Are recent cholesterol treatment guidelines still controversial?

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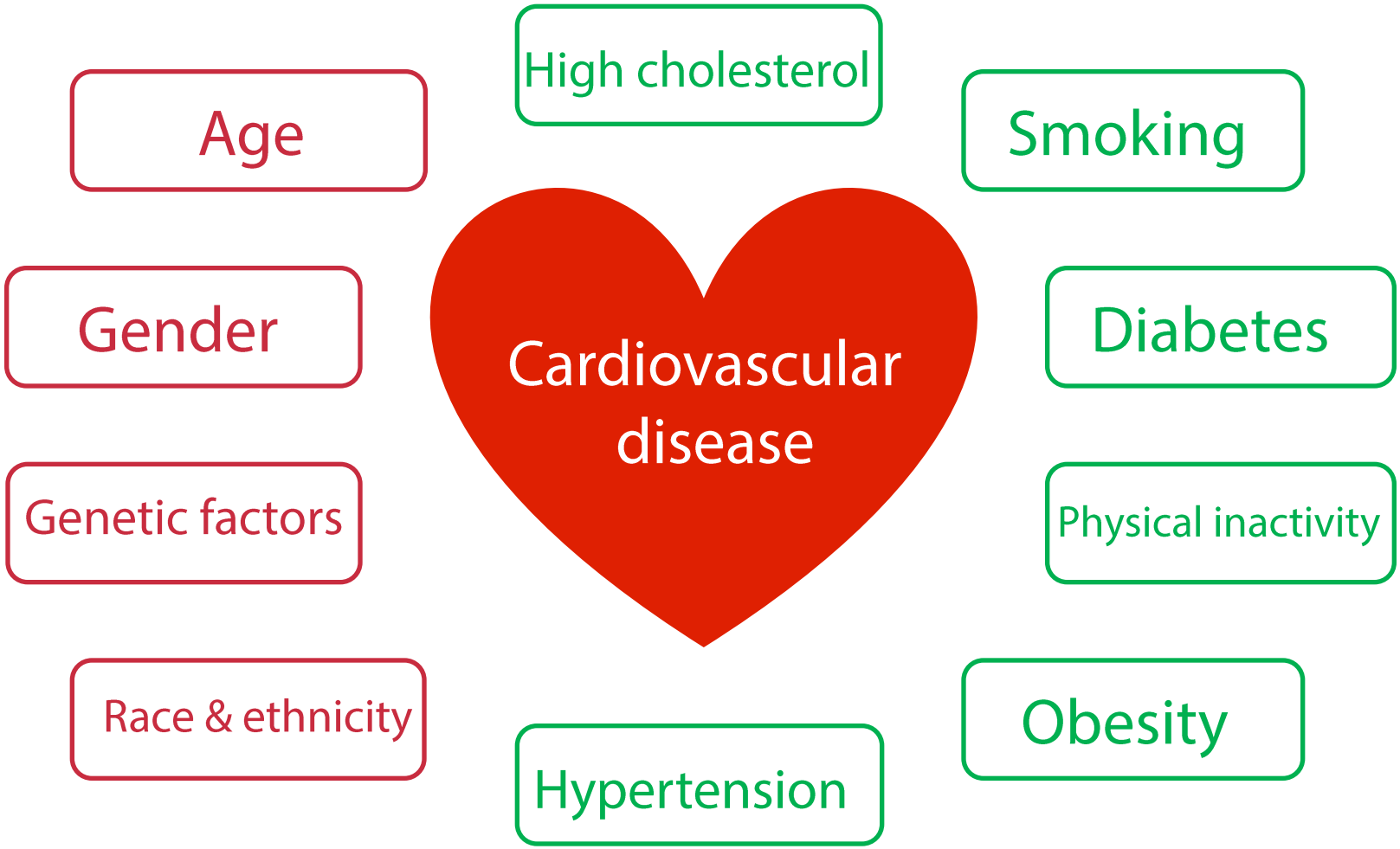
Conflict of interest disclosure

None

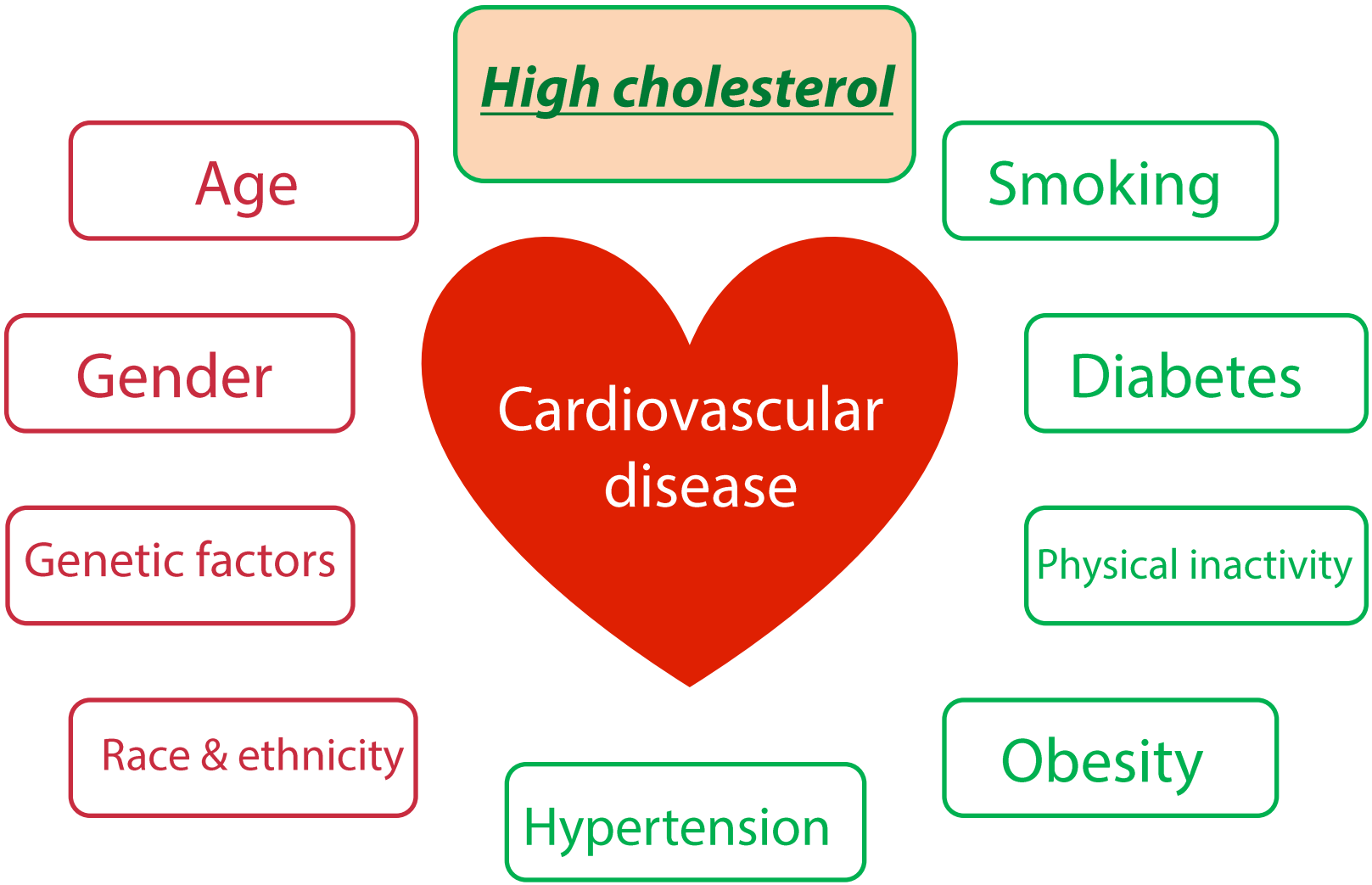
Content Overview

- Dyslipidemia and Cardiovascular Disease
- 2013 ACC/AHA Guideline
- Controversies on 2013 ACC/AHA Guideline
- Summary & Conclusion

Major risk factors for cardiovascular disease



Major risk factors for cardiovascular disease



Management of dyslipidemia (NCEP ATP III)

