To Screen of Not to Screen
The Italian /European and American Point of View

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Venice Arrhythmia
Consiglio Room 12:30-14:00
Friday October 16, 2015

American Reaction To the Italian/European

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No Conflicts of Interest

October 16 - 18
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- Background
- Evidence Based Medicine
- U.S. Screening Strategy
- Knowledge Gaps
- NHLBI Working Group Recommendations
- Economic/Legal/Ethical
- AEDs
- Conclusions

Background

- CV screening is widely recommended by professional societies.
- In the USA, current AHA recommendations-H &P.
- Limitations of the H &P are acknowledged, the AHA cites overwhelming support for the principle of this public health initiative as part of the rationale.
- AHA also acknowledges that efficacy of the various athlete screening strategies is not easily resolved in the context of evidence-based medicine.

American Reaction To the Italian/European Guidelines

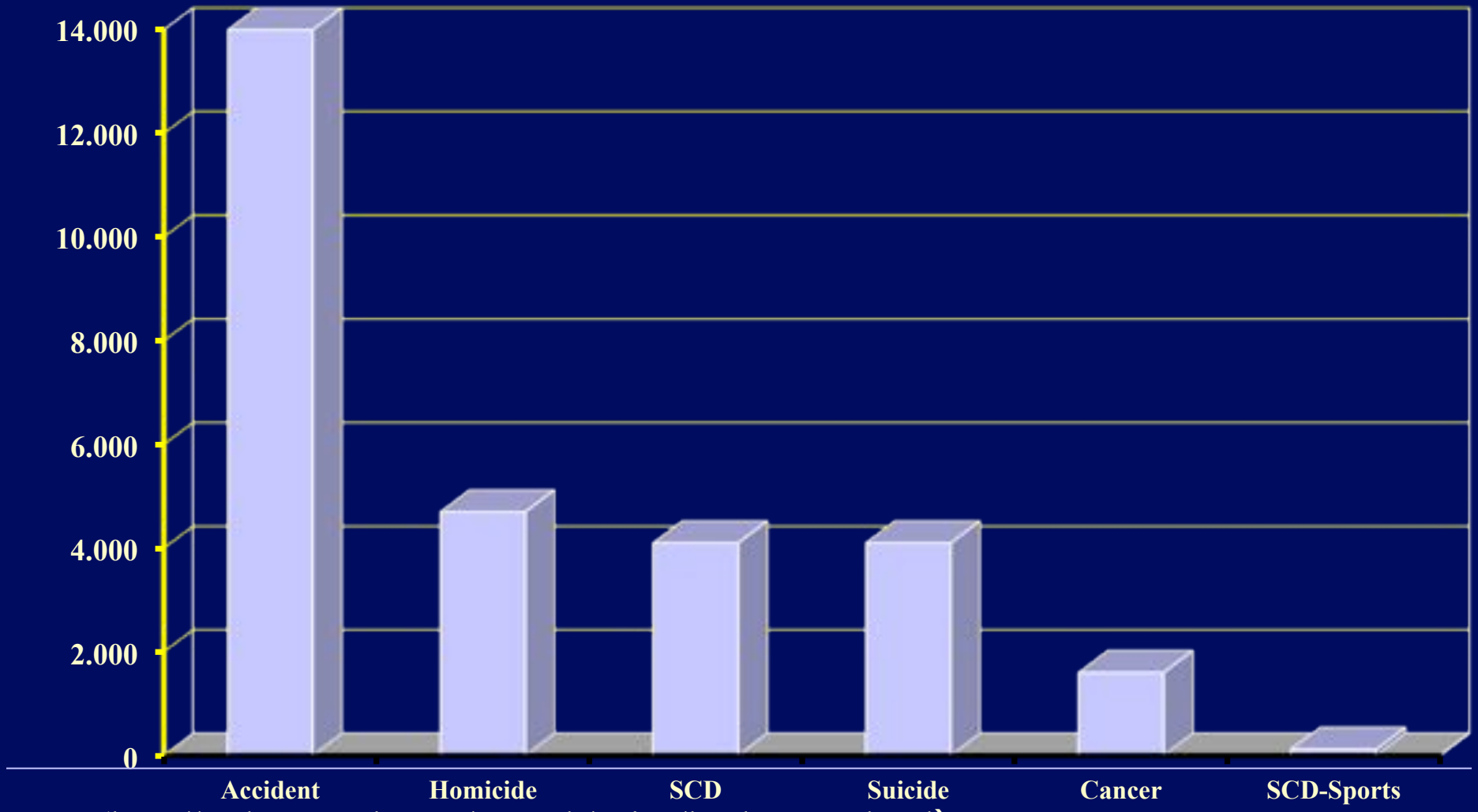
- Cardiac evaluation of athletes before participation is intuitively attractive to identify athletes at risk for SCD
- Screening to detect CV disease in athletes supported by the AHA and by the Sports Cardiology Study Group of the ESC
- Both guidelines recommend a personal and family history and physical examination, but the European guidelines recommend obtaining routine electrocardiograms (ECGs)
- AHA supports individual quality controlled local, community or student related ECG initiatives are supported if they are conducted properly with adequate resources

