

TYPE 2 DIABETES AND THE RISK OF SUDDEN CARDIAC DEATH

The Atherosclerosis Risk in Communities Study

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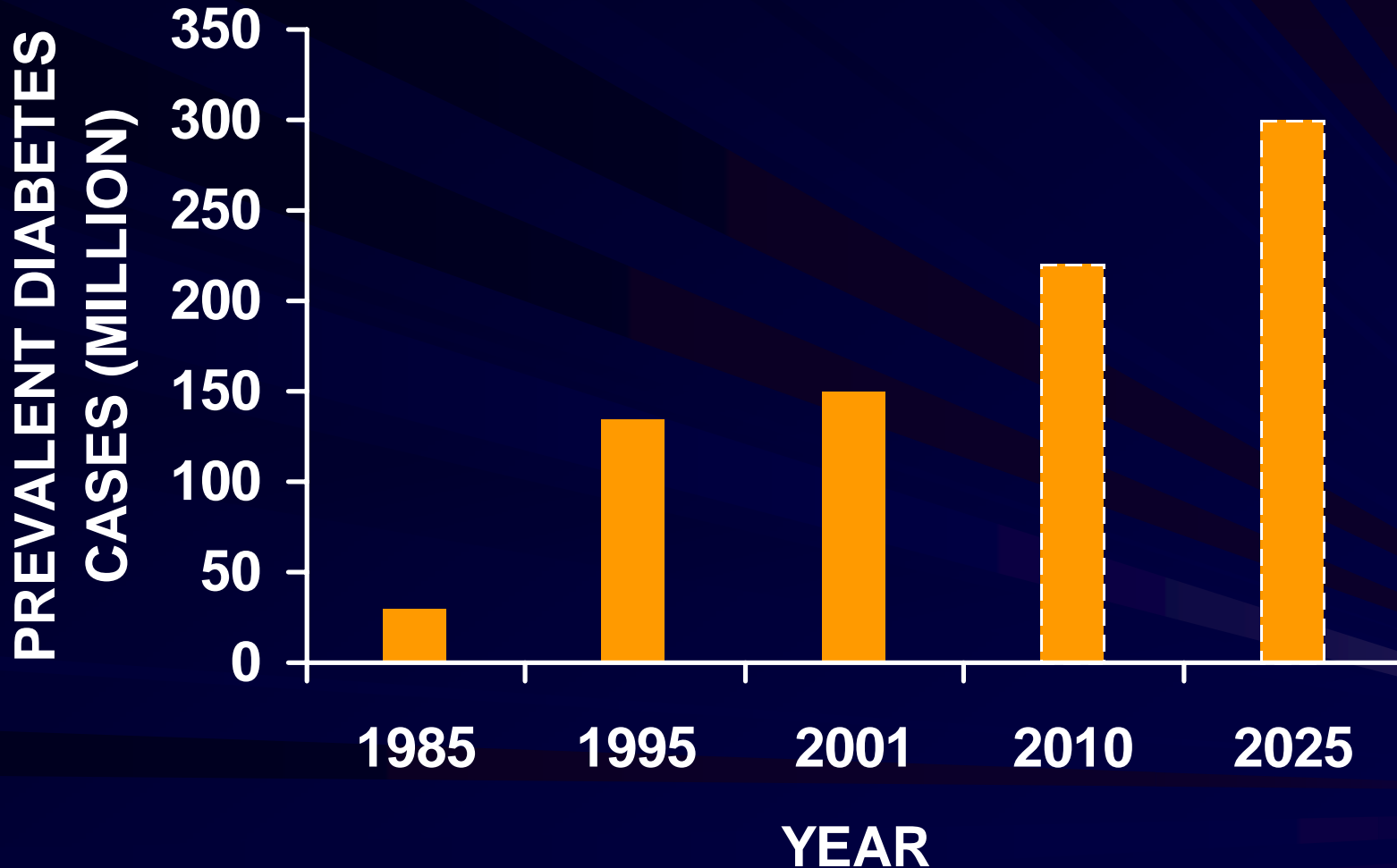
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We have no disclosures