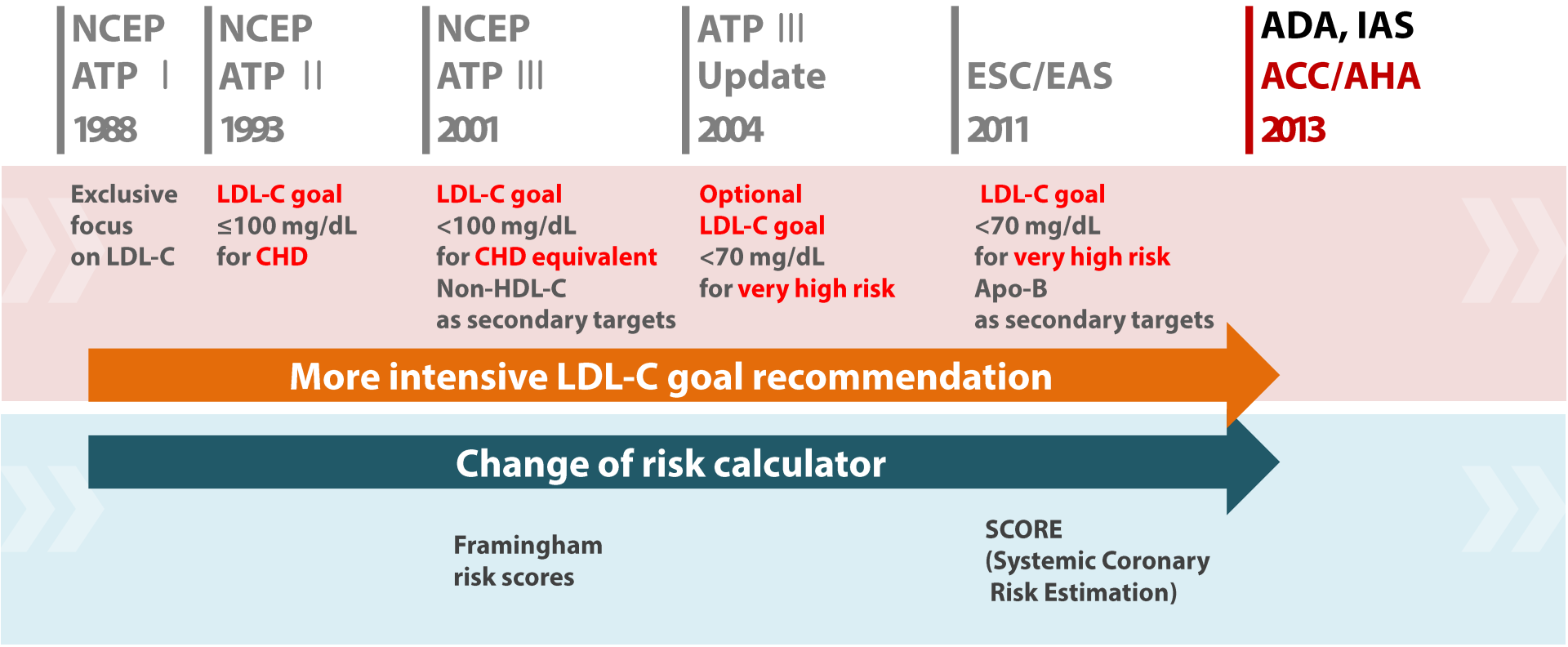
- Very high risk: established CHD + major risk factor(s)
  - LDL-C < 70 mg/dl ("option")

- High risk: CHD or CHD equivalent, or 10-yr risk > 20%
  - LDL-C < 100 mg/dl

- Secondary target: non-HDL-C

Circulation. 2004;110:227-239

Evolution of the lipid treatment guideline



2013 ACC/AHA guideline

- Update the clinical practice recommendations for the treatment of blood cholesterol levels to reduce atherosclerotic cardiovascular disease (ASCVD) risk

  - Evidences
    - **Randomized controlled trials** (**RCTs**) with CV outcomes
    - Systemic reviews of RCTs
    - Meta-analyses of RCTs

Circulation. 2014;129:S1-45

Major changes compared to ATP III guideline

1. Four major statin benefit groups

2. Development of the Pooled Cohort Equations

3. High- or moderate-intensity statin therapy

4. No specific LDL-cholesterol target

5. No routine use of non-statin drugs combined with statin

Circulation. 2014;129:S1-45

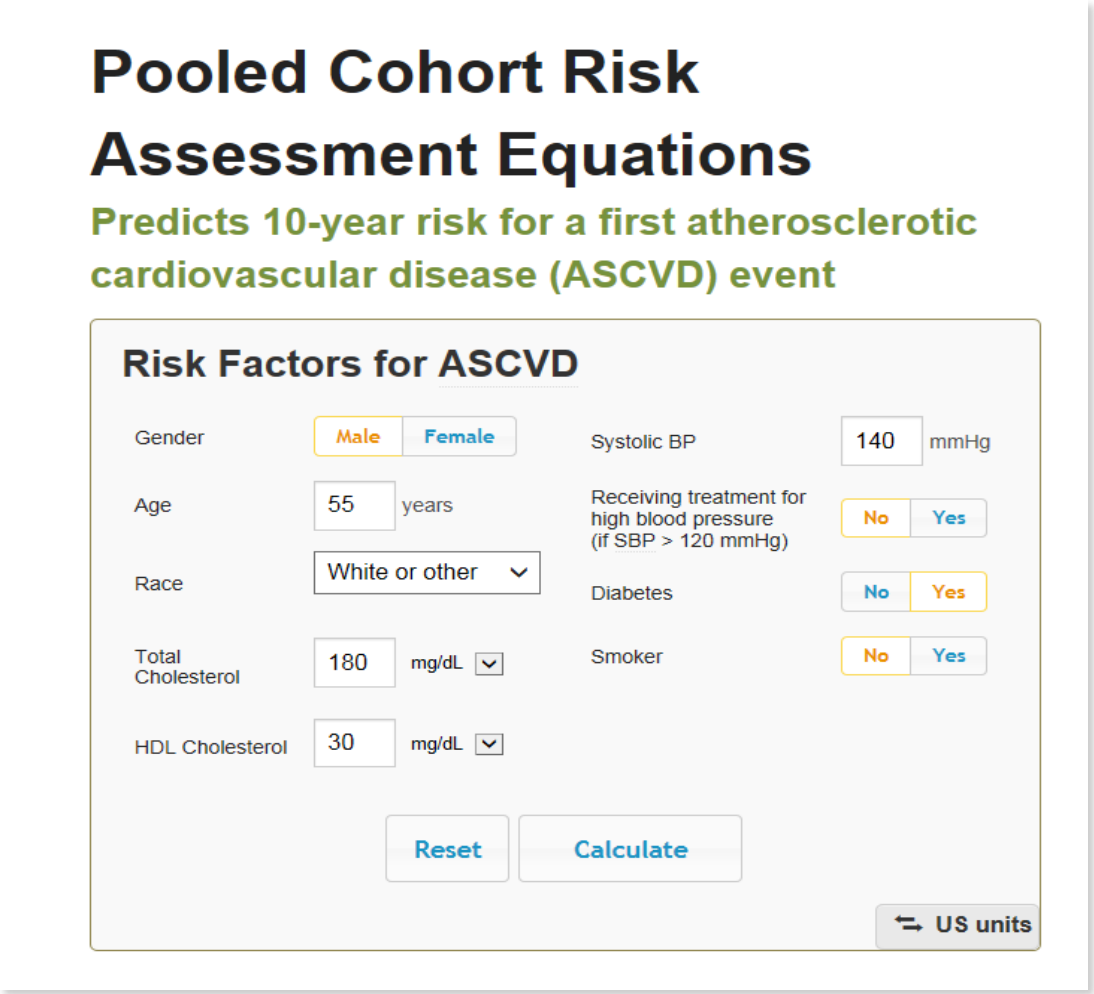
Target patient groups

Group 1	**Individuals with clinical ASCVD***
Group 2	Individuals with primary elevations of **LDL–C ≥190 mg/dL**
Group 3	Individuals 40 to 75 years of age with **diabetes** with LDL– C 70-189 mg/dL
Group 4	Individuals without clinical ASCVD or diabetes who are 40 to 75 years of age with LDL-C 70-189 mg/dL and an **estimated 10-year ASCVD risk of 7.5% or higher (*New Pooled Cohort risk equation)**

* Clinical ASCVD is defined by the inclusion criteria for the secondary prevention statin RCTs (**acute coronary syndromes, or a history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease presumed to be of atherosclerotic origin**).

