Maximizing statin benefit of treating patients with dyslipidemia for primary prevention
From safety to efficacy

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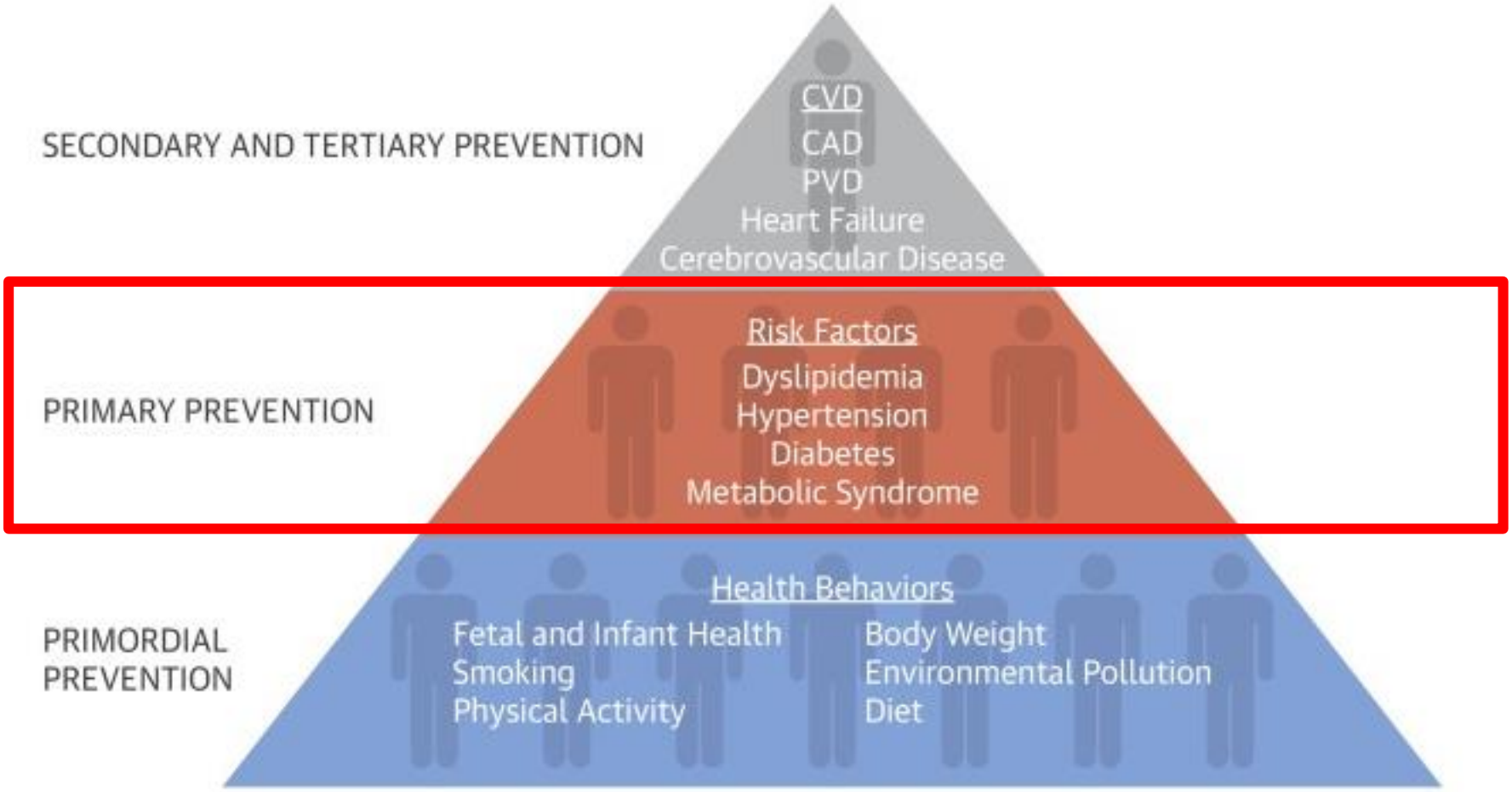
Outlines

- Aggressive “Primary Prevention” Era
  - More accurate risk estimate
  - What “ESC 2019 dyslipidemia treatment guideline” tell us ?
- Variation of statin efficacy between Asian and Western dyslipidemia
- Asian real world statin prescription condition
- Tailored lipid control in Asian primary prevention
- Conclusions

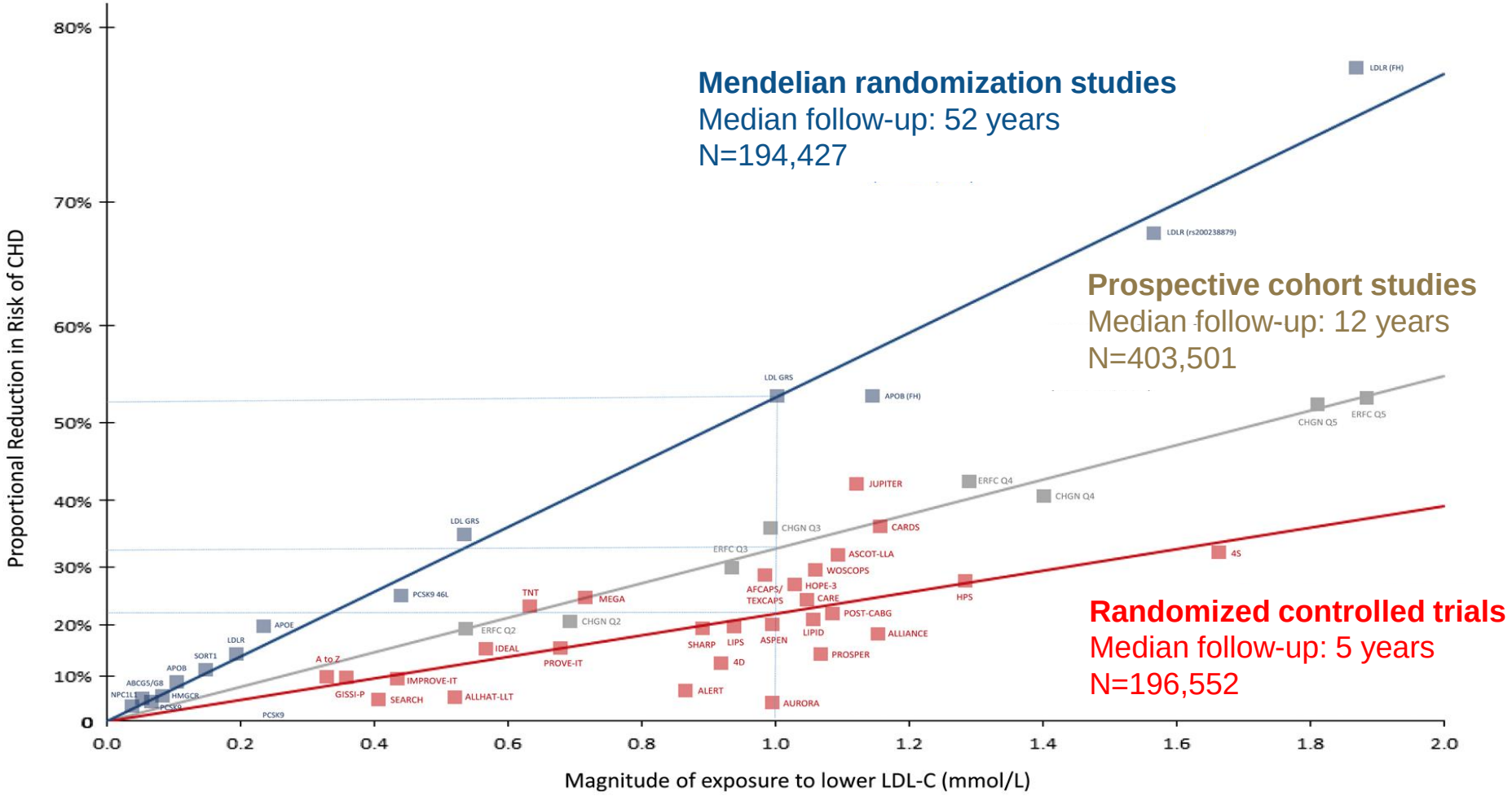
Cardiovascular disease prevention



J Am Coll Cardiol. 2017; 70 (17): 2171-85

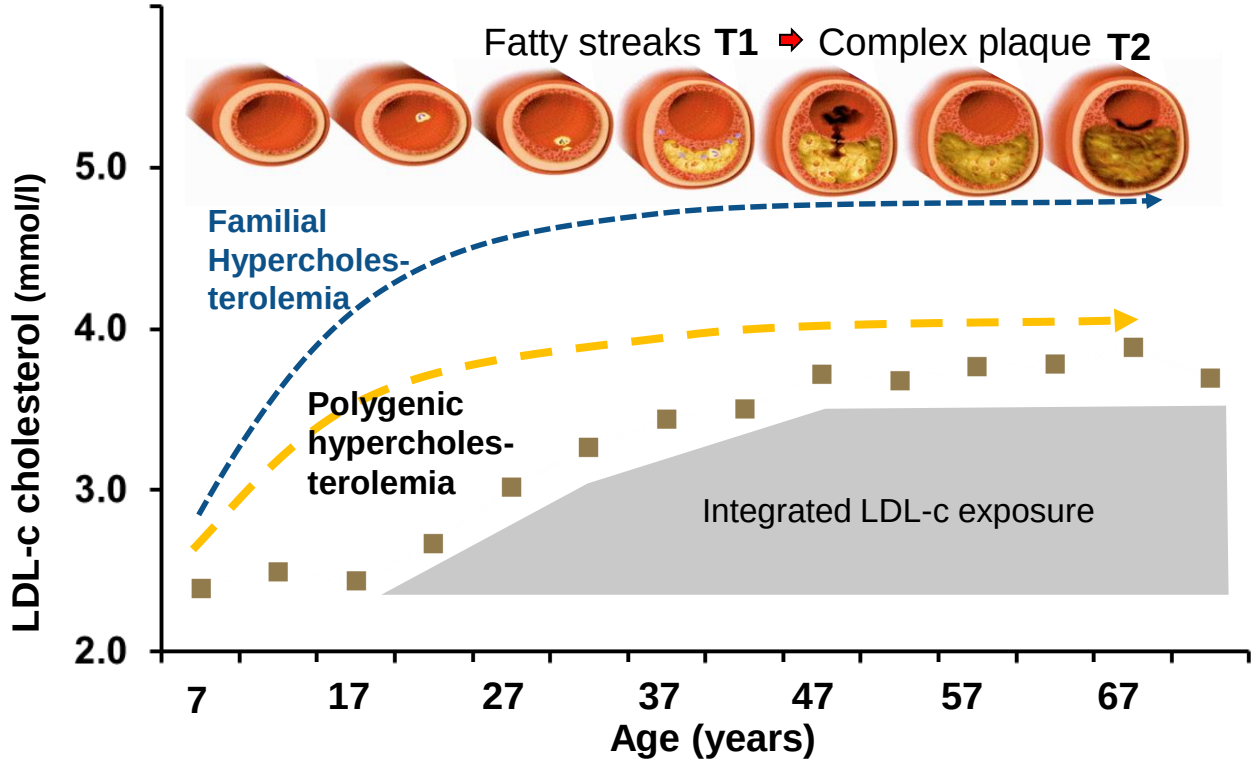
LDL is causal of atherosclerosis

Evidence from meta-analyses of **Mendelian randomization studies**, **prospective cohort studies**, and **randomized controlled trials** unequivocally establishes that LDL causes ASCVD.



Ference BA *et al*., Eur Heart J. 2017;38(32):2459-2472

LDL-c level increases with age, so does the risk of atherogenesis



Transitioning pathology

LDL-c rise with age

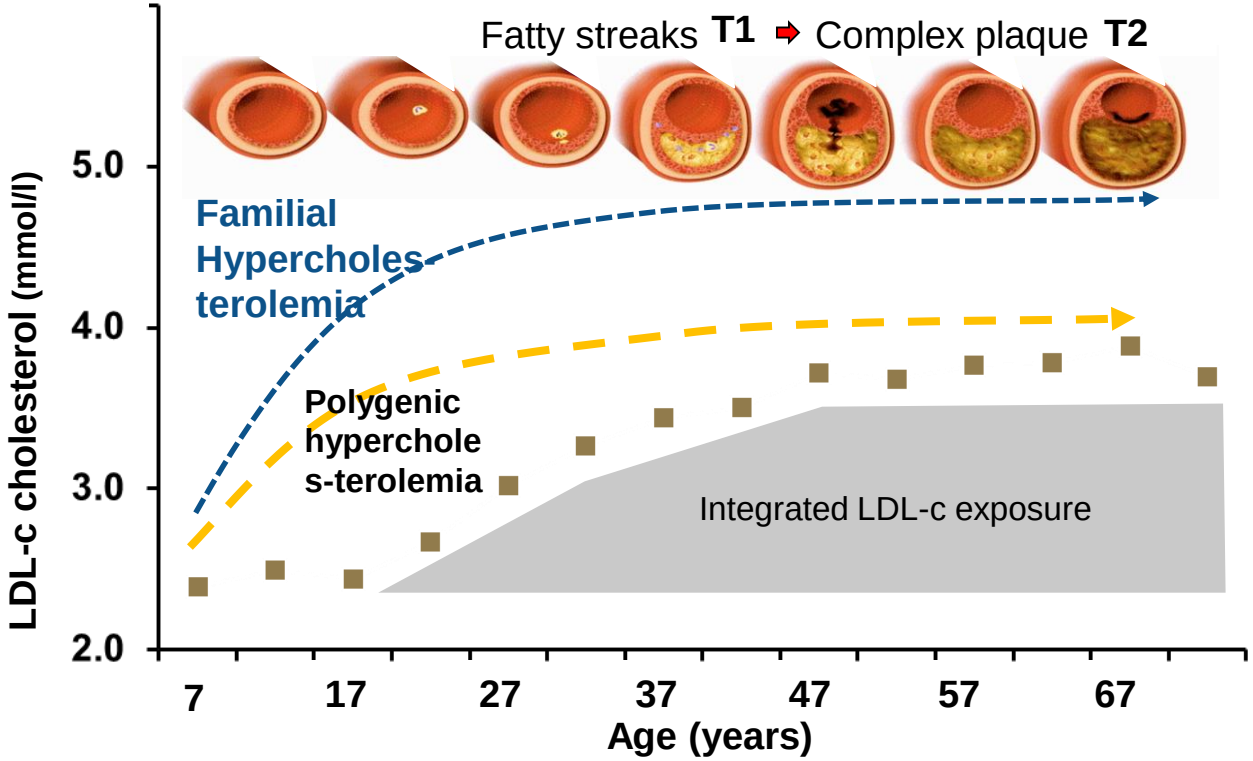
Packard CJ. Trends Cardiovasc Med. 2018 Jul;28(5):348-354

The atherosclerosis disease process changes with time and LDL-c level, and treatment effect depends on the disease phase

Greater RRR per mmol/l reduction
Plaque resolution

Lesser RRR
Plaque stabilisation

Response to initiation of LDL-c lowering



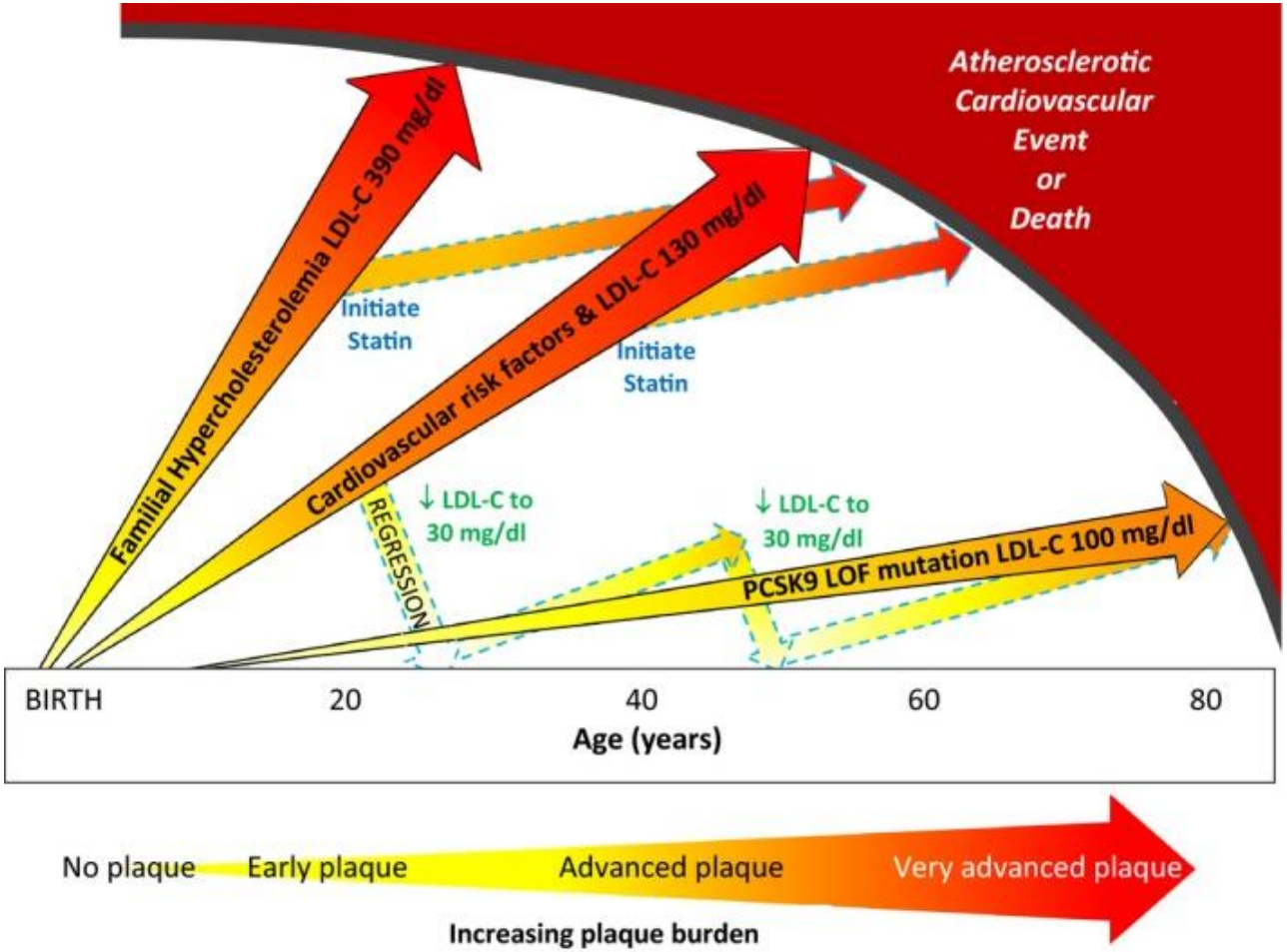
Transitioning pathology

LDLc rise with age

Packard CJ. Trends Cardiovasc Med. 2018 Jul;28(5):348-354

LDL-c lowering treatment impacts disease progression before clinical manifestation

Life course trajectory of atherosclerotic progression for different CV risk categories and the hypothesized effects of intensive LDL-c lowering.



Robinson JG *et al.*, J Am Heart Assoc. 2018 Oct 16;7(20):e009778

HMG-CoA reductase inhibitor evidence: Degree of Benefit in Prevention Types

Meta-analysis of randomized controlled trials comparing risk reductions between primary and secondary prevention patients

	Relative Risk Reduction		Absolute Risk Reduction		Number Needed To Treat	
	Primary	Secondary	Primary	Secondary	Primary	Secondary
Major CHD events	29.2	20.8	1.66	2.4	60	33
Major CV events	14.4	17.8	0.37	0.8	268	125
Nonfatal MI	31.7	NA	1.65	NA	61	NA
PCI or CABG	33.8	20.3	1.08	2.7	93	37

CABG=Coronary artery bypass graft surgery, CHD=Coronary heart disease, CV=Cardiovascular, MI=Myocardial infarction, PCI=Percutaneous coronary intervention

Source: Thavendiranathan P et al. *Arch Intern Med* 2006;166:2307-2313

2018 ACC/AHA Guideline on the Management of Blood Cholesterol

Group 1

Secondary ASCVD Prevention

ACS, MI, angina, coronary arterial revascularization, stroke, TIA or PAD

Group 2

Severe Hypercholesterolemia

LDL-C ≥190 mg/dL(4.9 mmol/L)

Group 3

Diabetes mellitus in Adults

+ age of 40–75 years

Group 4

Primary Prevention

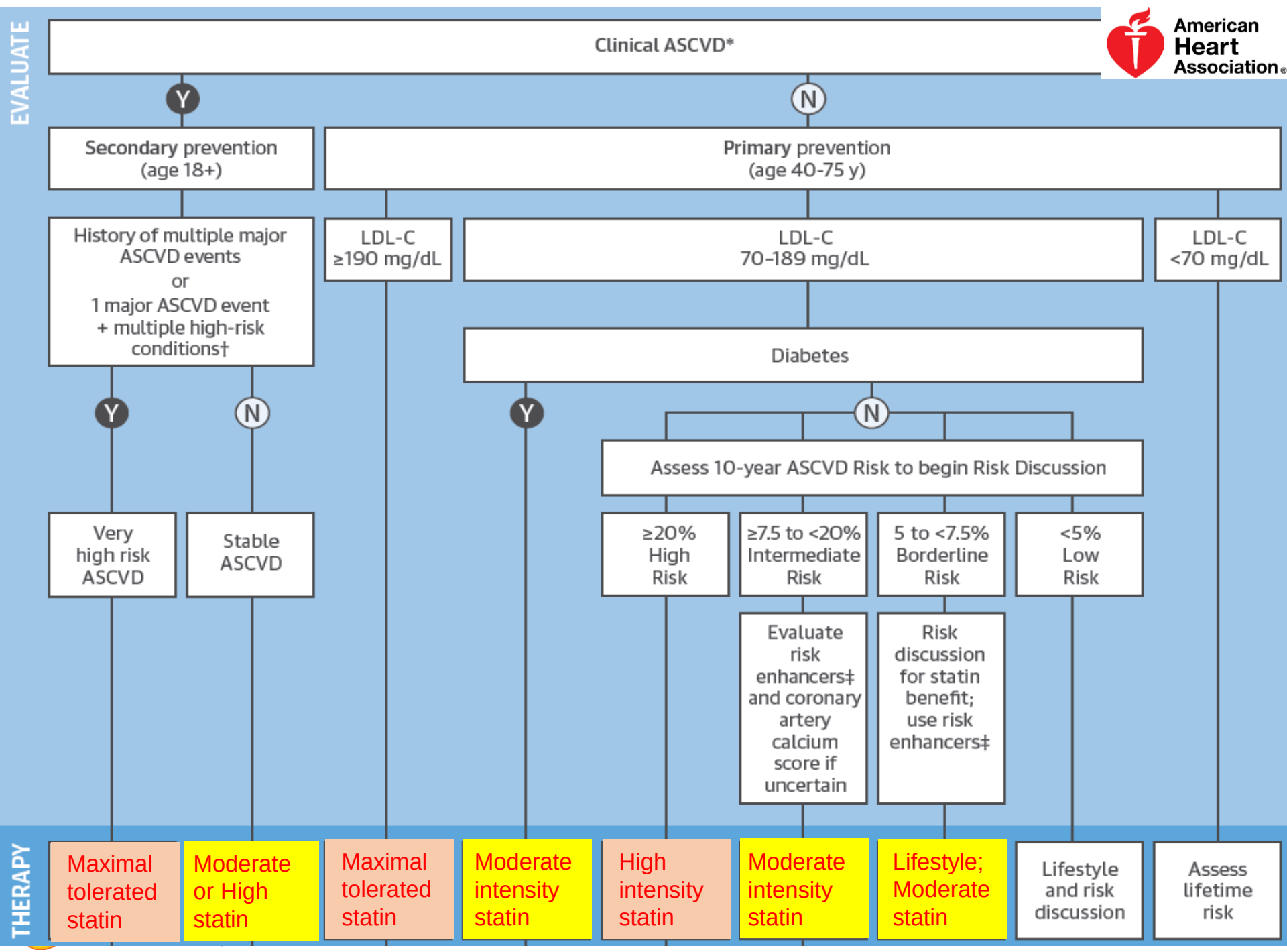
+ age of 40–75 years & LDL-C 70–189 mg/dL
+ 10-year ASCVD risk≥7.5%(intermediate-risk)

