“Getting to the Heart of the Matter”

Practical Implications of the New Lipid Guidelines

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Disclosure of Financial Relationships

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What are the key messages of the 2013 ACC/AHA Cardiovascular (CV) and Cholesterol Guideline*?

1) RCT evidence was re-examined
   - Shift of perspective…..CV benefit more related to statin than LDL reduction
   - NO RCT evidence to support continued use of specific LDL-C or non–HDL-C treatment targets
   - Non statin therapies generally provide little additional benefit, especially when factoring in risk and cost.

*2013 AHA/ACC Cholesterol Guideline http://circ.ahajournals.org/content/129/25_suppl_2/S1.full.pdf+html

What are the key messages of the 2013 ACC/AHA Cardiovascular (CV) and Cholesterol Guideline*?

2) Based on reassessment of benefit/risk--and using a more inclusive risk calculator

MORE PATIENTS should be considered for CV prevention than is now the case

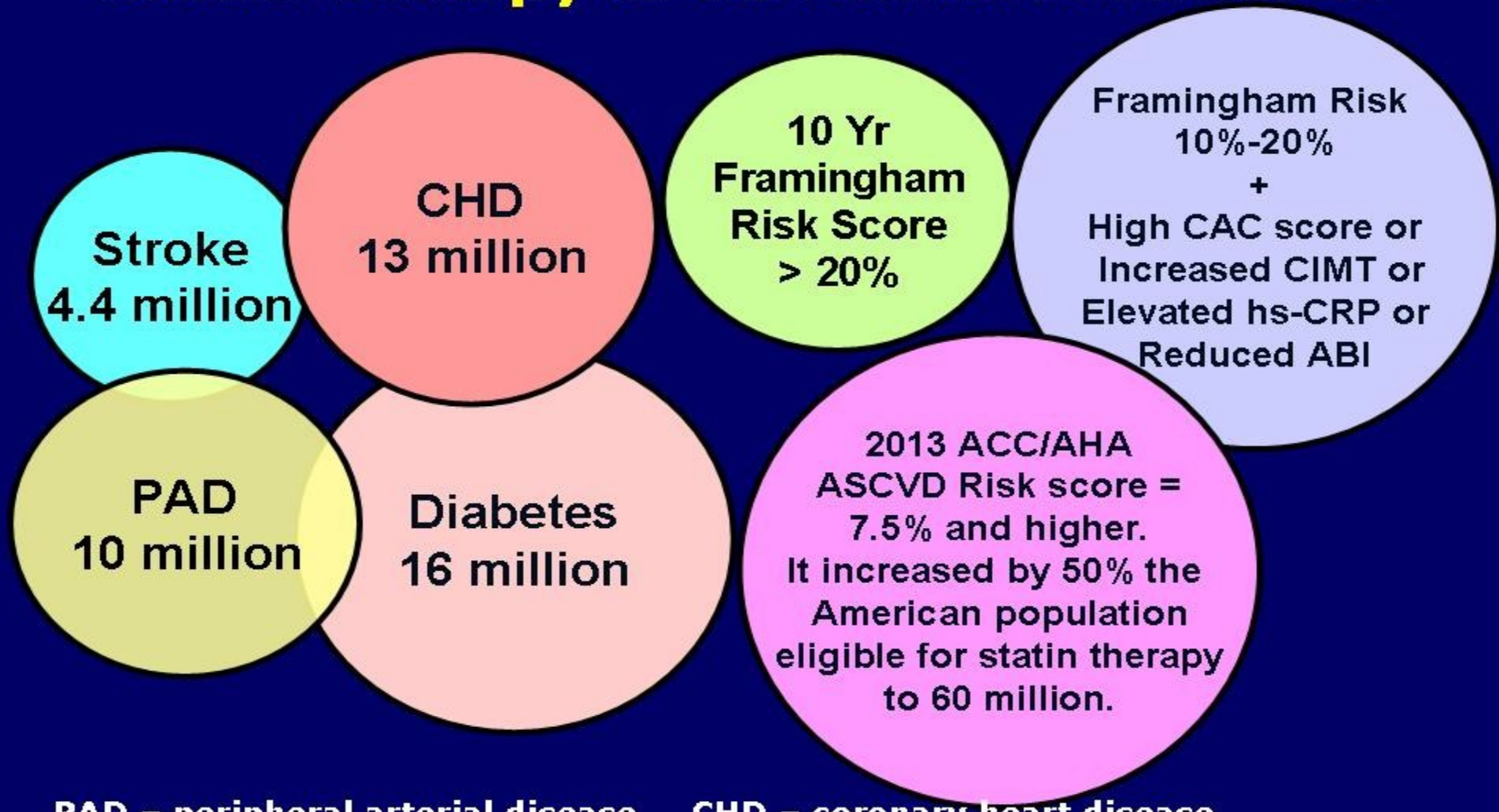
- Prevention extended from coronary artery disease to atherosclerotic vascular disease (ASCVD)
- Enhanced patient–provider dialogue is essential

