‘ABCDEF’ Approach for CVD Prevention: Focus on Aspirin

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(No Disclosures)

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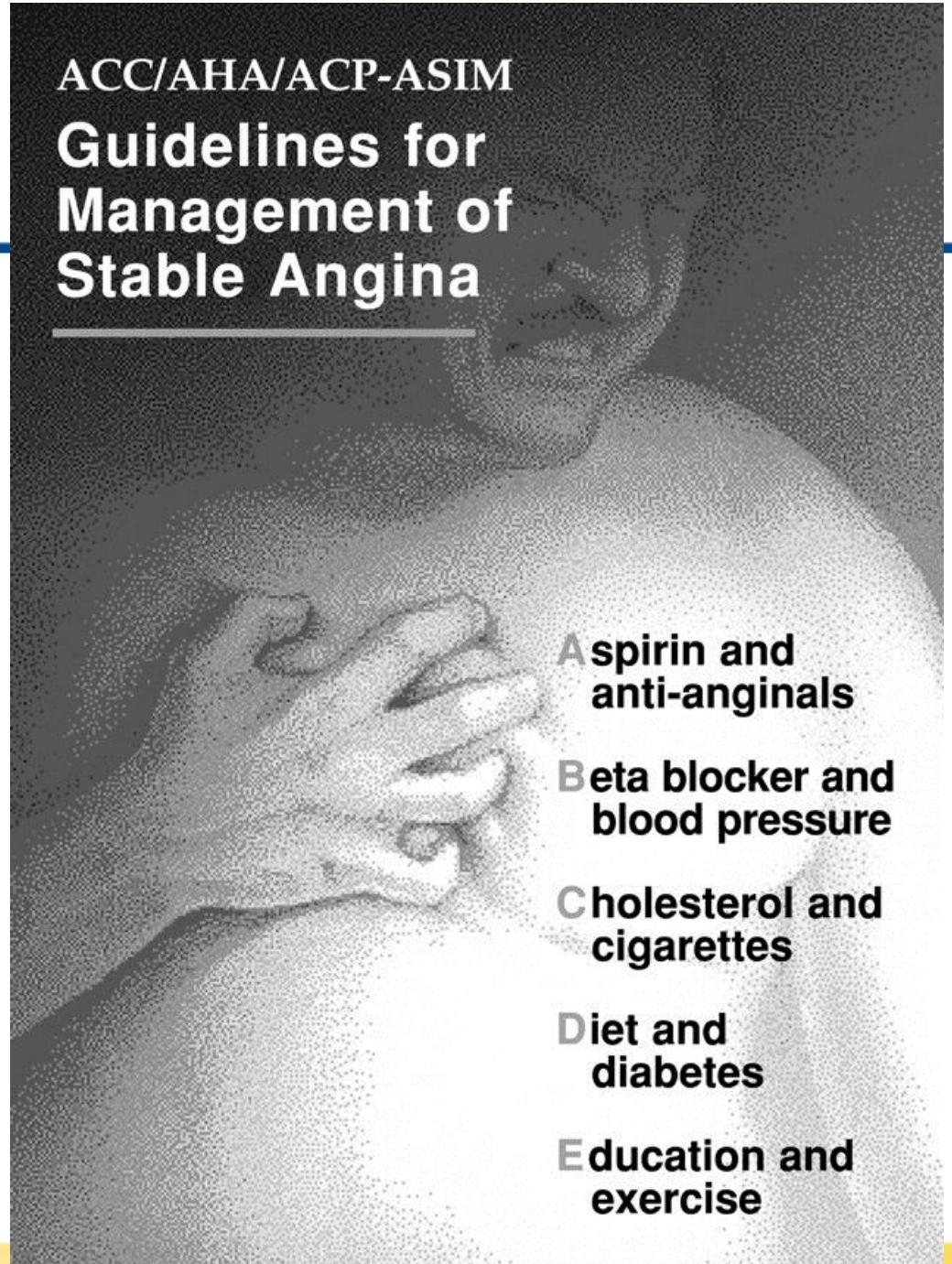

Raymond J Gibbons, et al.

Circulation. 1999;99:2829-2848

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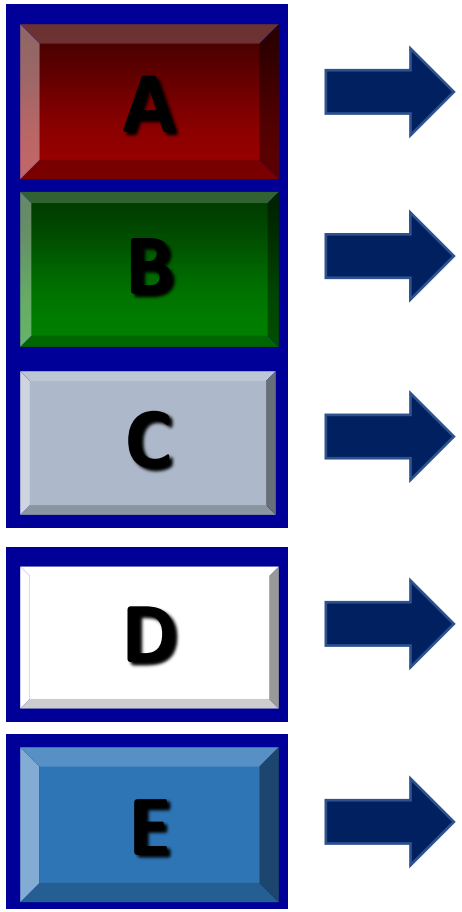
“ABCs” of CVD Prevention & Management



Assessment of Risk
Antiplatelet/Anticoagulant Rx

Blood pressure

Cholesterol
Cigarette Cessation

Diabetes/Glucose Management
Diet/Weight

Exercise/Education

2019 ACC/AHA CVD Prevention Guideline Writing Committee

- Routine use of an ‘ABCDEF’ approach for patient management can help keep track of latest prevention-related guidelines.

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Assessment of CVD Risk

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Shared Decision Making

Team-Based Approach to Prevention

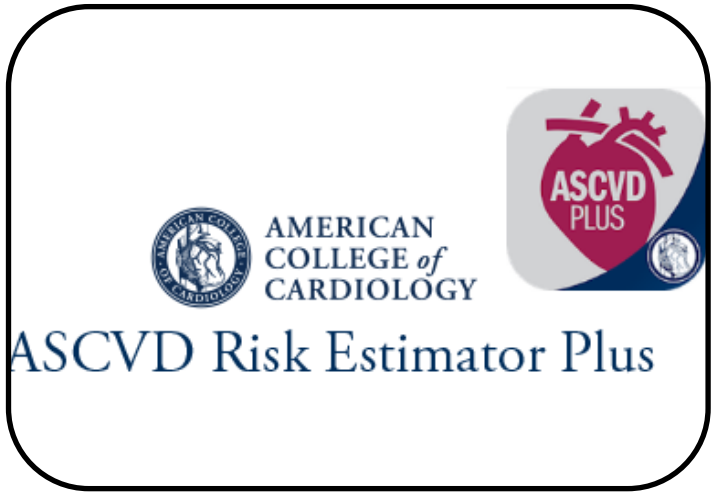
Social Determinants of Health

- Socioeconomic factors: limit effectiveness of recommendations
- Socioeconomic disadvantages: not captured by existing CVD risk estimators
- Medicare/Medicaid developed 5 domain screening tool:

Assessment of Cardiovascular Risk

ASSESSMENT		
COR	LOE	Recommendations
I	B-NR	1. For adults 40-75 y/o, clinicians should routinely assess traditional CVD risk factors & calculate 10-yr risk of ASCVD by using pooled cohort equations (PCE).
IIa	B-NR	2. For 20-39 y/o, it is reasonable to assess traditional ASCVD risk factors at least every 4 - 6 yrs.
IIa	B-NR	3. If borderline risk (5% to <7.5% 10-yr ASCVD risk) or intermediate risk (≥7.5% to <20%), it is reasonable to use additional risk-enhancing factors to guide decisions about preventive interventions (e.g. statin Rx)

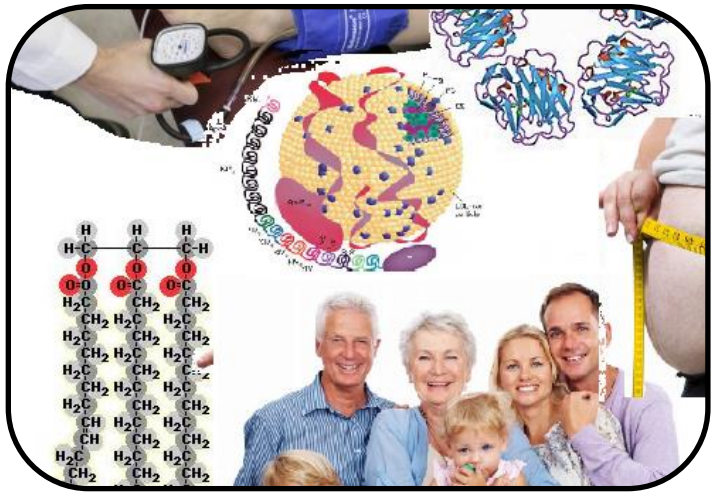
Toolbox for Estimating ASCVD Risk



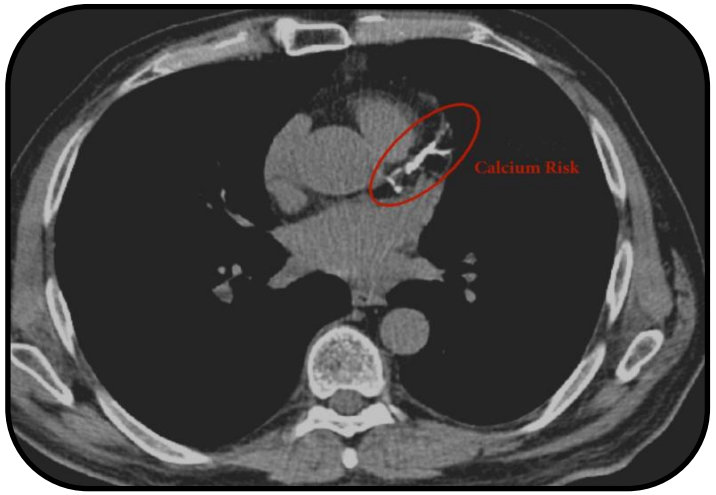
PCE: (Class I)

30-yr ASCVD risk:

(Class IIb)



Risk-Enhancing Factors: (Class IIa)



Coronary artery calcium: (Class IIa)

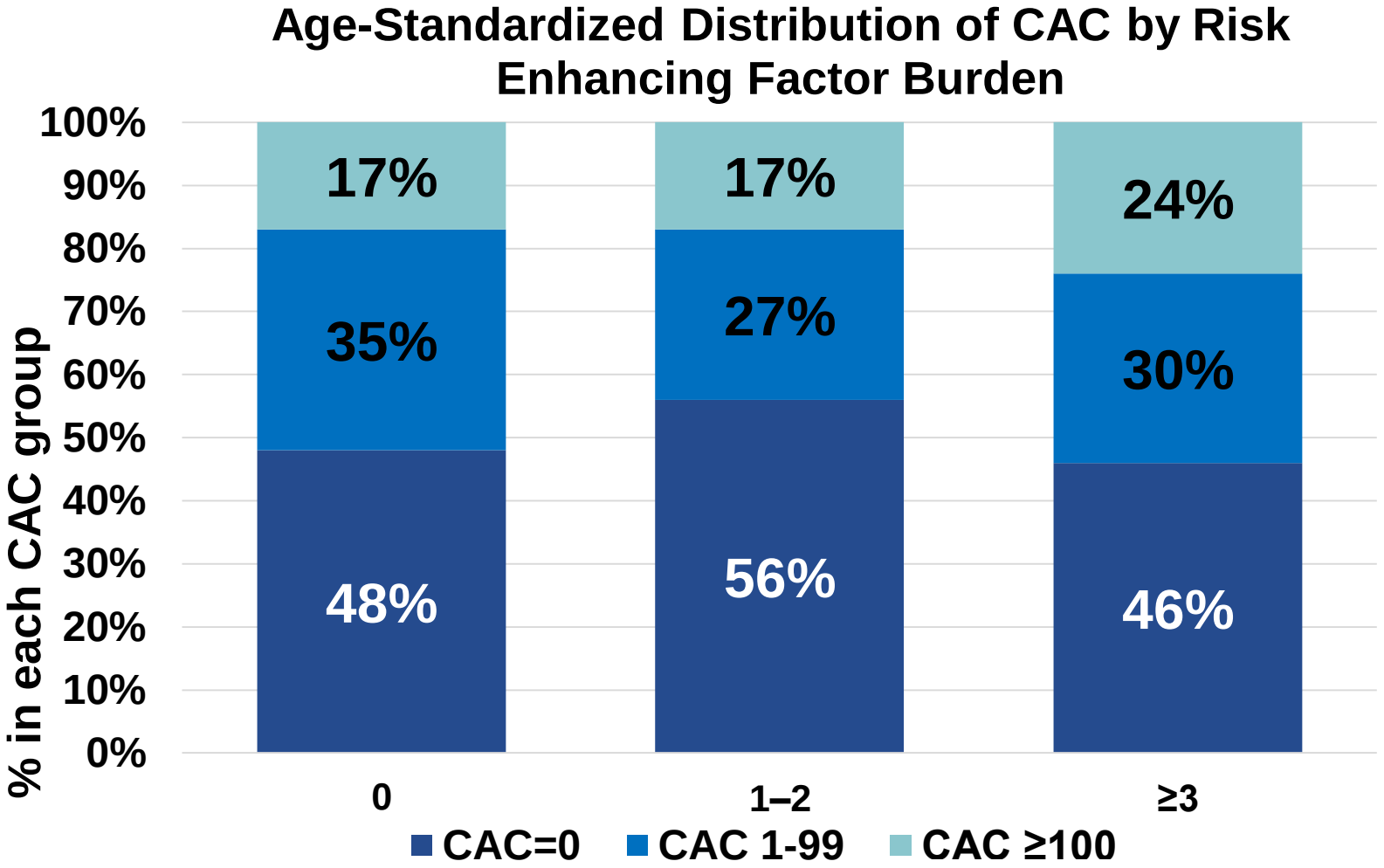
Risk-Enhancing Factors

- *When* to use?
  - **Uncertainty** of PCE estimate
  - Or
    If **further** risk stratification needed

- *Whom* to use in?
  - **Borderline** (5% to <7.5%) or
  - **Intermediate** (≥7.5% to <20%) 10-yr ASCVD risk

Table. ASCVD risk enhancers
• Family history of premature ASCVD • Primary hypercholesterolemia (LDL-C ≥160) • Chronic kidney disease • Metabolic syndrome • Conditions specific to women (e.g. preeclampsia, premature menopause) • Chronic inflammatory conditions (especially rheumatoid arthritis, psoriasis, HIV) • High risk race/ethnicity (e.g. south Asian ancestry) **Lipid/Biomarkers:** • Persistently elevated triglycerides (≥175 mg/dL) ***In selected individuals if measured:*** • hsCRP ≥2 mg/L • Lp(a) levels ≥50 mg/dL or ≥125 nmol/L • ApoB levels ≥130 mg/dL • Ankle-brachial index <0.9