Group 5

Other Populations at Risk

Ethnicity, Hypertriglyceridemia, Women, CKD & Chronic Inflammatory Disorders and HIV

Grundy SM, et al. 2018 AHA Cholesterol Clinical Practice Guidelines


EVALUATE
Clinical ASCVD*
Y
N
Secondary prevention (age 18+)
Primary prevention (age 40-75 y)
History of multiple major ASCVD events or 1 major ASCVD event + multiple high-risk conditions†
LDL-C ≥190 mg/dL
LDL-C 70-189 mg/dL
LDL-C <70 mg/dL
Diabetes
Y
N
Assess 10-year ASCVD Risk to begin Risk Discussion
Very high risk ASCVD
Stable ASCVD
≥20% High Risk
≥7.5 to <20% Intermediate Risk
5 to <7.5% Borderline Risk
<5% Low Risk
Evaluate risk enhancers‡ and coronary artery calcium score if uncertain
Risk discussion for statin benefit; use risk enhancers‡
THERAPY
Maximal tolerated statin
Moderate or High statin
Maximal tolerated statin
Moderate intensity statin
High intensity statin
Moderate intensity statin
Lifestyle; Moderate statin
Lifestyle and risk discussion
Assess lifetime risk

Treatment algorithm summary:

Clinical Status[a]	Age Range, y	Statin Intensity[b]	Goal LDL-C Reduction, %	Goal LDL-C Level, mg/dL[c]
Secondary prevention				
Very high-risk ASCVD	>18	High	≥50	<70
All other ASCVD	>18	High	≥50	
Primary prevention				
LDL-C ≥190 mg/dL	20-75	High	≥50	<100
Diabetes, LDL-C ≥70 mg/dL	40-75	Moderate	≥30	
High risk, LDL-C ≥70 mg/dL	40-75	High	≥50	
Intermediate risk, LDL-C ≥70 mg/dL[d]	40-75	Moderate	≥30	
All others (low-borderline risk, LDL-C <70 mg/dL, or outside age range)		Select cases[d]		

2019 ADA : Recommendations for statin and combination treatment in adults with diabetes

Age	ASCVD	Recommended statin intensity^ and combination treatment*
<40 years	No	None†
	Yes	High • If LDL cholesterol ≥70 mg/dL despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)#
≥40 years	No	Moderate‡
	Yes	High • If LDL cholesterol ≥70 mg/dL despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)

1. ≥40 years : Moderate intensity statin

2. ASCVD : High intensity statin

Diabetes American Association

2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)

5 groups

Very-high-risk	People with any of the following: Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke and TIA, and peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound. DM with target organ damage,[a] or at least three major risk factors, or early onset of T1DM of long duration (>20 years). Severe CKD (eGFR <30 mL/min/1.73 m^2). A calculated SCORE ≥10% for 10-year risk of fatal CVD. FH with ASCVD or with another major risk factor.
High-risk	People with: Markedly elevated single risk factors, in particular TC A calculated SCORE ≥5% and <10% for 10-year risk of fatal CVD.
Moderate-risk	Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years, without other risk factors. Calculated SCORE ≥1 % and <5% for 10-year risk of fatal CVD.
Low-risk	Calculated SCORE <1% for 10-year risk of fatal CVD.

Consider Risk first then primary or secondary prevention

High risk or very high risk Primary prevention

Lower target for European

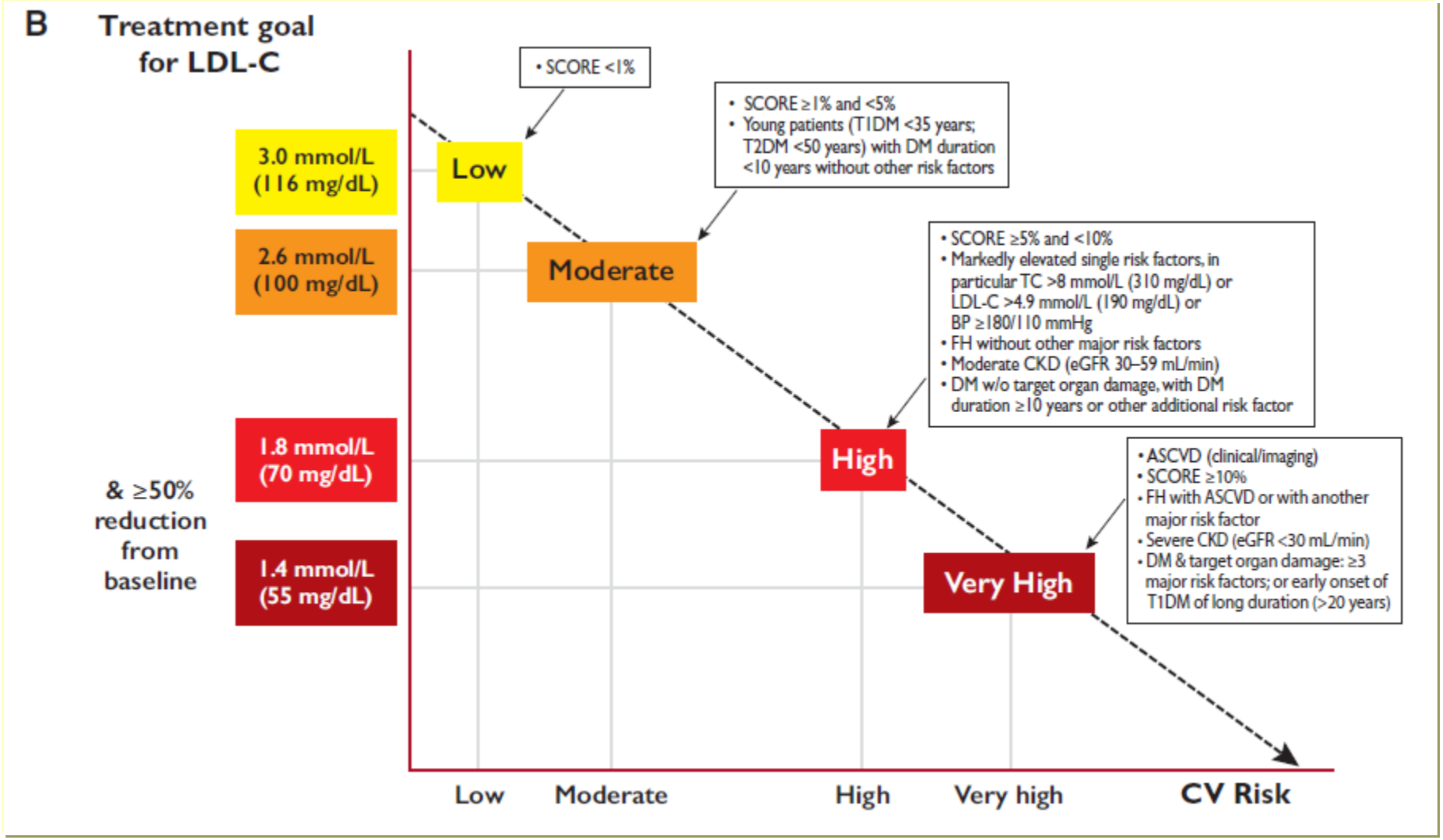
Recommendations for treatment goals for low-density lipoprotein cholesterol

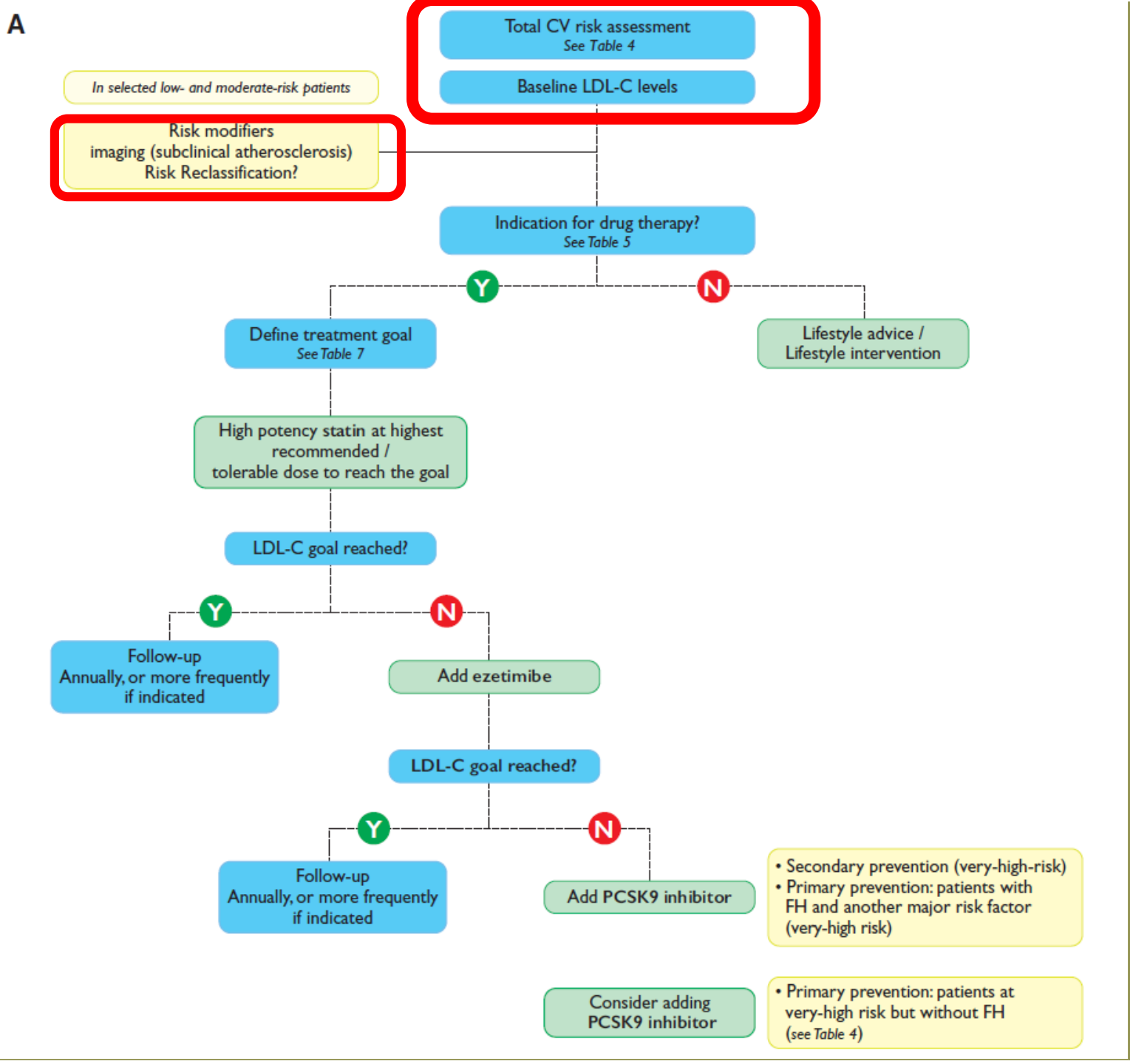
Recommendations	Class[a]	Level[b]
In secondary prevention for patients at very-high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[33–35,119,120]	I	A
In primary prevention for individuals at very-high risk but without FH,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[34–36]	I	C
In primary prevention for individuals with FH at very-high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) should be considered.	IIa	C
For patients with ASCVD who experience a second vascular event within 2 years (not necessarily of the same type as the first event) while taking maximally tolerated statin-based therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered.[119,120]	IIb	B
In patients at high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) are recommended.[34,35]	I	A
In individuals at moderate risk,[c] an LDL-C goal of <2.6 mmol/L (<100 mg/dL) should be considered.[34]	IIa	A
In individuals at low risk,[c] an LDL-C goal <3.0 mmol/L (<116 mg/dL) may be considered.[36]	IIb	A

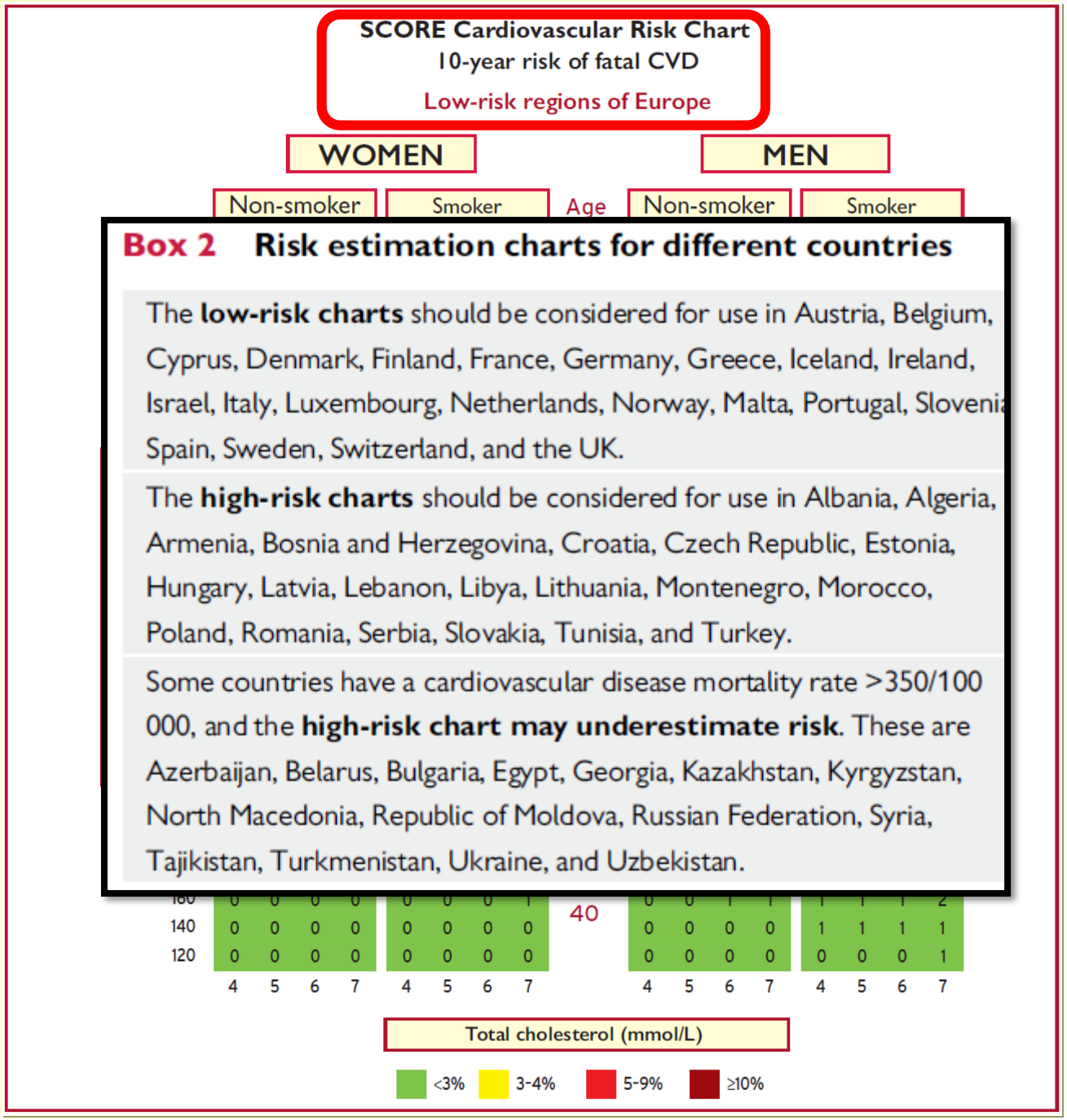
Table 7 **Treatment targets and goals for cardiovascular disease prevention**

Smoking	No exposure to tobacco in any form.
Diet	Healthy diet low in saturated fat with a focus on wholegrain products, vegetables, fruit, and fish.
Physical activity	3.5–7 h moderately vigorous physical activity per week or 30–60 min most days.
Body weight	BMI 20–25 kg/m^2, and waist circumference <94 cm (men) and <80 cm (women).
Blood pressure	<140/90 mmHg.[a]
LDL-C	**Very-high risk in primary or secondary prevention:** A therapeutic regimen that achieves ≥50% LDL-C reduction from baseline[b] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL). No current statin use: this is likely to require high-intensity LDL-lowering therapy. Current LDL-lowering treatment: an increased treatment intensity is required. **High risk:** A therapeutic regimen that achieves ≥50% LDL-C reduction from baseline[b] and an LDL-C goal of <1.8 mmol/L (<70 mg/dL). **Moderate risk:** A goal of <2.6 mmol/L (<100 mg/dL). **Low risk:** A goal of <3.0 mmol/L (<116 mg/dL).
Non-HDL-C	Non-HDL-C secondary goals are <2.2, 2.6, and 3.4 mmol/L (<85, 100, and 130 mg/dL) for very-high-, high-, and moderate-risk people, respectively.
ApoB	ApoB secondary goals are <65, 80, and 100 mg/dL for very-high-, high-, and moderate-risk people, respectively.
Triglycerides	No goal, but <1.7 mmol/L (<150 mg/dL) indicates lower risk and higher levels indicate a need to look for other risk factors.
Diabetes	HbA1c: <7% (<53 mmol/mol).

Updated ESC lipid treatment goals




A
Total CV risk assessment
See Table 4
Baseline LDL-C levels
In selected low- and moderate-risk patients
Risk modifiers
imaging (subclinical atherosclerosis)
Risk Reclassification?
Indication for drug therapy?
See Table 5
Y
N
Define treatment goal
See Table 7
Lifestyle advice /
Lifestyle intervention
High potency statin at highest
recommended /
tolerable dose to reach the goal
LDL-C goal reached?
Y
N
Follow-up
Annually, or more frequently
if indicated
Add ezetimibe
LDL-C goal reached?
Y
N
Follow-up
Annually, or more frequently
if indicated
Add PCSK9 inhibitor
• Secondary prevention (very-high-risk)
• Primary prevention: patients with
FH and another major risk factor
(very-high risk)
Consider adding
PCSK9 inhibitor
• Primary prevention: patients at
very-high risk but without FH
(see Table 4)


SCORE Cardiovascular Risk Chart
10-year risk of fatal CVD
Low-risk regions of Europe
WOMEN
MEN
Non-smoker
Smoker
Age
Non-smoker
Smoker
Box 2 Risk estimation charts for different countries
The low-risk charts should be considered for use in Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Netherlands, Norway, Malta, Portugal, Sloveni
Spain, Sweden, Switzerland, and the UK.
The high-risk charts should be considered for use in Albania, Algeria, Armenia, Bosnia and Herzegovina, Croatia, Czech Republic, Estonia, Hungary, Latvia, Lebanon, Libya, Lithuania, Montenegro, Morocco, Poland, Romania, Serbia, Slovakia, Tunisia, and Turkey.
Some countries have a cardiovascular disease mortality rate >350/100 000, and the high-risk chart may underestimate risk. These are Azerbaijan, Belarus, Bulgaria, Egypt, Georgia, Kazakhstan, Kyrgyzstan, North Macedonia, Republic of Moldova, Russian Federation, Syria, Tajikistan, Turkmenistan, Ukraine, and Uzbekistan.
140
120
40
4 5 6 7 4 5 6 7 4 5 6 7 4 5 6 7
Total cholesterol (mmol/L)
<3%
3-4%
5-9%
≥10%

Risk Estimate Matters in Primary Prevention

Recommendations for cardiovascular disease risk estimation

Recommendations	Class[a]	Level[b]
Total risk estimation using a risk estimation system such as SCORE is recommended for asymptomatic adults >40 years of age without evidence of CVD, DM, CKD, familial hypercholesterolaemia, or LDL-C >4.9 mmol/L (>190 mg/dL).	I	C
It is recommended that high- and very-high-risk individuals are identified on the basis of documented CVD, DM, moderate-to-severe renal disease, very high levels of individual risk factors, FH, or a high SCORE risk. It is recommended that such patients are considered as a priority for advice and management of all risk factors.	I	C
Risk scores developed for the general population are not recommended for CV risk assessment in patients with DM or FH.	III	C

CV Risk Prediction Models Are Important for Preventing CVD Events

Risk prediction model for clinical assessment

↓

Identification of high-risk populations

Effective communication of risk

↓

Appropriate treatment options

Several CV risk prediction models have been validated for use in clinical practice:

- Framingham risk score[1]
- QRISK2 model[2]
- ASCVD risk score calculator[3]
- WHO/ISH models[4]
- SCORE model[5]

CV risk prediction models utilize data of multiple risk factors, and are ideal and **cost-effective** options for clinical decision-making in **primary prevention** of CVDs[6]

ASCVD, atherosclerotic cardiovascular disease; SCORE, Systematic Coronary Risk Evaluation; WHO/ISH, World Health Organization/International Society of Hypertension

1. Wilson PW, D'Agostino RB, Levy D *et al. Circulation.* 1998;97:1837–1847;
2. Collins GS, Altman DG. *BMJ.* 2012;344:e4181;
3. Goff DC Jr, Lloyd-Jones DM, Bennett G *et al. J Am Coll Cardiol.* 2014;63:2935–2959;
4. World Health Organization/International Society for Hypertension. Available at http://ish-world.com/downloads/activities/colour_charts_24_Aug_07.pdf Accessed July 2018;
5. Conroy RM, Pyörälä K, Fitzgerald AP *et al. Eur Heart J* 2003; 24:987–1003;
6. Sun C, Xu F, Liu X *et al. Sci Rep.* 2017;7:43227.

