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Race, Ethnicity, and the Risk of Sudden Death

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Abstract

Sudden cardiac death (SCD) is a major cause of death worldwide, with an estimated U.S. annual incidence of 350,000.(1) This review will examine the influence of race and ethnicity on SCD burden and risk factors, and review the available literature on resuscitation outcomes and primary prevention of SCD. An improved understanding of associations between race, ethnicity, and SCD may provide clues to mechanisms, lead to improved prevention of SCD, and ultimately reduce racial and ethnic disparities in the burden of SCD.

Introduction

Risk of sudden cardiac death (SCD) may be influenced by race and ethnicity through cultural, social, genetic and environmental differences, including health behaviors, risk factor and comorbidity burden, socioeconomic status, and access to health care. We obtained relevant literature on these topics from the PubMed database (1948 – Apr 1, 2018), Scopus, and Google Scholar and included articles if they presented original data stratified by race or ethnicity, including incidence rates, risk factors for SCD, circumstances and outcomes of SCD, and/or implantable cardioverter defibrillator (ICD) use for adults ≥18 years of age. We considered race as typically defined in the U.S. (white, black/African American, Asian, American Indian/Alaska Native, and Native Hawaiian/Pacific Islander) and ethnicity as Hispanic/Latino or non-Hispanic, but also included alternative definitions of race.

Definitions of sudden cardiac arrest and SCD

Sudden cardiac arrest (SCA) is a sudden and unexpected collapse with loss of pulse.(2) Because out-of-hospital SCA has a case fatality rate of ~90–92%,(1, 3) sudden cardiac death (SCD) is often used as a synonym for SCA. In this review, we will use the term SCD throughout, except when discussing resuscitation or survivors of SCA. SCD can occur due to various etiologies, including non-cardiac causes such as drug overdose and terminal illness. In this review, we will focus on out-of-hospital SCD with likely cardiac cause.

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Race, ethnicity, and SCD epidemiology

SCD incidence

Early studies of SCD incidence by race include data from EMS systems, such as the Seattle Fire Department (1984–86), which found age-adjusted rates for non-traumatic SCD among blacks were two times greater than among whites.(4) The CPR Chicago Project (1987–88) reported higher SCD rates among blacks than whites at all ages, with relative risks >2 at younger ages.(5) In a more recent study in New York City (2002–2003) among approximately 4,000 SCDs with EMS response and attempted resuscitation, the age-adjusted rate among blacks was 40% higher than among whites (10.1 vs 5.8 per 10,000), and the rate among Hispanics was approximately 10% higher (6.5 per 10,000).(6)

An analysis of vital statistics data from >18,000 SCDs (1992) from the National Center for Health Statistics defined SCD by ICD-9 codes for coronary heart disease that occurred outside of the hospital or in the emergency room. In this study, blacks had a higher rate than non-Hispanic whites at each age category, while Hispanics had the lowest rates.(7) A later study using a decade of NCHS vital statistics data (1989–98) with similar methods reported that among ~450,000 SCDs per year among adults age ≥35, blacks had rates approximately 20% higher than whites, while rates were 50% lower among American Indians/Alaska Natives and Asians/Pacific Islanders; Hispanics had rates 40% lower than non-Hispanics.(8) It is important to keep in mind that a more recent study comparing prospective ascertainment of SCD to the use of death certificates to determine SCD found that death certificates result in significant overestimation of SCD and a low positive predictive value of 19%.(9)

In more recent studies, the Women's Health Initiative (418 SCDs in ~10 years of follow-up through 2009) reported annual rates of 4.3 per 10,000 per year in post-menopausal black women and 2.3 per 10,000 per year in their white counterparts; after multivariable adjustment, black women had a 30–60% higher risk of SCD.(10) In the Atherosclerosis Risk in Communities (ARIC) study (209 SCD cases in ~12 years of follow-up through 2001), incidence of SCD was 2–3 times higher among blacks than whites (19.8 vs. 5.8 per 10,000 person-years in non-diabetics, and 35.8 vs 16.8 per 10,000 person-years in diabetics), while rates of non-fatal MI did not differ.(11) In San Francisco (2007), the rate of autopsy-confirmed SCD with arrhythmic etiology was 3-fold higher among blacks than among whites 63.3 vs 20.1 per 100,000.(12) In the Oregon Sudden Unexpected Death Study (1077 cases identified using multiple-source ascertainment, 2002 – 2005), rates of SCD were twice as high in blacks as in whites, in both men (age-adjusted annual incidence 175 vs 84 per 100,000) and women (90 vs 40 per 100,000) (Figure 1).(13)

