Managing, Pooling and Evaluating Large Datasets

WHF ELF

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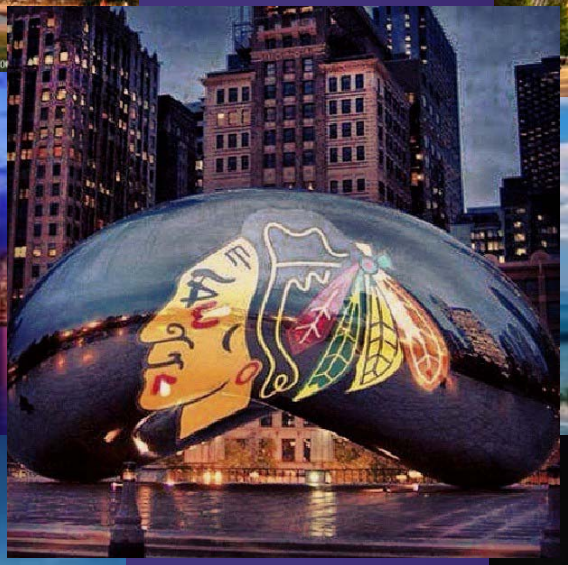
Greetings from Chicago!



Disclosures

- No relevant RWI
- Funding from NHLBI, NCATS, NIH

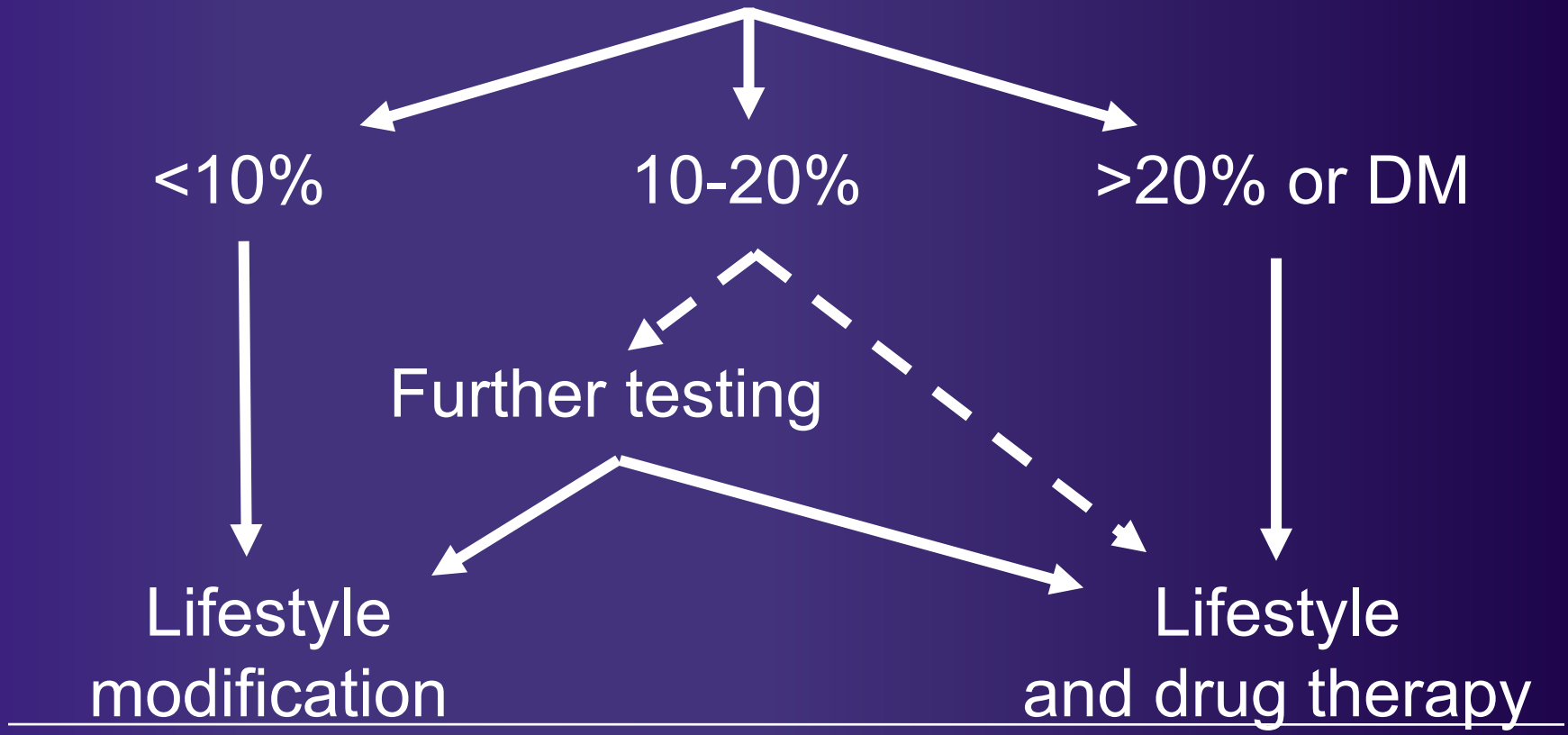
Outline

- Discovering lifetime risks for CVD (and other NCDs/chronic diseases of aging)
  - Power, pitfalls, promise of 10-year risk assessment
  - Lifetime Risk Pooling Project
    - Design
    - Analysis
    - Results

Current Paradigm for Risk Estimation and Treatment: ATP-III

"Intensity of prevention efforts should match the absolute risk of the patient"

Estimate 10-year absolute risk (FRS)



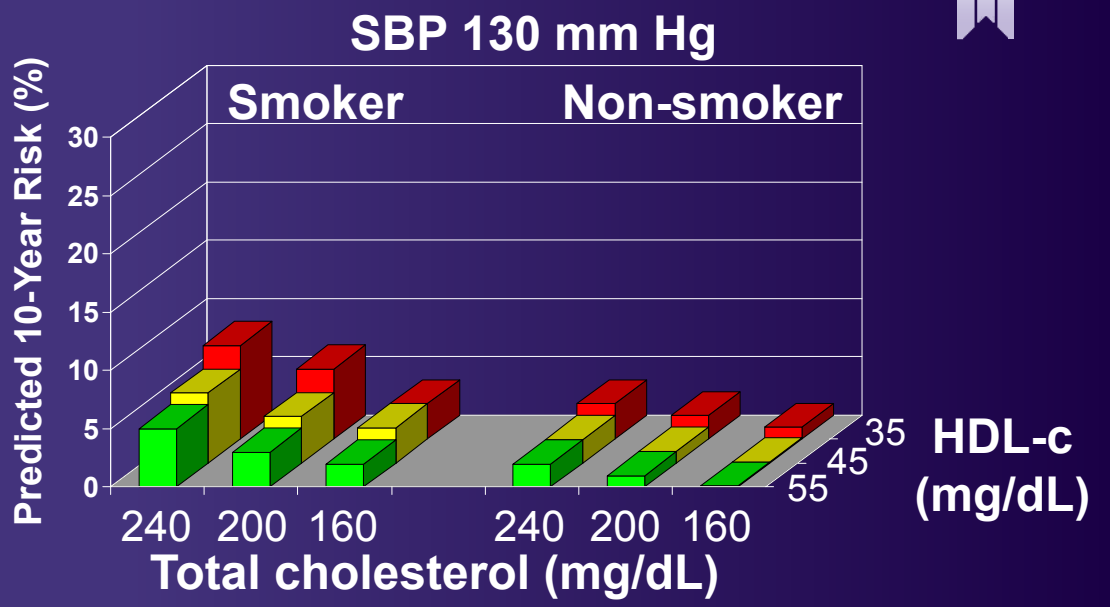
Rationale: Lifetime Risk Estimation

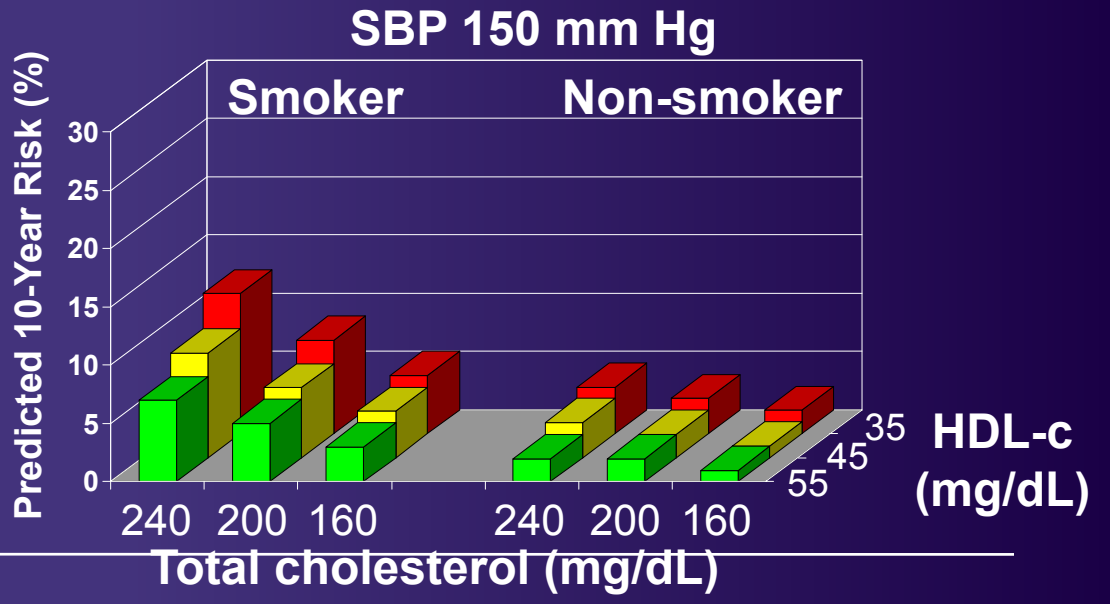
- Reliance solely on estimates of *short-term* absolute risk to communicate risk and make treatment decisions is problematic
  - Atherosclerosis is a lifecourse disease
  - Any single risk factor can produce cumulative damage and high risk if left untreated for years
  - Almost all men <50 and women <70 are considered to be at "low" short-term risk *regardless of risk factor burden*

AHA Prevention Conference V, Circulation 2000; Cavanaugh-Hussey, Prev Med 2008; Marma, Circ CQO 2010

10-Year Predicted Risks in ATP Risk Assessment Tool: Woman, Age 55

Cavanaugh-Hussey, Berry, Lloyd-Jones, Prev Med 2008.





Rationale: Lifetime Risk Estimation

- Lifetime risk
  - The absolute cumulative risk of an individual developing a given disease before death
  - Accounts for risk of disease of interest, remaining life expectancy, and competing causes of death
  - Reflects real-life risks and population burden of disease better than Kaplan-Meier cumulative incidence
  - Allows for comparison of disease burden now and in future
  - May provide adjunctive information for individual risk assessment

