

Sudden Cardiac Death in Asians: Insights from the San Francisco **POST SCD** Study

8 October 2016

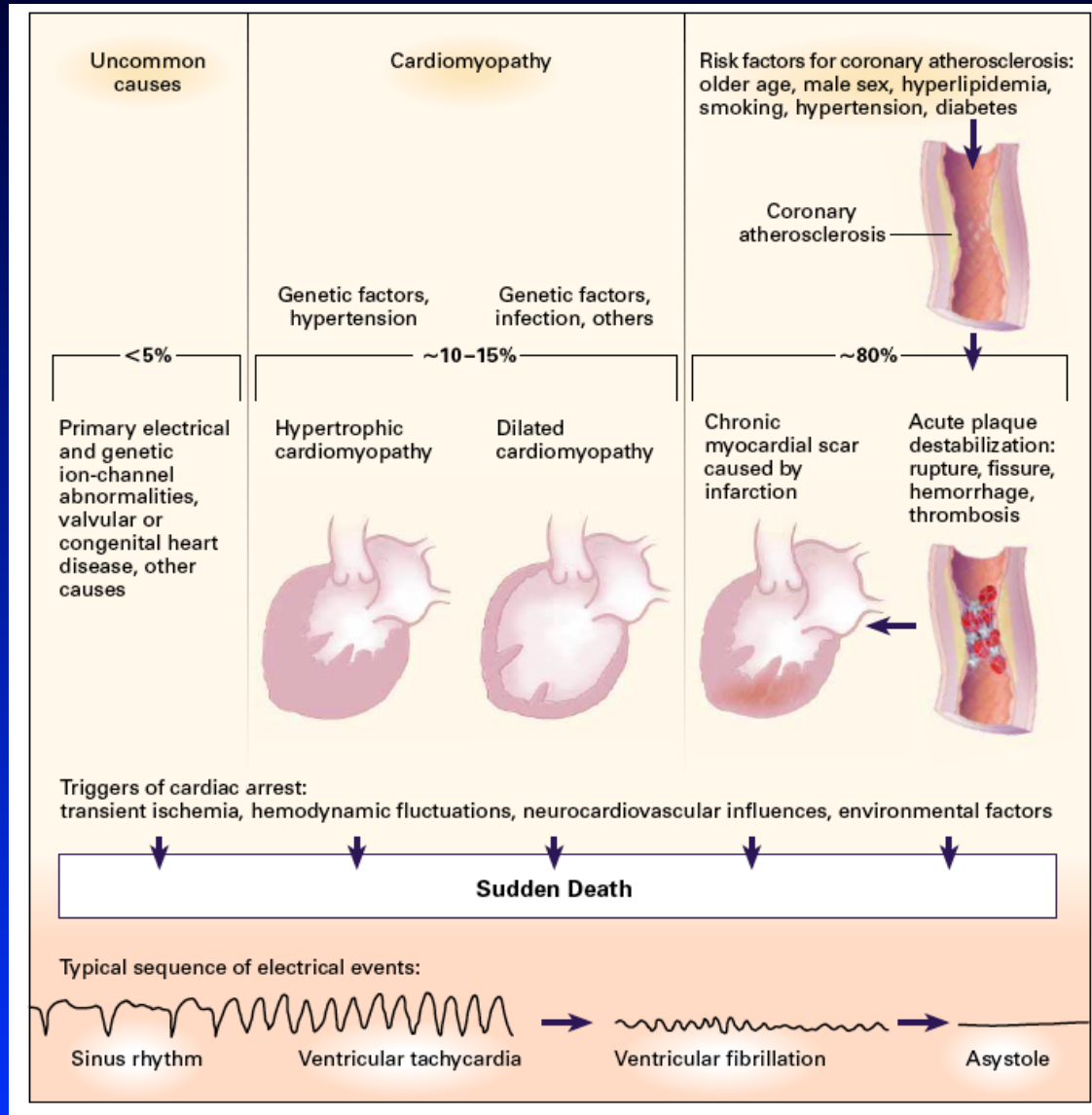
18th Conference on Healthcare of the Chinese in North
America

Zian H. Tseng, M.D., M.A.S.
Associate Professor of Medicine in Residence
Murray Davis Endowed Professor
Cardiac Electrophysiology Section
University of California, San Francisco

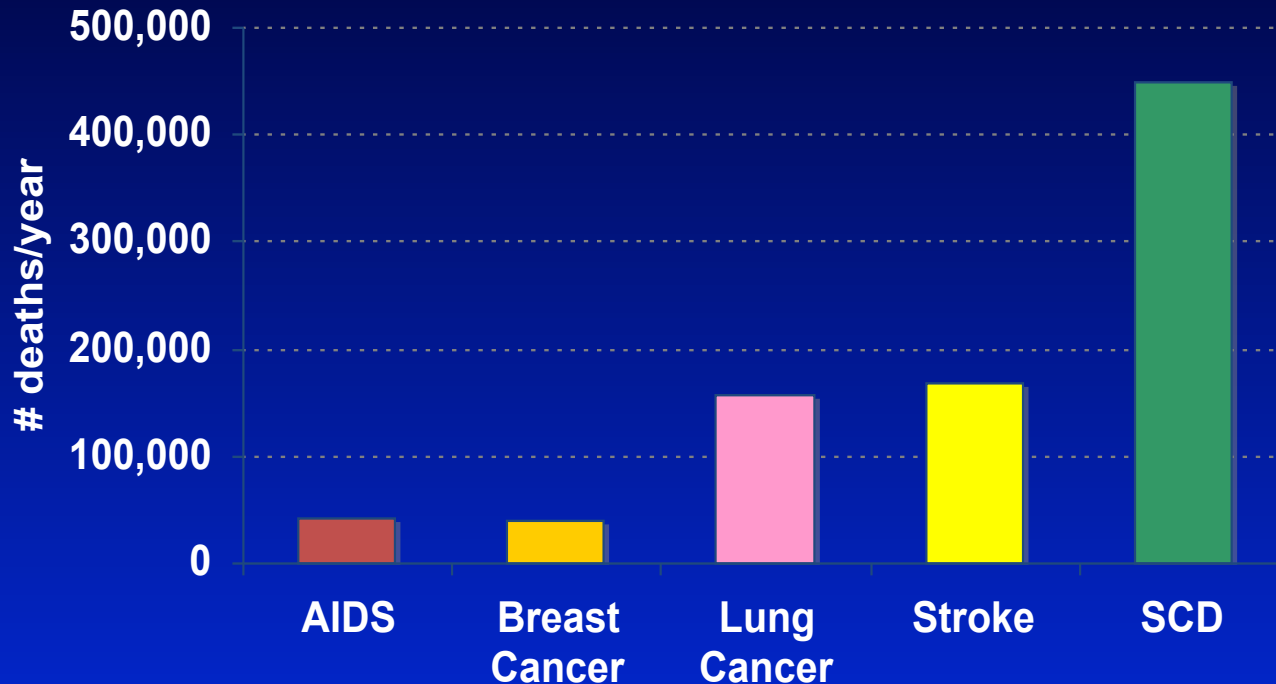
Disclosures

- Major
 - Research grant: R01 HL102090 (NIH / NHLBI)
 - Research grant: R01 HL126555 (NIH / NHLBI)
 - Research grant: DP14-1403 (CDC)
 - Research grant: R24 A1067039 (NIH)
- Minor
 - Honorarium: Biotronik

Etiology of Sudden Cardiac Death



Magnitude of Sudden Cardiac Death in the U.S.



¹ U.S. Census Bureau, *Statistical Abstract of the United States: 2001*.

² American Cancer Society, Inc., *Surveillance Research, Cancer Facts and Figures 2001*.

³ *2002 Heart and Stroke Statistical Update*, American Heart Association.

⁴ *Circulation*. 2001;104:2158-2163.

Sudden Cardiac Death: Definitions

ACC/AHA/HRS, 2006:

“SCA is the **sudden cessation of cardiac activity** so that the victim becomes **unresponsive**, with no normal breathing and no signs of circulation. If corrective measures are not taken rapidly, this condition **progresses to sudden cardiac death.**”

Sudden Cardiac Death: Definitions

- **VALIANT trial: Valsartan after acute MI and HF**
 - “The cause of death was considered as SCD if death occurred suddenly and unexpectedly in a patient in otherwise stable condition, with no premonitory HF, MI, or another clear cause of death. These could have been witnessed deaths (with or without documentation of arrhythmias) or unwitnessed deaths if the patient had been seen within 24 hours before death.”
- **MERIT-HF trial: Metoprolol for Heart Failure**
 - “SCD: Witnessed instantaneous death in the absence of progressive circulatory failure lasting for 60 min or more, unwitnessed death in the absence of pre-existence progressive circulatory failure or other causes of death”

Sudden Cardiac Death: Definitions

World Health Organization (WHO), 1969:

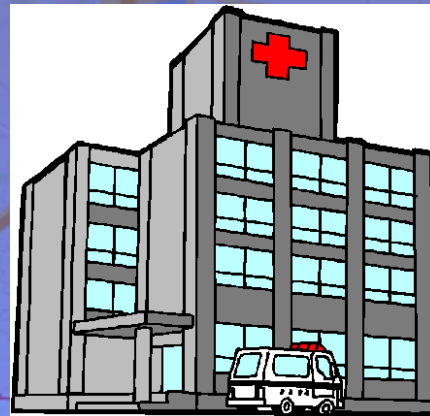
- Unexpected death within 1 h of symptom onset if witnessed
 - Unexpected death within 24 h of having been observed alive and sx-free if unwitnessed
-
- Out-of-hospital
 - Presumed sudden pulseless condition
 - Absence of obvious noncardiac condition

Methodological Issues in Population Studies of SCD

- Estimates in the US range from 184,000-450,000 annually due to subjective/inconsistent methods of data collection
 - Most data predates modern era of PPCI, statins, etc
 - Derived from homogenous populations
- Where does the data come from?
 - Death record review of listed COD
 - Retrospective review of paramedic/ER narratives
 - Incomplete medical records
- Which definition should we use for SCD?
 - WHO (Hinkle-Thaler) criteria?
 - Documented VF?
 - Witnessed cases only?