A few epidemiologic studies of SCD in predominantly Asian populations report substantially lower incidence rates than in US studies. A nationwide database in Korea of non-traumatic out of hospital SCA with presumed cardiac etiology (2006–07) reported rates of ~20 per 100,000.(14) In a population-based longitudinal study of middle-aged men in Japan, the age-adjusted rate of SCD was 36.8 per 100,000 in 2001–05.(15).

While more studies are needed, the available literature indicates a significant association of race and ethnicity with SCD burden, higher in blacks compared to whites, variable in Hispanics compared to whites, and possibly lowest among Asians.

Premature SCD

More years of life are lost due to premature SCD among blacks and perhaps other non-white groups. Studies consistently show higher rates for blacks even among young adults.(4, 5) In the Oregon SUDS study, the mean age of black SCD cases was approximately 6 years younger than white cases.(13) Using National Health and Nutrition Examination Survey (NHANES, 1999–2006) and national mortality data, blacks had a nearly two-fold higher cardiovascular disease mortality at young and middle ages, while the race difference diminished at older ages.(16)

Risk Factors

Coronary artery disease and related factors

Coronary artery disease is present in the majority (~75%) of SCD cases, though SCD is the first manifestation of heart disease in up to 50% of individuals.(17) Given this phenomenon, many risk factors for SCD are similar to those for coronary artery disease, and include male sex, older age, diabetes, hypertension, obesity, and smoking.(18–20) Many of these risk factors, particularly hypertension and diabetes, as well as prevalent coronary artery disease, are more prevalent in blacks than in whites in the general population.(1, 21, 22) A comparison of black vs. white SCD cases also found higher prevalence of most CV risk factors in blacks.(13)

Among Hispanics, prevalence of obesity, abnormal lipid profiles, and diabetes is notably higher than among non-Hispanic whites, while prevalence of hypertension and smoking are lower.(1, 23, 24) In the Hispanic Community Health Survey/Study of Latinos (HCHS/SOL) which enrolled >15,000 Hispanics with baseline exams 2008–2011, 80% of men and 71% of women had at least one cardiovascular disease risk factor, though the prevalence varied substantially by Hispanic/Latino background.(25) However, self-reported CHD prevalence was low, at 4.2% in men and 2.4% in women.(25) Overall, published studies show a markedly lower heart disease mortality in Hispanics despite a higher burden of several cardiovascular disease risk factors,(23, 24) a phenomenon labeled the Hispanic Paradox.(24, 26) It is not yet clear whether this paradox also applies to SCD, and there are currently no published data for Hispanics on risk factors for SCD specifically.

Among Asians, cardiovascular disease risk factor burden is similar to or lower than among whites, particularly lower rates of obesity and hypertension.(1) Recent NCDR data from 34 US states showed that although standardized cardiovascular disease mortality rates were lower among Asians compared to non-Hispanic whites, there was substantial variation by Asian-American subgroup, with Asian Indians and Filipino men having the highest rates and Vietnamese the lowest.(27)

Non-coronary cardiac risk factors

Compared with whites, blacks have a higher prevalence of several cardiac conditions associated with higher risk of SCD, including heart failure and left ventricular hypertrophy. In the Coronary Artery Risk Development in Young Adults (CARDIA) study of healthy black and white individuals at baseline, risk of incident heart failure under age 50 was particularly high among blacks.(28) In the Dallas Heart Study, blacks had a larger left ventricular mass and a 2- to 3-fold higher prevalence of left ventricular hypertrophy than whites.(29) In the LIFE study of hypertensive patients with electrocardiographic left ventricular hypertrophy, risk of SCD was twice as high among blacks as whites.(30) In the REGARDS study, major ECG abnormalities were more common among blacks than whites under age 65, but not over age 65.(31) In the CARDIA cohort, both major and minor ECG abnormalities were twice as common in blacks as in whites.(32)