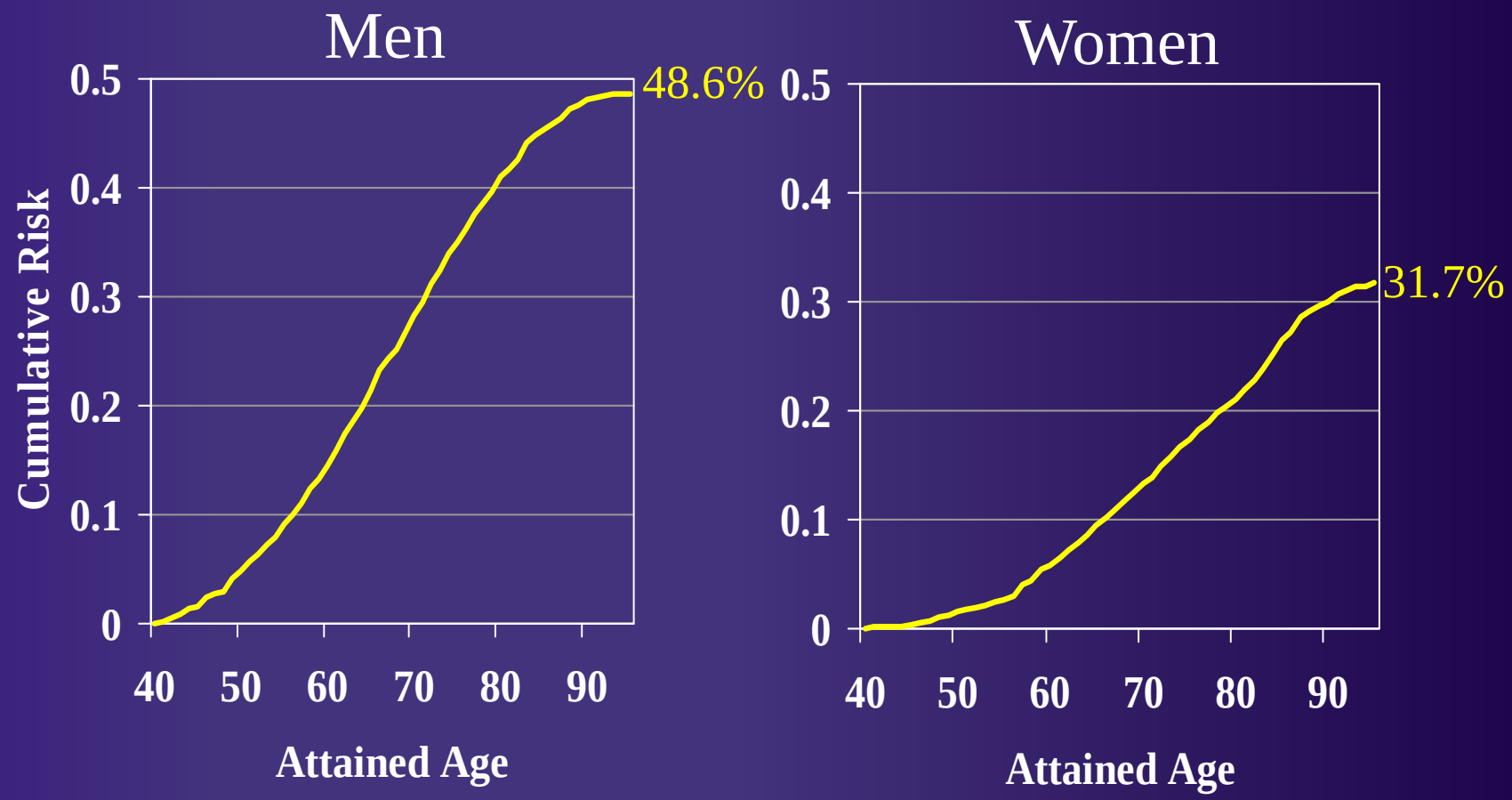
Methods

- Calculation of lifetime risk
  - Need to account for competing risk of death
    - Standard epidemiologic methods do not, yielding over-estimates of risk
  - Multiple-decrement life-table analysis
    - Accounts for risk of disease and competing risk of death

Study Sample

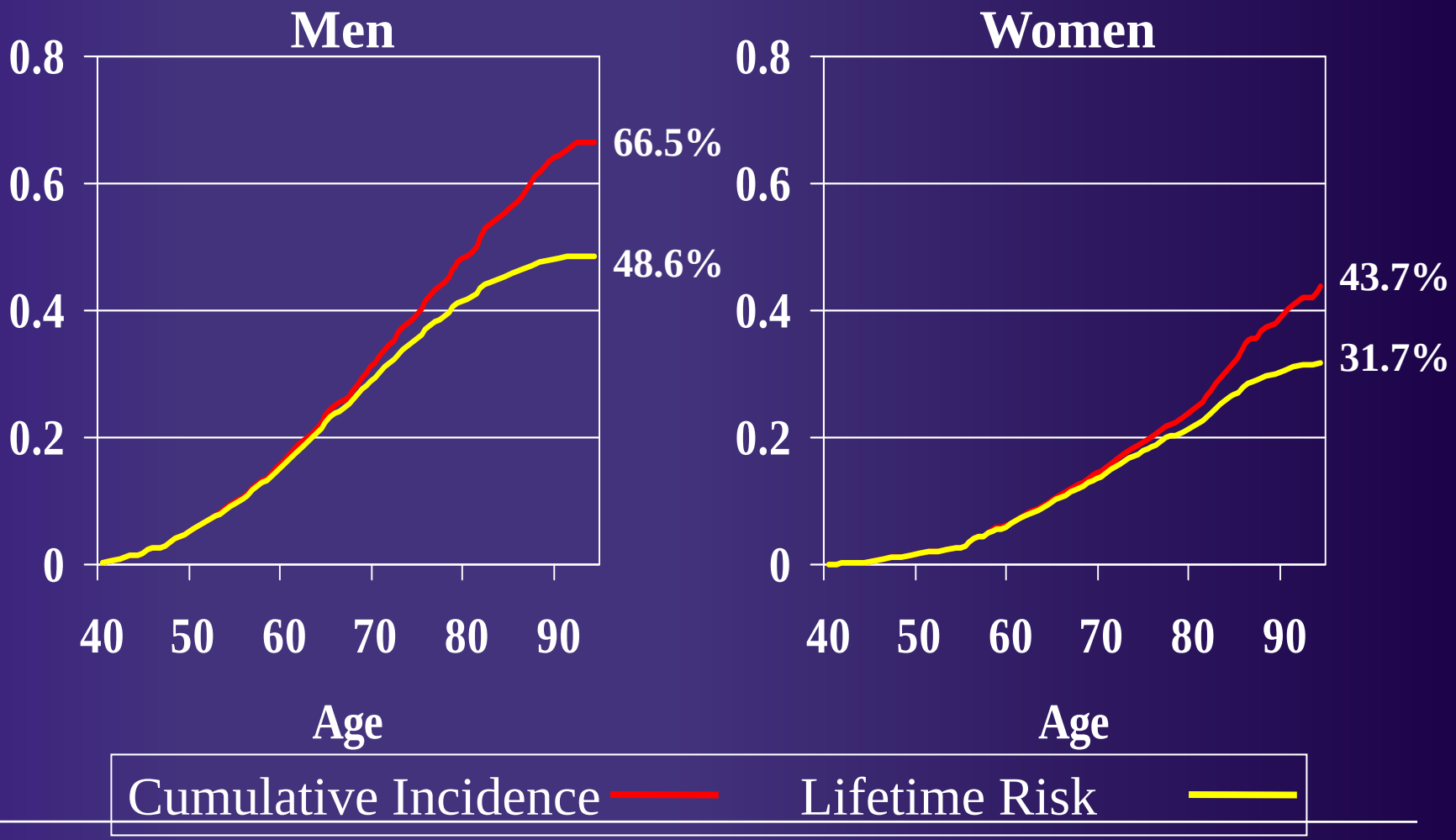
- Population needed for stable estimates
  - Huge cohort with wide age range and moderate follow up
  - At least moderate size cohort with longer term follow up
  - Especially if stratifying by RF levels
    - Mutable vs immutable factors

Lifetime Risk for CHD by Age and Sex

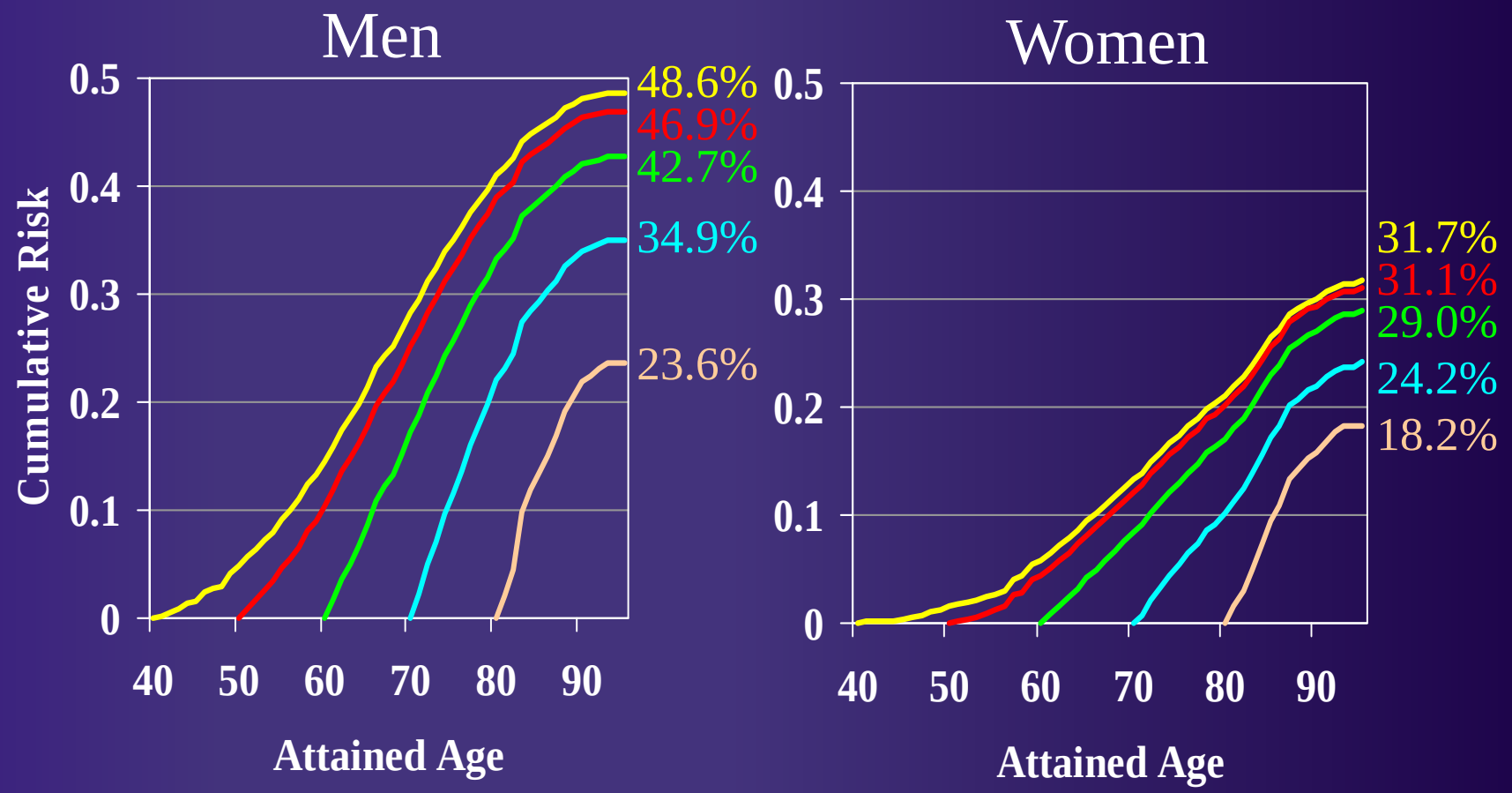


Lloyd-Jones et al. Lancet 1999;353:89.

KMCI vs. Lifetime Risk for CHD Age 40

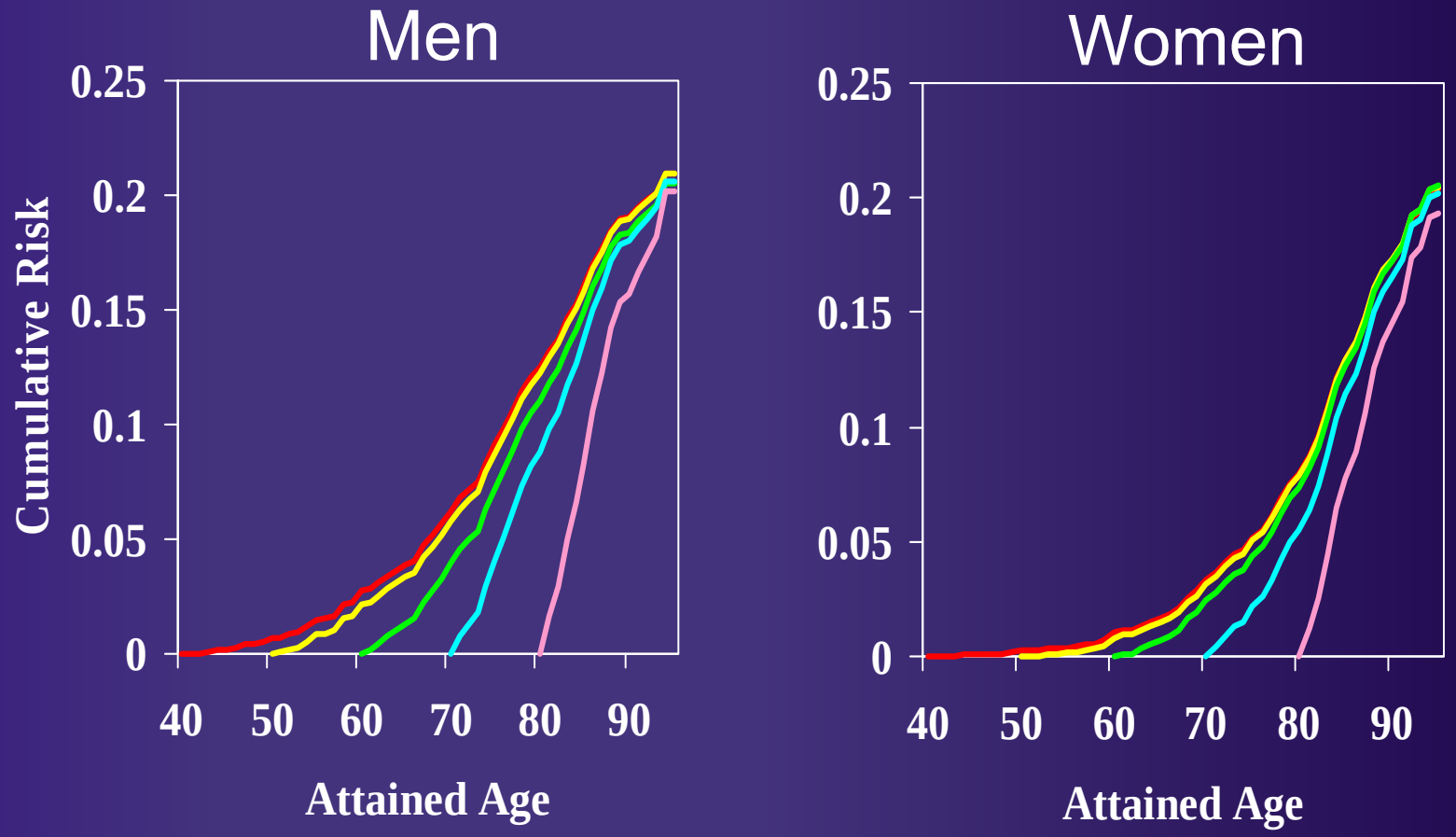


Lifetime Risk for CHD by Age and Sex



Lloyd-Jones et al. Lancet 1999;353:89.

