

# ESC/EAS Guidelines for the management of dyslipidaemias: Addenda

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

Developed with the special contribution of: European Association for Cardiovascular Prevention & Rehabilitation<sup>†</sup>

**Authors/Task Force Members: Željko Reiner\* (ESC Chairperson) (Croatia), Alberico L. Catapano\* (EAS Chairperson) (Italy), Guy De Backer (Belgium), Ian Graham (Ireland), Marja-Riitta Taskinen (Finland), Olov Wiklund (Sweden), Stefan Agewall (Norway), Eduardo Alegria (Spain), M. John Chapman (France), Paul Durrington (UK), Serap Erdine (Turkey), Julian Halcox (UK), Richard Hobbs (UK), John Kjekshus (Norway), Pasquale Perrone Filardi (Italy), Gabriele Riccardi (Italy), Robert F. Storey (UK), David Wood (UK).**

**ESC Committee for Practice Guidelines (CPG) 2008–2010 and 2010–2012 Committees: Jeroen Bax (CPG Chairperson 2010–2012), (The Netherlands), Alec Vahanian (CPG Chairperson 2008–2010) (France), Angelo Auricchio (Switzerland), Helmut Baumgartner (Germany), Claudio Ceconi (Italy), Veronica Dean (France), Christi Deaton (UK), Robert Fagard (Belgium), Gerasimos Filippatos (Greece), Christian Funck-Brentano (France), David Hasdai (Israel), Richard Hobbs (UK), Arno Hoes (The Netherlands), Peter Kearney (Ireland), Juhani Knuuti (Finland), Philippe Kolh (Belgium), Theresa McDonagh (UK), Cyril Moulin (France), Don Poldermans (The Netherlands), Bogdan A. Popescu (Romania), Željko Reiner (Croatia), Udo Sechtem (Germany), Per Anton Sirnes (Norway), Michal Tendera (Poland), Adam Torbicki (Poland), Panos Vardas (Greece), Petr Widimsky (Czech Republic), Stephan Windecker (Switzerland)**

**Document Reviewers: Christian Funck-Brentano (CPG Review Coordinator) (France), Don Poldermans (Co-Review Coordinator) (The Netherlands), Guy Berkenboom (Belgium), Jacqueline De Graaf (The Netherlands), Olivier Descamps (Belgium), Nina Gotcheva (Bulgaria), Kathryn Griffith (UK), Guido Francesco Guida (Italy), Sadi Gulec (Turkey), Yaakov Henkin (Israel), Kurt Huber (Austria), Y. Antero Kesaniemi (Finland), John Lekakis (Greece), Athanasios J. Manolis (Greece), Pedro Marques-Vidal (Switzerland), Luis Masana (Spain), John McMurray (UK), Miguel Mendes (Portugal), Zurab Pagava (Georgia), Terje Pedersen (Norway), Eva Prescott (Denmark), Quitéria Rato (Portugal), Giuseppe Rosano (Italy), Susana Sans (Spain), Anton Stalenhoef (The Netherlands), Lale Tokgozoglul (Turkey), Margus Viigimaa (Estonia), M. E. Wittekoek (The Netherlands), Jose Luis Zamorano (Spain).**

\* Corresponding authors: Željko Reiner (ESC Chairperson), University Hospital Center Zagreb, School of Medicine, University of Zagreb, Salata 2, 10 000 Zagreb, Croatia. Tel: +385 1 492 0019, Fax: +385 1 481 8457, Email: [zreiner@kbc-zagreb.hr](mailto:zreiner@kbc-zagreb.hr), Alberico L. Catapano (EAS Chairperson), Department of Pharmacological Science, University of Milan, Via Balzaretti, 9, 20133 Milano, Italy. Tel: +39 02 5031 8302, Fax: +39 02 5031 8386, Email: [Alberico.Catapano@unimi.it](mailto:Alberico.Catapano@unimi.it)

<sup>†</sup> Other ESC entities having participated in the development of this document: Associations: Heart Failure Association.

Working Groups: Cardiovascular Pharmacology and Drug Therapy, Hypertension and the Heart, Thrombosis.

Councils: Cardiology Practice, Primary Cardiovascular Care, Cardiovascular Imaging.

The content of these European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS) Guidelines has been published for personal and educational use only. No commercial use is authorized. No part of the ESC Guidelines may be translated or reproduced in any form without written permission from the ESC. Permission can be obtained upon submission of a written request to Oxford University Press, the publisher of the *European Heart Journal* and the party authorized to handle such permissions on behalf of the ESC.

**Disclaimer.** The ESC Guidelines represent the views of the ESC and the EAS, and were arrived at after careful consideration of the available evidence at the time they were written. Health professionals are encouraged to take them fully into account when exercising their clinical judgement. The guidelines do not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patients, in consultation with that patient, and where appropriate and necessary the patient's guardian or carer. It is also the health professional's responsibility to verify the rules and regulations applicable to drugs and devices at the time of prescription.

©2011 The European Society of Cardiology and the European Atherosclerosis Association. All rights reserved. For permissions please email: [journals.permissions@oup.com](mailto:journals.permissions@oup.com).

The disclosure forms of the authors and reviewers are available on the ESC website [www.escardio.org/guidelines](http://www.escardio.org/guidelines)

## Keywords

dyslipidaemia • cholesterol • triglycerides • treatment • cardiovascular diseases • guidelines

## Table of Contents

Addenda on the ESC website:

Addendum I. SCORE charts with high-density lipoprotein-cholesterol

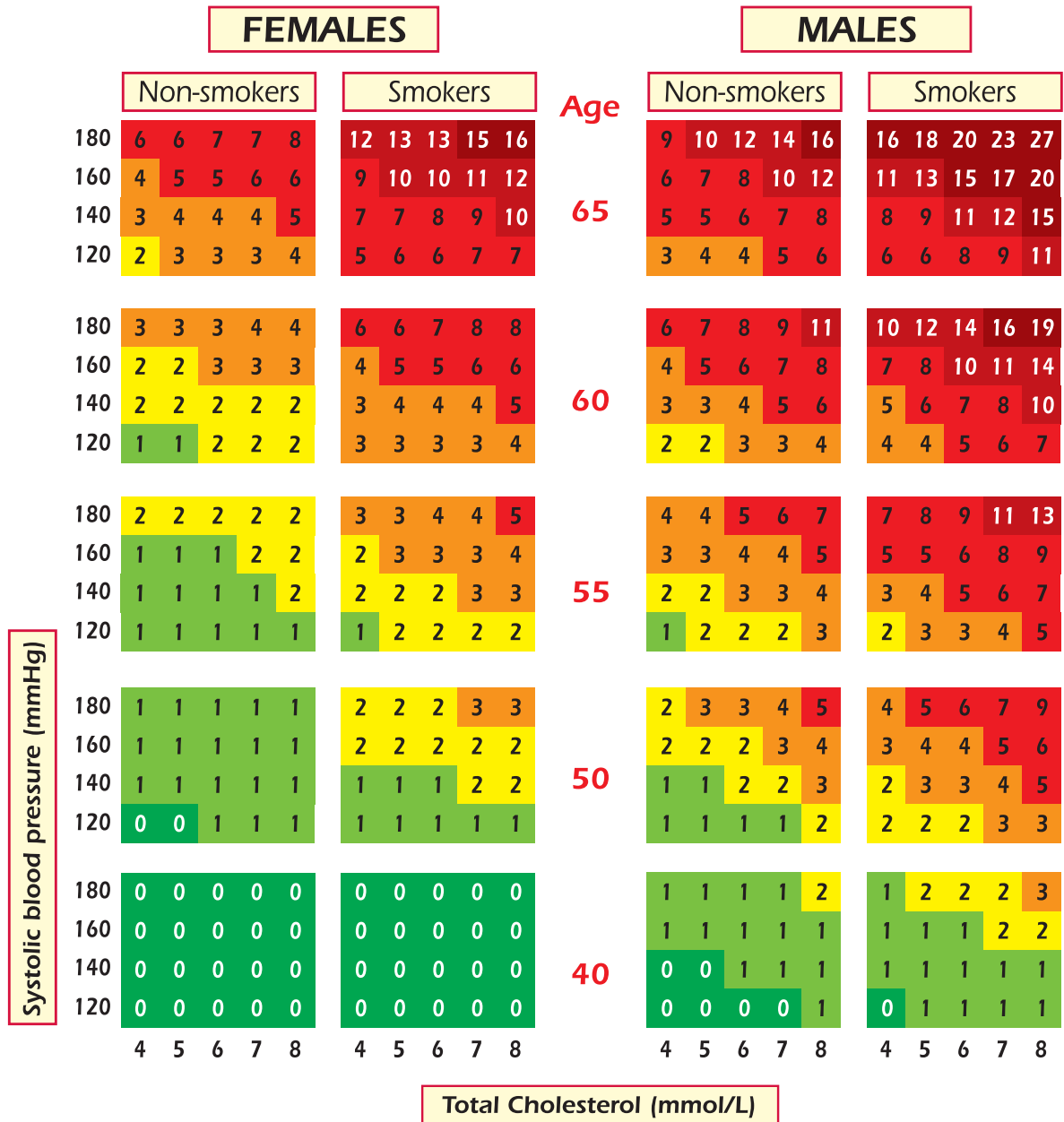
Addendum II. Practical approach to reach low-density lipoprotein-cholesterol goal

Addendum III. Inhibitors and inducers of enzymatic pathways involved in statin metabolism

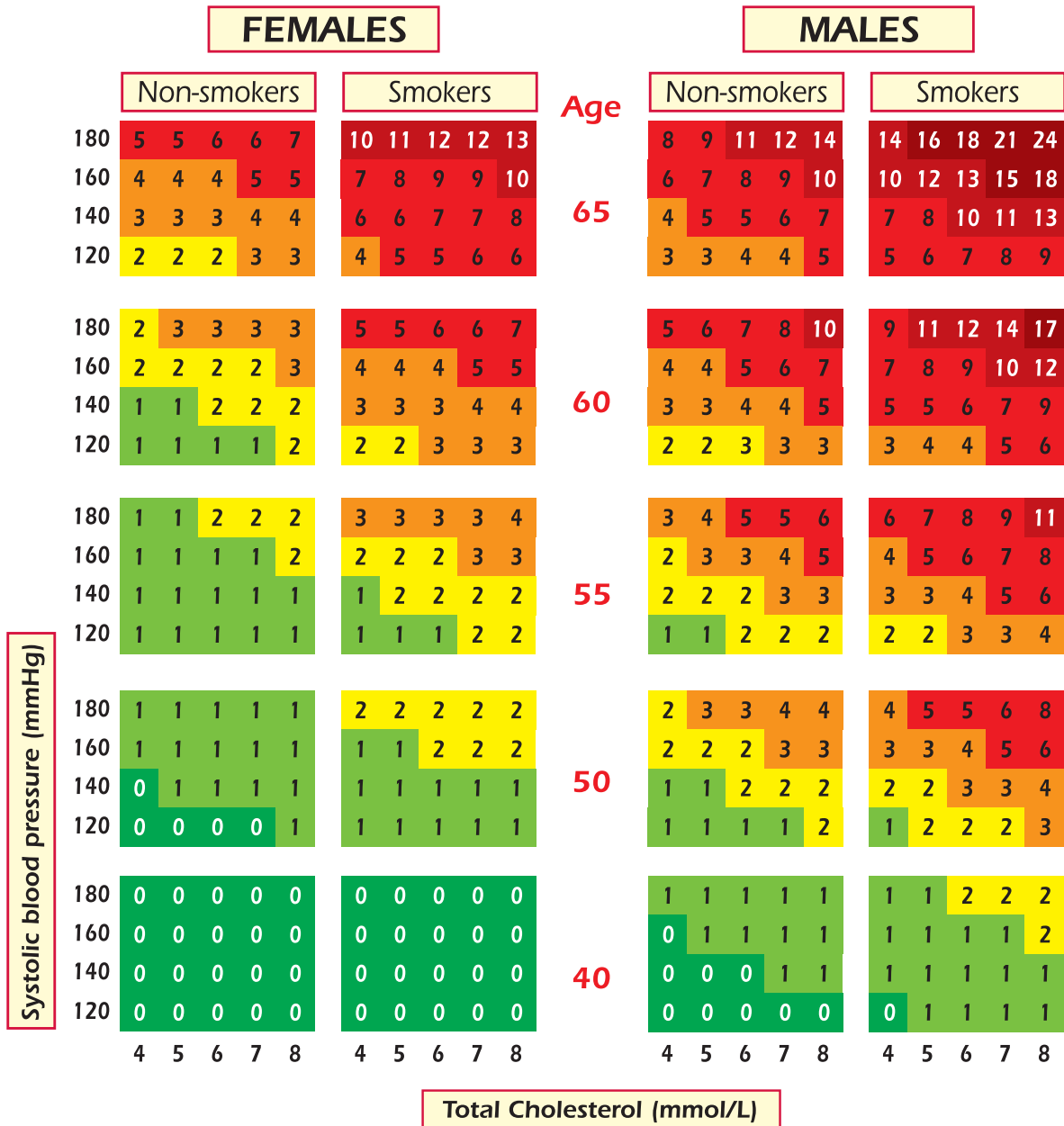
Addendum IV. Additional references (given by sections of the Table of contents of the Guidelines)