*2013 AHA/ACC Cholesterol Guideline http://circ.ahajournals.org/content/129/25_suppl_2/S1.full.pdf+html

What are the 4 groups where benefit of statin generally exceeds risks?

- Clinical ASCVD
- LDL ≥ 190
- Diabetes with LDL 70-189, and without clinical ASCVD
- Estimated 10-year ASCVD risk ≥7.5% (pooled cohort equation)

The 2013 ACC/AHA Guidelines Expanded Statin Therapy to 60 Million Americans



PAD – peripheral arterial disease
CHD – coronary heart disease
CAC – coronary artery calcification
CIMT – carotid intima media thickness
ABI – ankle brachial index

Source: New Jersey Preventive Cardiology & Cholesterol Clinic 2014

The majority of CVD events occur in patients without previous history of ASCVD events**

**Colorado Kaiser Quarter 1 2014 CV event analysis	
“First event” patients	65%
Age (21-98)	Average 66 yr
Not on statin	61%
Smokers/unknown status	30%
DM	17%
BP not controlled	22%
CV Risk Unknown	21%
Low Framingham Risk	10%
Moderate Framingham Risk	10%

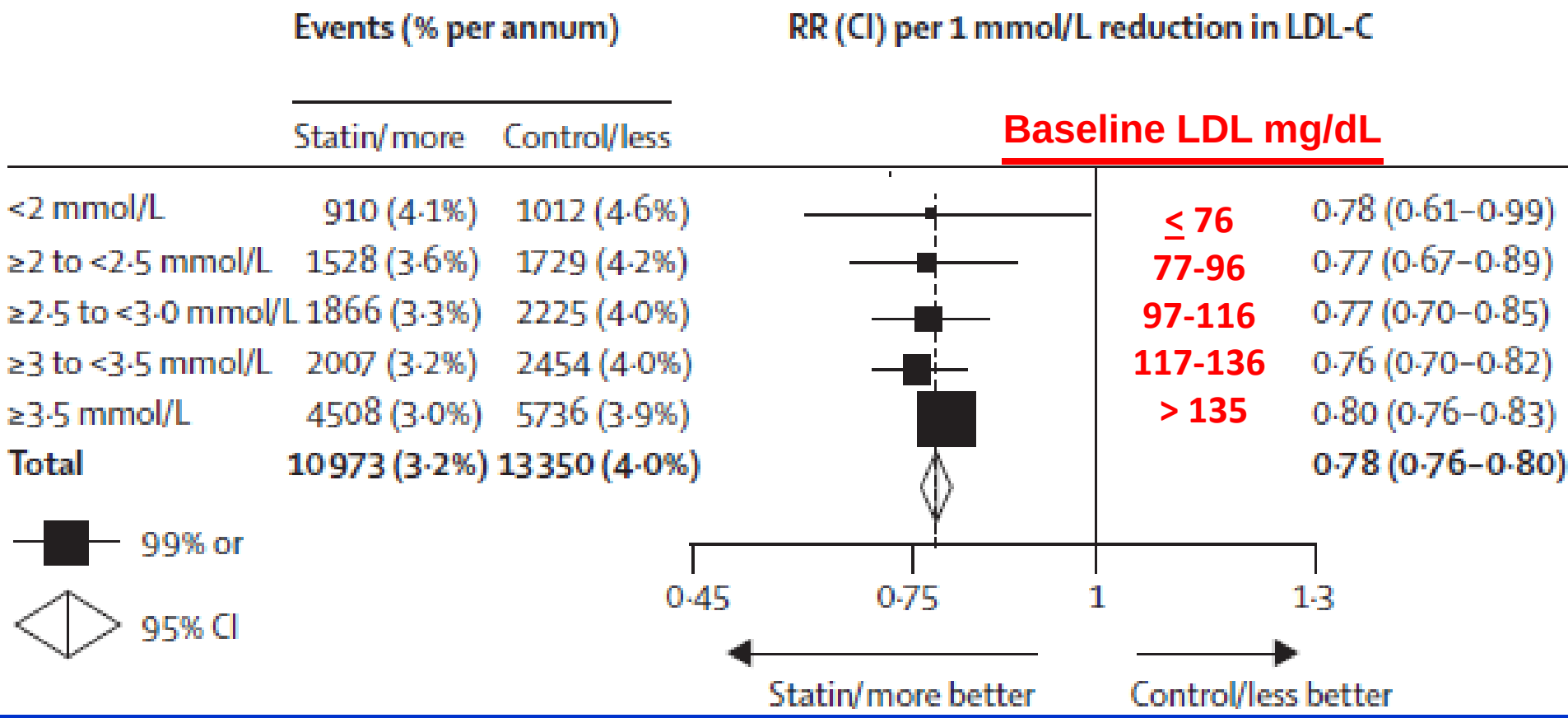
What is the rationale supporting statin over specific LDL targets?