Incidence of sudden death stratified by athletic or general population and the years of the study population

Country	Author	Population	Years	Incidence / 100,000/year
Italy	Corrado	Athletes	1980-1981	**3.6**
Italy	Corrado	Athletes	2007-2008	**0.40**
US	Maron	Athletes	1985-2006	**0.44**
Israel	Steinvil	Athletes	1985-1997	**2.54**
Israel	Steinvil	Athletes	1998-2009	**2.66**
US	Van Camp	Athletes	1983-1993	**0.33**
Denmark	Holst	Athletes	2000-2006	**1.21**
Denmark	Holst	All children	2000-2006	**3.76**
Japan	Tanaka	All children	1989-1996	**1.32**
Canada	Atkins	Children 1-11	2005-2007	**3.73**
Canada	Atkins	Children 12-19	2005-2007	**6.37**

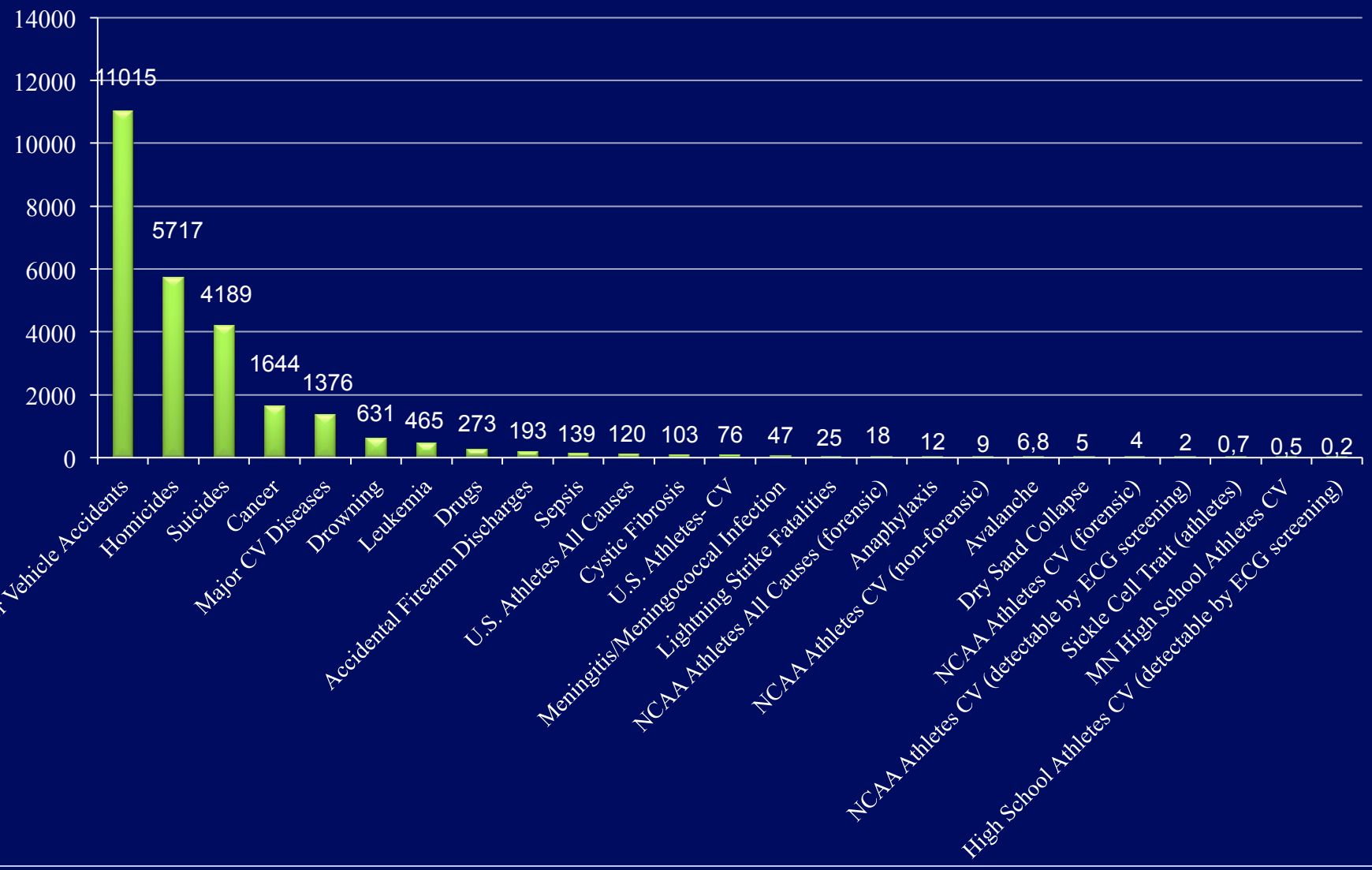
Doherty et al J Interv Card Electrophysiol (2013) 36:167–175