These patterns may explain, at least in part, the higher incidence of SCD among blacks (Figure 2); current data in Hispanics is inadequate to draw conclusions. In a meta-analysis of data from >250,000 men and women enrolled in 18 cohort studies, individuals with an optimal risk factor profile had 4–5 times lower risk of cardiovascular death than patients with 2 or more risk factors, and these trends were similar in blacks and whites.(33)

The role of socioeconomic status (SES)

At least five studies have reported that lower SES is associated with higher incidence of SCD, a finding that persists across different health care systems.(34–38) Low SES is also associated with a higher burden of cardiovascular disease risk factors, less use of preventive care, and lower rates of bystander CPR. Because SES is associated with race and ethnicity in the US,(24) racial and ethnic differences in SCD may be partially explained by differences in SES.

Genetics

With the availability of improved sequencing technology, there has been a resurgence of studies investigating genetic variants that could explain racial differences in disease, for example, higher CHD risk in blacks. Published studies have revealed some findings that are of both mechanistic and clinical significance for SCD. Hypertrophic cardiomyopathy is genetically-determined, may be more prevalent among blacks,(13) and is a common cause of sudden death in young athletes.(39) However, this rare phenotype likely plays a small role in SCD risk in the general population. Polymorphisms leading to altered amino acid sequences encoding potassium and sodium channel have been more commonly found in blacks compared to whites.(40) A meta-analysis of 18 reports of ion channelopathy genes associated with SCD found significant racial and ethnic differences in mean allele frequencies: Asians carried the highest frequencies of *NOS1AP* and *SCN5A*, whites had the highest *KCNH2* frequency, and Hispanics had the highest *KCNQ1* frequency.(41) The common variant S1103Y of the sodium channel gene SCN5A, found almost exclusively in people of African descent, may predispose to ventricular arrhythmias.(42) Associations between single nucleotide polymorphisms of the NOS1AP gene and the QT interval, which is associated with SCD risk, differed across race and ethnic groups in the Multi-Ethnic Study of Atherosclerosis (MESA), and were strongest in the white group.(43) While many studies

have focused on differences between races and ethnicities, ancestry informative marker studies from the MESA study as well as from the Hispanic Community Health Survey / Study of Latinos (HSCS/SOL) indicate that there is substantial genetic diversity among Hispanics based on their region of origin (Mexican, Central/South American, Puerto Rican, Dominican, and Cuban)(44) and that cardiovascular risk factors vary substantially among these Hispanic/Latino subgroups.(25) Given the ongoing investigational focus on genetics of race, additional novel findings are anticipated in the next several years.

Sudden cardiac arrest resuscitation and outcomes

In a 2014 review of SCA outcomes by race, non-whites were generally less likely than whites to receive bystander CPR and less likely to present with a shockable rhythm (ventricular fibrillation/tachycardia; VF/VT), both factors that would negatively affect survival (Table 1).(45) Several of these studies did find lower survival in blacks compared to whites, but the data were mixed (Table 1); newer studies also suggest differences in survival based on race, ethnicity or region.(45–47) Teasing out the effects of race and ethnicity vs. SES is difficult. In a paper examining the probability of receiving bystander-initiated CPR, Sasson et al (48) classified neighborhoods as high- or low-income, and as predominantly (>80%) white, black, or integrated. Compared to high-income white neighborhoods, bystander-initiated CPR rates were lowest in low-income black neighborhoods, but were also lower in low-income white, low-income integrated, and high-income black neighborhoods, suggesting that both SES and race/ethnicity play a role.