1. Preamble
2. Introduction
  - 2.1 Scope of the problem
  - 2.2 Dyslipidaemias
3. Total cardiovascular risk
  - 3.1 Total cardiovascular risk estimation
  - 3.2 Risk levels
4. Evaluation of laboratory lipid and apolipoprotein parameters
5. Treatment targets
6. Lifestyle modifications to improve the plasma lipid profile
  - 6.1 The influence of lifestyle on total cholesterol and low-density lipoprotein-cholesterol levels
  - 6.2 The influence of lifestyle on triglyceride levels
  - 6.3 The influence of lifestyle on high-density lipoprotein-cholesterol levels
  - 6.4 Dietary supplements and functional foods active on plasma lipid values
  - 6.5 Lifestyle recommendations
7. Drugs for treatment of hypercholesterolaemia
  - 7.1 Statins
  - 7.2 Bile acid sequestrants
  - 7.3 Cholesterol absorption inhibitors
  - 7.4 Nicotinic acid
  - 7.5 Drug combinations
    - 7.5.1 Statins and bile acid sequestrants
    - 7.5.2 Statins and cholesterol absorption inhibitors
    - 7.5.3 Other combinations
  - 7.6 Low-density lipoprotein apheresis
  - 7.7 Future perspectives
8. Drugs for treatment of hypertriglyceridaemia
  - 8.1 Management of hypertriglyceridaemia
  - 8.2 Fibrates
  - 8.3 Nicotinic acid
  - 8.4 *n*-3 fatty acids
  - 8.5 Drug combinations
    - 8.5.1 Statins and fibrates
    - 8.5.2 Statins and nicotinic acid
    - 8.5.3 Statins and *n*-3 fatty acids
9. Drugs affecting high-density lipoprotein
  - 9.1 Statins
  - 9.2 Fibrates
  - 9.3 icotinic acid
  - 9.4 Cholesterylester transfer protein inhibitors
  - 9.5 Future perspectives
10. Management of dyslipidaemias in different clinical settings
  - 10.1 Familial dyslipidaemias
    - 10.1.1 Familial combined hyperlipidaemia
    - 10.1.2 Familial hypercholesterolaemia
    - 10.1.3 Familial dysbetalipoproteinaemia
    - 10.1.4 Familial lipoprotein lipase deficiency
    - 10.1.5 Other genetic disorders of lipoprotein metabolism
  - 10.2 Children
  - 10.3 Women
  - 10.4 The elderly
  - 10.5 Metabolic syndrome and diabetes
  - 10.6 Patients with acute coronary syndrome and patients undergoing percutaneous coronary intervention
  - 10.7 Heart failure and valvular disease
  - 10.8 Autoimmune diseases
  - 10.9 Renal disease
  - 10.10 Transplantation patients
  - 10.11 Peripheral arterial disease
  - 10.12 Stroke
  - 10.13 Human immunodeficiency virus patients
11. Monitoring of lipids and enzymes in patients on lipid-lowering drug therapy
12. How to improve adherence to lifestyle changes and compliance with drug therapy

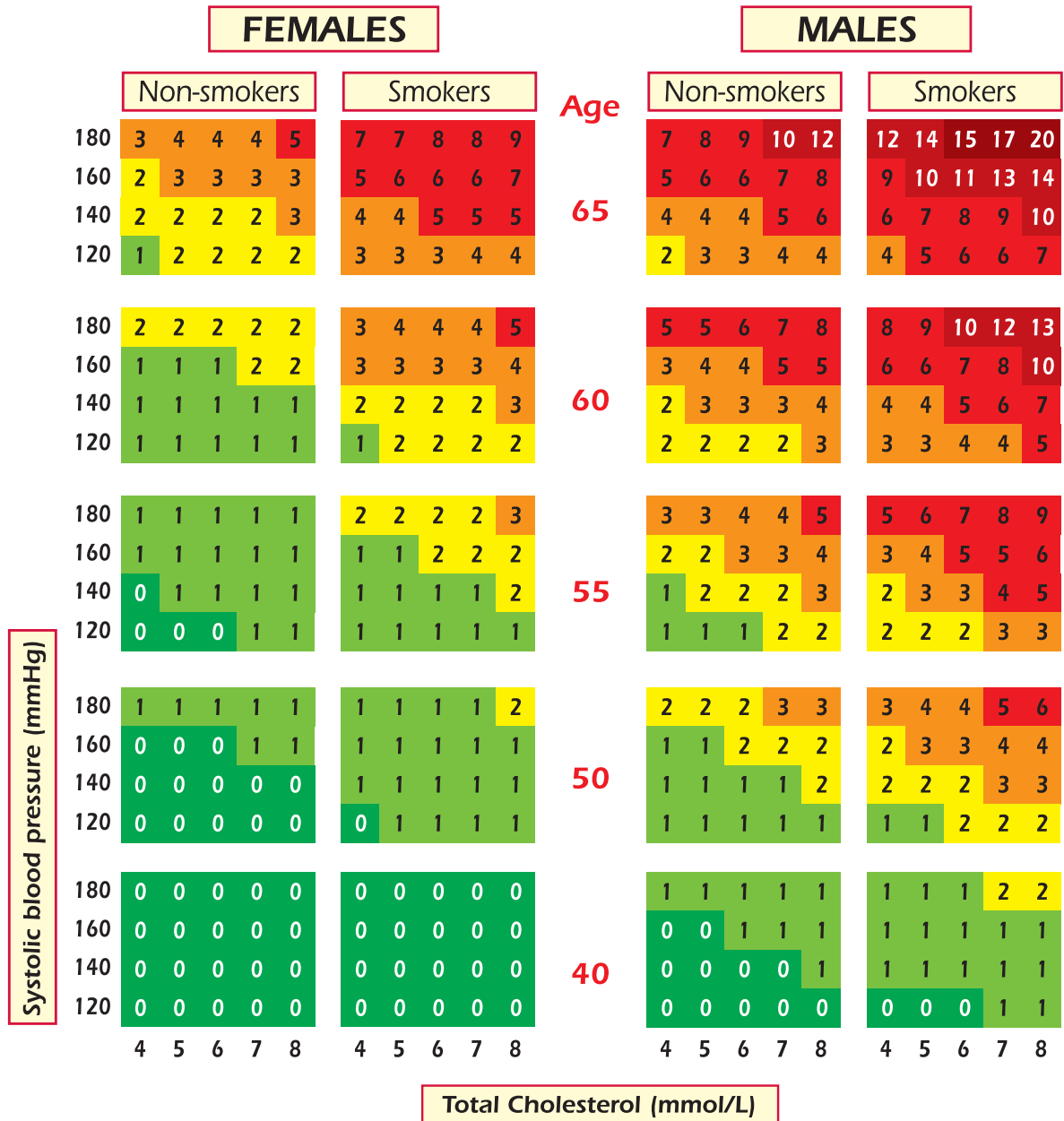
## Addendum I. SCORE charts with high-density lipoprotein-cholesterol included



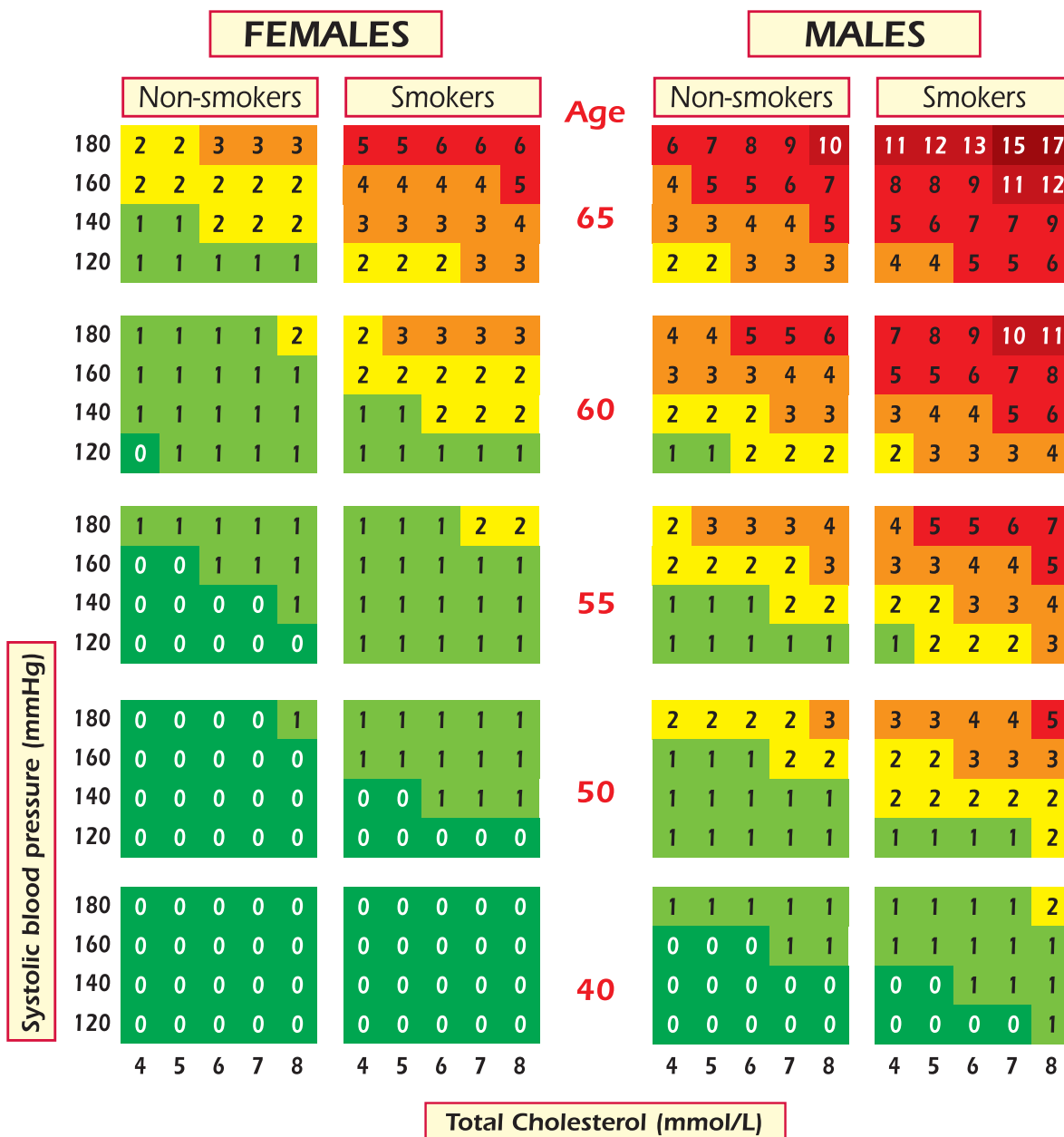
SCORE chart for use in low risk regions - HDL 0.8 mmol/L