- Statins:
  - Have pleotropic effects beyond LDL reduction
  - Stabilize endothelium and effective within weeks of therapy start
  - Effective even when LDL minimally reduced
  - Effective in patients with LDL < 100 at baseline

For those still advocating LDL-targets

STATINS are - by far - the most effective agents available to reduce LDL

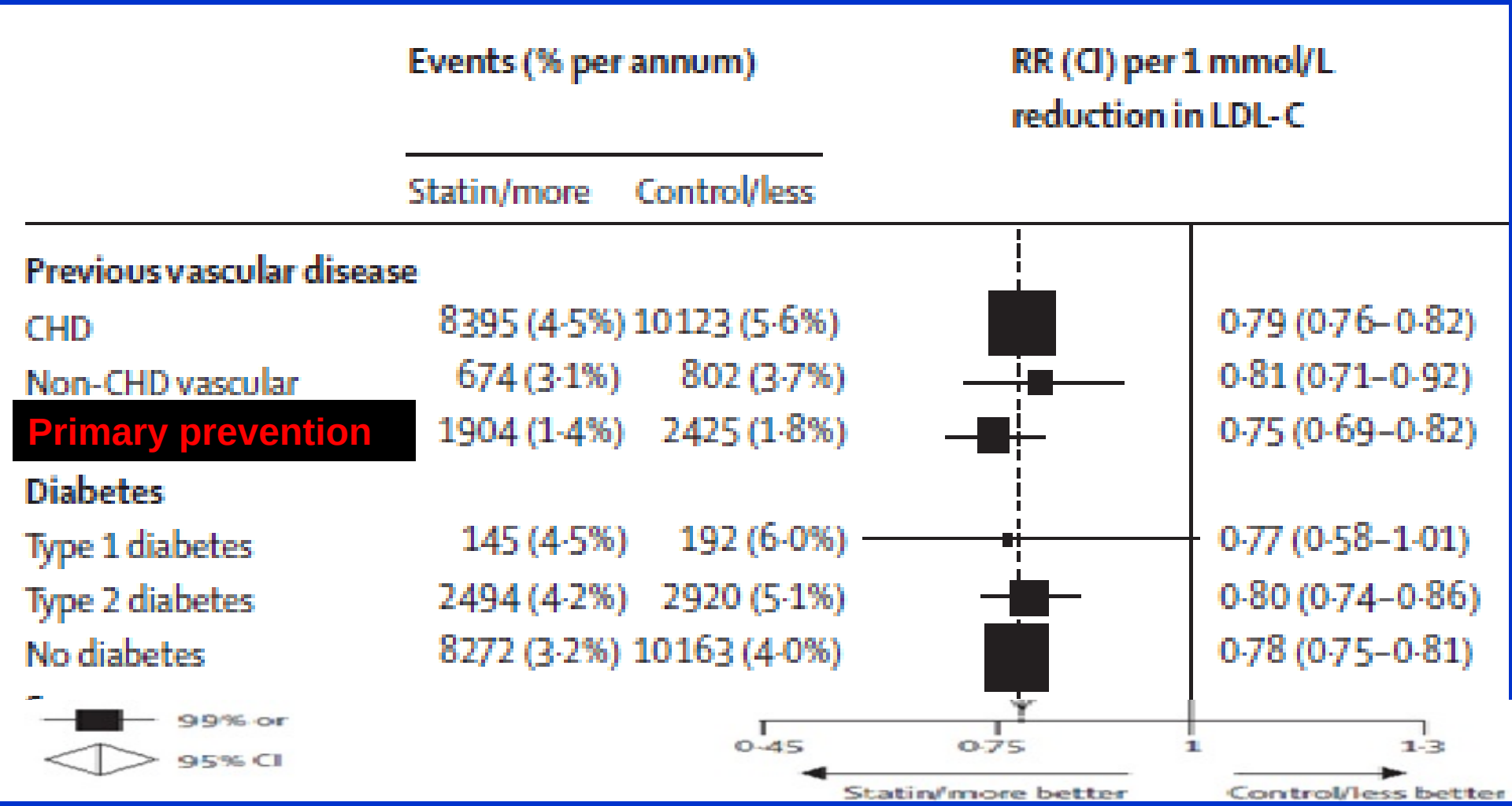
Statins benefit across range of baseline lipids