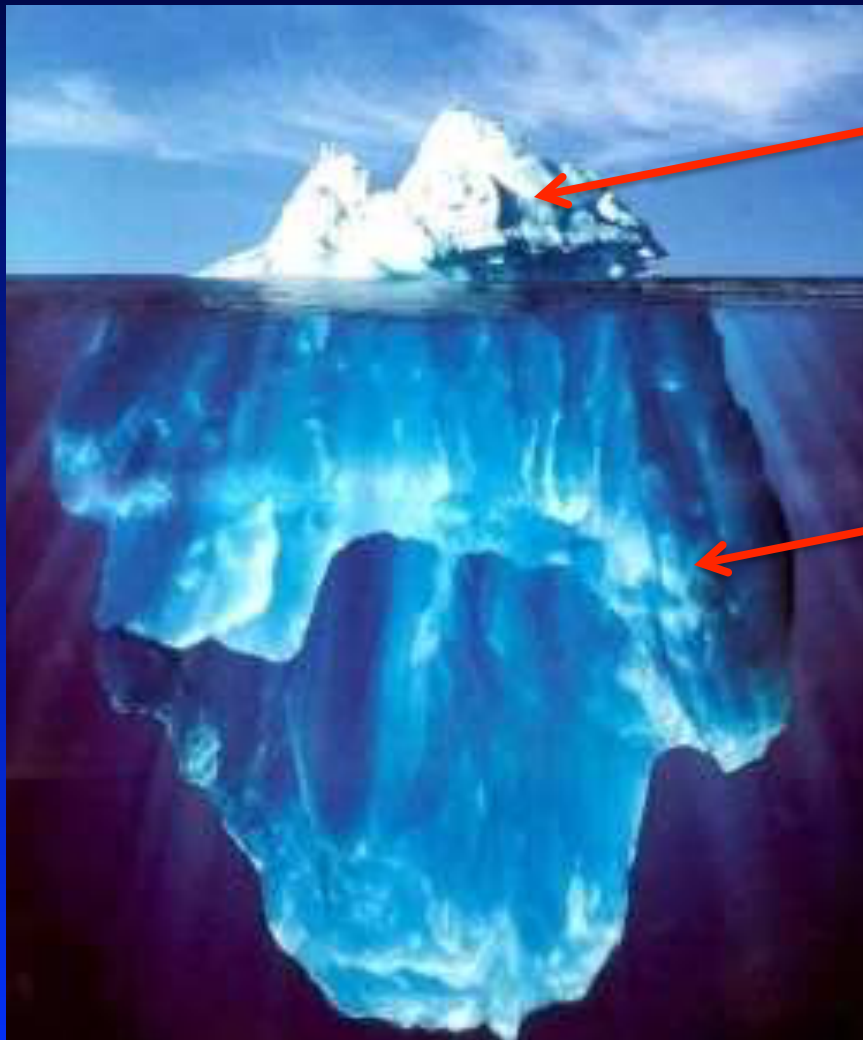
Comprehensive Surveillance of SCD

- Oregon—SUDS (Chugh, JACC, 2004)
 - WHO criteria
 - Portland, OR: population 1,000,000
 - Track dozens of ambulance companies and area hospitals
 - Review of all available records
 - **SCA+SCD: 53/100,000**



Autopsy rate: 11%

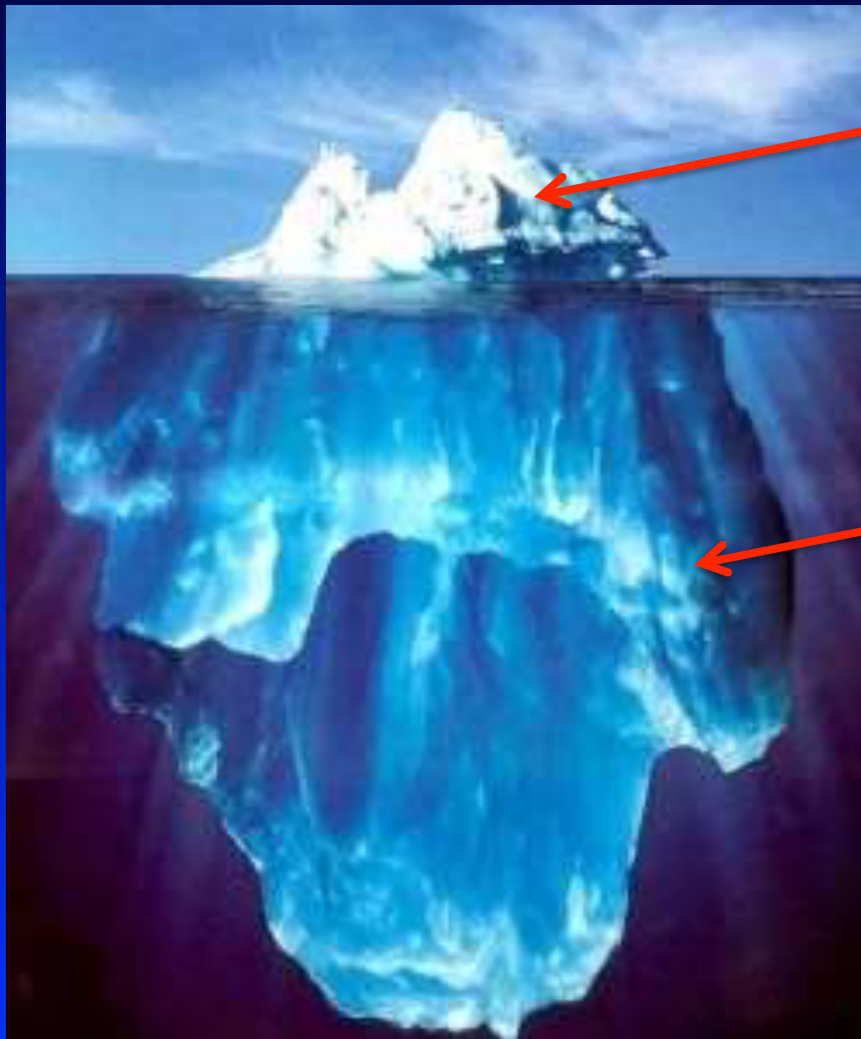
Sudden Cardiac Arrest vs. Sudden Cardiac Death



SCA

SCD

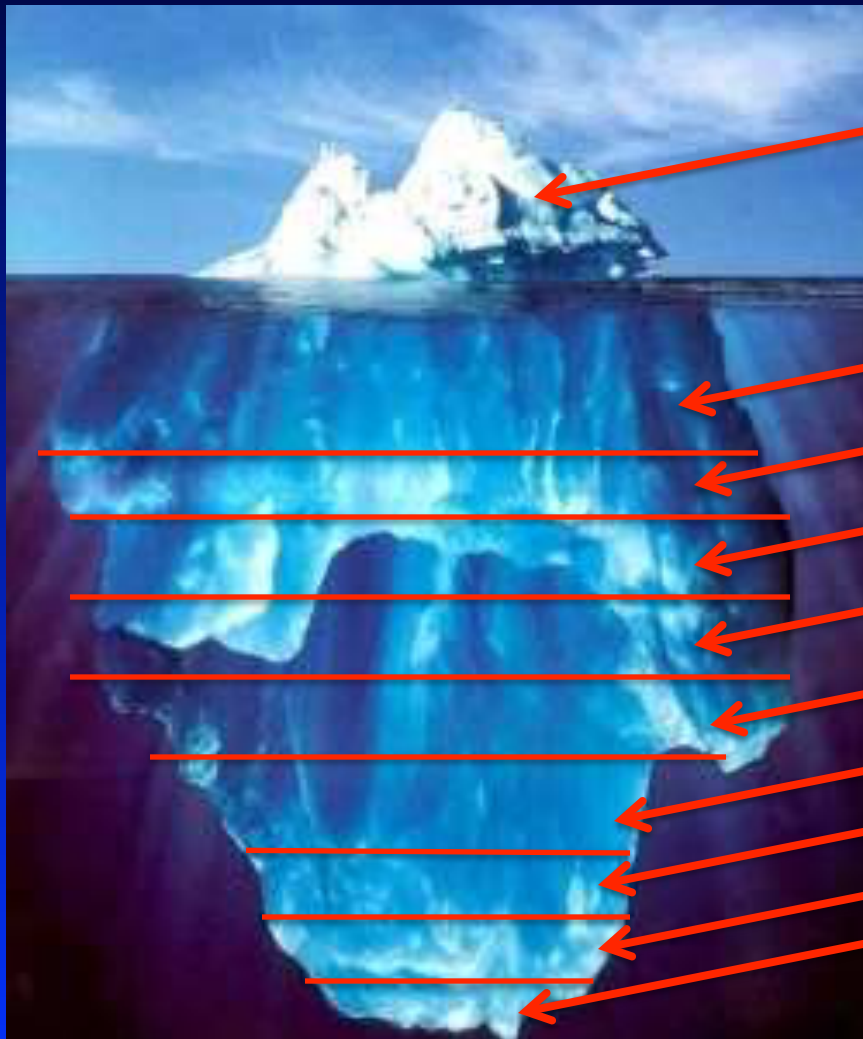
Sudden Cardiac Arrest vs. Sudden Cardiac Death



SCA

SCD?