Circulation. 2014;129:S1-45

The new pooled cohort equations to estimate 10-year ASCVD risk



http://clincalc.com/Cardiology/ASCVD/PooledCohort.aspx

Specific dose of statins by the percent reduction in LDL-C level

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL-C on average, by approximately ≥ 50%	Daily dose lowers LDL-C on average, by approximately 30% to < 50%	Daily dose lowers LDL-C on average, by < 30%
Atorvastatin(40)-80 mg **Rosuvastatin 20 (*40*) mg**	**Atorvastatin 10 *(20)* mg** **Rosuvastatin *(5)* 10 mg** **Simvastatin 20-40 mg** **Pravastatin 40 *(80)* mg** **Lovastatin 40 mg** *Fluvastatin XL 80 mg* **Fluvastatin 40 mg bid** *Pitavastatin 2-4 mg*	*Simvastatin 10 mg* **Pravastatin 10-20 mg** **Lovastatin 20 mg** *Fluvastatin 20-40 mg* *Pitavastatin 1 mg*

Circulation. 2014;129:S1-45

No evidences for target goals and non-statin drug use

- No more LDL-C / non-HDL goal
- No routine use of non-statin drugs combined with statin

Circulation. 2014;129:S1-45

Controversies on 2013 ACC/AHA guideline

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- Too many statin eligible patients
- Pooled cohort equations
- Intensity of statins
- No lipid target goals
- Role of non-statin drugs

Controversies on 2013 ACC/AHA guideline

- **Too many statin eligible patients**
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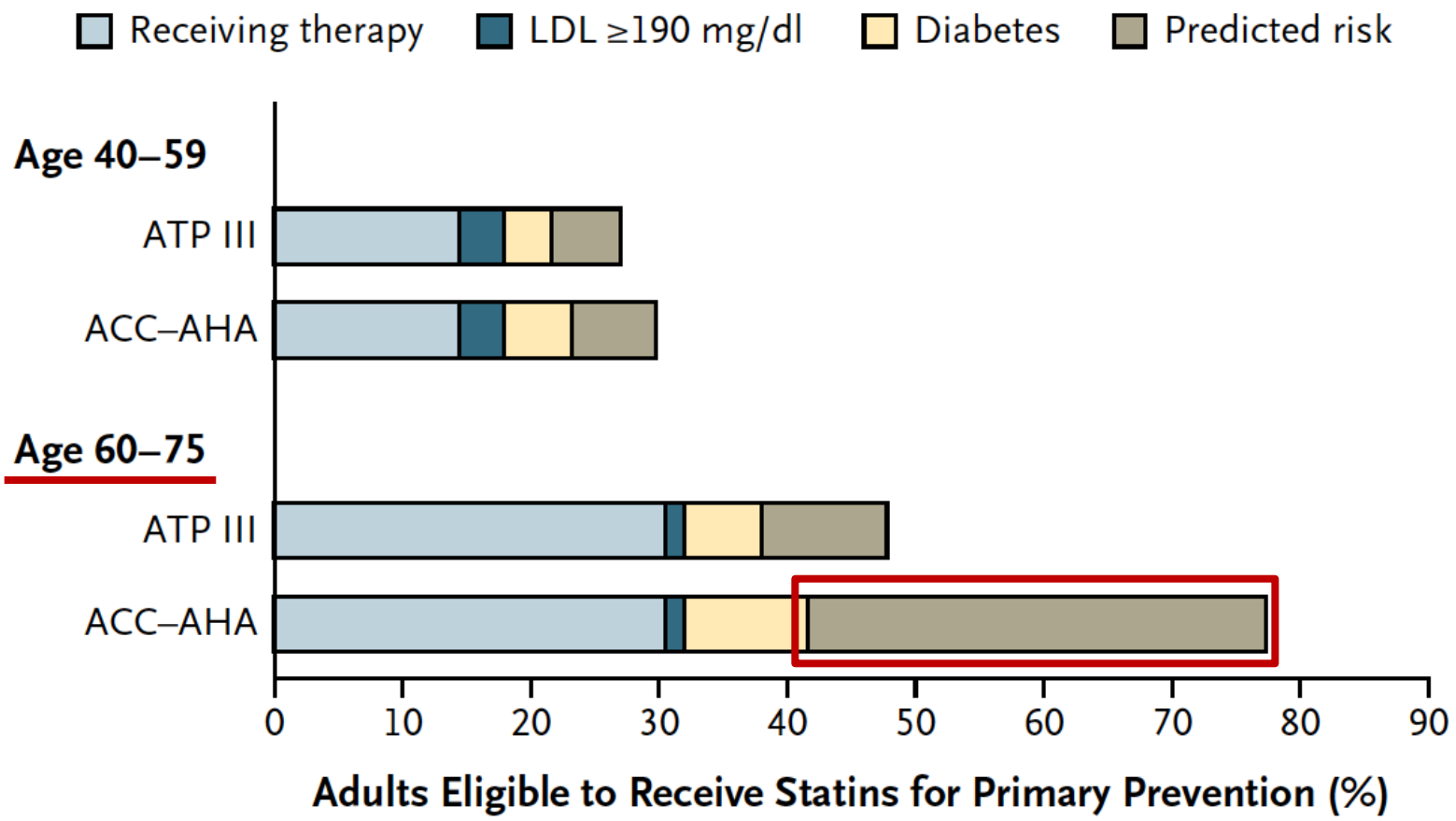
Too many statin eligible patients

	ATP-III guideline	**ACC/AHA** guideline	**New Candidates** for statin therapy
American (115.4 million)	43.2 milion (37.5%)	56.0 million (48.6%)	**14.4** million (12%)
Korean (19 million)	3.5 million (18.6%)	6.7 million (35.1%)	**3.6** million (19%)

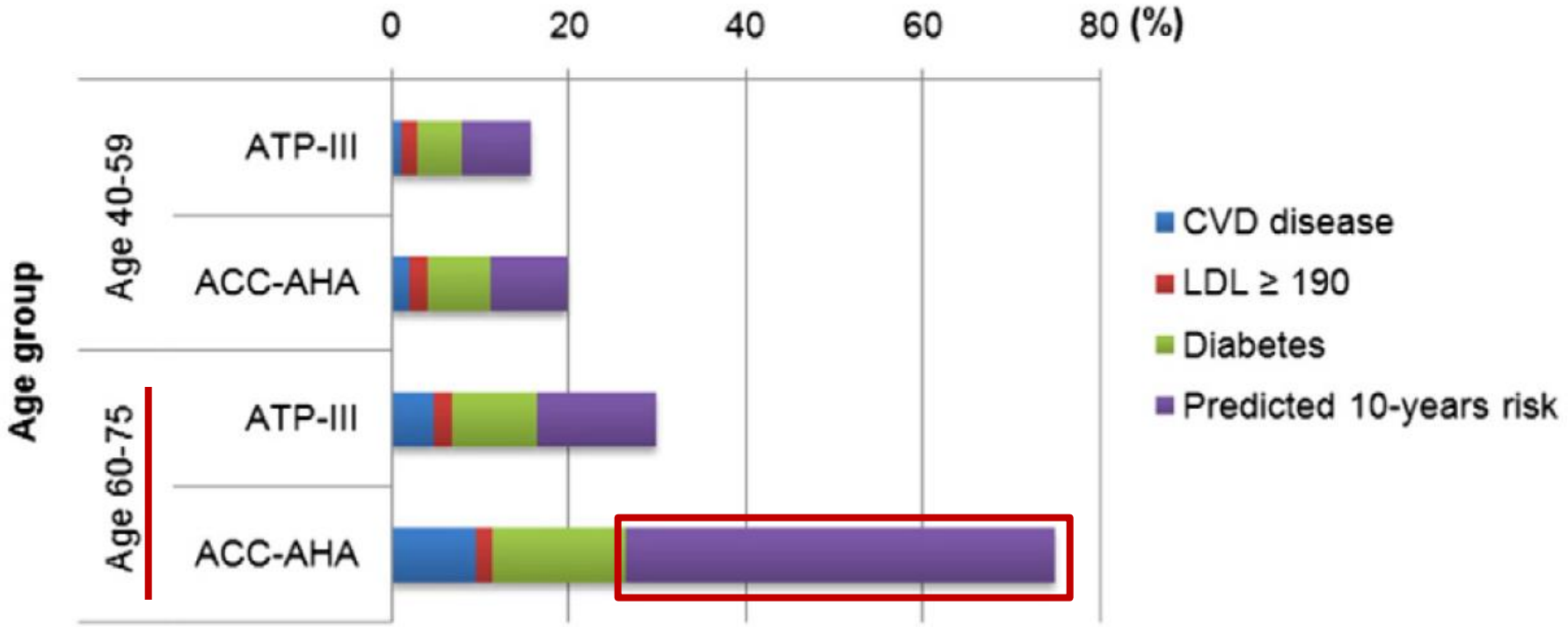
NEJM. 2014;370:1422-31
Am Heart J. 2015;170:598-605.e7

Too many statin eligible patients in U.S.