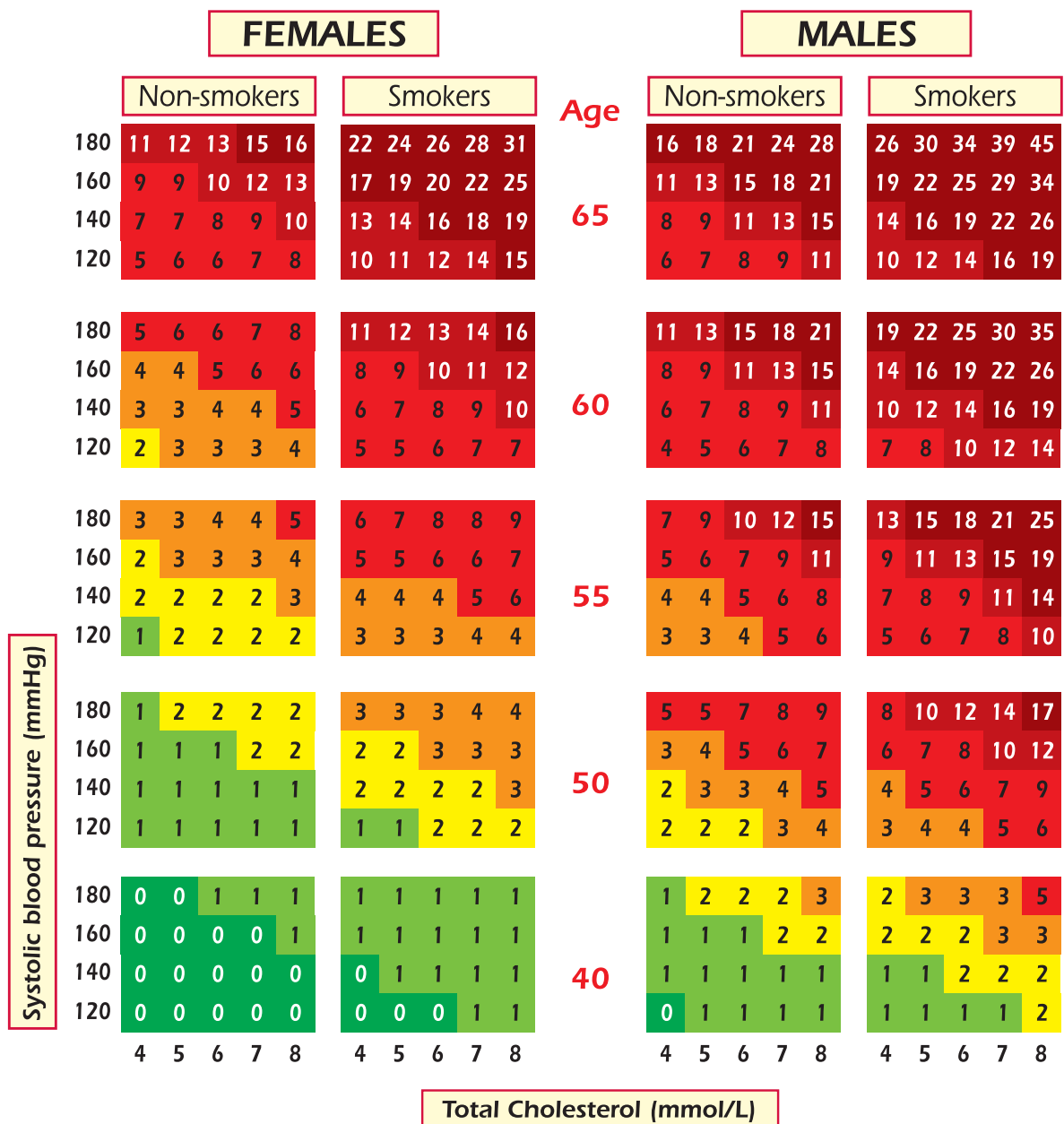
SCORE chart for use in low risk regions - HDL 1.0 mmol/L



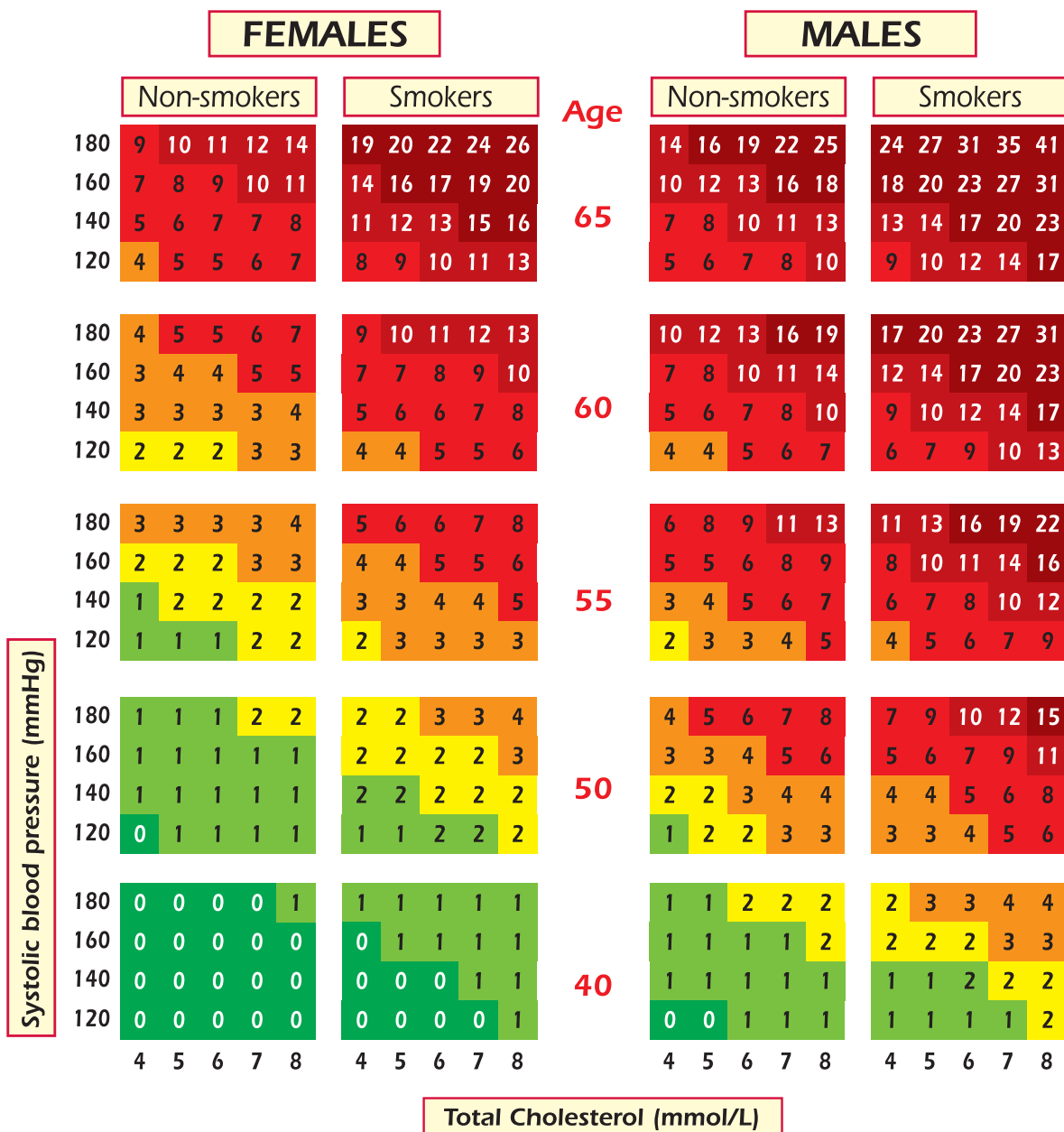
SCORE chart for use in low risk regions - HDL 1.4 mmol/L