Presence of CAC in Those With REFs From MESA

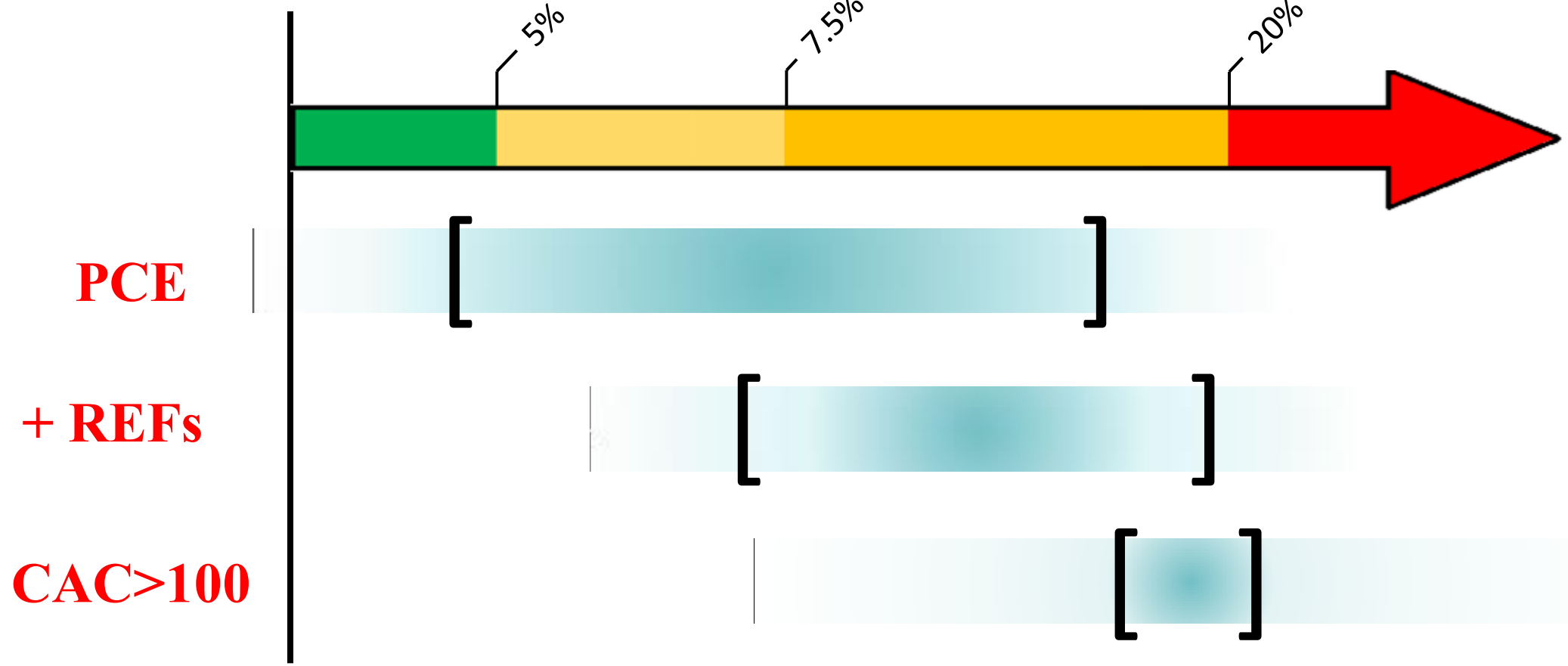


Dudum R*, Patel J* … Al-Rifai M. AHA abstract. 2019.
*Both authors contributed equally to this work.

Assessment of Cardiovascular Risk

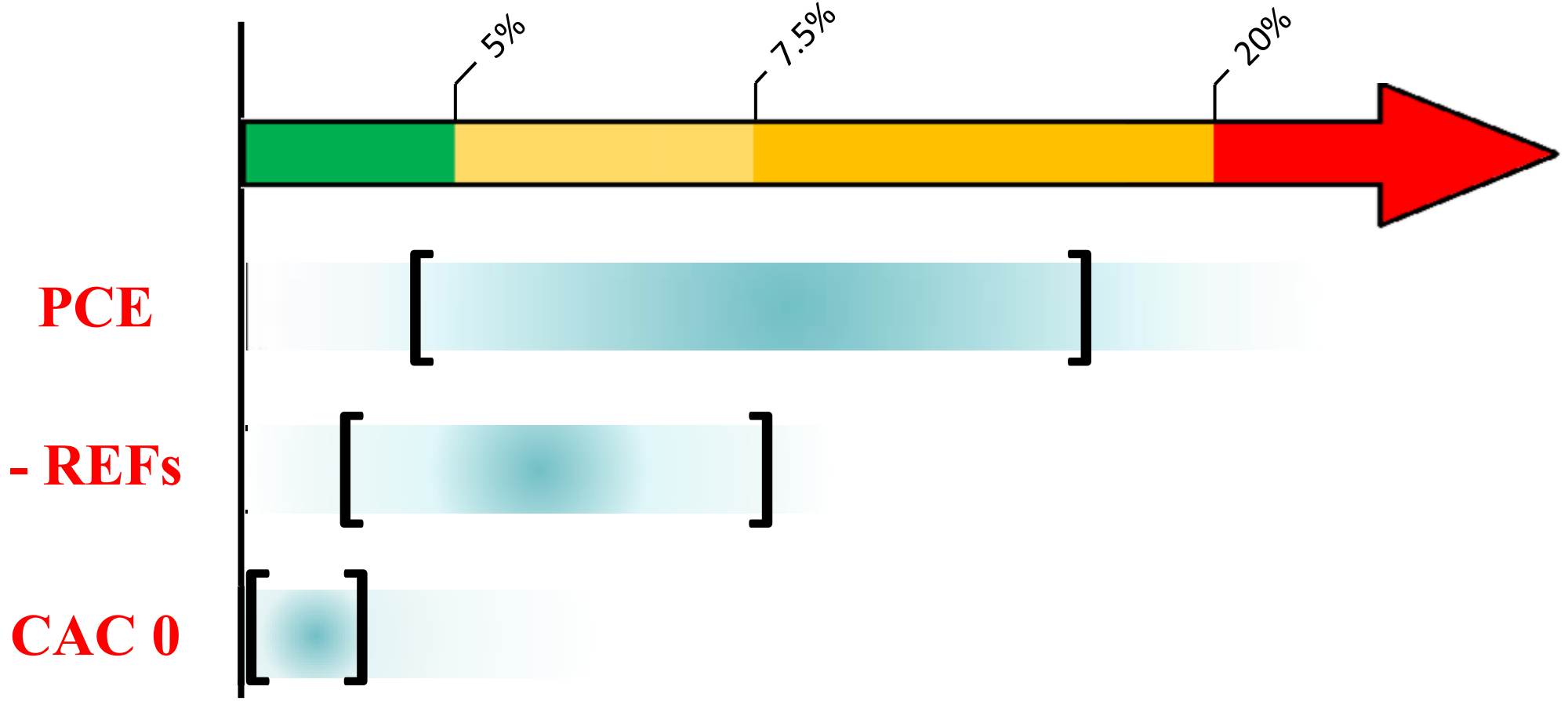
ASSESSMENT		
COR	LOE	Recommendations
IIa	B-NR	4. In adults at intermediate risk (≥7.5% to <20% 10-yr ASCVD risk) or selected adults at borderline risk (5% to <7.5%), if risk-based decisions for preventive interventions (e.g., statin Rx) remain uncertain, it is reasonable to measure a coronary artery calcium score to guide risk discussion.
IIb	B-NR	5. For adults 20-39 y/o and for those 40-59 y/o who have <7.5% 10-yr risk, estimating lifetime or 30-yr risk may be considered.

Risk Reclassification for Primary Prevention



#CAC>100
#SecondaryPrevention

Risk Reclassification for Primary Prevention

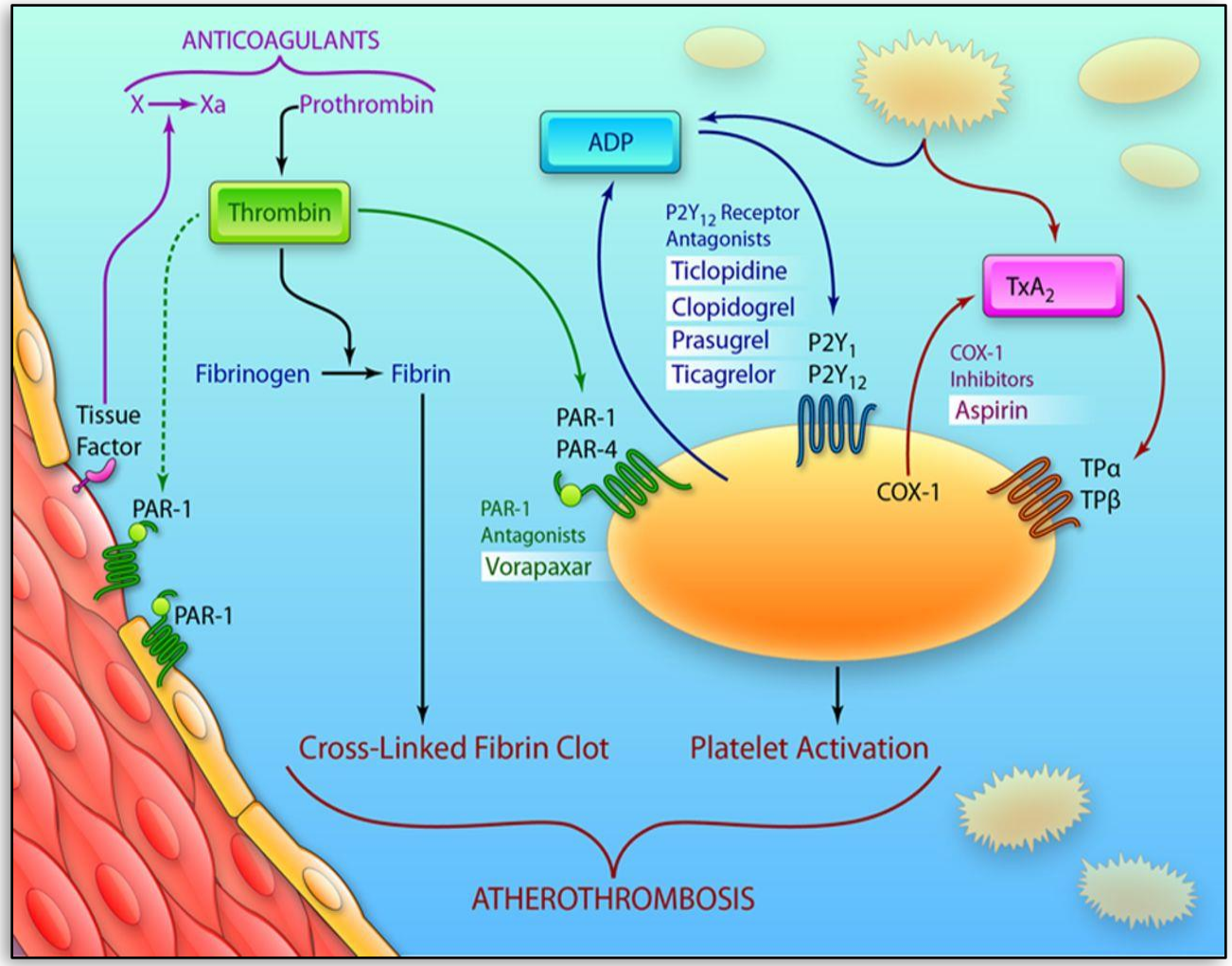


#ThePowerofZero

Aspirin

ASPIRIN		
COR	LOE	Recommendations
IIb	A	1. Low-dose aspirin (75-100 mg orally daily) might be considered for primary prevention of ASCVD among select adults 40-70 y/o at higher ASCVD risk but not at increased bleeding risk.
III: Harm	B-R	2. Low-dose aspirin (75-100 mg orally daily) should not be administered on routine basis for primary prevention among adults >70 y/o.
III: Harm	C-LD	3. Low-dose aspirin (75-100 mg orally daily) should not be administered for primary prevention among adults at increased risk of bleeding.

Targets for Oral Antiplatelet Rx



ASPIRIN – Irreversible Inhibitor of COX-1 which halts production of Thromboxane A2 and thus platelet aggregation

Bonaca MP, Creager MA. *Circ Res.* 2015;116:1579-1598.

Aspirin for Major CV Events (MACE): SECONDARY PREVENTION

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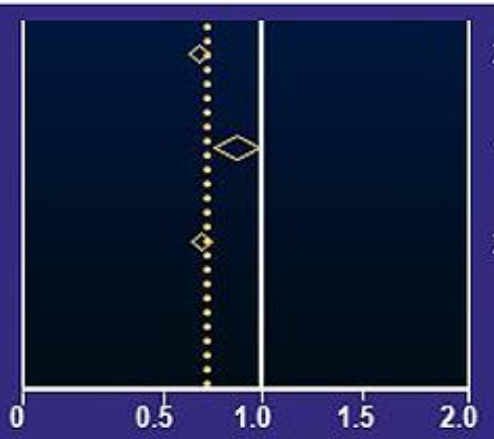
SECONDARY PREVENTION – 27% RRR in MACE

Category of trial	No of trials with data	MI, STROKE OR VASCULAR DEATH: Anti-platelet	MI, STROKE OR VASCULAR DEATH: Adjusted controls	STRATIFIED STATISTICS: O–E	STRATIFIED STATISTICS: variance	% odds reduction (SD)
ALL HIGH RISK**	142	4183/36,536 (14.7%)	5400/36,711	-568.8	1810.9	27% (2)
ALL LOW RISK (primary prevention)	3	652/14,608 (4.46%)	708/14,504 (4.85%)	-28.5	273.5	10% (6)
ALL TRIALS (high or low risk)	145	4835/51,144 (9.5%)	6108/51,315 (11.9%)	-597.3	2084.4	25% (2)



** All high risk: Prior MI, acute MI, prior stroke/TIA, other high risk

Antiplatelet Trialists Collaboration. *BMJ.* 1994;308:81-106.

Role of aspirin in primary prevention

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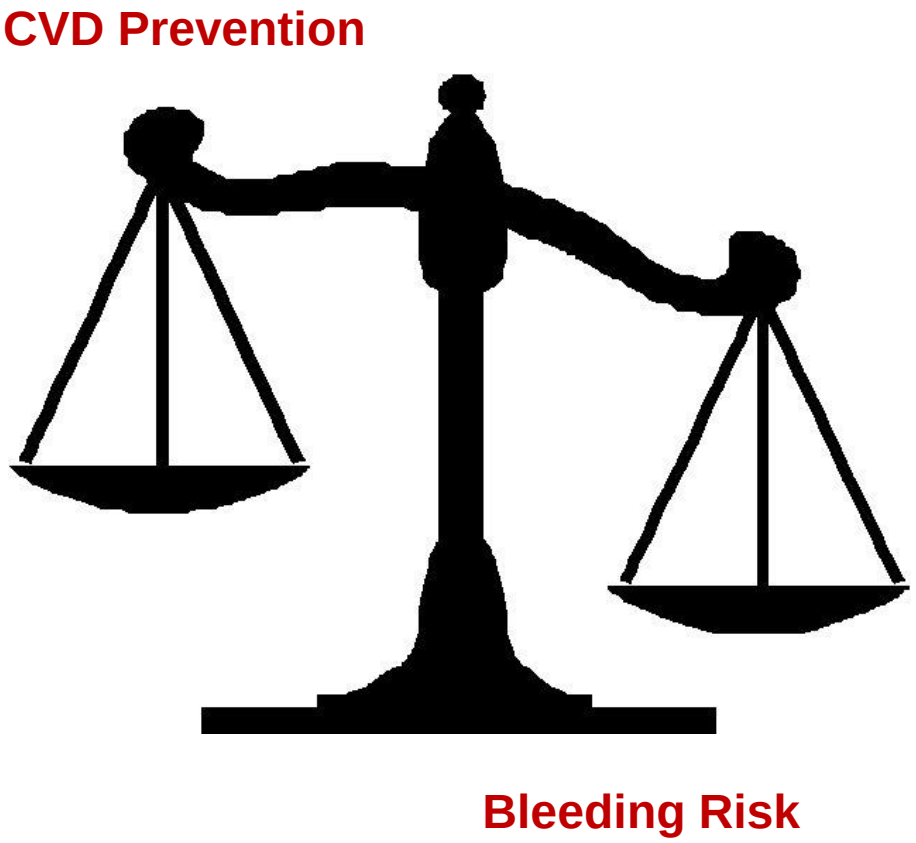
- Absolute risks of vascular events: lower than in secondary prevention
- Complication rates (bleeding) comparable



Aspirin Use in Primary Prevention in U.S.