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DIABETES, A GLOBAL EPIDEMIC



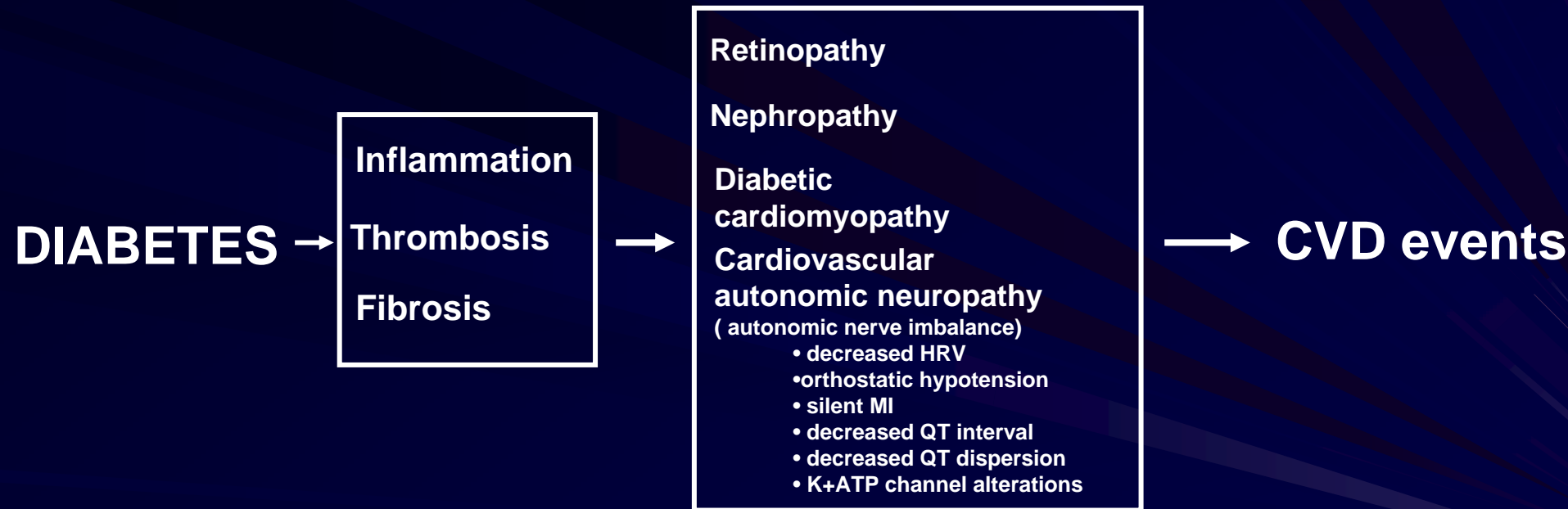
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Zimmet P. et al., Global and societal implications of the diabetes epidemic ; Nature, 2001;414:782-787

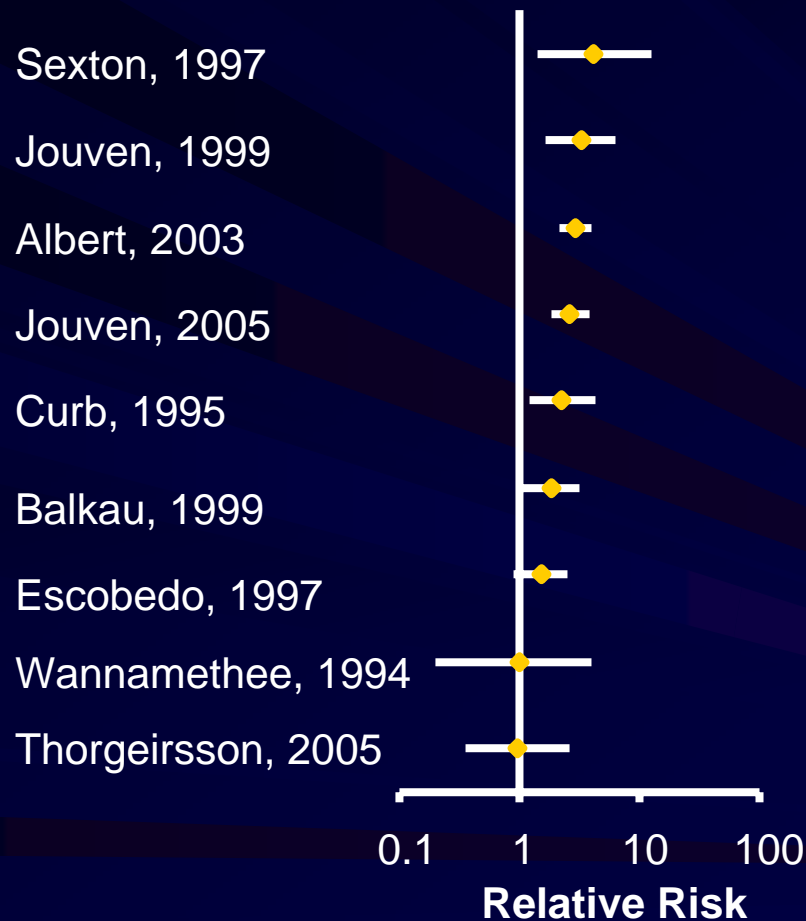
SUDDEN CARDIAC ARREST, A PUBLIC HEALTH BURDEN