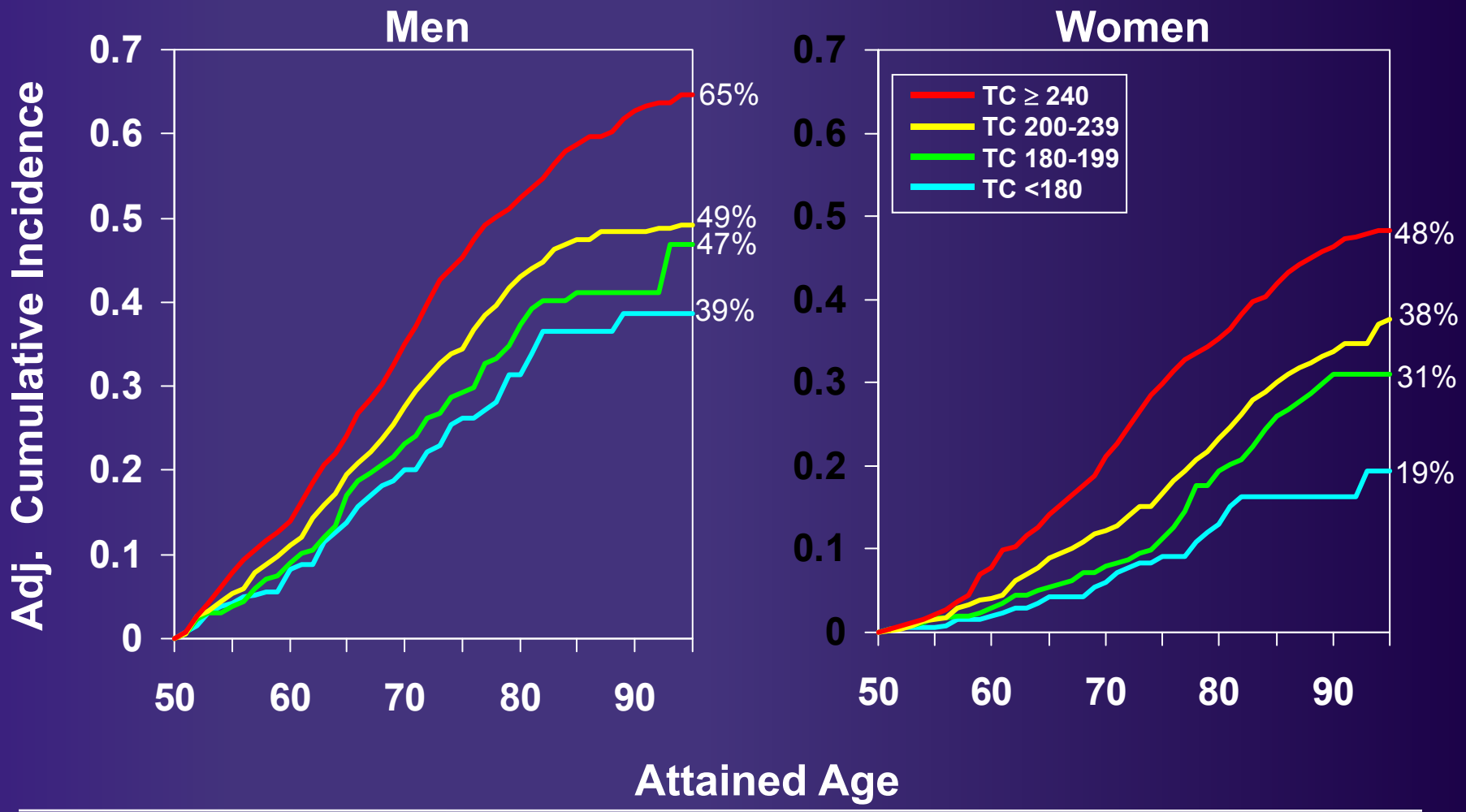
Lifetime Risk for CHF by Age and Sex



Lloyd-Jones et al. *Circulation* 2002

Lifetime Risk for ASCVD

Total Cholesterol at Age 50



Lloyd-Jones, *Circulation* 2006

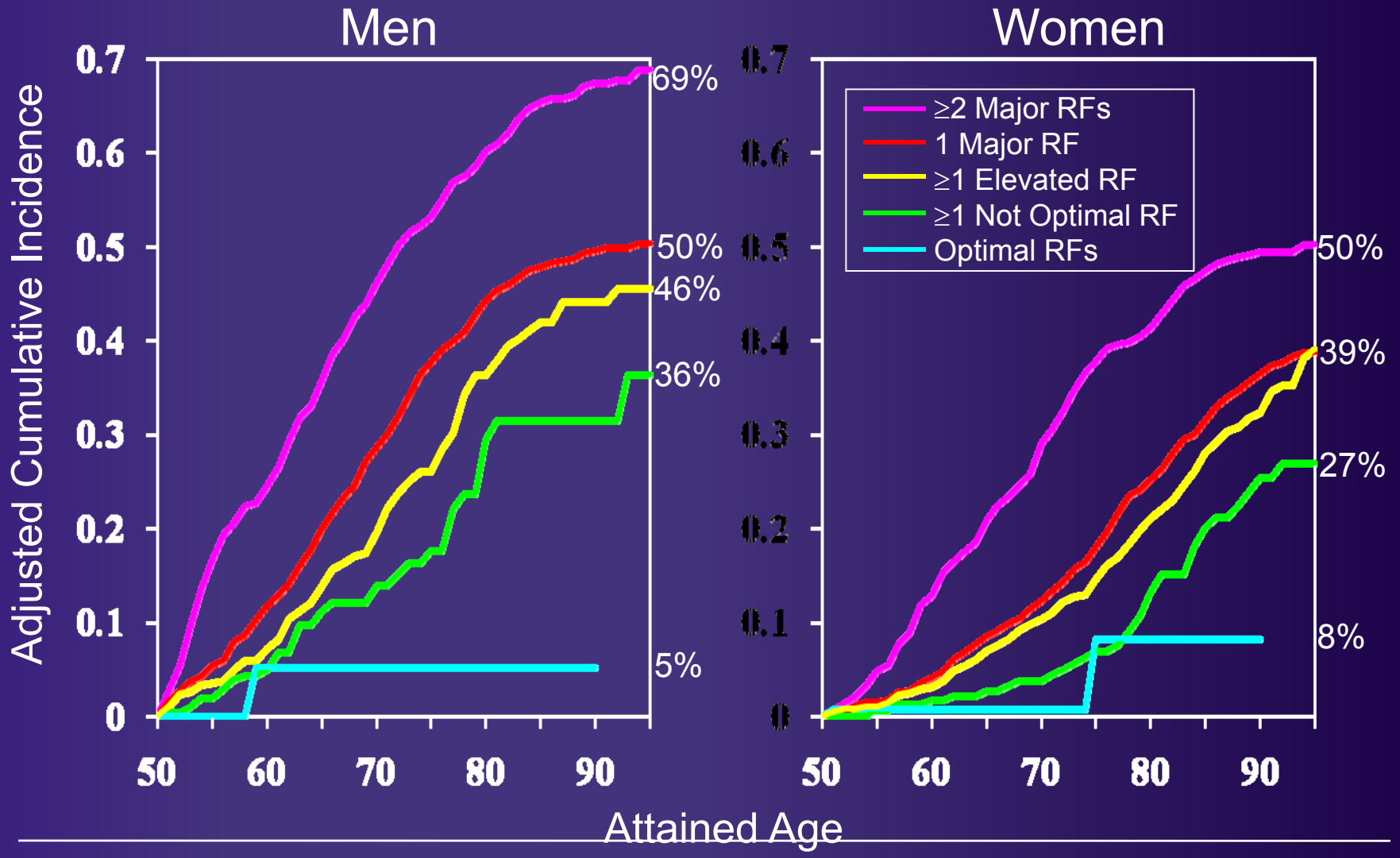
Aggregate Risk Factor Burden

	All Optimal	Not Optimal	Elevated	1 Major / ≥2 Major
SBP/ DBP	<120 and <80	120-139 or 80-89	140-159 or 90-99	≥160 or ≥100
TC	<180	180-199	200-239	≥240
DM	No	No	No	Yes
Smoking	No	No	No	Yes

Lloyd-Jones, *Circulation* 2006; 113: 791-798

Lifetime Risk for ASCVD by RF Strata

Framingham Heart Study, Age 50



Lloyd-Jones, *Circulation* 2006

Lifetime Risks for Common Diseases at Age 40

Disease	Men	Women
Any CVD*	>1 in 2	>1 in 2
CHD[1]	1 in 2	1 in 3
AF[2]	1 in 4	1 in 4
CHF[3]	1 in 5	1 in 5
Stroke[4]	1 in 5	1 in 5
Hip fracture[5]	1 in 20	1 in 6
Breast cancer[6,7]	1 in 1000	1 in 8
Prostate cancer[6]	1 in 6	--
Lung cancer[6]	1 in 12	1 in 17
Colon cancer[6]	1 in 16	1 in 17
Diabetes[8]	1 in 3	1 in 3

* Unpublished data , FHS 1. Lloyd-Jones, Lancet 1999 2. Lloyd-Jones Circulation 2004 3. Lloyd-Jones, Circulation 2002. 4. Seshadri, Stroke 2006. 5. Cummings, Arch Intern Med 1989. 6. SEER cancer statistics review, 1975-2000. 7. Feuer, J Natl Cancer Inst 1993. 8. Narayan, JAMA 2003.