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From: Prevalence of Aspirin Use for Primary Prevention of CVD in the US: 2017 National Health Interview Survey

	Aspirin Use %	Estimated US Population using Aspirin
Women	**21.8%**	**14.5 Million**
Men	25.5%	14.5 Million
Age		
40-49 y	7.0%	2.6 Million
50-59 y	18.4%	6.7 Million
60-69 y	34.7%	10.2 Million
70-79 y	**44.6%**	**6.5 Million**
≥80 y	**46.2%**	**3.05 Million**

O'Brien CW et al. Ann Intern Med. Published online July 23, 2019. doi:10.7326/M19-0953

Aspirin for Primary Prevention of CVD

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"An aspirin a day will help prevent a heart attack if you have it for lunch instead of a cheeseburger."

Aspirin for Primary Prevention of CVD

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- Based on older trials, prior US guidelines had recommended low dose aspirin for primary ASCVD prevention only in setting of elevated 10-yr CVD risk

Prior AHA/ACC Aspirin Recommendations ('97 and '02)

Primary Prevention

Aspirin (75-162 mg daily) should be used in adults at intermediate risk (10-year risk of CHD ≥10%)

CHD=Coronary heart disease

Source: Pearson TA et al. *Circulation* 2002;106:388-391

Grundy SM et al. *Circulation* 1997; 95: 2329–2331

Aspirin for Primary Prevention of CVD

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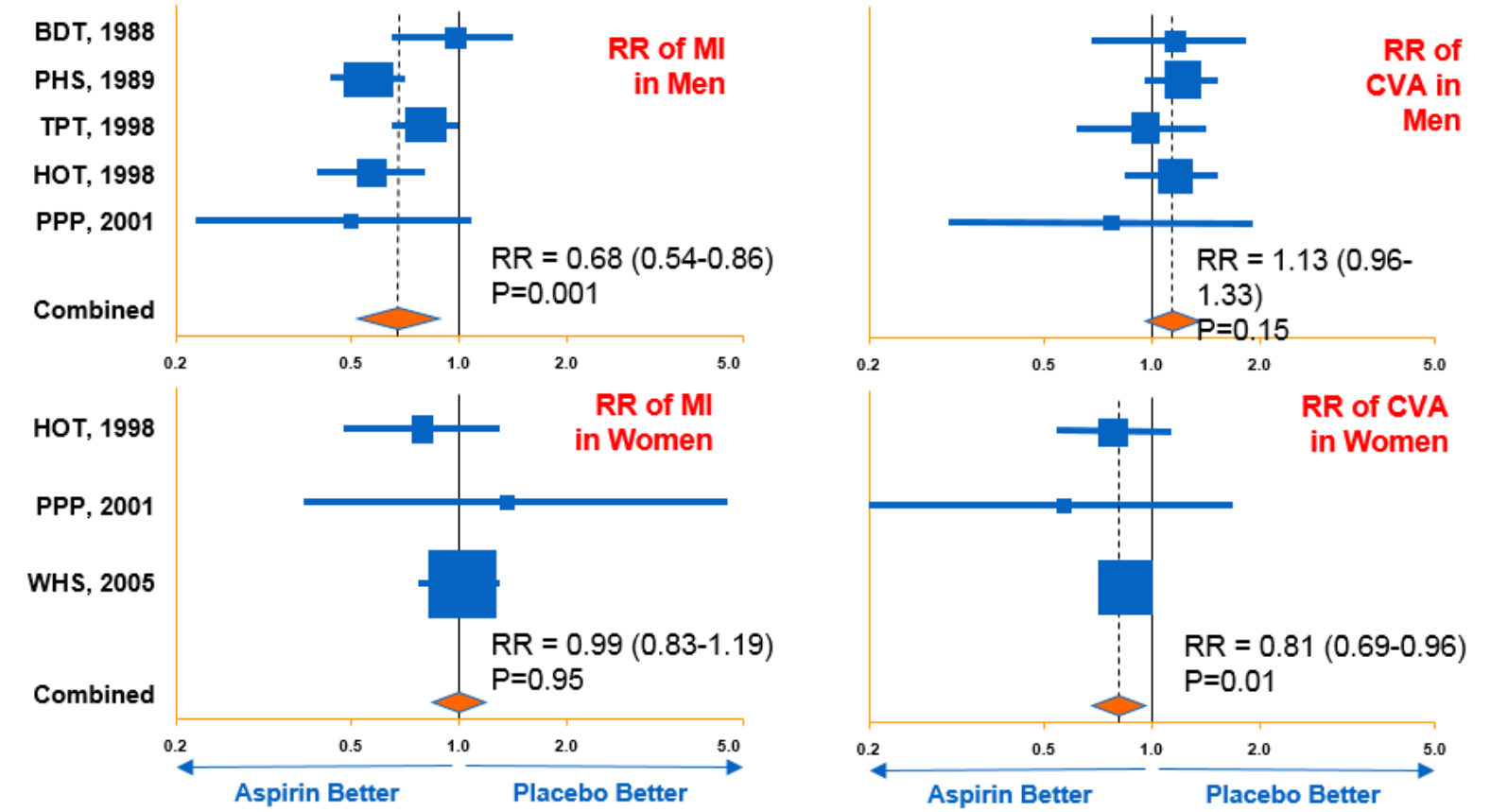
What data are the prior recommendations based on?



CVA=Cerebrovascular accident, MI=Myocardial infarction, RR=Relative risk

Source: Ridker P et al. *NEJM* 2005;352:1293-1304

Aspirin for Primary Prevention of ASCVD:
2014 Meta-analysis

Xie M et al. PLoS ONE 2014; 9(10): e90286

- **ASCVD Events – 10% ↓**
  RR 0.90 (95% CI 0.85, 0.95)
- **Major Bleeding – 55% ↑**
  RR 1.55 (1.35, 1.78)
- NNT to prevent 1 major ASCVD event over a mean f/u of 6.8 years = 284.
- NNH to cause 1 major bleeding = 299

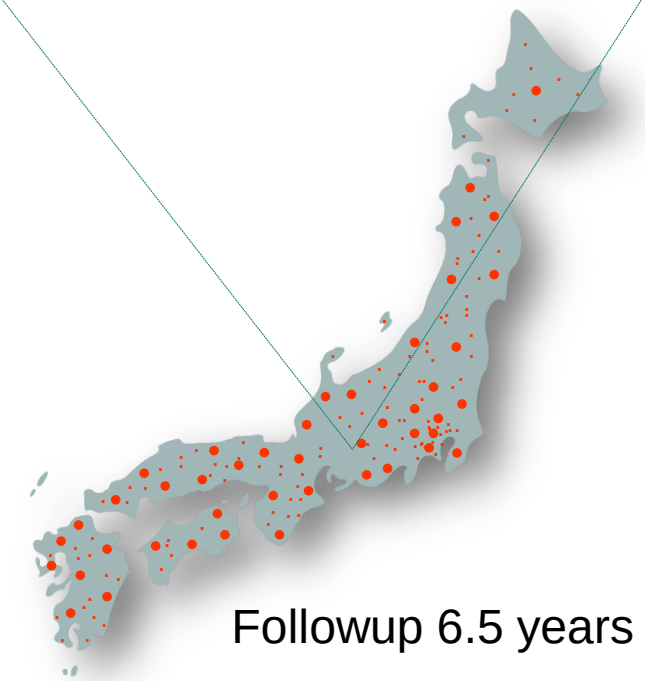
NNT = number needed to treat; NNH = number need to harm

2014 – the Japanese Primary Prevention Project (JPPP)

Ikeda et al. JAMA 2014

Patients aged 60–85 years
- Hypertension
- Dyslipidemia
- Diabetes mellitus

(one or more condition)



Followup 6.5 years

Eligible ✓

1:1 randomization

Enteric-coated aspirin 100 mg/day

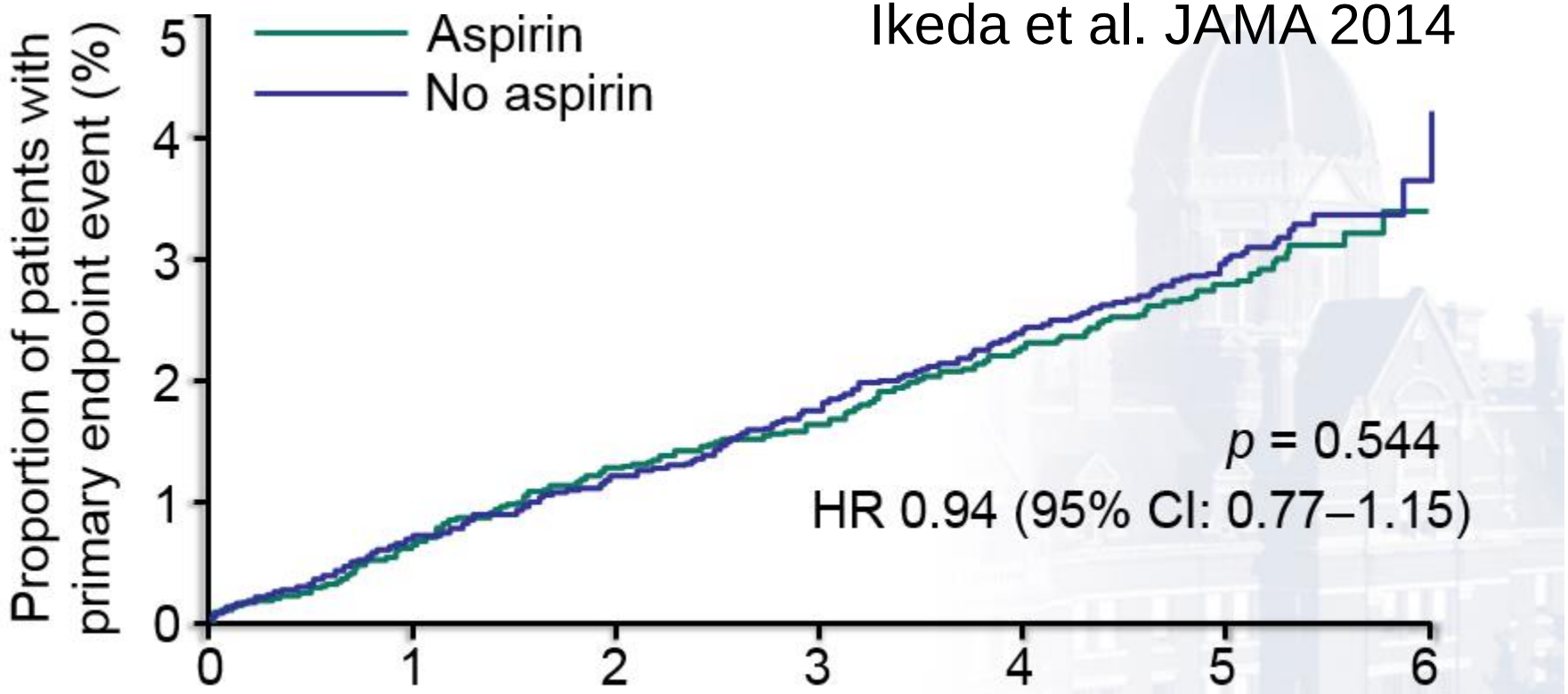
No aspirin

Ongoing medications to control underlying disease(s)

JPPP Primary endpoint:

death from CV causes, nonfatal stroke and nonfatal MI

Ikeda et al. JAMA 2014



Number at risk							
Aspirin	7220	7021	6771	6583	6322	3639	169
No aspirin	7244	7073	6861	6645	6359	3711	182

ARRIVE:
Aspirin in Primary Prevention

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- Enrolled **12,546 patients** followed for **mean of 60 months**
- Adults ≥55 y/o (men) or ≥60 y/o (women) with moderate *estimated* CV risk (10-yr ASCVD risk 17.4%)
- However, **observed event rates were lower (<10% 10-years**)
  - – Thus, population was low to moderate risk
- Excluded patients at high risk of bleeding or diabetes
- Randomized enteric-coated aspirin (100 mg) or placebo daily

Gaziano JM et al. The Lancet. 2018; 392

ARRIVE: Primary Outcome Intention to Treat

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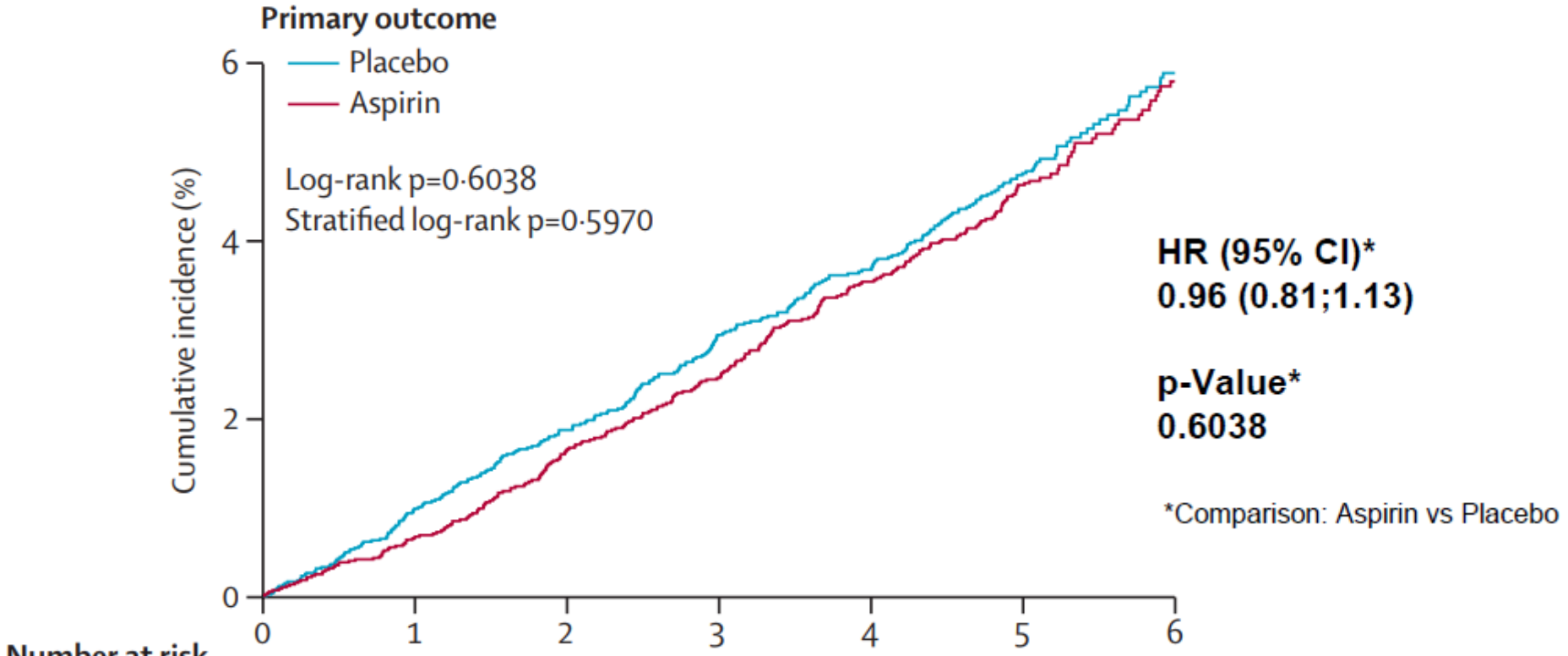
Time to First Occurrence of CV Death, MI, UA, Stroke or TIA (Intent-to-Treat population)