One Size *Does Not* Fit All!

The Framingham risk equations have been shown to **overestimate** global cardiovascular risk in other (non-US) populations[1]

Equations derived from Western population samples have **limited applicability** to other populations[2]

Successful and meaningful prediction of CV risk is dependent on:

1. **Selection** of the best-fitting model for the study population → Applicability of predicted risk score to a local patient setting

2. **Risk factors** and **demographic characteristics** of the population → Calibration to local settings

1. Asia Pacific Cohort Studies Collaboration. *J Epidemiol Community Health*. 2007;61:115–121;
2. Yang X, Li J, Hu D, *et al. Circulation*. 2016;134:1430–1440.

Treatment Guidelines Underline the Need for CV Risk Prediction Tools for Asian Populations

- Models for predicting CVDs in Asian populations are currently limited[1]
- According to the ACC/AHA guidelines on CV risk assessment:[2]
  - The **lack of ethnic-specific risk algorithms** is an important **obstacle** to understanding and preventing ASCVD in Asian populations
  - The **development** of algorithms **specific to these race/ethnic groups** should be **encouraged**, and
  - When providers use equations developed for non-Hispanic White populations for other populations, their risks may be overestimated

Therefore, it is important to develop an Asian-specific risk prediction model for primary prevention of CVDs

1. Park GM, Kim YH. *Pulse* 2015;3:153–157; 2. Lackland DT, Levy D, O'Donnell CJ, *et al. J Am Coll Cardiol.* 2014;63:2935–2959.

Guideline-Recommended CV Risk Prediction Models Are Currently Available in a Few Asian Countries

Chinese Guidelines for Prevention of Cardiovascular Disease recommend sex ediction models for ICVD (including vents)[1]

- Recently nd validated the first equation n a Chinese population[2]

According to th ion of India, "*the risk calculator propo 3rd Iteration (JBS3) appears to prov tes in Indians*"[3]

The Japanese A s recommend a 10-year probability (absolute risk) calculator of CAD death, derived from the NIPPON DATA80 risk charts[4]

ASCVD, atherosclerotic cardiovascular disease; CAD, coronary artery disease; ICVD, ischemic cardiovascular disease

1. Chinese Society of Cardiology of Chinese Medical Association, Editorial Board of Chinese Journal of Cardiology. *Zhonghua Xin Xue Guan Bing Za Zhi*. 2011;39:3–22; 2. Yang X, Li J, Hu D, *et al. Circulation*. 2016;134:1430–1440; 3. Iyengar SS, Puri R, Narasingan SN, *et al. J Assoc Physicians India*. 2016;64:7–52; 4. Teramoto T, Sasaki J, Ishibashi S , *et al. J Atheroscler Thromb*. 2013;20:603–615.

Cardiovascular risk prediction tools for populations in Asia

Asia Pacific Cohort Studies Collaboration

J Epidemiol Community Health 2007;**61**:115–121. doi: 10.1136/jech.2005.044842

See end of article for authors' affiliations

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Accepted 2 April 2006

Background: Cardiovascular risk equations are traditionally derived from the Framingham Study. The accuracy of this approach in Asian populations, where resources for risk factor measurement may be limited, is unclear.

Objective: To compare "low-information" equations (derived using only age, systolic blood pressure, total cholesterol and smoking status) derived from the Framingham Study with those derived from the Asian cohorts, on the accuracy of cardiovascular risk prediction.

Design: Separate equations to predict the 8-year risk of a cardiovascular event were derived from Asian and Framingham cohorts. The performance of these equations, and a subsequently "recalibrated" Framingham equation, were evaluated among participants from independent Chinese cohorts.

Setting: Six cohort studies from Japan, Korea and Singapore (Asian cohorts); six cohort studies from China; the Framingham Study from the US.

Participants: 172 077 participants from the Asian cohorts; 25 682 participants from Chinese cohorts and 6053 participants from the Framingham Study.

Main results: In the Chinese cohorts, 542 cardiovascular events occurred during 8 years of follow-up. Both the Asian cohorts and the Framingham equations discriminated cardiovascular risk well in the Chinese cohorts; the area under the receiver–operator characteristic curve was at least 0.75 for men and women. However, the Framingham risk equation systematically overestimated risk in the Chinese cohorts by an average of 276% among men and 102% among women. The corresponding average overestimation using the Asian cohorts equation was 11% and 10%, respectively. Recalibrating the Framingham risk equation using cardiovascular disease incidence from the non-Chinese Asian cohorts led to an overestimation of risk by an average of 4% in women and underestimation of risk by an average of 2% in men.

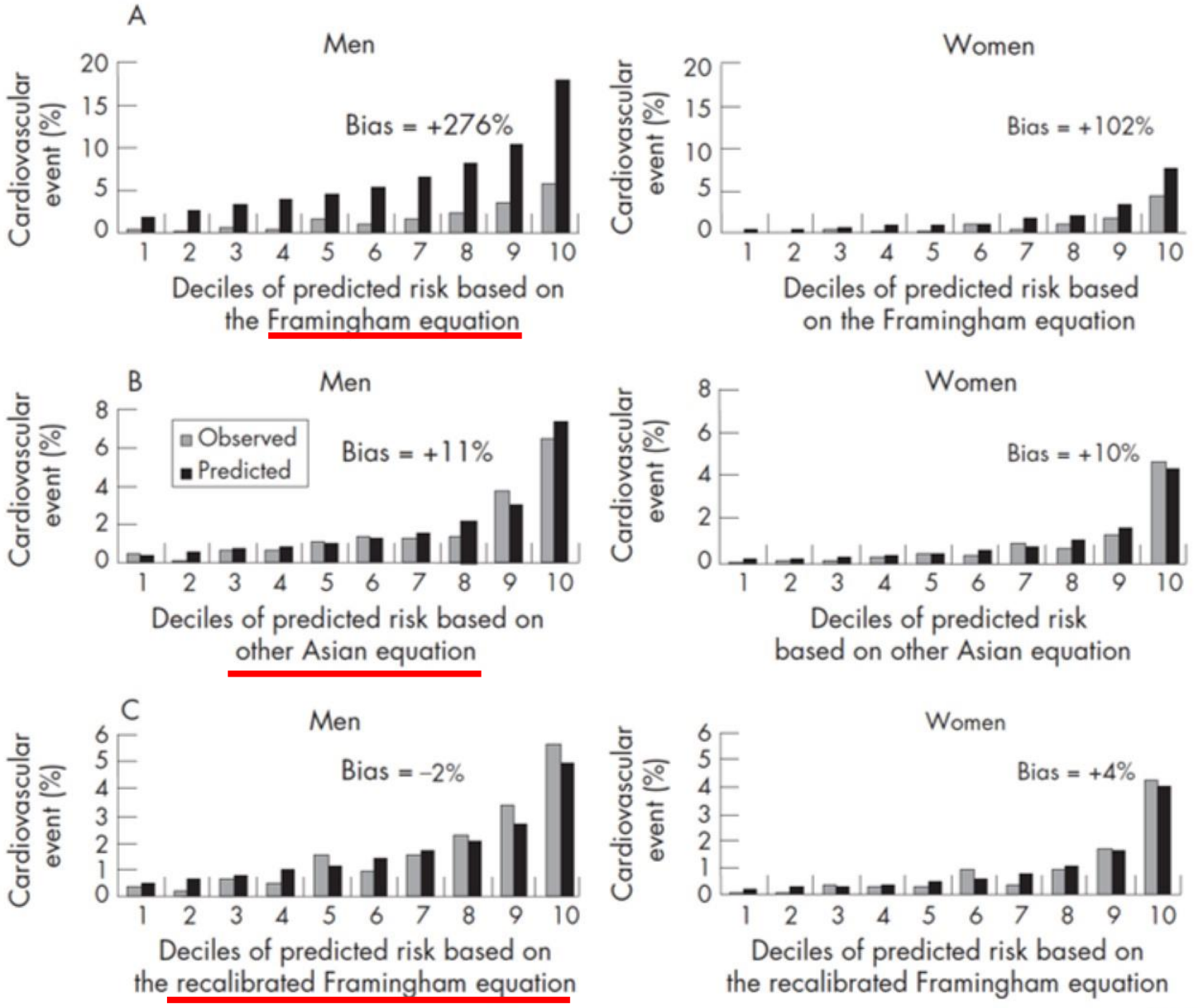
Interpretation: A low-information Framingham cardiovascular risk prediction tool, which, when recalibrated with contemporary data, is likely to estimate future cardiovascular risk with similar accuracy in Asian populations as tools developed from data on local cohorts.

Methods

- Six cohort studies from Japan, Korea and Singapore (Asian cohorts); six cohort studies from China and Framingham Study (USA)
- 'Low information' (age, sex, SBP, total cholesterol and smoking status)
- Participants:
  - 172,077 participants from the Asian cohorts
  - 25,682 participants from Chinese cohorts
  - 6053 participants from the Framingham Study
- 8-year risk of any cardiovascular event, defined as CV death, non-fatal MI or non-fatal CVA

CV, cardiovascular; CVA, cerebrovascular accident; MI, myocardial infarction; SBP, systolic blood pressure

Asia Pacific Cohort Studies Collaboration. *J Epidemiol Community Health*. 2007;61:115-21.



Asia Pacific Cohort Studies Collaboration. *J Epidemiol Community Health*. 2007;61:115-21.

Predictive Value for the Chinese Population of the Framingham CHD Risk Assessment Tool Compared With the Chinese Multi-provincial Cohort Study

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Wei Wang, MD
Jiayi Sun, BS
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William B. Kannel, MD
Dong Zhao, MD, PhD

Context The Framingham Heart Study helped to establish tools to assess coronary heart disease (CHD) risk, but the homogeneous nature of the Framingham population prevents simple extrapolation to other populations. Recalibration of Framingham functions could permit various regions of the world to adapt Framingham tools to local populations.

Objective To evaluate the performance of the Framingham CHD risk functions, directly and after recalibration, in a large Chinese population, compared with the performance of the functions derived from the Chinese Multi-provincial Cohort Study (CMCS).

Design, Setting, and Participants The CMCS cohort included 30 121 Chinese adults aged 35 to 64 years at baseline. Participants were recruited from 11 provinces and were followed up for new CHD events from 1992 to 2002. Participants in the Framingham Heart Study were 5251 white US residents of Framingham, Mass, who were 30 to 74 years old at baseline in 1971 to 1974 and followed up for 12 years.

Main Outcome Measures "Hard" CHD (coronary death and myocardial infarction) was used as the end point in comparisons of risk factors (age, blood pressure, smoking, diabetes, total cholesterol, and high-density lipoprotein cholesterol [HDL-C]) as evaluated by the CMCS functions, original Framingham functions, and recalibrated Framingham functions.

Results The CMCS cohort had 191 hard CHD events and 625 total deaths vs 273 CHD events and 293 deaths, respectively, for Framingham. For most risk factor categories, the relative risks for CHD were similar for Chinese and Framingham participants, with a few exceptions (ie, age, total cholesterol of 200-239 mg/dL [5.18-6.19 mmol/L], and HDL-C less than 35 mg/dL [0.91 mmol/L] in men; smoking in women). The discrimination using the Framingham functions in the CMCS cohort was similar to the CMCS functions: the area under the receiver operating characteristic curve was 0.705 for men and 0.742 for women using the Framingham functions vs 0.736 for men and 0.759 for women using the CMCS functions. However, the original Framingham functions systematically overestimated the absolute CHD risk in the CMCS cohort. For example, in the 10th risk decile in men, the predicted rate of CHD death was 20% vs an actual rate of 3%. Recalibration of the Framingham functions using the mean values of risk factors and mean CHD incidence rates of the CMCS cohort substantially improved the performance of the Framingham functions in the CMCS cohort.

Conclusions The original Framingham functions overestimated the risk of CHD for CMCS participants. Recalibration of the Framingham functions improved the estimates and demonstrated that the Framingham model is useful in the Chinese population. For regions that have no established cohort, recalibration using CHD rates and risk factors may be an effective method to develop CHD risk prediction algorithms suited for local practice.

JAMA. 2004;291:2591-2599

THE FRAMINGHAM HEART STUDY has contributed to the identification of risk factors for coronary heart disease (CHD)[1-3] and has developed multivariable functions to predict absolute CHD risk.[4-7] Risk reduction programs now focus on absolute risk of disease rather than on modification of individual risk factors.[8-11] The Framingham prediction algorithms have been widely adopted to assess absolute risk and guide the intensity of risk factor interventions.[12-14] However, since more than 99% of Framingham participants are of European descent, the Framingham functions cannot be generalized to other populations without evaluation of their appropriateness. Directly applying Framingham functions in some populations overestimates CHD risk.[7,15,16]

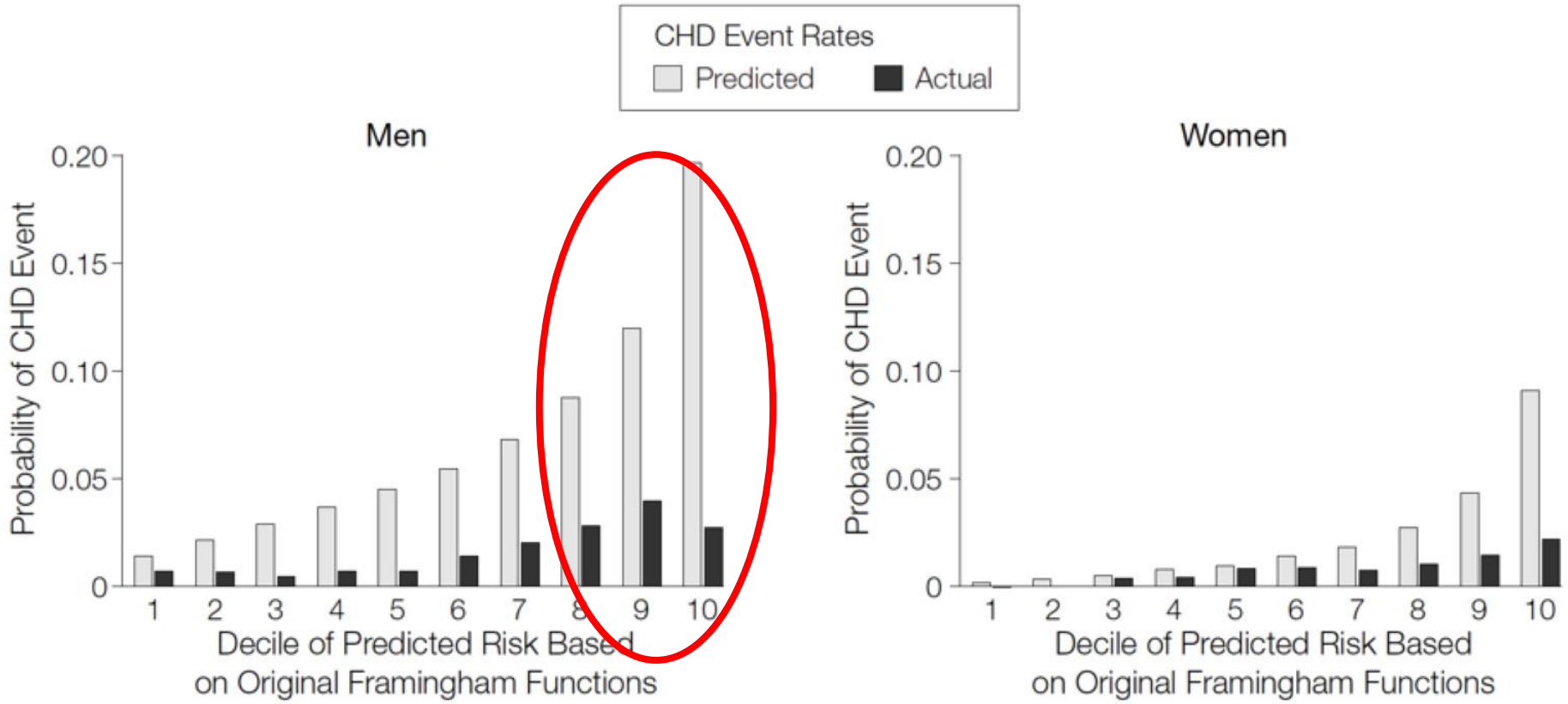
Recalibrating Framingham functions can substantially improve predictive ability and, thus, can be a useful

Chinese Multi-Provincial Cohort Study

- Adaptation of risk scores to Chinese population
- 30,121 Chinese adults from 16 centers in 11 provinces
- Age 35 to 64 years at baseline
- Followed for up to 10 years(follow-up rate of 86%)

Liu J. *et al. JAMA.* 2004;291:2591-9.

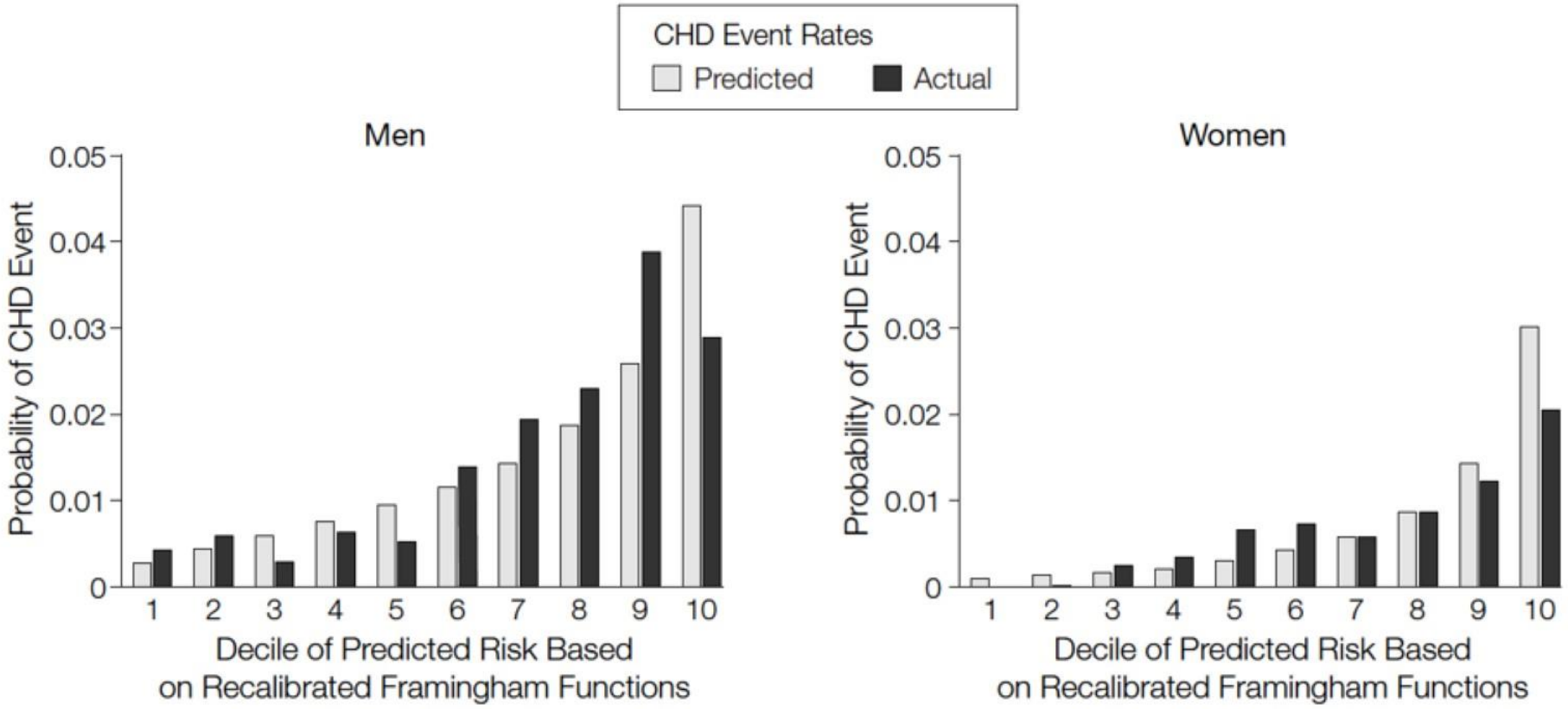
Figure 2. Ten-Year Prediction of CHD Events in CMCS Men and Women Using the Original Framingham Functions



CMCS indicates Chinese Multi-provincial Cohort Study. Coronary heart disease (CHD) events included coronary death and myocardial infarction.