Lifetime Risk for CVD: Current Status pre-LRPP

- Until recently, all estimates from white cohorts
  - Lifetime risks for CVD in blacks (other race/ethnic groups) unknown
    - Blacks have higher RF burden for some RFs
    - Blacks have higher short-term CHD and stroke rates
    - Blacks (esp men) also have higher all-cause and non-CVD mortality
    - Effects on lifetime risk?
- CIs around estimates for lifetime risks by RF burden are wide, especially for low risk groups
- Further research needed to understand burden of CVD now and in future

The Cardiovascular Lifetime Risk Pooling Project

- Rationale
  - Robust estimates of long-term/lifetime risk by age, sex, race or RF status infeasible from single cohort studies
  - Pooling of cohort studies smooths birth cohort effects present in single cohorts
  - Other pooling projects (GBD, PSC, ERFC, etc.) have not focused on long-term risks

- Objective
  - To collect and pool high-quality longitudinal data from community- and population-based cohorts in order to provide estimates for long-term and lifetime risks of CVD in the general US population and in subgroups

The Cardiovascular Lifetime Risk Pooling Project

- Criteria for cohort inclusion
  - Community- or population-based (not from RCT)
  - Directly measured RFs
  - ≥10 years' follow up

The Cardiovascular Lifetime Risk Pooling Project

- Methods – 18 datasets collected
  - Limited access datasets from NHLBI
    - ARIC, FHS, FOS, HHP, PRHHP
  - Datasets from NCHS
    - NHEFS, NHANES II Mortality, NHANES III FU Studies
  - University of Michigan IUC
    - EPESE, Hisp EPESE, Kaiser Old, Tecumseh
  - Internal study datasets
    - CHS, MRFIT screenees, WHI-OS
  - NU DPM datasets
    - CHA, PG, WE
- Next: Much gnashing of teeth

Issues in Pooling Datasets

- Similarity/appropriateness of cohorts
  - Selection criteria
  - Exclusion criteria
- Exposure ascertainment
  - Blood pressure
- Outcomes ascertainment
  - Adjudication vs administrative data
- Aligning data points
  - Person-exams by age

Lifetime Risk Pooling Project

Cohort	Age at Entry	Baseline Exam	White		Black		Hispanic		Asian	
			Men	Women	Men	Women	Men	Women	Men	Women
ARIC	45-64	1987-89	5429	6036	1631	2639				
CHS	65-100	1989-93	2152	2813	343	580				
CHA	18-74	1967-73	20195	14358	1494	2329				
EPESE										
FHS										
FOS										
Hisp EPES										
Honolulu										
Kaiser Ol										50
MRFIT sc										
NHEFS										
NHANES										
People's (										
People's (										
Puerto Ri										
Tecumsel										
WE	40-59	1957-58	2057		47					
WHI-OS	50-79	1993-98		78013		7639		2623		3741
Total (N=620612)			**384672**	**135135**	**29639**	**17137**	**17800**	**4382**	**8056**	**3791**

- >620,000 unique individuals
- ~11 million p-y of follow up
- 55,000 CVD deaths
- 6600 non-fatal MIs
- 4400 non-fatal strokes

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Lifetime Risks of Cardiovascular Disease

Jarett D. Berry, M.D., Alan Dyer, Ph.D., Xuan Cai, M.S., Daniel B. Garside, B.S., Hongyan Ning, M.D., Avis Thomas, M.S., Philip Greenland, M.D., Linda Van Horn, R.D., Ph.D., Russell P. Tracy, Ph.D., and Donald M. Lloyd-Jones, M.D.

N Engl J Med 2012; 366; 321-329

Prevalence (%) of RF Strata at Selected Index Ages

	Index Age (y)							
	45		55		65		75	
RF Burden	M	W	M	W	M	W	M	W
All Optimal	2.9	7.1	2.9	3.6	2.8	1.7	2.8	1.3
≥1 Not Optimal	9.5	14.4	8.2	8.4	8.8	6.6	10.0	6.4
≥1 Elevated	19.1	22.0	18.8	21.5	19.2	18.8	20.4	18.2
1 Major	46.5	40.1	45.9	40.7	44.2	41.6	43.3	43.3
≥2 Major	22.0	16.4	24.2	25.8	25.0	31.3	23.5	30.8

Prevalence (%) of RF Strata at Selected Index Ages

	Index Age (y)							
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RF Burden	M	W	M	W	M	W	M	W
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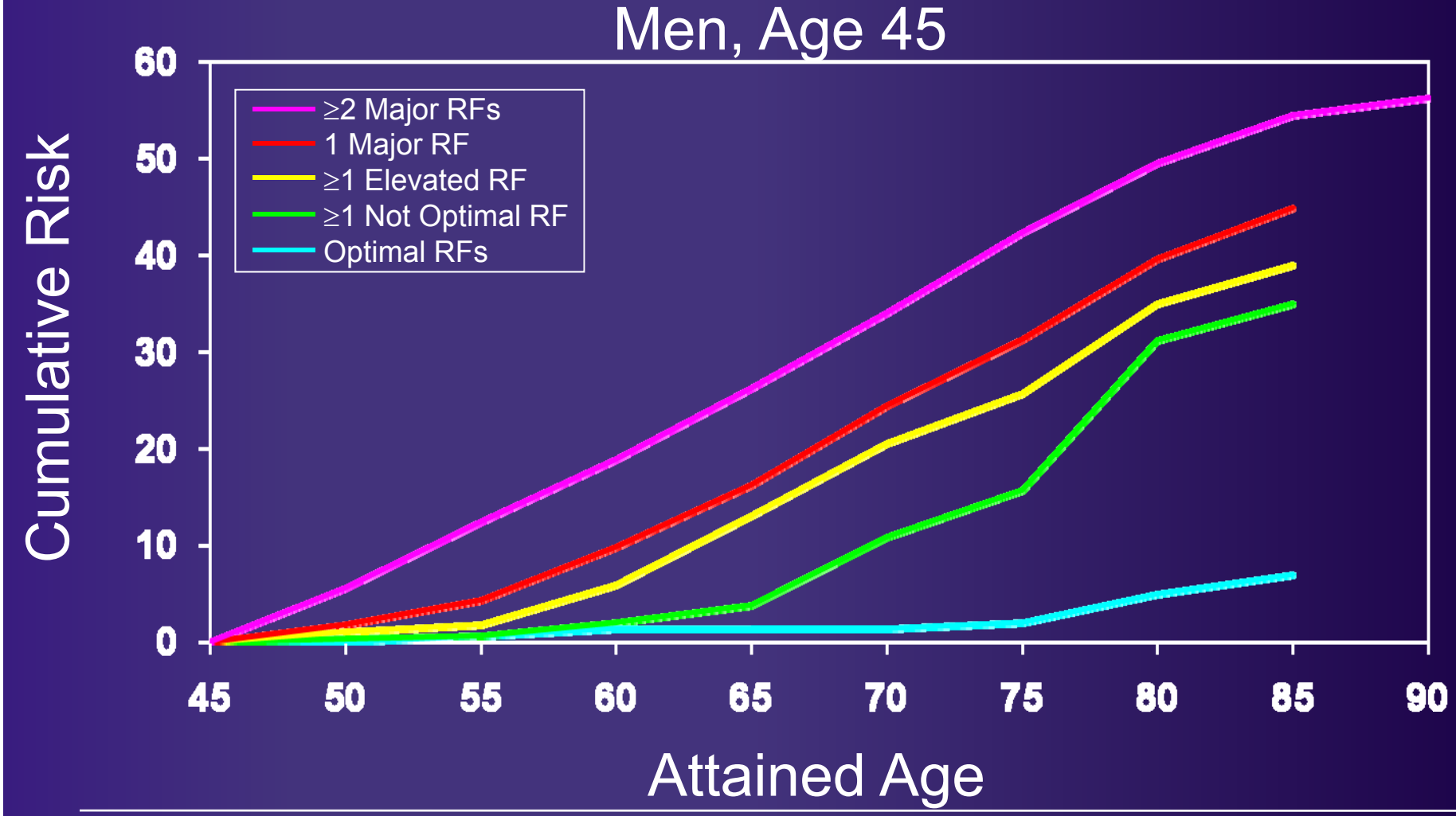
≥1 Elevated	19.1	22.0	18.8	21.5	19.2	18.8	20.4	18.2
1 Major	46.5	40.1	45.9	40.7	44.2	41.6	43.3	43.3
≥2 Major	22.0	16.4	24.2	25.8	25.0	31.3	23.5	30.8

Lifetime Risks for All ASCVD

Cardiovascular Lifetime Risk Pooling Project



Lifetime Risks* for ASCVD: Men

RF Burden	Index Age			
	Age 45*	Age 55*	Age 65†	Age 75†
All Optimal	1.4% (0-3.4)	14.6% (1.0-28.3)	29.5% (17.0-42.0)	17.5% (3.0-32.0)
≥1 Not Optimal	31.2% (17.6-44.7)	19.7% (11.9-27.4)	29.4% (20.7-38.1)	22.8% (14.4-31.2)
≥1 Elevated	35.0% (26.8-43.2)	33.9% (27.9-39.8)	38.2% (32.4-43.9)	28.9% (22.7-35.2)
1 Major	39.6% (35.7-43.6)	32.2% (29.1-35.2)	37.2% (33.7-40.8)	36.1% (31.6-40.5)
≥2 Major	49.5% (45.0-53.9)	46.8% (43.0-50.7)	49.5% (45.2-53.8)	38.5% (32.0-45.0)

* To age 80; † to age 90

Lifetime Risks* for ASCVD: Women

RF Burden	Index Age			
	Age 45*	Age 55*	Age 65†	Age 75†
All Optimal	4.1% (0-8.2)	10.1% (0-25.0)	12.4% (2.8-22.0)	12.4% (0-25.6)
≥1 Not Optimal	12.2% (4.6-19.7)	13.3% (5.5-21.1)	25.0% (15.4-34.5)	19.9% (10.9-29.0)
≥1 Elevated	15.6% (10.3-20.9)	15.3% (11.3-19.3)	29.3% (23.8-34.7)	21.8% (16.8-26.8)
1 Major	20.2% (17.2-23.2)	16.7% (14.5-19.0)	31.9% (28.8-34.9)	29.4% (26.1-32.7)
≥2 Major	30.7% (26.3-35.0)	29.2% (26.2-32.3)	38.7% (35.3-42.1)	36.3% (32.2-40.4)

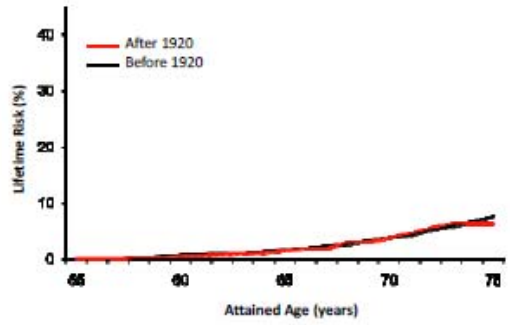
* To age 80; † to age 90

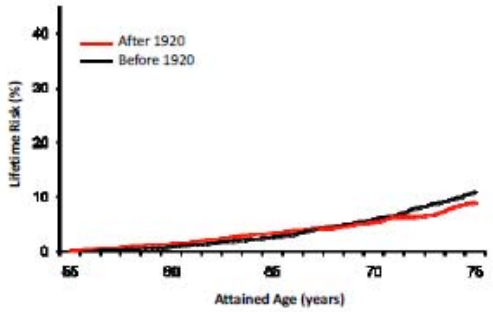
Internal Validation

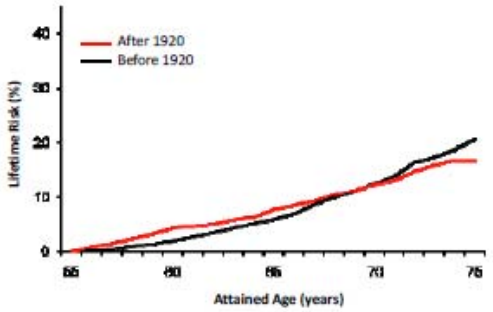
- Check for similar patterns in adjusted cumulative incidence curves in each cohort before pooling
- Happily, these have always been there!
  - Range of absolute values
  - Very similar relative and absolute risk estimates once stratified by aggregate RF burden