SCORE chart for use in low risk regions - HDL 1.8 mmol/L

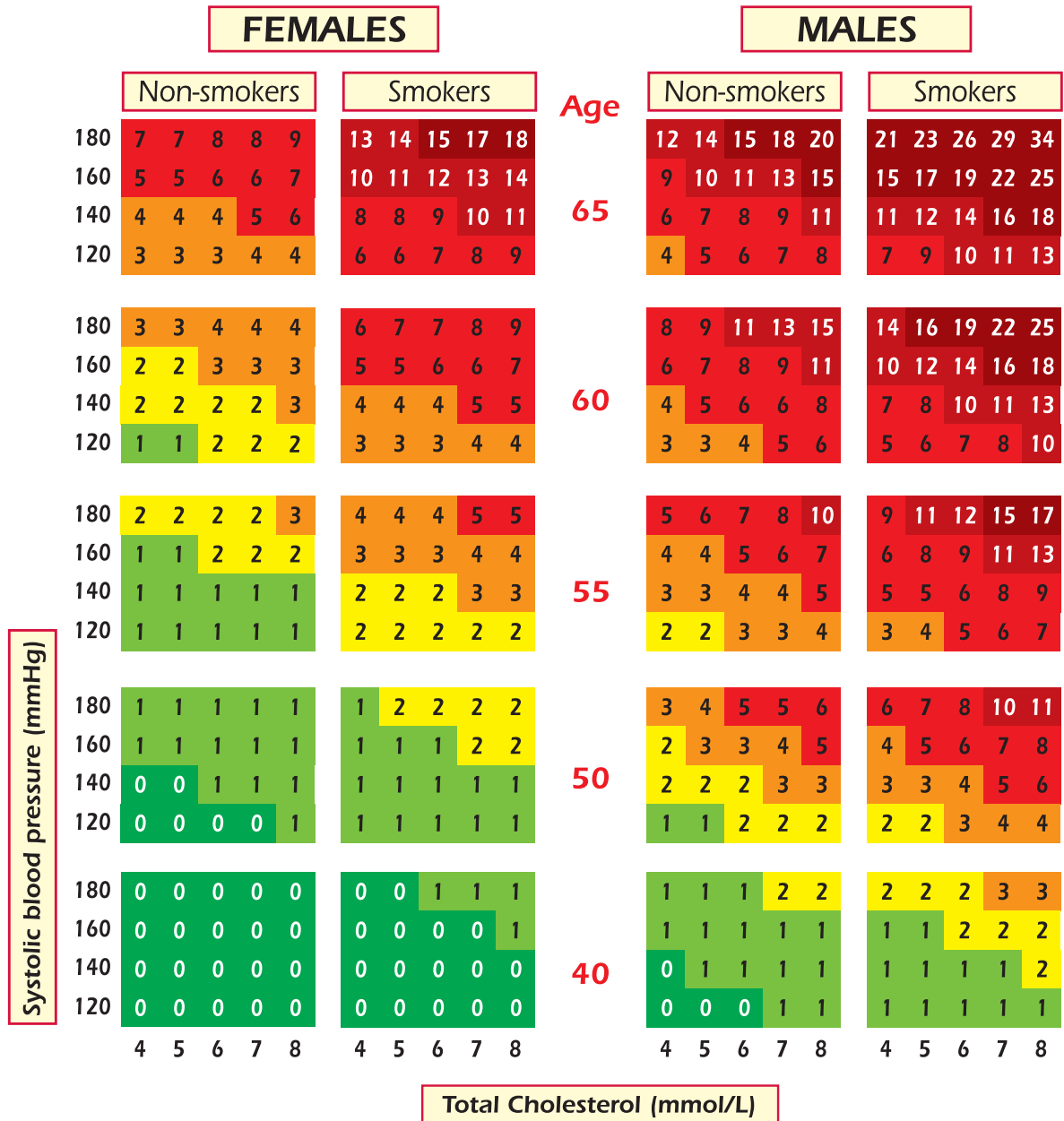


SCORE chart for use in high risk regions - HDL 0.8 mmol/L

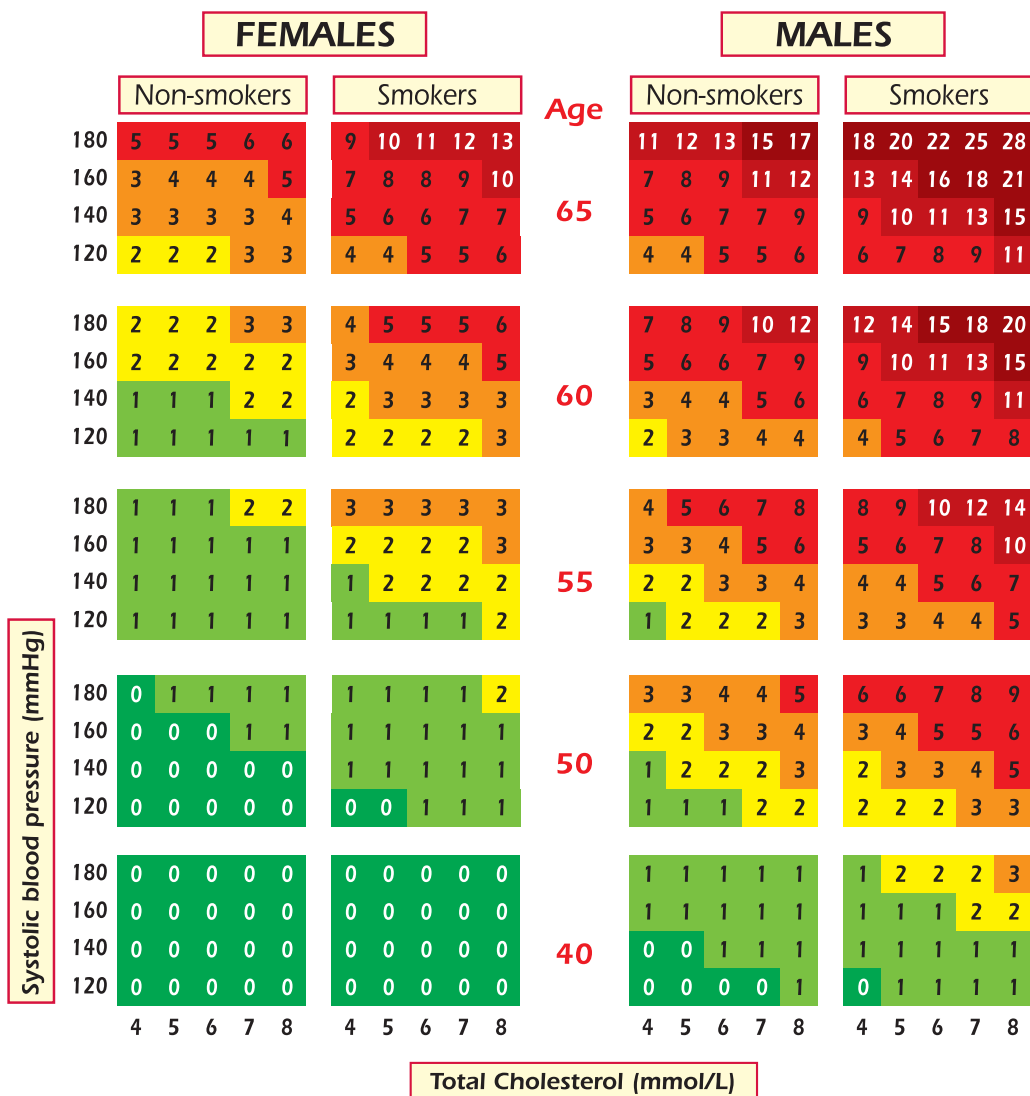


SCORE chart for use in high risk regions - HDL 1.0 mmol/L





SCORE chart for use in high risk regions - HDL 1.4 mmol/L



SCORE chart for use in high risk regions - HDL 1.8 mmol/L

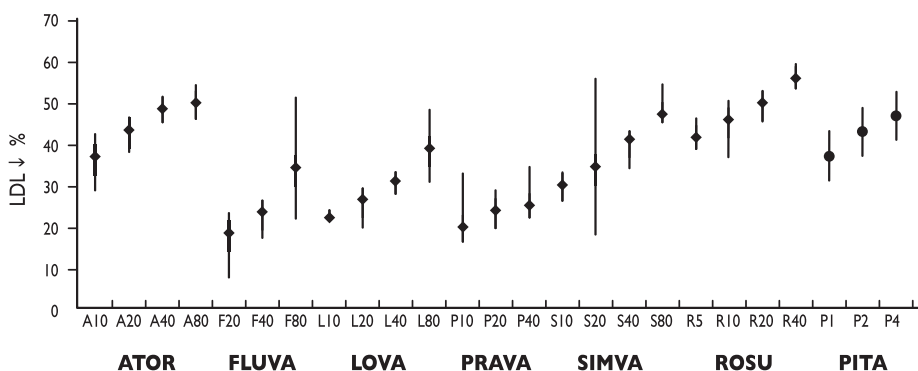
## Addendum II. Practical approach to reach low-density lipoprotein-cholesterol goal

The proposed approach requires the estimation of the distance from the target that can easily be obtained by the use of the following table. Once the distance from a target is determined, then by interpolation the average response to a statin can be determined and the drugs that can help in reaching that target identified from the figure.

Intolerance to a statin, clinical conditions of the patient, and possible interactions with concomitant drugs should also be taken in account.

**Table** Percentage reduction of LDL-C requested to achieve goals as a function of the starting value

STARTING LDL-C		% REDUCTION TO REACH LDL-C		
mmol/L	~mg/dL	<1.8 mmol/L (~70 mg/dL)	<2.5 mmol/L (~100 mg/dL)	<3 mmol/L (~115 mg/dL)
>6.2	>240	>70	>60	>55
5.2-6.2	200-240	65-70	50-60	40-55
4.4-5.2	170-200	60-65	40-50	30-45
3.9-4.4	150-170	55-60	35-40	25-30
3.4-3.9	130-150	45-55	25-35	10-25
2.9-3.4	110-130	35-45	10-25	<10
2.3-2.9	90-110	22-35	<10	-
1.8-2.3	70-90	<22	-	-



Weng TC, et al. *J Clin Pharm Ther*. 2010;35:139-151  
 Mukhtar RY, et Al. *Int J Clin Pract*. 2005;59(2):239-252

**Figure** A systematic review and meta-analysis on the therapeutic equivalence of statins.

## Addendum III. Inhibitors and inducers of enzymatic pathways involved in statin metabolism

For more information, see US FDA website with information for health professionals (drugs): [www.fda.gov/Drugs/ResourcesFor You/HealthProfessionals/default.htm](http://www.fda.gov/Drugs/ResourcesForYou/HealthProfessionals/default.htm)

<b>CYP substrates</b>	<b>Inhibitors</b>	<b>Inducers</b>
CYP3A4 Atorvastatin, lovastatin, simvastatin	Ketoconazole, itraconazole, fluconazole, erythromycin, clarithromycin, tricyclic antidepressants, nefazodone, venlafaxine, fluvoxamine, fluoxetine, sertraline, cyclosporin A, tacrolimus, mibefradil, amiodarone, danazol, diltiazem, verapamil, protease inhibitors, midazolam, corticosteroids, grapefruit juice, tamoxifen	Phenytoin, phenobarbital, barbiturates, rifampin, dexamethasone, cyclophosphamide, carbamazepine, omeprazole, St John's Wort
CYP2C9 Fluvastatin, rosuvastatin, pitavastatin	Ketoconazole, fluconazole, amiodarone, sulfaphenazole, oxandrolone, dronedarone, warfarin	Rifampicin, phenobarbital, phenytoin
<b>Transporter protein substrates</b>	<b>Inhibitors</b>	<b>Inducers</b>
MDR/P-gp Atorvastatin, lovastatin, pravastatin, simvastatin, pitavastatin	Ritonavir, ciclosporin, verapamil, erythromycin, ketoconazole, itraconazole, quinidine, elacridar	Rifampicin, St John's Wort
OATP1B1 All statins	Ciclosporin, rifampicin, gemfibrozil, gemfibrozil-O-glucuronide, clarithromycin, erythromycin, roxithromycin, telithromycin, indinavir, ritonavir, saquinavir	
<b>UGT substrates</b>	<b>Inhibitors</b>	<b>Inducers</b>
Atorvastatin, lovastatin, pravastatin, simvastatin	Gemfibrozil, ciclosporin	Rifampicin

## Addendum IV. Additional references

References in addition to those listed in the full text document of the ESC/EAS Guidelines on the management of dyslipidaemias.

These additional references are given by section.

1. Preamble
2. Introduction

No additional references

3. Total cardiovascular risk

- Ankle Brachial Index Collaboration, Fowkes FG, Murray GD, Butcher I, Heald CL, Lee RJ, Chambless LE, Folsom AR, Hirsch AT, Dramaix M, DeBacker G, Wautrecht JC, Kornitzer M, Newman AB, Cushman M, Sutton-Tyrrell K, Fowkes FG, Lee AJ, Price JF, d'Agostino RB, Murabito JM, Norman PE, Jamrozik K, Curb JD, Masaki KH, Rodriguez BL, Dekker JM, Bouter LM, Heine RJ, Nijpels G, Stehouwer CD, Ferrucci L, McDermott MM, Stoffers HE, Hooi JD, Knottnerus JA, Ogren M, Hedblad B, Witteman JC, Breteler MM, Hunink MG, Hofman A, Criqui MH, Langer RD, Fronck A, Hiatt WR, Hamman R, Resnick HE, Guralnik J, McDermott MM. Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: a meta-analysis. *JAMA* 2008;**300**:197–208.
- Stein JH, Korcarz CE, Hurst RT, Lonn E, Kendall CB, Mohler ER, Najjar SS, Rembold CM, Post WS; American Society of Echocardiography Carotid Intima-Media Thickness Task Force. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force. Endorsed by the Society for Vascular Medicine. *J Am Soc Echocardiogr* 2008;**21**:93–111.
- Miller JM, Rochitte CE, Dewey M, Arbab-Zadeh A, Niinuma H, Gottlieb I, Paul N, Clouse ME, Shapiro EP, Hoe J, Lardo AC, Bush DE, de Roos A, Cox C, Brinker J, Lima JA. Diagnostic performance of coronary angiography by 64-row CT. *N Engl J Med* 2008;**359**:2324–2336.
- Aktas MK, Ozduran V, Pothier CE, Lang R, Lauer MS. Global risk scores and exercise testing for predicting all-cause mortality in a preventive medicine program. *JAMA* 2004;**292**:1462–1468.
- Catapano AL, Pedersen TR, De Backer G. Averting a pandemic health crisis in Europe by 2020: what physicians need to know regarding cholesterol management. *Eur J Cardiovasc Prev Rehabil* 2007;**14**:340–345.
- Vartiainen E, Jousilahti P, Alftan G, Sundvall J, Pietinen P, Puska P. Cardiovascular risk factor changes in Finland, 1972–1997. *Int J Epidemiol* 2000;**29**:49–56.
- Wilson P, Pencina M, Jacques P, Selhub J, D'Agostino R, O'Donnell. C-reactive protein and reclassification of cardiovascular risk in the Framingham Heart Study. *Circ Cardiovasc Qual Outcomes* 2008;**1**:92–97.

4. Evaluation of laboratory lipid and apolipoprotein parameters

- Ridker PM, Rifai N, Cook NR, Bradwin G, Buring JE. Non-HDL cholesterol, apolipoproteins A-I and B100, standard lipid measures, lipid ratios, and CRP as risk factors for cardiovascular disease in women. *JAMA* 2005;**294**:326–333.
- Gotto AM Jr. Triglyceride as a risk factor for coronary artery disease. *Am J Cardiol* 1998;**82**:22Q–25Q.
- Ridker PM. Fasting versus nonfasting triglycerides and the prediction of cardiovascular risk: do we need to revisit the oral triglyceride tolerance test? *Clin Chem* 2008;**54**:11–13.
- Abdel-Maksoud MF, Hokanson JE. The complex role of triglycerides in cardiovascular disease. *Semin Vasc Med* 2002;**2**:325–333.
- Briel M, Ferreira-Gonzalez I, You JJ, Karanicolos PJ, Akl EA, Wu P, Blechacz B, Bassler D, Wei X, Sharmar A, Whitt I, Alves da Silva S, Khalid Z, Nordmann AJ, Zhou Q, Walter SD, Vale N, Bhatnagar N, O'Regan C, Mills EJ, Bucher HC, Montori VM, Guyatt GH. Association between change in high density lipoprotein cholesterol and cardiovascular disease morbidity and mortality: systematic review and meta-regression analysis. *BMJ* 2009;**338**:b92.
- Barter PJ, Ballantyne CM, Carmena R, Castro Cabezas M, Chapman MJ, Couture P, de Graaf J, Durrington PN, Faergeman O, Frohlich J, Furberg CD, Gagne C, Haffner SM, Humphries SE, Jungner I, Krauss RM, Kwitterovich P, Marcovina S, Packard CJ, Pearson TA, Reddy KS, Rosenson R, Sarrafzadegan N, Sniderman AD, Stalenhoef AF, Stein E, Talmud PJ, Tonkin AM, Walldius G, Williams KM. Apo B versus cholesterol in estimating cardiovascular risk and in

guiding therapy: report of the thirty-person/ten-country panel. *J Intern Med* 2006;**259**:247–258.