Bystander CPR was also less likely among Hispanics (33.7%) than whites (40.7%) in the nationwide CARES registry (>31,000 SCA cases, 2005–2010).(49) In a statewide registry in Arizona (~4800 cases, 2010–2012), SCAs in predominantly (>80%) Hispanic neighborhoods were less likely than those in predominantly (>80%) white neighborhoods to receive bystander CPR, have shockable rhythms, and survive to hospital discharge.(50) In the CARE-LA database in Los Angeles, California, Hispanics were about half as likely to receive bystander CPR as whites.(51)

A study of EMS-attended SCD cases in Korea had low overall survival (2.3%)(14). In the Oregon SUDS and Seattle/King County studies, Asians appear more likely to present with asystole than whites, a factor that is associated with poor survival outcomes.(46, 52)

Primary prevention of SCD

Implantable cardioverter-defibrillators (ICDs): disparities in availability

Because of a high case fatality rate, prevention of SCD is a high priority. Reducing cardiovascular disease risk factors and treating existing coronary artery disease can prevent SCD, while the primary prevention ICD can abort SCD and improve survival in high risk patients. However, among eligible patients, non-whites appear less likely to be implanted with an ICD. Among 233 patients with cardiomyopathy and EF ≤35% and no prior history of SCA (2006), ICD implantation over 4 years was significantly lower in blacks, and findings persisted after adjustment for multiple comorbidities (Figure 3, Panel A).(53) Among >13,000 patients hospitalized for heart failure with EF ≤30% and eligible for ICD

therapy (Get With The Guidelines (GTWG) Program database, 2005–2007), ICD use was 30% lower in black patients than in white patients.(54) In newer data from the GWTG-Heart Failure program among patients admitted for heart failure with EF ≤35%, rates of counseling regarding primary prevention ICD were lower among blacks and Hispanics than whites, and among those counseled, both black and Hispanic patients were less likely to receive an ICD. (55)

Evidence of benefit from ICD implantation

Data are mixed on primary prevention ICD outcomes by race. In the MADIT-II clinical trial, total mortality was reduced among whites (n=1073, hazard ratio (HR) 0.75, 95% CI 0.55–1.02), but not among blacks (n=102, HR 1.25, 95% CI 0.42–3.60), and sudden cardiac death was also reduced in whites (HR 0.29, 95% CI 0.17–0.49) but not blacks (HR 1.71, 95% CI 0.33–8.84). However, the small sample size among blacks likely resulted in insufficient power to test the effectiveness of the ICD among blacks in this trial.(56) In the SCD-HeFT clinical trial, mortality was equally reduced in white and black patients (425 blacks, 1932 whites).(57) In the PROSE-ICD observational study of primary prevention ICDs (477 blacks, 712 non-blacks), blacks had a higher rate of mortality without appropriate shock, indicating less arrhythmic death.(58) In the Longitudinal Study of Implantable Cardioverter Defibrillators (LS-ICD) among 2621 patients including 32.7% minorities, the rate of appropriate therapy was lower among Hispanics than non-Hispanic whites, but no differences were reported for blacks or other races vs. whites.(59) The GWTG-HF and National Cardiovascular Disease Registry ICD Registries found a similar benefit of primary prevention ICDs for 3-year adjusted mortality in 852 minority (564 black, 189 Hispanic, and 99 other) and 2070 white Medicare patients (Figure 3, Panel B).(60)

Important caveats related to investigation of race and ethnicity effects

Using existing data on race, ethnicity and SCD risk to inform current practice has several limitations. In the studies described above, absolute rates of SCD varied greatly between studies (from ~20 per 100,000 to >400 per 100,000), likely due to a number of reasons, including the source of SCD data, SCD definitions, study dates, and denominators for rate calculations. In addition, the prevalence and management of heart disease has changed in the past decades. The Framingham study reported a 49% reduction in SCD risk from 1950–1999 concurrent with a reduction in overall heart disease.(61) It is also important to account for regional variation in SCD incidence and risk factor prevalence, which is often as large as variation due to race and ethnicity. For example, adjusted incidence rates of EMS-treated SCA ranged from 45.1 to 86.1 per 100,000 across 10 sites in the U.S. and Canada,(3) and the age-adjusted prevalence of coronary heart disease from the 2010 US Behavioral Risk Factor Surveillance System ranged from 3.7 (Hawaii) to 8.2 (Kentucky) per 100,000.(62) Finally, race and ethnicity are primarily social constructs, though they may correlate with genetic ancestry. The practice of separating race and ethnicity as separate categories has been criticized. In addition, within each race and ethnic category, there is substantial variability in factors that could influence health outcomes, including access to adequate nutrition, housing, education, and health care; and the experience of racism and/or discrimination.