LDL 130 to 90 same benefit as LDL 90 to 50

Cholesterol Treatment Trialists' (CTT) Collaboration Lancet 376:1671, 2010.

Statin benefit across “disease” state



Cholesterol Treatment Trialists’ (CTT) Collaboration Lancet 376:1671, 2010.

BUT ARE STATINS SAFE???

"….Because the absolute benefit of statins is related to an individual's baseline risk, it is only in those individuals whose baseline risk is very low that the benefits of statin therapy may not outweigh the risk of adverse events…"

NLA Task Force on Statin Safety - 2014 update

Statin safety has been reconfirmed**

- Rarely and sporadically associated with impaired cognition
- Increase risk for the development of diabetes ~10% to 12%
- Certain drugs(especially gemfibrozil) increase risk of statin toxicity
- Liver toxicity extremely rare; check LFT routinely at baseline only
- Myopathy risk ~10%; Rhabodmyolysis 0.1% (No need for routine CPK)

**Journal of Clinical Lipidology 8 Suppl 3, 2014.

Closer look at statin risk/benefit

At 4 years from statin initiation:

- NNT of patients with 10 year CV risk = 10% to prevent 1 MI ~ 60-70

- NNH development of Diabetes: ~ 255 (meta analysis**)

Rhabdo risk on statin ~ 0.5 per 1000 statin users/year (most cases NOT directly related to statin!!)

**Statins and risk of incident diabetes:
Cholesterol Treatment Trialists' (CTT) Collaboration Lancet 376:1671, 2010

With all the emphasis on better benefit/risk determination, what is the controversy concerning use of the new AHA/ACC global risk calculator?