Sudden "Cardiac" Death



SCA

CAD

Tamponade

Valvular

Neurologic

DCM

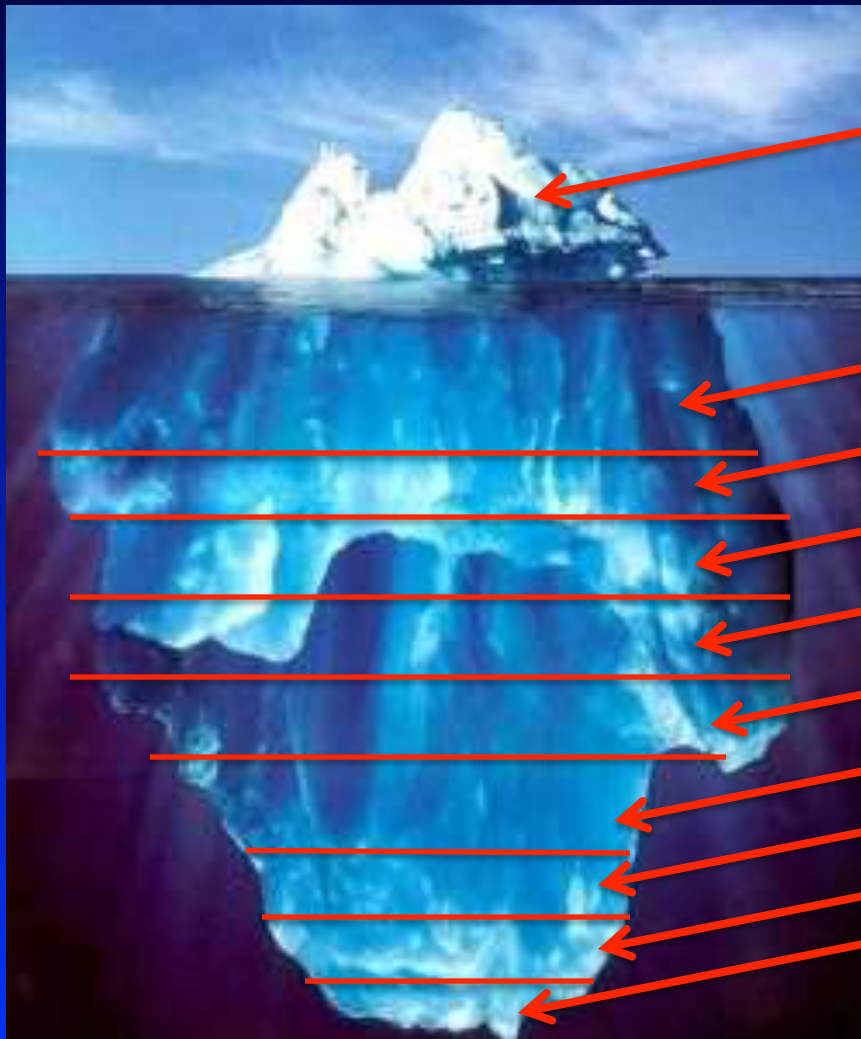
HCM

Ao Dissection

Hemorrhage

1° electrical disease

Sudden Arrhythmic Death



SCA

CAD

Tamponade

Valvular

Neurologic

DCM

HCM

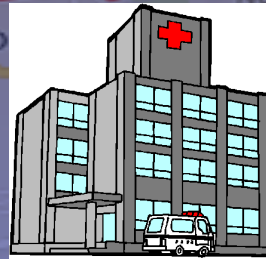
Hemorrhage

Ao Dissection

1° electrical disease

San Francisco **POST SCD** Study

Postmortem Systematic InvesTigation of Sudden Cardiac Death



All out of hospital and ER deaths reported
by law to ME

Every Incident
SCD
2011-

San Francisco

SF Medical Examiner



UCSF Cardiology

Study Design

1. Complete capture of all OOH SCDs for accurate population incidence
 - Single surveillance source, County ME, to which all OOH deaths are reported by law
 - SF DPH death certificate cross-check to confirm complete capture
2. Comprehensive autopsy of all SCDs to refine to arrhythmic deaths
 - Cranial vault, cardiac mass, LV measurements, Coronary vessels sectioned every 5mm, histology
3. Prediction model to help refine external registry SCDs to arrhythmic SDs
 - Future precision genotype-phenotype correlations within POST SCD cases
4. Identify pathologic correlates and predictors of arrhythmic SD

Case Adjudication

IRBs with all county hospitals

All outside medical records obtainable via medicolegal authority

- PMH (active problems, prescriptions, recent visits)
- Medications (e.g., QT-prolonging, methadone)
- Paramedic runsheets and rhythms
- Autopsy findings (including toxicology and histology)
- CIED interrogations if present

Adjudication panel



Dr. Phil Ursell
Chief Cardiac
Pathologist
UCSF



Dr. Ellen Moffatt
Medical Examiner,
City and County of
San Francisco



Dr. Zian H. Tseng
Study PI
Cardiac
Electrophysiologist,
UCSF



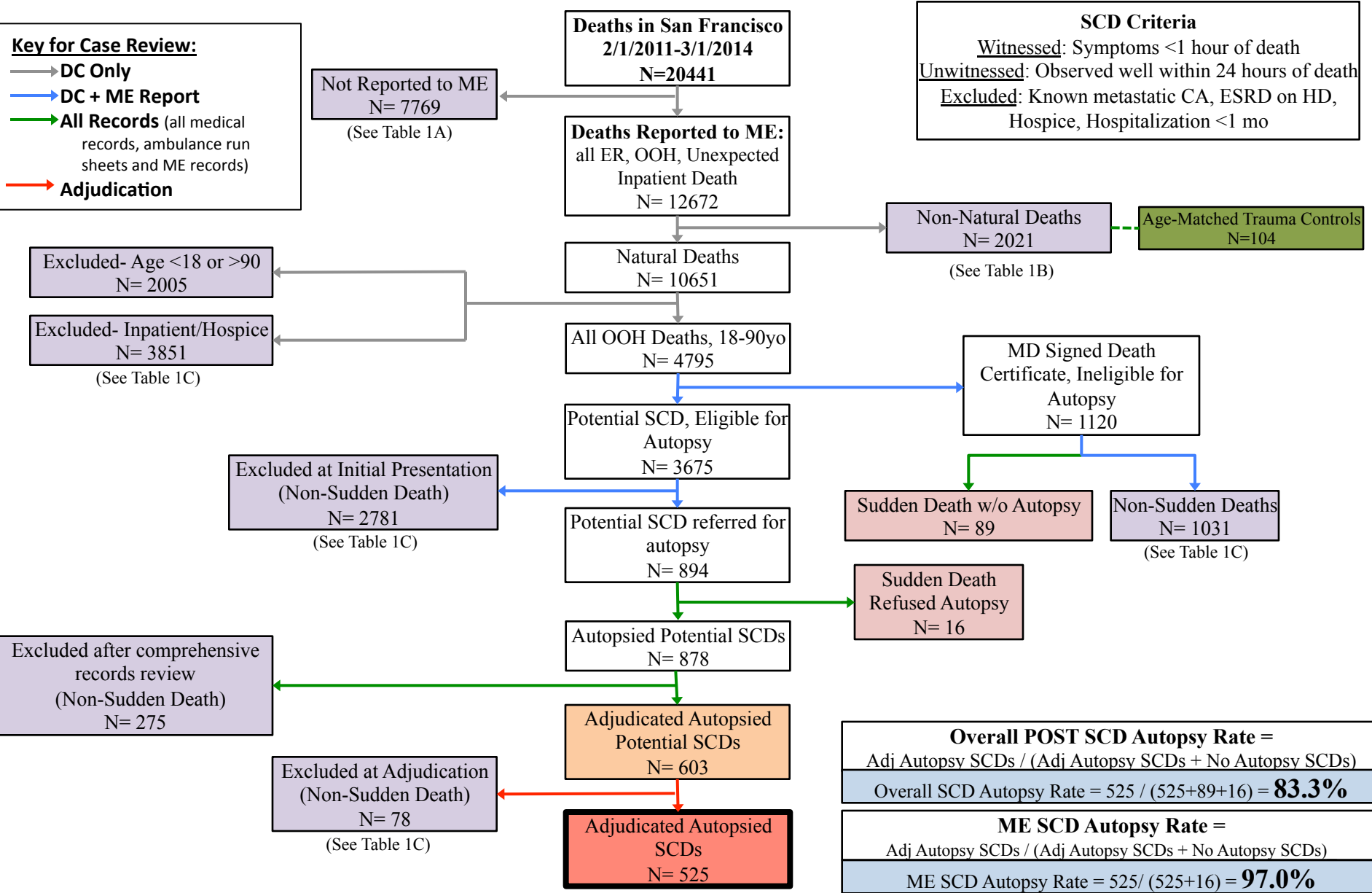
Dr. Jeff Olgin
Chief of Cardiology,
UCSF



Dr. Anthony Kim
Neurologist
Director of UCSF
Stroke Center

Key for Case Review:
 —→ DC Only
 —→ DC + ME Report
 —→ All Records (all medical records, ambulance run sheets and ME records)
 —→ Adjudication

SCD Criteria
Witnessed: Symptoms <1 hour of death
Unwitnessed: Observed well within 24 hours of death
Excluded: Known metastatic CA, ESRD on HD, Hospice, Hospitalization <1 mo



Overall POST SCD Autopsy Rate =
 $\text{Adj Autopsy SCDs} / (\text{Adj Autopsy SCDs} + \text{No Autopsy SCDs})$
 Overall SCD Autopsy Rate = $525 / (525+89+16) = \mathbf{83.3\%}$

ME SCD Autopsy Rate =
 $\text{Adj Autopsy SCDs} / (\text{Adj Autopsy SCDs} + \text{No Autopsy SCDs})$
 ME SCD Autopsy Rate = $525 / (525+16) = \mathbf{97.0\%}$

Table 1: Non-Sudden Deaths

Table 1: Non-Sudden Deaths	
<u>1A: Deaths not Reported to ME</u>	
	Total (%)
Inpatient Death	5462 (70.3%)
SNF/Hospice Death	2094 (27.0%)
Death OOH – Under Physician Care	197 (2.5%)
ER/OP Death – Under Physician Care	16 (0.2%)
<u>1B: Non-Natural Deaths</u>	
	Total (%)
Accidental Overdose	818 (40.5%)
Trauma Death	572 (28.3%)
Suicide	355 (17.6%)
Homicide	228 (11.3%)
Other Accidental Death	48 (2.4%)
<u>1C: Excluded Natural Deaths</u>	
	Total (%)
Nursing Home/Hospice	3861 (38.5%)
ES Disease/Metastatic CA	2249 (22.4%)
Age (<18, >90)	2012 (20.1%)
Non-sudden presentation (includes OD at scene)	1009 (10.1%)
Recent Complaints	427 (4.2%)
Recent Major Procedure/Hospitalization(<1month)	395 (3.9%)
DNR/Refused Treatment	39 (0.4%)
Arrested Out of County	29 (0.3%)

Table 2: Cause of Sudden Deaths without Autopsy

Table 2: Cause of Sudden Deaths without Autopsy	
<u>2A: Sudden Deaths without Autopsy</u>	
	Total (%)
Cardiac Causes	85 (95%)
Complications of Diabetes Mellitus	1 (1%)
Complications of Stroke	2 (2%)
Respiratory Failure	1 (1%)
<u>2B: Sudden Deaths Refused Autopsy</u>	
	Total (%)
Cardiac Causes	16 (100%)

POST SCD Demographics

	SCD with Autopsy	SCD without Autopsy	p* SCD with Autopsy vs. without Autopsy	SF Adult Population 2011	US Adult Population 2011
N	525	105	-	690,689	232,556,019
Age, mean ±SD	62.8 ± 14.5	73.1 ± 11.6	0	-	-
	18-90	37-89	-	-	-
Male, n (%)	362 (69%)	74 (70%)	0.82	350,179 (51%)	112,848,136 (49%)
Race (%)					
White	279 (53%)	44 (42%)		290,089 (42%)	149,300,964 (64%)
Black	81 (15%)	8 (8%)		40,751 (6%)	28,371,834 (12%)
Hispanic	40 (8%)	8 (8%)	0.001	102,913 (15%)	37,441,519 (16%)
Asian	110 (21%)	37 (35%)		232,762 (34%)	11,395,245 (5%)
Other	15 (3%)	8 (8%)		24,174 (3%)	6,046,457 (3%)
<i>Median Income</i>					
Tertile 1	248 (50%)	43 (45%)		266,642 (39%)	184,288,905 (79%)
Tertile 2	82 (16%)	14 (13%)	0.3446	230,900 (33%)	16,631,720 (7%)
Tertile 3	171 (34%)	43 (42%)		193,147 (28%)	31,635,394 (14%)

- for age, t-test assuming unequal variance; for categorical, Fisher's exact test
- Population data from American Community Survey 2011