Clinical implications

A special report from over a decade ago called for a multipronged approach to reduce disparities in cardiovascular health by race, ethnicity, gender, socioeconomic status, education level, and geography.(63) Ongoing efforts in all of these arenas are also likely to reduce race and ethnic disparities in SCD incidence. Physician training to reduce disparities in counseling and placement of ICDs may reduce mortality from SCD in high-risk minority populations.

There are also opportunities for immediate interventions, including increased public education about SCA and the need for bystander CPR in minority communities. Because bystander CPR approximately doubles survival, CPR training and placement of automated external defibrillators (AEDs) in minority communities could improve SCA survival and reduce disparities by race and ethnicity. Recent studies have shown the need to improve training in minority communities. Lower rates of CPR training have been reported in black and Hispanic residents and in areas with lower SES,(64) and while less than half of all respondents to a nationwide survey had been trained in AED use, Hispanics were less likely to be trained compared to whites and blacks.(65)

Future directions

SCD is a major cause of mortality in all population subgroups. Accordingly, well-designed and consistent, high quality studies that target strategies for prevention in the major racial and ethnic groups are needed. More contemporary data on SCD risk in blacks is needed, and there is a conspicuous lack of studies evaluating SCD risk in Hispanics, Asians, and other minorities. A growing body of literature demonstrates that CV risk factor prevalence and disease outcomes vary substantially within race and ethnic groups (e.g., among Hispanics based on region of origin,(25) and among Asian-American subgroups(66)); this level of detailed information is needed for SCD burden and risk.

Conclusions

Race and ethnicity may have a significant effect on SCD burden and risk factors, with major public health implications for prevention. Studies have consistently reported higher rates of SCD and SCD at younger age among blacks compared to whites. A higher risk factor burden in blacks could explain some of these differences. Both blacks and Hispanics are less likely to receive primary prevention ICDs when indicated. However, there is little available data on SCD epidemiology among Hispanics and non-black minorities, which limits the current understanding of SCD in these groups. The existing literature strongly suggests the need for a renewed investigative focus on race, ethnicity and SCD, with initiation of prospective studies large enough to feasibly evaluate SCD burden and risk factors in these populations.

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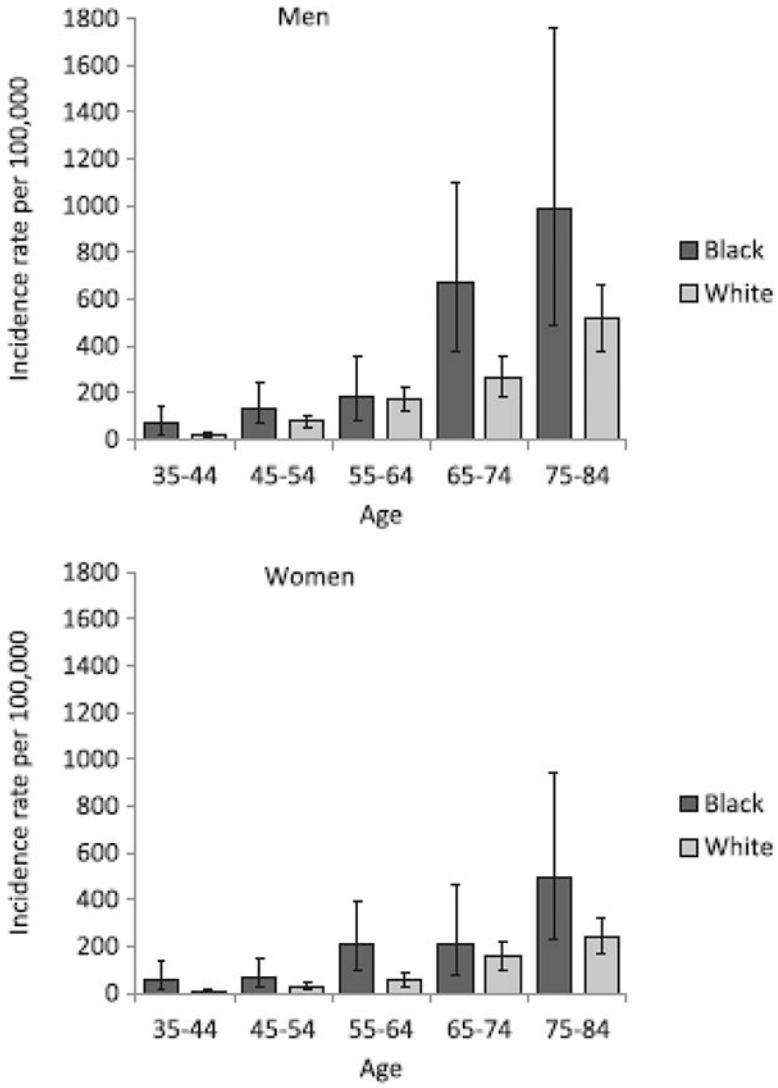