Annual Causes of Death in U.S. Population Age 1-21 (CDC)
79,000,000



(http://webappa.cdc.gov/sasweb/ncipc/leadcaus10.html)

Causes of Death in U.S. Population Age 1-25 (CDC)
90,000,000



(http://webappa.cdc.gov/sasweb/ncipc/leadcaus10.html)

U. S. Screening Strategy

The 14-Element AHA Recommendations for Pre-participation Cardiovascular Screening of Competitive Athletes

Medical history & Personal history

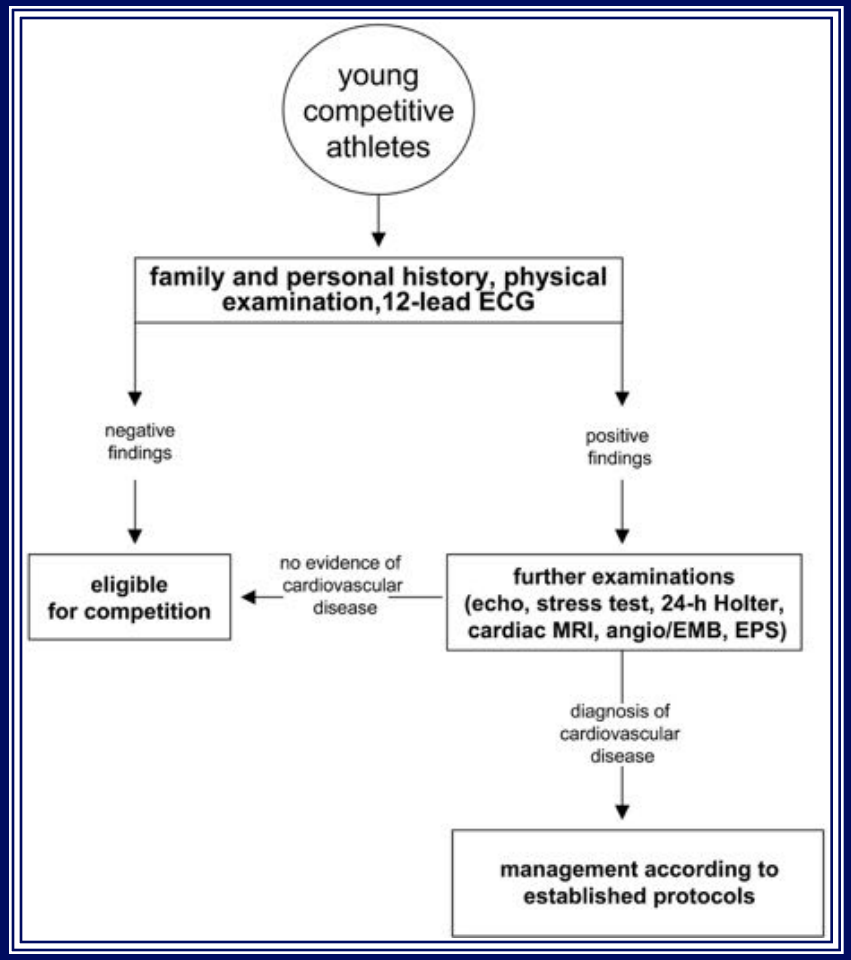
- 1. Chest pain/discomfort/tightness/pressure related to exertion
- 2. Unexplained syncope/near-syncope†
- 3. Excessive and unexplained dyspnea/fatigue or palpitations, associated with exercise
- 4. Prior recognition of a heart murmur
- 5. Elevated systemic blood pressure
- 6. Prior restriction from participation in sports
- 7. Prior testing for the heart, ordered by a physician
- Family history
- 8. Premature death (sudden and unexpected, or otherwise) before 50 y of age attributable to heart disease in ≥1 relative
- 9. Disability from heart disease in close relative <50 y of age
- 10. Hypertrophic or dilated cardiomyopathy, long-QT syndrome, or other, or clinically significant arrhythmias;