SCD Case Study #1

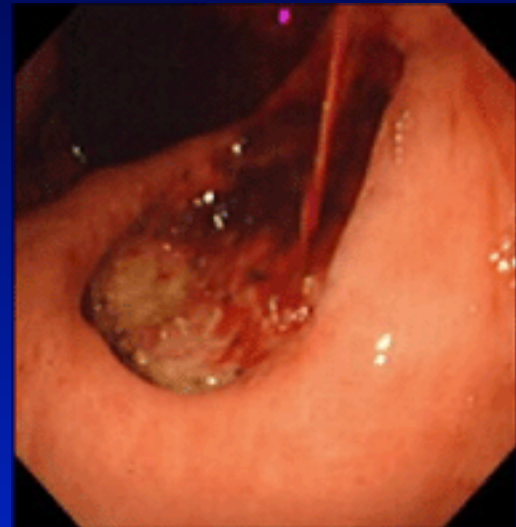
- 74 yo Filipino gentleman
 - 4 V CABG 2002
 - EF 22%, fixed defect anterior, inferior walls
 - Diabetes
- Admitted for fever and bronchitis, receiving IV antibiotics
- Troponin negative, slightly fluid overloaded
- Called to consult on several asymptomatic runs of NSVT (5-7 beats) and to consider primary prevention ICD

SCD Case Study #1

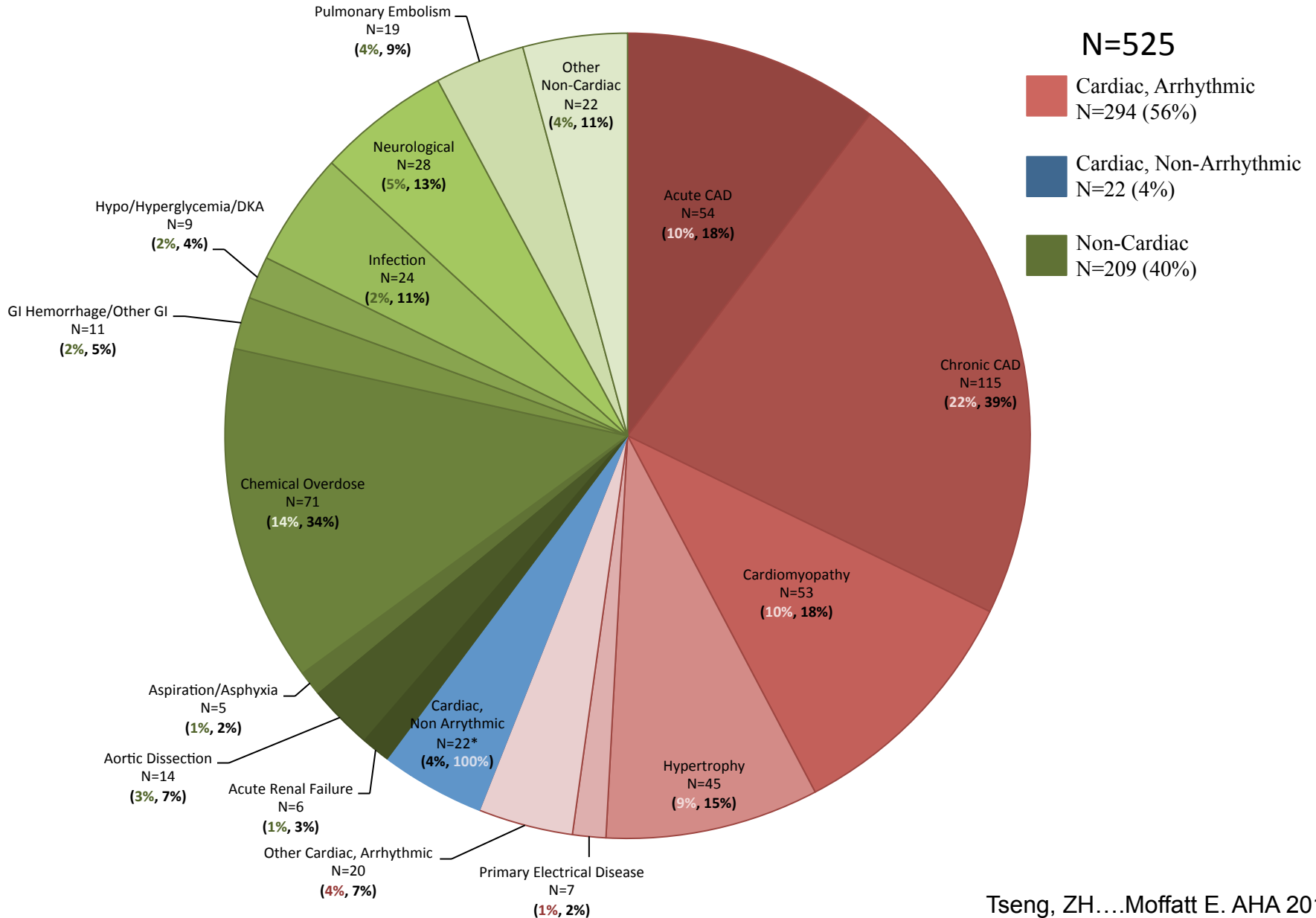
- Recommended uptitration of β blocker, ICD implant as an outpatient after completing antibiotic treatment
- ICD scheduled for 1 month after discharge
- 2 weeks later patient found dead in the morning by wife
- Pt had returned to usual state of health, no complaints the night before

“Non-Cardiac SCD”

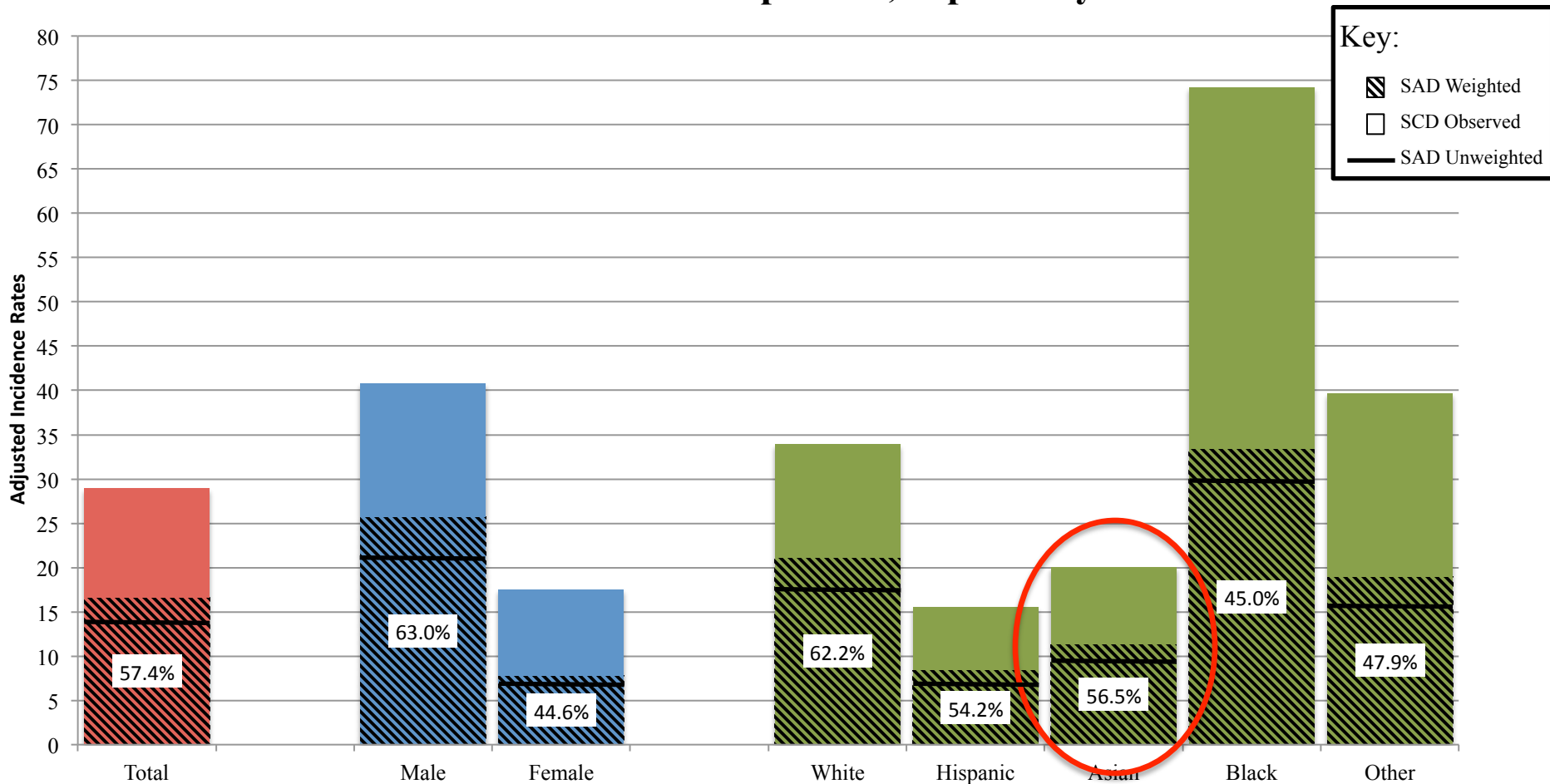
- Referring MD
- At autopsy, 2.5 L fresh blood in stomach and duodenum
- Heart: no acute coronary lesions
- Cause of death: exsanguination
- ICD would not have prevented SCD, pt may not have survived procedure