Figure 1.

A comparison of age-specific sudden cardiac arrest incidence between blacks and whites from the Oregon Sudden Unexpected Death Study (Oregon SUDS), 2002 to 2005. (Used with permission from ref 13)

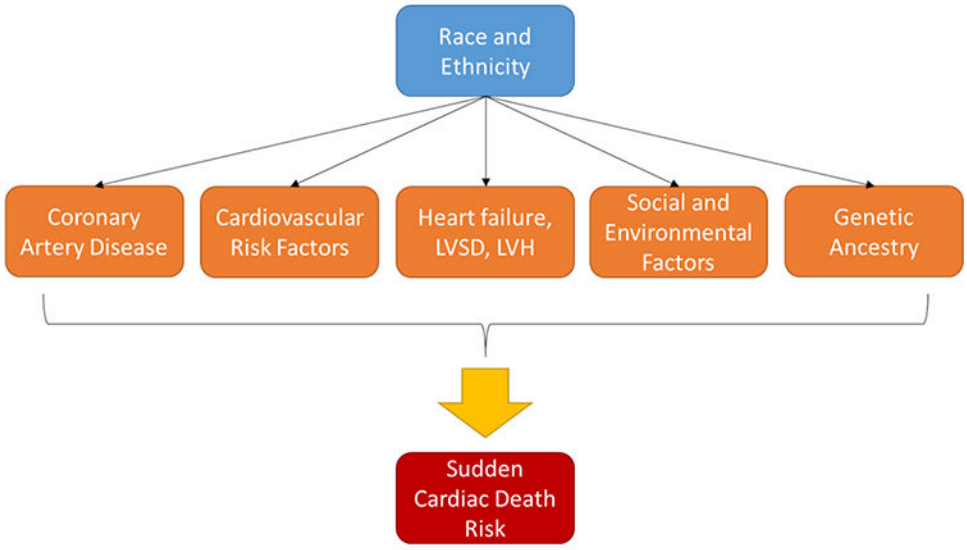


Figure 2.

Race and ethnicity may influence risk of SCD through coronary disease burden, cardiovascular risk factor burden, non-coronary heart disease, social and environmental factors (including health behaviors, socioeconomic status, and access to health care), and genetic ancestry. LVSD = left ventricular systolic dysfunction. LVH = left ventricular hypertrophy.