- van der Steeg WA, Boekholdt SM, Stein EA, El-Harchaoui K, Stroes ES, Sandhu MS, Wareham NJ, Jukema JW, Luben R, Zwiderman AH, Kastelein JJ, Khaw KT. Role of the apolipoprotein B–apolipoprotein A-I ratio in cardiovascular risk assessment: a case–control analysis in EPIC-Norfolk. *Ann Intern Med* 2007;**146**:640–648.
- Langlois MR, Blaton VH. Historical milestones in measurement of HDL-cholesterol: impact on clinical and laboratory practice. *Clin Chim Acta* 2006;**369**:168–178.
- Nazir DJ, Roberts RS, Hill SA, McQueen MJ. Monthly intra-individual variation in lipids over a 1-year period in 22 normal subjects. *Clin Biochem* 1999;**32**:381–389.
- Hellerud C, Burlina A, Gabelli C, Ellis JR, Nyholm PG, Lindstedt S. Glycerol metabolism and the determination of triglycerides—clinical, biochemical and molecular findings in six subjects. *Clin Chem Lab Med* 2003;**41**:46–55.
- Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 1972;**18**:499–502.
- Wilder LB, Bachorik PS, Finney CA, Moy TF, Becker DM. The effect of fasting status on the determination of low-density and high-density lipoprotein cholesterol. *Am J Med* 1995;**99**:374–377.
- Bachorik PS, Ross JW. National Cholesterol Education Program recommendations for measurement of low-density lipoprotein cholesterol: executive summary. The National Cholesterol Education Program Working Group on Lipoprotein Measurement. *Clin Chem* 1995;**41**:1414–1420.
- Nauck M, Warnick GR, Rifai N. Methods for measurement of LDL-cholesterol: a critical assessment of direct measurement by homogeneous assays versus calculation. *Clin Chem* 2002;**48**:236–254.
- Benn M, Nordestgaard BG, Jensen GB, Tybjaerg-Hansen A. Improving prediction of ischemic cardiovascular disease in the general population using apolipoprotein B: the Copenhagen City Heart Study. *Arterioscl Thromb Vasc Biol* 2007;**27**:661–670.
- Warnick GR, Nauck M, Rifai N. Evolution of methods for measurement of HDL-cholesterol: from ultracentrifugation to homogeneous assays. *Clin Chem* 2001;**47**:1579–1596.
- Marcovina S, Packard CJ. Measurement and meaning of apolipoprotein AI and apolipoprotein B plasma levels. *J Intern Med* 2006;**259**:437–446.
- Ritchie RF, Palomaki GE, Neveux LM, Ledue TB, Craig WY, Marcovina S, Navolotskaia O. Reference distributions for apolipoproteins AI and B and the apolipoprotein B/AI ratios: a practical and clinically relevant approach in a large cohort. *J Clin Lab Anal* 2006;**20**:209–217.
- Ritchie RF, Palomaki GE, Neveux LM, Ledue TB, Marcovina S, Navolotskaia O. Reference distributions for apolipoproteins AI and B and B/AI ratios: comparison of a large cohort to the world's literature. *J Clin Lab Anal* 2006;**20**:218–226.
- Walldius G, Jungner I. The apoB/apoA-I ratio: a strong, new risk factor for cardiovascular disease and a target for lipid-lowering therapy – a review of the evidence. *J Intern Med* 2006;**259**:493–519.
- Thompson A, Danesh J. Associations between apolipoprotein B, apolipoprotein AI, the apolipoprotein B/AI ratio and coronary heart disease: a literature-based meta-analysis of prospective studies. *J Intern Med* 2006;**259**:481–492.
- McQueen MJ, Hawken S, Wang X, Ounpuu S, Sniderman A, Probstfield J et al. Lipids, lipoproteins, and apolipoproteins as risk markers of myocardial infarction in 52 countries (the INTERHEART study): a case–control study. *Lancet* 2008;**372**:224–233.
- Sniderman AD. The apoB/apoA-I ratio and insulin resistance: sorting out the metabolic syndrome. *Eur Heart J* 2007;**28**:2563–2564.
- Sniderman AD, Faraj M. Apolipoprotein B, apolipoprotein A-I, insulin resistance and the metabolic syndrome. *Curr Opin Lipid* 2007;**18**:633–637.
- Sniderman AD, Hogue JC, Bergeron J, Gagne C, Couture P. Non-HDL cholesterol and apoB in dyslipidaemia. *Clin Sci (Lond)* 2008;**114**:149–155.
- Sniderman AD, Marcovina SM. Apolipoprotein A1 and B. *Clin Lab Med* 2006;**26**:733–750.
- Kastelein JJ, van der Steeg WA, Holme I, Gaffney M, Cater NB, Barter P, Deedwania P, Olsson AG, Boekholdt SM, Demicco DA, Szarek M, LaRosa JC, Pedersen TR, Grundy SM; TNT Study Group; IDEAL Study Group. Lipids, apolipoproteins, and their ratios in relation to cardiovascular events with statin treatment. *Circulation* 2008;**117**:3002–3009.
- Kamstrup PR, Tybjaerg-Hansen A, Steffensen R, Nordestgaard BG. Genetically elevated lipoprotein(a) and increased risk of myocardial infarction. *JAMA* 2009;**301**:2331–2339.
- Anuurad E, Boffa MB, Koschinsky ML, Berglund L. Lipoprotein(a): a unique risk factor for cardiovascular disease. *Clin Lab Med* 2006;**26**:751–772.
- Berglund L, Anuurad E. Role of lipoprotein(a) in cardiovascular disease current and future perspectives. *J Am Coll Cardiol* 2008;**52**:132–134.
- Berglund L, Ramakrishnan R. Lipoprotein(a): an elusive cardiovascular risk factor. *Arterioscler Thromb Vasc Biol* 2004;**24**:2219–2226.
- El Harchaoui K, van der Steeg WA, Stroes ES, Kuivenhoven JA, Otvos JD, Wareham NJ et al. Value of low-density lipoprotein particle number and size as

- predictors of coronary artery disease in apparently healthy men and women: the EPIC-Norfolk Prospective Population Study. *J Am Coll Cardiol* 2007;**49**:547–553.
- St-Pierre AC, Cantin B, Dagenais GR, Mauriege P, Bernard PM, Despres JP, Hutten BA, Kastelein JJ, Khaw KT, Boekholdt SM. Low-density lipoprotein subfractions and the long-term risk of ischemic heart disease in men: 13-year follow-up data from the Quebec Cardiovascular Study. *Arterioscler Thromb Vasc Biol* 2005;**25**:553–559.
  - Koba S, Hirano T, Ito Y, Tsunoda F, Yokota Y, Ban Y, Iso Y, Suzuki H, Katagiri T. Significance of small dense low-density lipoprotein-cholesterol concentrations in relation to the severity of coronary heart diseases. *Atherosclerosis* 2006;**189**: 206–214.
  - Kathiresan S, Otvos JD, Sullivan LM, Keyes MJ, Schaefer EJ, Wilson PW, D'Agostino RB, Vasani RS, Robins SJ. Increased small low-density lipoprotein particle number: a prominent feature of the metabolic syndrome in the Framingham Heart Study. *Circulation* 2006;**113**:20–29.
  - Humphries SE, Norbury G, Leigh S, Hadfield SG, Nair D. What is the clinical utility of DNA testing in patients with familial hypercholesterolaemia? *Curr Opin Lipid* 2008;**19**:362–368.
  - Janssens AC, Aulchenko YS, Elefante S, Borsboom GJ, Steyerberg EW, van Duijn CM. Predictive testing for complex diseases using multiple genes: fact or fiction? *Genet Med* 2006;**8**:395–400.
  - Sarwar N, Danesh J, Eiriksdottir G, Sigurdsson G, Wareham N, Bingham S, Boekholdt SM, Khaw KT, Gudnason V. Triglycerides and the risk of coronary heart disease: 10,158 incident cases among 262,525 participants in 29 Western prospective studies. *Circulation* 2007;**115**:450–458.
- ## 5. Treatment targets
- Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, Kirby A, Sourjina T, Peto R, Collins R, Simes R; Cholesterol Treatment Trialists' (CTT) Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet* 2005;**366**:1267–1278.
  - Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002;**106**:3143–3421.
  - Brunzell JD, Davidson M, Furberg CD, Goldberg RB, Howard BV, Stein JH, Witztum JL. Lipoprotein management in patients with cardiometabolic risk: consensus conference report from the American Diabetes Association and the American College of Cardiology Foundation. *J Am Coll Cardiol* 2008;**51**:1512–1524.
  - Sniderman A, Solhpour A. Targeting targets for LDL-lowering therapy: lessons from the Collaborative Atorvastatin Diabetes Study (CARDS). *Clin Chem* 2009;**55**:391–393.
  - Gotto AM Jr. Establishing the benefit of statins in low- to-moderate-risk primary prevention: the Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS). *Atheroscler Suppl* 2007;**8**:3–8.
- ## 6. Lifestyle modifications to improve the plasma lipid profile
- Shaefer EJ. Lipoproteins, nutrition and heart disease. *Am J Clin Nutr* 2002;**75**: 191–212.
  - Keys A, Mickelsen O, Miller EO, Chapman CB. The relation in man between cholesterol levels in the diet and in the blood. *Science* 1950;**112**:79–81.
  - Denke MA. Dietary fats, fatty acids, and their effects on lipoproteins. *Curr Atheroscler Rep* 2006;**8**:466–471.
  - Lichtenstein AH. Thematic review series: patient-oriented research. Dietary fat, carbohydrate, and protein: effects on plasma lipoprotein patterns. *J Lipid Res* 2006;**47**:1661–1667.
  - Mensink RP. Effects of stearic acid on plasma lipid and lipoproteins in humans. *Lipids* 2005;**40**:1201–1205.
  - Connor WE, De Francesco CA, Connor SL. n-3 fatty acids from fish oil. Effects on plasma lipoproteins and hypertriglyceridemic patients. *Ann NY Acad Sci* 1993;**683**: 16–34.
  - Shekelle RB, Stamler J. Dietary cholesterol and ischaemic heart disease. *Lancet* 1989;**1**:1177–1179.
  - Ye SQ Jr., Kwiterovich PO Jr. Influence of genetic polymorphisms on responsiveness to dietary fat and cholesterol. *Am J Clin Nutr* 2000;**72**:p1275S–1284S.
  - Riccardi G, Rivellese AA. Dietary treatment of the metabolic syndrome: the optimal diet. *Br J Nutr* 2000;**83**:S143–S148.
  - Myers J. Exercise and cardiovascular health. *Circulation* 2003;**107**:E2–E5.
  - Riccardi G, Aggett P, Brighenti F, Delzenne N, Frayn K, Nieuwenhuizen A, Pannemans D, Theis S, Tuijelaars S, Vessby B. PASSCLAIM—body weight regulation, insulin sensitivity and diabetes risk. *Eur J Nutr* 2004;**43**(Suppl 2):I17–I146.
  - Chan DC, Watts GF, Ng TW, Yamashita S, Barrett PH. Effect of weight loss on markers of triglyceride-rich lipoprotein metabolism in the metabolic syndrome. *Eur J Clin Invest* 2008;**38**:743–751.
  - Riccardi G, Giacco R, Rivellese AA. Dietary fat, insulin sensitivity and the metabolic syndrome. *Clin Nutr* 2004;**23**:447–456.
  - Rivellese AA, Giacco R, Annuzzi G, De Natale C, Patti L, Di Marino L, Minerva V, Costabile G, Santangelo C, Masella R, Riccardi G. Effects of monounsaturated vs. saturated fat on postprandial lipemia and adipose tissue lipases in type 2 diabetes. *Clin Nutr* 2008;**27**:133–141.
  - Riccardi G, Rivellese AA, Giacco R. Role of glycemic index and glycemic load in the healthy state, in prediabetes, and in diabetes. *Am J Clin Nutr* 2008;**87**:269S–274S.
  - Mann JI, Cummings JH, Englyst HN, Key T, Liu S, Riccardi G, Summerbell G, Uauy R, van Dam RM, Venn B, Vorster HH, Wiseman M. FAO/WHO Scientific Update on carbohydrates in human nutrition: conclusions. *Eur J Clin Nutr* 2007;**61**(Suppl 1):S132–S137.
  - Stanhope KL, Havel PJ. Fructose consumption: considerations for future research on its effects on adipose distribution, lipid metabolism, and insulin sensitivity in humans. *J Nutr* 2009;**139**:1236S–1241S.
  - Hollenbeck CB. Dietary fructose effects on lipoprotein metabolism and risk for coronary artery disease. *Am J Clin Nutr* 1993;**58**(5 Suppl):800S–809S.
  - Taskinen MR, Nikkilä EA, Välimäki M, Sane T, Kuusi T, Kesäniemi A, Ylikahri R. Alcohol-induced changes in serum lipoproteins and in their metabolism. *Am Heart J* 1987;**113**:458–464.
  - Rivellese AA, Iovine C, Ciano O, Costagliola L, Galasso R, Riccardi G, Vaccaro O. Nutrient determinants of postprandial triglyceride response in a population-based sample of type II diabetic patients. *Eur J Clin Nutr* 2006;**60**:1168–1173.
  - Annuzzi G, De Natale C, Iovine C, Patti L, Di Marino L, Coppola S, Del Prato S, Riccardi G, Rivellese AA. Insulin resistance is independently associated with postprandial alterations of triglyceride-rich lipoproteins in type 2 diabetes mellitus. *Arterioscler Thromb Vasc Biol* 2004;**24**:2397–2402.
  - Iovine C, Gentile A, Hattemer A, Pacioni D, Riccardi G, Rivellese AA. Self-monitoring of plasma triglyceride levels to evaluate postprandial response to different nutrients. *Metabolism* 2004;**53**:620–623.
  - Rivellese AA, Maffettone A, Vessby B, Uusitupa M, Hermansen K, Berglund L, Louheranta A, Meyer BJ, Riccardi G. Effects of dietary saturated, monounsaturated and n-3 fatty acids on fasting lipoproteins, LDL size and post-prandial lipid metabolism in healthy subjects. *Atherosclerosis* 2003;**167**:149–158.
  - Ford ES, Liu S. Glycemic index and serum high-density lipoprotein cholesterol concentration among US adults. *Arch Intern Med* 2001;**161**:572–576.
  - Bellisle F, Diplock AT, Hornstra G, Koletzko B, Roberfroid M, Salminen S, Saris WHM. Functional food science in Europe. *Br J Nutr* 1998;**80**(Suppl 1):S3–S4.
  - Rudkowska I, Jones PJ. Functional foods for the prevention and treatment of cardiovascular diseases: cholesterol and beyond. *Expert Rev Cardiovasc Ther* 2007;**5**: 477–490.
  - Plat J, Mensink RP. Plant stanol and sterol esters in the control of blood cholesterol levels: mechanism and safety aspects. *Am J Cardiol* 2005;**96**:15D–22D.
  - Ostlund RE Jr. Phytosterols and cholesterol metabolism. *Curr Opin Lipidol* 2004;**15**: 37–41.
  - Tikkanen MJ. Plant sterols and stanols. *Handb Exp Pharmacol* 2005;**170**:215–230.
  - Anderson JW, Johnstone BM, Cook-Newell ME. Meta-analysis of the effects of soy protein intake on serum lipids. *N Engl J Med* 1995;**333**:276–282.
  - Reiner Z, Tedeschi-Reiner E. Rice policosanols does not have any effects on blood coagulation factors in hypercholesterolemic patients. *Coll Antropol* 2007;**31**:315–319.
  - Berthold HK, Unverdorben S, Degenhardt R, Bulitta M, Gouni-Berthold I. Effect of policosanols on lipid levels among patients with hypercholesterolemia or combined hyperlipidemia: a randomized controlled trial. *JAMA* 2006;**295**:2262–2269.
  - Lichtenstein AH, Appel LJ, Brands M, Carnethon M, Daniels S, Franch HA, Franklin B, Kris-Etherton P, Harris WS, Howard B, Karanja N, Lefevre M, Rudel L, Sacks F, Van Horn L, Winston M, Wylie-Rosett J. Diet and lifestyle recommendations revision 2006: a scientific statement from the American Heart Association Nutrition Committee. *Circulation* 2006;**114**:82–96.
  - Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002;**346**:393–403.
  - Orchard TJ, Temprosa M, Goldberg R, Haffner S, Ratner R, Marcovina S, Fowler S; Diabetes Prevention Program Research Group. The effect of metformin and intensive lifestyle intervention on the metabolic syndrome: the Diabetes Prevention Program randomized trial. *Ann Intern Med* 2005;**142**:611–619.
  - Rydén L, Standl E, Bartnik M, Van den Bergh G, Betteridge J, de Boer MJ, Cosentino F, Jönsson B, Laakso M, Malmberg K, Puri S, Ostergren J, Tuomilehto J, Thrainsdottir I, Vanhorebeek I, Stramba-Badiale M, Lindgren P, Qiao Q, Priori SG, Blanc JJ, Budaj A, Camm J, Dean V, Deckers J, Dickstein K, Lekakis J, McGregor K, Metra M, Morais J, Osterspey A, Tamargo J, Zamorano JL, Deckers JW, Bertrand M, Charbonnel B, Erdmann E,