Adjudicated Etiologies of SCD: 56% Arrhythmic



SCD and SAD Event Rates per 100,00 person-years

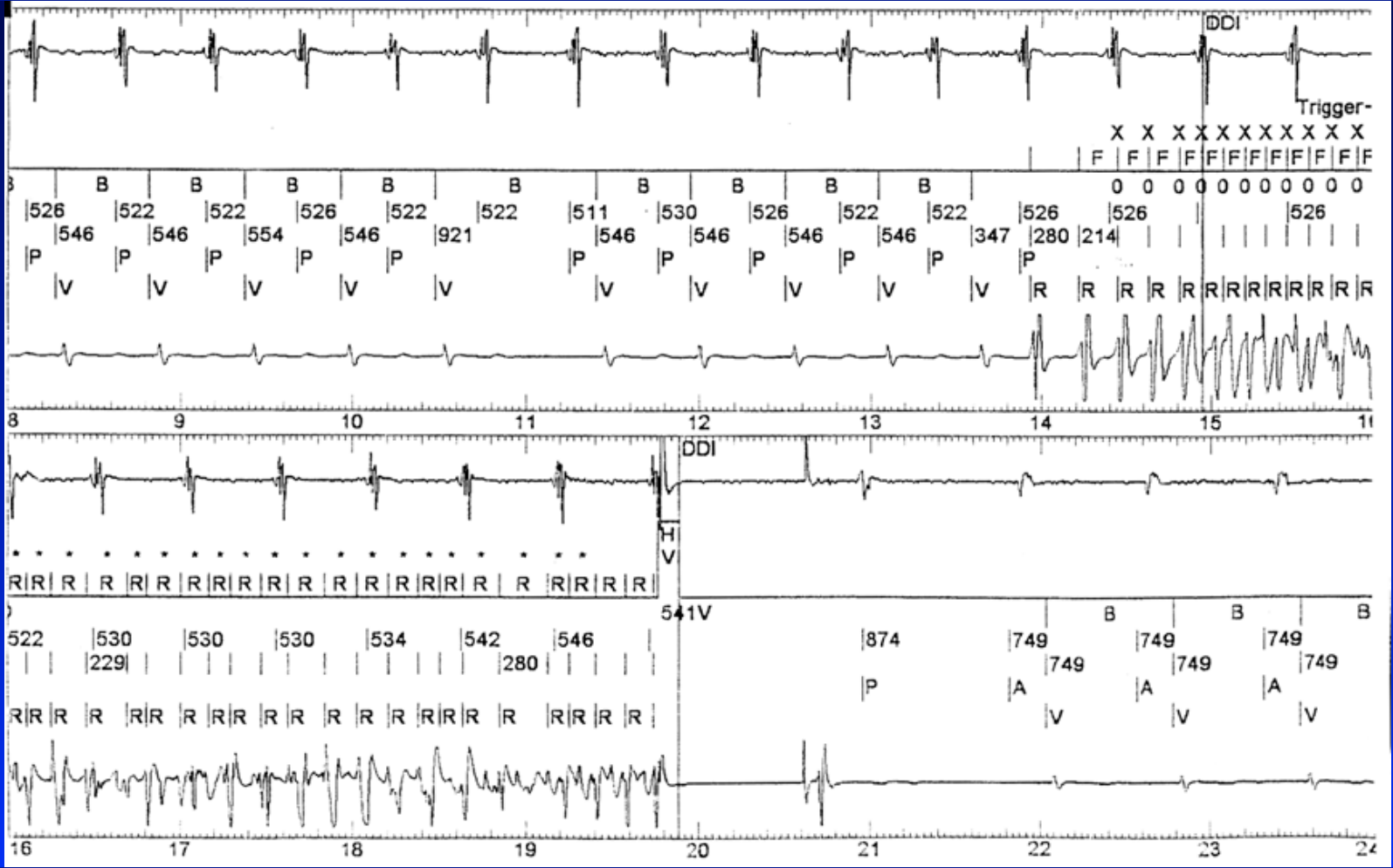


	All SCD		Weighted SAD	
	IRR	P-value	IRR	P-value
Male vs. Female	2.4	<0.00005	3.37	<0.00005
Hispanic vs. White	0.46	<0.00005	0.39	<0.00005
Asian vs. White	0.55	0.002	0.49	0.0007
Black vs. White	2.15	0.0006	1.54	0.093
Other vs. White	1.13	0.28	0.86	0.51

SCD Case Study #2

- 78 yo Chinese man
 - Dilated cardiomyopathy, stable EF 25%
 - Paroxysmal AF
 - Primary prevention ICD implanted 3 years ago, no shocks
- In usual state of health when wife went shopping
- 3 hours later wife found him unresponsive
- Paramedics called, asystole on arrival, no resuscitation attempted

ICD Interrogation



x 30

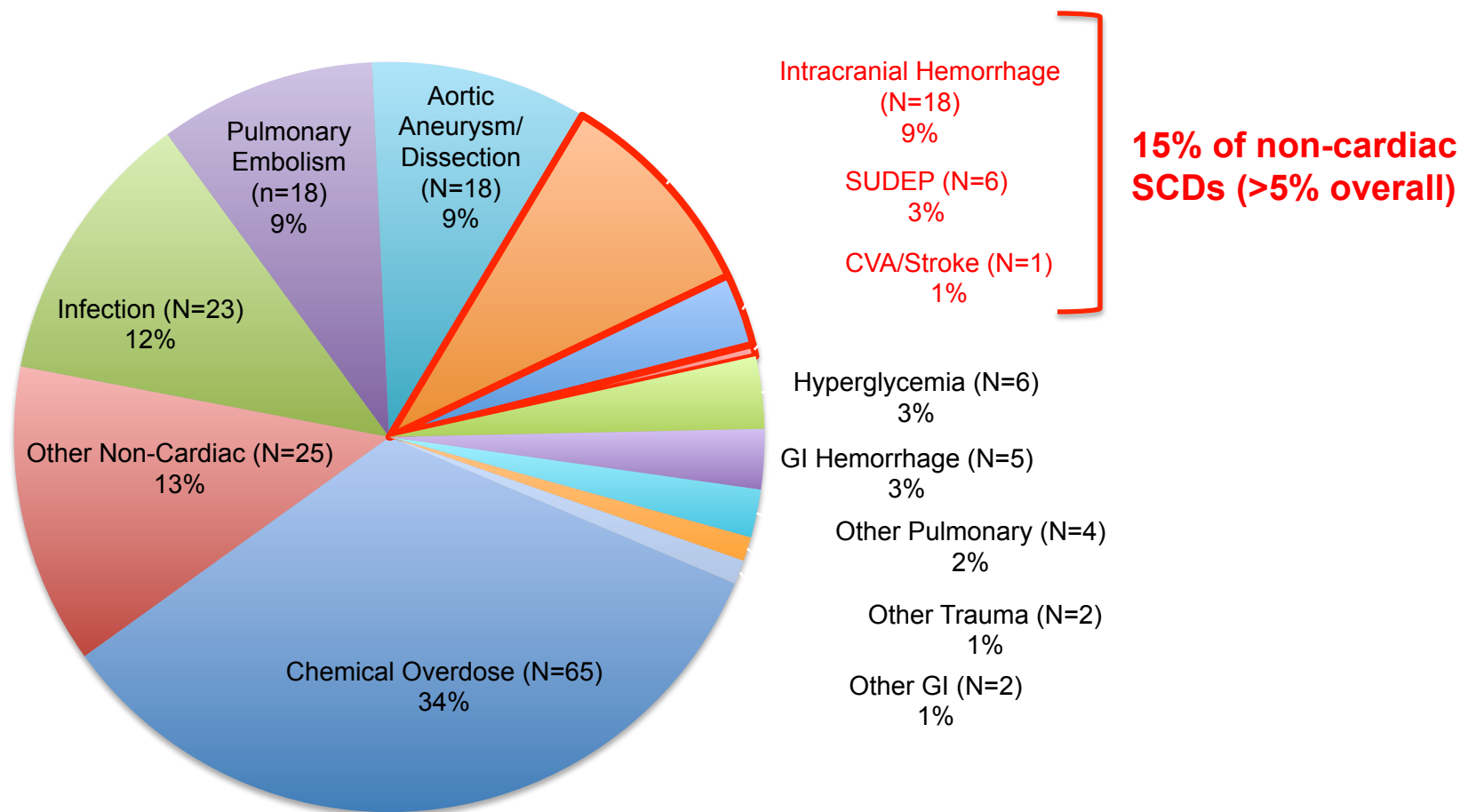
VF ≠ Sudden Arrhythmic Death

- At autopsy
 - Massive subarachnoid hemorrhage (requires perfusing rhythm)
 - Heart 760 g
- Neurocardiogenic injury
 - VF due to acute adrenergic surge
- Despite rhythm documentation of VF, cause of death was neurologic