Birth Cohort Effects

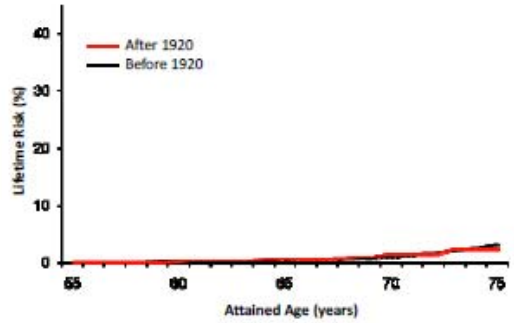
Men

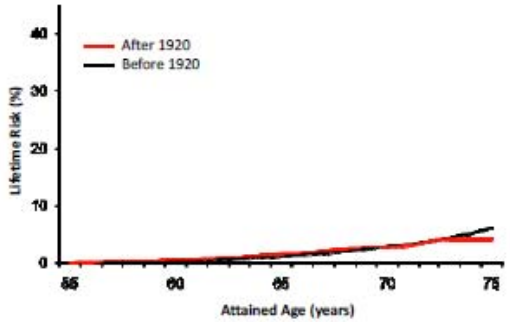


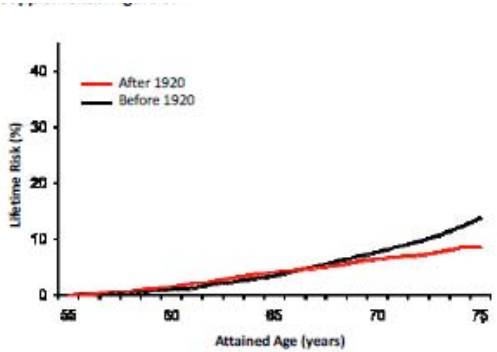




Women







1 Elevated RF 1 Major RF ≥2 Major RFs

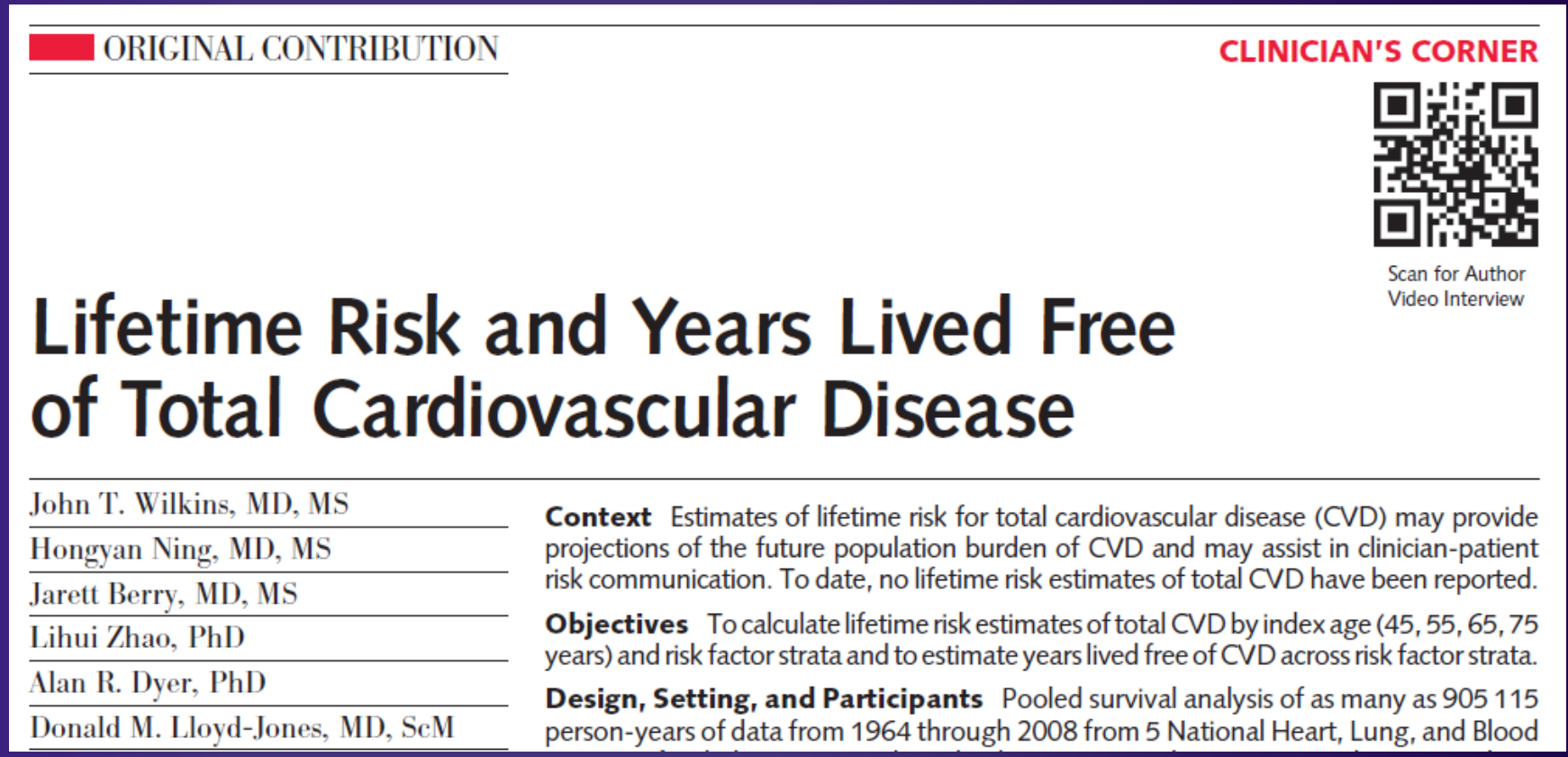
…Similar patterns seen in NHANES I, II, and III cohorts

Summary

- Lifetime risks for CVD are overall high
- Differences in risk factor burden in middle and older ages associated with marked differences in remaining LR for CVD
  - …despite similar short-term risks
  - Optimal risk profile associated with very low LRs
  - 7- to 30-fold gradient in LR for 45 yo men and women
- LRs similar in whites and blacks
  - … but for different reasons
- LRs similar across birth cohorts

Implications

- Competing risks are important to consider in long-term risk estimation
- Effect of RFs remarkably consistent over time and across races and birth cohorts
- Secular trends of declining CVD rates due to changes in prevalence of RFs>>effect of RFs



ORIGINAL CONTRIBUTION

CLINICIAN'S CORNER

Scan for Author Video Interview

Lifetime Risk and Years Lived Free of Total Cardiovascular Disease

John T. Wilkins, MD, MS
Hongyan Ning, MD, MS
Jarett Berry, MD, MS
Lihui Zhao, PhD
Alan R. Dyer, PhD
Donald M. Lloyd-Jones, MD, ScM

Context Estimates of lifetime risk for total cardiovascular disease (CVD) may provide projections of the future population burden of CVD and may assist in clinician-patient risk communication. To date, no lifetime risk estimates of total CVD have been reported.

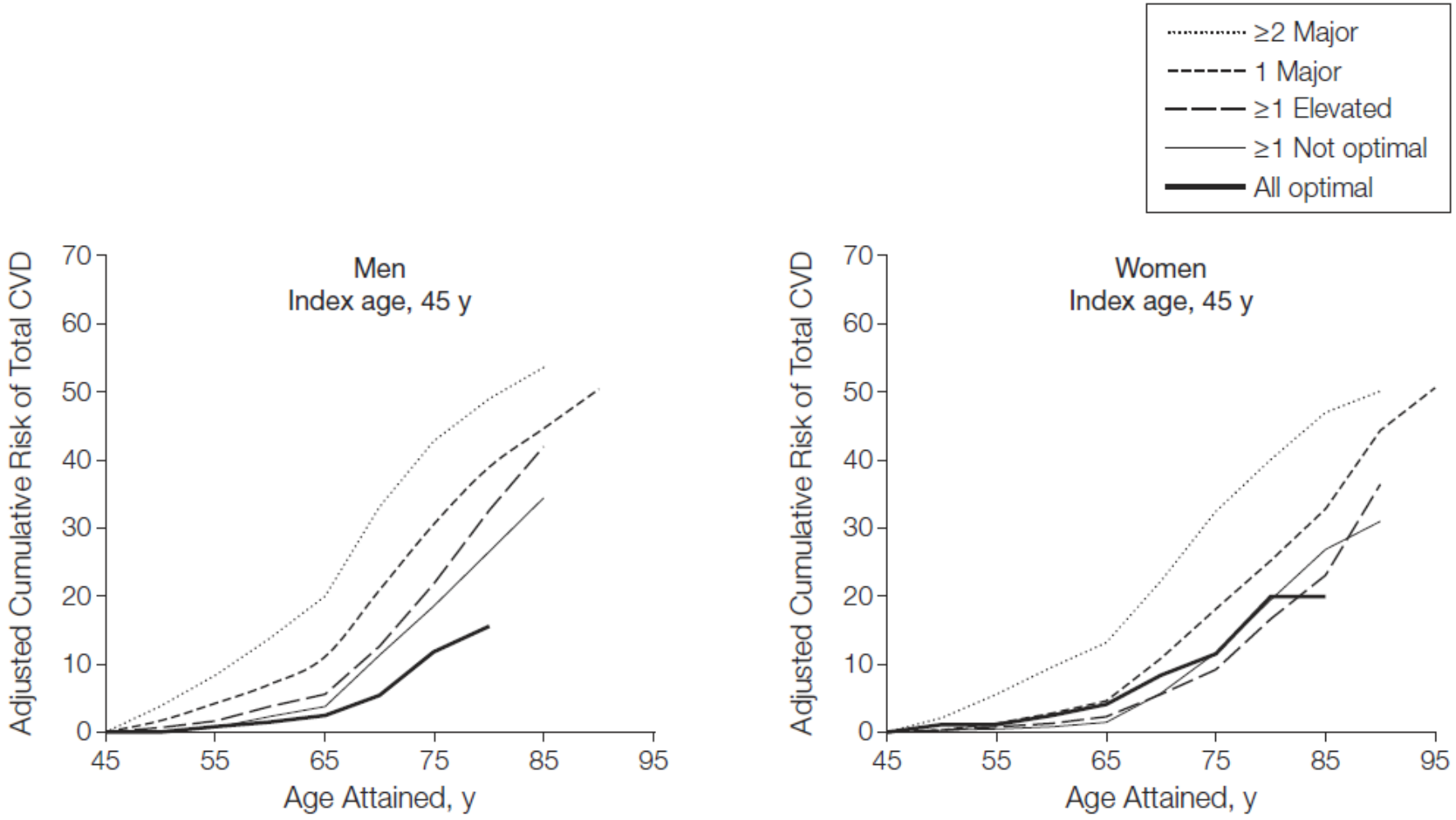
Objectives To calculate lifetime risk estimates of total CVD by index age (45, 55, 65, 75 years) and risk factor strata and to estimate years lived free of CVD across risk factor strata.

Design, Setting, and Participants Pooled survival analysis of as many as 905 115 person-years of data from 1964 through 2008 from 5 National Heart, Lung, and Blood

- LR for Total CVD (CHD, Stroke, HF, CVD death):
  - Men: 60%; Women: 56%
  - Varies by aggregate RF burden

Wilkins, JAMA 2012

Lifetime Risk for Total CVD by Aggregate RF Burden: Age 45



Wilkins, JAMA 2012

Compression of Morbidity: Methods

- Censoring precludes estimation of mean CVD-free and overall survival times
- Irwin's restricted mean
  - Mean of the survival time restricted to a given time point
  - Mathematically equivalent to the area under the survival curve up to the selected restriction time
  - For each index age the restriction time point was set as 95 years old or the oldest age such that the SE of the survival estimate is ≤10%

Wilkins, JAMA 2012

Compression of Morbidity

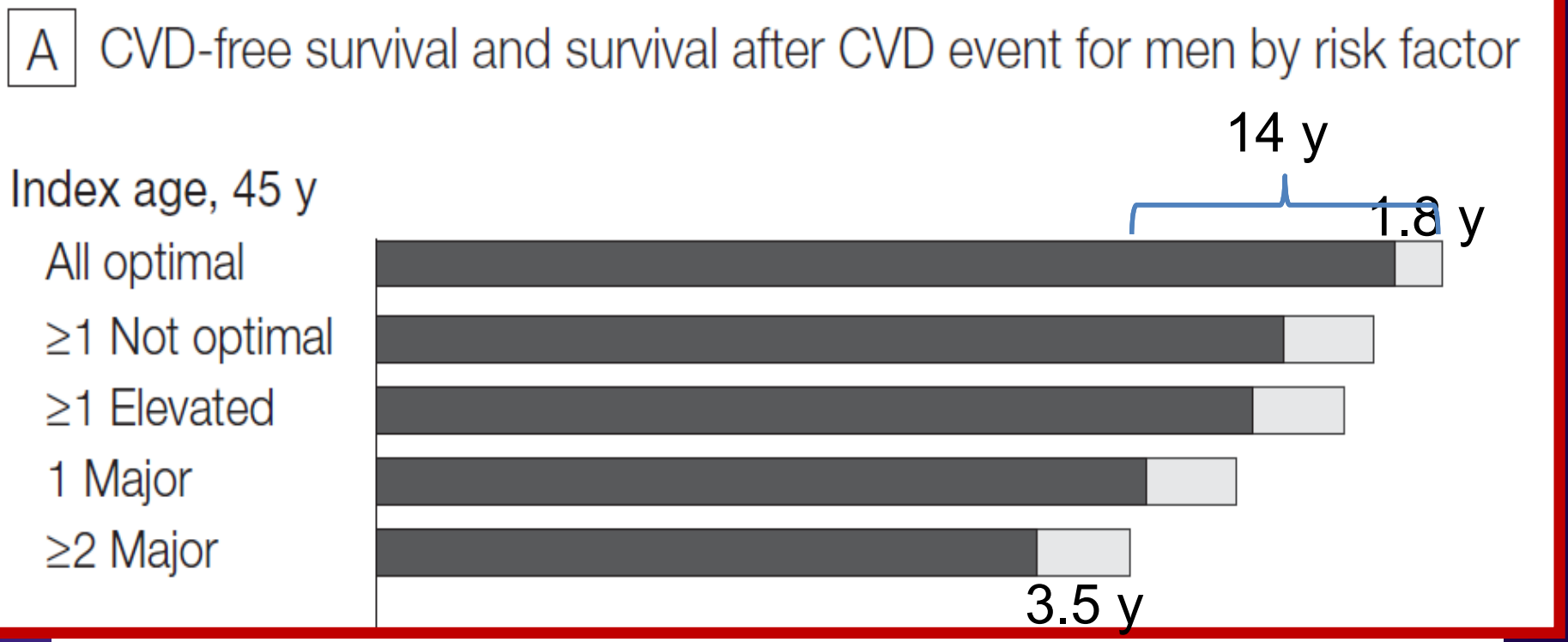
Figure 2. CVD-Free Survival and Survival After CVD Events for Men and Women by Index Age and Aggregate Risk Factor Burden