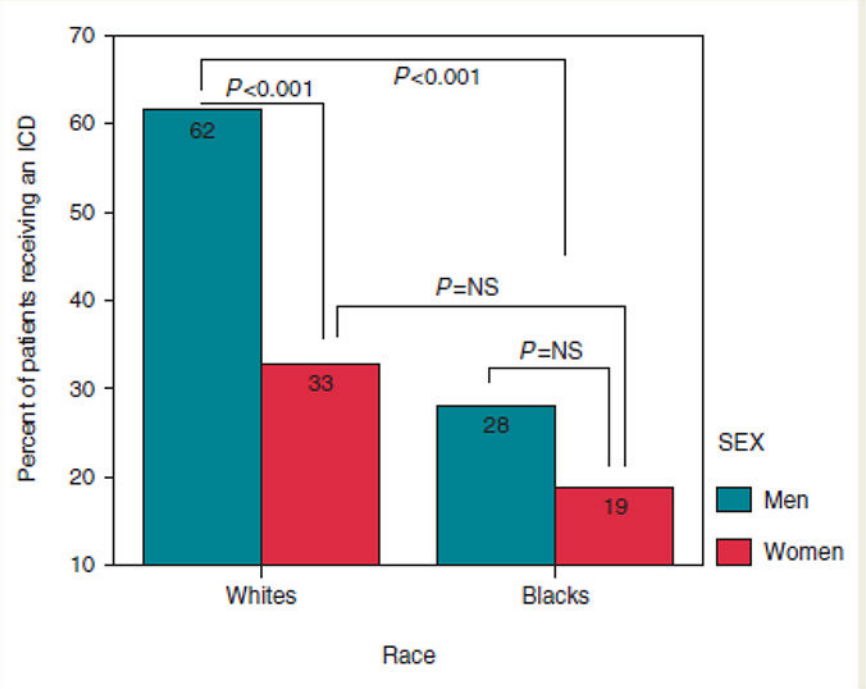
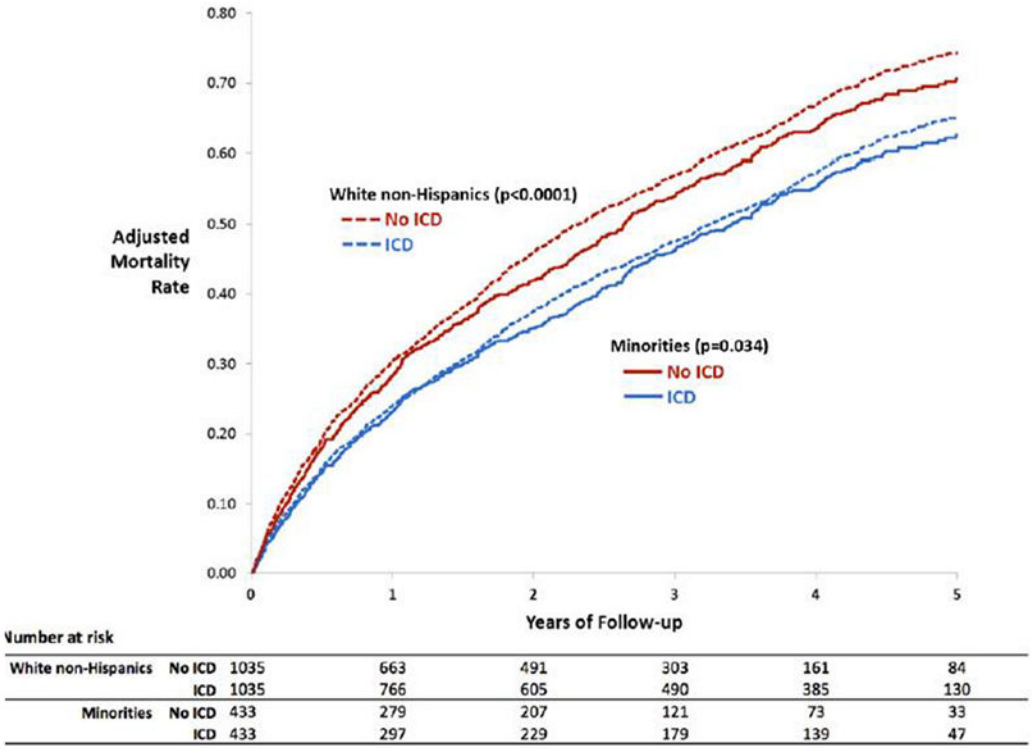


Figure 3. Panel A.