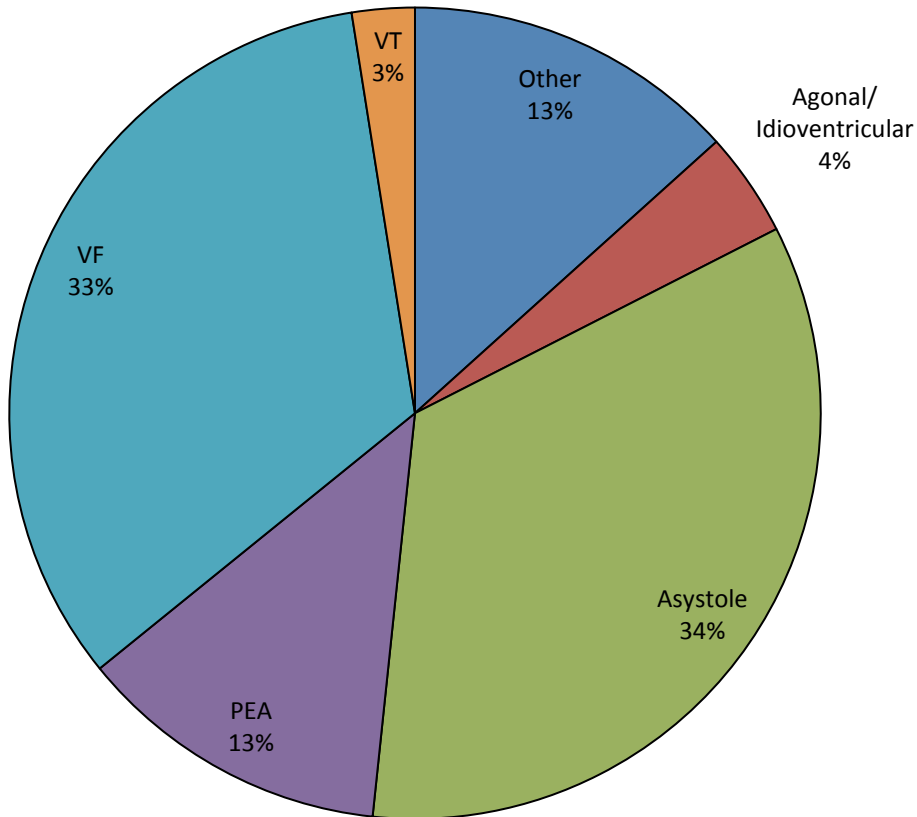
Sudden Neurologic Death

15% of Non-Cardiac Causes

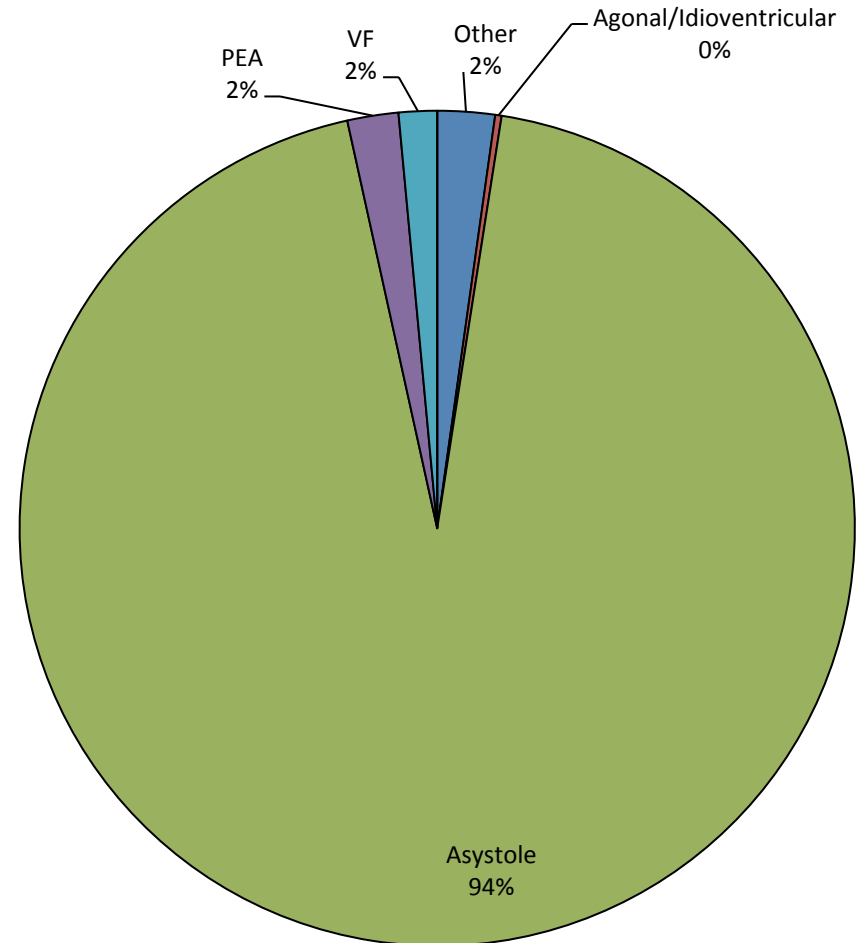


Presenting Rhythms at EMS Arrival: Witnessed and Unwitnessed SCDs

**Witnessed
N=120**



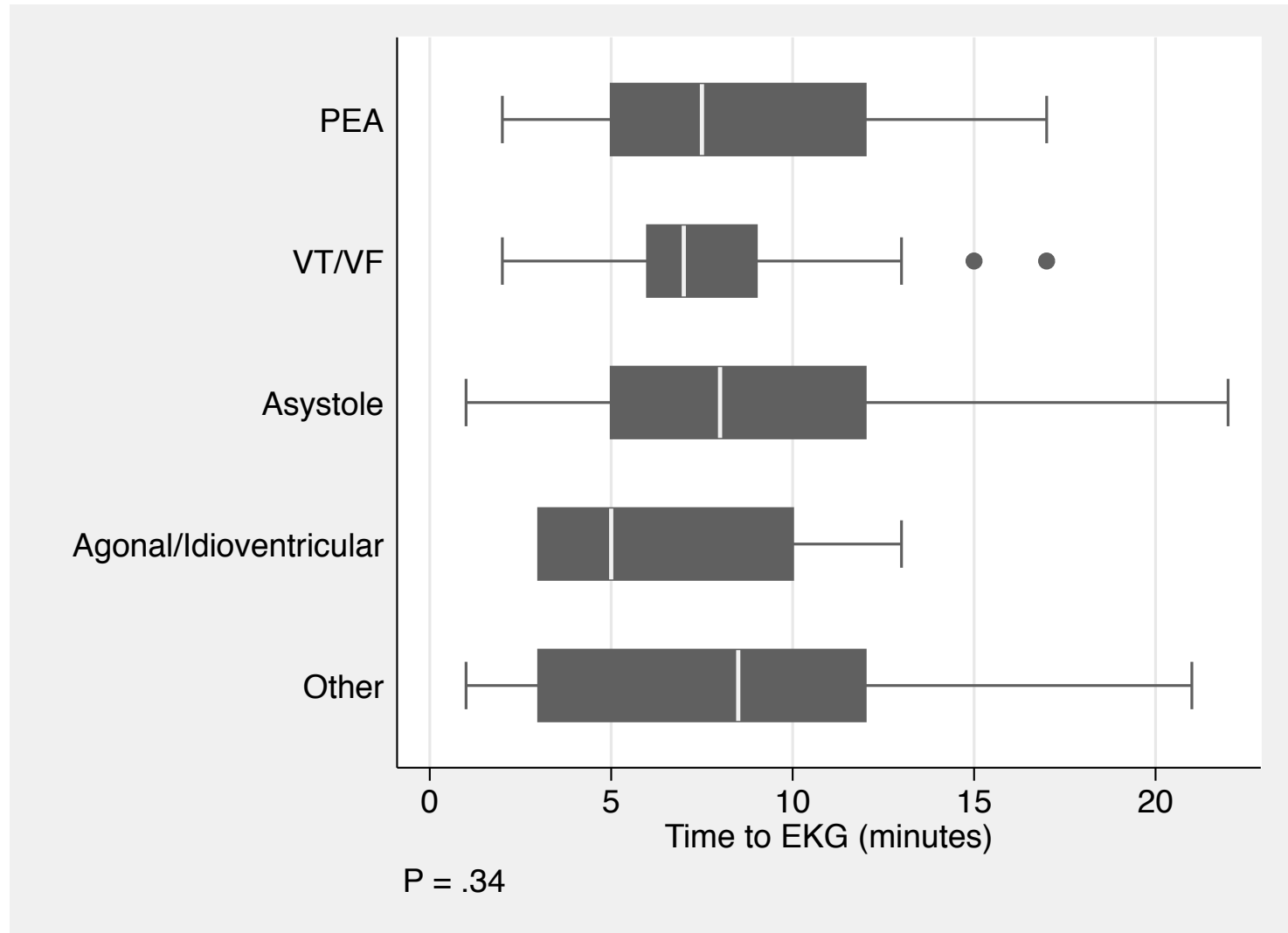
**Unwitnessed
N=405**



*Other: NSR (STEMI), AF/L (STEMI), Sinus Brady (STEMI and NSTEMI)

Time from Arrest to Initial Rhythm

Collapsed and Trimmed *witnessed cases only



COD by Initial Rhythm

Witnessed cases only

Initial Rhythm	Arrhythmic COD N=78	Non- Arrhythmic COD N=42	Fisher's Exact	Total
Agonal/Idioventricular	3 (60%)	2 (40%)	1.0	5
Asystole	26 (63%)	15 (37%)	0.84	41
NSR	3 (60%)	2 (40%)	1.0	5
PEA	2 (13%)	13 (87%)	<0.0001	15
Sinus Brady	2 (40%)	3 (60%)	0.34	5
VT/VF	39 (91%)	4 (9%)	<0.0001	43
Other	2 (67%)	1 (33%)	1.0	3
Unknown	1 (33%)	2 (67%)	0.61	3

Sudden Cardiac Death in Patients With Human Immunodeficiency Virus Infection

Zian H. Tseng, MD, MAS,* Eric A. Secemsky, MD,† David Dowdy, MD, PHD, SCM,‡
Eric Vittinghoff, PHD, MPH,§ Brian Moyers, MD,* Joseph K. Wong, MD,|| Diane V. Havlir, MD,¶
Priscilla Y. Hsue, MD#

San Francisco, California; and Baltimore, Maryland

The New York Times

Health

WORLD U.S. N.Y. / REGION BUSINESS TECHNOLOGY SCIENCE HEALTH SPORTS OPINION A

Search Health 3,000+ Topics

Inside Health

Heart Trouble Early and Often in H.I.V. Patients



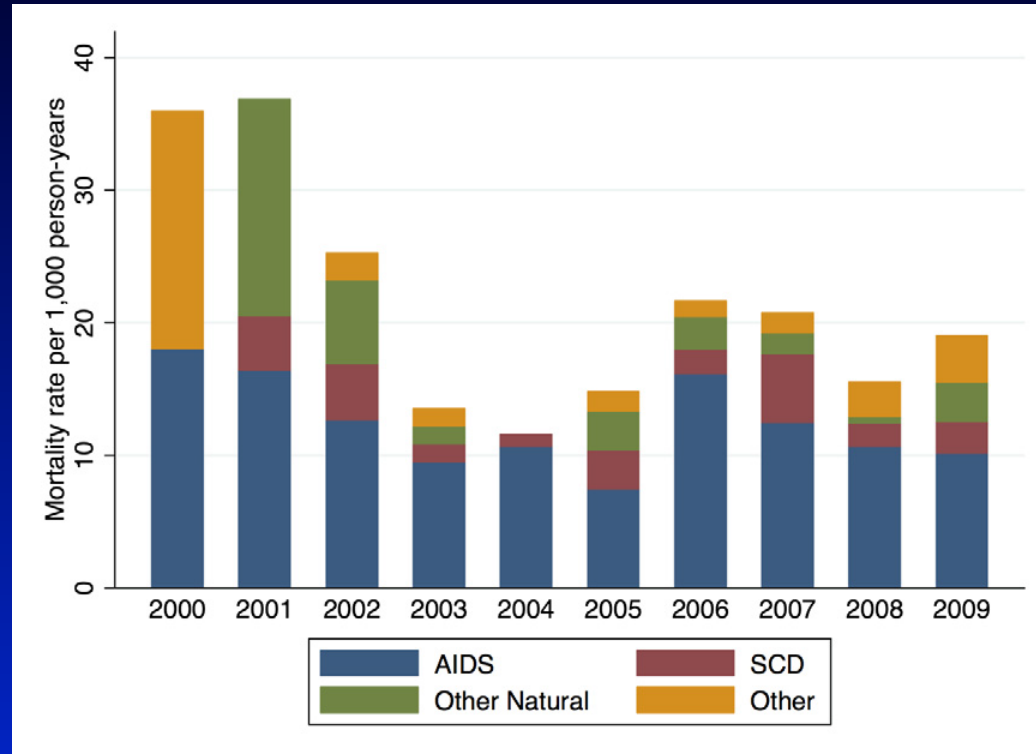
Jim Wilson/The New York Times

Mark Abramson has been HIV positive since 1988 and writes about his experiences in San Francisco.

By DONALD G. McNEIL Jr.