NEJM. 2014;370:1422-31

Too many statin eligible patients in Korea



Am Heart J. 2015;170:598-605.e7

Controversies on 2013 ACC/AHA guideline

- Too many statin eligible patients
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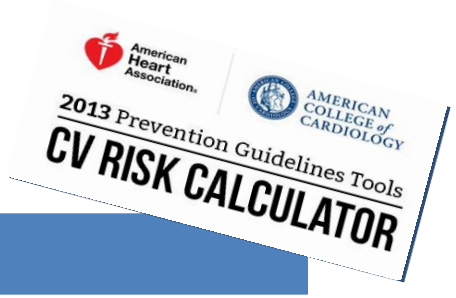
Pitfalls of the new risk calculator

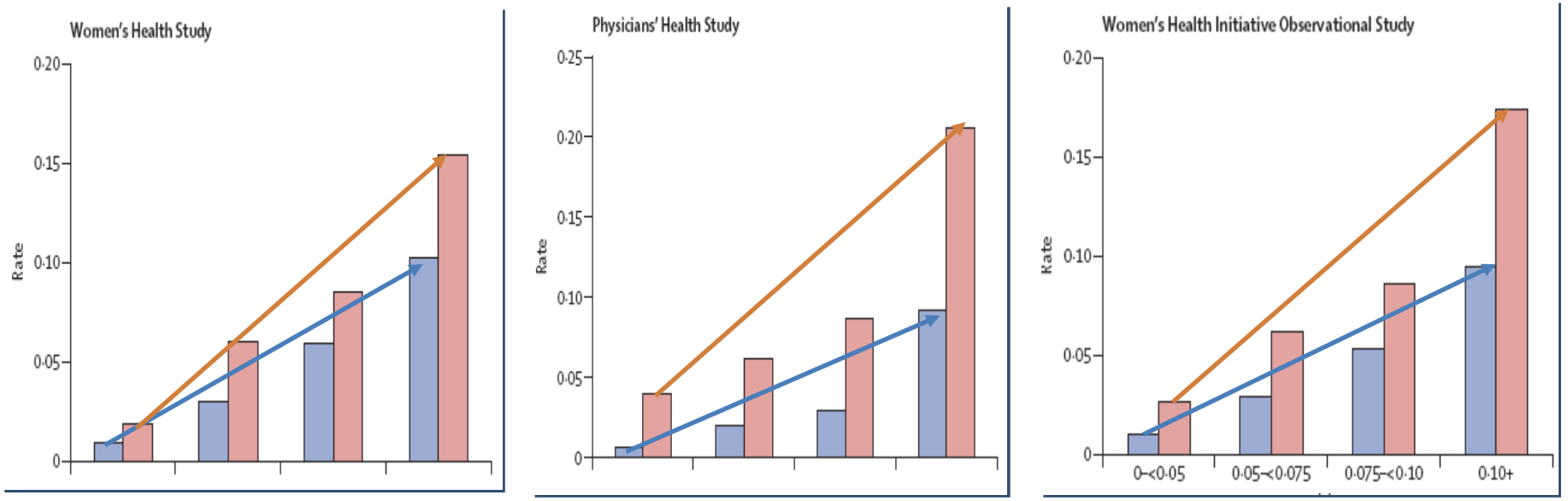
- Individuals in the fourth group can be identified by using **the new Pooled Cohort Equations for ASCVD risk prediction**, developed by the Risk Assessment Work Group



Risk Factor	Units
• Sex	• M or F
• Age	• Years
• Race	• African/Americans or whites/others
• Total Cholesterol	• mg/dL
• HDL-C	• mg/dL
• Systolic BP	• mm Hg
• Treatment for High Blood Pressure	• Y or N
• Diabetes	• Y or N
• Smoker	• Y or N

Circulation. 2014;129:S1-45

Pitfalls of the new risk calculator



Observed event rates

Event rates predicted by new ACC/AHA risk prediction algorithm

Lancet. 2013;382:1762-5

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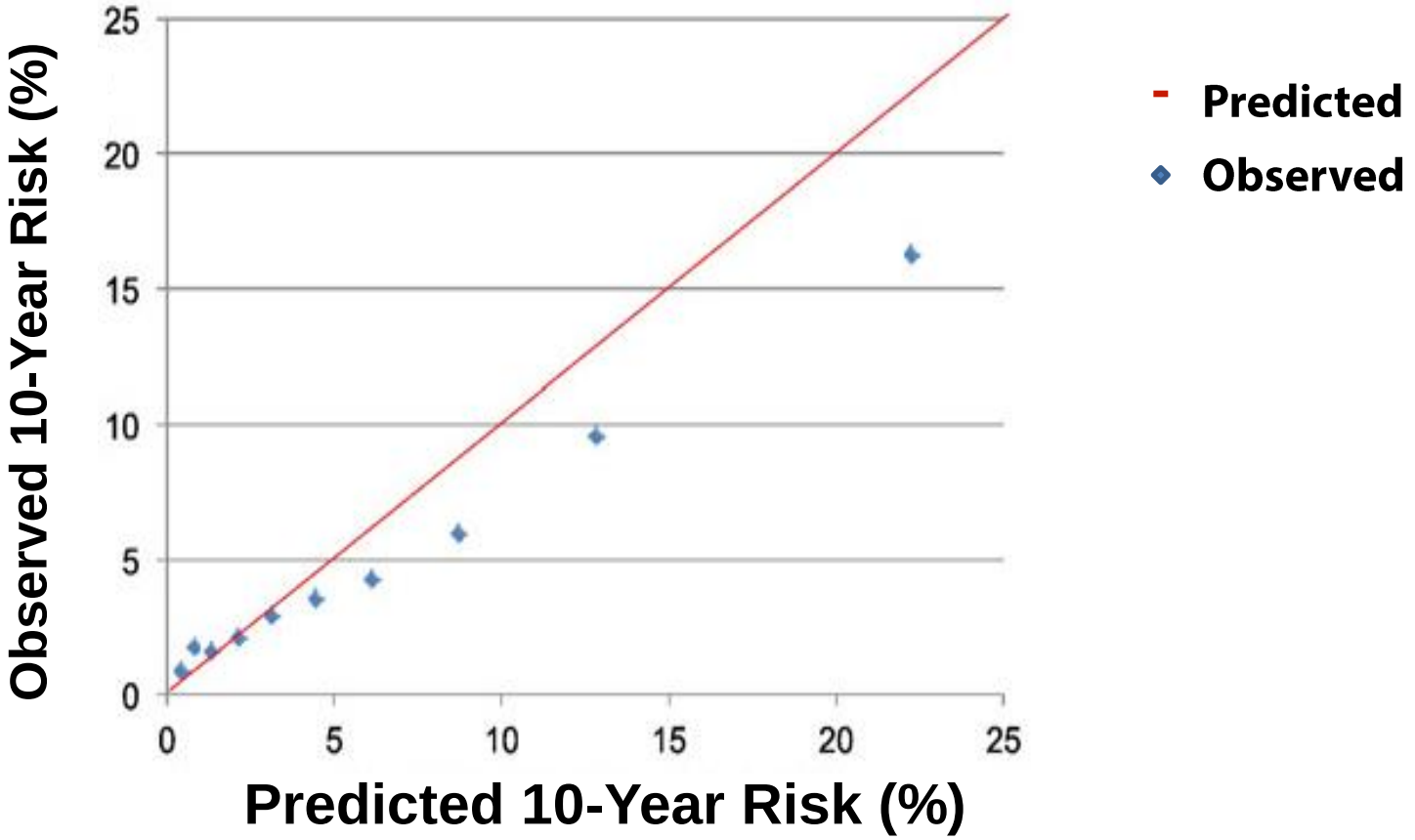