Gaziano JM et al. The Lancet. 2018; 392

ARRIVE: Bleeding Intention to Treat

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Gastrointestinal Bleeding Adjudication	Placebo Arm (n=6276)	Aspirin Arm (n=6270)
Time to First GI Bleeding		
Patients with events, n (%)	29 (0.46%)	61 (0.97%)
Hazard Ratio (95% CI)*	2.11 [1.36;3.28]	
p-Value*	0.0007	
Severity of adjudicated first GI Bleeding		
Mild, n (%)	22 (0.35%)	42 (0.67%)
Moderate, n (%)	5 (0.08%)	15 (0.24%)
Severe, n (%)	2 (0.03%)	4 (0.06%)

*Comparison: Aspirin vs Placebo; p-Value from log-rank test of time to first event
Note: Percentages based on number of subjects randomized to the indicated treatment group

Gaziano JM et al. The Lancet. 2018; 392

ASPREE: Aspirin in Primary Prevention in Older Adults

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- Adults in Australia (>70 y.o) & U.S. (>65 y.o among Blacks/Hispanics)
  - 19,114 participants – excluded those with CVD, dementia, disability - followed for mean of 4.7 yrs
- Randomized to EC aspirin 100 mg daily vs. placebo
- 50% were age ≥74 years, 56% women
- primary end point was a composite of death, dementia, or persistent physical disability

McNeil JJ et al. N Engl J Med 2018;379

ASPREE: Death, Dementia, Disability

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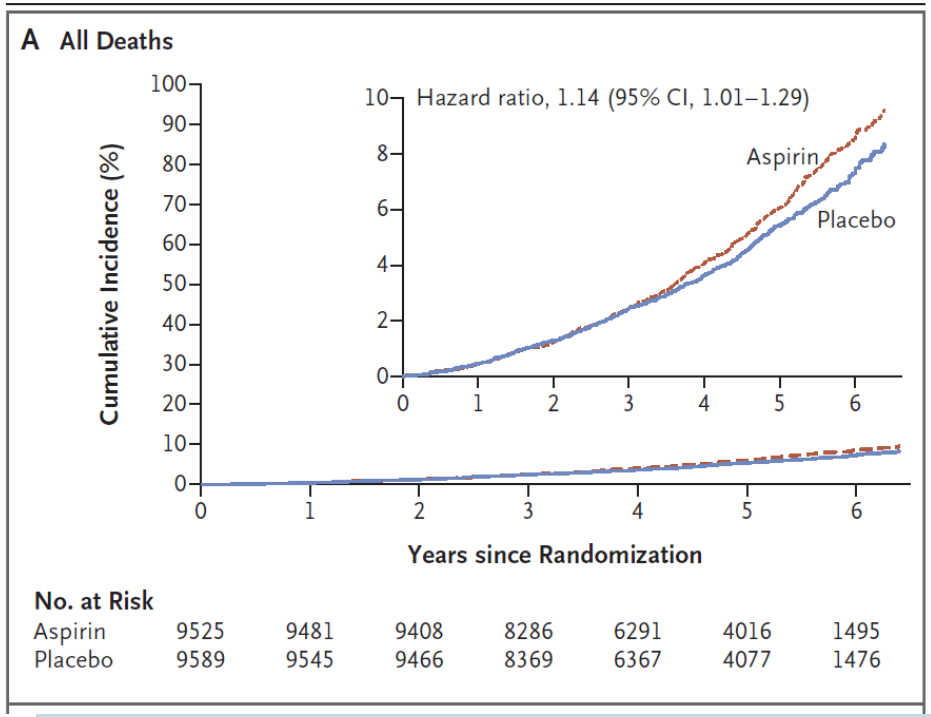
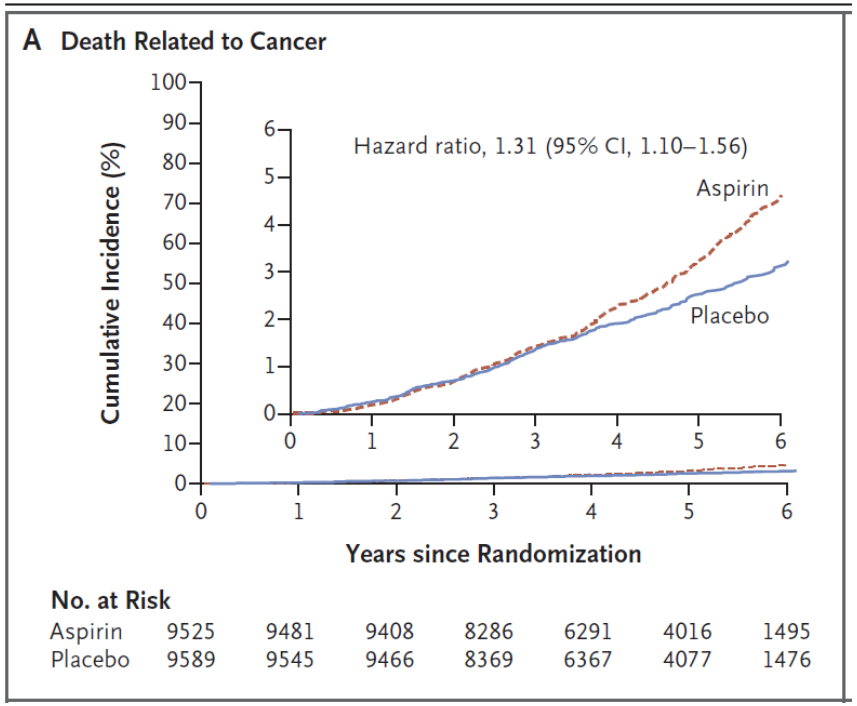
- All Deaths

HR 1.14 (1.01-1.29)



- Cancer Deaths

HR 1.31 (1.01-1.29)



No benefit on Dementia or Persistent Physical Disability

McNeil JJ et al. N Engl J Med 2018;379

ASPREE:
CV outcomes and Bleeding

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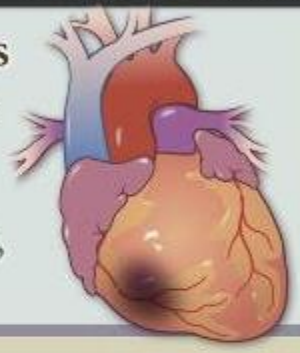
Effect of Aspirin on Cardiovascular Events in the Elderly

RANDOMIZED, DOUBLE-BLIND, MULTICENTER TRIAL

19,114 Patients

≥70 yr of age with no known cardiovascular disease, dementia, or disability

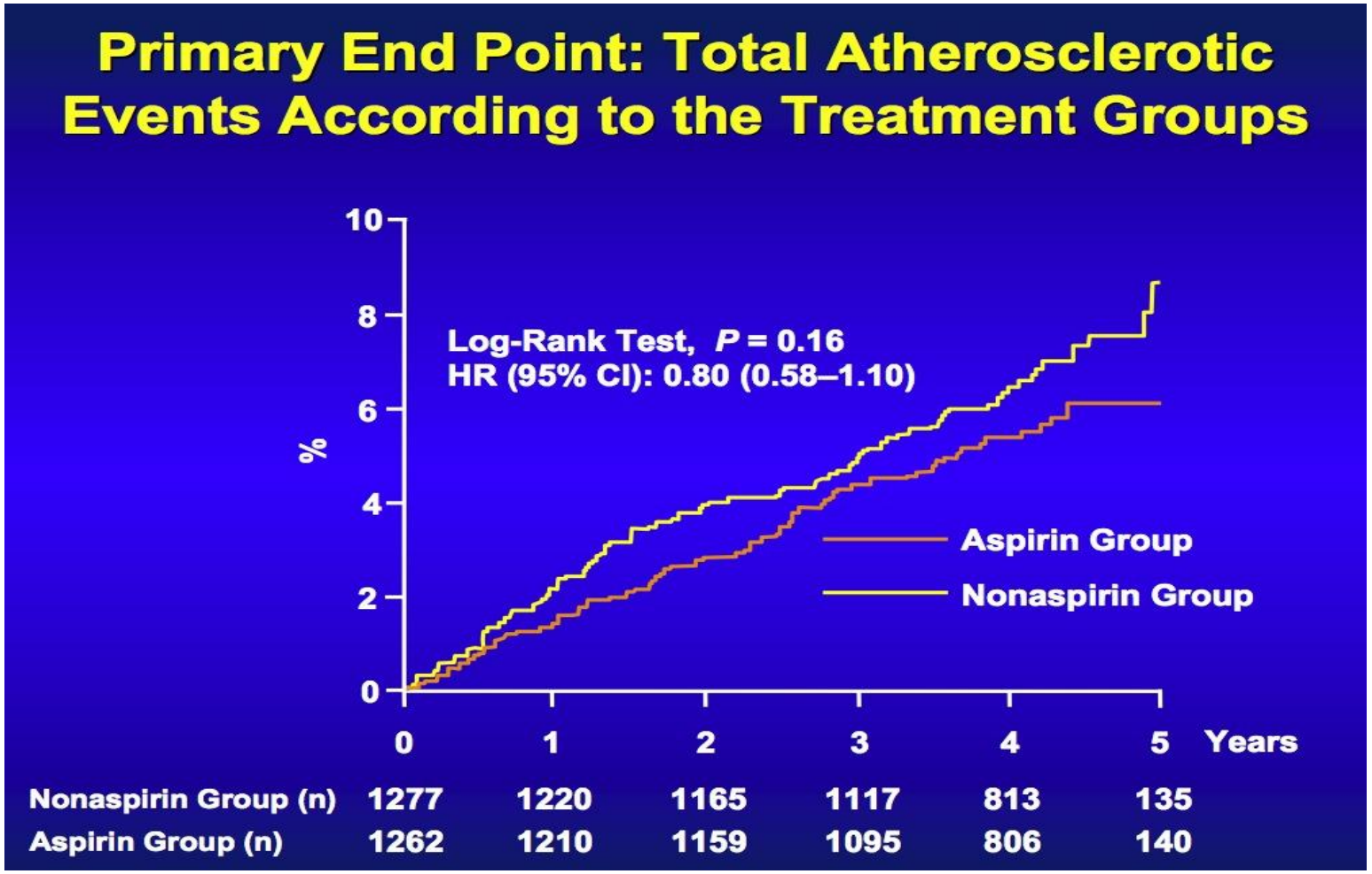


	Aspirin	Placebo
	N=9525	N=9589
	Events per 1000 person-yr	
Cardiovascular disease	10.7	11.3
	HR, 0.95 95% CI, 0.83–1.08	
Major hemorrhage	8.6	6.2
	HR, 1.38 95% CI, 1.18–1.62, P<0.001	

The NEW ENGLAND JOURNAL of MEDICINE

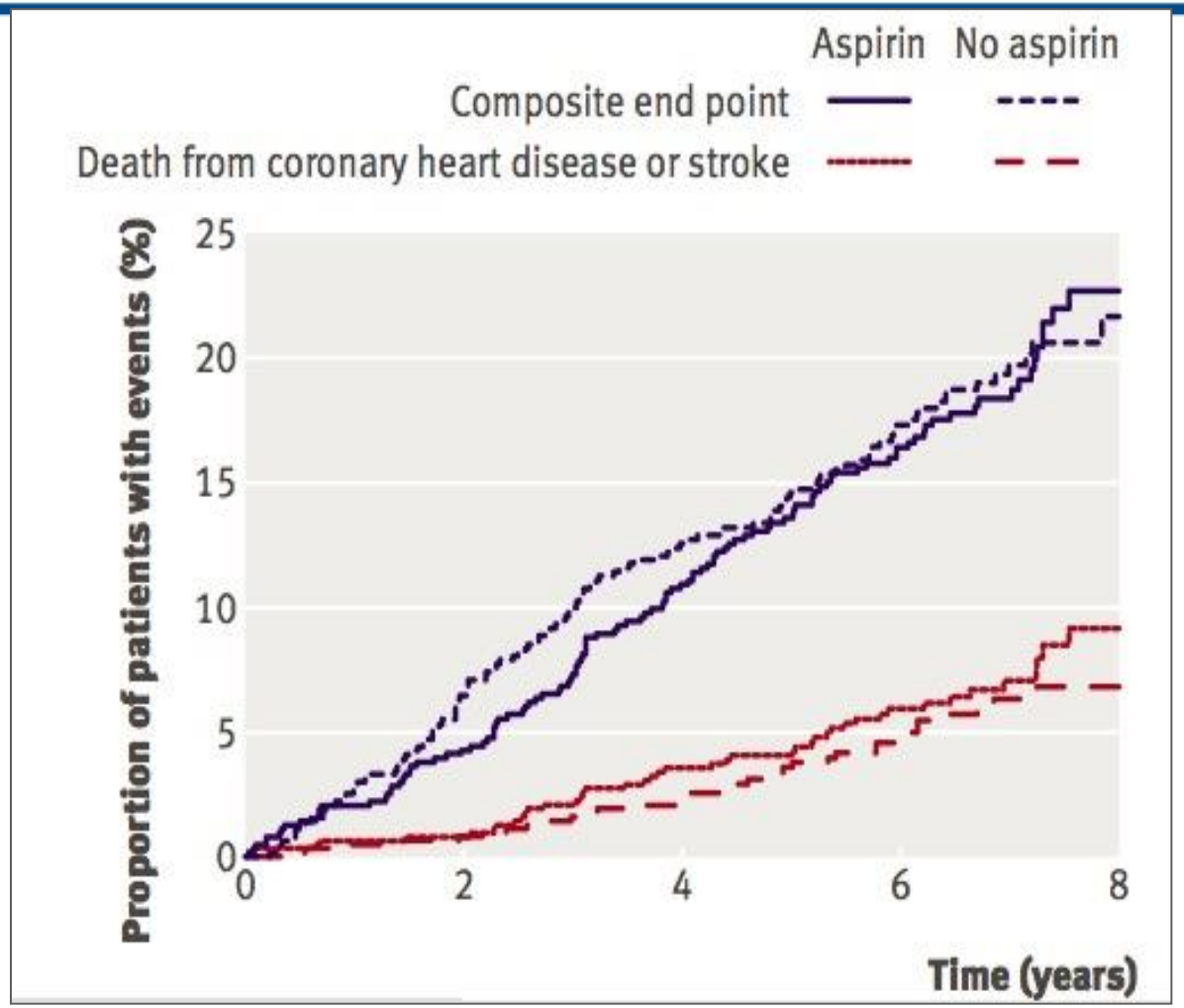
McNeil et al. 2018

Low dose ASA for primary prevention among pts with Type 2 diabetes: 2008 JPAD RCT



Ogawa H et al. JAMA 2008 (300) 18; 2134-2141

POPADAD: Asymptomatic "PAD" & diabetes: ASA ineffective



POPADAD Belch J et al. BMJ 2008

- 1276 adults age >40 with diabetes and ABI <0.99, but no clinical CVD
- RCT of ASA 100 mg/d vs. placebo ±antioxidant in 2 x 2 factorial design
- Median follow-up 6.7 yrs

ASCEND: Aspirin in Primary Prevention in DM

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- Adults with diabetes, but no CVD
  - **15,480 participants** followed for mean of **7.4 yrs**
- Randomized to aspirin 100 mg daily vs. placebo
- Mean age 63 years, 38% women
- Primary outcome – major vascular event (MI, stroke/TIA, vascular death)

Bowman L et al. ASCEND Collaborative Group. N Engl J Med 2018;379:1529-39.

