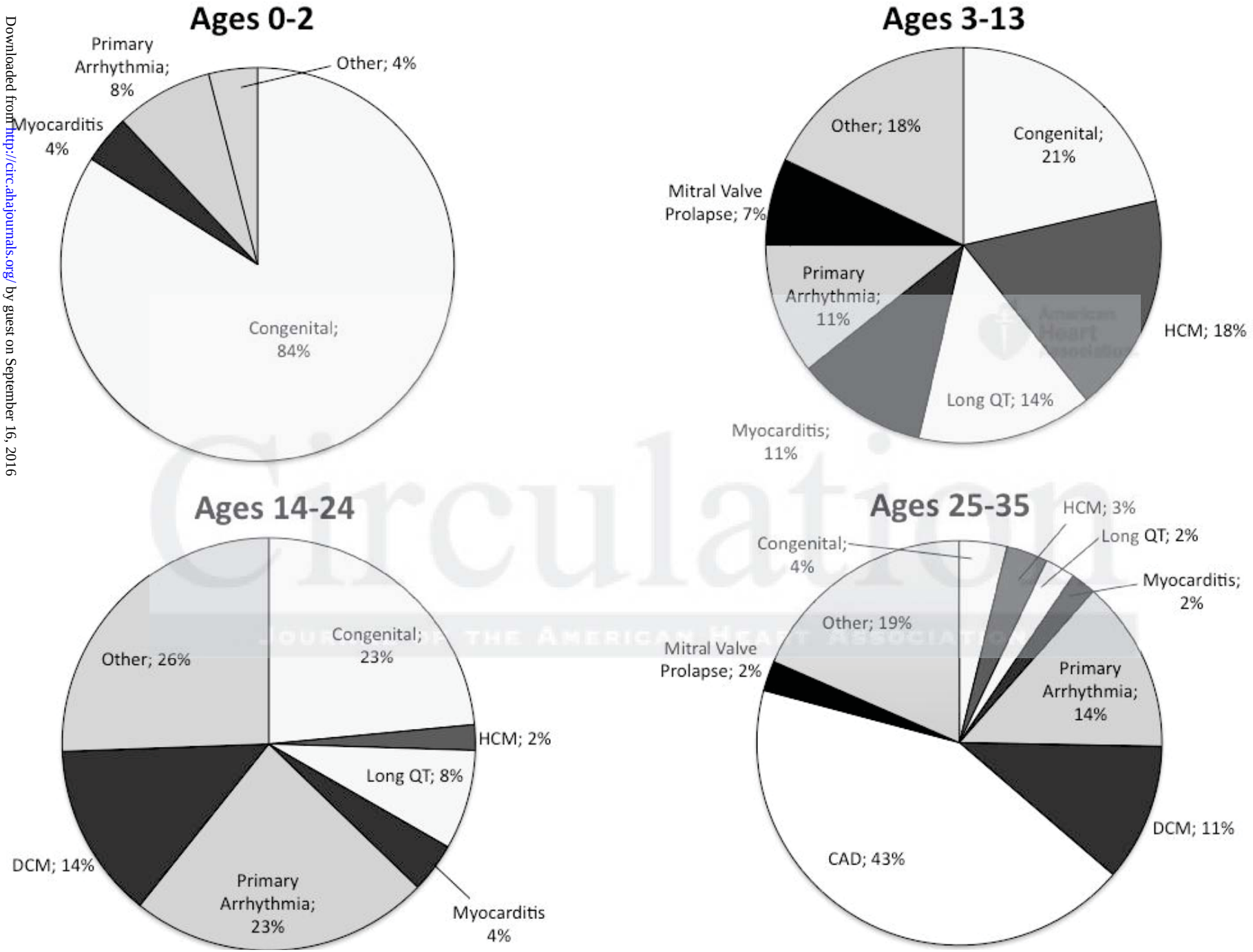

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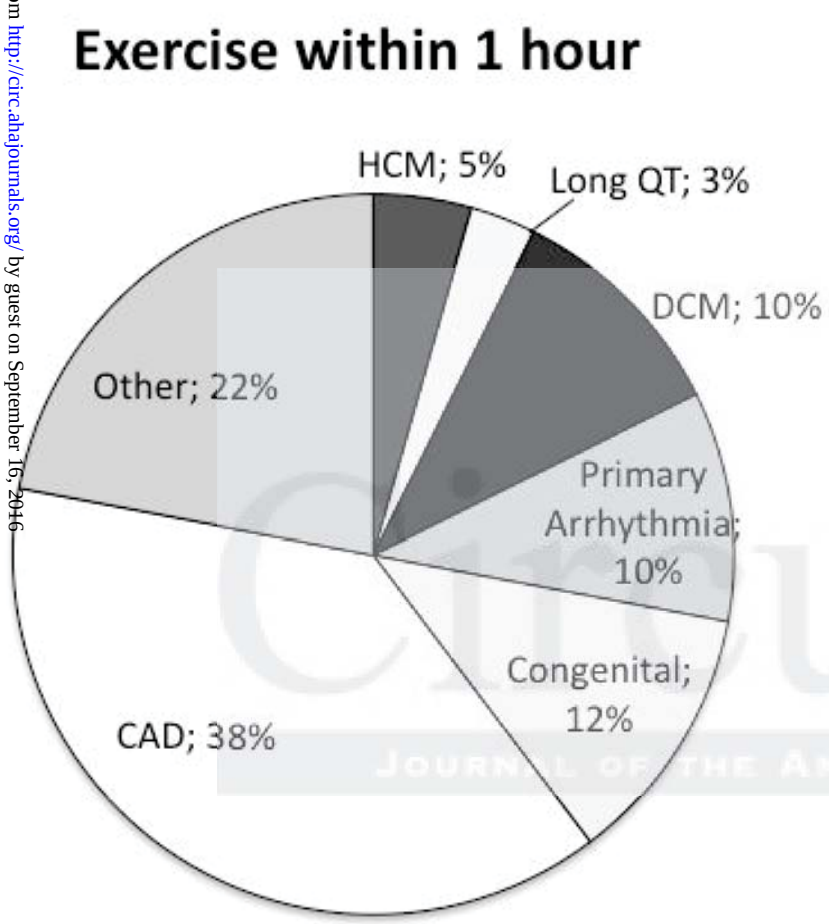

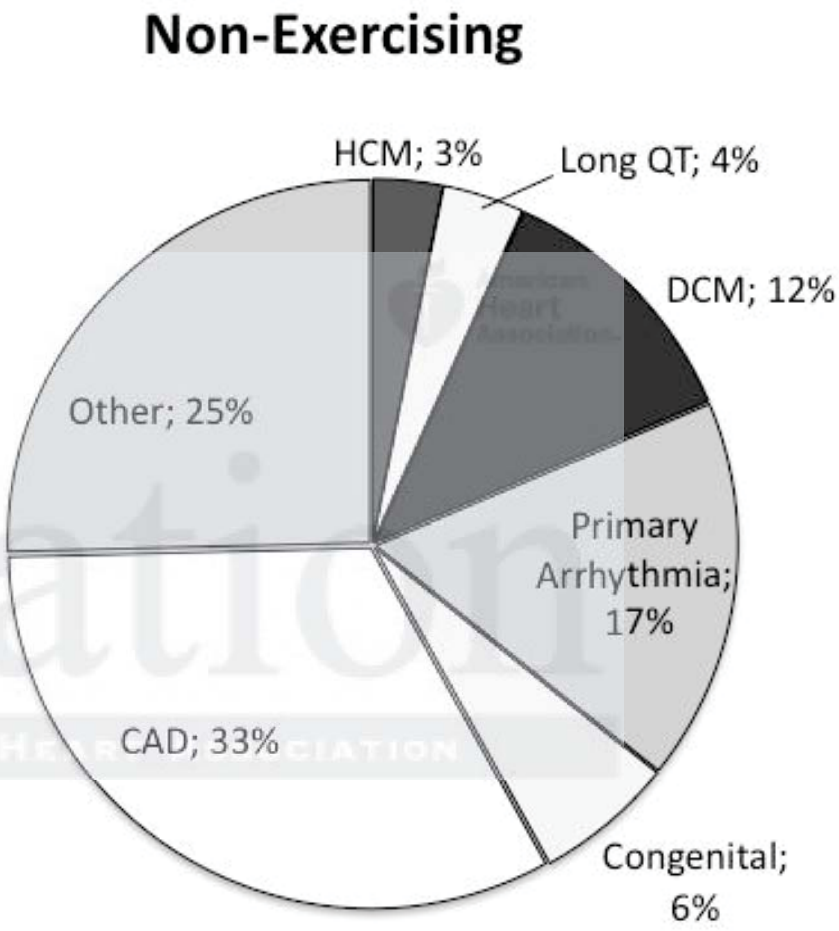

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Lauren Meyer, Benjamin Stubbs, Carol Fahrenbruch, Chris Maeda, Kimberly Harmon, Mickey Eisenberg and Jonathan Drezner

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