Am Heart J. 2015;170:598-605.e7

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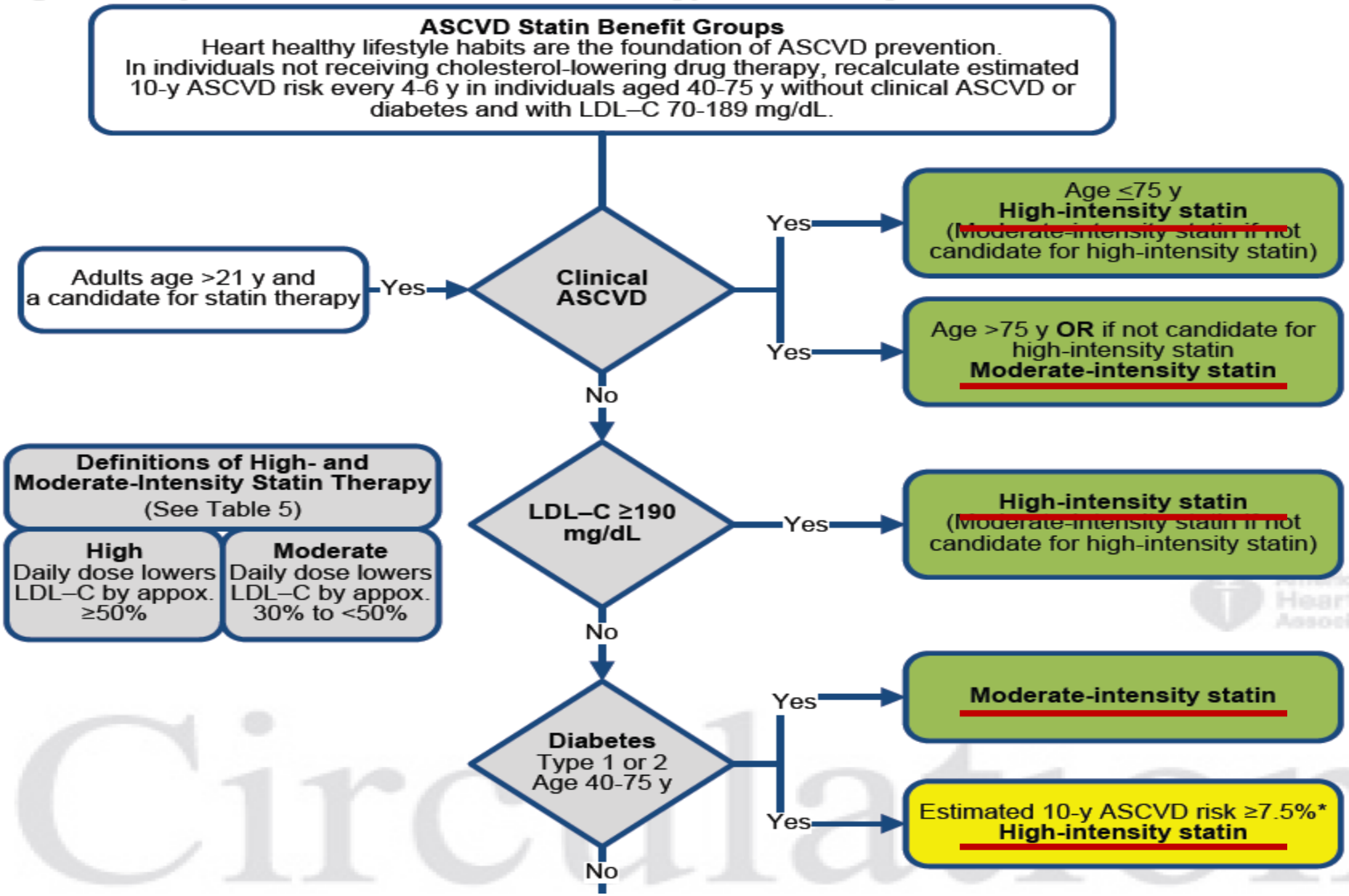
High- or moderate-intensity statin therapy



Circulation. 2014;129:S1-45

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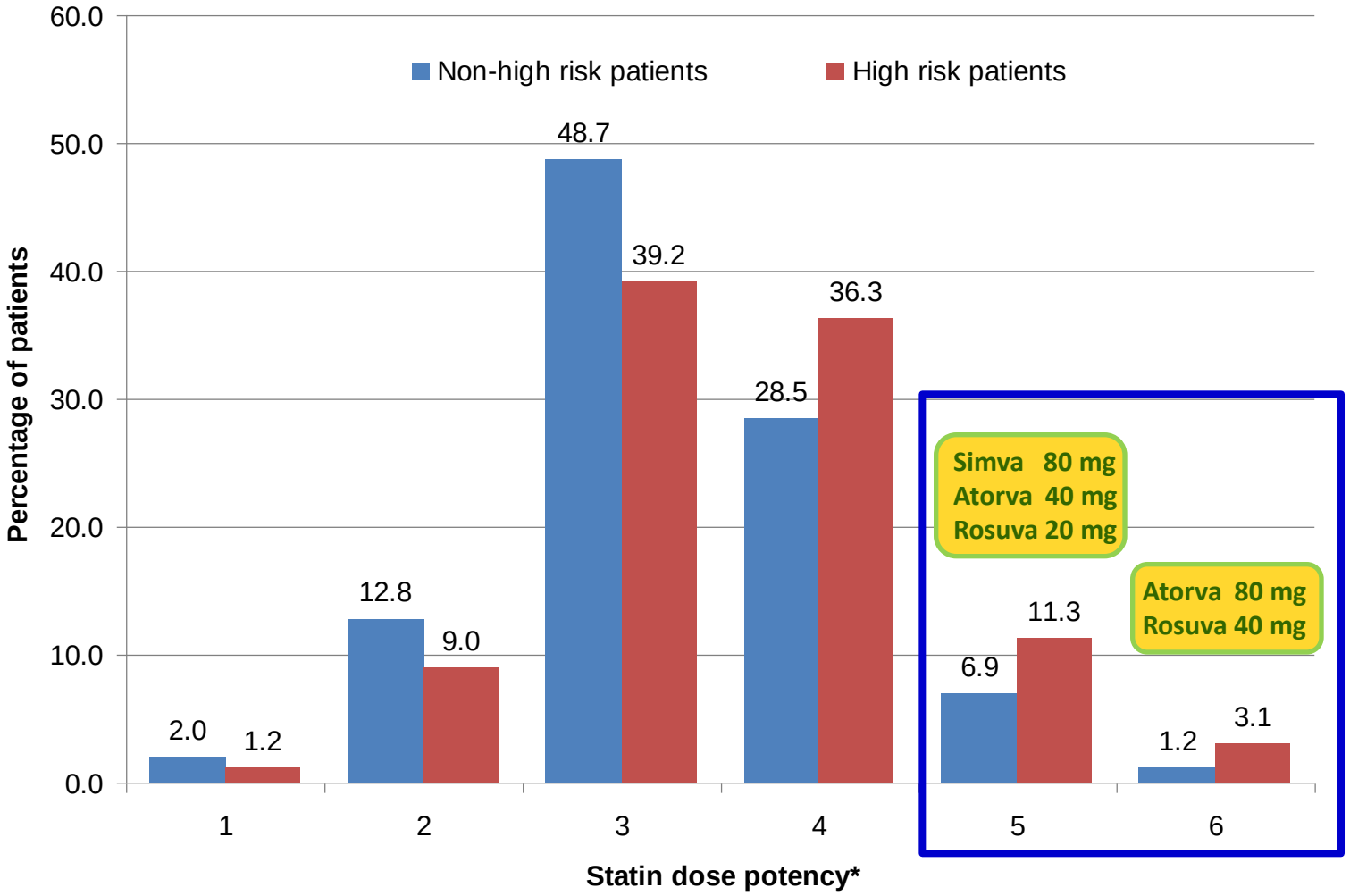
Circulation. 2014;129:S1-45