Published: June 18, 2012 | 63 Comments

Mortality Rates by Cause and Year



- 230 deaths over 3.7 median years' follow-up
- 13% SCDs, 86% (30/35) of all cardiac deaths
- Mean HIV SCD rate: 2.6/1,000 PY (95% CI 1.8-3.8), **4.5-fold higher** than background HIV- SCD rate

SCD Case Study #3

- 76-year-old male with mild CAD history of CHB with DDD PPM implanted in 2008
 - Underlying rate < 30 bpm
 - ERI reached 3 weeks prior
- Without complaint, found dead by his wife the morning before scheduled generator change

SCD Case Study #3

- 74 yo man with CAD, PPM for CHB
- Gen change scheduled for 5 weeks after ERI
- Did not show up to UCSF EP lab: died in sleep
- Autopsy negative (no MI, PE, or bleed)

Battery Status

Estimated remaining longevity: 6 months, < 1-13 months

Based on Past History

Voltage/Impedance

2.63 V / 3,767 ohms

Pacing (% of total):

AS - VS 2.2%

AS - VP 0.7%

AP - VS 2.3%

AP - VP 94.9%

Battery Status

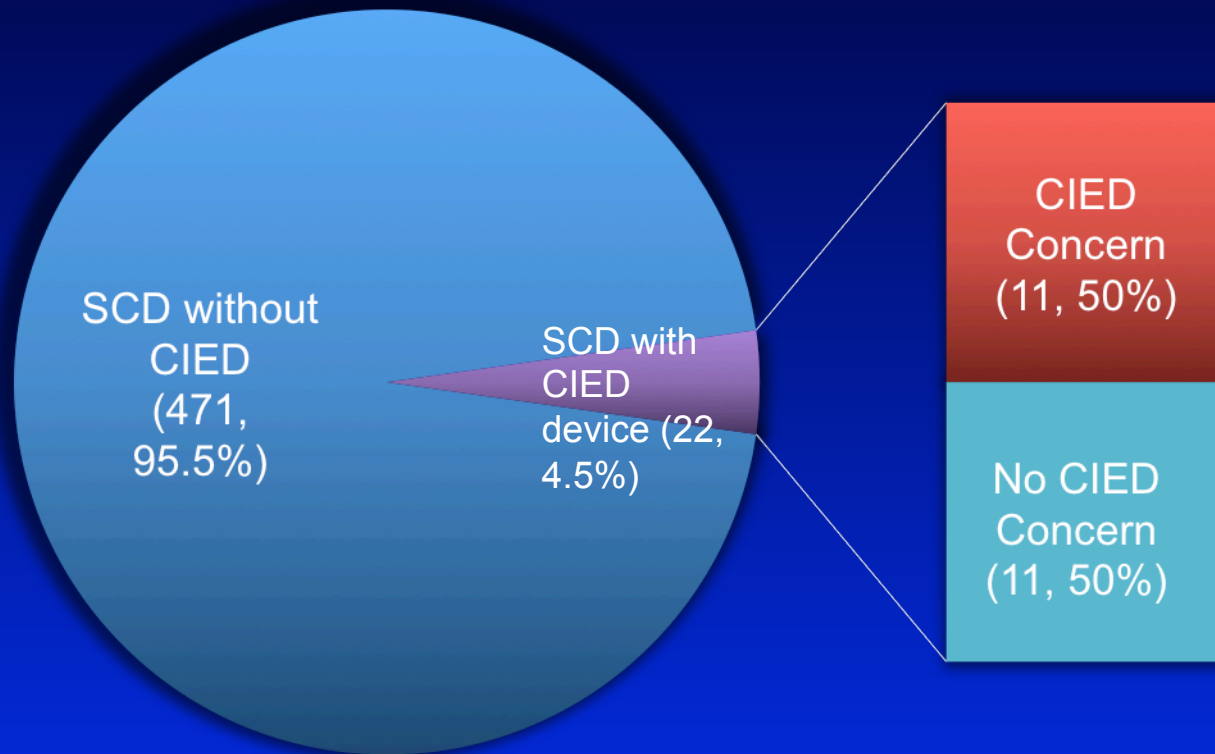
Estimated remaining longevity: Replace Pacer

Voltage/Impedance

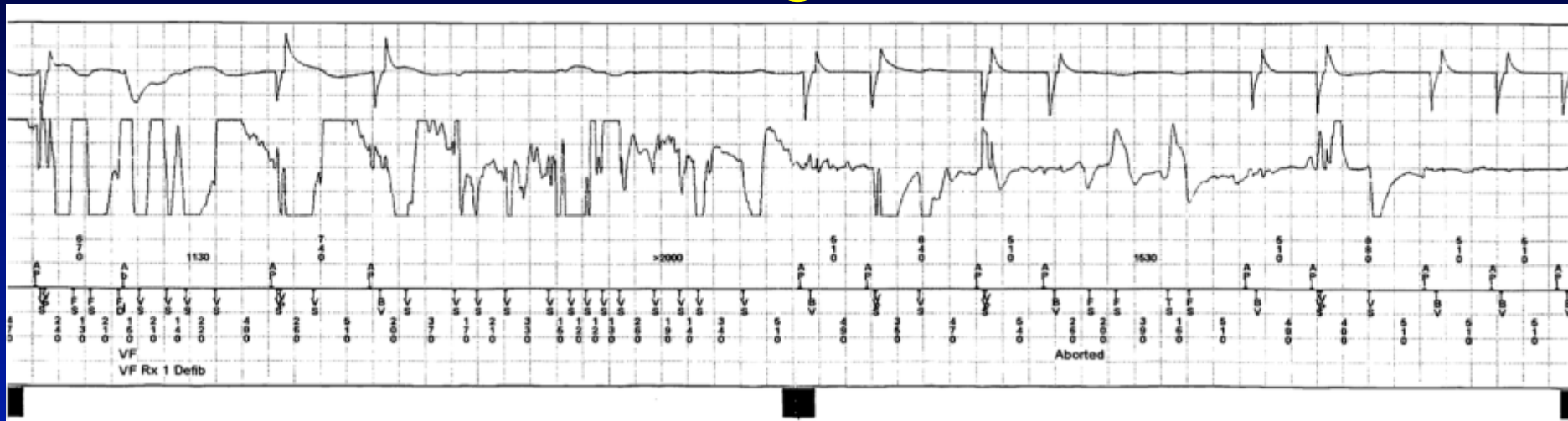
2.17 V / 22,108 ohms

Ventricular High Rate Episodes: 0

Sudden Death in Patients with CIEDs

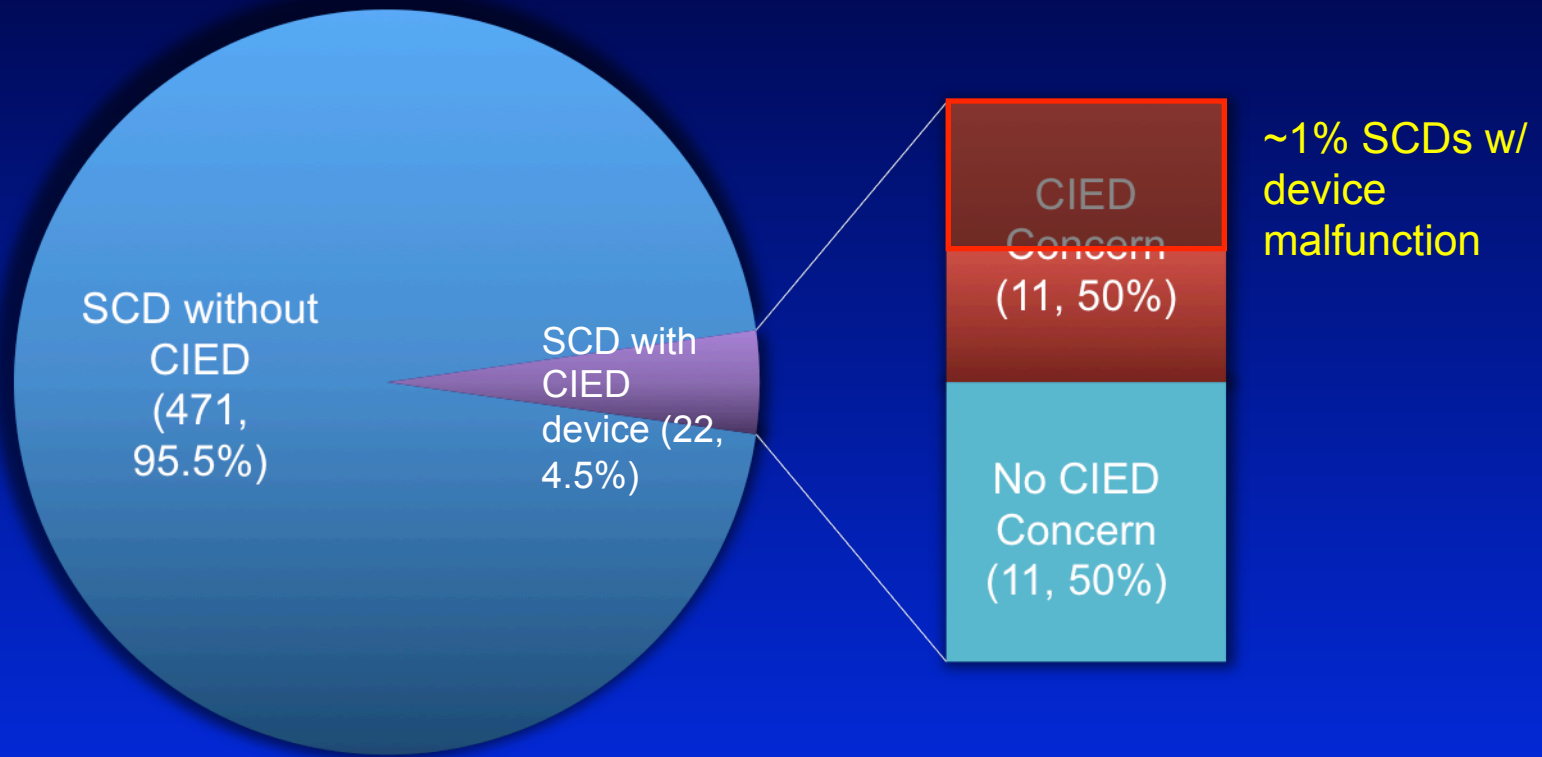


ICD Lead Fracture During Shock Resulting in SCD

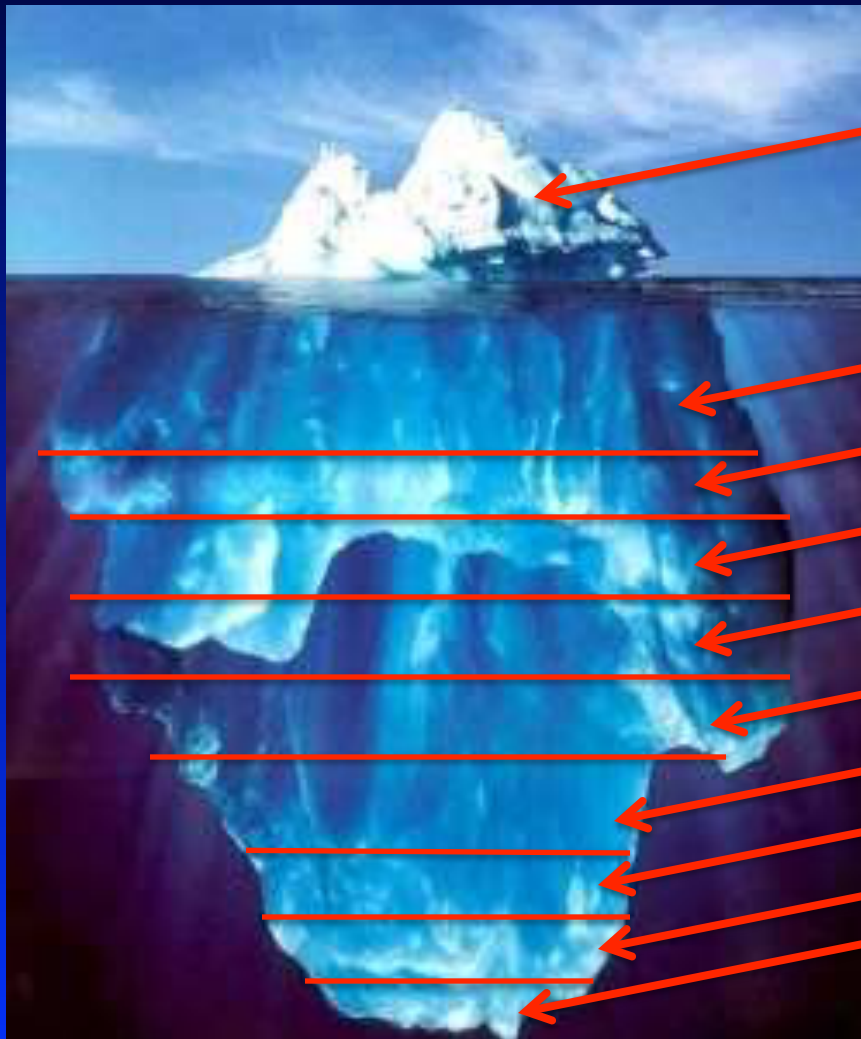


- Improved post-market surveillance
- More accurate device failure rates
- Opportunities MD practice improvement: device selection, programming