A CVD-free survival and survival after CVD event for men by risk factor

Index age, 45 y

B CVD-free survival and survival after CVD event for women by risk factor

Index age, 45 y



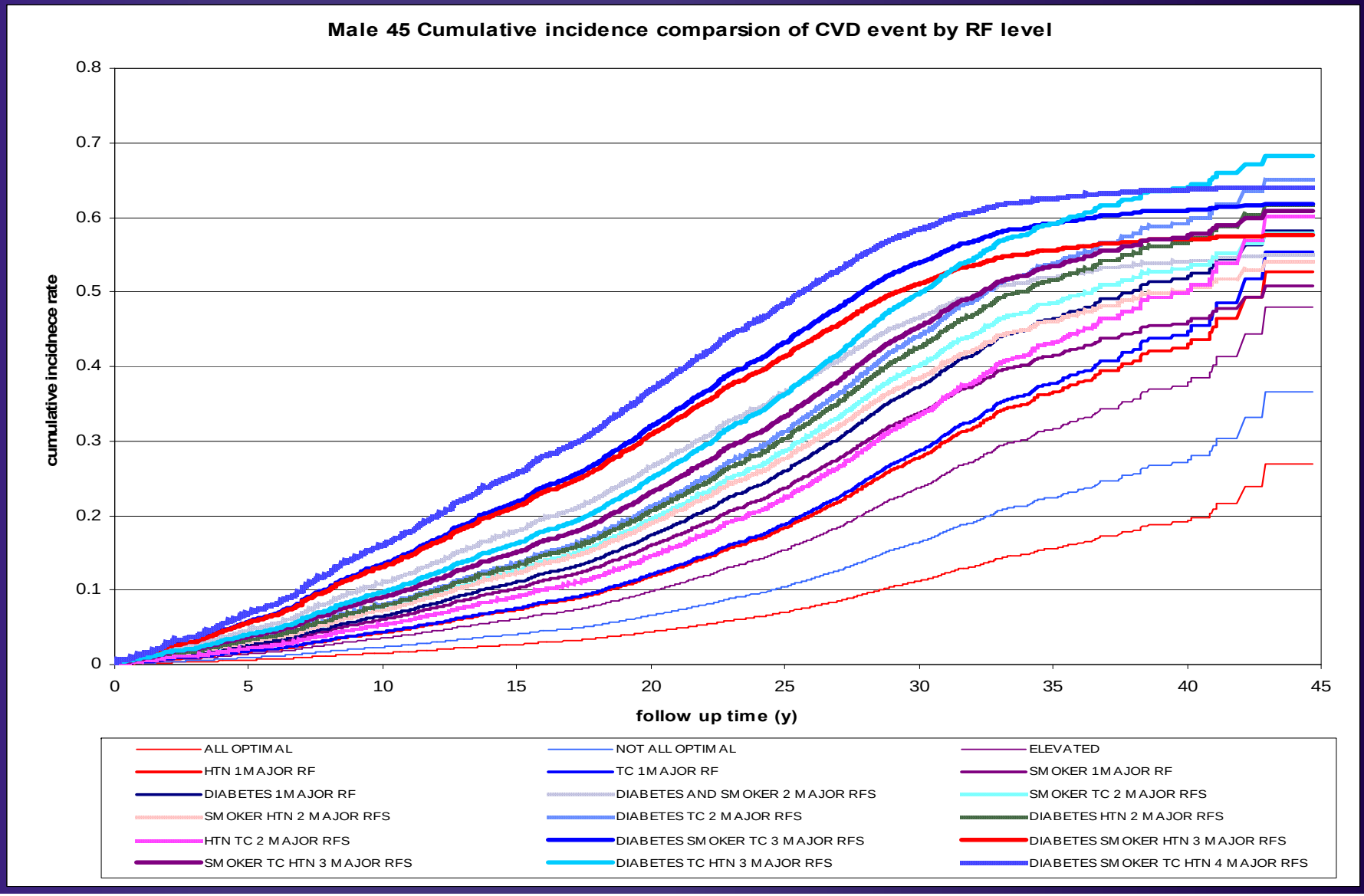
CVD indicates cardiovascular disease.

Wilkins, JAMA 2012

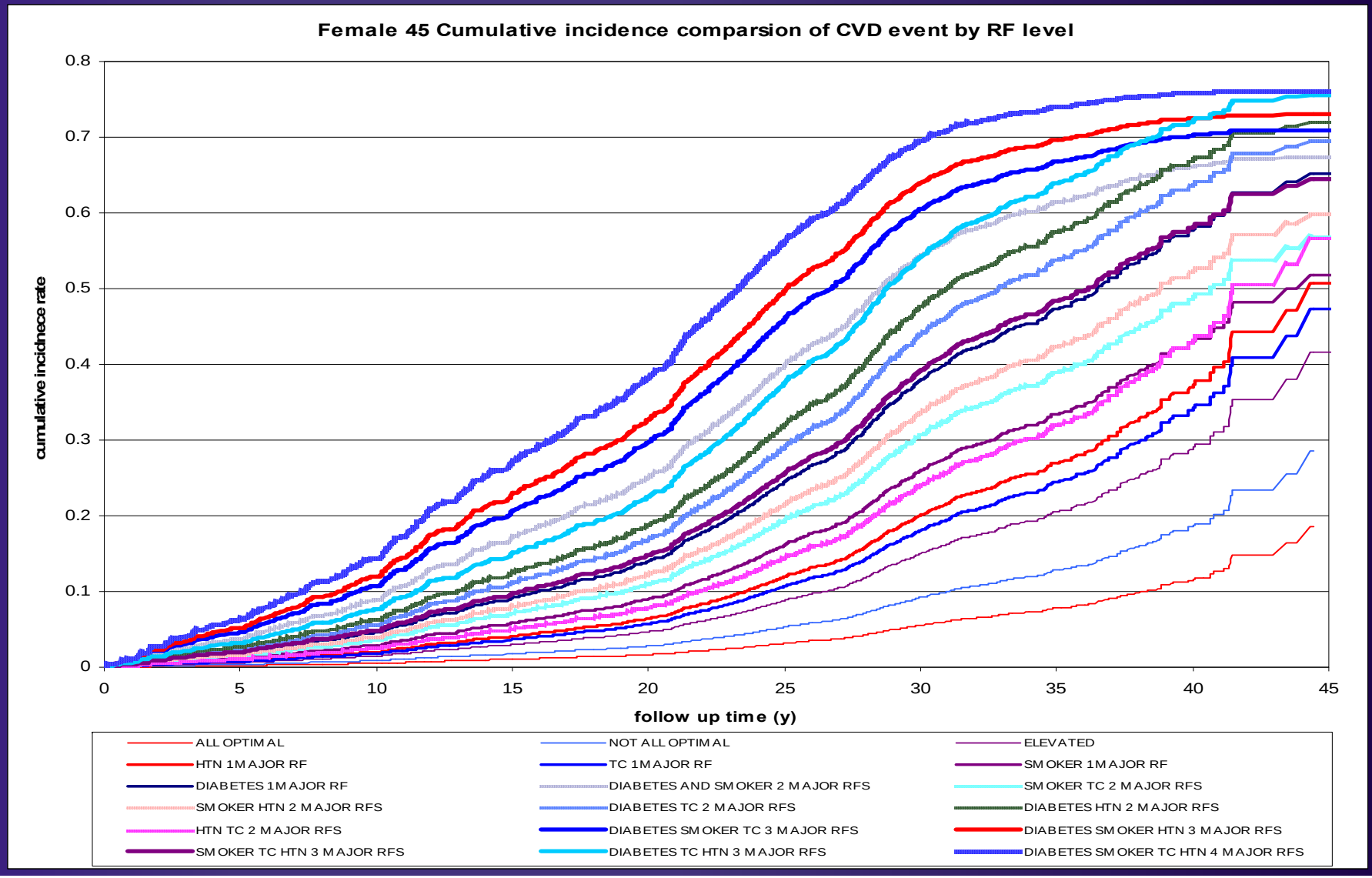
Competing Cox Methodology

- Lets the outcomes compete to be first, rather than considering them one at a time
- Provides robust estimates of hazards and cumulative incidences for multiple endpoints simultaneously
  - And gives a total cumulative incidence for events through the end of follow up

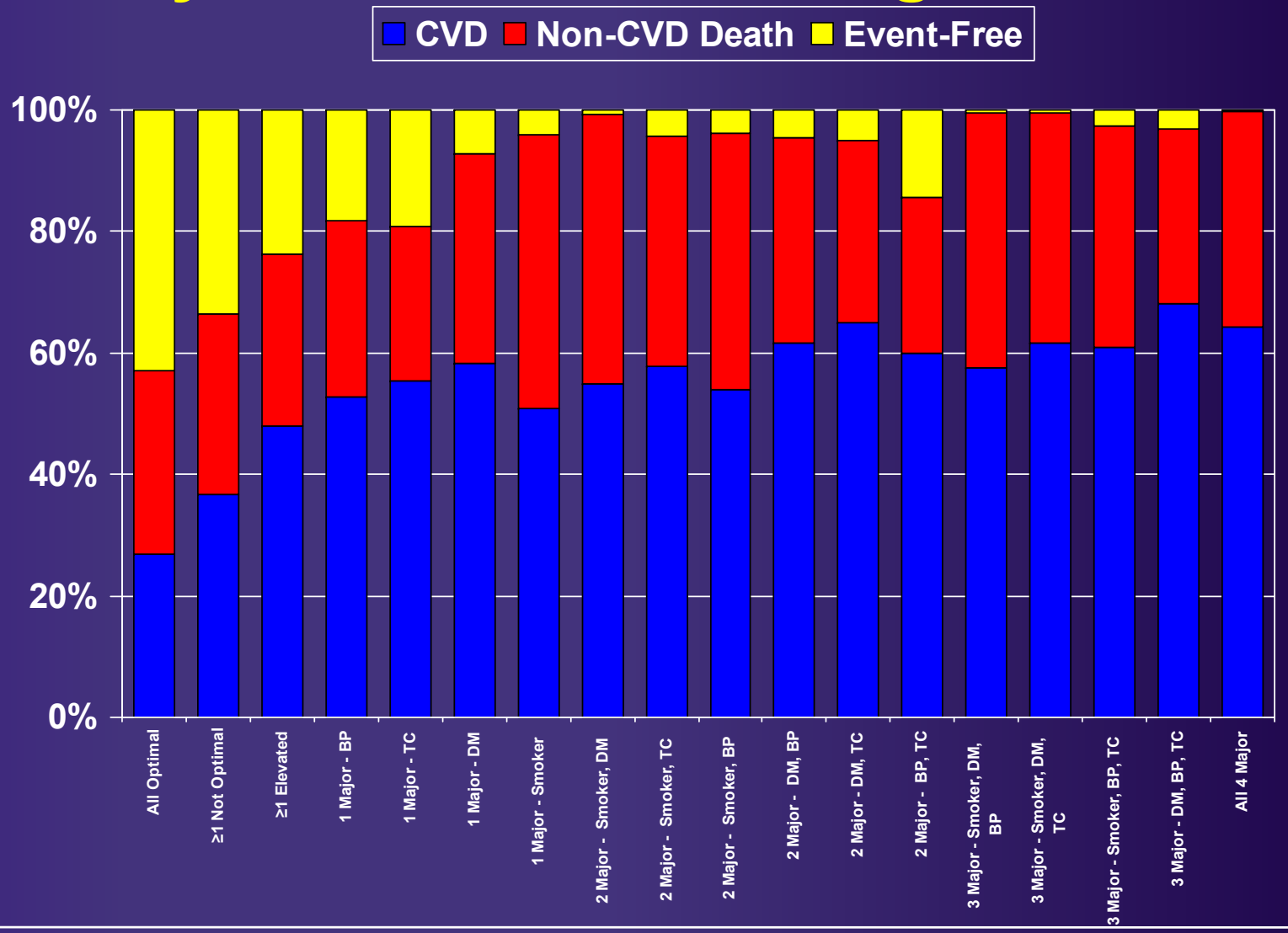
Competing CI for CVD Events by RF Burden: Male, Age 45