ASCEND
Primary Outcome

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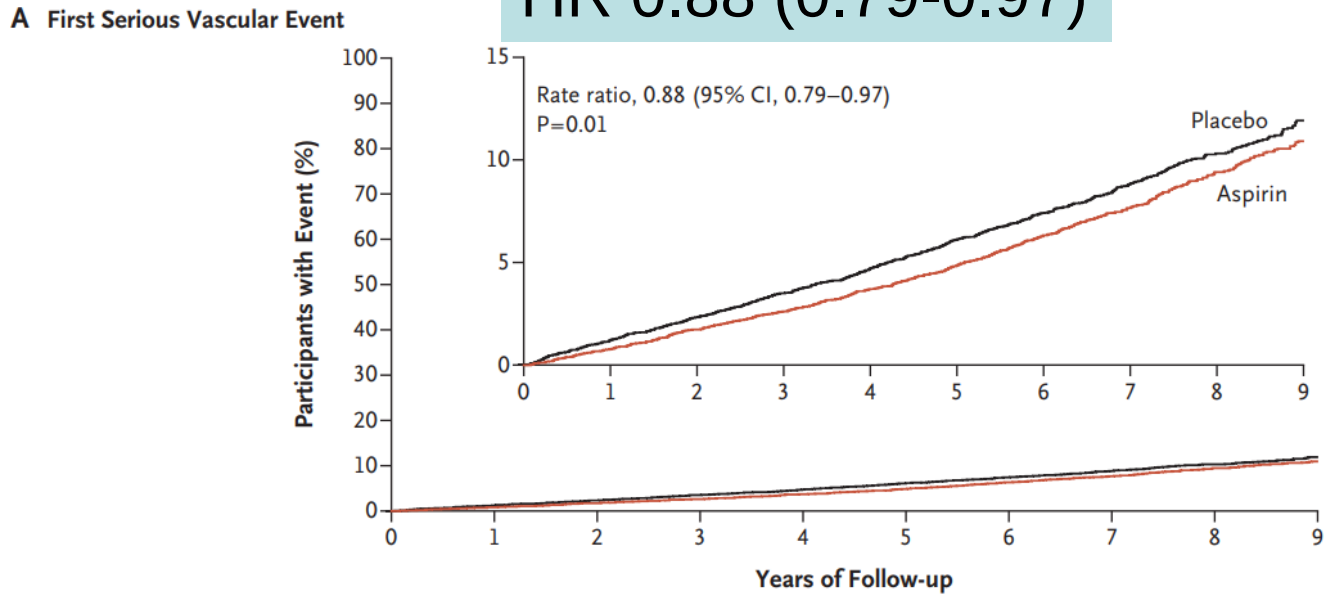
BENEFIT: Vascular Events

- Aspirin group [8.5%] vs. Placebo group [9.6%]

HR 0.88 (0.79-0.97)



No. at Risk										
Placebo	7740	7618	7486	7342	7188	7001	5771	3890	2200	1430
Aspirin	7740	7655	7536	7404	7252	7096	5825	3966	2222	1428
Cumulative benefit per 1000 participants in aspirin group		4±2	6±2	9±3	10±3	13±4	11±4	12±5	9±6	10±7

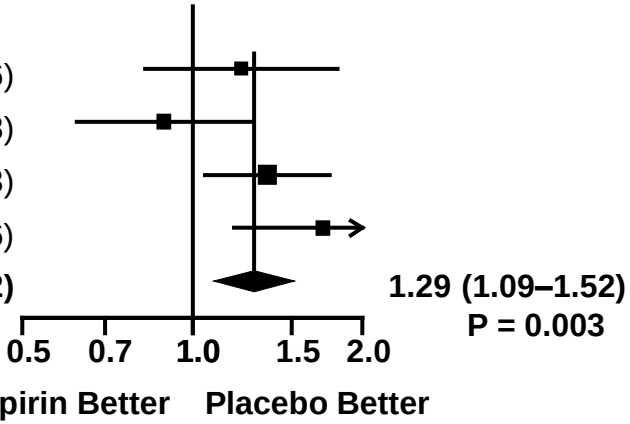
12% RRR

Bowman L et al. ASCEND Collaborative Group. N Engl J Med 2018;379:1529-39.

ASCEND:

Effect of aspirin on major BLEED

Type of Event	Aspirin (N=7740) no. of participants with events (%)	Placebo (N=7740) no. of participants with events (%)	Rate Ratio (95% CI)	Absolute Difference (%)
Major bleed				
Intracranial hemorrhage	55 (0.7)	45 (0.6)		0.1
Sight threatening eye bleed	57 (0.7)	64 (0.8)		-0.1
Serious gastrointestinal hemorrhage	137 (1.8)	101 (1.3)		0.5
Other major bleed	74 (1.0)	43 (0.6)		0.4
Any major bleed	**314 (4.1)**	**245 (3.2)**	**1.29 (1.09–1.52) P = 0.003**	**0.9**



Rate Ratio 1.29 (1.09-1.52)

Bowman L et al. ASCEND Collaborative Group. N Engl J Med 2018;379:1529-39.

2019 ACC/AHA Primary Prevention Guidelines

Can I use a 10-year ASCVD risk estimate for aspirin?

- In recent cohort studies/trials, estimated ASCVD risk has exceeded actual risk observed during follow-up.
- In addition, ASCVD risk generally tracks with bleeding risk.
- The committee felt there was **insufficient evidence** to recommend a specific PCE risk threshold as an inclusion criterion for aspirin.
- Instead clinicians should consider the totality of evidence for ASCVD risk [inclusive, where appropriate, of risk-enhancing factors, such as **strong family history of premature MI, inability to achieve lipid or BP or glucose targets, or significant elevation in coronary artery calcium score**] & to also tailor decisions about prophylactic aspirin to patient and clinician preferences.

Arnett DK, Blumenthal RS,….**Michos ED**…et al. Circulation 2019

2019 ACC/AHA Primary Prevention Guidelines

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- A non-exhaustive list of scenarios associated with increased risk of bleeding includes;
  - a history of previous GI bleeding or peptic ulcer disease or bleeding from other sites,
  - age >70 years,
  - thrombocytopenia, coagulopathy,
  - chronic kidney disease,
  - or concurrent use of other medications that increase bleeding risk such as NSAIDs, steroids, DOACs, or warfarin.

Role of Aspirin in Primary Prevention in Modern Era:

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- Three recent large-scale primary prevention trials suggest aspirin may do more harm than good. **Why?**
- Compared to prior decades, in modern preventive practice:
  - Less smoking
  - Increased utilization of statins/aggressive lipid lowering
  - Better BP control
- Percent taking **statin Rx** in ASPREE, ARRIVE, & ASCEND was 34%, 43%, and 75%, respectively.
- Aspirin may reduce incidence of colorectal cancers (but cancer reduction not seen in ASCEND or ASPREE)

Aspirin for Cancer Prevention

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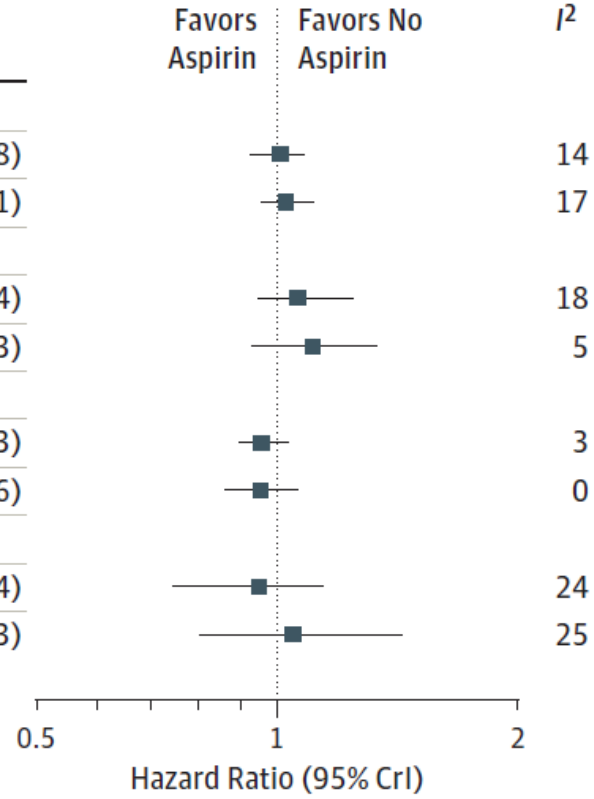
Figure 3. Exploratory Cancer Outcomes

Efficacy	No. of Studies	Aspirin		No Aspirin		Absolute Risk Difference, % (95% CI)	HR (95% CrI)	I^2
		No. of Events	No. of Participants	No. of Events	No. of Participants			
All participants								
Incident cancer	10	4507	63 048	4409	61 475	0.03 (-0.37 to 0.46)	1.01 (0.93-1.08)	14
Cancer mortality	12	1530	75 353	1447	73 781	0.05 (-0.11 to 0.23)	1.03 (0.96-1.11)	17
Low CV risk participants								
Incident cancer	4	2837	38 905	2730	39 044	0.41 (-0.13 to 1.01)	1.06 (0.95-1.24)	18
Cancer mortality	5	823	49 942	748	50 078	0.16 (-0.06 to 0.42)	1.11 (0.93-1.33)	5
High CV risk participants								
Incident cancer	6	1670	24 143	1679	22 431	-0.30 (-0.76 to 0.19)	0.96 (0.90-1.03)	3
Cancer mortality	7	707	25 411	699	23 703	-0.13 (-0.41 to 0.17)	0.96 (0.86-1.06)	0
Participants with diabetes								
Incident cancer	3	1091	9640	1116	9655	-0.68 (-2.09 to 0.95)	0.95 (0.74-1.14)	24
Cancer mortality	4	445	10 667	438	10 685	0.16 (-0.56 to 1.02)	1.05 (0.80-1.43)	25



Zheng SL et al. JAMA. 2019;321(3):277-287. doi:10.1001/jama.2018.20578

2019 Meta-Analysis: *Aspirin Use for Primary Prevention with CVD & Bleeding Events*

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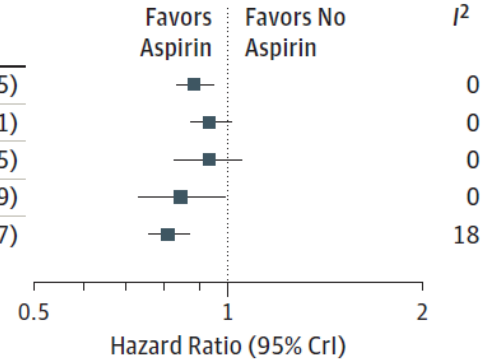
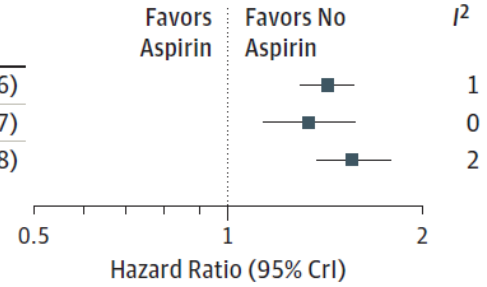
Figure 1. Cardiovascular and Bleeding Outcomes in all Participants

Cardiovascular Outcomes	No. of Studies	Aspirin		No Aspirin		Absolute Risk Reduction, % (95% CI)	HR (95% CrI)
		No. of Events	No. of Participants	No. of Events	No. of Participants		
Composite CV outcome	11	2911	79717	3072	78147	0.38 (0.20 to 0.55)	0.89 (0.84-0.95)
All-cause mortality	13	3622	81623	3588	80057	0.13 (-0.07 to 0.32)	0.94 (0.88-1.01)
CV mortality	13	995	81623	997	80057	0.07 (-0.04 to 0.17)	0.94 (0.83-1.05)
Myocardial infarction	13	1469	81623	1599	80057	0.28 (0.05 to 0.47)	0.85 (0.73-0.99)
Ischemic stroke	10	831	65316	942	63752	0.16 (0.06 to 0.30)	0.81 (0.76-0.87)



Bleeding Outcomes	No. of Studies	Aspirin		No Aspirin		Absolute Risk Increase, % (95% CI)	HR (95% CrI)
		No. of Events	No. of Participants	No. of Events	No. of Participants		
Major bleeding	11	1195	74715	834	73143	0.47 (0.34 to 0.62)	1.43 (1.30-1.56)
Intracranial bleeding	12	349	80985	257	79419	0.11 (0.04 to 0.18)	1.34 (1.14-1.57)
Major GI bleeding	10	593	70336	380	70465	0.30 (0.20 to 0.41)	1.56 (1.38-1.78)



CVD prevention: Number Needed to Treat: **265**

Major Bleeding: Number Needed to Harm: **210**

Zheng SL et al. JAMA. 2019;321(3):277-287.

Net benefit vs Net Harm with ASA at 5 yrs (New Zealand)

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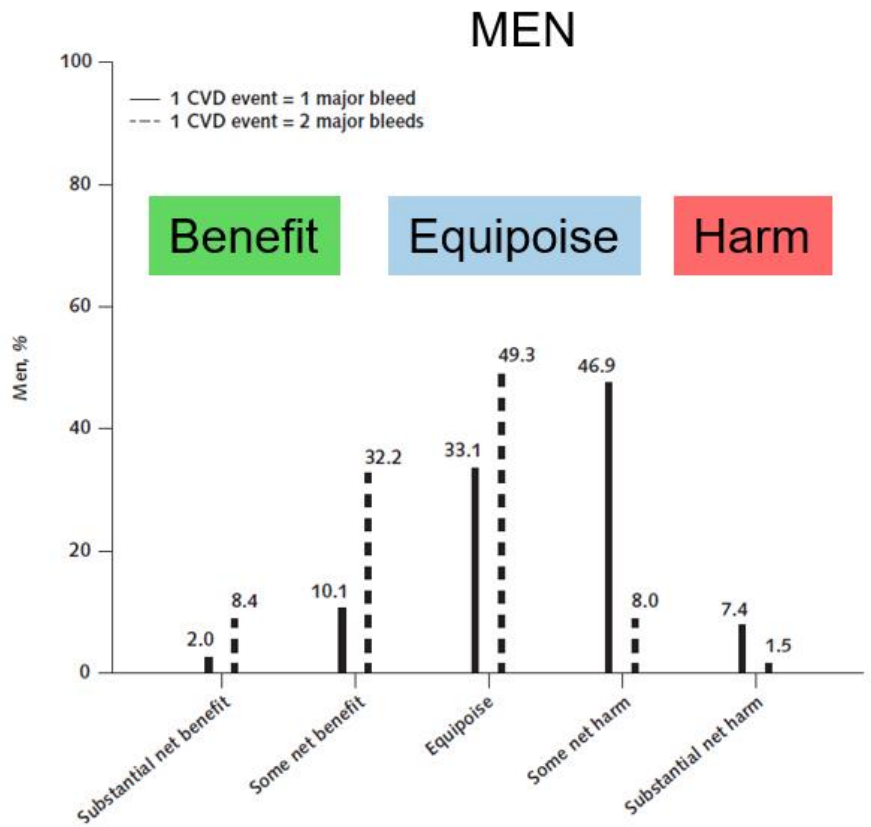
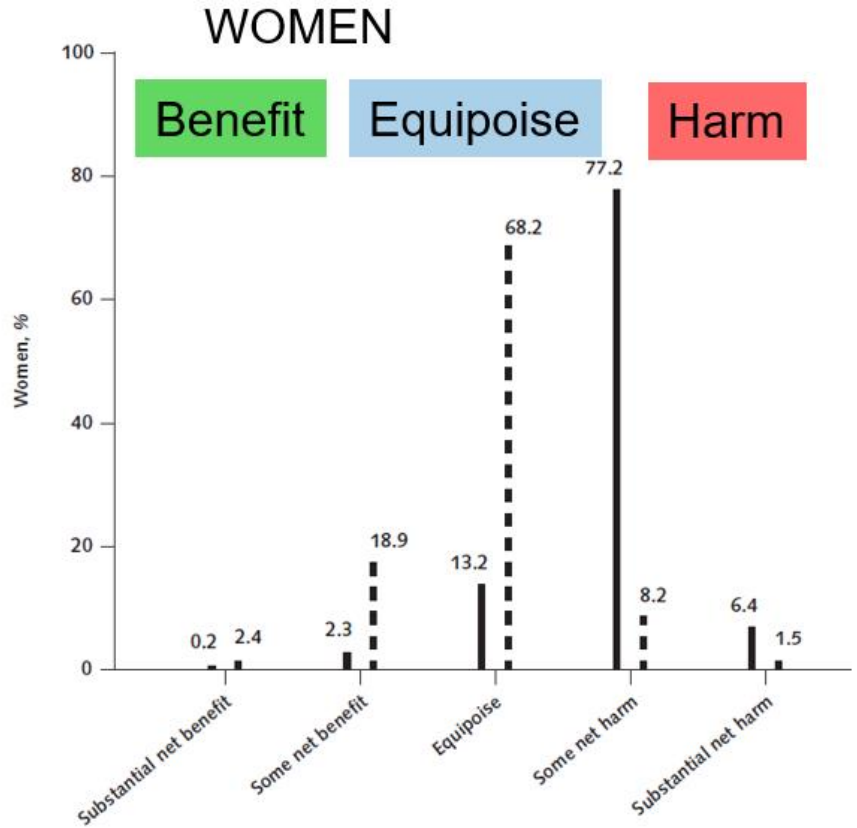
- 2.5% of women & 2% of men likely to have net benefit if 1 CVD event = 1 major bleed,
- 21.4% of women & 41% of men likely to have net benefit if 1 CVD event = 2 major bleeds.