- Ferrannini E, Flyvbjerg A, Gohlke H, Juanatey JR, Graham I, Monteiro PF, Parhofer K, Pyörälä K, Raz I, Scherthaner G, Volpe M, Wood D; Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC); European Association for the Study of Diabetes (EASD). Guidelines on diabetes, pre-diabetes, and cardiovascular diseases: executive summary. The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD). *Eur Heart J* 2007;**28**:88–136.
- Poli A, Marangoni F, Paoletti R, Mannarino E, Lupattelli G, Notarbartolo A, Aureli P, Bernini F, Cicero A, Gaddi A, Catapano A, Cricelli C, Gattone M, Marrocco W, Porrini M, Stella R, Vanotti A, Volpe M, Volpe R, Cannella C, Pinto A, Del Toma E, La Vecchia C, Tavani A, Manzato E, Riccardi G, Sirtori C, Zambon A; Nutrition Foundation of Italy. Non-pharmacological control of plasma cholesterol levels. *Nutr Metab Cardiovasc Dis* 2008;**18**:S1–S16.
  - Kris-Etherton P, Daniels SR, Eckel RH, Engler M, Howard BV, Krauss RM, Lichtenstein AH, Sacks F, St Jeor S, Stampfer M, Eckel RH, Grundy SM, Appel LJ, Byers T, Campos H, Cooney G, Denke MA, Howard BV, Kennedy E, Krauss RM, Kris-Etherton P, Lichtenstein AH, Marckmann P, Pearson TA, Riccardi G, Rudel LL, Rudrum M, Sacks F, Stein DT, Tracy RP, Ursin V, Vogel RA, Zock PL, Bazzarre TL, Clark J. Summary of the scientific conference on dietary fatty acids and cardiovascular health: conference summary from the nutrition committee of the American Heart Association. *Circulation* 2001;**103**:1034–1039.
  - Levitan EB, Wolk A, Mittleman MA. Fish consumption, marine omega-3 fatty acids, and incidence of heart failure: a population-based prospective study of middle-aged and elderly men. *Eur Heart J* 2009;**30**:1495–1500.
  - Montonen J, Järvinen R, Reunanen A, Knekt P. Fish consumption and the incidence of cerebrovascular disease. *Br J Nutr* 2009;**9**:1–7.
  - Yashodhara BM, Umakanth S, Pappachan JM, Bhat SK, Kamath R, Choo BH. Omega-3 fatty acids: a comprehensive review of their role in health and disease. *Postgrad Med J* 2009;**85**:84–90.
  - Kloner RA, Rezkalla SH. To drink or not to drink? That is the question. *Circulation* 2007;**116**:1306–1317.
  - Van Horn L, McCoin M, Kris-Etherton PM, Burke F, Carson JA, Champagne CM, Karmally W, Sikand G. The evidence for dietary prevention and treatment of cardiovascular disease. *J Am Diet Assoc* 2008;**108**:287–331.
  - Reiner Z, Tedeschi-Reiner E. The effects of plant sterols on hypercholesterolemia. *Lijec Vjesn* 2007;**129**:276–281.
  - Goldberg AC, Ostlund RE Jr., Bateman JH, Schimmoeller L, McPherson TB, Spilburg CA. Effect of plant stanol tablets on low-density lipoprotein cholesterol lowering in patients on statin drugs. *Am J Cardiol* 2006;**97**:376–379.
  - Kelly S, Summerbell C, Brynes A, Whittaker V, Frost G. Wholegrain cereals for coronary heart disease. *Cochrane Database Syst Rev* 2007;**18**:CD005051.
  - Veltri EP, Marais AD, de Groot E; ENHANCE Investigators. Simvastatin with or without ezetimibe in familial hypercholesterolemia. *N Engl J Med* 2008;**358**:1431–1443.
  - Stalenhoef AFH, De Graaf J. Association of fasting and nonfasting serum triglycerides with cardiovascular disease and the role of remnant-like lipoproteins and small dense LDL. *Curr Opin Lipidol* 2008;**19**:355–361.
  - Domanski M, Tian X, Fleg J, Coady S, Goslen C, Kirby R, Sachdev V, Knatterud G, Braunwald E. Pleiotropic effect of lovastatin, with and without cholestyramine, in the post coronary artery bypass graft (Post CABG) trial. *Am J Cardiol* 2008;**102**:1023–1027.
  - Brown BG, Bardsley J, Poulin D, Hillger LA, Dowdy A, Maher VM, Zhao XQ, Albers JJ, Knopp RH. Moderate dose, three-drug therapy with niacin, lovastatin, and colestipol to reduce low-density lipoprotein cholesterol <100 mg/dl in patients with hyperlipidemia and coronary artery disease. *Am J Cardiol* 1997;**80**:111–115.
  - Lal SM, Katyal A. Effects of nicotinic acid and lovastatin in combination with cholestyramine in renal transplant patients. *Mol Med* 2002;**99**:580–584.
  - Florentin M, Liberopoulos EN, Mikhailidis DP, Elisaf MS. Colesevelam hydrochloride in clinical practice: a new approach in treatment of hypercholesterolemia. *Curr Med Res Opin* 2008;**24**:995–1009.
  - Ballantyne CM, Hourji J, Notarbartolo A, Melani L, Lipka LJ, Suresh R, Sun S, LeBeaut AP, Sager PT, Veltri EP; Ezetimibe StudyGroup. Effect of ezetimibe coadministered with atorvastatin in 628 patients with primary hypercholesterolemia. *Circulation* 2003;**107**:2409–2415.
  - Birjmohun RS, Kastelein JJ, Poldermans D, Stroes ES, Hostalek U, Assmann G. Safety and tolerability of prolonged-release nicotinic acid in statin-treated patients. *Curr Med Res Opin* 2007;**23**:1707–1713.
  - Taylor AJ, Sullenberger LE, Lee HJ, Lee JK, Grace KA. Arterial Biology for the Investigation of the Treatment Effects of Reducing cholesterol (ARBITER) 2. A double-blind, placebo-controlled study of extended-release niacin on atherosclerosis progression in secondary prevention patients treated with statins. *Circulation* 2004;**110**:3512–3517.
  - Pauciuolo P, Borgnino C, Paoletti R et al. Efficacy and safety of a combination of fluvastatin and bezafibrate in patients with mixed hyperlipidemia (FACT study). *Atherosclerosis* 2000;**150**:429–436.
  - Reiner Z, Galić M, Hanževački M, Tedeschi-Reiner E. Concomitant use of statins and cytochrome P 450 inhibitors. *Lijec Vjesn* 2005;**127**:65–68.
  - Zeman M, Zák A, Vecka M, Tvrzická E, Pšaríková A, Stanková B. N-3 fatty acid supplementation decreases plasma homocysteine in diabetic dyslipidemia treated with statin fibrate combination. *J Nutr Biochem* 2006;**17**:379–384.
  - Reiner Z, Tedeschi-Reiner E, Štajminger G. The role of omega-3 fatty acids from fish in prevention of cardiovascular diseases. *Lijec Vjesn* 2007;**129**:350–355.
  - Patterson D, Slack J. Lipid abnormalities in male and female survivors of myocardial infarction and their first-degree relatives. *Lancet* 1972;**1**:393–399.
  - Brown BG, Hillger L, Zhao XQ, Poulin D, Albers JJ. Types of change in coronary stenosis severity and their relative importance in overall progression and regression of coronary disease. Observations from the FATS Trial. Familial Atherosclerosis Treatment Study. *Ann NY Acad Sci* 1995;**748**:407–417.
  - Sharma M, Ansari MT, Abou-Setta AM, Soares-Weiser K, Chye Ooi T, Sears M, Yazdi F, Tsertsvadze A, Moher D. Systematic review: comparative effectiveness and harms of combination therapy and monotherapy for dyslipidemia. *Ann Intern Med* 2009;**151**:622–630.
  - Corsini A, Windler E, Farnier M. Colesevelam hydrochloride: usefulness of a specifically engineered bile acid sequestrant for lowering LDL-cholesterol. *Eur J Cardiovasc Prev Rehabil* 2009;**16**:1–9.
  - Neuvonen PJ, Niemi M, Backman JT. Drug interaction with lipid-lowering drugs: mechanisms and clinical relevance. *Clin Pharmacol Ther* 2006;**80**:565–581.
- ## 7. Drugs for treatment of hypercholesterolaemia
- Johnson C, Waters DD, DeMicco DA, Breazna A, Bittner V, Greten H, Grundy SM, LaRosa JC. Comparison of effectiveness of atorvastatin 10 mg versus 80 mg in reducing major cardiovascular events and repeat revascularization in patients with previous percutaneous coronary intervention (post hoc analysis of the Treating to New Targets [TNT] Study). *Am J Cardiol* 2008;**102**:1312–1317.
  - Wiviott SD, de Lemos JA, Cannon CP, Blazing M, Murphy SA, McCabe CH, Califf R, Braunwald E. A tale of two trials: a comparison of the post-acute coronary syndrome lipid-lowering trials A to Z and PROVE IT-TIMI 22. *Circulation* 2006;**113**:1406–1414.
  - Gotto AM Jr., Whitney E, Stein EA, Shapiro DR, Clearfield M, Weis S, Jou JY, Langendörfer A, Beere PA, Watson DJ, Downs JR, de Cani JS. Relation between baseline and on-treatment lipid parameters and first acute major coronary events in the Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS). *Circulation* 2000;**101**:477–484.
  - Jones PH, Davidson MH, Bais HE, Bays HE, McKenney JM, Miller E, Cain VA, Blasetto JW; STELLAR Study Group. Comparison of the efficacy and safety of rosuvastatin versus atorvastatin, simvastatin, and pravastatin across doses (STELLAR Trial). *Am J Cardiol* 2003;**92**:152–160.
  - Glynn RJ, Danielson E, Fonseca FA, Genest J, Gotto AM Jr., Kastelein JJ, Koenig W, Libby P, Lorenzatti AJ, MacFadyen JG, Nordestgaard BG, Shepherd J, Willerson JT, Ridker PM. A randomized trial of rosuvastatin in the prevention of venous thromboembolism. *N Engl J Med* 2009;**360**:1851–1861.
  - Cholesterol Treatment Trialists (CTT) Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet* 2005;**366**:1267–1278.
  - The Lipid Research Clinics Coronary Primary Prevention Trial results. I. Reduction in incidence of coronary heart disease. *JAMA* 1984;**251**:351–364.
  - Kastelein JJ, Akdim F, Stroes ES, Zwiderman AH, Bots ML, Stalenhoef AF, Visseren FL, Sijbrands EJ, Trip MD, Stein EA, Gaudet D, Duivenvoorden R,
- ## 8. Drugs for treatment of hypertriglyceridaemia
- Ford ES, Li C, Zhao G, Pearson WS, Mokdad AH. Hypertriglyceridemia and its pharmacologic treatment among US adults. *Arch Intern Med* 2009;**169**:572–579.
  - Simes RJ, Voysey M, O'Connell R, Glasziou P, Best J, Scott R, Pardy C, Byth K, Sullivan D, Ehnholm C, Keech AC; FIELD Study Investigators. Effects of fenofibrate on cardiovascular events in patients with type 2 diabetes after adjustment for use of statins and other drugs. *PLoS One* 2010;**5**:8580.
  - Birjmohun RS, Hutten BA, Kastelein JJP, Stroes ESG. Efficacy and safety of high-density lipoprotein cholesterol-increasing compounds. A meta-analysis of randomized controlled trials. *J Am Coll Cardiol* 2005;**45**:185–197.
  - Remick J, Weintraub H, Setton R, Offenbacher J, Fisher E, Schwartzbard A. Fibrate therapy. An update. *Cardiol Rev* 2008;**16**:129.
  - Jacobson TA, Miller M, Schaefer EJ. Hypertriglyceridemia and cardiovascular risk reduction. *Clin Ther* 2007;**29**:763–777.
  - Kamanna VS, Kashyap ML. Nicotinic acid (niacin) receptor agonists: will they be useful therapeutic agents? *Am J Cardiol* 2007;**100**(suppl):53N–61N.