"OVER-RISKING"

Pooled Cohort Risk Equations for predicting atherosclerotic cardiovascular disease events in adults considered for initiation of statin therapy*

Estimated 10-y risk (*n*)†	Event rates‡ at 5-y follow-up		C index (95% CI)
	Observed	Predicted	
< 5% (3453)	0.93%	0.95%	0.72 (0.70 to 0.75)
5% to < 7.5% (1578)	2.38%	2.40%	
7.5% to < 10% (1332)	3.06%	3.43%	
≥ 10% (4634)	5.99%	7.56%	

**CI defined in Glossary. Atherosclerotic cardiovascular disease events were coronary heart disease death, nonfatal myocardial infarction, and fatal or nonfatal stroke. Participants considered for initiation of statin therapy did not have diabetes, were not currently using statins, and had a low-density lipoprotein cholesterol level of 70 to 189 mg/dL.*

†Based on Pooled Cohort Risk Equations.

‡Calculated using number of events at 5 years estimated from the Kaplan–Meier curve (observed events) and Pooled Cohort Risk Equations (predicted events) and the number of participants in the 10–y risk groups.

Validation of the atherosclerotic cardiovascular disease Pooled Cohort risk equations. JAMA. 2014;311:1406-15.

What are some of the factors that may sway (UNDERESTIMATE) ASCVD risk?

- Primary genetic hyperlipidemias
- Family history of premature ASCVD
- High-sensitivity C-reactive protein >2 mg/L
- Coronary artery calcium score ≥75 percentile for age, sex, and ethnicity
- Ankle-brachial index <0.9
- Elevated lifetime(attributable)risk of ASCVD
- Incidentally found atherosclerosis on imaging

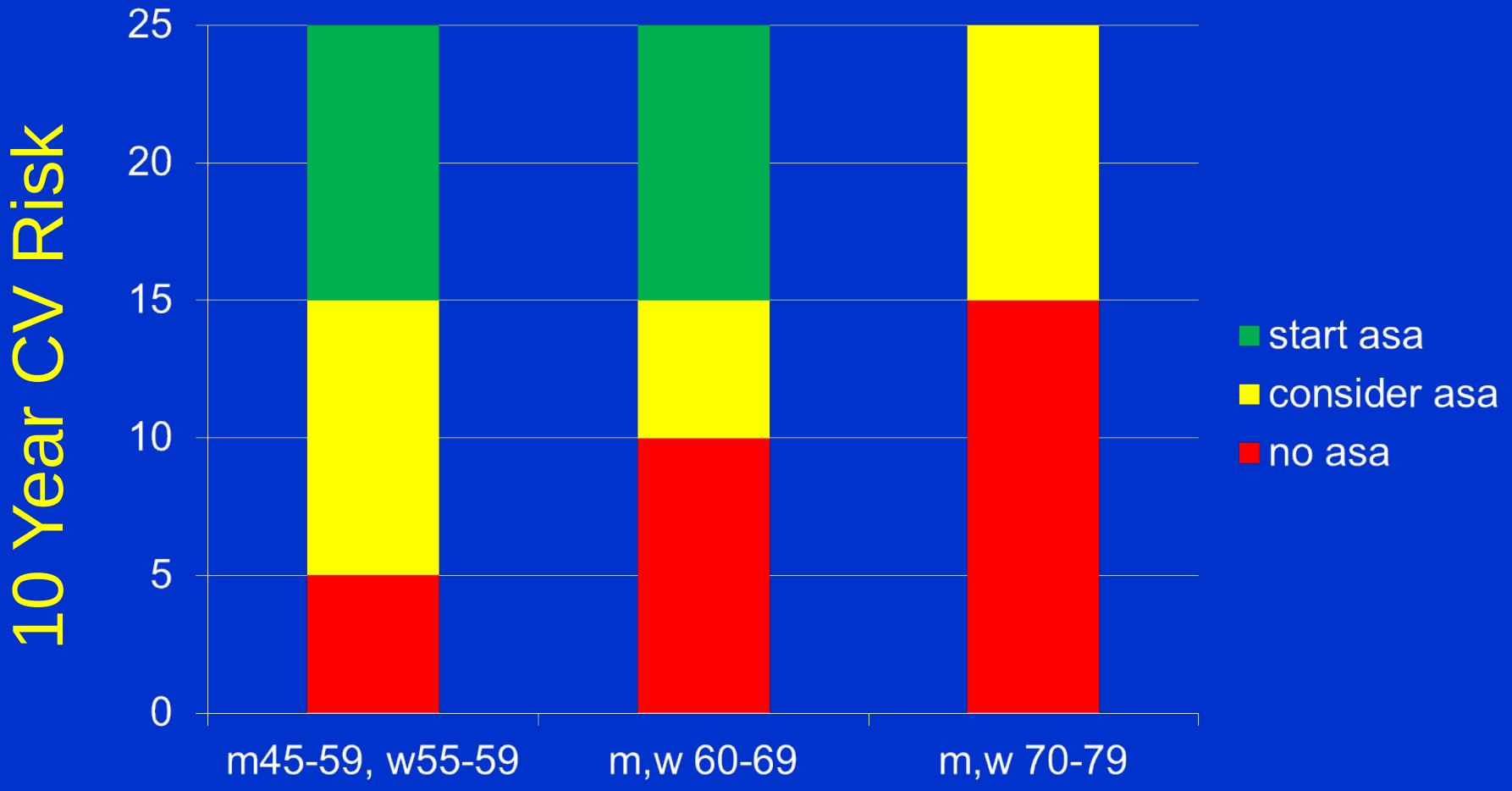
A few more commonly asked questions…..