- 1-5% survival
- Sudden cardiac death: 25-50% of all cardiovascular deaths
- Lack of specific, modifiable risk factors

DIABETES SEQUELAE



DIABETES AND SUDDEN CARDIAC DEATH, EXISTING STUDIES



STUDY QUESTION

What is the strength of the association of Type 2 Diabetes with the risk of sudden cardiac death in comparison with the risk of non-fatal myocardial infarction?

STUDY DESIGN

- Study
Population: Atherosclerosis Risk in Communities (ARIC) Study
 - probability sample of 15,792 men and women
 - age: 45-64 years at baseline
 - four U.S. communities
 - follow-up: 1987-2001
- Endpoint
Classification:
 - Incident sudden cardiac death 1987-2001
 - Incident non-fatal MI 1987-2001
- Exclusions:
 - missing data on exposure and outcome variables
 - race other than Black or White
 - final sample size: 14,999
- Statistical Analysis: -Cox proportional hazard ratios

EXPOSURE DEFINITION

- **Diabetes** - defined as either a physician's diagnosis of diabetes, use of hypoglycemic medications, non-fasting glucose level greater than 200 mg/dL, or fasting blood glucose level greater than 126 mg/dL.
- **Pre-diabetes** - fasting plasma glucose levels 100-126 mg/dL

OUTCOME DEFINITIONS

- **Sudden cardiac death:** death meeting ARIC study criteria for definite fatal MI, definite fatal CHD, or possible fatal CHD, adjudicated by a physician panel on the basis of data from death certificates, informant interviews, physician questionnaires, coroner reports, and hospital discharge summaries, to be a sudden, pulseless condition without a known non-cardiac cause.
- **Non-fatal MI:** incident definite, or probable myocardial infarction that did not result in a fatal outcome within 28 days.

Selected baseline characteristics, ARIC cohort

CHARACTERISTIC	SUDDEN CARDIAC DEATH		NON-FATAL MI	
	Yes (n=304)	No (n=14,695)	Yes (n=930)	No (n=14,069)
Age (years, (SD))	56.7 (5.3)	54.1 (5.8)	55.5 (5.5)	54.1 (5.8)
Gender, % Male	63.6	44.5	64.6	43.8
Race, % Black	40.7	25.0	24.0	25.4
BMI (SD)	28.9 (5.8)	27.7 (5.3)	28.3 (5.0)	27.6 (5.4)
Hypertension, %	60.9	33.9	49.4	33.6
Systolic blood pressure (mm Hg, (SD))	132.8 (23.1)	120.9 (18.6)	126.5 (20.3)	120.8 (18.6)
Smoking, % Ever	68.1	57.7	71.3	57.1
Prevalent CHD	30.7	4.4	15.0	4.3
Prevalent HF	11.4	4.8	7.1	4.8
Type 2 DM at baseline, %	33.6	11.3	24.5	11.0
Incident type 2 DM, %	19.2	11.8	15.7	11.7
Glucose (mg/dL, (SD))	136.9 (74.3)	108.2 (39.1)	122.0 (53.8)	108.0 (39.3)

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COX PROPORTIONAL HAZARD REGRESSION OF THE ASSOCIATION OF TYPE 2 DIABETES WITH THE RELATIVE RISK OF SUDDEN CARDIAC DEATH OR NON-FATAL MI

OUTCOME	Unexposed		Exposed		Crude	Adjusted*
	Events	p-years	Events	p-years	HR (95% CI)	
SCD	202	168,895	102	20,296	4.22 (3.32, 5.35)	2.53 (1.97, 3.25)
Non-fatal MI	680	165,179	250	19,274	3.22 (2.78, 3.72)	2.51 (2.15, 2.92)