- Goldberg RB, Jacobson TA. Effects of niacin on glucose control in patients with dyslipidemia. *Mayo Clin Proc* 2008;**83**:470–478.
  - McKenney JM, Sica D. Role of prescription omega-3 fatty acids in the treatment of hypertriglyceridemia. *Pharmacotherapy* 2007;**27**:715–728.
  - Balk EM, Lichtenstein AH, Chung M, Kupelnick B, Chew P, Lau J. Effects of omega-3 fatty acids on serum markers of cardiovascular disease risk: a systematic review. *Atherosclerosis* 2006;**189**:19–30.
  - Hartweg J, Farmer AJ, Holman RR, Neil A. Potential impact of omega-3 treatment on cardiovascular disease in type 2 diabetes. *Curr Opin Lipidol* 2009;**20**:30–38.
  - Sharrett AR, Ballantyne CM, Coady SA, Heiss G, Sorlie PD, Catellier D, Patsch W; Atherosclerosis Risk in Communities Study Group. Coronary heart disease prediction from lipoprotein cholesterol levels, triglycerides, lipoprotein(a), apolipoproteins A-I and B, and HDL density subfractions: The Atherosclerosis Risk in Communities (ARIC) Study. *Circulation* 2001;**104**:1108–1113.
  - Coronary Drug Project Research Group. Clofibrate and niacin in coronary heart disease. *JAMA* 1975;**231**:360–381.
  - Gille A, Bodor ET, Ahmed K, Offermanns S. Nicotinic acid: pharmacological effects and mechanisms of action. *Annu Rev Pharmacol Toxicol* 2008;**48**:79–106.
  - Brown BG, Zhao XQ, Chait A, Frohlich J, Cheung M, Heise N, Dowdy A, DeAngelis D, Fisher LD, Albers J. Lipid altering or antioxidant vitamins for patients with coronary disease and very low HDL cholesterol? The HDL-Atherosclerosis Treatment Study Design. *Can J Cardiol* 1998;Suppl A:6A–13A.
- ### 9. Drugs affecting high-density lipoprotein
- Assmann G, Schulte H, von Eckardstein A, Huang Y. High-density lipoprotein cholesterol as a predictor of coronary heart disease risk. The PROCAM experience and pathophysiological implications for reverse cholesterol transport. *Atherosclerosis* 1996;**124**(Suppl):S11–S20.
  - Luc G, Bard JM, Ferrières J, Evans A, Amouyel P, Arveiler D, Fruchart JC, Ducimetière P. Value of HDL cholesterol, apolipoprotein A-I, lipoprotein A-I, and lipoprotein A-I/A-II in prediction of coronary heart disease: the PRIME Study. Prospective Epidemiological Study of Myocardial Infarction. *Arterioscler Thromb Vasc Biol* 2002;**22**:1155–1161.
  - Chapman MJ. Therapeutic elevation of HDL-cholesterol to prevent atherosclerosis and coronary heart disease. *Pharmacol Ther* 2006;**111**:893–903.
  - Wolfram RM, Brewer HB, Xue Z, Satler LF, Pichard AD, Kent KM, Waksman R. Impact of low high-density lipoproteins on in-hospital events and one-year clinical outcomes in patients with non-ST-elevation myocardial infarction acute coronary syndrome treated with drug-eluting stent implantation. *Am J Cardiol* 2006;**98**:711–717.
  - Genest JJ, McNamara JR, Salem DN, Schaefer EJ. Prevalence of risk factors in men with premature coronary artery disease. *Am J Cardiol* 1991;**67**:1185–1189.
  - Kannel WB. High-density lipoproteins: epidemiologic profile and risks of coronary artery disease. *Am J Cardiol* 1983;**52**:9B–12B.
  - Kontush HA, Chapman MJ. Functionally defective HDL: a new therapeutic target at the crossroads of dyslipidemia, inflammation and atherosclerosis. *Pharmacol Rev* 2006;**58**:342–374.
  - Le Goff W, Guerin M, Chapman MJ. Pharmacological modulation of cholesteryl ester transfer protein, a new therapeutic target in atherogenic dyslipidemia. *Pharmacol Ther* 2004;**101**:17–38.
  - Chapman MJ, Le Goff W, Guerin M, Kontush A. CETP—at the heart of the action of lipid-modulating therapy with statins, fibrates, niacin and CETP inhibitors. *Eur Heart J* 2010;**31**:149–164.
  - Hausenloy DJ, Yellon DM. Targeting residual cardiovascular risk: raising high-density lipoprotein cholesterol levels. *Heart* 2008;**94**:706–714.
  - McTaggart F, Jones P. Effects of statins on high-density lipoproteins: a potential contribution to cardiovascular benefit. *Cardiovasc Drugs Ther* 2008;**22**:321–338.
  - Ashen MD, Blumenthal RS. Clinical practice. Low HDL cholesterol levels. *N Engl J Med* 2005;**353**:1252–1260.
  - Smilde TJ, Van Wissen S, Wollersheim H, Trip MD, Kastelein JJ, Stalenhoef AF. Effect of aggressive versus conventional lipid lowering on atherosclerosis progression in familial hypercholesterolemia (ASAP): a prospective, randomised, double-blind trial. *Lancet* 2001;**357**:577–581.
  - Brewer HB Jr. Benefit–risk assessment of rosuvastatin 10 to 40 milligrams. *Am J Cardiol* 2003;**92**:23K–29K.
  - Ballantyne CM, Herd JA, Ferlic LL, Dunn JK, Farmer JA, Jones PH. Influence of low HDL on progression of coronary artery disease and response to fluvastatin therapy. *Circulation* 1999;**99**:736–743.
  - Fruchart JC, Staels B, Duriez P. The role of fibric acids in atherosclerosis. *Curr Atheroscl Rep* 2001;**3**:83–92.
  - Chapman MJ. Fibrates in 2003: therapeutic action in atherogenic dyslipidaemia and future perspectives. *Atherosclerosis* 2003;**171**:1–13.
  - Chapman MJ, Assmann G, Fruchart JC, Shepherd J, Sirtori C. Raising high-density lipoprotein cholesterol with reduction of cardiovascular risk: the role of nicotinic acid—a position paper developed by the European Consensus Panel on HDL-C. *Curr Med Res Opin* 2004;**20**:1253–1268.
  - Singh IM, Shishehbor MH, Ansell BJ. High-density lipoprotein as a therapeutic target: a systematic review. *JAMA* 2007;**298**:786–798.
  - Zambon A, Gervois P, Pauletto P, Fruchart JC, Staels B. Modulation of hepatic inflammatory risk markers of cardiovascular diseases by PPAR-alpha activators: clinical and experimental evidence. *Arterioscler Thromb Vasc Biol* 2006;**26**:977–986.
- ### 10. Treatment of dyslipidemias in different clinical settings
- Barter PJ, Rye KA. Is there a role for fibrates in the management of dyslipidemia in the metabolic syndrome? *Arterioscler Thromb Vasc Biol* 2008;**28**:39–46.
  - Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 2004;**351**:1296–1305.
  - Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Culleton B, Hamm LL, McCullough PA, Kasiske BL, Kelepouris E, Klag MJ, Parfrey P, Pfeffer M, Raij L, Spinosa DJ, Wilson PW; American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. *Circulation* 2003;**108**:2154–169.
  - van der Graaf A, Kastelein JJ, Wiegman A. Heterozygous familial hypercholesterolaemia in childhood: cardiovascular risk prevention. *J Inherit Metab Dis* 2009;**32**:699–705.
  - Ward MM. Premature morbidity from cardiovascular and cerebrovascular diseases in women with systemic lupus erythematosus. *Arthritis Rheum* 1999;**42**:338–346.
  - DAD Study Group, Friis-Møller N, Reiss P, Sabin CA, Weber R, Monforte A, El-Sadr W, Thiébaud R, De Wit S, Kirk O, Fontas E, Law MG, Phillips A, Lundgren JD. Class of antiretroviral drugs and the risk of myocardial infarction. *N Engl J Med* 2007;**356**:1723–1735.
  - Abifadel M, Varret M, Rabès JP, Allard D, Ouguerram K, Devillers M, Cruaud C, Benjannet S, Wickham L, Erlich D, Derré A, Villéger L, Farnier M, Beucler I, Bruckert E, Chambaz J, Chanu B, Lecerf JM, Luc G, Moulin P, Weissenbach J, Prat A, Krempf M, Junien C, Seidah NG, Boileau C. Mutations in PCSK9 cause autosomal dominant hypercholesterolemia. *Nat Genet* 2003;**34**:154–156.
  - Whittall RA, Scartezini M, Li K, Hubbard C, Reiner Ž, Abraha A, Neil HA, Dedoussis G, Humphries SE. Development of a high-resolution melting method for mutation detection in familial hypercholesterolaemia patients. *Ann Clin Biochem* 2010;**47**:44–55.
  - Hadfield SG, Horara S, Starr BJ, Yazdgerdi S, Bhatnagar D, Cramb R, Egan S, Everdell R, Ferns G, Jones A, Marenah CB, Marples J, Prinsloo P, Sneyd A, Stewart MF, Sandle L, Wang T, Watson MS, Humphries SE. Are patients with familial hypercholesterolaemia well managed in lipid clinics? An audit of eleven clinics from the Department of Health Familial Hypercholesterolaemia Cascade Testing project. *Ann Clin Biochem* 2008;**45**:199–205.
  - Staels B, Maes M, Zambon A. Fibrates and future PPARalpha agonists in the treatment of cardiovascular disease. *Nat Clin Pract Cardiovasc Med* 2008;**5**:542–553.
  - Mungall M, Gaw A, Shephard J. Statin therapy in the elderly. Does it make good clinical and economic sense? *Drugs Aging* 2003;**20**:263–275.
  - Ducharme N, Radhama R. Hyperlipidemia in the elderly. *Clin Geriatr Med* 2008;**24**:471–487.
  - Grundy SM, Cleeman JJ, Rifkind BM, Kuller LH. Cholesterol lowering in the elderly population. Coordinating Committee of the National Cholesterol Education Program. *Arch Intern Med* 1999;**159**:1670–1678.
  - National Lipid Education Council. Treating dyslipidemia in the elderly: are we doing enough? *Lipid Management Newsletter* 1999;**4**:1.
  - Kagansky N, Levy S, Berner Y, Rimon E, Knobler H. Cholesterol lowering in the older population: time for reassessment? *QJM* 2001;**94**:457–463.
  - Lemaitre RN, Psaty BM, Heckbert SR, Kronmal RA, Newman AB, Burke GL. Therapy with hydroxymethylglutaryl coenzyme A reductase inhibitors (statins) and associated risk of incident cardiovascular events in older adults: evidence from the Cardiovascular Health Study. *Arch Intern Med* 2002;**162**:1395–1400.
  - Sever PS, Poulter NR, Dahlof B, Wedel H, Beevers G, Caulfield M, Collins R, Kjeldsen SE, Kristinsson A, McInnes G, Mehlsen J, Nieminen MS, O'Brien ET, Ostergren J, ASCOT Investigators. The Anglo-Scandinavian Cardiac Outcomes Trial lipid lowering arm: extended observations 2 years after trial closure. *Eur Heart J* 2008;**29**:499–508.
  - Aronow W. Treatment of older persons with hypercholesterolemia with and without cardiovascular disease. *J Gerontol A Biol Sci Med Sci* 2001;**56A**(3):M138–M145.
  - Dornbrook-Lavender KA, Roth MT, Pieper JA. Secondary prevention of coronary heart disease in the elderly. *Ann Pharmacother* 2003;**37**:1867–1876.