What is the role of Aspirin in prevention of ASCVD?

- General trend: use aspirin less frequently for primary prevention
  - Other interventions often lowers added benefit of ASA**
- Risk/benefit ratio changes with age and gender
- Where is benefit most clear?
  - CAD and stroke (thrombotic): ASA considered for all
  - PAD, DM, CKD, AAA: ASA when 10yr risk >10%**
  - For all others when 10yr risk > 15% AND:
    - Men 45-69 yo**
    - Women 55-69 yo**

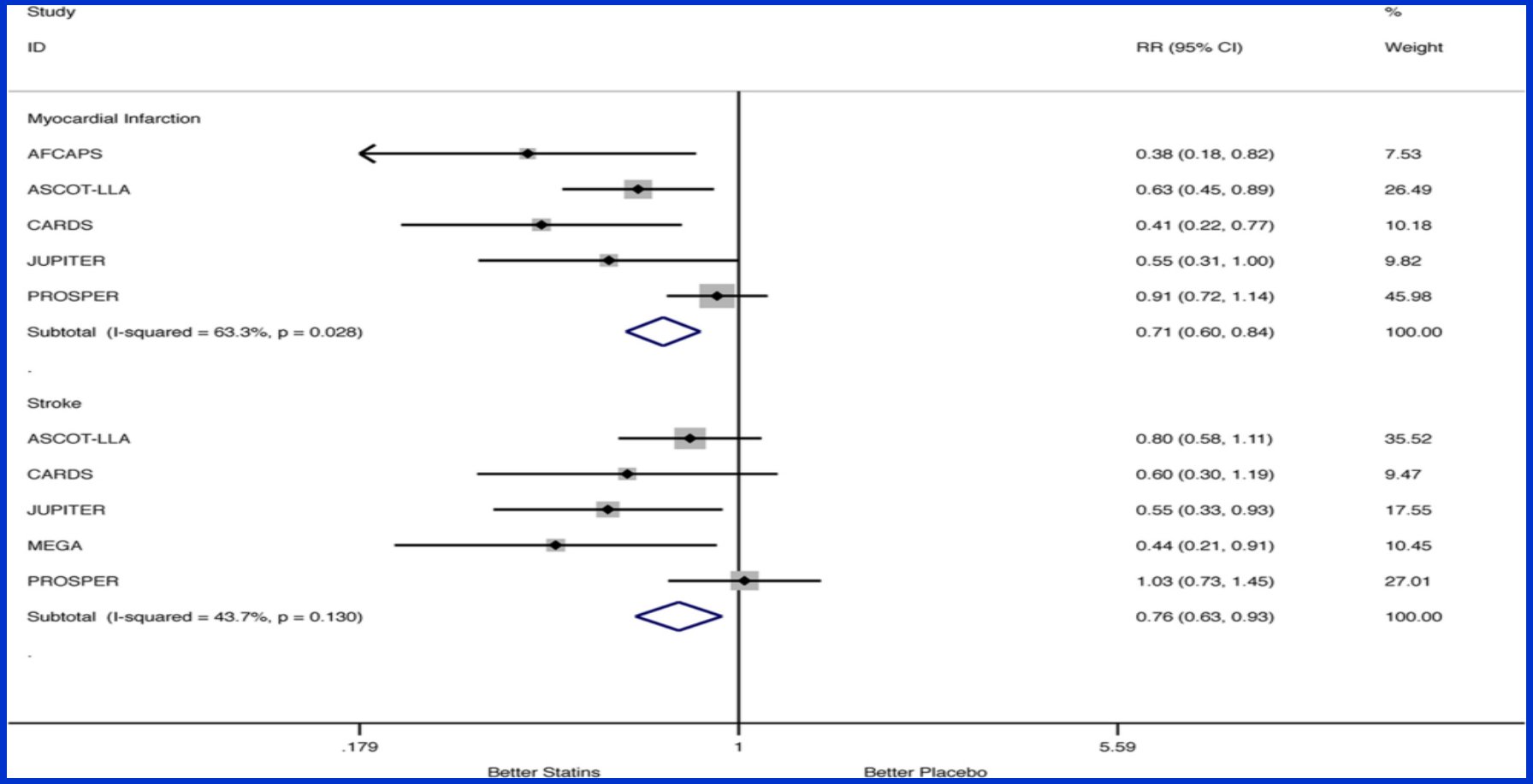
**Risk often falls below risk threshold when patient treated with other modalities!!