ICD implantation lags among blacks. In patients eligible for primary prevention implantable cardioverter defibrillator (cardiomyopathy and ejection fraction ≤35%), implantation over 4 years was significantly lower in blacks, and findings persisted after adjustment for multiple comorbidities. (Used with permission from Ref 53)



Number at risk

White non-Hispanics	No ICD	1035	663	491	303	161	84
	ICD	1035	766	605	490	385	130
Minorities	No ICD	433	279	207	121	73	33
	ICD	433	297	229	179	139	47

Figure 3. Panel B.

The ICD benefit for overall survival was similar in white non-Hispanics and minorities (of whom 66% were black and 22% were Hispanic). (Used with permission from Ref 60)

Table 1.

Arrest circumstances and outcomes of SCD by race

Author	Witnessed arrest	Shockable rhythm (VF/VT)	Response time	Bystander CPR	Survival to hospital discharge
Studies within the US					
Becker et al.,(5) 1993 *Chicago*	B 42% W 49% p**	B 17% W 26% p**	B 6 min W 6 min (B 18 seconds longer, p**)	B 18% W 25% p**	B 0.8% W 2.6% p**
Cowie et al.,(4) 1993 *Seattle*	B 53% W 61% p=NS	B 40% W 51% p=NS	B 3.4 min W 3.4 min p=NS	B 18% W 32% p**	B 9% W 17% p*
Brookoff et al.,(67) 1994 *Memphis*	B 60% W 64% p=NS	B 44% W 54% p*	No diff (mean times not stated)	B 10% W 21% p**	B 7% W 9% p=NS
Chu et al.,(68) 1998 *Michigan*	B 57% W 61% p=NS	B 37% W 51% p**	B 5.3 min W 7.0 min p**	B 11% W 20% p**	B 6% W 7% p=NS
Sayegh et al.,(69) 1999 *Michigan*	B 53% W 56% p=NS	B 43% W 46% p=NS	Response <9 min B 88% W 83% p*	B 3% W 6% p*	B 18% W 25% p**
Galea et al.,(6) 2007 *New York*	H 43% B 36% W 42% p**	H 15% B 12% W 17% p=NS	H 5.0 min B 4.7min W 4.5 min p*	H 25% B 31% W 31% p*	H 2% B 1% W 3% p**
Vadeboncoeur et al., (70) 2008 *Arizona*	H 44% NH 50% p=NS	H 21% NH 27% p*	H 5.1 min NH 5.5 min p**	H 16% NH 26% p**	H 8% NH 7% p NR
Benson et al.,(51) 2009 *Los Angeles*	H 40% B 36% W 48% p**	H 35% B 24% W 31% p=NS	NR	H 13% B 13% W 24% p NR	H 5% B 3% W 6% p=NS
McNally et al.,(49) 2011 *Multiple states*	NR	NR	NR	H 40.2% B 32.8% W 33.7% p**	H 9.4% B 8% W 10% p NR
Reinier et al.,(13) 2015 *Portland, OR*	B 67% W 68% p=NS	B 34% W 43% p=NS	B 6.4 min W 6.7 min p=NS	NR	B 8% W 13% p=NS
Studies Outside the US					
Hamaad et al.,(71) 2006 *UK*	NR	I-Asian 30% Afro-Car 30% W 45% p NR	Call to collection time, min: I-Asian 22.6 Afro-Car 31.7 W 28.2 p NR	NR	NR
Shah et al.,(72) 2010 *UK*	S-Asian 70% W 62% p*	S-Asian 30% W 30% p=NS	S-Asian 7.46 min W 7.48 min p=NS	S-Asian 30% W 34% p=NS	S-Asian 9% W 9% p NR

Adapted from Tables 2 and 3 in Ref 45, with permission.

p* = p<0.05;

p** = p<0.01;

NS = not significant; NR = not reported.

B = Black/African American; H = Hispanic/Latino; W = White/Caucasian; I-Asian = Indo-Asian; Afro-Car = Afro-Caribbean; S-Asian = South Asian.