Sudden Death in Patients with CIEDs



Autopsy-Proven Sudden Cardiac Death



SCA

CAD

Tamponade

Valvular

Neurologic

DCM

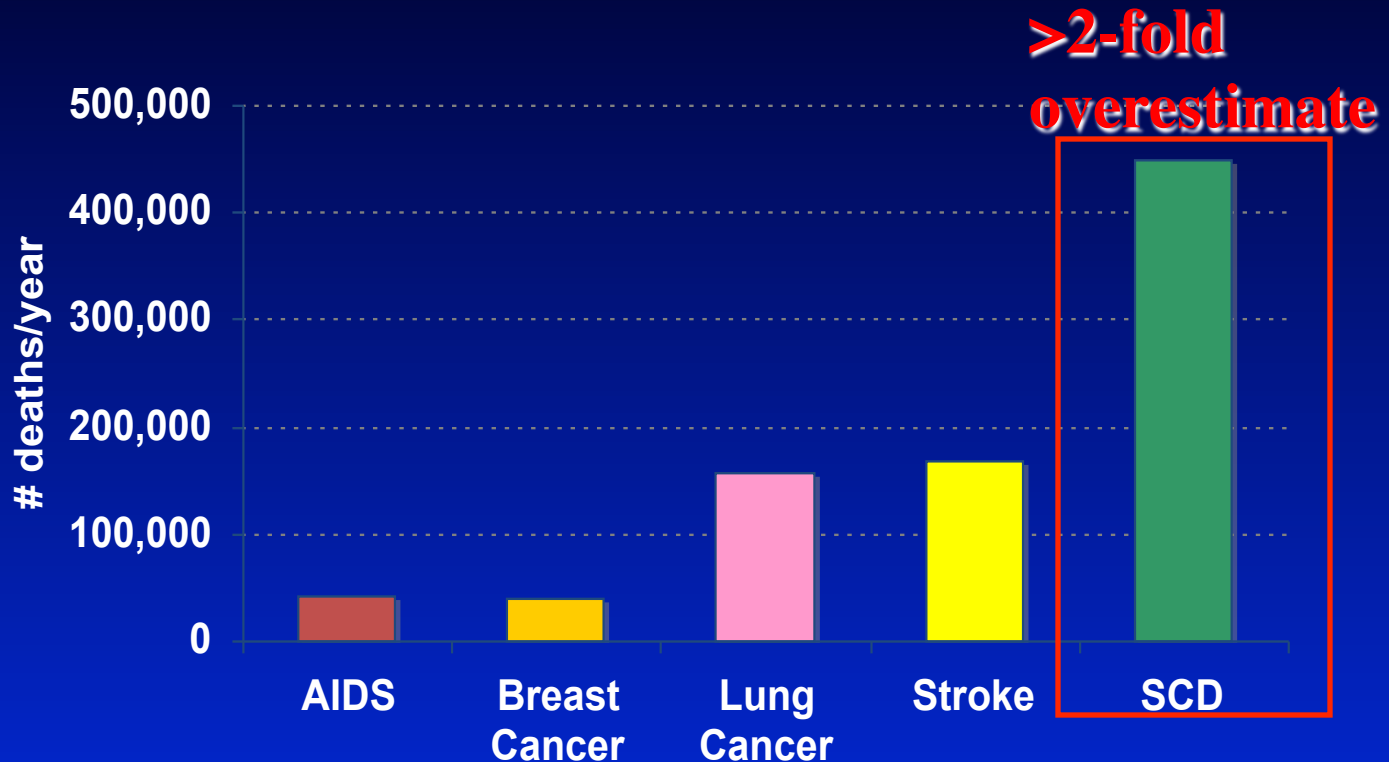
HCM

HIV

CIEDs

1° electrical disease

Magnitude of Sudden Cardiac Death in the U.S.



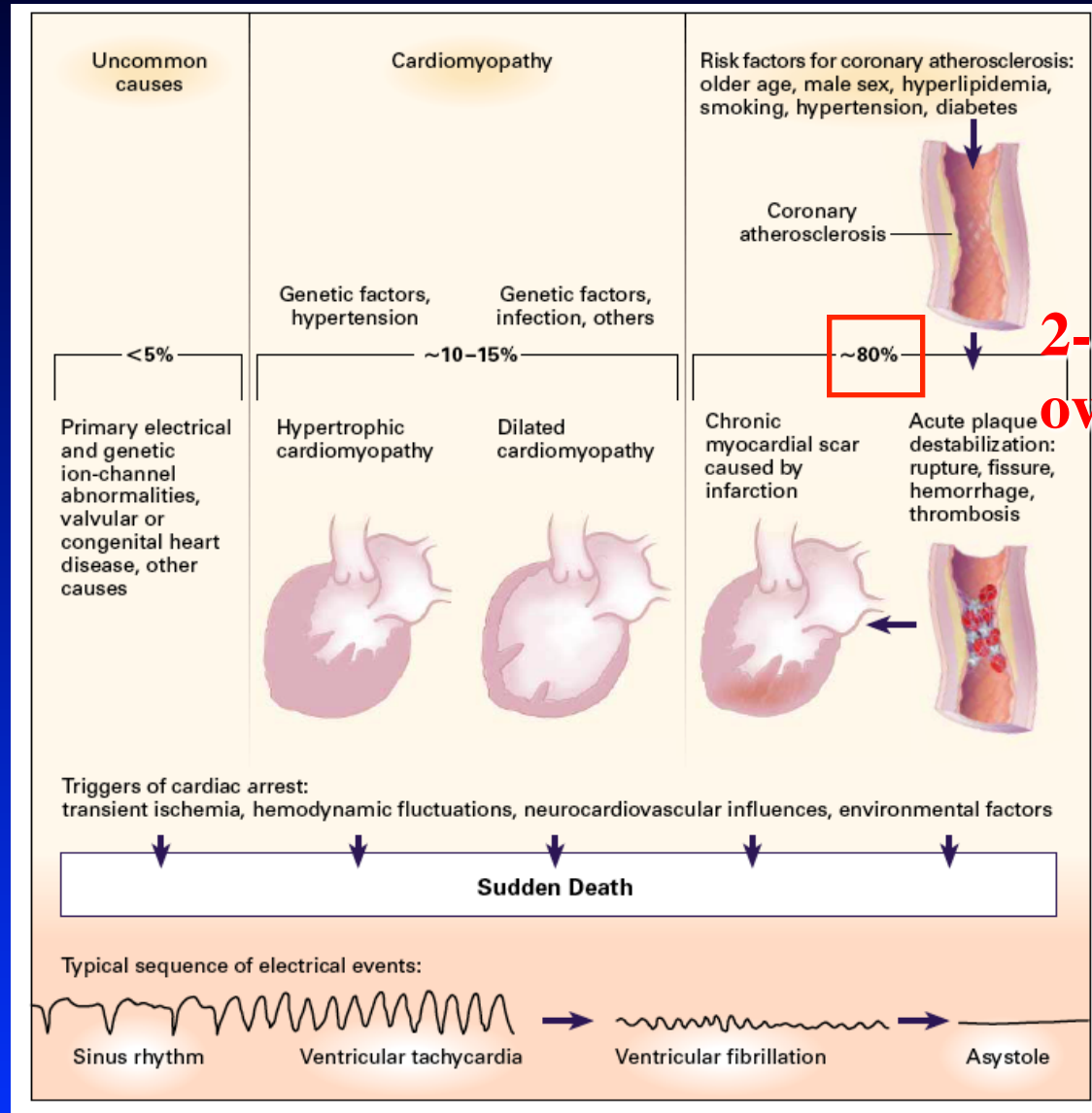
¹ U.S. Census Bureau, *Statistical Abstract of the United States: 2001*.

² American Cancer Society, Inc., *Surveillance Research, Cancer Facts and Figures 2001*.

³ 2002 *Heart and Stroke Statistical Update*, American Heart Association.

⁴ *Circulation*. 2001;104:2158-2163.

Etiology of Sudden Cardiac Death



2-fold overestimate

Early and Anticipated Insights

- SAD only account for just over half of all “SCDs”
- Men, blacks have 2-fold higher incidence of SAD than reference – Asians have intermediate risk
- SCD rates are up to 4-fold higher in HIV+
- CIED problems underestimated: postmortem surveillance necessary
- Sudden neurologic death most common non-cardiac cause after OD, higher risk in Asians and women
- Precise phenotypes for future genetic association studies
- Precision EMS protocols
- Prediction modeling for true arrhythmic causes in existing SCD cohorts
- Hemorrhage risk with anticoagulants, antiplatelets

Acknowledgements

- SF Medical Examiner's Office
 - Ellen Moffatt
 - Amy Hart
- UCSF Pathology
 - Phil Ursell
- UCSF EP Section
 - Jeff Olgin
 - Robert Hayward
 - Brian Moyers
 - Nina Clark
 - Rana Khan
- UCSF Epidemiology/Biostatistics
 - Eric Vittinghoff
- SFGH
 - Priscilla Hsue
 - Diane Havlir
- UCSF Pediatrics
 - Ronn Tanel
- SF VAMC
 - Joseph Wong
- UCSF Cardiology
 - Elyse Foster
 - Ian Harris
- UCSF Neurology
 - Anthony Kim
 - Michael Wilson
- SFFD/SFGH Emergency Medicine
 - Karl Sporer
 - Clement Yeh
- UCSF Human Genetics
 - Brad Aouizerat
 - Pui-Yan Kwok
- UCSF Medical Ethics
 - Bernie Lo