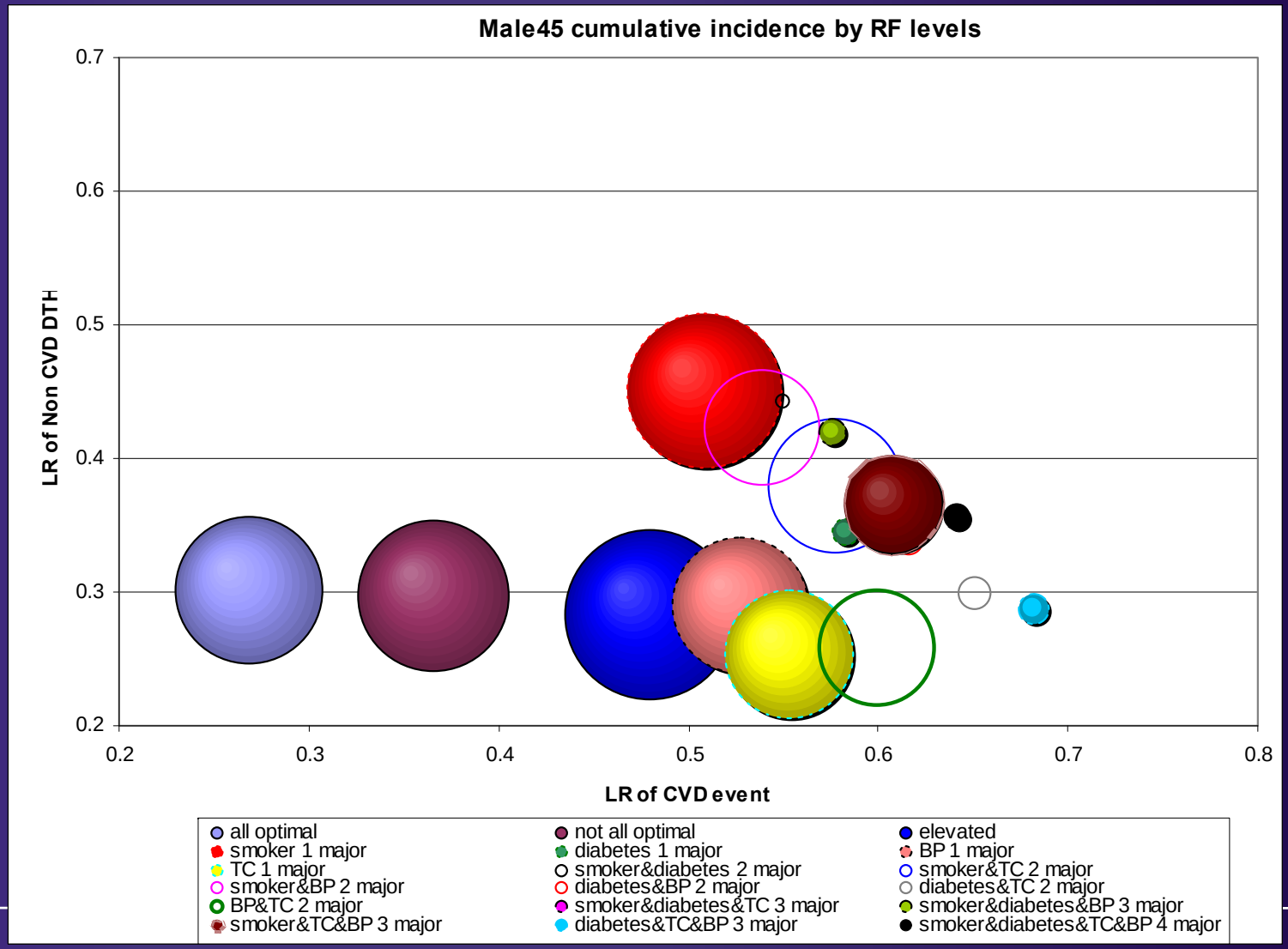
Competing CI for CVD Events by RF Burden: Female, Age 45



Competing CI for CVD and Non-CVD Events by RF Burden: Male, Age 45



Competing CI for CVD Events and Non-CVD Death by RF Burden: Male, Age 45



Racial Differences in Risks for First Cardiovascular Events and Noncardiovascular Death

The Atherosclerosis Risk in Communities Study, the Cardiovascular Health Study, and the Multi-Ethnic Study of Atherosclerosis

Matthew Feinstein, MD; Hongyan Ning, MD, MS; Joseph Kang, PhD; Alain Bertoni, MD, MPH; Mercedes Carnethon, PhD; Donald M. Lloyd-Jones, MD, ScM

Competing vs Standard Cox Models (B vs W)

	Men*		Women*	
	Competing Risks Method (Fine and Gray Method)	Standard Cox Model Method	Competing Risks Method (Fine and Gray Method)	Standard Cox Model Method
Model 1: unadjusted				
Non-CVD death	1.87 (1.53, 2.29)	1.76 (1.49, 2.07)	1.39 (1.10, 1.77)	1.59 (1.33, 1.90)
CHD death/nonfatal MI	0.77 (0.60, 1.00)	1.06 (0.90, 1.26)	1.24 (0.94, 1.65)	1.72 (1.40, 2.10)
Stroke	2.18 (1.63, 2.90)	2.37 (1.84, 3.04)	2.91 (2.15, 3.92)	2.92 (2.23, 3.82)
HF	1.17 (0.91, 1.49)	1.24 (1.02, 1.50)	2.07 (1.65, 2.59)	2.14 (1.78, 2.57)
Other CVD death	1.85 (1.34, 2.56)	N/A	2.20 (1.42, 3.42)	N/A
Any CVD event (overall)	1.27 (1.11, 1.45)	1.29 (1.14, 1.46)	2.03 (1.76, 2.34)	2.07 (1.81, 2.37)

Feinstein, Circulation 2012

External validation

Lifetime risk for cancer death by sex and smoking status: the lifetime risk pooling project

Andrew Gawron · Lifang Hou · Hongyan Ning · Jarett D. Berry · Donald M. Lloyd-Jones

Gawron, *Cancer Causes & Control*, 2012

External validation

Table 1 Cohort characteristics and proportion of participants with death from cancer during observed follow-up

	ARIC	CHA	FHS	FHSOFF	HHP	HISEP	NHEF	NHEFII	PRHHP	WHI-OS
Total *N*	15,371	33,902	5,079	4,739	8,006	3,042	11,399	12,504	9,475	91,294
Entry age, mean (years)	54.2	40.4	44.2	36.9	54.4	74.6	49.8	46.2	54.9	63.6
Entry age, range (years)	45–64	18–90	28–64	20–62	45–68	65–99	25–74	18–74	47–77	50–79
Follow-up years, mean	10.8	29	35.5	24.1	21.3	5.4	16.2	13.2	14.2	7.7
Follow-up years, range	0.0–13.1	0.1–37.0	24.0–54.8	0.1–31.6	7.0–33.1	0.0–7.9	0–22.1	0.0–16.0	14.0–20.0	0.1–10.6
Cancer deaths (%)	61 (0.4)	3,987 (10.5)	1,034 (20.4)	260 (5.5)	1,532 (19.1)	106 (3.5)	982 (8.7)	568 (4.5)	212 (2.2)	2,575 (2.8)

Index age (years)	Pooled cohorts				Total follow-up (person-years)	Cancer deaths, *N*	Total deaths, *N*
	Male		Female				
	Smokers	Non-smokers	Smokers	Non-smokers			
45	4,586	3,823	1,827	2,492	164,212	1,375	3,942
55	7,266	6,635	1,729	3,057	203,993	2,583	8,815
65	3,463	4,081	1,071	2,801	108,590	1,678	6,990
75	601	711	358	1,548	24,088	463	2,356

ARIC Atherosclerosis Risk in Communities, *CHA* Chicago Heart Association, *FHS* Framingham Heart Study, *FHOSFF* Framingham Heart Study Offspring Cohort, *HHP* Healthy Heart Program, *HISEP* Hispanic Established Populations for Epidemiologic Studies of the Elderly, *NHEF* National Health and Nutrition Examination Survey, *NHEFII* National Health and Nutrition Examination Survey II, *PRHHP* Puerto Rico Heart Health Program, *WHI* Women's Health Initiative Observational Study

Gawron, *Cancer Causes & Control*, 2012

External validation

Table 2 Lifetime risks for death from cancer at selected index ages to age 90 (% and 95 % CI), by individual cohort and compared to SEER national surveillance data

Index ages (years)	CHA	FHS	HHP	HISEP	NHEF	NHEFII	PRHP	WHI-OS	SEER
Male									
45	22.7 (21.7–23.6)	22.8 (21.0–24.5)	26.8 (25.6–28.0)	N/A	15.6 (13.9–17.4)	21.0 (18.4–23.6)	N/A	N/A	22.3
55	22.7 (21.5–23.8)	22.8 (21.0–24.6)	26.8 (25.5–28.0)	N/A	14.7 (12.9–16.5)	20.5 (17.8–23.2)	12.3 (8.4–16.3)	N/A	22.3
65	21.3 (19.3–23.4)	22.4 (20.5–24.4)	25.5 (24.1–26.9)	7.6 (5.0–10.2)	12.2 (10.4–14.0)	18.6 (15.8–21.4)	11.9 (7.7–16.1)	N/A	20.9
75	20.8 (12.3–29.4)	19.9 (17.6-22.3)	23.8 (21.6–26.0)	6.8 (4.1–9.5)	7.7 (5.5–10.0)	15.9 (11.9–20.0)	8.3 (3.1–13.5)	N/A	16.8
Female									
45	18.3 (17.3–19.2)	18.5 (17.0–20.0)	N/A	N/A	17.4 (15.7–19.0)	13.0 (11.3–14.8)	N/A	N/A	17.8
55	17.1 (16.0–18.2)	18.0 (16.5–19.5)	N/A	N/A	12.1 (10.6–13.6)	11.8 (10.1–13.5)	N/A	20.7 (11.5–30.0)	17.2
65	16.4 (14.4–18.5)	15.9 (14.4–17.4)	N/A	11.0 (8.3–13.7)	8.9 (7.4–10.3)	9.5 (7.9–11.1)	N/A	19.6 (10.1–29.1)	15.4
75	10.1 (4.7–15.5)	12.2 (10.6–13.8)	N/A	10.0 (7.1–13.0)	6.2 (4.3–8.0)	7.0 (4.9–9.2)	N/A	17.3 (7.0–27.6)	11.6

CHA Chicago Heart Association, *FHS* Framingham Heart Study, *HHP* Healthy Heart Program, *HISEP* Hispanic Established Populations for Epidemiologic Studies of the Elderly, *NHEF* National Health and Nutrition Examination Survey, *NHEFII* National Health and Nutrition Examination Survey II, *PRHHP* Puerto Rico Heart Health Program, *WHI* Women's Health Initiative Observational Study, *SEER* Surveillance Epidemiology and End Results (http://seer.cancer.gov)

Gawron, *Cancer Causes & Control*, 2012

Effect of TC Changes over Time
Lifetime Risk Age 55 to 85 y

MEN	One Measurement N=18,026	Two Measurements N=1,316
TC <160 mg/dL	21.3 (17.1-25.4)	6.2 (0-14.7)
TC 160-199 mg/dL	24.9 (23.1-26.7)	22.7 (15.1-24.1)
TC 200-239 mg/dL	30.9 (29.4-32.5)	43.5 (36.5-50.5)
TC ≥ 240 mg/dL or Rx	38.7 (36.7-40.6)	45.6 (39.2-52.0)
WOMEN	**One Measurement N=15,274**	**Two Measurements N=1,200**
TC <160 mg/dL	10.2 (3.6-16.8)	0
TC 160-199 mg/dL	20.4 (17.7-23.1)	8.1 (2.8-13.5)
TC 200-239 mg/dL	20.8 (19.0-25.1)	13.9 (7.9-19.8)
TC ≥ 240 mg/dL or Rx	26.2 (24.5-27.9)	25.7 (22.9-33.4)