Physical examination

- 11. Heart murmur
- 12. Femoral pulses to exclude aortic coarctation
- 13. Physical stigmata of Marfan syndrome
- 14. Brachial artery blood pressure (sitting position)§

Maron et al *Circulation*. 2014;130:1303-1334.)

Italian/European Screening Strategy



Corrado, D. et al. Eur Heart J 2005 26:516-524

Pre-particpation athletic screening and athletic restriction in Italy, the United States and Israel

Country	Years	Screening	Initial	Examiner	Death
Italy 	1981-2008	Mandatory	History, PE, ECG ETT, Echo	Sports Medicine MD	Decreased
United States 	1985-2006	Recommended	History, PE	MD Non-MD	No decrease
Israel 	1985-2009	Mandatory	History, PE, ECG, ETT, Echo	Certified MD	No decrease

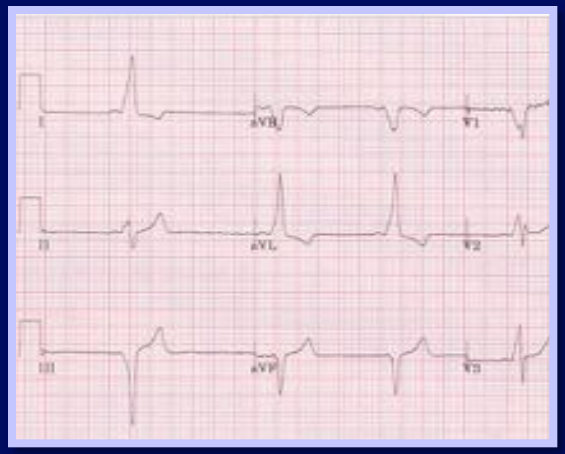
American Reaction To the Italian/European Guidelines

- ESC Sports Cardiology Study Group recommend systematic pre-participation screening for young competitive athletes with personal and family history, physical exam, and 12 lead ECG in the Italian mode
- This strategy has not been translated on a national basis to other countries other than Israel
- A recent NIH/NHLBI position paper did not support mass screening of young athletes (< 40 year old) with ECGs concluding that insufficient evidence was currently available
- The group recommended pilot screening studies in target populations

Maron et al *Circulation*. 2014;130:1303-1334.

Screening tests in young athletes

Currently in use
Cheap
Nondiagnositic
Poor sensitivity
Poor specificity



Useful for electrical diseases
Suggestive for some CVD
Relatively cheap
Moderate sensitivity
Moderate to high specificity
Low PPV

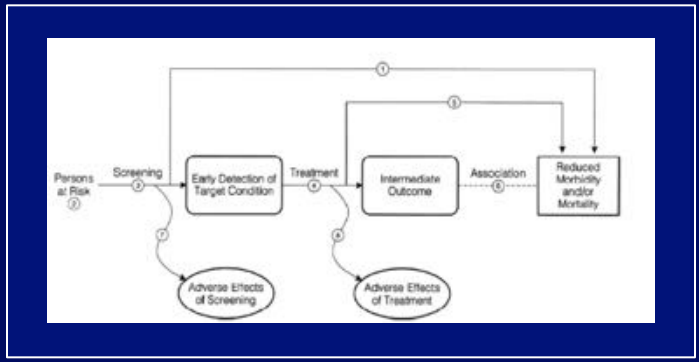
Useful for structural CVD
Misses electrical disease
Expensive
Poor sensitivity
High specificity

Slide courtesy of : Kaltman J, MD Chief, Heart Development and Structural Diseases Branch National Heart, Lung, and Blood Institute

Kaltman J et al .Screening for Sudden Cardiac Death in the Young: Report From a National Heart, Lung *C*irculation. 2011;123:1911-1918

U.S. Preventive Services Task Force's Analytic Framework Screening

(1)Evidence - screening reduces morbidity and/or mortality?
(2) Disease prevalence?
(3) Sensitivity and specificity of the test?
Is there significant variation between examiners in how the test is performed?
(4) Does treatment reduce the incidence of the intermediate outcome?
How do the efficacy and effectiveness of treatments compare in community settings?
(5) Does treatment improve health outcomes for people diagnosed clinically?
Do people diagnosed by screening to have even better outcomes than those diagnosed clinically?
(6) Is the intermediate outcome reliably associated with reduced morbidity and/or mortality?
(7) Does screening result in adverse effects? Is the test acceptable to patients?
What are the potential harms, and how often do they occur?
(8) Does treatment result in adverse effects?