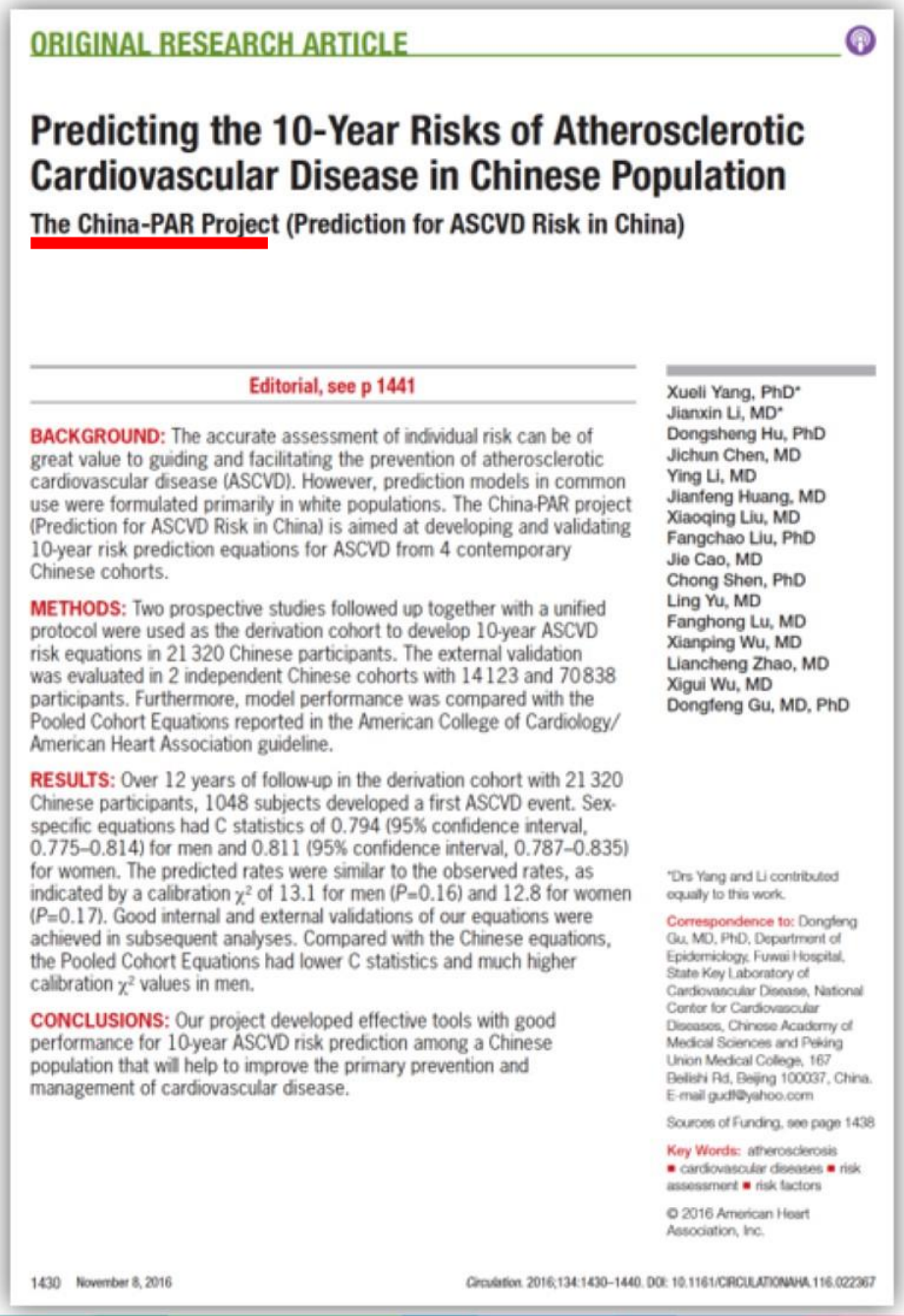
Liu J. *et al. JAMA.* 2004;291:2591-9.

Figure 3. Ten-Year Prediction of CHD Events in CMCS Men and Women Using the Recalibrated Framingham Functions



CMCS indicates Chinese Multi-provincial Cohort Study. Coronary heart disease (CHD) events included coronary death and myocardial infarction.

Liu J. *et al. JAMA.* 2004;291:2591-9.



ORIGINAL RESEARCH ARTICLE

Predicting the 10-Year Risks of Atherosclerotic Cardiovascular Disease in Chinese Population

The China-PAR Project (Prediction for ASCVD Risk in China)

Editorial, see p 1441

BACKGROUND: The accurate assessment of individual risk can be of great value to guiding and facilitating the prevention of atherosclerotic cardiovascular disease (ASCVD). However, prediction models in common use were formulated primarily in white populations. The China-PAR project (Prediction for ASCVD Risk in China) is aimed at developing and validating 10-year risk prediction equations for ASCVD from 4 contemporary Chinese cohorts.

METHODS: Two prospective studies followed up together with a unified protocol were used as the derivation cohort to develop 10-year ASCVD risk equations in 21 320 Chinese participants. The external validation was evaluated in 2 independent Chinese cohorts with 14 123 and 70 838 participants. Furthermore, model performance was compared with the Pooled Cohort Equations reported in the American College of Cardiology/American Heart Association guideline.

RESULTS: Over 12 years of follow-up in the derivation cohort with 21 320 Chinese participants, 1048 subjects developed a first ASCVD event. Sex-specific equations had C statistics of 0.794 (95% confidence interval, 0.775–0.814) for men and 0.811 (95% confidence interval, 0.787–0.835) for women. The predicted rates were similar to the observed rates, as indicated by a calibration χ^2 of 13.1 for men (P=0.16) and 12.8 for women (P=0.17). Good internal and external validations of our equations were achieved in subsequent analyses. Compared with the Chinese equations, the Pooled Cohort Equations had lower C statistics and much higher calibration χ^2 values in men.

CONCLUSIONS: Our project developed effective tools with good performance for 10-year ASCVD risk prediction among a Chinese population that will help to improve the primary prevention and management of cardiovascular disease.

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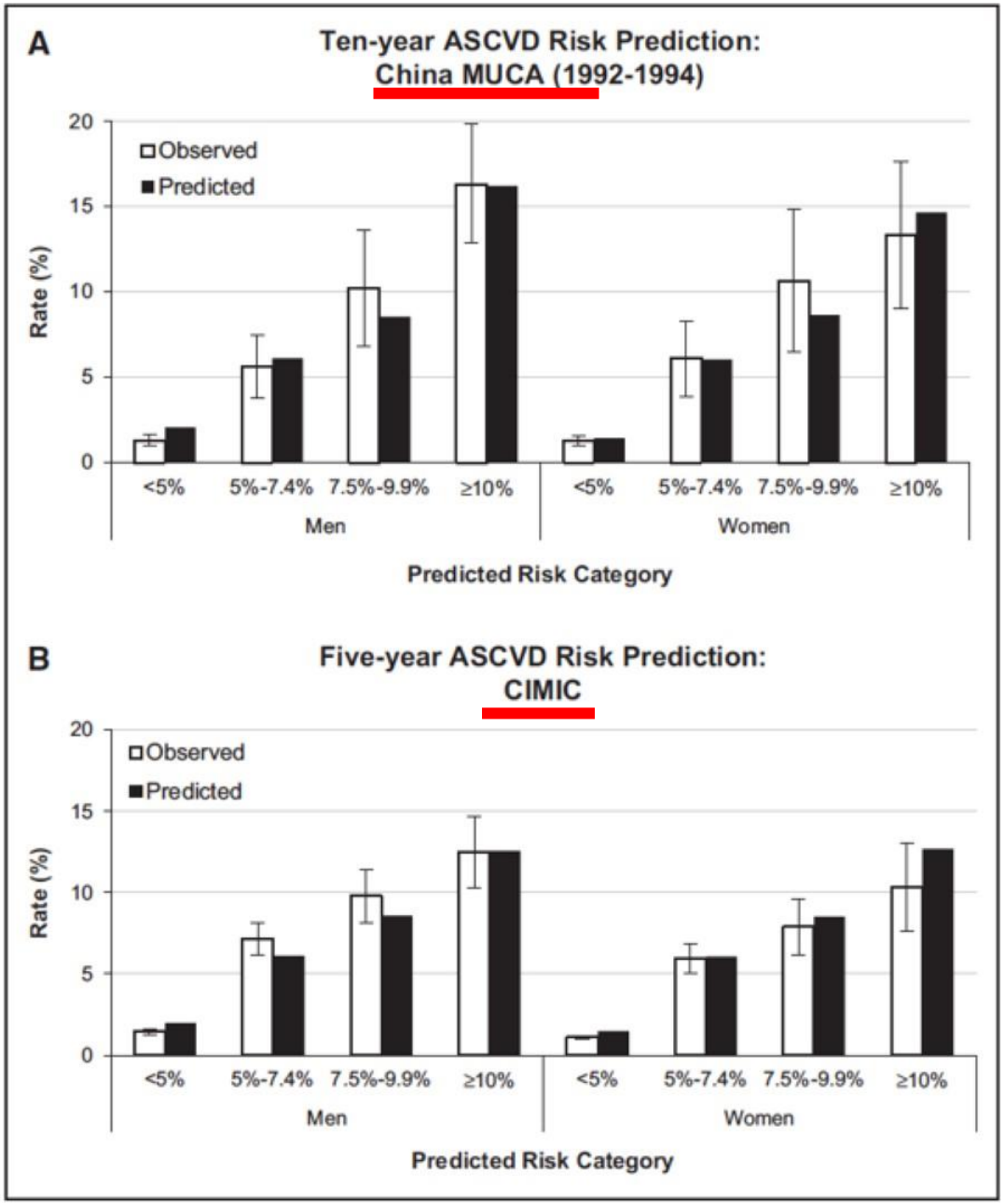
Sources of Funding, see page 1438

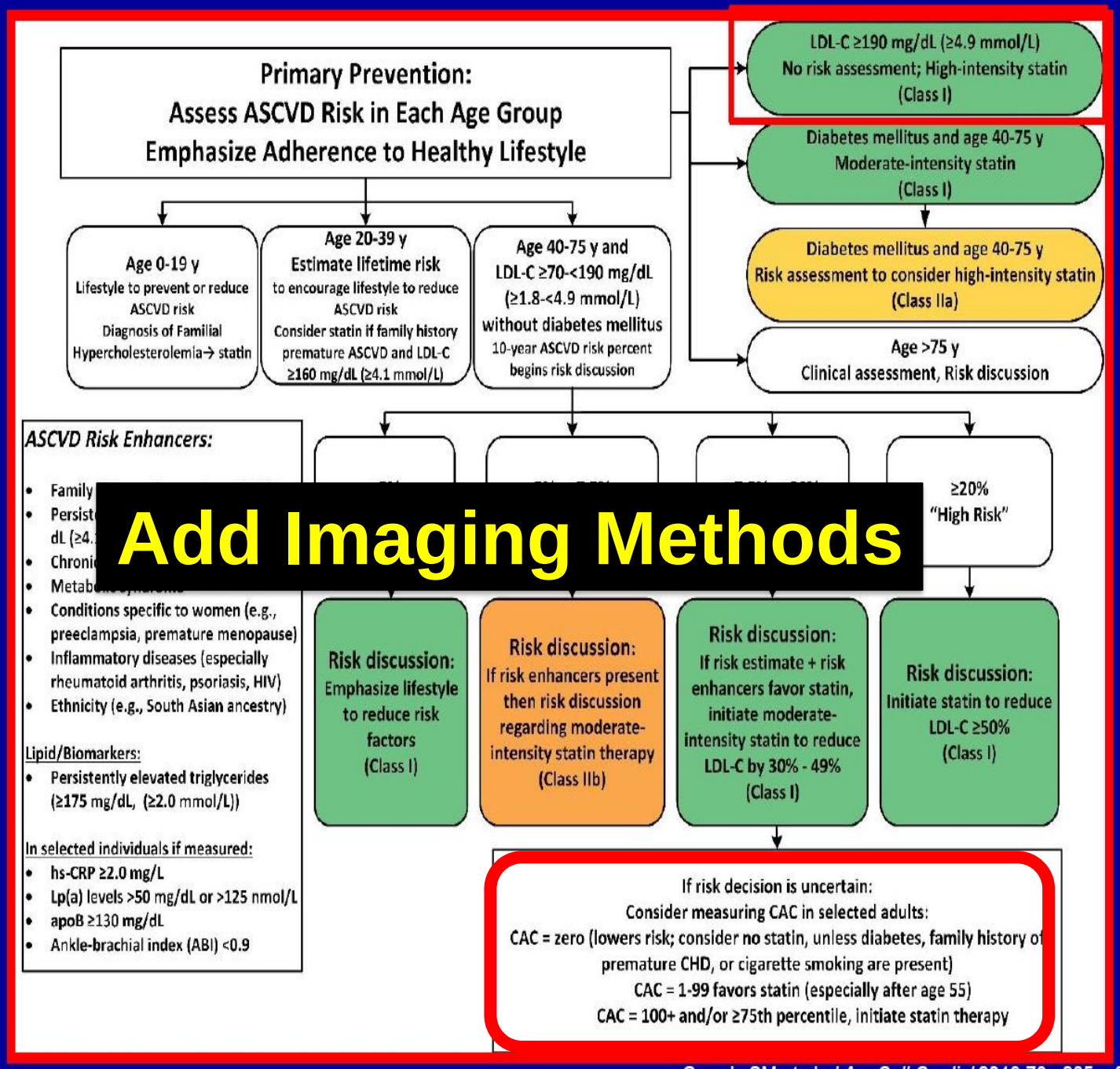
Key Words: atherosclerosis ■ cardiovascular diseases ■ risk assessment ■ risk factors

Circulation. 2016;134:1430–1440. DOI: 10.1161/CIRCULATIONAHA.116.022367

- Two prospective studies used as derivation cohort to develop 10-year ASCVD risk equations in 21 320 Chinese participants
- External validation evaluated in 2 independent Chinese cohorts with 14,123 and 70,838 participants



Yang X. *et al. Circulation.* 2016;134:1430-1440.



Grundy SM et al. *J Am Coll Cardiol* 2019;73:e285–e350.

CENTRAL ILLUSTRATION: Proposed Decision-Making Approach to Selective Use of Coronary Artery Calcium Measurement for Risk Prediction

Using 10-year ASCVD risk estimate plus coronary artery calcium (CAC) score to guide statin therapy

Patient's 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimate:	<5%	5-7.5%	>7.5-20%	>20%
Consulting ASCVD risk estimate alone	Statin not recommended	Consider for statin	Recommend statin	Recommend statin
Consulting ASCVD risk estimate + CAC				
If CAC score =0	Statin not recommended	Statin not recommended	Statin not recommended	Recommend statin
If CAC score >0	Statin not recommended	Consider for statin	Recommend statin	Recommend statin
Does CAC score modify treatment plan?	✗ CAC not effective for this population	✓ CAC can reclassify risk up or down	✓ CAC can reclassify risk up or down	✗ CAC not effective for this population

Greenland, P. et al. J Am Coll Cardiol. 2018;72(4):434-47.

Imaging Helps for Risk Stratification

2019 ESC guideline

Recommendations for cardiovascular imaging for risk assessment of atherosclerotic cardiovascular disease

Recommendations	Class[a]	Level[b]
Arterial (carotid and/or femoral) plaque burden on arterial ultrasonography should be considered as a risk modifier in individuals at low or moderate risk.[29,30]	IIa	B
CAC score assessment with CT should be considered as a risk modifier in the CV risk assessment of asymptomatic individuals at low or moderate risk.[14–16,24,26]	IIa	B

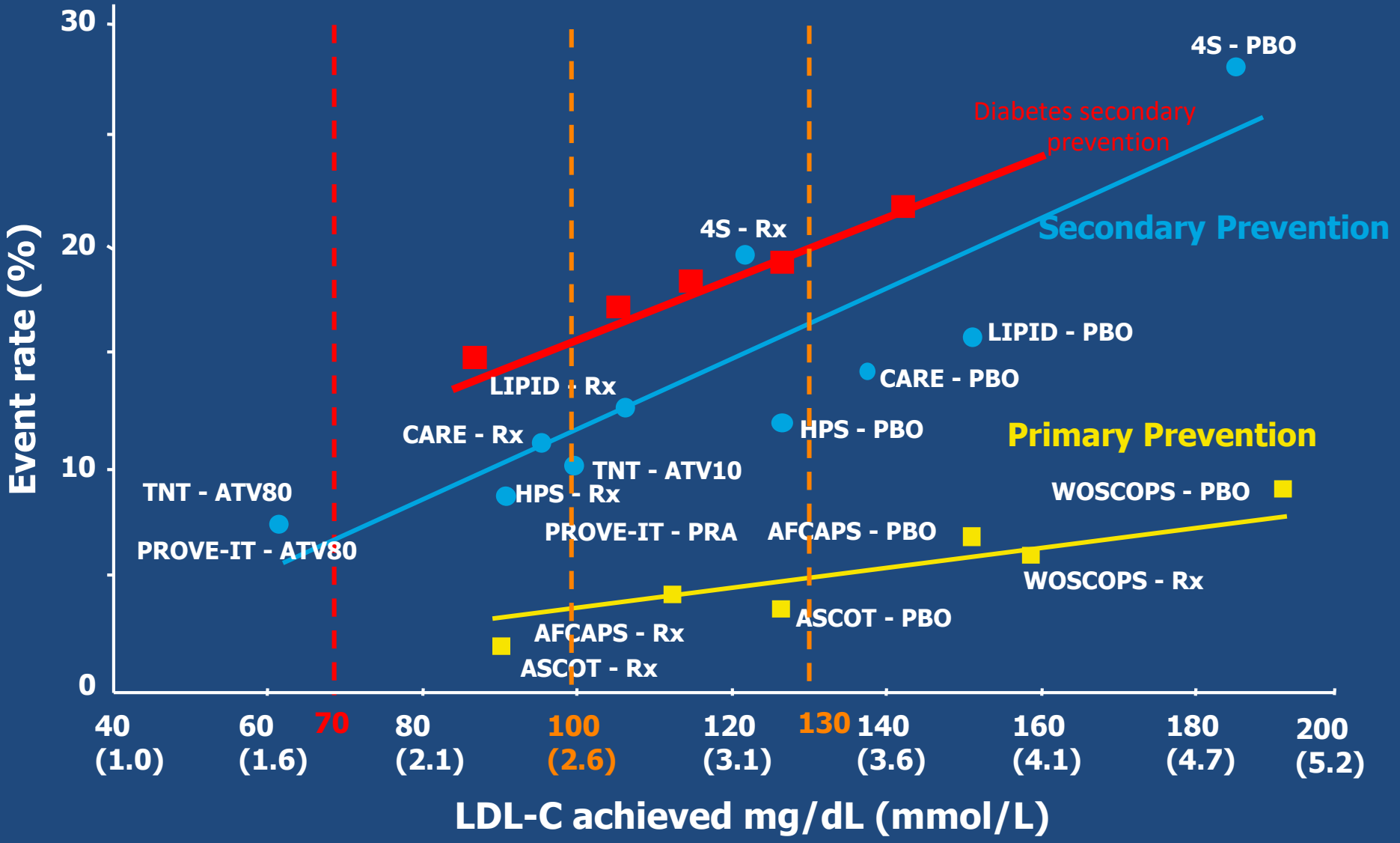
Risk Assessment 2018

1. Clinical characteristics and blood test (biomarkers): Yes but not all biomarkers routinely
2. Imaging in selected individuals with CT for coronary calcium or ultrasound for CIMT plus plaque: Yes in some individuals
3. Polygenic risk scores and genetic panels: Exciting but not ready for prime time in routine practice

Differences between 2018 AHA/ACC and 2019 ESC/EAS Guidelines: Risk assessment

1. Definition of risk groups – ESC guidelines do not confine very high risk to secondary prevention,
2. Recommendation that Lp(a) be checked once in everyone in ESC versus as a risk enhancer in AHA/ACC
3. Stronger support for apo B measurement in risk assesment
4. Although both recommend Coronary Artery Calcium Scores as risk enhancers, ultrasound is only recommended by ESC/EAS

Abundant Statin treatment evidence in primary prevention



Adapted from Rosensen, Exp Opin Emerg Drugs 2004;9:269;
LaRosa J et al, N Engl J Med, 2005;352:1425

Statin therapy is remarkably safe

Typically, treating 10.000 patients for 5 years with a standard statin regimen, is expected

to prevent:
1000 major vascular events (secondary prevention)
500 major vascular events (primary prevention)

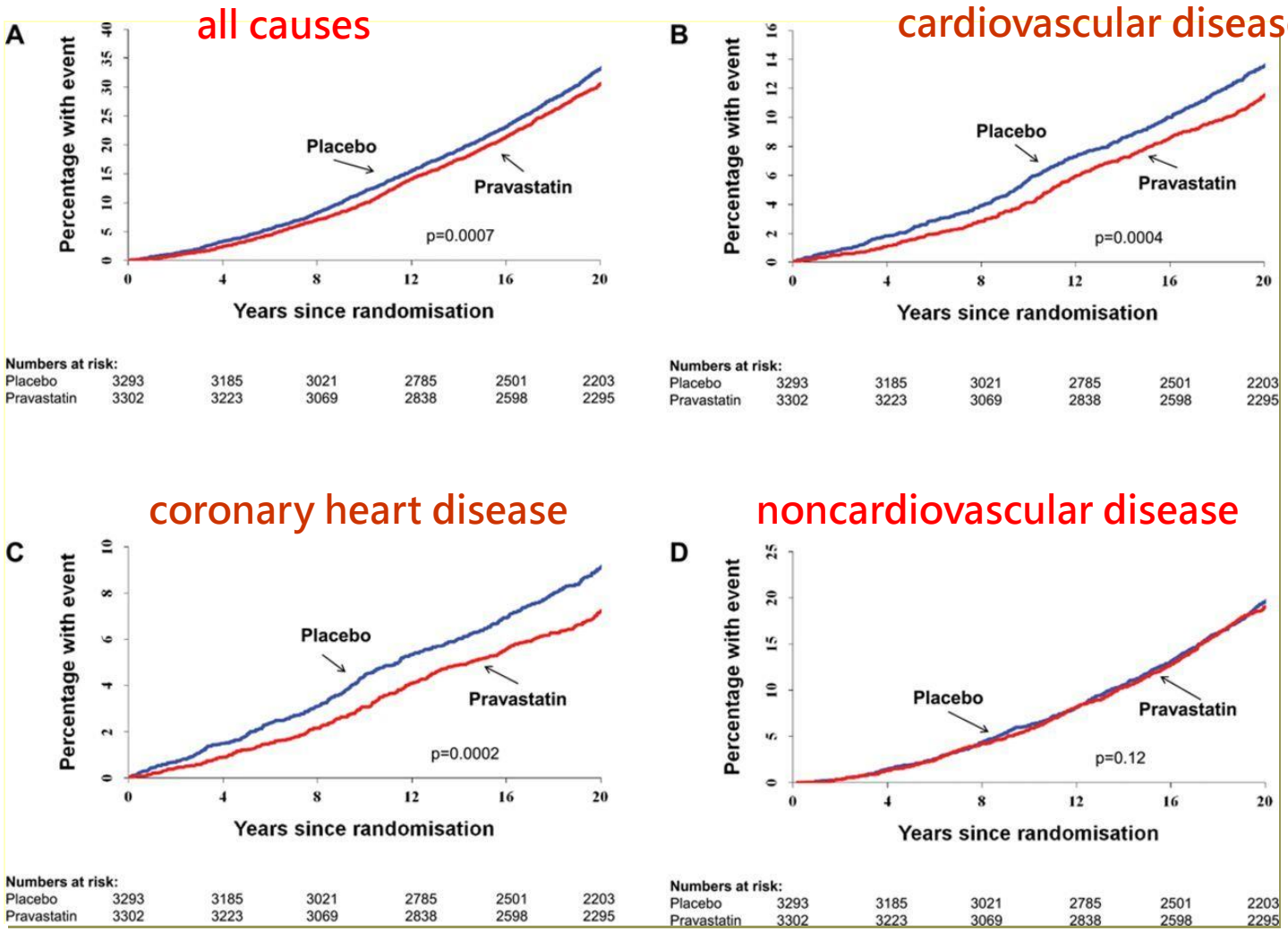
to cause:
5 cases of myopathy
50-100 new cases of diabetes
5-10 hemorrhagic strokes (in those with prior stroke)
50-100 patients may experience symptomatic adverse events such as muscle pain or weakness. Placebo-controlled randomized trials show that almost all of these cases are misattributed.