Aspirin recommendations for primary prevention of ASCVD



Is there evidence to support statin use in elderly patients without known ASCVD?

Benefits of Statins in Elderly Subjects Without Established Cardiovascular Disease: A Meta-Analysis**



**J Am Coll Cardiol 62(22):2090-2099, 2013.

Considerations for statin therapy in patients older than 75 years

- Consider life expectancy and quality of life years than chronologic age
- Start statin in anticipation of
  - --5 years of expected therapy and quality years for primary prevention
  - --2 years of expected therapy and quality years for primary prevention
- Avoid combination lipid lowering therapy and be aware of renal function
- Employ a shared decision approach
- Safe to stop statin in patients with significant comorbidities

Is there any role for treat to target?

A contrarian view based on observational studies and expert opinion:

- "Statin and stop" sufficient for most patients treated for primary prevention
- High Intensity statin for all patients with new ASCVD events is a cornerstone of therapy
- Treatment targets ("hybrid approach") will still be used-- and adjunct lipid therapy considered-- when:
  - LDL> 130mg after max statin achieved OR
  - LDL> 100mg/dL when other clinical confounders exist
- Niacin and/or ezetimibe therapy for patients who are statin intolerant

IMPROVE-IT: 'Modest' Benefit When Adding Ezetimibe to Statins in Post-ACS Patients

Primary End Point and Individual Components (7-Year Event Rates)

Clinical Outcomes	Simvastatin, n=9077 (%)	Ezetimibe/Simvastatin, n=9067 (%)	*P*
Primary end point (Cardiovascular death, MI, unstable angina, coronary revascularization, or stroke)	34.7	32.7	0.016
All-cause death	15.3	15.4	0.782
MI	14.8	13.1	0.002
Stroke	4.8	4.2	0.052
Ischemic stroke	4.1	3.4	0.008
Unstable angina	1.9	2.1	0.618
Coronary revascularization	23.4	21.8	0.107

http://www.medscape.com/viewarticle/835030#vp_2

Do I need to monitor lipids regularly for patients on statins?

- Lipids should be checked 6-8 weeks after statin initiation to insure adequate LDL response & compliance
- Serial lipid monitoring is not essential
  - --Especially if pharmacy utilization provides evidence of adherence
  - --Documentation of LDL can motivate some patients
  - --Reinforces importance of diet and exercise
- Routine CPK and LFT monitoring is not necessary
- Non fasting lipid determination is adequate in most cases when lab follow-up is deemed desirable

ARS Case 1: Mr. Smith

65 yr old healthy male presents for his annual HME

PMH: No history of HTN, Diabetes
Non-smoker
Takes a multivitamin daily
CV Risk 11%

Auto order lab results:

TC 171
Trig 91
HDL 42
LDL 95

ARS Case 1:
What would you do with his lab results?