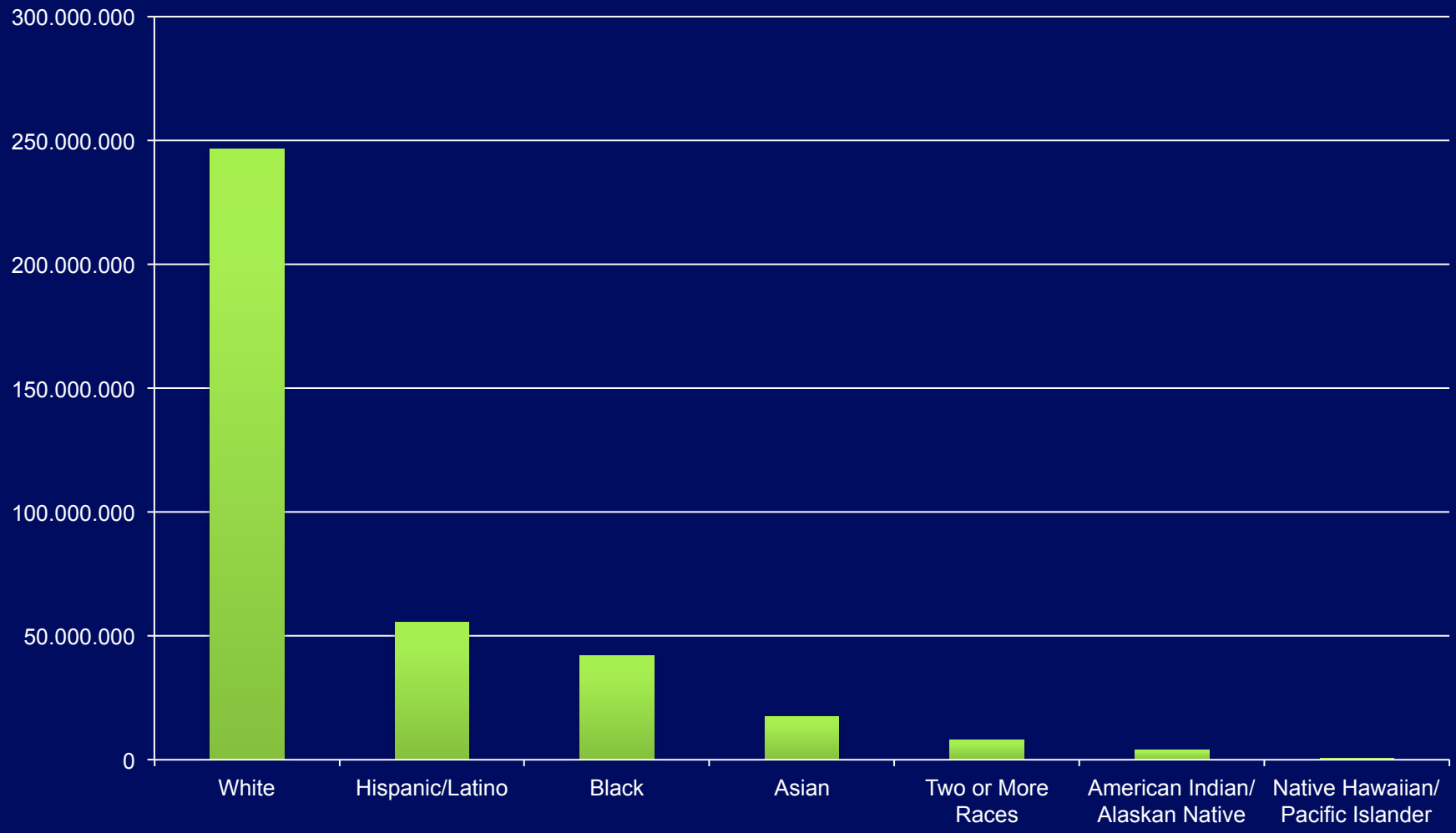


Screening for Sudden Cardiac Death in the Young **:** NIH Study Group. *2011;123:1911-1918*