NO evidence to support adverse effects of statins on:
Cognitive function, clinically significant renal deterioration, risk of cataract and risk of haemorrhagic stroke in patients without prior stroke

Mach F *et al.,* Eur Heart J. 2018;39(27):2526-2539, Collins R *et al.*, Lancet. 2016; 388(10059):2532-2561

WOSCOPS (West of Scotland Coronary Prevention Study)

5-Year Randomized Trial and 20-Year Observational Follow-Up



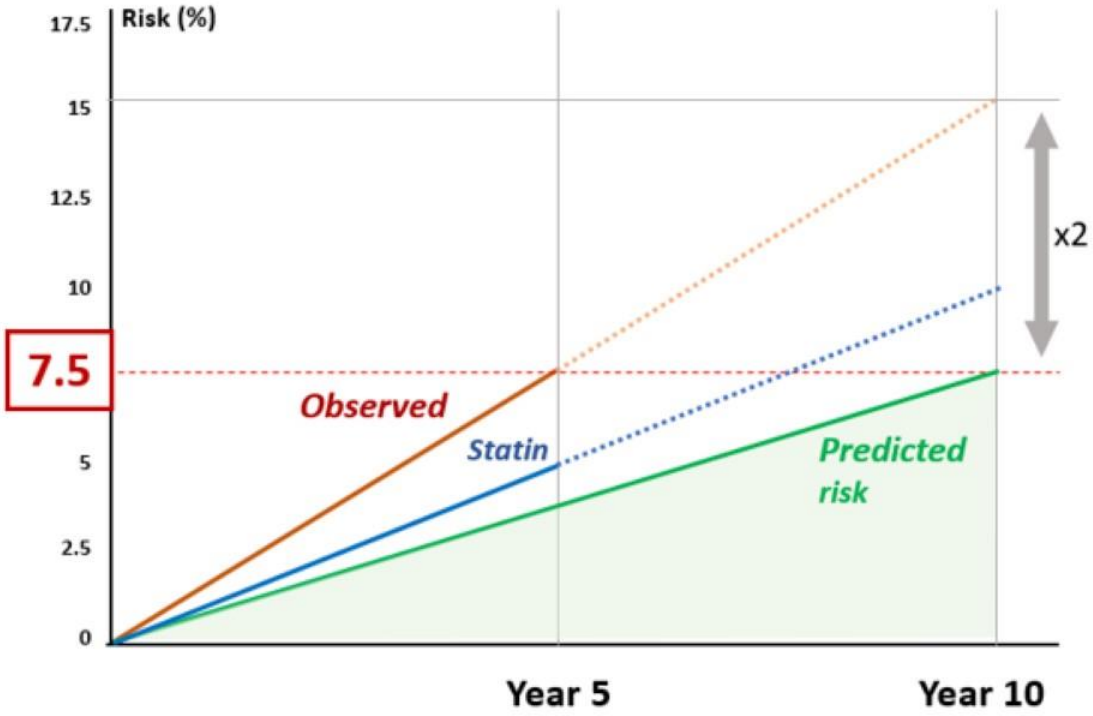
Circulation. 2016;133:1073–1080

WOSCOPS (West of Scotland Coronary Prevention Study)

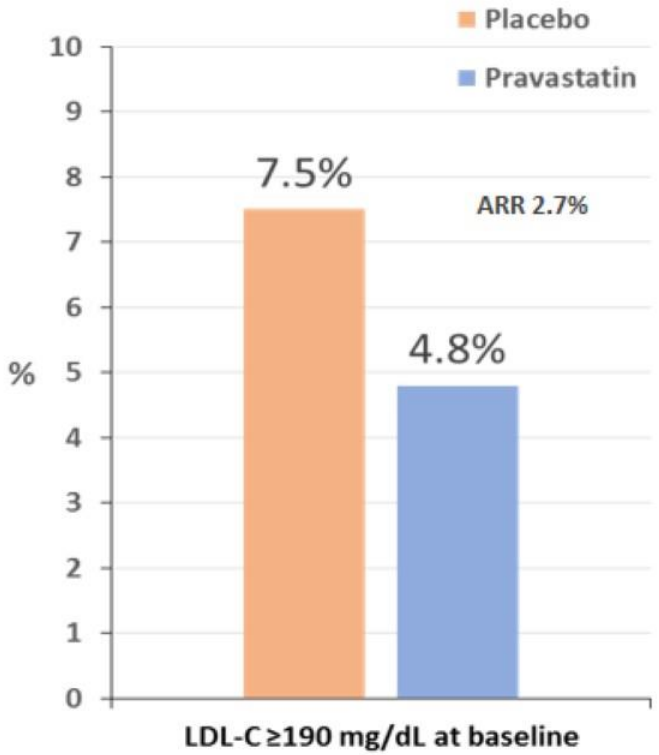
5-Year Randomized Trial and 20-Year Observational Follow-Up

Risk of MACE at 5 years with Pravastatin vs placebo
HR **0.62 (95% CI 0.42, 0.92)**, *P*=0.018

LDL-C ≥190 mg/dL



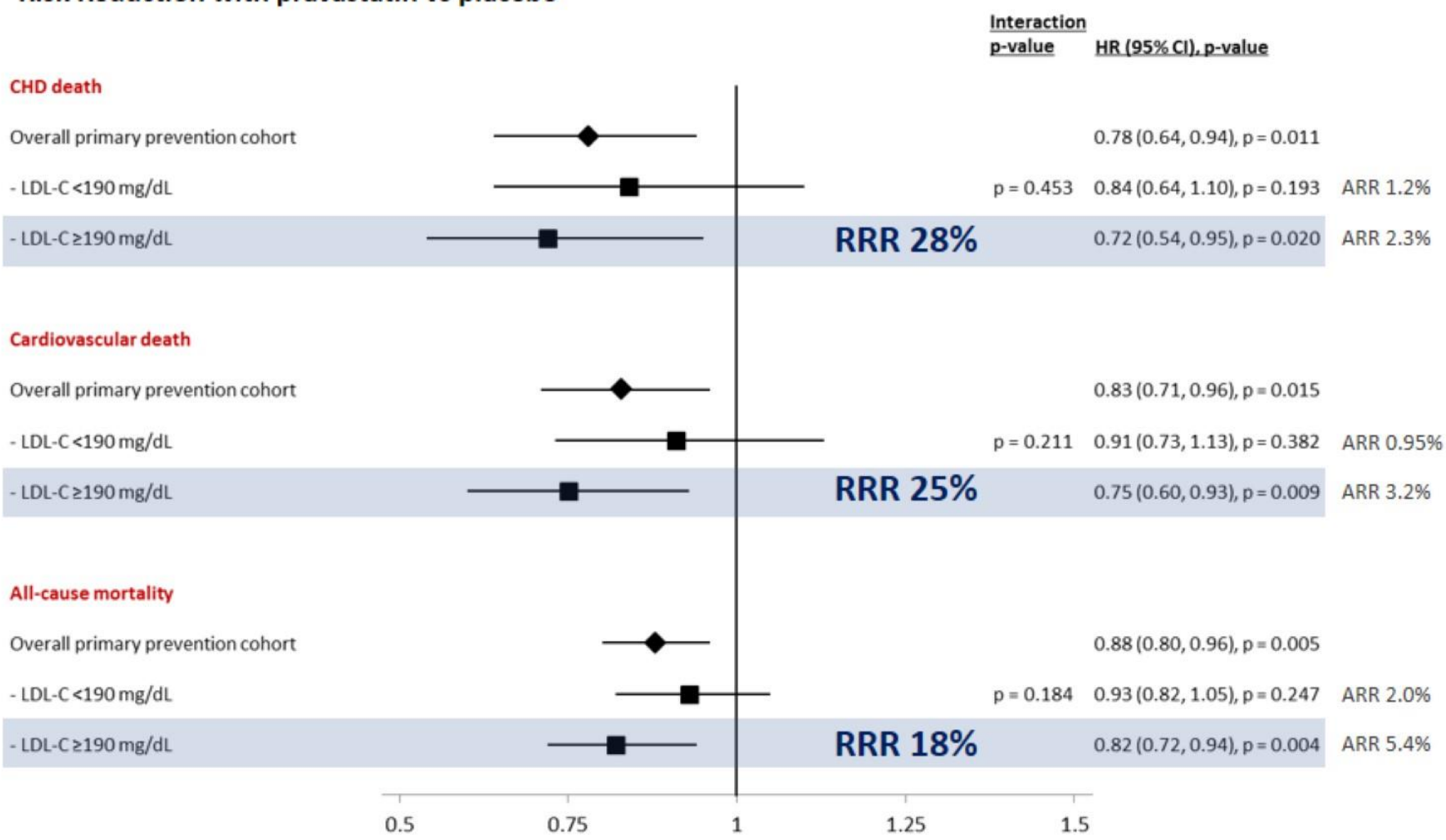
OBSERVED MACE event rates at **5 years**



Vallejo-Vaz AJ, et al. Circulation 2017;136:1878–91

LDL-C, low-density lipoprotein cholesterol; MACE, major adverse cardiovascular events

Long-term mortality endpoints at 20 years of follow-up

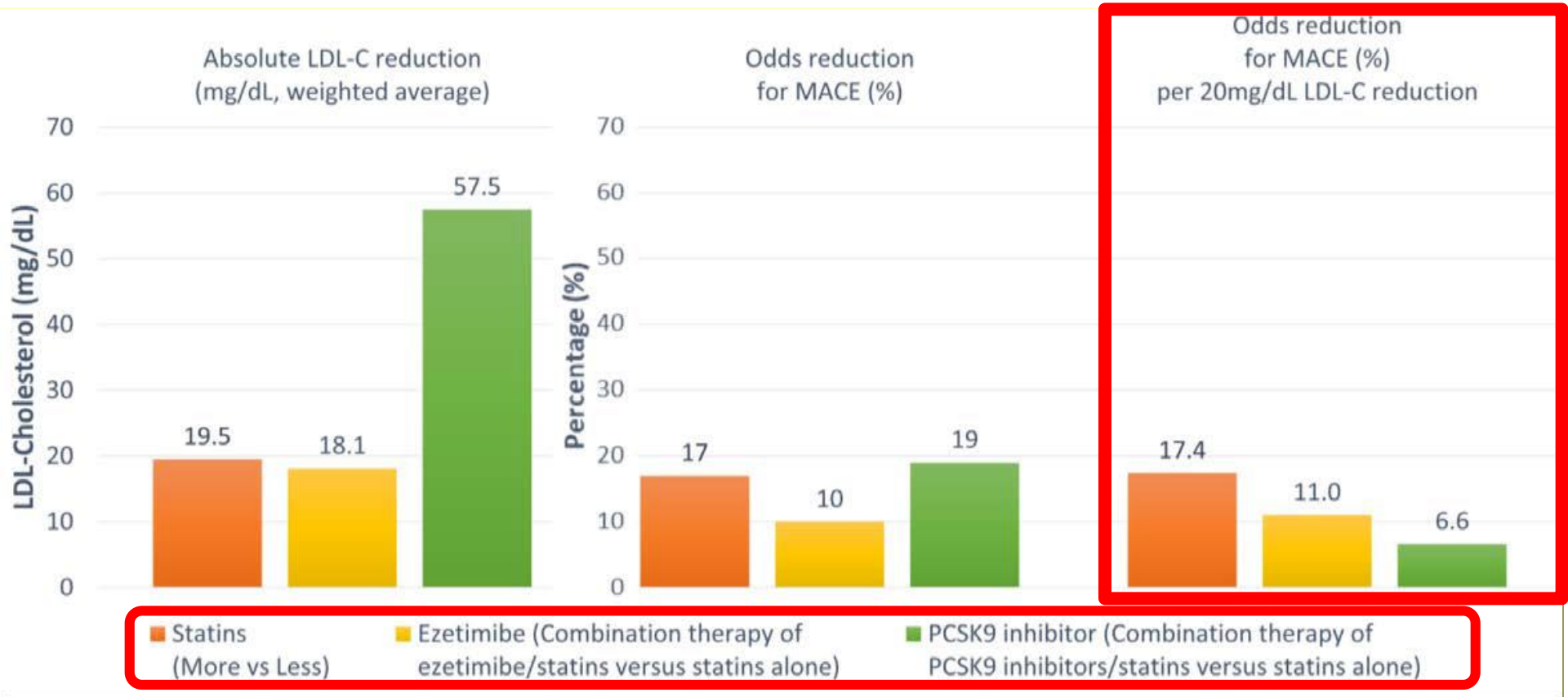


Vallejo-Vaz AJ, et al. Circulation 2017;136:1878–91

CHD, coronary heart disease; LDL-C, low-density lipoprotein cholesterol

Reduction of LDL-C and the odds reduction for MACE according to the 3 lipid-lowering therapy strategies

Statin reduce MACE most per 20mg/dL LDL reduction



	Statins (N=57,672)	Ezetimibe (N=20,688)	PCSK9 inhibitor (N=54,677)
Baseline LDL-C (mg/dL, weighted average)	101.9	105.4	94.1
LDL-C at follow-up (mg/dL, weighted average)	84.6	66.4	50.8

Circ Cardiovasc Qual Outcomes. 2019;12:e005460.

Outlines

- Aggressive “Primary Prevention” Era
  - More accurate risk estimate
  - What “ESC 2019 dyslipidemia treatment guideline” tell us ?
- Variation of statin efficacy between Asian and Western dyslipidemia
- Asian real world statin prescription condition
- Tailored lipid control in Asian primary prevention
- Conclusions

Asian patients are more sensitive in statin therapy due to Pharmacokinetics

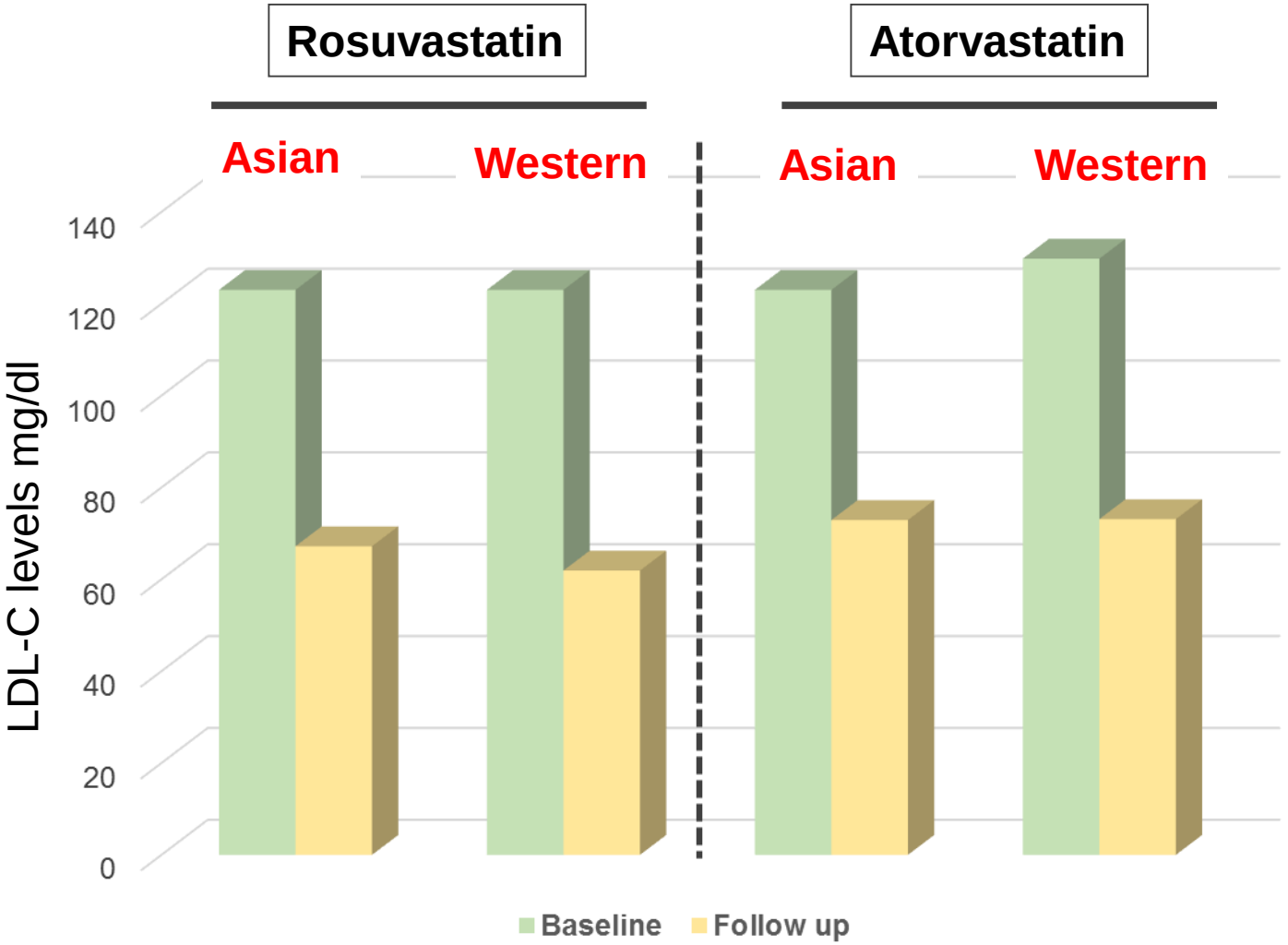
Table 2. Variant allele frequency (percentage) of polymorphisms having effects on statin pharmacokinetics in different ethnic groups

SNP	Chinese	Japanese		Caucasian	Indian[a]
SLCO1B1 521T>C	14.6-15.1	11.0		15.0	2.3
SLCO1B1 388A>G	81.7-83.7	65.1	>	40.3	55.7
ABCG2 421C>A	28.9-29.3	31.1-34.3		11.1-11.7	6.2

The *SLCO1B1* 521C allele results in the *SLCO1B1**5, *15 and *17 haplotypes.
Data from HapMap. [a]Gujarati Indians in Houston, Texas.