1. Inform patient lipids are fine

2. Send patient to “Preventing Diabetes and Heart Disease” class/webinar

3. Start patient on moderate dose statin:
   Simvastatin 40 mg

4. Start patient on moderate dose statin:
   Simvastatin 40 mg and ASA 81 mg

Case 1 continued…

- You convince Mr. Smith to start Simvastatin 40mg

- Mr. Smith returns for a repeat lipid test in eight weeks:

  TC 145

  Trig 80

  HDL 46

  LDL 80

CV risk is now 6.5%

ARS Case 1 Question 2
What do you do now?

1. Stop statin because CV risk is now below 7.5%

2. Start ASA 81mg

3. Encourage patient to stay on current dose because statins only protect your heart while you are taking them

4. Option 3 and encourage patient to have a yearly lipid test

Case #1 Summary

- CV Risk trumps LDL level!
- Document risk discussion with patient
- Use statin patient instruction information to help convince patients to start statin

Case #1 Summary

- Encourage med adherence at every opportunity as Primary Prevention patients are most likely to stop their statin
- Use standardized letters and emails to notify patients of importance of continued use
- In future a med adherence monitoring program may make yearly lipid tests less important

ARS Case #2: Mr. Green

59 yr old emails you about his lipid results

PMH: Controlled HTN

10 yr CV Risk 6%

Labs: Non fasting

Total Cholesterol	192
Triglyceride	831
HDL	44
LDL direct	55
HBA1c	6.1 (unchanged from 6 months)

BMI: 36

EVS: 20 min of moderate intensity exercise q wk

ARS Case #2:
What would you do for Mr. Green?

1. Ask pt come return to medical office for repeat lipid in FASTING state

2. Refer to “Preventing Diabetes and Heart Disease” class/webinar and start Metformin

3. Order fibrate to pharmacy

4. Order both fibrate and statin

Initial Questions to Address

- Should I accept non-fasting lipid test?
- What is patient's CV risk?
- Should I treat triglycerides based on a non-fasting level?
- What is the best way to treat?

Summary Case #2

- Treat patient based on non-fasting lipid profile
- Diet, exercise, and Omega 3 Fatty Acids for most
- Metformin for appropriate patients with Prediabetes
- Good blood sugar control for DM
- THEN consider fibrate if TG ≥ 700, especially for patients with a history of pancreatitis.

ARS Case #3: Ms. Jones

38 year old female with a new diagnosis of Type 2 DM, here for a Diabetes visit.

PMH: HTN, smoker
PSH: Tubal Ligation

Pre-visit labs:

TC: 220
TG: 245
LDL: 130
HDL: 41

10 year CV risk is 12%

ARS Case #3: Ms. Jones
What would you recommend?

1: Tell patient to quit smoking and attend DM class

2: Option 1 plus offer Quitline referral medication to help her quit

3: Option 1 & 2 plus Simvastatin 40 mg

4: Option 1,2 & 3 plus ASA 81 mg

Summary Slide for Ms. Jones

- Colorado Quitline and tobacco cessation medications for tobacco cessation
- Even with pts < 40, assess risk to determine need for statin
- For pts with Diabetes consider ASA when 10 year CV risk is > 10% AFTER STATIN

ARS Case #4: Mr. Adams ASCVD patient

79 y/o male new KP member. Had AMI 3 years ago, was recently discharged from hospital with recurrent ACS and continued on pre-admission dose of simvastatin 40 mg qd

Total cholesterol: 166 mg/dL

TG: 230 mg/dL

LDL-c: 85 mg/dL

HDL-c: 35 mg/dL

ARS Case #3: Mr. Adams
What would be the best treatment option?

1. Intensify Statin
2. Continue current therapy
3. Add niacin to further lower LDL and improve HDL
4. Add ezetimibe

Questions?