U.S. Screening Gaps in Knowledge

- Precise frequency of SCD in athletes and non-athletes
  Numerator/Demoninator
- Pre-participating screening strategies
  Effectiveness, Predictive Accuracy, Cost
- Athletic restriction
  Effectiveness, Predictive Accuracy, Cost
- The ongoing debate related to screening persists because of:
  Knowledge gaps
  Absence of RCTs

2014 Estimated Total U.S. Population: 318,857,056



(http://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?src=bkmk)

Prevalence of Electrocardiographic Anomalies in Young Individuals- Relevance to Nationwide Cardiac Screening Program

Prevalence of Electrocardiographic Anomalies in Young Individuals

Relevance to a Nationwide Cardiac Screening Program

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Objectives This study sought to investigate the prevalence of potentially abnormal electrocardiographic (ECG) patterns in young individuals to assess the implications for a nationwide screening program for conditions causing sudden cardiac death (SCD).

Background The Italian experience suggests that pre-participation screening with ECG reduces the incidence of SCD in athletes. However, the majority of SCDs occur in nonathletes. In the United Kingdom, screening for cardiac disorders is confined to symptomatic individuals or those with a family history of inherited cardiac conditions or premature cardiac death.

Methods Between 2008 and 2012, 7,764 nonathletes ages 14 to 35 years underwent ECG screening. Electrocardiograms were analyzed for group 1 (training-related) and group 2 (potentially pathological) patterns presented in the 2010 European Society of Cardiology position paper, which advocates further evaluation for individuals with group 2 ECG patterns. Results were compared with 4,081 athletes.

Results Group 1 patterns occurred in 49.1% of nonathletes and 87.4% of athletes ($p < 0.001$). Group 2 patterns occurred in 21.8% of nonathletes and 33% of athletes ($p < 0.001$). In nonathletes, QTc interval abnormalities comprised the majority (52%) of group 2 changes, whereas T-wave inversions constituted 11%. Male sex and African/Afro-Caribbean ethnicity demonstrated the strongest association with group 2 ECG patterns.

Conclusions The study demonstrates that 1 in 5 young people have group 2 ECG patterns. The low incidence of SCD in young people suggests that in most instances such patterns are non-specific. These findings have significant implications on the feasibility and cost-effectiveness of nationwide screening programs for cardiovascular disease in young nonathletes and athletes alike, on the basis of current guidelines. (J Am Coll Cardiol 2014;63:2028–34)

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Chandra J Am Coll Cardiol 2014;63:2028–34

Prevalence of Electrocardiographic Anomalies in Young Individuals- Relevance to Nationwide Cardiac Screening Program

Table 1 European Society of Cardiology Classification of Changes of the Athlete's Electrocardiogram

Group 1: Common and Training-Related ECG Changes	Group 2: Uncommon and Training-Unrelated ECG Changes
Sinus bradycardia	T-wave inversion
First-degree AV block	ST-segment depression
Incomplete RBBB	Pathological Q-waves
ERI	LA enlargement
Isolated QRS voltage criteria for LVH	RA enlargement
	LAD
	RAD
	RVH
	Ventricular pre-excitation
	LBBB
	RBBB
	Long QTc interval (>440 ms, men; >460 ms, women)
	Short QTc interval (<360 ms)
	Brugada-like ER