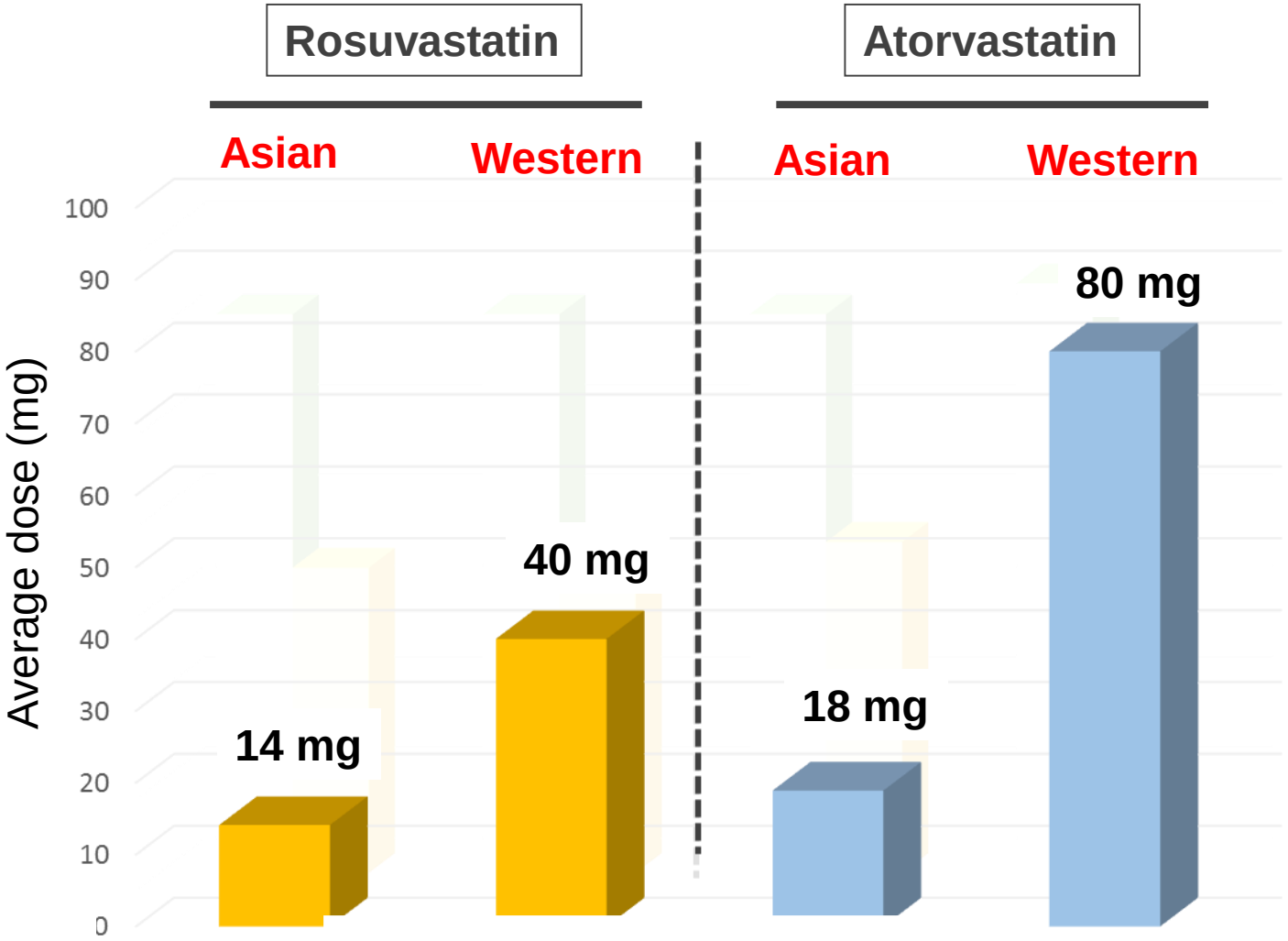
J Atheroscler Thromb, 2017; 24: 00-00

Asian patients are more sensitive in statin therapy



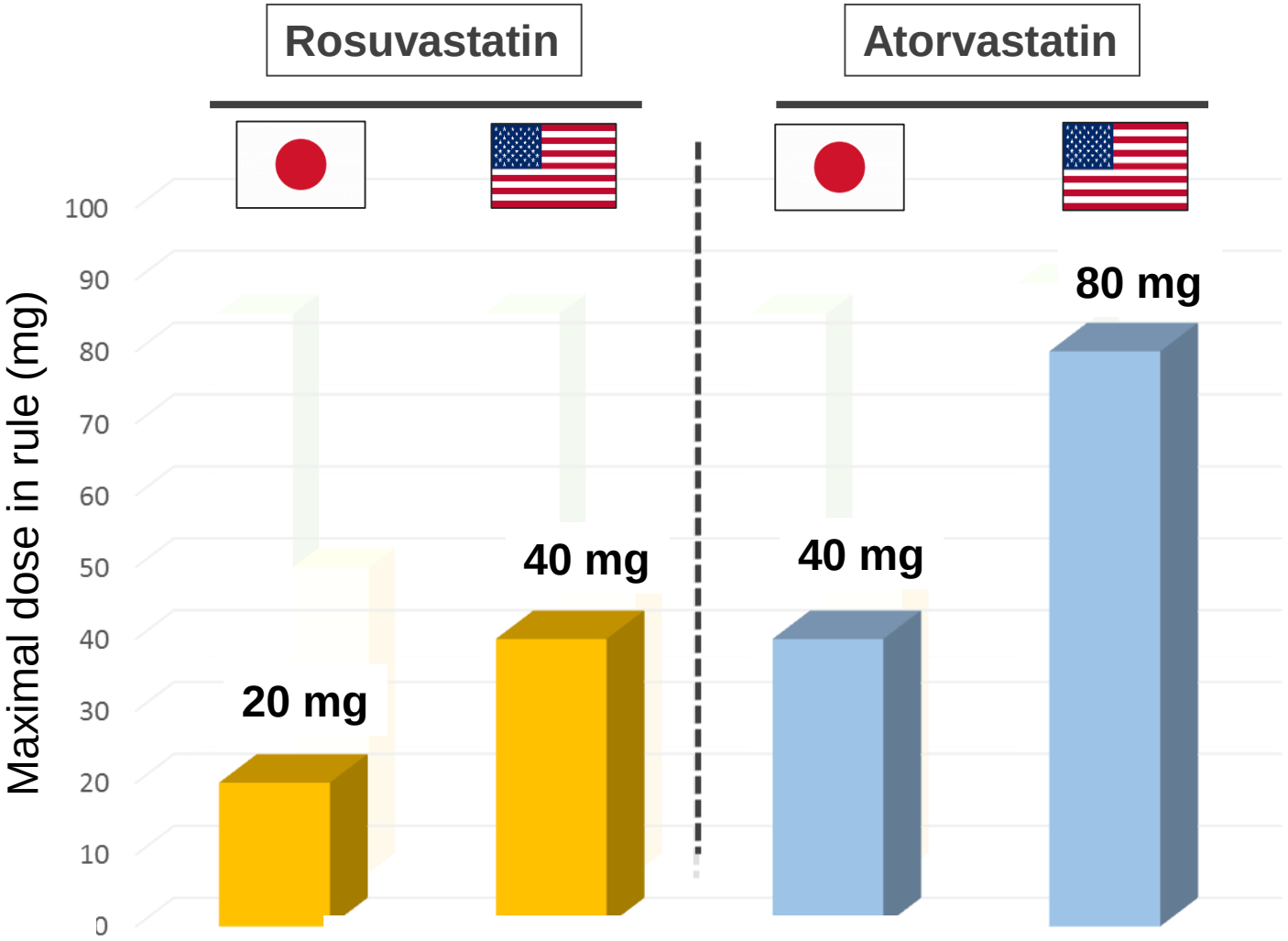
J Atheroscler Thromb, 2017; 24: 19-25

Asian patients are more sensitive in statin therapy



J Atheroscler Thromb, 2017; 24: 19-25

Maximal dose of statins in Japan and U.S



J Atheroscler Thromb, 2017; 24: 19-25

2018 ACC/AHA Guideline on the Management of Blood Cholesterol

Racial/ethnic issues in intensity of statin therapy & response to LDL-C lowering

- Japanese patients may be sensitive to statin dosing. In an open-label, randomized primary- prevention trial, Japanese participants had a reduction in CVD events with low-intensity doses of pravastatin as compared with placebo (S4.5.1- 33)

- In a secondary prevention trial, Japanese participants with CAD benefitted from a [moderate-intensity] dose of pitavastatin (S4.5.1-34)

- Using a lower statin intensity in Japanese patients may give results similar to those seen with higher intensities in non- Japanese patients

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Atherosclerosis 266 (2017) 158–166

Contents lists available at ScienceDirect

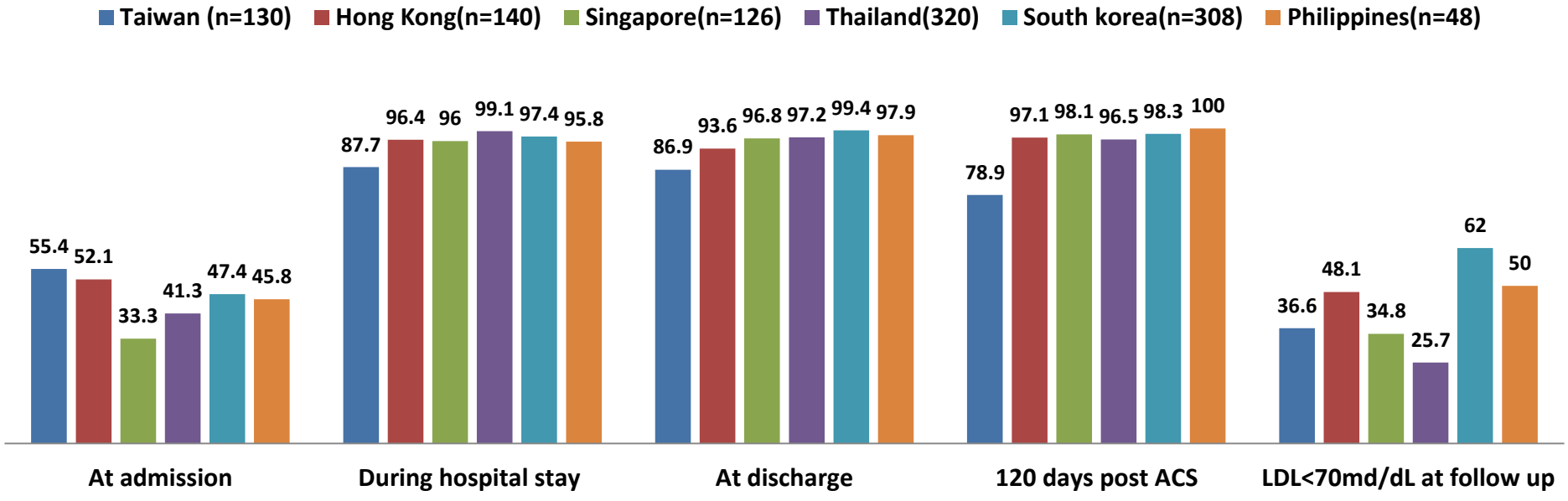
Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

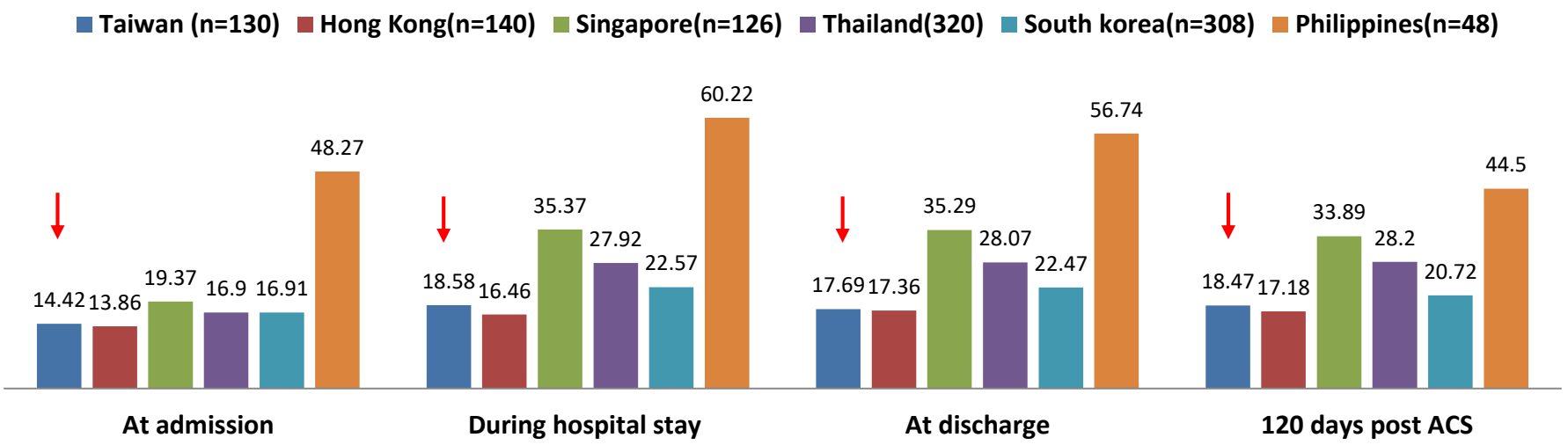
Cholesterol target value attainment and lipid-lowering therapy in patients with stable or acute coronary heart disease: Results from the Dyslipidemia International Study II

Anselm K. Gitt [a, b, *], Dominik Lautsch [c], Jean Ferrières [d], Gaetano M. De Ferrari [e], Ami Vyas [f], Carl A. Baxter [g], Lori D. Bash [c], Veronica Ashton [h], Martin Horack [b], Wael Almahmeed [i, j], Fu-Tien Chiang [k], Kian Keong Poh [l, m], Philippe Brudi [c], Baishali Ambegaonkar [c]

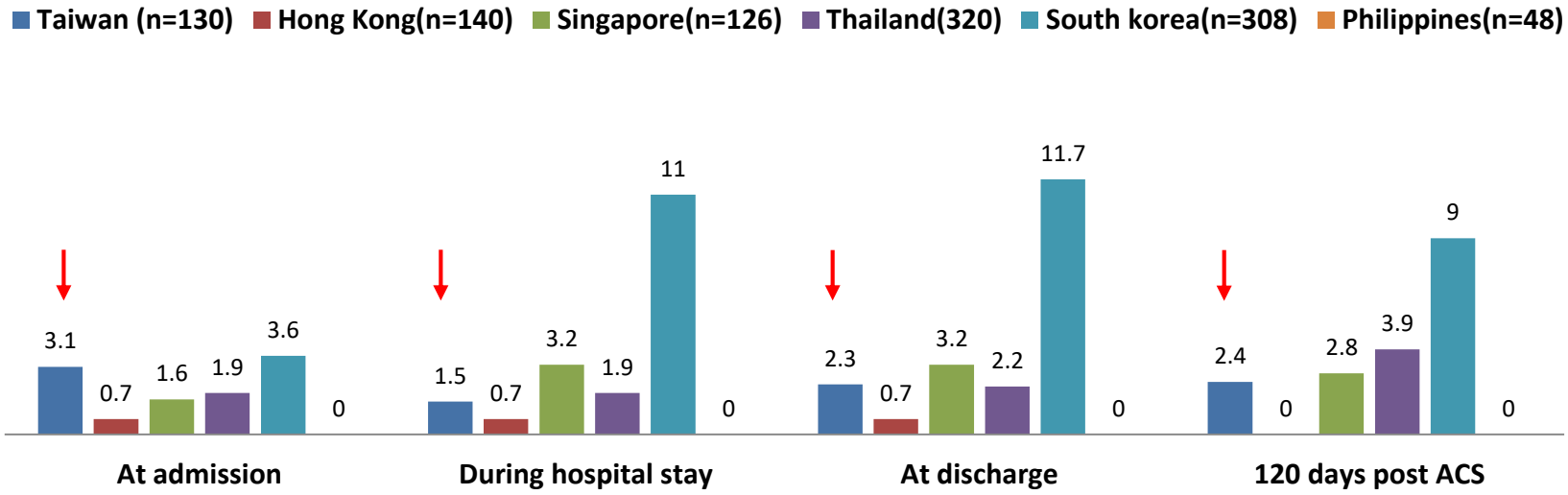
Lipid lowering treatment (%) in ACS



Atorvastatin equivalent dose



Ezetimibe in combination with any statin(%)

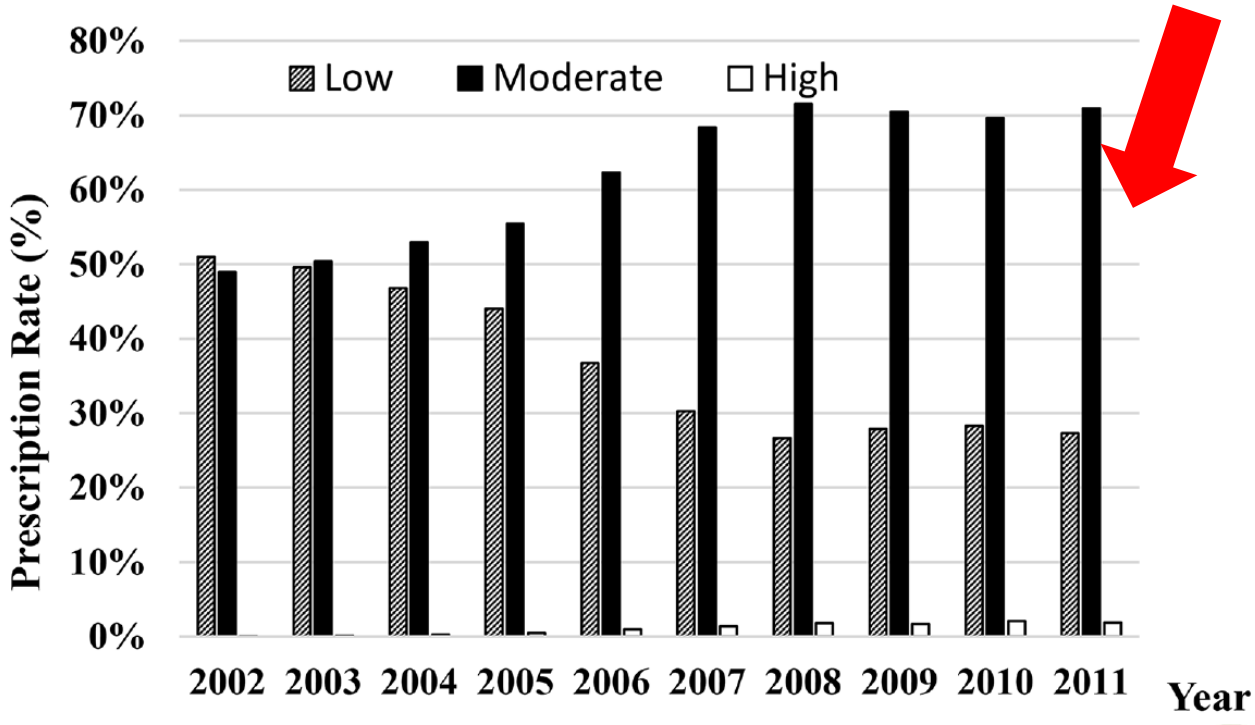


BMJ Open

10-year trends in statin utilization in Taiwan: a retrospective study using Taiwan's National Health Insurance Research Database

Hsing-Chun Hsieh,[1,2] Jason C Hsu,[1] Christine Y Lu[3]

Moderate intensity



Outlines

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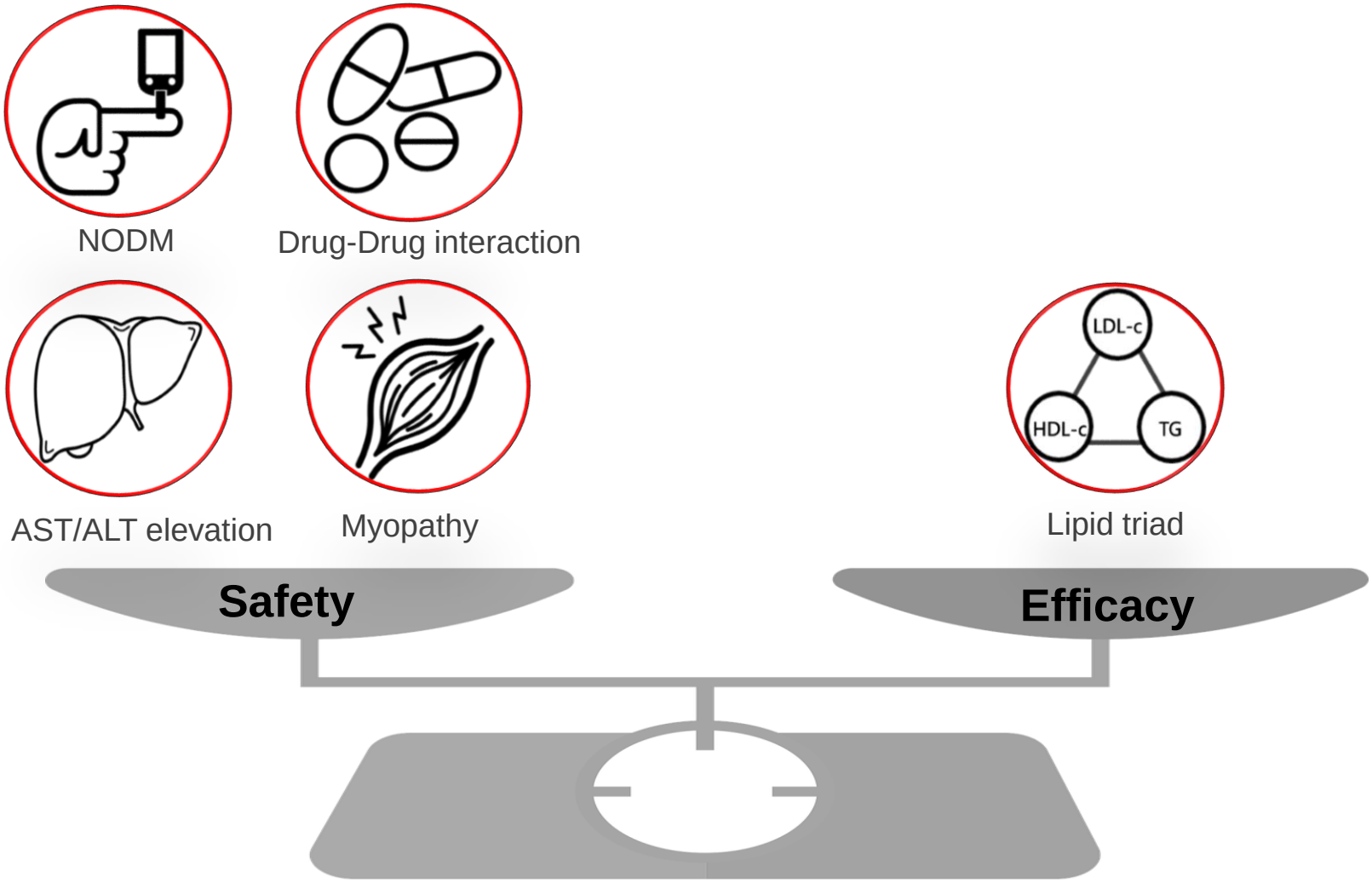
- Conclusions

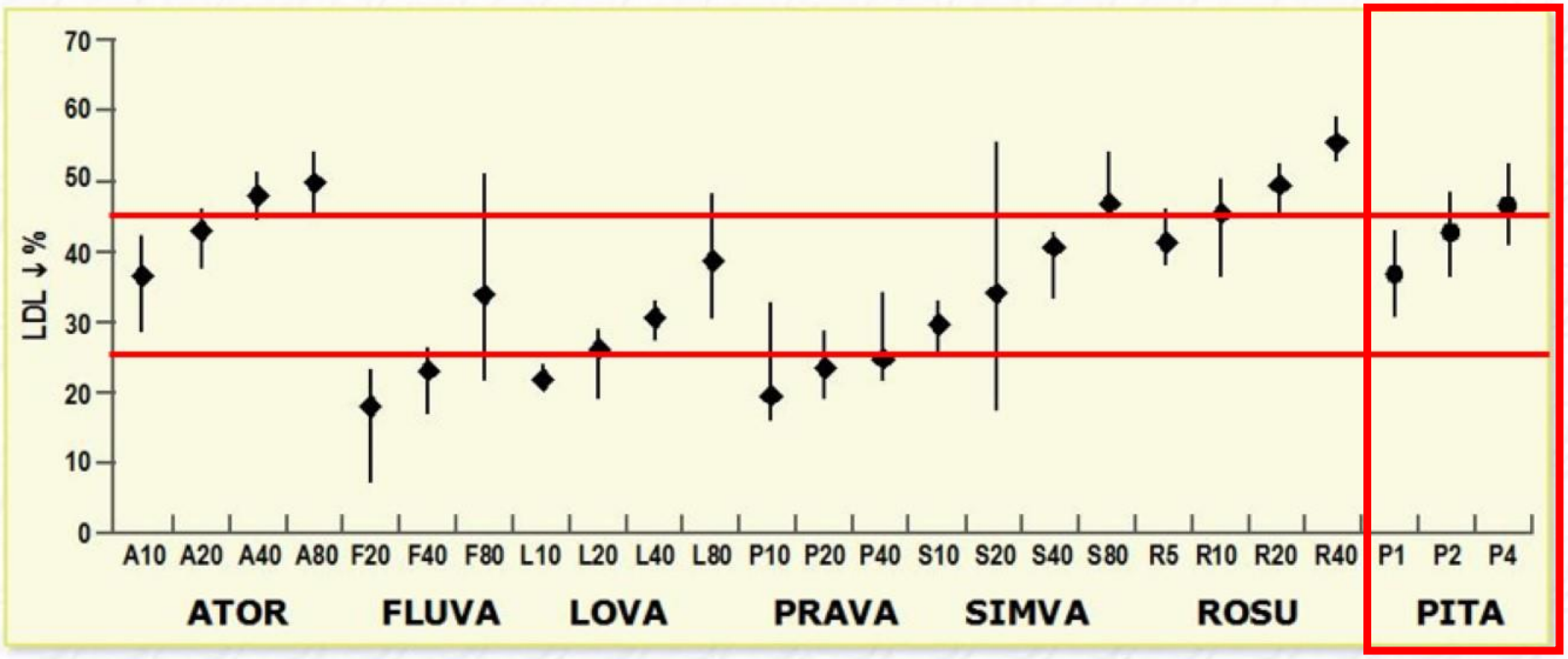
Primary prevention:

Balance of efficacy and safety



A systematic review and meta-analysis of the therapeutic equivalence of statins

47%



Pitavastatin 4 mg ≒ Atorvastatin 40 mg ≒ Rosuvastatin 10mg[1]

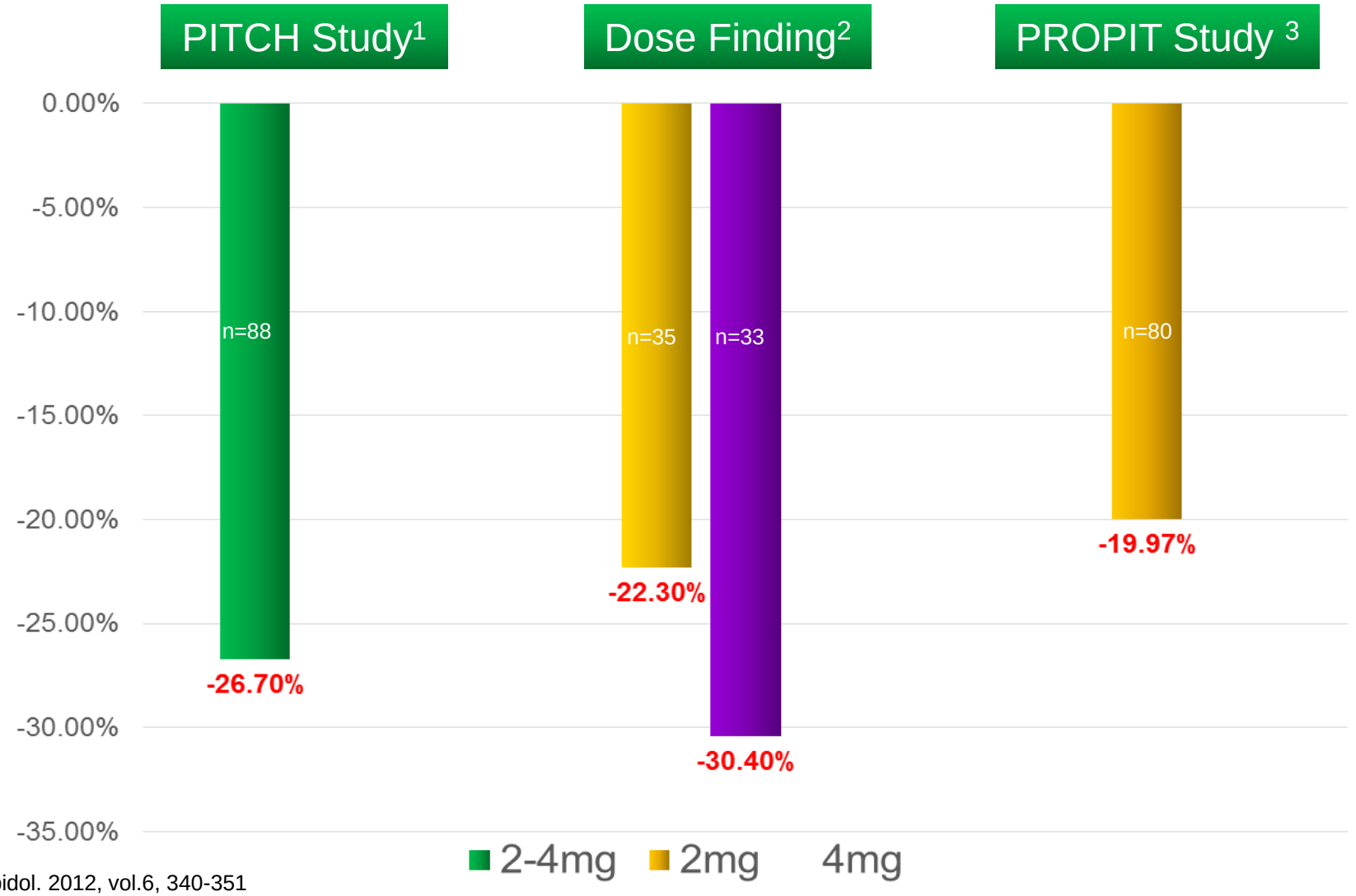
EAS

www.escardio.org/guidelines

European Heart Journal 2016; 37:2999–3058 - doi:10.1093/eurheartj/ehv272
Atherosclerosis 253 (2016) 281-344-d oi:10.1016/j.atherosclerosis.2016.08.018

EUROPEAN SOCIETY OF CARDIOLOGY®

Efficacy of Pitavastatin on TG



1.J of Clin. Lipidol. 2012, vol.6, 340-351
2.Drug Res. 2002,vol.52,NO.4 : 251-255
3.Clin. Endo. 2014,vol.82,NO.5 : 670-677

European Heart Journal (2016) **37**, 2999–3058
doi:10.1093/eurheartj/ehw272

2016 ESC/EAS Guidelines for the Management of Dyslipidaemias

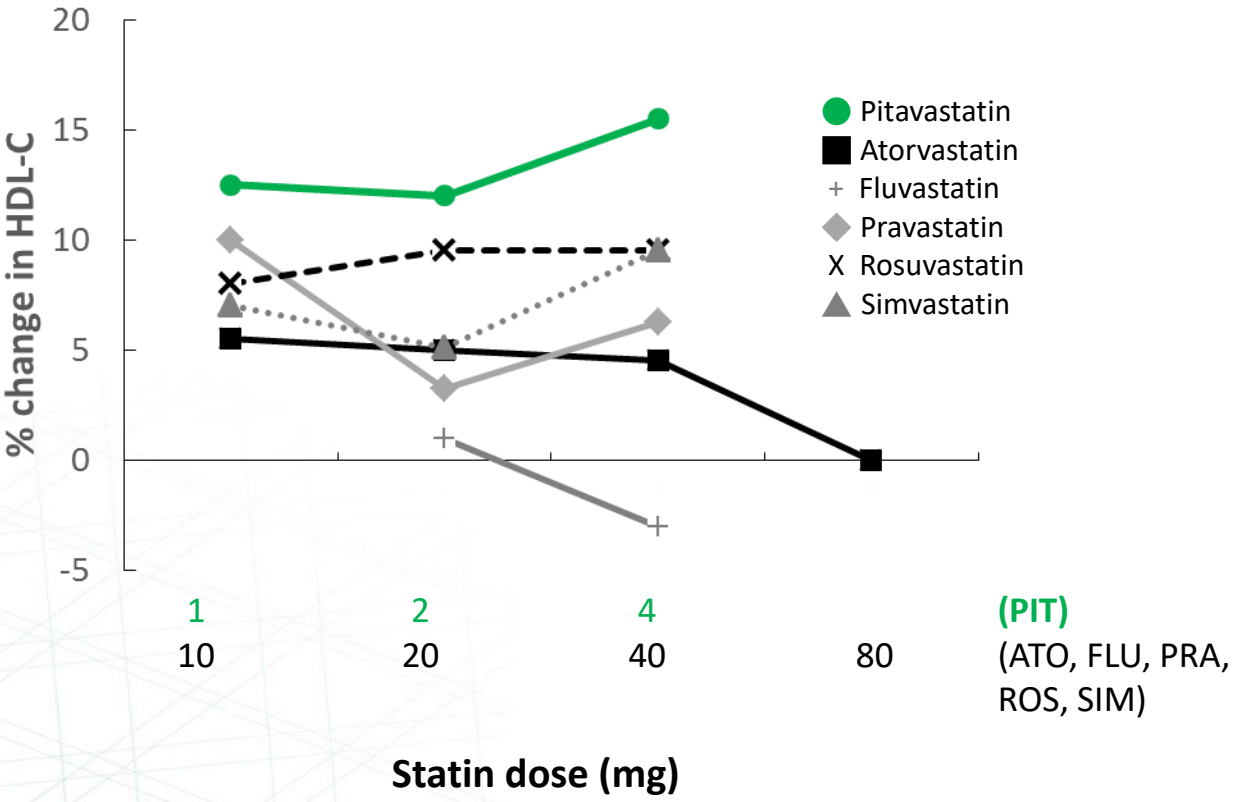
7.4 Statins

Since statins have significant effects on mortality as well as most CVD outcome parameters, these drugs are the first choice to reduce both total CVD risk and moderately elevated TG levels.

More potent statins (atorvastatin, rosuvastatin and pitavastatin) demonstrate a robust lowering of TG levels, especially at high doses and in patients with elevated TGs. In subgroup analyses from statin trials, the risk reduction is the same in subjects with HTG as in normotriglyceridaemic subjects.

Effect of each statin dose on HDL-C level

Pitavastatin showed the greatest increase in HDL-C than other statins.



ATO=atorvastatin; FLU=fluvastatin; PIT=pitavastatin; PRA=pravastatin; ROS=rosuvastatin; SIM=simvastatin.
HDL-C=high-density lipoprotein cholesterol.
Yamashita S, et al. J Atheroscler Thromb. 2010;17(5):436-51.

Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials

Naveed Sattar, David Preiss, Heather M Murray, Paul Welsh, Brendan M Buckley, Anton J M de Craen, Sreenivasa Rao Kondapally Seshasai, John J McMurray, Dilys J Freeman, J Wouter Jukema, Peter W Macfarlane, Chris J Packard, David J Stott, Rudi G Westendorp, James Shepherd, Barry R Davis, Sara L Pressel, Roberto Marchioli, Rosa Maria Marfisi, Aldo P Maggioni, Luigi Tavazzi, Gianni Tognoni, John Kjekshus, Terje R Pedersen, Thomas J Cook, Antonio M Gotto, Michael B Clearfield, John R Downs, Haruo Nakamura, Yasuo Ohashi, Kyoichi Mizuno, Kausik K Ray, Ian Ford

用statin治療255 個病人4 年會額外增加1 個DM, 但可預防5.4 個心血管事件發生

Methods We searched Medline, Embase, and the Cochrane Central Register of Controlled Trials from 1994 to 2009, for randomised controlled endpoint trials of statins. We included only trials with more than 1000 patients, with identical follow-up in both groups and duration of more than 1 year. We excluded trials of patients with organ transplants or who needed haemodialysis. We used the I^2 statistic to measure heterogeneity between trials and calculated risk estimates for incident diabetes with random-effect meta-analysis.

Findings We identified 13 statin trials with 91140 participants, of whom 4278 (2226 assigned statins and 2052 assigned control treatment) developed diabetes during a mean of 4 years. Statin therapy was associated with a 9% increased risk for incident diabetes (odds ratio [OR] 1·09; 95% CI 1·02–1·17), with little heterogeneity (I^2=11%) between trials. Meta-regression showed that risk of development of diabetes with statins was highest in trials with older participants, but neither baseline body-mass index nor change in LDL-cholesterol concentrations accounted for residual variation in risk. Treatment of 255 (95% CI 150–852) patients with statins for 4 years resulted in one extra case of diabetes.

Interpretation Statin therapy is associated with a slightly increased risk of development of diabetes, but the risk is low both in absolute terms and when compared with the reduction in coronary events. Clinical practice in patients with moderate or high cardiovascular risk or existing cardiovascular disease should not change.

Lancet 2010; 375: 735–42

Effect of pitavastatin on new onset DM

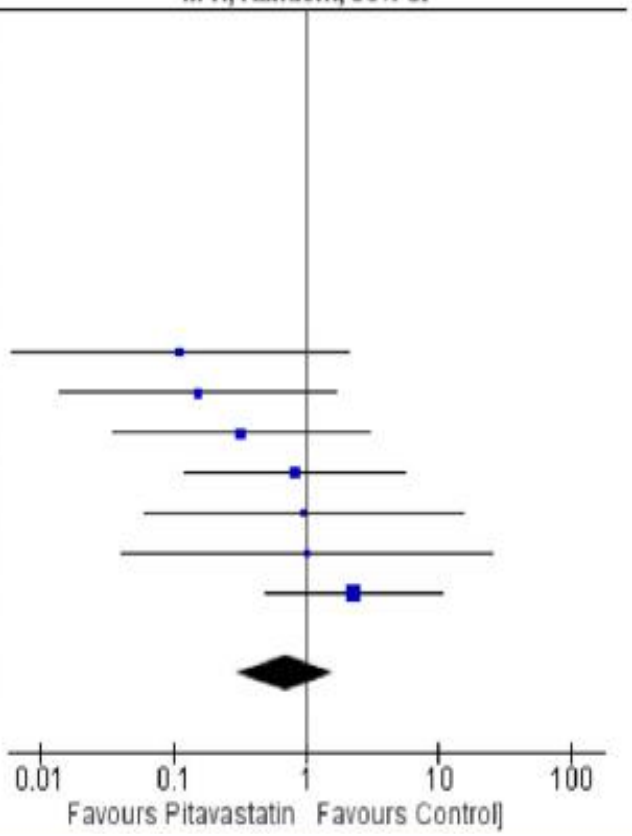
C. New onset diabetes – Risk Ratio

Study or Subgroup	Pitavastatin Events	Pitavastatin Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Eriksson M et al, 2011	0	218	0	111		Not estimable
NK-104-203	0	202	0	49		Not estimable
PREVAIL-US	0	143	0	131		Not estimable
NK-104-202	0	206	0	54		Not estimable
PAPAGO-T	0	50	0	50		Not estimable
PEACE	0	70	0	81		Not estimable
VISION	0	21	0	21		Not estimable
Stender S et al, 2013	0	597	0	288		Not estimable
INTREPID	0	123	4	124	8.2%	0.11 [0.01, 2.06]
Budinski D et al, 2009	1	576	2	179	12.1%	0.16 [0.01, 1.70]
COMPACT-CAD	1	36	3	35	14.2%	0.32 [0.04, 2.97]
TRUTH	2	38	2	31	19.3%	0.82 [0.12, 5.46]
Saito Y et al, 2002	1	84	1	81	9.2%	0.96 [0.06, 15.16]
Ose L et al, 2009	1	592	0	202	6.8%	1.03 [0.04, 25.11]
NK-104-4.01CH	9	280	2	142	30.2%	2.28 [0.50, 10.42]
Total (95% CI)		**3236**		**1579**	**100.0%**	**0.70 [0.30, 1.61]**
Total events	15		14			

Pr
At
At
Pr
Pr
Si
At

Heterogeneity: Tau² = 0.00; Chi² = 5.97, df = 6 (P = 0.43); I² = 0%

Test for overall effect: Z = 0.84 (P = 0.40)

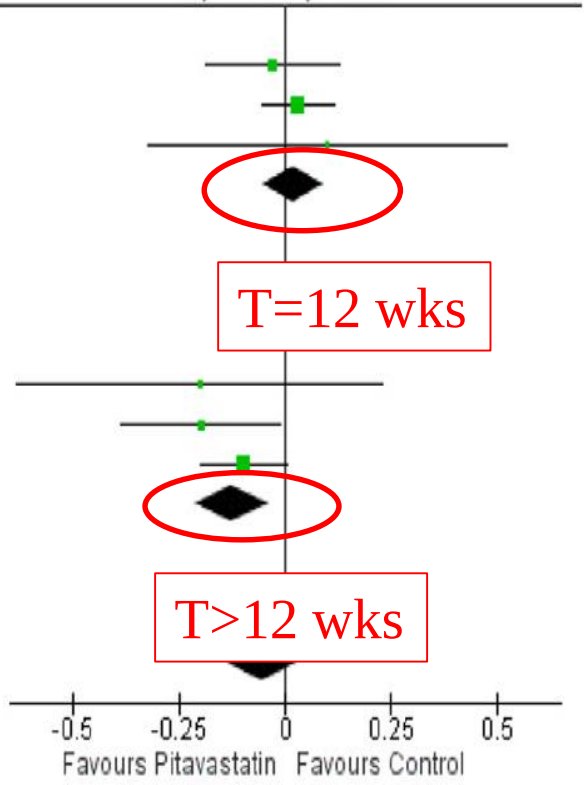


Atherosclerosis 2015 Volume 241, Issue 2, Pages 409–418

Effect of pitavastatin on HbA1c based on follow-up time

B – HbA1c (%)

Study or Subgroup	Pitavastatin Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.9.1 Follow-up =12 weeks								
PAPAGO-T	5.83	0.34	50	5.86	0.46	50	17.5%	-0.03 [-0.19, 0.13]
PREVAIL-US	5.77	0.34	143	5.74	0.36	131	33.3%	0.03 [-0.05, 0.11]
VISION	5.8	0.7	21	5.7	0.7	21	3.5%	0.10 [-0.32, 0.52]
Subtotal (95% CI)			**214**			**202**	**54.2%**	**0.02 [-0.05, 0.09]**
Heterogeneity: Tau² = 0.00; Chi² = 0.57, df = 2 (P = 0.75); I² = 0%								
Test for overall effect: Z = 0.53 (P = 0.60)								
1.9.2 Follow-up >12 weeks								
TRUTH	5.7	0.6	38	5.9	1.1	31	3.4%	-0.20 [-0.63, 0.23]
COMPACT-CAD	5.55	0.44	36	5.75	0.35	35	14.2%	-0.20 [-0.38, -0.02]
INTREPID	5.3	0.43	123	5.4	0.39	124	28.3%	-0.10 [-0.20, 0.00]
Subtotal (95% CI)			**197**			**190**	**45.8%**	**-0.13 [-0.21, -0.04]**
Heterogeneity: Tau² = 0.00; Chi² = 0.98, df = 2 (P = 0.61); I² = 0%								
Test for overall effect: Z = 2.83 (P = 0.005)								
Total (95% CI)			**411**			**392**	**100.0%**	**-0.06 [-0.14, 0.03]**
Heterogeneity: Tau² = 0.00; Chi² = 7.89, df = 5 (P = 0.16); I² = 37%								
Test for overall effect: Z = 1.32 (P = 0.19)								
Test for subgroup differences: Chi² = 6.34, df = 1 (P = 0.01), I² = 84.2%								

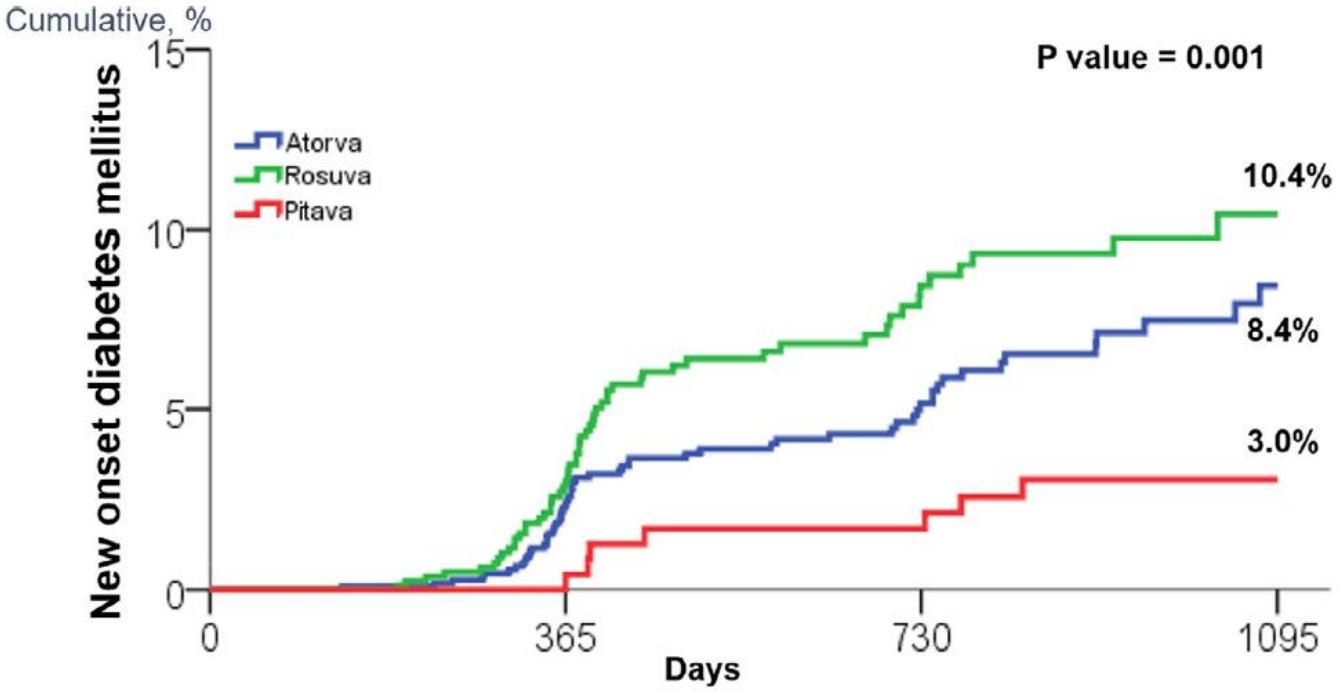


Atherosclerosis 2015 Volume 241, Issue 2, Pages 409–418

The American Journal of Cardiology®

Pitavastatin had lower NODM rate in AMI patients

Korean prospective, multicenter, real-world treatment, Asian patients diagnosed with AMI