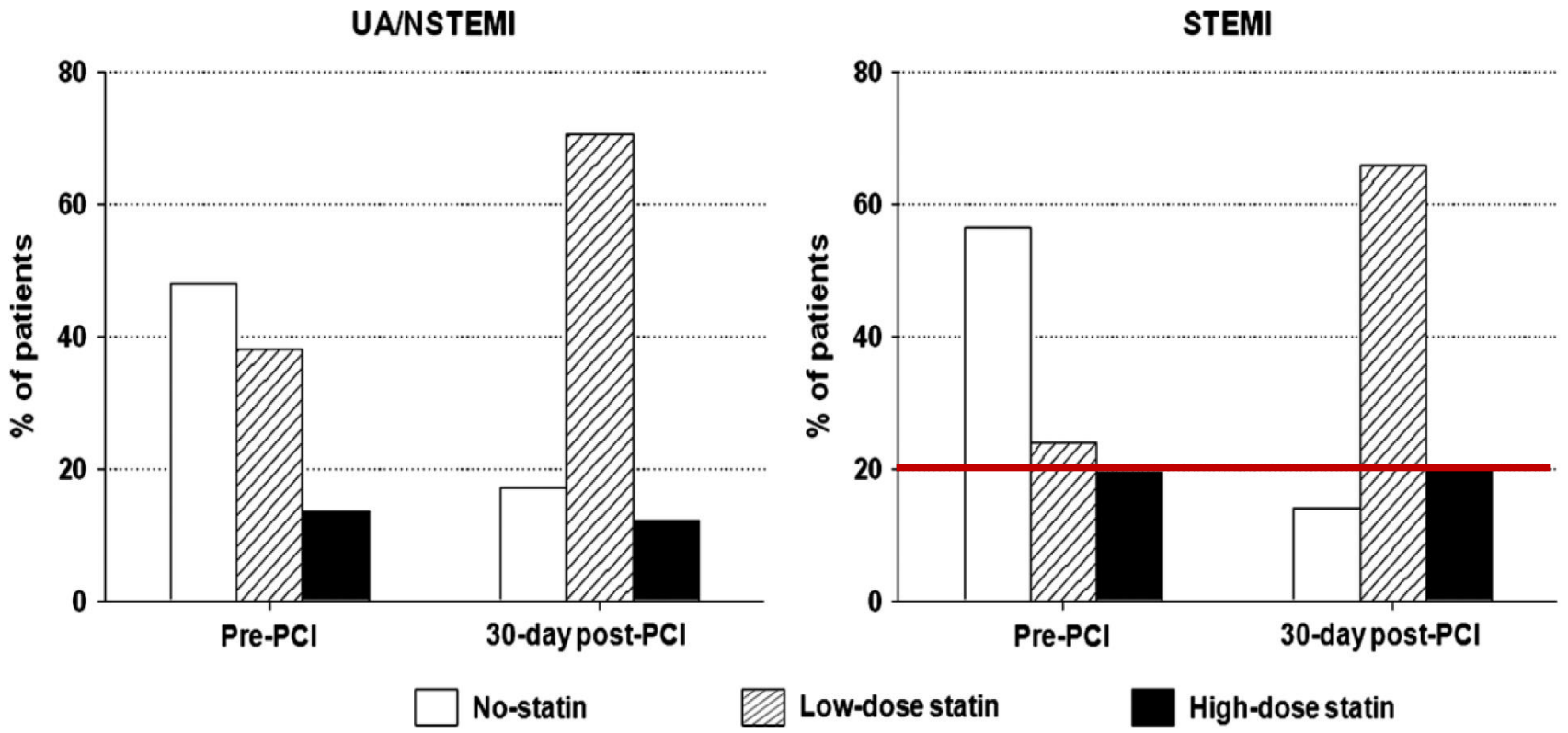
Statin use in real world practice

In Europe & Canada



Eur J Prev Cardiol. 2012;19:221-30

Statin use in Korea



Atorva ≥ 40 mg
Rosuva ≥ 20 mg

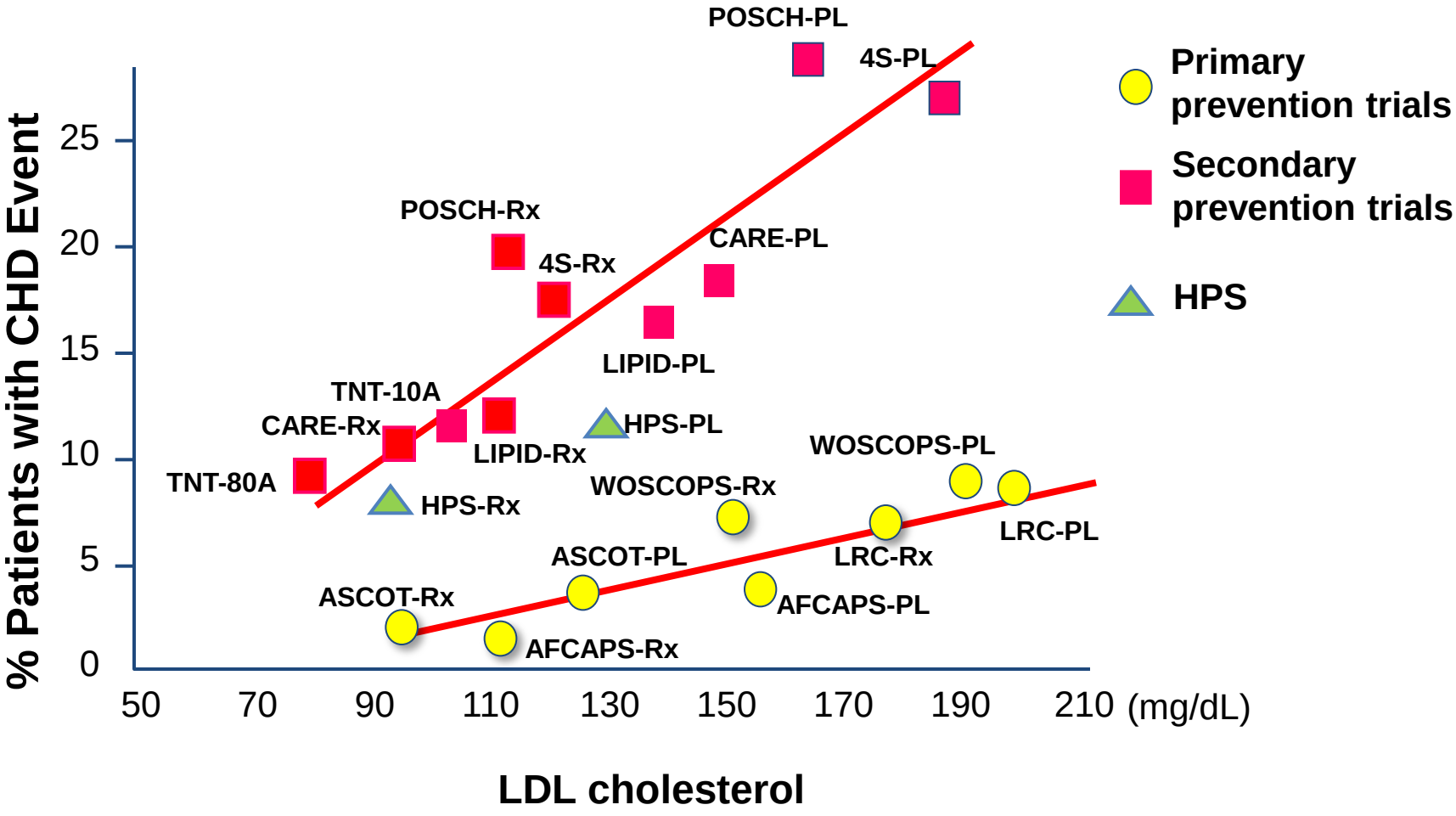
Clin Cardiol. 2012;35:700-6

Controversies on 2013 ACC/AHA guideline

- Too many statin eligible patients
- Pooled cohort equations
- Intensity of statins
- **No lipid target goals**
- Role of non-statin drugs

No lipid target goals

For LDL-C; ”Lower is better”



NEJM. 2005;352:1425–1435

Expert Opin Emerg Drugs. 2004;9:269–279

LDL-C target goals in recent guidelines

	LDL-C Targets	
	Very high risk	**High** risk
NLA (2016)	< 70 mg/dL	< 100 mg/dL
ESC/EAS (2016)	< 70 mg/dL	< 100 mg/dL
AACE (2016)	< 70 mg/dL	< 100 mg/dL
IAS (2014)		< 70 mg/dL (optimal level for 1° prevention)

J Clin Lipidol. 2016;10:S1-43
Eur Heart J. 2016 [Epub ahead of print]
Endocr Pract. 2016;22:84-113
J Clin Lipidol. 2014;8:29-60