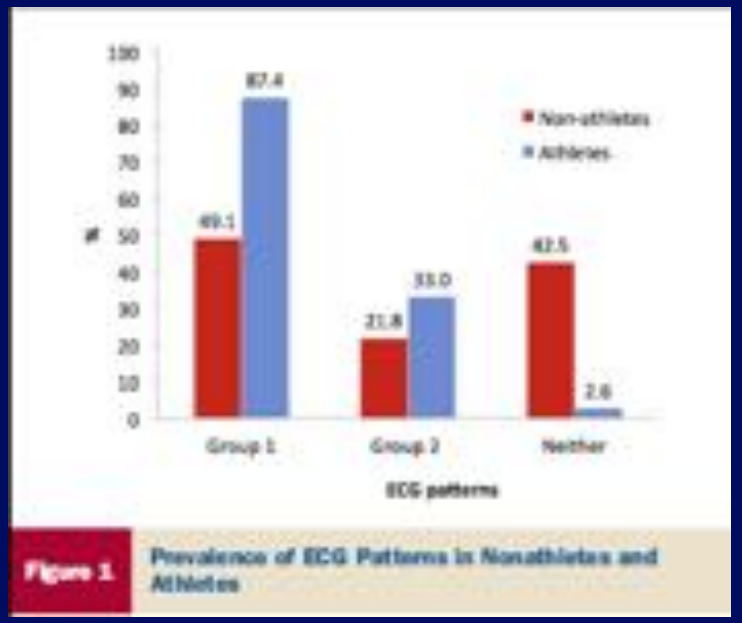


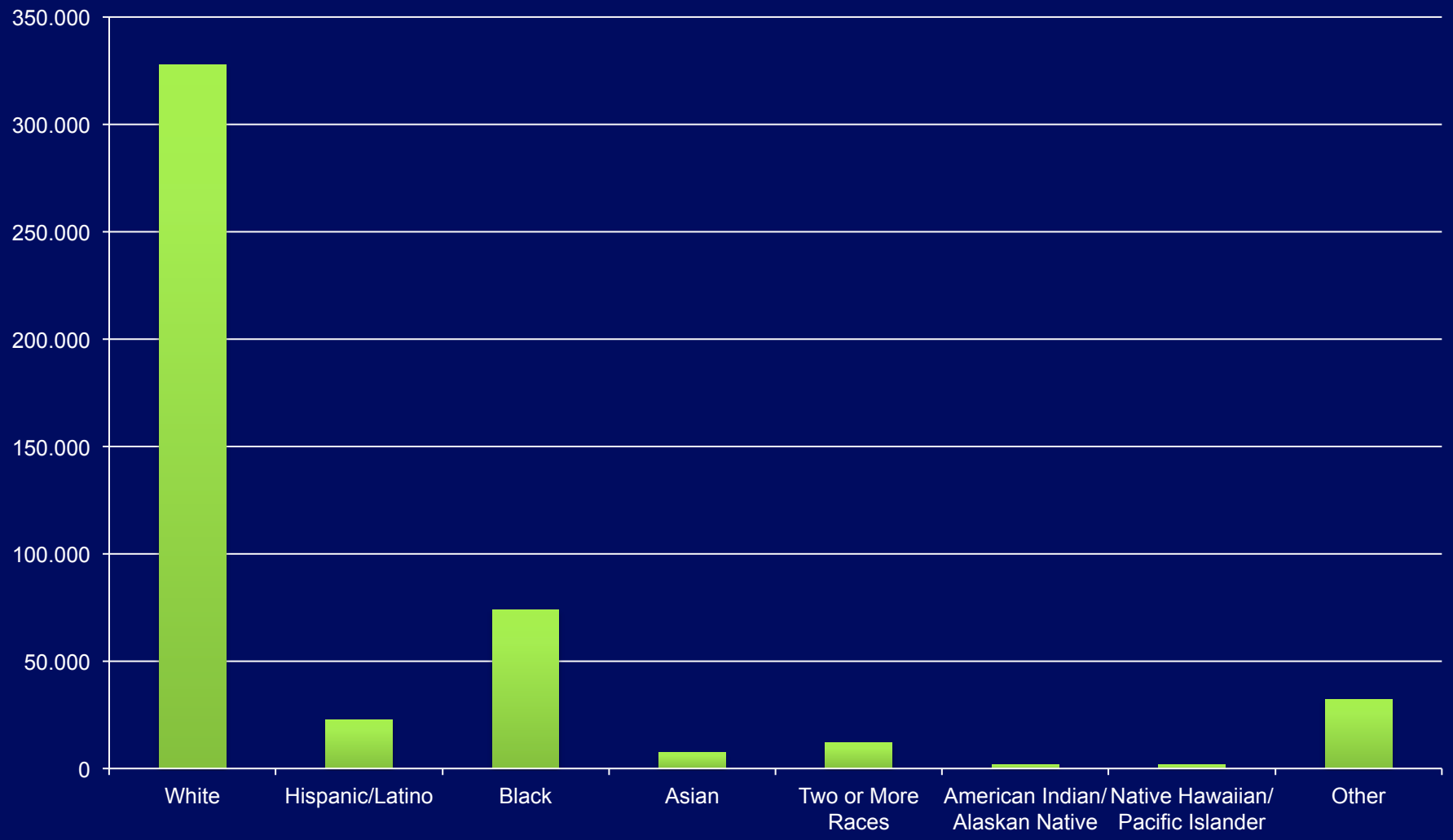
Figure 1 Prevalence of ECG Patterns in Nonathletes and Athletes