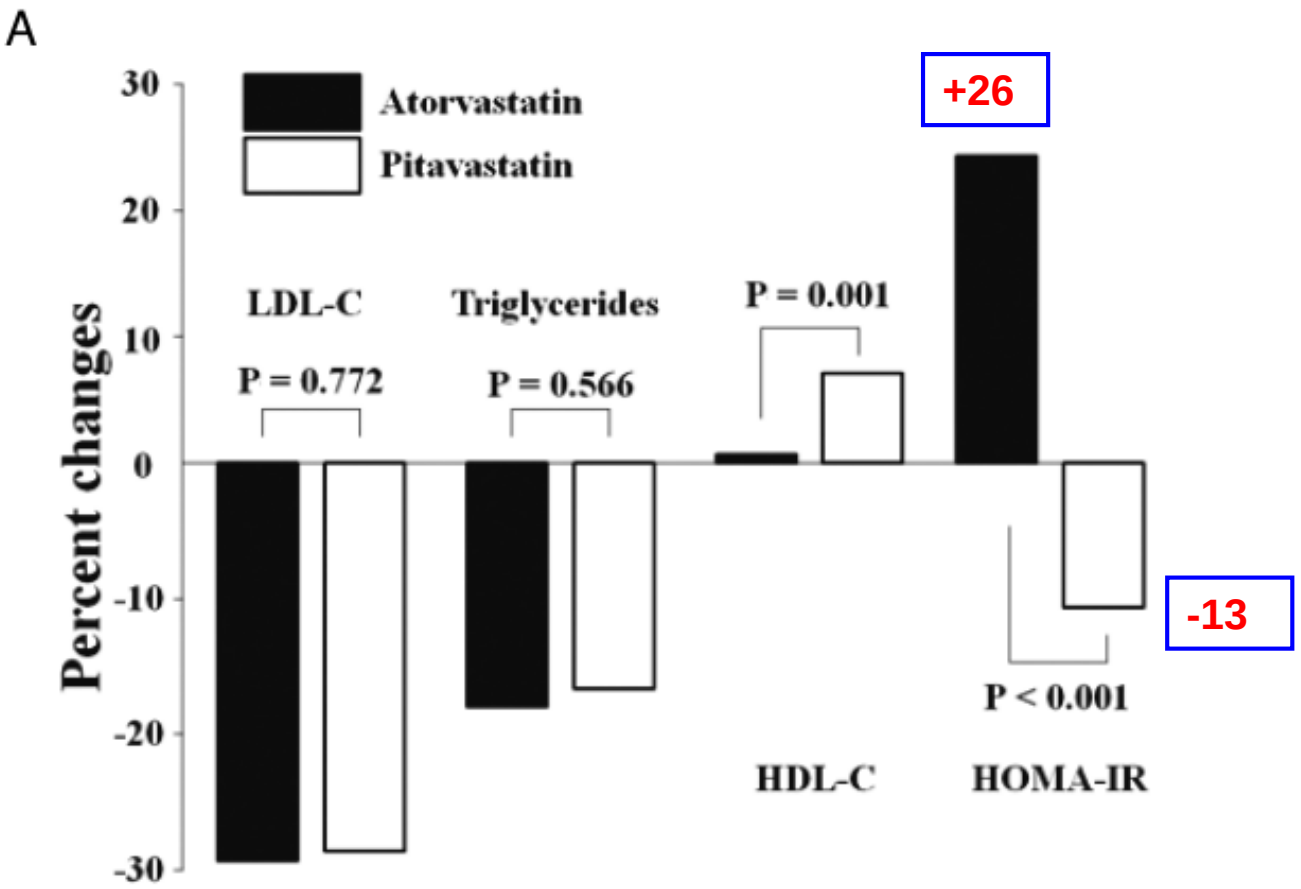


Atorva	1267	1243	1221	1209
Rosuva	961	939	910	905
Pitava	255	254	251	248

Am J Cardiol2018;122:922 928

Pitavastatin may have greater benefits for improving insulin resistance

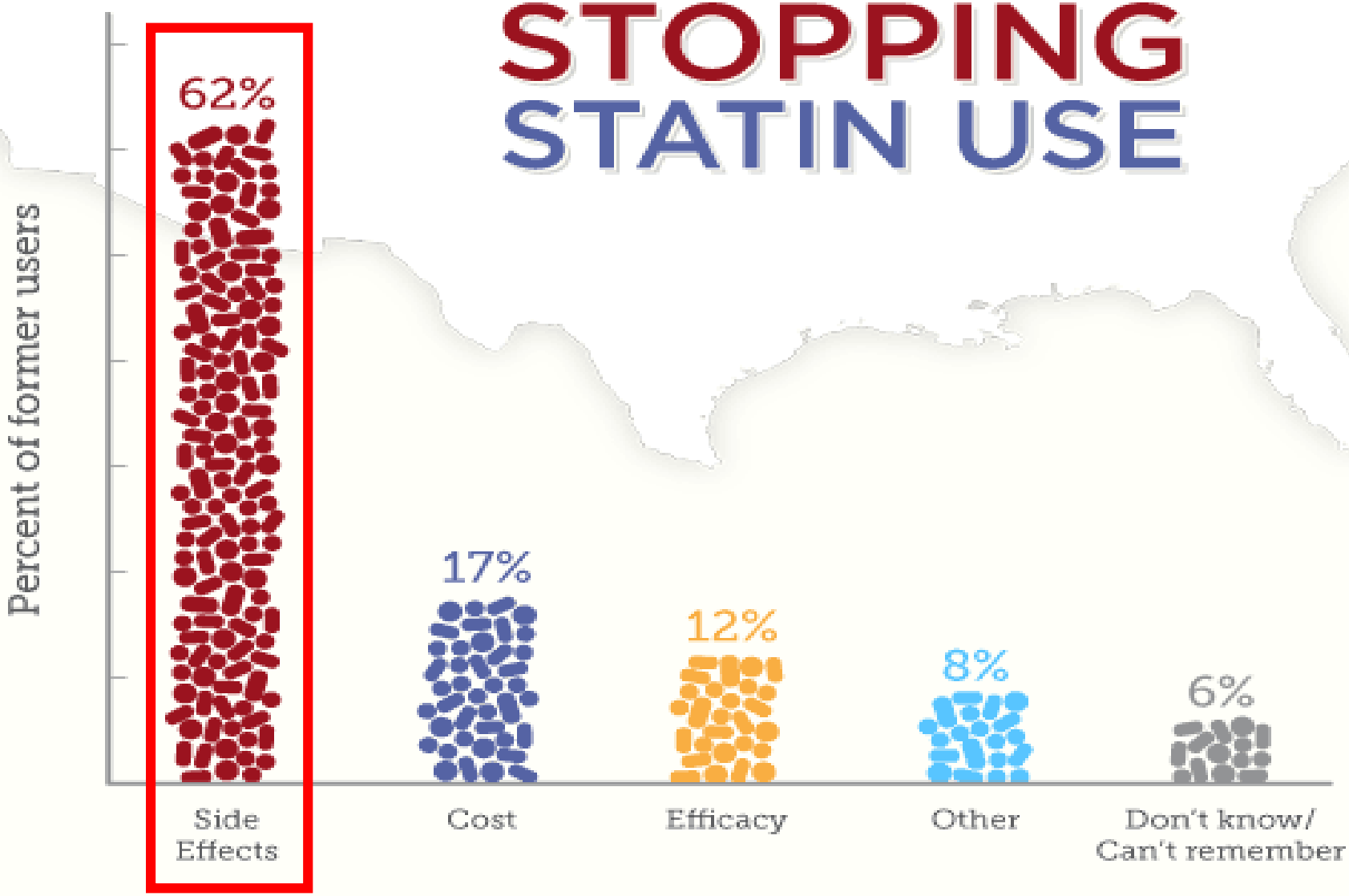
(A) Changes in the lipid profiles and HOMA-IR



J Atheroscler Thromb, 2015; 22: 1158-1171.

Most Common Reasons for

STOPPING STATIN USE



Reasons for stopping statin use among former statin users

The USAGE survey is supported by Kowa Pharmaceuticals America, Inc. and the National Lipid Association.
GEN-1014

Association of Clinician Knowledge and Statin Beliefs With Statin Therapy Use and Lipid Levels (A Survey of US Practice in the PALM Registry)

Angela Lowenstern, MD[a,b,*], Ann Marie Navar, MD, PhD[a,b], Shuang Li, MS[a], Salim S. Virani, MD, PhD[c], Anne C. Goldberg, MD[d], Michael J. Louie, MD, MPH, MSc[e], L. Veronica Lee, MD[f], Eric D. Peterson, MD, MPH[a,b], and Tracy Y. Wang, MD, MHS, MSc[a,b]

Guideline implementation requires clinician knowledge but may be influenced by pre-existing beliefs and biases. We assessed the association of these clinician factors with lipid management following the release of the 2013 American College of Cardiology/American Heart Association cholesterol guidelines. In the PALM registry, 774 clinicians completed a survey to assess their knowledge of the 2013 American College of Cardiology/American Heart Association guidelines, belief in statin benefit, and statin safety concerns. The association of these factors with statin use, statin dosing, and low-density lipoprotein cholesterol (LDL-C) levels were assessed in the 6,839 patients treated by these clinicians between May and November 2015. Overall, 63.9% of clinicians responded to at least 3 out of 4 hypothetical scenarios in concordance with guideline recommendations (good tested knowledge), 88.4% reported belief in statin benefit, and 15.4% raised concerns about statin safety. Belief in statin benefit was more prevalent among cardiologists, who represented 48.8% of the clinicians surveyed, and concerns regarding statin safety were higher among noncardiologists and clinicians in an academic setting. Guideline knowledge was not associated with a difference in statin use (74.1% vs 73.8%, p = 0.84) and achievement of LDL-C level <100 mg/dl (54.7% vs 52.4%, p = 0.07). However, patients treated by clinicians who reported belief in statin benefit were more likely to receive guideline-recommended statin intensity (41.9% vs 36.9%, p = 0.03), whereas patients treated by clinicians expressing statin safety concerns were less likely receive statins of at least guideline-recommended intensity (36.8% vs 42.5%, p = 0.001) and to achieve an LDL-C <100 mg/dl (44.1% vs 56.1%, p <0.001); the latter persisted after multivariable adjustment (odds ratio 0.75, 95% confidence interval 0.63 to 0.89). In conclusion, clinician beliefs regarding benefits and risks of statins were significantly associated with guideline adherence and patients' achieved LDL-C levels, whereas clinician knowledge of guideline recommendations was not. (Am J Cardiol 2019;123:1011–1018)

Guideline knowledge, belief in statin benefit, and concerns regarding statin risk based on clinician characteristics

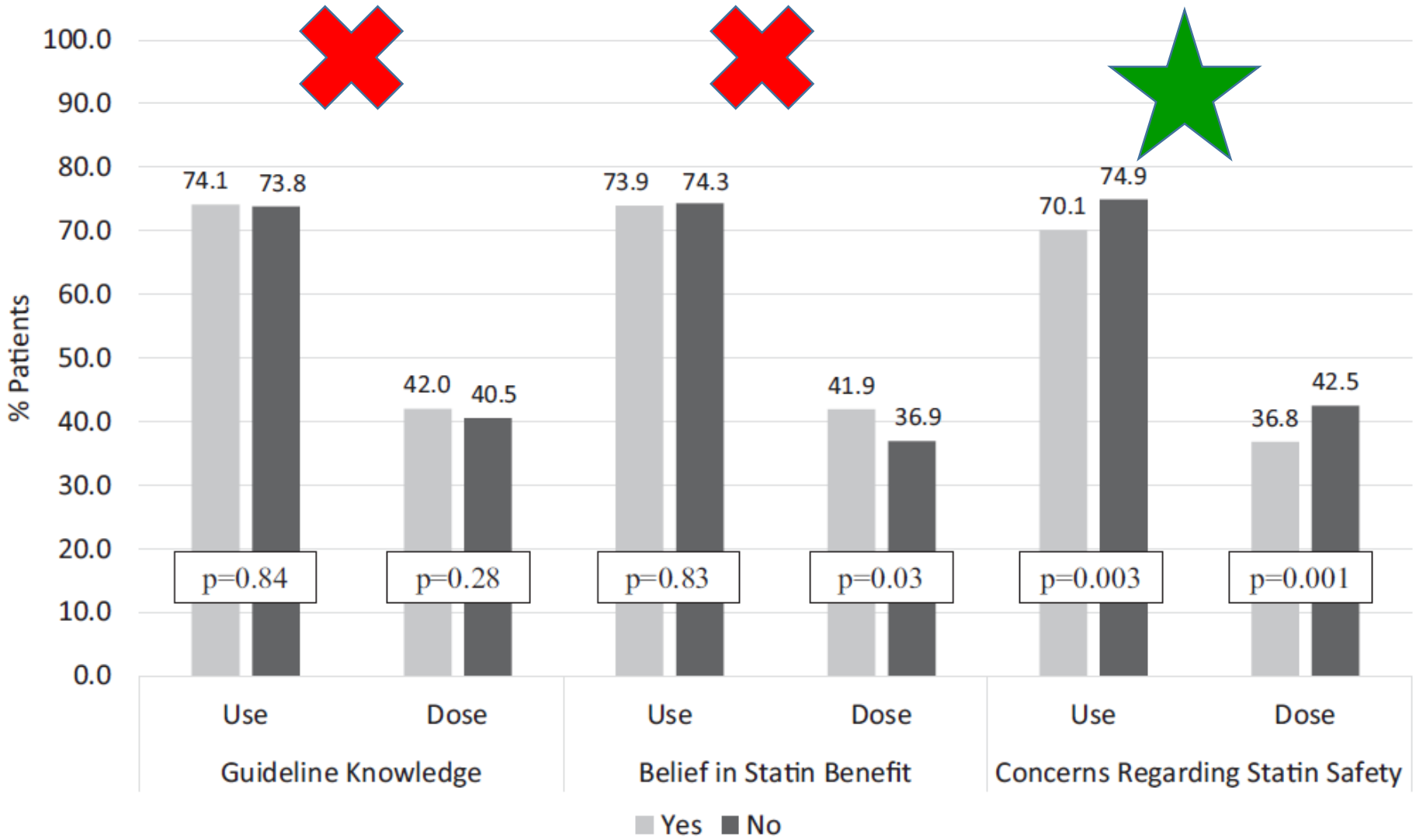
Guideline knowledge, belief in statin benefit, and concerns regarding statin risk based on clinician characteristics

Clinician-reported	Cardiologists	Noncardiologists	Board certified	Not board certified	>10 years in practice	≤10 years in practice	Academic	Nonacademic
Guideline knowledge	66.8%	61.3%	63.5%	66.4%	62.6%	66.5%	65.7%	63.5%
p value	0.11		0.58		0.28		0.56	
Belief of statin benefit	91.5%	85.5%	89.6%	80.8%	90.8%	83.6%	85.9%	89.4%
p value	**0.009**		**0.009**		**0.003**		0.17	
Concern regarding statin safety	10.1%	20.3%	15.1%	17.3%	14.5%	17.2%	20.2%	13.3%
p value	**<0.001**		0.55		0.32		**0.02**	

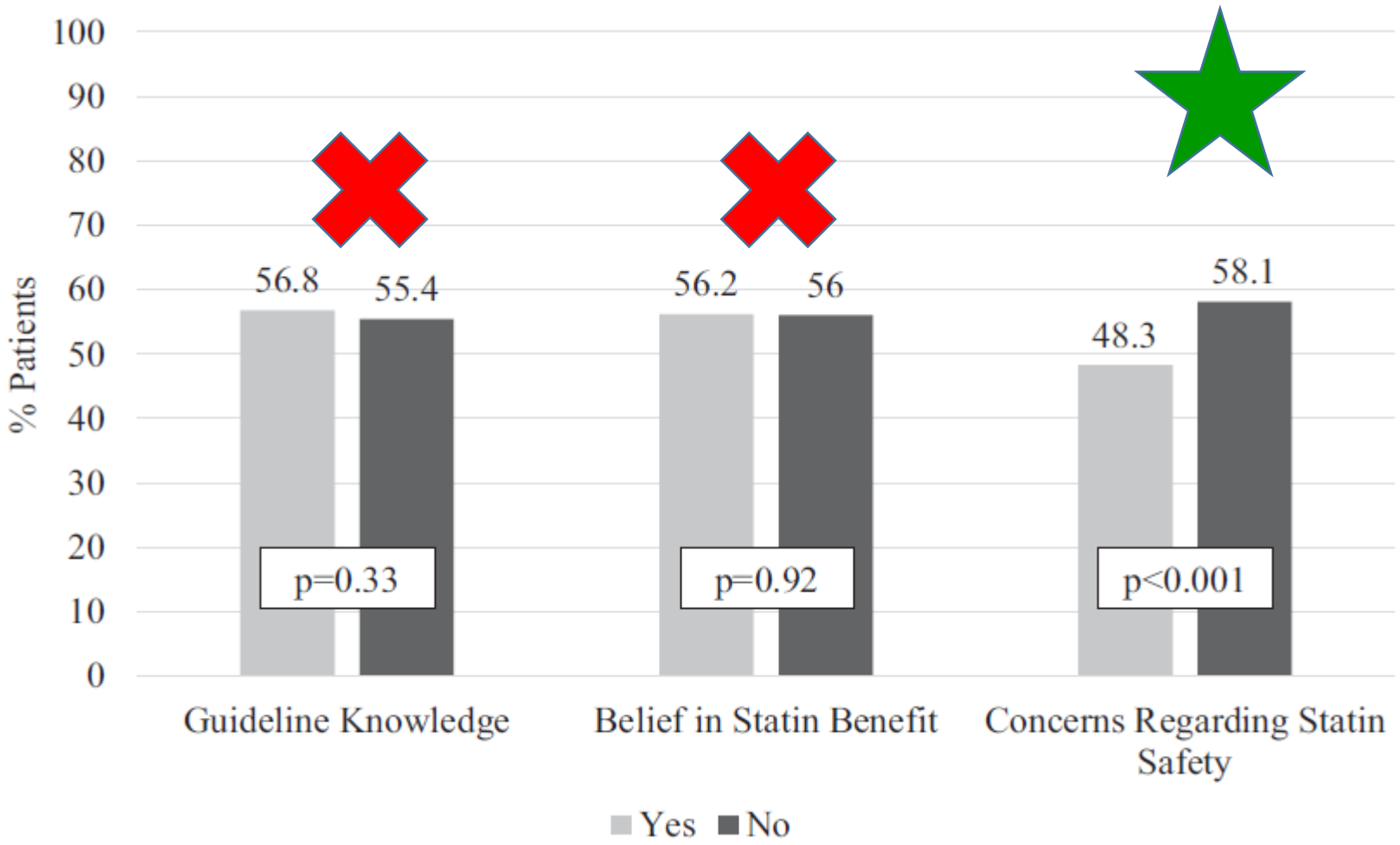
Guideline knowledge: ≥3/4 scenario questions answered in accordance with guidelines.
Belief of statin benefit: sum score >0.
Concern regarding statin safety: sum score >0.

Am J Cardiol 2019;123:1011−1018

Statin use and guideline-concordant statin dosing among patients with a guideline indication for statin therapy



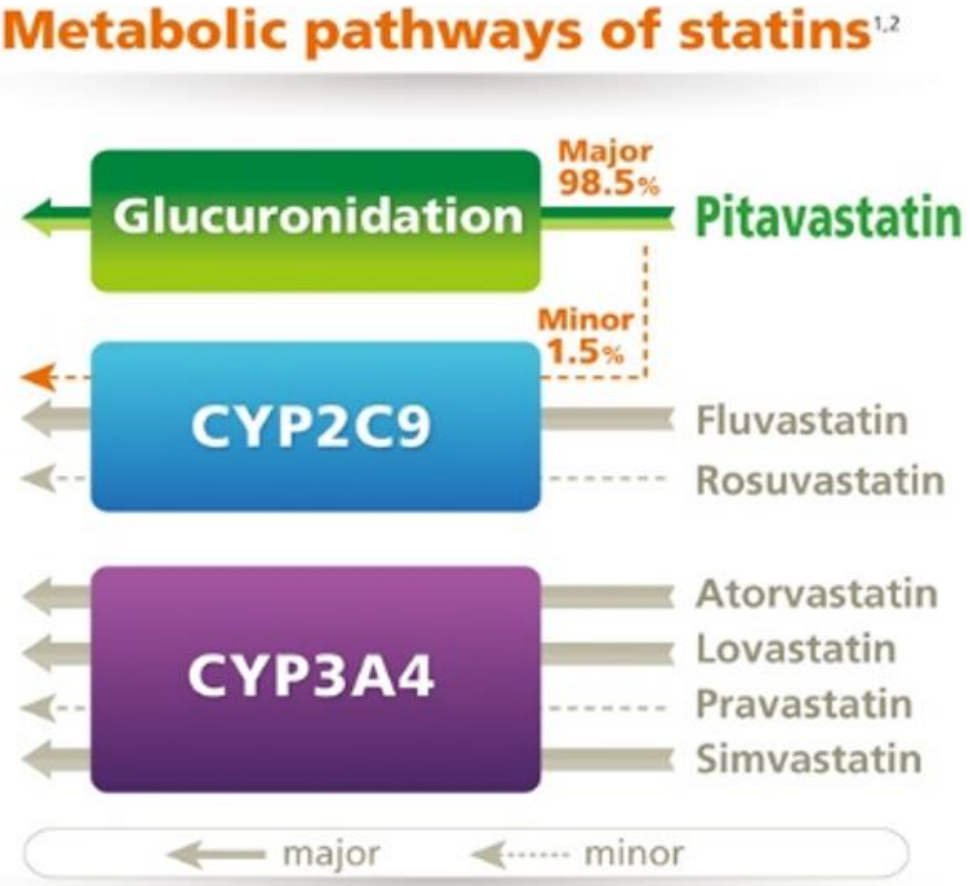
Achievement of LDL-C <100 mg/dl among patients with a guideline indication for statin therapy



Am J Cardiol 2019;123:1011–1018

Pitavastatin: unique metabolic profile
Minor metabolism via CYP pathways

Pitavastatin is minimally metabolized by CYP enzymes, and is therefore expected to have a low risk of DDIs and related ADRs[1].



ADR=adverse drug reaction; CYP=cytochrome P450; DDI=drug-drug interaction.

1. Corsini A, Ceska R. Curr Med Res Opin. 2011;27(8):1551-62. 2. Kawai Y, et al. Drug Des Devel Ther. 2011;5:283-97.

Safety and tolerability of pitavastatin

Postmarketing survey in Japan

pitavastatin was well tolerated with a good safety profile

Adverse reaction	Pitavastatin (N=19,921)	Atorvastatin (N=4,805)	Rosuvastatin (N=8,795)
Incidence of adverse reactions	6.1%	12.0%	11.1%
Increased CK (CPK)	1.4%	2.2%	2.3%
Increased ALT (GPT)	0.9%	1.8%	0.7%
Increased AST (GOT)	0.7%	1.1%	0.5%
Increased γ-GTP	0.5%	1.9%	0.6%
Increased plasma glucose	0.01%	0.37%	0.01%
Increased HbA1c	0.02%	0.25%	0.01%
Hematuria	–	–	0.7%
Proteinuria	–	0.2%	0.3%

ALT=alanine transaminase; AST=aspartate transaminase; CK=creatine kinase; CPK=creatine phosphokinase; GOT=glutamic oxaloacetic transaminase; GPT=glutamate pyruvate transaminase; GTP=glutamyltranspeptidase; HbA1c=hemoglobin A1c.

Hayashi T, et al. Expert Opin Pharmacother. 2007;8(14):2315-27.

Conclusions

- Updated lipid treatment guidelines suggest more aggressive LDL-c management in primary prevention according to risk stratification
- Accurate risk calculator, incorporate imaging method, should be the key in individual primary prevention treatment
- We need "Taiwan CVD risk calculator"
- Statin for lipid lowering strategy in primary prevention was suggested by most guidelines but still have barriers in real world and Asians
- Why Pitavastatin: the 1st consideration statin for primary prevention for
  - Non-diabetogenic , HDL elevation
  - Lower drug-drug interaction probability
  - Lower side effect

Thank you for your attention