*Adjustment: race-by-ARIC center, age, gender, systolic blood pressure, cigarette years of smoking, smoking status, hypertension, anti-hypertensive medication

EFFECT OF RACE ON THE ASSOCIATION OF DIABETES WITH THE RELATIVE RISK OF SUDDEN CARDIAC DEATH

Outcome	Total sample*	Whites **	Blacks**
HR (95% CI)			
Sudden cardiac death	2.53 (1.97, 3.25)	2.18 (1.51, 3.17)	2.90 (2.08, 4.05)
Non-fatal MI	2.51 (2.15, 2.92)	2.49 (1.89, 3.29)	2.51 (2.09, 3.01)

*Adjustment: race-by-ARIC center, age, gender, systolic blood pressure, cigarette years of smoking, smoking status, hypertension, anti-hypertensive medication

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EFFECT OF GENDER ON THE ASSOCIATION OF DIABETES WITH SUDDEN CARDIAC DEATH AND NON-FATAL MI

MODEL	SUDDEN CARDIAC DEATH (n=304)		NON-FATAL MI (n=930)	
	Women (n=111)	Men (n=193)	Women (n=311)	Men (n=599)
Crude	6.26 (4.30, 9.13)	3.30 (2.42, 4.52)	4.27 (3.39, 5.38)	2.82 (2.25, 3.28)
Model 1	4.04 (2.72, 6.00)	2.85 (2.08, 3.91)	3.81 (3.00, 4.85)	2.63 (2.17, 3.18)
Model 2	2.97 (1.99, 4.44)	2.35 (1.70, 3.26)	3.04 (2.37, 3.89)	2.25 (1.85, 2.74)

Model 1: race-by-ARIC center, age

Model 2: race-by-ARIC center, age, systolic blood pressure, cigarette years of smoking, smoking status, hypertension, anti-hypertensive medication

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DIABETES AS A TIME-VARYING EXPOSURE

Outcome	Crude	Adjusted*
Sudden cardiac death	4.33 (3.45, 5.45)	2.68 (2.11, 3.40)
Non-fatal MI	2.65 (2.31, 3.05)	2.04 (1.77, 2.36)

*Adjustment: race-by-ARIC center, age, gender, systolic blood pressure, cigarette years of smoking, smoking status, hypertension, anti-hypertensive medication

GLUCOSE LEVELS AND THE RELATIVE RISK OF SUDDEN CARDIAC DEATH

FASTING GLUCOSE LEVEL	SUDDEN CARDIAC DEATH HR (95 % CI)	
	Adjusted for age and race	Fully adjusted*
<100 mg/dL	1.00 (referent)	1.00 (referent)
100-126 mg/dL	1.56 (1.19, 2.05)	1.21 (0.92, 1.59)
>126 mg/dL	3.51 (2.56, 4.83)	2.49 (1.80, 3.44)