Take Home Observations

- You can make useful new insights through data mining
  - But don’t make a career out of it
- Traditional RFs have fairly universal *relative* associations with CVD incidence/prevalence
  - But to understand local incidence need local hazard functions and RF prevalence/burden info
- Competing risks should be a part of our thinking from the population/prevention perspective

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Managing, Pooling and Evaluating Large Datasets

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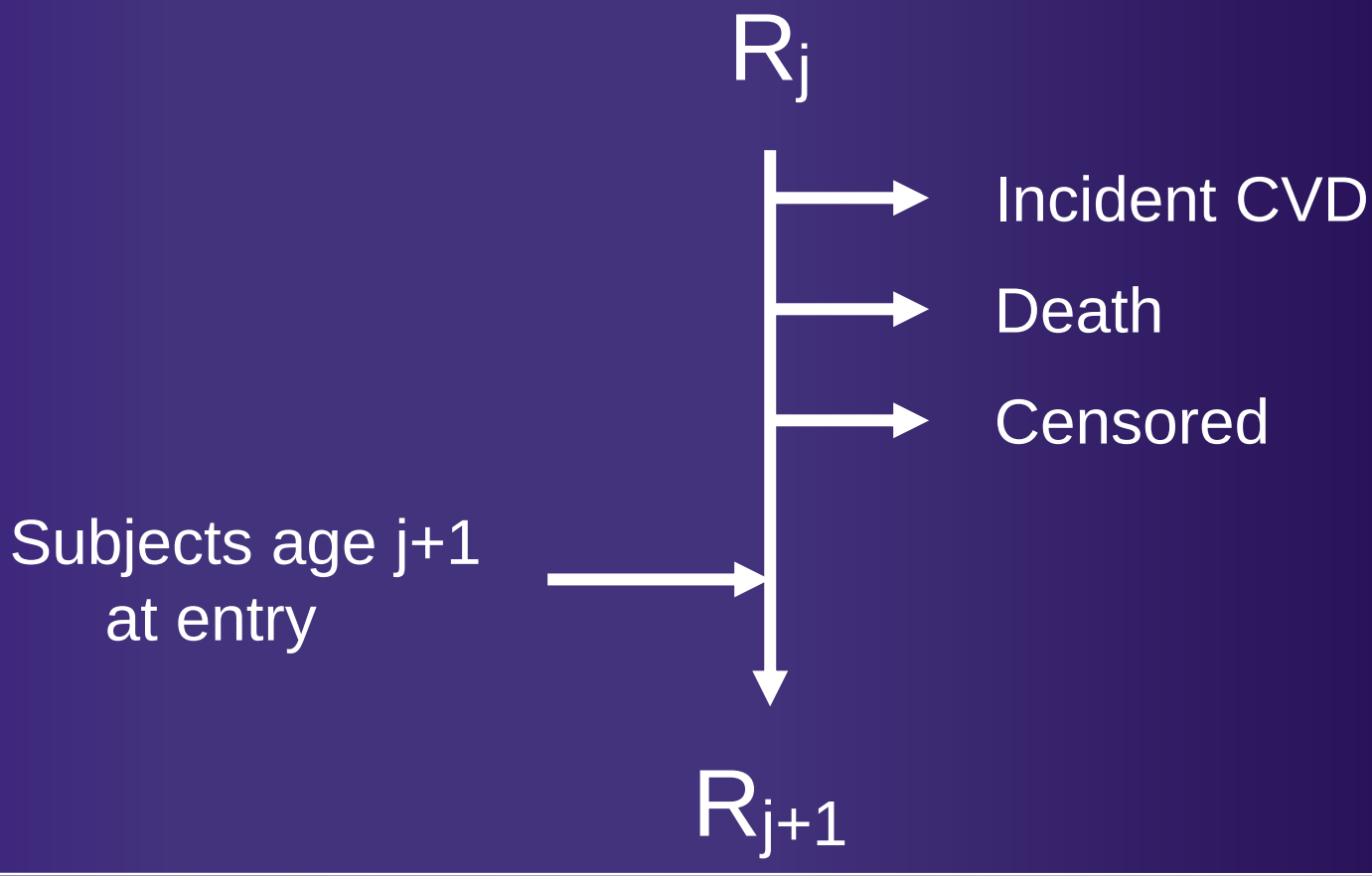
Methods - Lifetime Risk Calculation

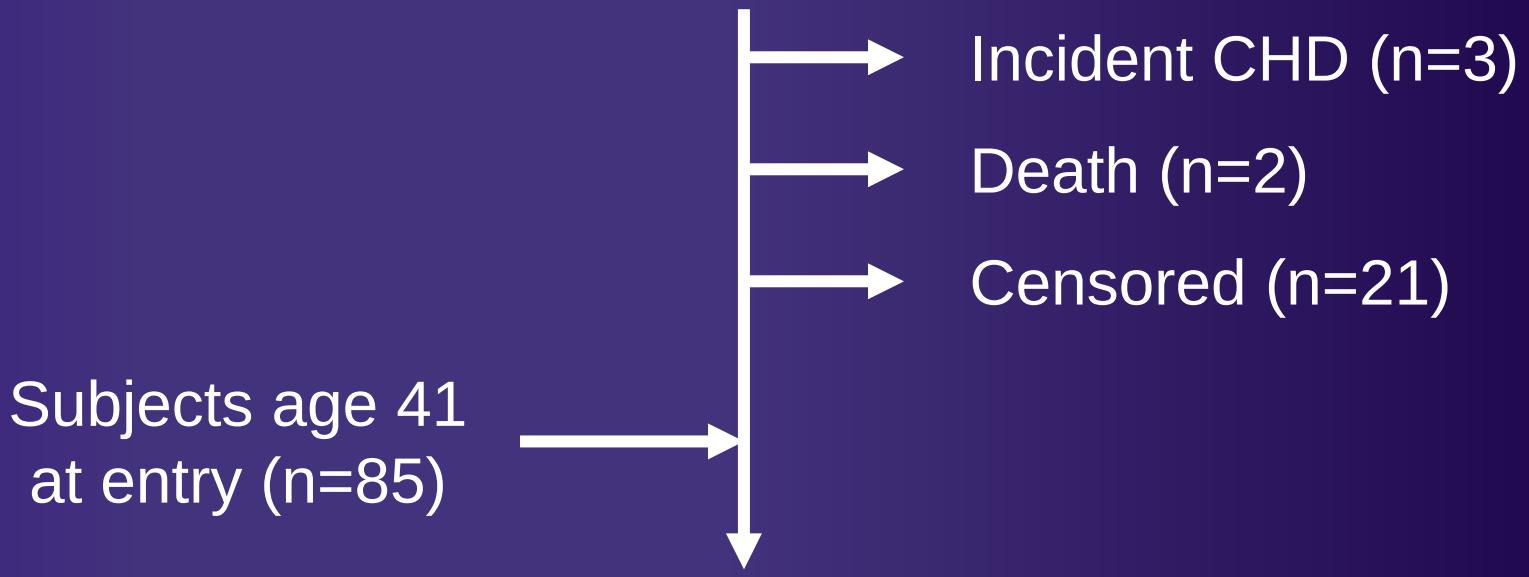
Risk set for age j during F/U



Methods - Lifetime Risk Calculation

Risk set for age j during F/U

$R_{40} = 57 + 1281 = 1338$



$R_{41} = 1397$

Methods - Lifetime Risk Calculation

- Kaplan-Meier estimate
  - Hazard: $h_j = e_j / R_j$
  - Age-specific incidence: $f_j = h_j \times S_{j-1}$
  - Where e_j = number of events at age j, $F_{39} = 0$, and $S_{39} = 1$
  - Cumulative incidence: $F_j = \Sigma^j_{i=40} f_i$
  - Survival probability: $S_j = 1 - F_j$

Methods - Lifetime Risk Calculation

- Cumulative incidence (F_j) does not reflect competing risk of death from other causes
  - Decedents counted as withdrawals
  - Assumed to have same risk of CVD as those censored alive
  - Subjects who die free of CVD before age j have escaped CVD, therefore future risk = 0
- Therefore, a separate survival curve, U_j, calculated with death included as an event rather than a withdrawal

Methods - Lifetime Risk Calculation

- Adjusted cumulative risk
  - $f_j^* = h_j \times U_{j-1}$
  - $F_j^* = \Sigma_{i=40} f_j^*$
  - $S_j^* = 1 - F_j^*$
- Same method used to generate curves for index starting ages other than 40
- 95% CI calculated as per Gaynor et al (J Am Stat Assoc 1993; 88:402)

Methods - Lifetime Risk Calculation

Survival Analysis = $\sum$ (Hazard x Survival Probability)

- K-M estimate
  - Hazard:

    h = Events/Risk set
  - Survival Probability:

$$1 - \left(\frac{\text{Events}}{\text{Risk Set}}\right)$$

- Lifetime risk estimate
  - Hazard:

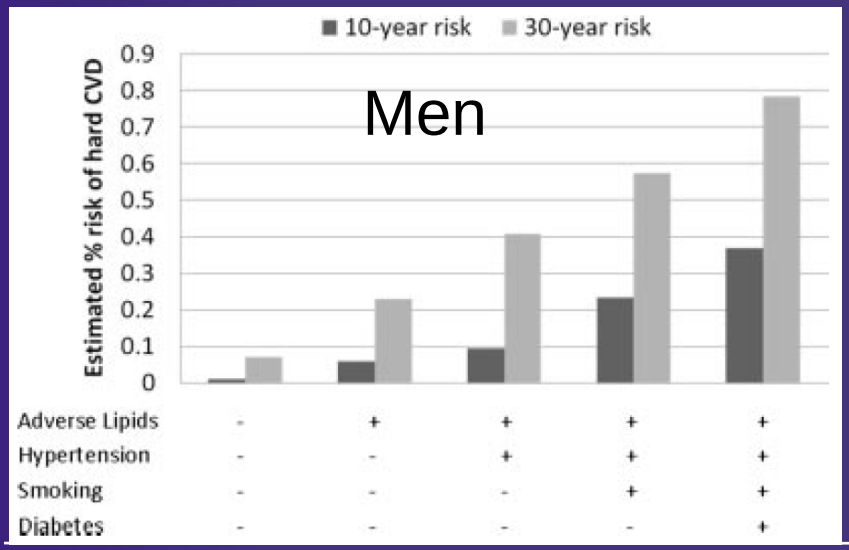
    h = Events/Risk set
  - Survival Probability:

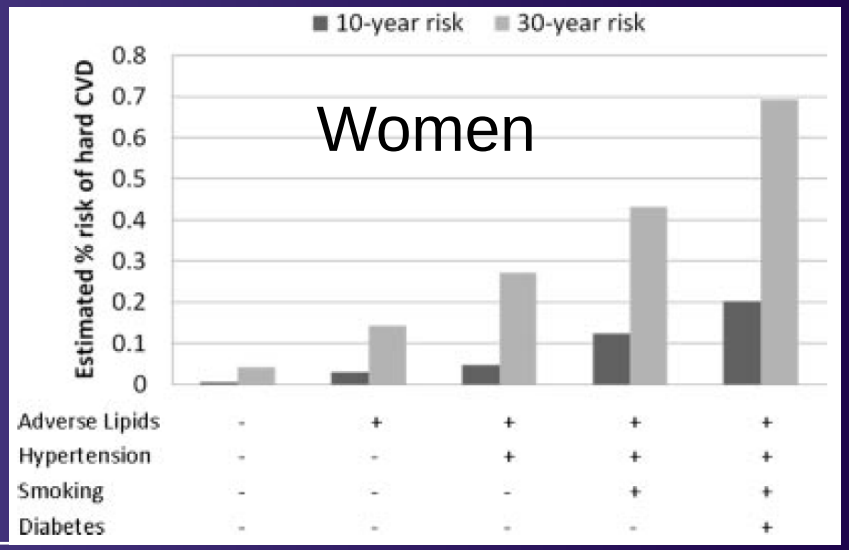
$$1 - \left(\frac{\text{Events + Other Deaths}}{\text{Risk Set}}\right)$$

Can't we just take the 10-year risk estimate and fudge it to give us a long-term risk estimate?

10-Year vs. 30-Year Risks for CVD

- Rank order generally maintained
- Estimating 30 year risk
  - 10-year risk x3 does not work (underestimates risk)
  - Updating age does not work (overestimates high/underestimates low risk)
  - Unadjusted model does not work (overestimates risk)





Pencina et al, Circ 2009