Controversies on 2013 ACC/AHA guideline

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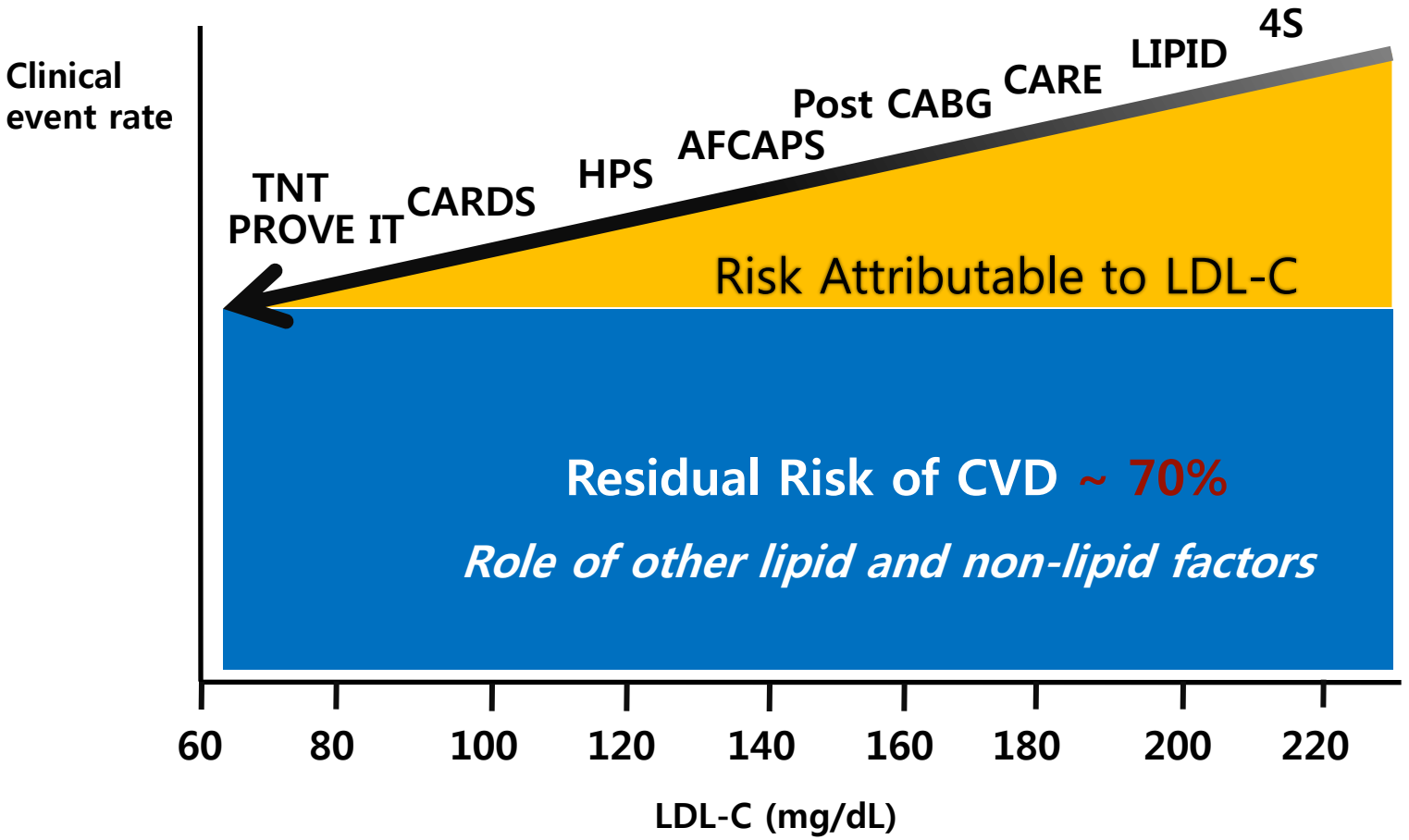
- No lipid target goals
- **Role of non-statin drugs**

Residual CVD risk despite optimal LDL-C reduction



TNT = Treating to New Targets study, PROVE IT = Pravastatin or Atorvastatin Evaluation and Infection Therapy study, CARDS = Collaborative Atorvastatin Diabetes Study, Post CABG = Post Coronary Artery Bypass Graft Study

J Am Coll Card. 2005;46:1225-8
Curr Atheroscler Rep. 2012;14: 1–10

No evidences for non-statin drug use

- FIELD
- ILLUMINATE
- ACCORD-LIPID
- AIM-HIGH
- HPS2-THRIVE

Lancet. 2005;366:1849-61; *NEJM*. 2007;357:2109-22
NEJM. 2010;362:1563-74; *NEJM*. 2011;365:2255-67
NEJM. 2014;371:203-212

IMProved Reduction of Outcomes: Vytorin Efficacy International Trial: IMPROVE-IT

The NEW ENGLAND JOURNAL of MEDICINE

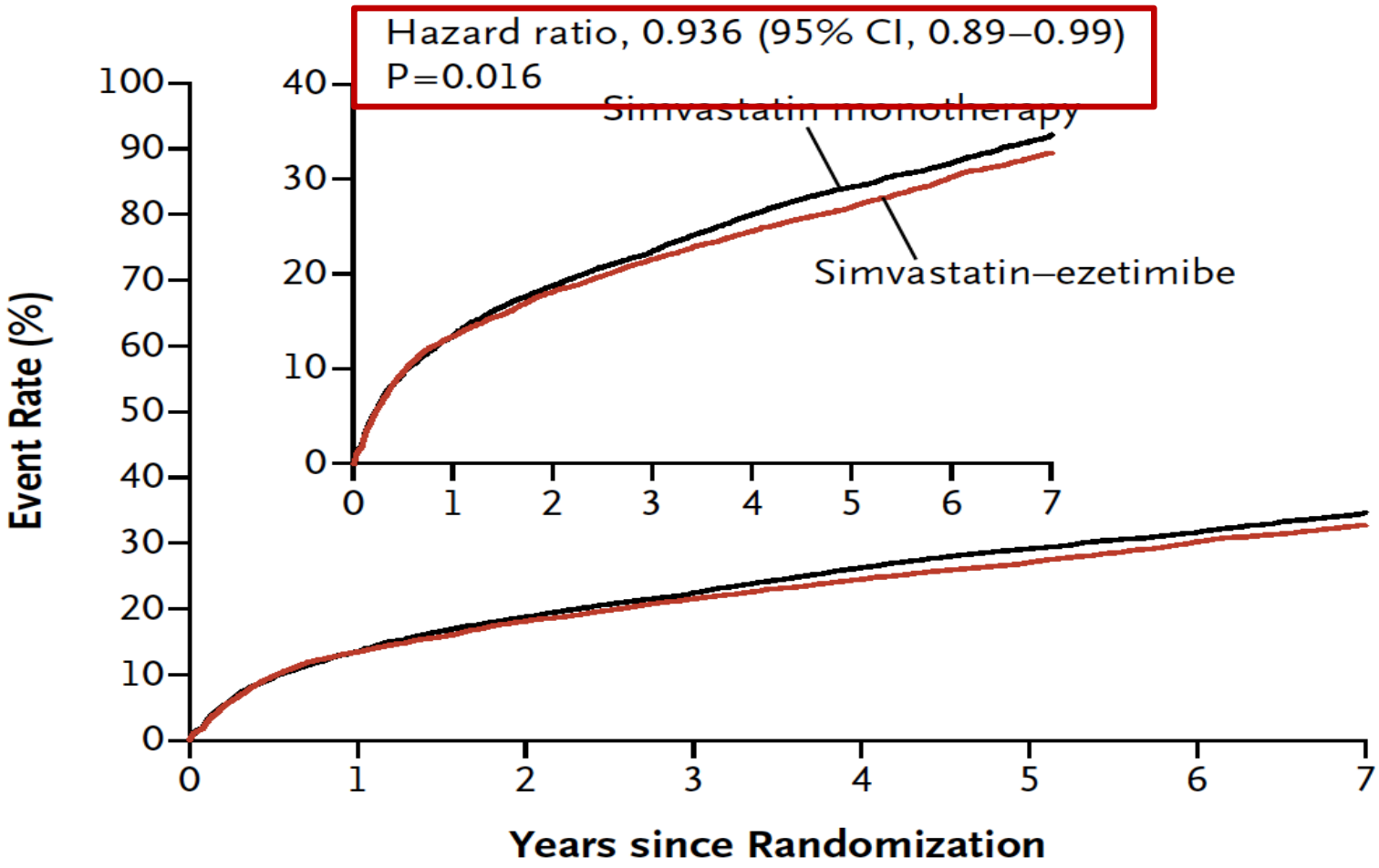
ESTABLISHED IN 1812 JUNE 18, 2015 VOL. 372 NO. 25

Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes

Christopher P. Cannon, M.D., Michael A. Blazing, M.D., Robert P. Giugliano, M.D., Amy McCagg, B.S., Jennifer A. White, M.S., Pierre Theroux, M.D., Harald Darius, M.D., Basil S. Lewis, M.D., Ton Oude Ophuis, M.D., Ph.D., J. Wouter Jukema, M.D., Ph.D., Gaetano M. De Ferrari, M.D., Witold Ruzyllo, M.D., Paul De Lucca, Ph.D., KyungAh Im, Ph.D., Erin A. Bohula, M.D., D.Phil., Craig Reist, Ph.D., Stephen D. Wiviott, M.D., Andrew M. Tershakovec, M.D., M.P.H., Thomas A. Musliner, M.D., Eugene Braunwald, M.D., and Robert M. Califf, M.D., for the IMPROVE-IT Investigators*

Primary efficacy endpoint

Cardiovascular death, MI, documented unstable angina requiring rehospitalization, coronary revascularization (≥30 days), or stroke



NEJM. 2015;372:2387-97

(Possible) Evidences for non-statin drug use

- IMPROVE-IT
- PCSK-9 inhibitors (OSLER & ODYSSEY LONG TERM)

NEJM. 2015;372:2387-97
NEJM. 2015;372:1489-99
NEJM. 2015;372:1500-09

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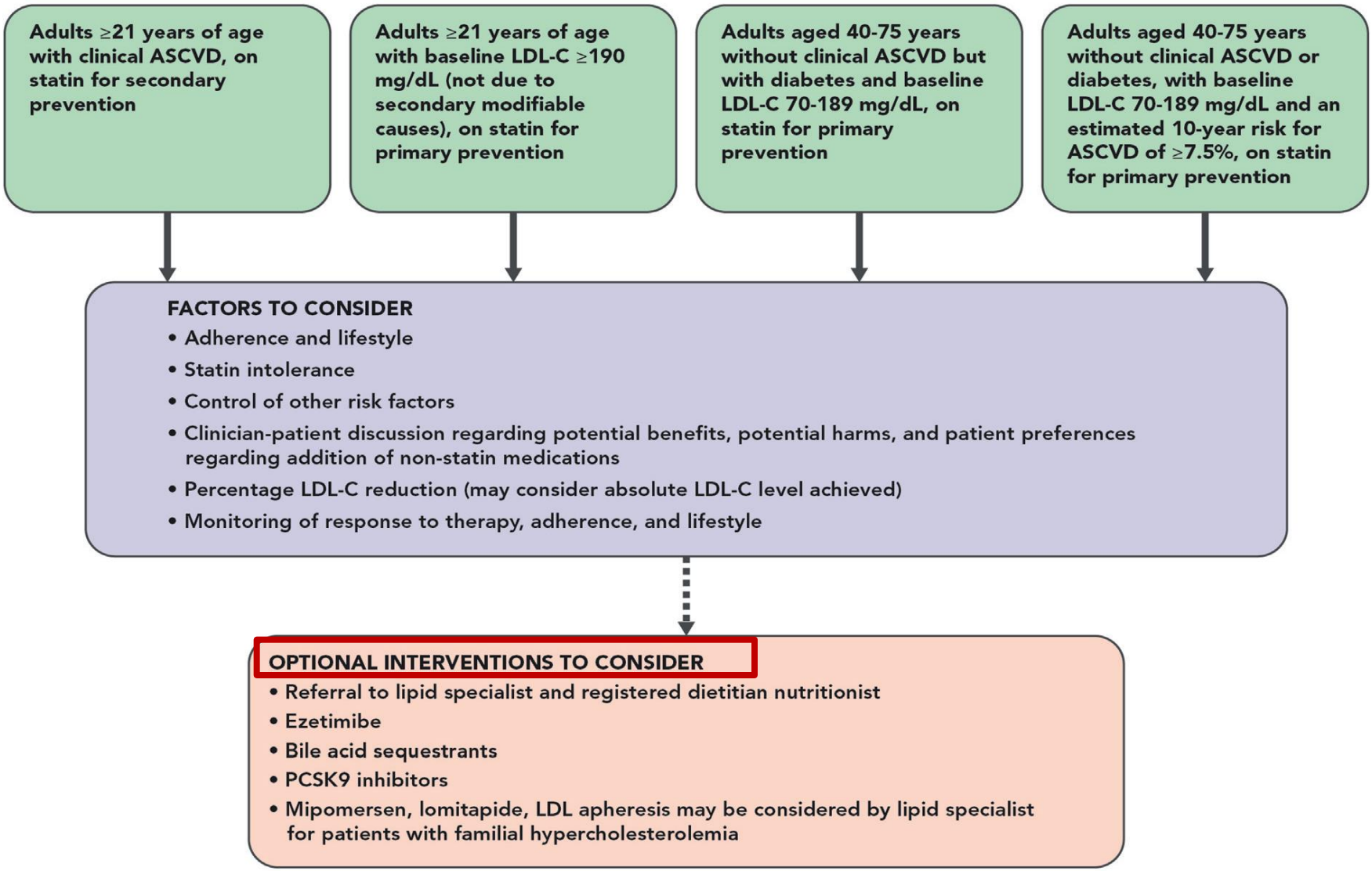
EXPERT CONSENSUS DECISION PATHWAY

2016 ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk

A Report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents

Endorsed by the National Lipid Association

The role of non-statin therapies



JACC. 2016;68:92-125

Summary

- Choice of statin eligible patients using Pooled Cohort Equations
- Which is better? fixed dose vs. treat to target approach
- Non-statin therapies are non-effective?

Conclusion

Are recent cholesterol treatment guidelines still controversial?

YES!

Thank you!

Different risk assessment tools in different guidelines

Guidelines	Risk Assessment Tool	Population Cohorts
ACC/AHA	Pooled cohort equations (PCE)	USA (non-Hispanic Whites & African-Americans)
CCS	Framingham risk score (FRS) for total CVD	USA
NICE	QRISK2	European
ESC/EAS	Systemic coronary risk evaluation (SCORE)	European
NLA	Consider 10yr-FRS, 30yr- FRS, or PCE	USA

Circulation. 2014;129:S1-45 / *Can J Cardiol*. 2013;29:151-167 / *BMJ*. 2014;349:g4356
Eur Heart J. 2016 [Epub ahead of print] / *J Clin Lipidol.* 2016;10:S1-43

Efficacy of statins in Asians

Clinical trials of statin therapy in Asian patients: lipid-lowering efficacy

Trial	No.	Locale	Statin (Dose, mg)	Mean % LDL	p Value
Randomized					
ASIA[6]	157	Multiple*	Atorvastatin (10–20)	48%	0.003
			Simvastatin (10–20)	41%	
Chan et al[28]	76	China	Simvastatin (10)	33%	—
J-CLAS[29]	121	Japan	Atorvastatin (5–20)	36%–50%	<0.001
Saito et al[30]	112	Japan	Rosuvastatin (1–40)	36%–66%	<0.0001
Wang et al[31]	54	Taiwan	Atorvastatin (10)	42%	<0.001
Yamamoto et al[32]	60	Japan	Rosuvastatin (1–4)	30–42%	0.001
Open label					
GOALLS[9,33]	198	Multiple†	Simvastatin (20, 40, 80)	41%	—
Itoh et al[34]	201	Japan	Simvastatin (5)	28%	<0.001
Mabuchi et al[35]	37	Japan	Rosuvastatin (10–40)	49%–57%	<0.0001
STATT[36]	133	Multiple‡	Simvastatin (20, 40, 80)	45%	<0.001
Teramoto et al[37]	212	Japan	Fluvastatin (20, 30, 40)	29%	<0.001
Tomlinson et al[38]	31	Hong Kong	Fluvastatin (20, 40)	26%	<0.01
Yoshida et al[39]	22	Japan	Simvastatin (20)	40%	<0.001

Am J Cardiol. 2007; 99: 410-414