Selak V et al. *Ann Intern Med 2019.* doi:10.7326/M19-1132

Net benefit vs Net Harm with ASA at 5 yrs (New Zealand)

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- For some persons without CVD, aspirin is likely to result in net benefit.
- Net benefit subgroups had higher baseline CVD risk, higher levels of most established CVD risk factors, & lower levels of bleeding-specific risk factors than net harm subgroups.
- No matter which weighting is used (1:1 or 1:2), fewer than half of all patients ages 30-79 years without known CVD likely derive benefit from aspirin therapy for primary CVD prevention.
- (Prevention of cancer was not included in the analysis).

Selak V et al. *Ann Intern Med 2019.* doi:10.7326/M19-1132

Role of Aspirin in Primary Prevention in Modern Era:

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So who might benefit from aspirin for primary ASCVD prevention?

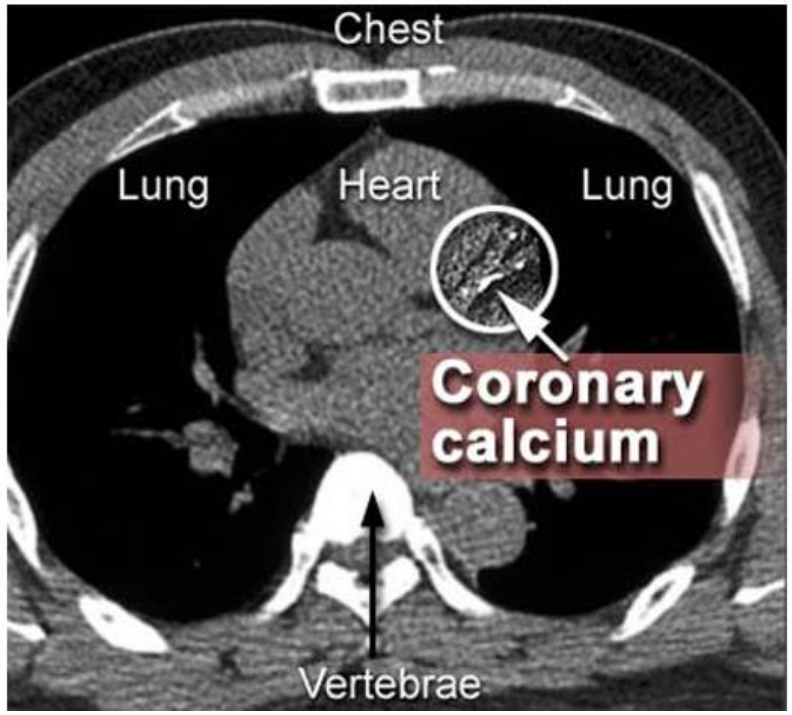
-Those with subclinical atherosclerosis (CAC)?

2019 ACC/AHA Primary Prevention Guideline

Assessment of ASCVD: Use of CAC

Coronary Artery Calcium (CAC) obtained by non-contrast cardiac CT

~1 mSv



Can CAC inform Aspirin Decision? (modeling from MESA)

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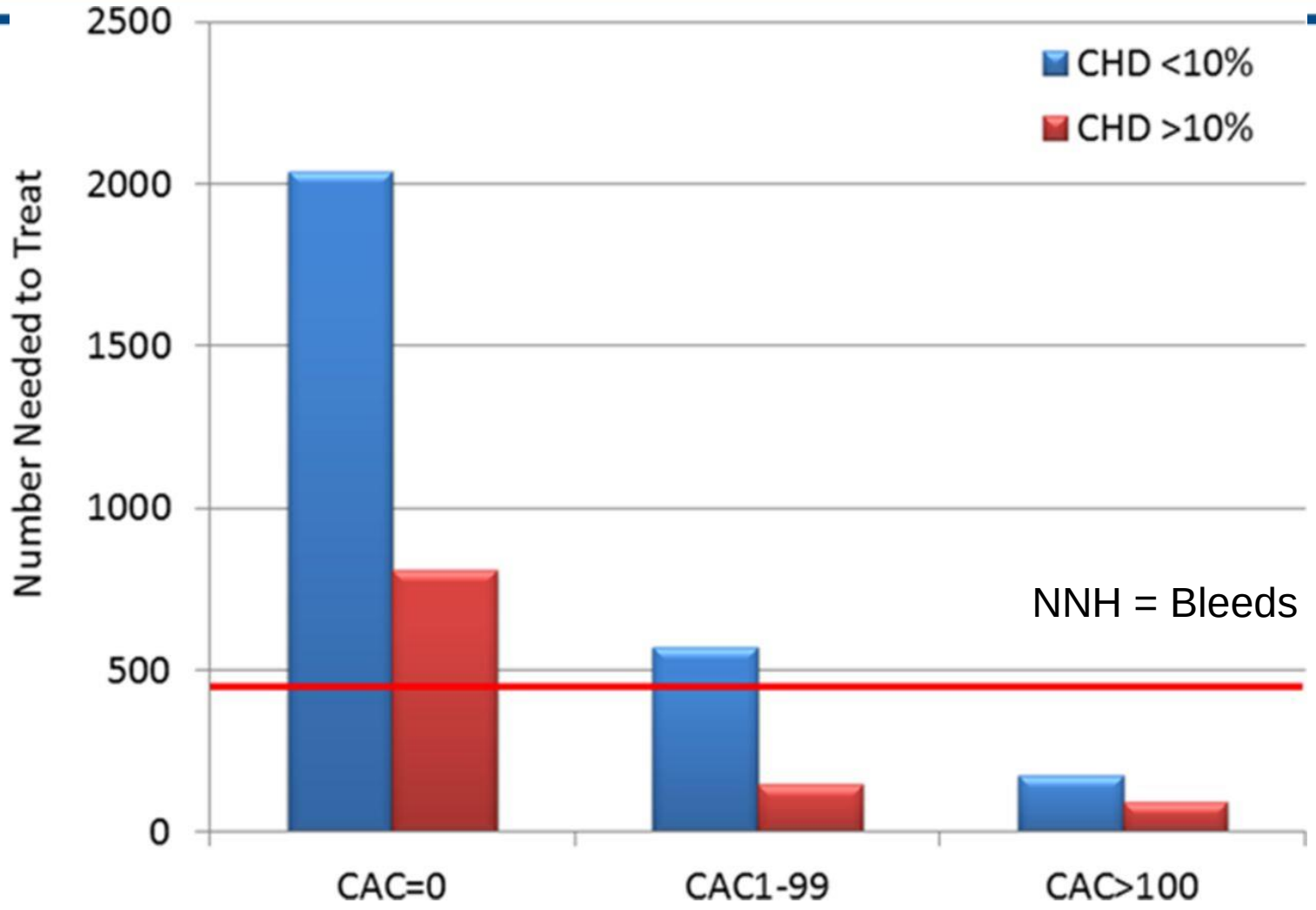

Michael D. Miedema et al. Circ Cardiovasc Qual Outcomes. 2014;7:453-460

Role of Aspirin in Primary Prevention in Modern Era:

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So who else might benefit from aspirin for primary ASCVD prevention?

Remaining questions:

Other subgroups that might benefit?

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- HIV
  - Increased platelet dysfunction & immune activation in HIV, which is decreased with aspirin
  - Do we need a “REPRIEVE”-like trial for aspirin?
- Auto-immune Disease
  - RA, SLE, & psoriatic arthritis are inflammatory disorders with increased burden of subclinical CAD & clinical CVD risk

What about aspirin in those age >70 for primary prevention?

- Avoid initiating in “healthy” older adults age >70
  - Taking it preventively will not increase survival.
  - **Given higher bleeding risk, difficult to justify routine use.**
  - Don't take it to prevent cancer, as we do not know whether it helps or hurts
- What if already on therapy & doing well, should we **de-prescribe**?
  - ➢ We say say **Yes**
  - ➢ But engage patient in a shared discussion making discussion about stopping vs continuing

Making sense of Aspirin for CV Prevention: Our thoughts

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- **Aspirin still strongly indicated for secondary prevention**
- Most healthy people should not take daily aspirin
- These recommendations differ from prior AHA guidelines recommending that aspirin is considered for patients with 10-yr ASCVD risk ≥10%.
- There may be **select** patients age 40 to 70 who have a very high risk of ASCVD, who may benefit if low risk for bleeding.

Making sense of Aspirin for CV Prevention: Our thoughts

JOHNS HOPKINS MEDICINE

- **Consider low-dose aspirin (75-100 mg/day) in:**
  - current smoking
  - strong family history of premature heart attacks
  - very elevated cholesterol with intolerance to statins
  - Subclinical atherosclerosis, **CAC >100**
  - Select patients with diabetes with ASCVD >10%?

Making Sense of Aspirin for CV Prevention

- Consider low-dose aspirin (75-100 mg/day) in:
  - Current smoking
  - Strong family history of early heart attacks
  - Very elevated cholesterol with statin intolerance
  - Subclinical atherosclerosis, **CAC >100**
  - Select patients with ASCVD >20%?
- Thoughtful decisions needed in context of risk discussion

Making sense of Aspirin for CV Prev: Another viewpoint

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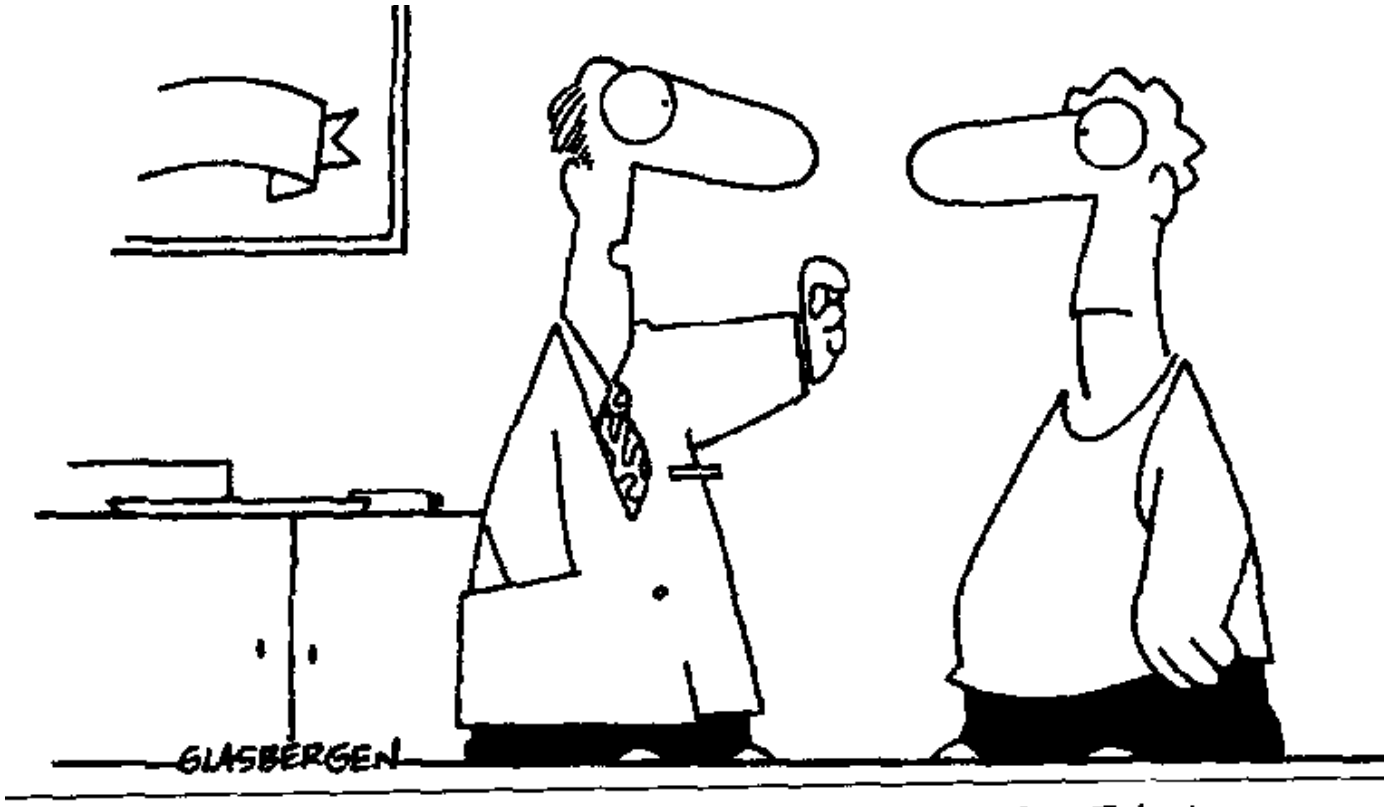
"Thus, beyond diet maintenance, exercise, and smoking cessation, the best strategy for the use of aspirin in the primary prevention of cardiovascular disease may simply be to prescribe a **statin** instead."

-Dr. Paul Ridker, NEJM 2018

Ridker PM. N Engl J Med 2018; 379(16):1572-1574.