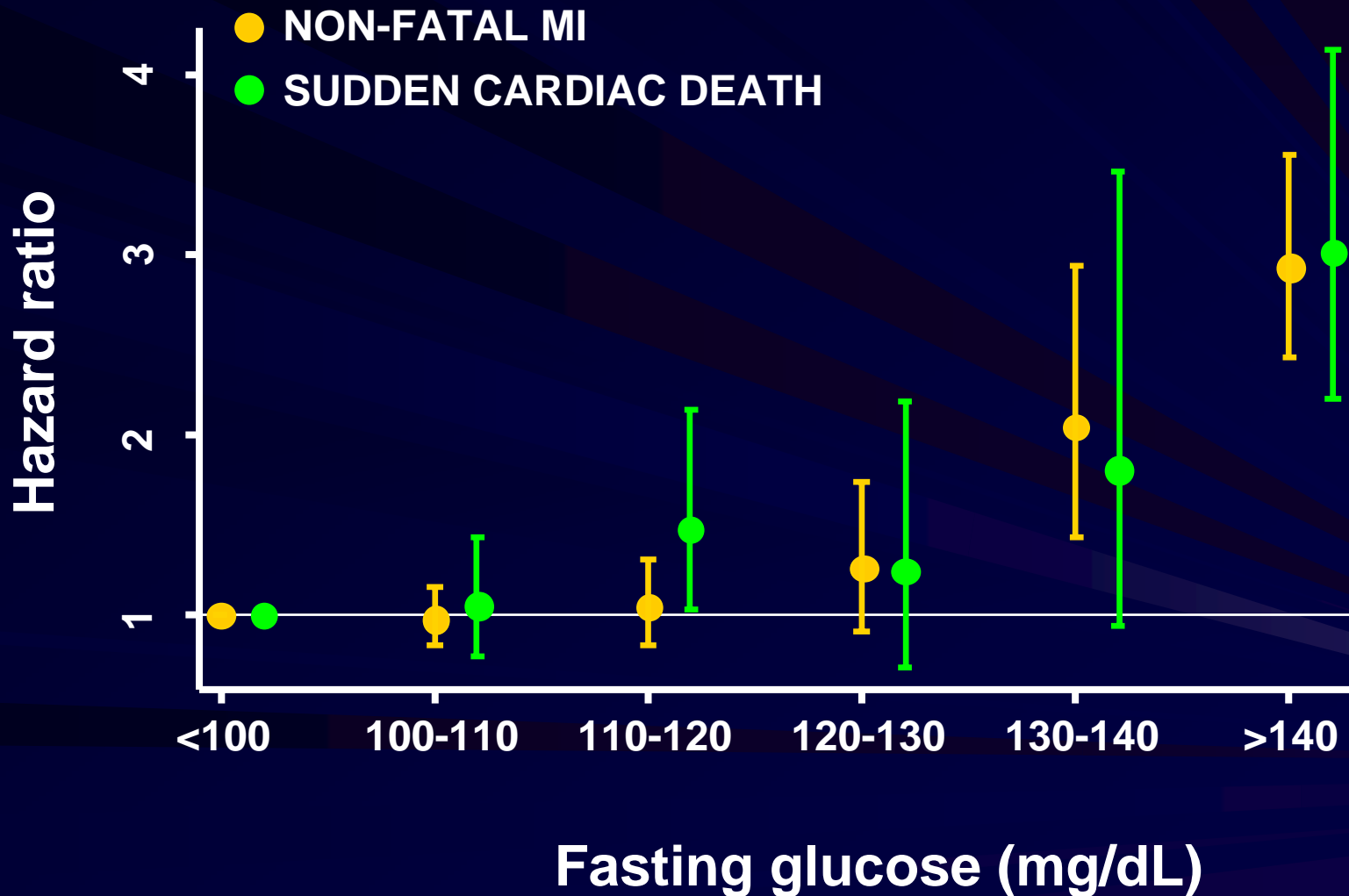
*Adjustment for race-by-ARIC center, age, gender, systolic blood pressure, cigarette years of smoking, smoking status, hypertension, anti-hypertensive medication

GLUCOSE LEVELS AND THE RELATIVE RISK OF NON-FATAL MI

FASTING GLUCOSE LEVEL	NON-FATAL MI HR (95 % CI)	
	Adjusted for age and race	Fully adjusted*
<100 mg/dL	1.00 (referent)	1.00 (referent)
100-126 mg/dL	1.25 (1.08, 1.45)	0.99 (0.85, 1.15)
>126 mg/dL	3.56 (3.00, 4.22)	2.64 (2.21, 3.14)

*Adjustment for race-by-ARIC center, age, gender, systolic blood pressure, cigarette years of smoking, smoking status, hypertension, anti-hypertensive medication

FASTING GLUCOSE LEVELS AND THE RELATIVE RISK OF SUDDEN CARDIAC DEATH OR NON-FATAL MI



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SUMMARY

- Strength of the association of type 2 diabetes is similar for sudden cardiac death and for non-fatal MI
- Association of type 2 diabetes with sudden cardiac death is not modified by gender
- Association of type 2 diabetes with sudden cardiac death is not modified by race
- Gradient of relative risk of sudden cardiac death and non-fatal MI across spectrum of fasting glucose levels

NEXT STEPS

- In 1975 Kannel et al., stated that: “Victims of sudden cardiac death are no different from the rest of the coronary-prone population”. Is this true?
- Understanding of the association of diabetes with the risk of sudden cardiac death perhaps needs to go beyond the dichotomized diabetic status to include broader measures of physiological imbalance.

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