	Group 2 ECG		
	Black	Non Black	p
Non-athlete	29%	21%	<0.003
Athlete	58%	21%	<0.001

High prevalence Group 2 ECG changes

Chandra J Am Coll Cardiol 2014;63:2028–34

2014 NCAA Population: 479,475



(http://web1.ncaa.org/rgdSearch/exec/saSearch)

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Author	Year	Population	Cost/Life Year H&P ($)
Fuller	1999	Athletes	84,000
Quaguli	2006	Children	15000
Wheeler	2010	Athletes	28,000-17,000
Leslie	2012	Children	91,000-204,000
Schoen	2013	Athletes	69,000
Halkin*	2012	Athletes	179,000-240,000

*4,813 lives would be saved over a 20-year span of screening at a cost-per-life-saved of $10.6 to $14.4 million

Halkin A, et al "Preventing sudden death of athletes with electrocardiographic screening" *J Am Coll Cardiol* 2012; 60: 2271–2276

Fuller, C. M. (2000). Cost effectiveness analysis of screening of high school athletes for risk of sudden cardiac death. Medicine and Science in Sports and Exercise, 32(5), 887–890.

Quaglini, S., Rognoni, C., Spazzolini, C., Priori, S. G., Mannarino, S., & Schwartz, P. J. (2006). Cost-effectiveness of neonatal ECG screening for the long QT syndrome [Research Support, Non-U.S. Gov't]. European Heart Journal, 27(15), 1824–1832.

Wheeler, M. T., Heidenreich, P. A., Froelicher, V. F., Hlatky, M. A., & Ashley, E. A. (2010). Cost-effectiveness of preparticipation screening for prevention of sudden cardiac death in young athletes. Annals of Internal Medicine, 152(5), 276–286.

Leslie, L. K., Cohen, J. T., Newburger, J. W., Alexander, M. E., Wong, J. B., Sherwin, E. D., et al. (2012). Costs and benefits of targeted screening for causes of sudden cardiac death in children and adolescents. Circulation, 125(21), 2621–2629.

Schoenbaum, M., Denchev, P., Vitiello, B., & Kaltman, J. R. (2012). Economic evaluation of strategies to reduce sudden cardiac death in young athletes. Pediatrics, 130(2), e380–e389.

American Reaction To the Italian/European Guidelines

- For screening protocol to be appropriate these conditions must be met:
  - + The condition being screened should have significant morbidity or mortality
  - ? The disease screened should have treatment that can effect it's outcome and not merely prematurely identify the inevitable
  - ? Treatment afforded by early detection produces superior results to the early treatment of symptomatic results
  - ± There must be a sufficiently high prevalence of the condition in the population to merit screening
  - − Sensitive and specific screening strategies must be identified
  - − The screening strategy must be cost effective

- Screening of athletes fails to meet the criteria necessary for a widespread screening as a public health strategy

Lynn LA Guidelines for Screening Tests: The American College of Physicians Hospital Physician 1993;45:29.
Katcher M Risk Profiling and Screening Strategies In Estes N Sudden Cardiac Death in the Athlete Futura 1998

American Reaction To the Italian/European Guidelines

- While intuitively appealing, screening programs have not yet been demonstrated to be effective in decreasing the risks inherent in athletics
- The Italian data provides the best evidence to date supporting the pre-participation screening of athletes
- There are many valuable lessons from the Italian experience useful in developing a rigorous, comprehensive registry to study the pre-participation screening process prospectively
- Based on the best available evidence pre-participation screening is effective in Italy but this strategy needs further study

American Reaction To the Italian/European Guidelines

- Cardiovascular pre-participation screening proposal is highly laudable, has the potential to save young lives, and merits further evaluation

- The principal US challenges:
  - Scientific
  - Demographic-Population diversity
  - Medical expertise
  - Screening infrastructure
  - Ethical
  - Legal
  - Economic

- Scientific perspective: the best approach is to assess the hypothesis that screening saves lives cost effectively with appropriately designed and while implementing PAD programs with AEDS

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Evidence Based Medicine

- A fundamental principle of evidence based medicine is that clinical practice should be based on a sound scientific foundation established by clinical studies.
- The level of evidence needed for adoption of new strategies should vary according to the clinical situation, and the higher the stakes, the better the evidence should be
- The stakes grow higher in proportion to the size of the affected population, the severity of the illness, the age of the population , and the risks and cost of the intervention
- The stakes are extremely high for pre-participation cardiovascular screening of athletes

Hlatky, MA , NEJM 2004;350;2126-2128