ASPIRIN

Healthy lifestyle is anti-inflammatory



"To prevent a heart attack, take one aspirin a day. Take it out for a jog, then take it to the gym, then take it for a bike ride…"

Blood Pressure

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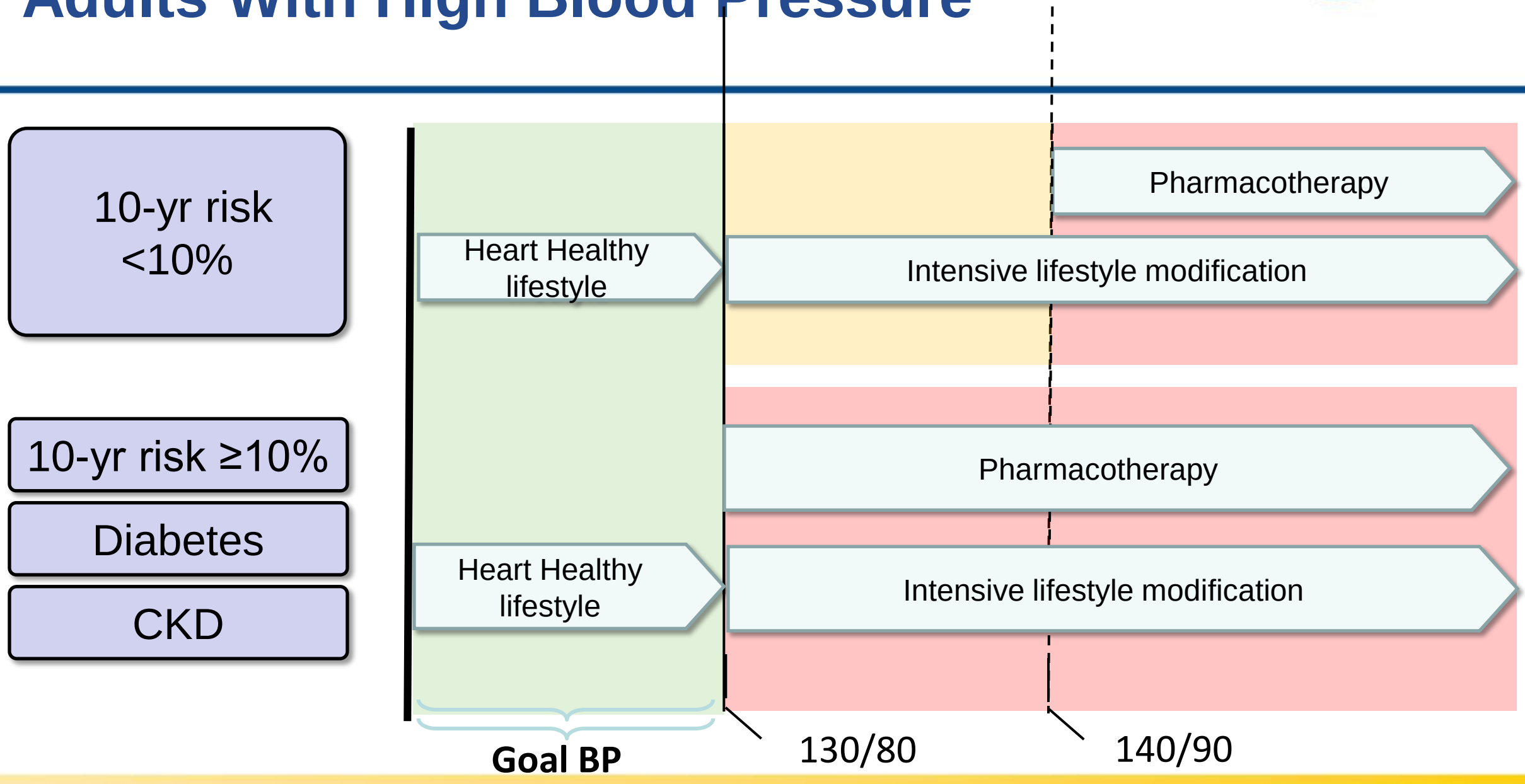
BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

Blood Pressure

BLOOD PRESSURE		
COR	**LOE**	**Recommendations**
I	A	1. In adults with elevated blood pressure (BP) including those requiring antihypertensive medications nonpharmacological interventions are recommended: • weight loss • heart-healthy dietary pattern • sodium reduction • dietary potassium supplementation • increased physical activity with a structured exercise program • limited alcohol

Adults With High Blood Pressure



Cholesterol Take Home Message

- STATIN Rx is 1st-line for primary prevention of ASCVD in patients:
  - Elevated LDL-C levels (≥190 mg/dl)
  - Those with diabetes mellitus who are age 40– 75
  - Those determined to be at sufficient ASCVD risk after risk discussion

Top 10 Take Home Messages of ’18 Guidelines

2. **If clinical ASCVD, reduce LDL-C with high-intensity statin or max. tolerated statin**

   The more LDL-C is reduced → the greater the risk reduction

   Use max. tolerated statin to lower LDL-C by ≥50%

Top 10 Take Home Messages of ’18 Guidelines

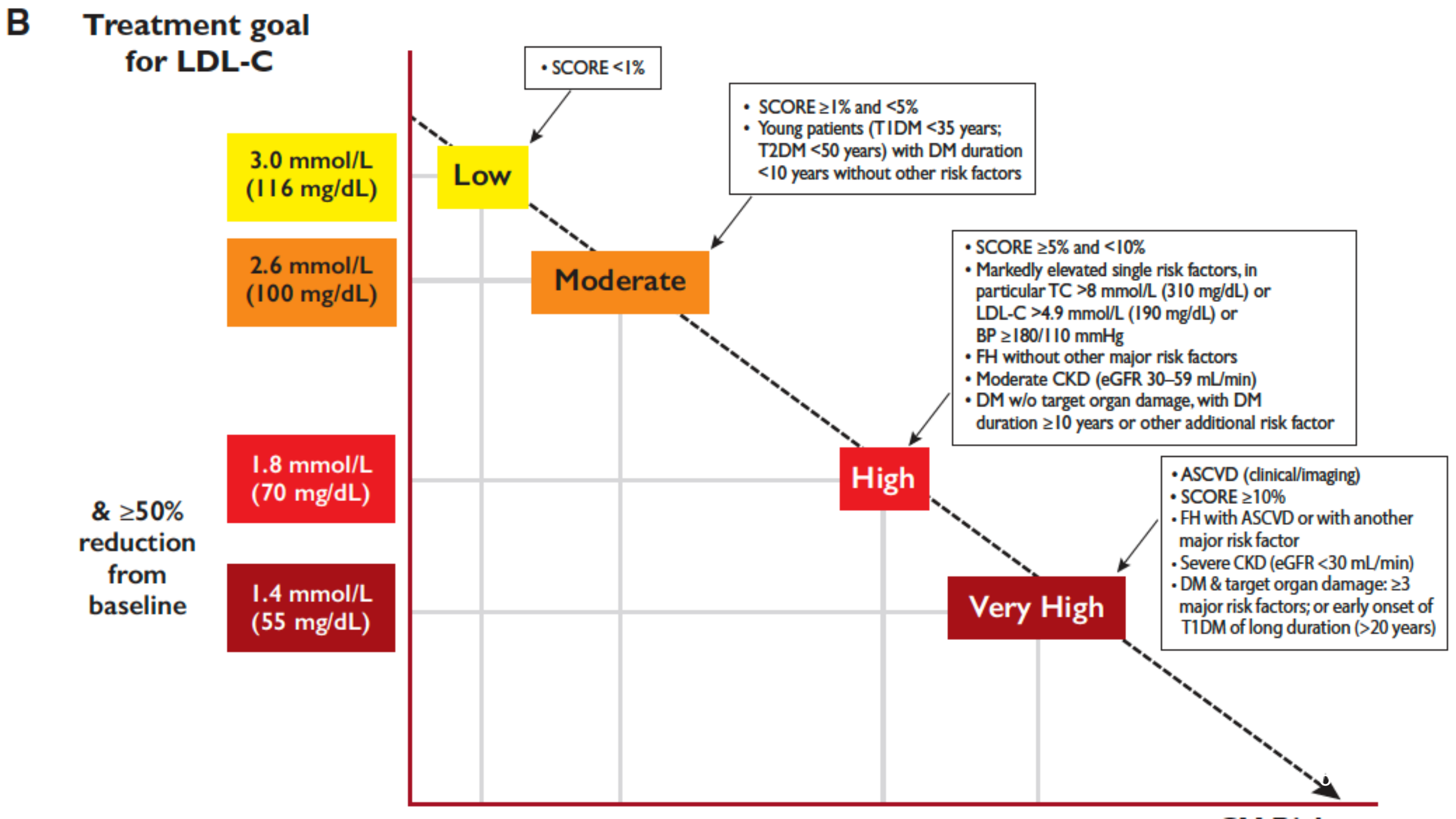
3. Very high-risk ASCVD: use LDL-C threshold of 70 mg/dL to consider nonstatin

- Very high-risk: multiple major events or 1 major event + high-risk conditions
- Reasonable to add ezetimibe to max. tolerated statin if LDL-C remains ≥70
- If LDL-C ≥70 on max. statin + ezetimibe → adding PCSK9i is reasonable
  * long-term (>3 yrs) cost-effectiveness less certain

Top 10 Take Home Messages of ’18 Guidelines

4. Severe primary hypercholesterolemia (LDL-C ≥190) → begin high-intensity statin

- If LDL-C ≥100 → ezetimibe reasonable
- If LDL-C on statin + ezetimibe remains ≥100 & other risk factors → consider PCSK9i, though long-term (>3 yrs) economic value less clear


B
Treatment goal for LDL-C
• SCORE <1%
• SCORE ≥1% and <5%
• Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years without other risk factors
• SCORE ≥5% and <10%
• Markedly elevated single risk factors, in particular TC >8 mmol/L (310 mg/dL) or LDL-C >4.9 mmol/L (190 mg/dL) or BP ≥180/110 mmHg
• FH without other major risk factors
• Moderate CKD (eGFR 30–59 mL/min)
• DM w/o target organ damage, with DM duration ≥10 years or other additional risk factor
• ASCVD (clinical/imaging)
• SCORE ≥10%
• FH with ASCVD or with another major risk factor
• Severe CKD (eGFR <30 mL/min)
• DM & target organ damage: ≥3 major risk factors; or early onset of T1DM of long duration (>20 years)
Low
Moderate
High
Very High
3.0 mmol/L (116 mg/dL)
2.6 mmol/L (100 mg/dL)
1.8 mmol/L (70 mg/dL)
1.4 mmol/L (55 mg/dL)
& ≥50% reduction from baseline

Key Inclusion Criteria – REDUCE-IT

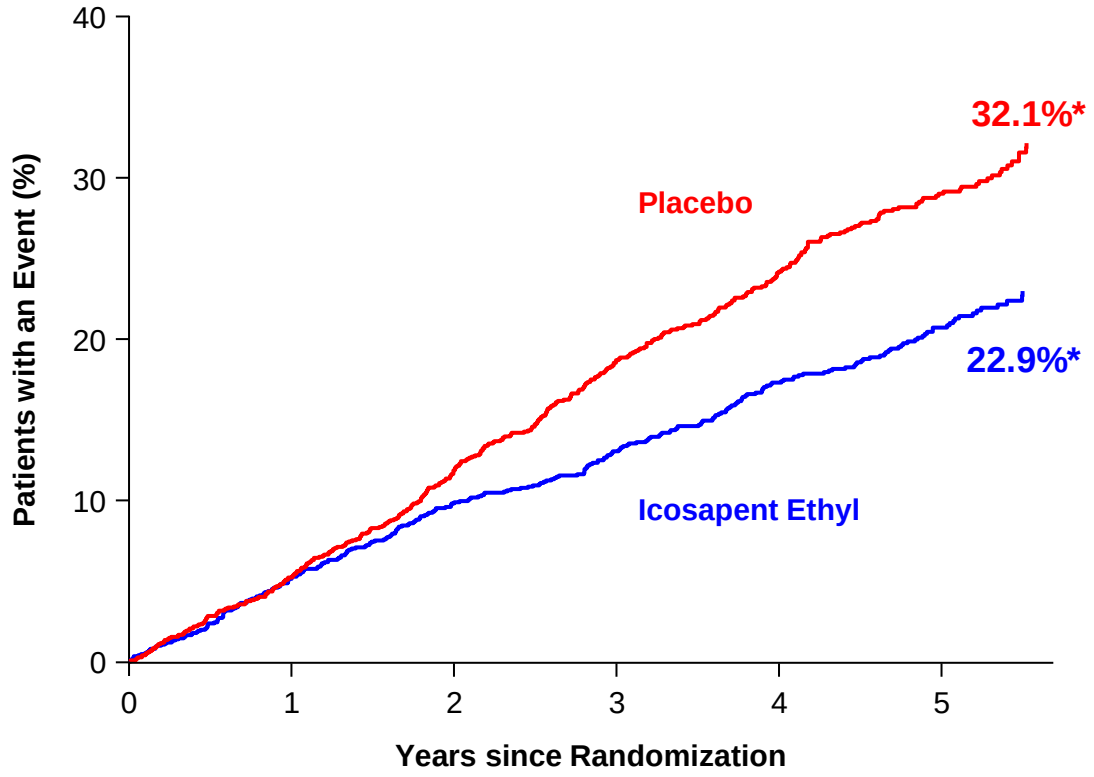
1. Age ≥45 years with established CVD (Secondary Prevention Cohort) *or* ≥50 years with DM with ≥1 additional risk factor for CVD (Primary Prevention Cohort)

2. Fasting TG levels ≥150 mg/dL & <500 mg/dL*

3. LDL-C >40 & ≤100 mg/dL and on stable statin Rx (± ezetimibe) for ≥4 weeks prior to qualifying measurements for randomization

*Due to the variability of triglycerides, a 10% allowance existing in the initial protocol, which permitted patients to be enrolled with qualifying triglycerides ≥135 mg/dL. protocol amendment 1 (May 2013) changed the lower limit of acceptable triglycerides from 150 mg/dL to 200 mg/dL, with no variability allowance.

Primary End Point:
USA Subgroup CV Death, MI, CVA, Revasc, UAP



Hazard Ratio, 0.69
(95% CI, 0.59–0.80)

RRR = 31%

ARR = 6.5%

NNT = 15 (95% CI, 11–27)

P = 0.000001

*Estimated Kaplan-Meier event rate at approximately 5.7 years. The curves were visually truncated at 5.7 years because a limited number of events occurred beyond that time point; all patient data were included in the analyses.

Bhatt DL, Miller M, Brinton EA, et al. *Circulation.* 2019. Bhatt DL. AHA 2019, Philadelphia.

Cigarettes: Rx Options for Cessation

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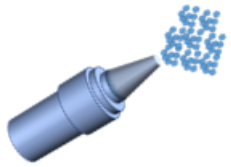
Nicotine replacement therapy		Patch	**If >10 cigarettes/day use 21 mg If <10 cigarettes/day use 14 mg or 7 mg**
		Gum	**2 mg or 4 mg (start with 4mg if first tobacco is ≤30 min from waking); max is 20 lozenges or 24 pieces of gum per day**
		Lozenge	
		Nasal spray	**10 mg/mL**
		Oral inhaler	**10 10-mg cartridge (max 6-16 cartridges/day)**
Other pharmacotherapies		Bupropion	**150 mg SR daily (up to twice daily)**
		Varenicline	**0.5 mg daily titrated to 1 mg twice daily**

Cigarette/Tobacco Cessation

CIGARETTES/TOBACCO		
COR	**LOE**	**Recommendations**
IIa	**B-R**	**To facilitate tobacco cessation, it is reasonable to dedicate trained staff to tobacco treatment in every healthcare system.**
III: Harm	**B-NR**	**All adults & adolescents should avoid secondhand smoke exposure to reduce risk.**

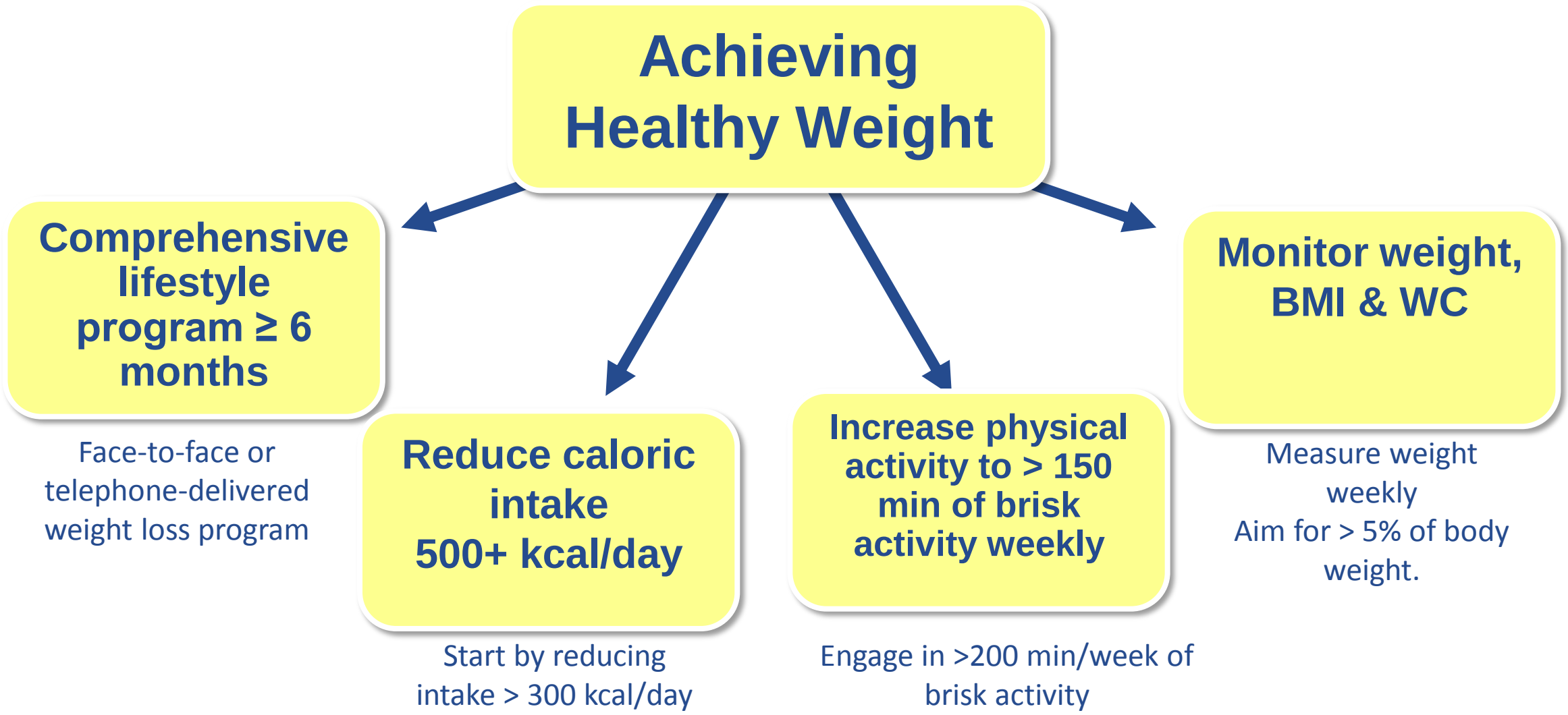
Diet/Nutrition

DIET		
COR	LOE	Recommendations
I	B-R	1. Diet emphasizing intake of vegetables, fruits, legumes, nuts, whole grains, & fish is recommended to decrease risk factors.
IIa	B-NR	2. Replacement of saturated fat with dietary monounsaturated & polyunsaturated fats can be beneficial.
IIa	B-NR	3. Diet containing reduced amounts of cholesterol & sodium can be beneficial.

Diet/Nutrition

DIET		
COR	LOE	Recommendations
IIa	B-NR	4. As part of a healthy diet, it is reasonable to minimize intake of processed meats, refined carbohydrates, & sweetened beverages.
III-Harm	B-NR	5. As part of a healthy diet, the intake of *trans* fats should be avoided to reduce risk.

Diet/Nutrition



Diabetes: Non-pharmacologic Recommendations for T2DM

- **Tailored Comprehensive Nutritional Plan**
  - Mediterranean, DASH, vegetarian/vegan
  - Team based approach: registered dietitian-nutritionist or DM education program.

- **Exercise**
  - A combination of aerobic and resistance is better than either alone.

- **Set A GOAL**
- Better glycemic control + improve weight

Diabetes Mellitus – Type 2

DIABETES		
COR	LOE	Recommendations
IIa	B-R	3. For adults with T2DM, it is reasonable to initiate metformin as 1st-line Rx along with lifestyle therapies at time of diagnosis to improve glycemic control & reduce risk.

Diabetes Mellitus – Type 2

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DIABETES		
COR	LOE	Recommendations
IIb	B-R	4. For adults with T2DM & additional ASCVD risk factors who require glucose-lowering Rx despite initial lifestyle modifications & metformin, it may be reasonable to initiate a sodium-glucose cotransporter 2 (SGLT-2) inhibitor or a glucagon-like peptide-1 receptor (GLP-1R) agonist to improve glycemic control & reduce risk.

CV risk categories in patients with DM

ESC
European Society of Cardiology

Very high-risk	Patients with DM **and** established CVD **or** other target organ damage[a] **or** three or more major risk factors[b] **or** early onset T1DM of long duration (>20 years)
High-risk	Patients with DM duration ≥10 years without target organ damage plus any other additional risk factor
Moderate-risk	Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years, without other risk factors

[a]Proteinurea, renal impairment defined as eGFR < 30mL/min/1.73m^2, left ventricular hypertrophy, or retinopathy.
[b]Age, hypertension, dyslipidaemia, smoking, obesity

ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi/10.1093/eurheartj/ehz486)

Spectrum of Physical Activity

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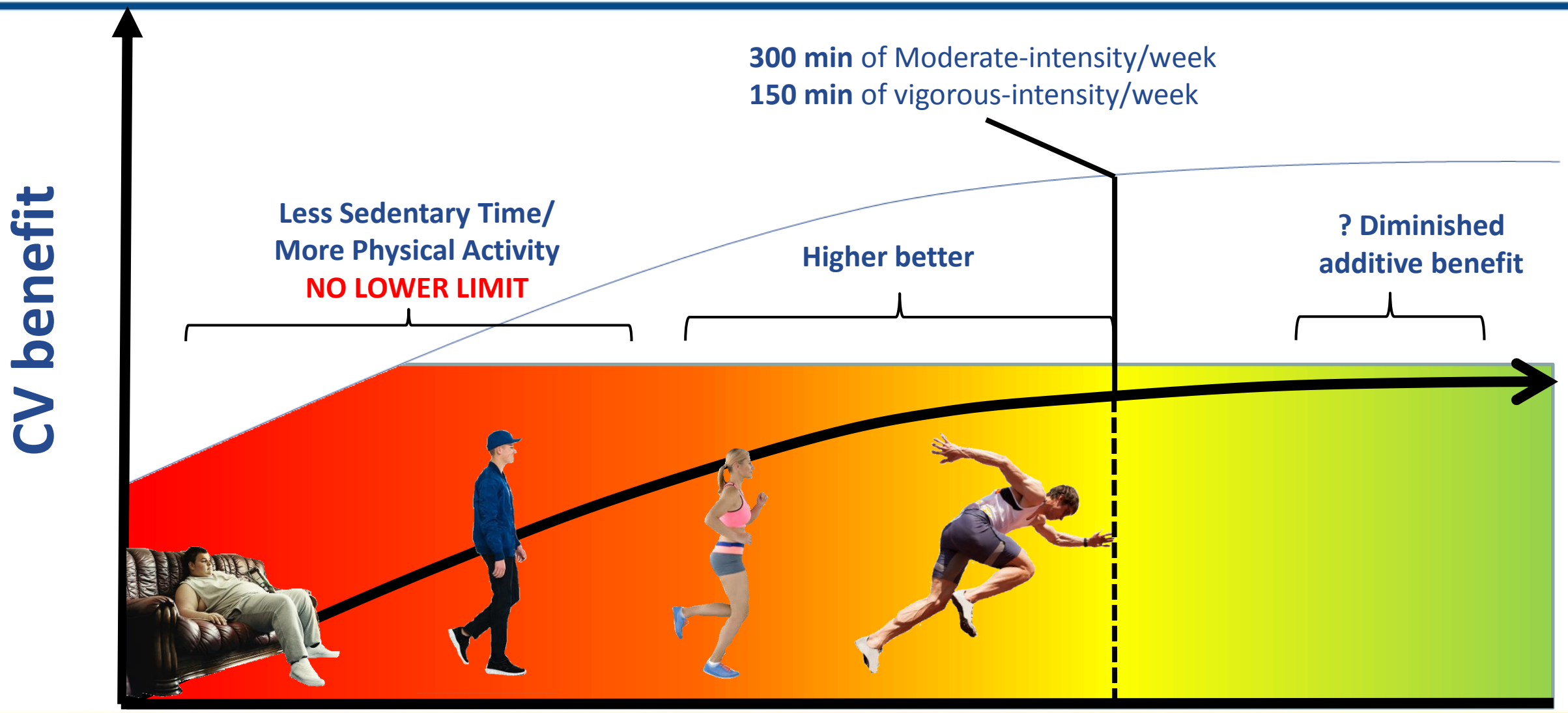

Cumulative Impact of Evidence-Based Heart Failure with Reduced EF Medical Therapies

	Relative-risk	2 yr Mortality
None	- -	35%
ACEI or ARB	↓ 23%	27%
Beta Blocker	↓ 35%	18%
Aldosterone Ant	↓ 30%	13%
ARNI (replacing ACEI/ARB)	↓ 16%	11%
SGLT2 inhibitor	↓ 17%	9%

Cumulative risk reduction if all evidence-based medical therapies are used:
Relative risk reduction 74.0%, Absolute risk reduction: 25.9%, NNT = 3.9

Updated from Fonarow GC, et al. Am Heart J 2011;161:1024-1030 and Lancet 2008;372:1195-1196.

A

Assess Risk: #PCE 1st → Personalized assessment (Low risk: <5%, Borderline/Intermediate risk: 5-<20% & high risk: ≥20%) → Refine by CAC;
CHA2DS2-VASc for CVA risk in case of Afib

Antiplatelet Therapy: #Rethink aspirin – Smoking, FamHx early MI, HeFH, CAC >100? ASCVD >20%?; P2Y12 inhibitor if recent PCI; Anticoagulate with NOAC or warfarin

B

Blood Pressure: #120 is new 140, Lifestyle 1st, If high risk → meds @ 130/80, If low risk →meds @ 140/90

C

Cholesterol: #PCE + REF; Shared decision making; Discuss statin if intermediate risk; Refine by CAC: Power of Zero!; If high-risk → target LDL-C <70mg/dl; Maximize statin → ezetimibe → PCSK9i

Cigarette: #Never too late to quit; 1st motivational interviewing →PharmacoRx next; Individualized and/or group social support counseling.

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D

Diabetes: #Screen for high risk (long duration, albuminuria, eGFR<60, retinopathy, neuropathy, ABI<0.9); Rx: Lifestyle →Metformin → SGLT2i/GLP1-RA; ACEI/ARB for BP.

Diet: #Calculate BMI; Eat vegetables, fruits, nuts, legumes, whole grains, fish; Counseling & caloric restriction for maintaining weight loss

---

E

Exercise: #target >150 min./week of moderate or >75 min./week of vigorous-intensity activity; Any moderate-intensity physical activity is beneficial; Consider mHealth!

F

Heart Failure: #ACEI/ARB/Aldosterone antagonist/ARNI/Beta Blocker should be considered; Consider ICD for those with low EF

‘ABCDEF’ of Cardiovascular Prevention

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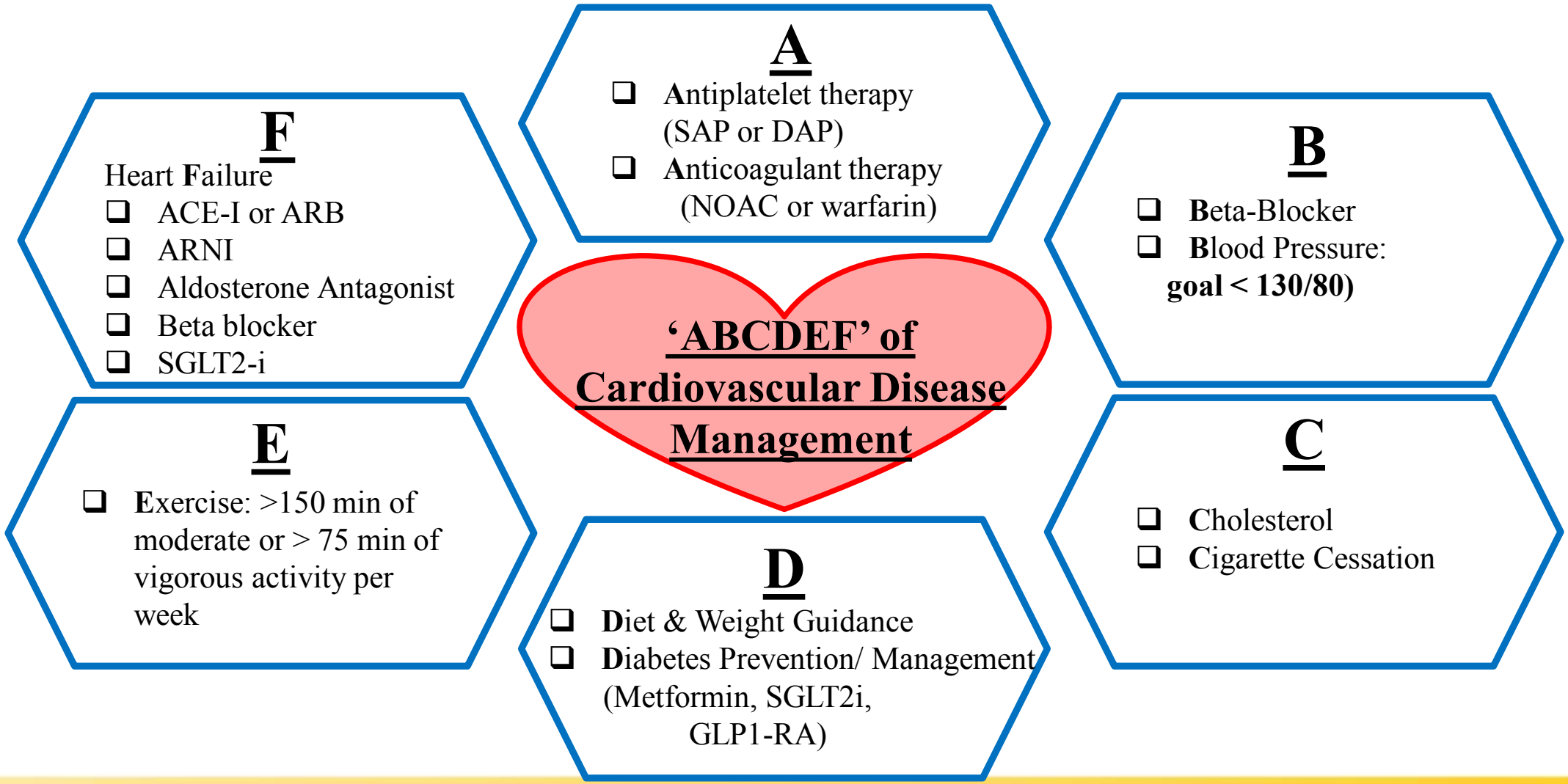

The Ciccarone Center for the Prevention of Cardiovascular Disease at Johns Hopkins

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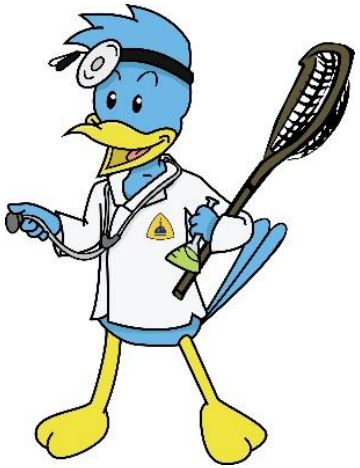
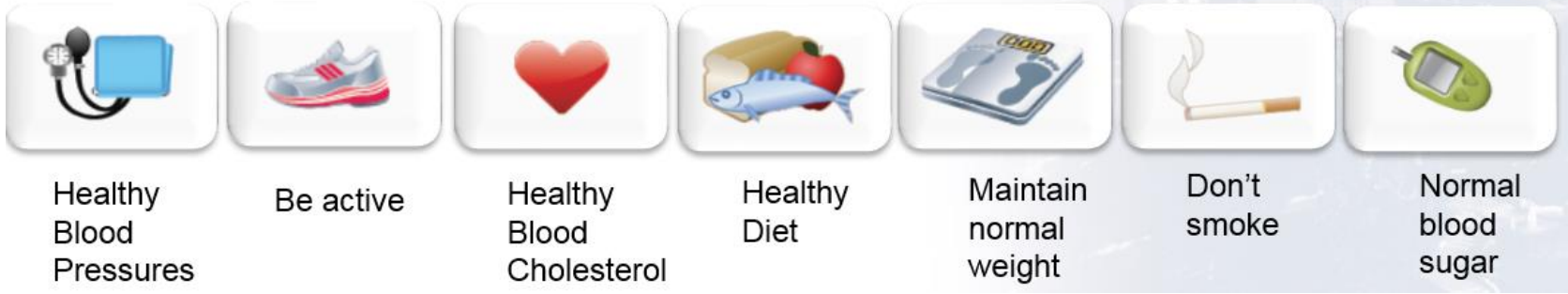
Thank you!



Life's Simple 7™



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