- Kalantzi KJ, Milionis HJ, Mikhailidis DP, Goudevenos JA. Lipid lowering therapy in the elderly: is there a benefit? *Curr Pharm Des* 2006;**12**:3945–3960.
- Ford I, Blauw GJ, Murphy MB, Shepherd J, Cobbe SM, Bollen EL, Buckley BM, Jukema JW, Hyland M, Gaw A, Lagaay AM, Perry IJ, Macfarlane P, Norrie J, Meinders AE, Sweeney BJ, Packard CJ, Westendorp RG, Twomey C, Stott DJ; The PROSPER Study Group. A Prospective Study of Pravastatin in the Elderly at Risk (PROSPER). *Curr Control Trials Cardiovasc Med* 2002;**3**:1–8.
- Grundy SM, Cleeman JI, Merz CN, Brewer HB Jr., Clark LT, Hunninghake DB, Pasternak RC, Smith SC Jr., Stone NJ; Coordinating Committee of the National Cholesterol Education Program. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation* 2004;**110**:227–239.
- Alexander KP, Blazing MA, Rosenson RS, Hazard E, Aronow WS, Smith SC Jr., Ohman EM. Management of hyperlipidemia in older adults. *J Cardiovasc Pharmacol Ther* 2009;**14**:49–58.
- Einarson TR, Metge CJ, Iskjedjian M, Mukherjee J. An examination of the effect of cytochrome P450 drug interactions of hydroxymethylglutaryl-coenzyme A reductase inhibitors on health care utilization: a Canadian population-based study. *Clin Ther* 2002;**24**:2126–2136.
- LaRosa JC, He J, Vupputuri S. Effect of statins on risk of coronary disease. A meta-analysis of randomized controlled trials. *JAMA* 1999;**282**:2340–2346.
- Feldman T, Davidson M, Shah A, MacCubbin D, Meehan A, Zakson M, Tribble D, Veltri E, Mitchell Y. Comparison of the lipid-modifying efficacy and safety profiles of ezetimibe coadministered with simvastatin in older versus younger patients with primary hypercholesterolemia: a post hoc analysis of subpopulations from three pooled clinical trials. *Clin Ther* 2006;**28**:849–859.
- Whiteley L, Padmanabhan S, Hole D, Isles C. Should diabetes be considered a coronary heart disease risk equivalent? *Diabetes Care* 2005;**28**:1588–1593.
- Juutilainen A, Lehto S, Rönnemaa T, Pyörälä K, Laakso M. Type 2 diabetes as a 'coronary heart disease equivalent'. *Diabetes Care* 2005;**28**:2901–2907.
- Preis SR, Hwang S-J, Coady S, Pencina MJ, D'Agostino RB, Savage PJ, Levy D, Fox CS. Trends in all-cause and cardiovascular disease mortality among women and men with and without diabetes mellitus in the Framingham heart study, 1950 to 2005. *Circulation* 2009;**7**:1728–1735.
- Alexander CM, Landsman PB, Teutsch SM, Haffner SM; Third National Health and Nutrition Examination Survey (NHANES III); National Cholesterol Education Program (NCEP). NCEP defined metabolic syndrome, diabetes, and prevalence of coronary heart disease among NHANES III participants age 50 years and older. *Diabetes* 2003;**52**:1210–1214.
- Mulnier HE, Seaman HE, Raleigh VS, Soedamah-Muthu SS, Colhoun HM, Lawrenson RA, de Vries CS. Risk of myocardial infarction in men and women with type 2 diabetes in the UK: a cohort study using the General Practice Research Database. *Diabetologia* 2008;**51**:1639–1645.
- Bonora E. The metabolic syndrome and cardiovascular disease. *Ann Med* 2006;**38**:64–80.
- Gami AS, Witt BJ, Howard DE, Erwin PJ, Gami LA, Somers VK, Montori VM. Metabolic syndrome and risk of incident cardiovascular events and death. *Am J Cardiol* 2007;**49**:403–414.
- Després J-P, Cartier A, Côté M, Arsenault BJ. The concept of cardiometabolic risk: bridging the fields of diabetology and cardiology. *Ann Med* 2008;**40**:514–523.
- Taskinen M-R. Type 2 diabetes as a lipid disorder. *Curr Mol Med* 2005;**5**:297–308.
- American Diabetes Association. Clinical practice recommendations 2009. *Diabetes Care* 2009;**32**:8–9, 29–31.
- Rosenzweig JL, Ferrannini E, Grundy SM, Haffner SM, Heine RJ, Horton ES, Kawamori R. Primary prevention of cardiovascular disease and type 2 diabetes in patients at metabolic risk: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2008;**93**:3671–3689.
- Cholesterol Treatment Trialists' (CTT) Collaborators, Kearney PM, Blackwell L, Collins R, Keech A, Simes J, Peto R, Armitage J, Baigent C. Efficacy of cholesterol-lowering therapy in 18,686 people with diabetes in 14 randomised trials of statins: a meta-analysis. *Lancet* 2008;**371**:117–125.
- Grundy SM, Vega GL, McGovern ME, Tulloch BR, Kendall DM, Fitz-Patrick D, Ganda OP, Rosenson RS, Buse JB, Robertson DD, Sheehan JP; Diabetes Multicenter Research Group. Efficacy, safety, and tolerability of once-daily niacin for the treatment of dyslipidemia associated with type 2 diabetes. *Arch Intern Med* 2002;**162**:1568–1576.
- Retnakaran R, Zinman B. Type 1 diabetes, hyperglycaemia, and the heart. *Lancet* 2008;**371**:1790–1799.
- Soedamah-Muthu SS, Fuller JH, Mulnier HE, Raleigh VS, Lawrenson RA, Colhoun HM. High risk of cardiovascular disease in patients with type 1 diabetes in the U.K.: a cohort study using the general practice research database. *Diabetes Care* 2006;**29**:798–804.
- ALLHAT Collaborative Research Group. Major outcomes in moderately hypercholesterolemic hypertensive patients randomized to pravastatin vs usual care. The antihypertensive and lipid lowering treatment to prevent heart attack trial (ALLHAT-LLT). *JAMA* 2002;**288**:2998–3007
- Koren MJ, Hunninghake DB, on behalf of the ALLIANCE Investigators. Clinical outcomes in managed-care patients with coronary heart disease treated aggressively in lipid-lowering disease management clinics. *J Am Coll Cardiol* 2004;**44**:1772–1779.
- Athyros VG, Papageorgiou AA, Mercouris BR, Athyrou VV, Symeonidis AN, Basayannis EO, Demetriadis DS, Kontopoulos AG. Treatment with atorvastatin to the National Cholesterol Educational Program goals versus usual care in secondary coronary heart disease prevention. The GREEK Atorvastatin and Coronary-heart-disease Evaluation (GREACE) Study. *Curr Med Res Opin* 2002;**4**:220–228.
- Sadek MM, Haddad T, Haddad H. The role of statins in chronic heart failure. *Curr Opin Cardiol* 2009;**24**:167–171.
- Reiner Z. Statins in heart failure—a failure? *Nutr Metab Cardiovasc Dis* 2008;**18**:397–401.
- Cleland JG, McMurray JJV, Kjekshus J, Cornel JH, Dunselman P, Fonseca C, Hjalmarson Å, Korewicki J, Lindberg M, Ranjith N, van Veldhuisen DJ, Waagstein F, Wedel H, Wikstrand J. Plasma concentration of amino-terminal pro-brain natriuretic peptide in chronic heart failure. Prediction of cardiovascular events and interaction with the effects of rosuvastatin. A report from the Controlled Rosuvastatin Multinational Trial in Heart Failure (CORONA). *J Am Coll Cardiol* 2009;**54**:1850–1859.
- Heart Protection Study Collaborative Group. N-terminal pro-B-type natriuretic peptide, vascular disease risk, and cholesterol reduction among 20536 patients in the MRC/BHF heart protection study. *J Am Coll Cardiol* 2007;**49**:311–319.
- Farivar RS, Cohn LH. Hypercholesterolemia is a risk factor for bioprosthetic valve calcification and explantation. *J Thorac Cardiovasc Surg* 2003;**125**:969–976.
- Peto R, Emberson J, Landray M, Baigent C, Collins R, Clare R, Califf R. Analyses of cancer data from three ezetimibe trials. *N Engl J Med* 2008;**359**:1357–1366.
- Sherer Y, Shoenfeld Y. Mechanisms of disease: atherosclerosis in autoimmune diseases. *Nat Clin Pract Rheumatol* 2006;**2**:99–104.
- Greenwood J, Steinman L, Zamvil SS. Statin therapy and autoimmune disease: from protein prenylation to immunomodulation. *Nat Rev Immunol* 2006;**6**:358–370.
- Muntner P, He J, Astor BC, Folsom AR, Coresh J. Traditional and nontraditional risk factors predict coronary heart disease in chronic kidney disease: results from the atherosclerosis risk in communities study. *Am Soc Nephrol* 2005;**16**:529–538.
- Parikh NI, Hwang S-J, Larson MG, Meigs JB, Levy D, Fox CS. Cardiovascular disease risk factors in chronic kidney disease. Overall burden and rates of treatment and control. *Arch Intern Med* 2006;**166**:1884–1891.
- Vaziri ND. Dyslipidemia of chronic renal failure: the nature, mechanisms and potential consequences. *Am J Physiol Renal Physiol* 2006;**290**:F262–F272.
- Kwan BCH, Kronenberg F, Beddhu S, Cheung AK. Lipoprotein metabolism and lipid management in chronic kidney disease. *J Am Soc Nephrol* 2007;**18**:1246–1261.
- Seliger SL, Weiss NS, Gillen DL, Kestenbaum B, Ball A, Sherrard DJ, Stehman-Breen CO. HMG-CoA reductase inhibitors are associated with reduced mortality in ESRD patients. *Kidney Int* 2002;**61**:297–304.
- Andreucci VE, Fissel RB, Bragg-Gresham JL, Ethier J, Greenwood R, Pauly M, Wizemann V, Port FK. Dialyses outcomes and practice patterns study (DOPPS) data on medications in hemodialysis patients. *Am J Kidney Dis* 2004;**44**:61–67.
- Harper CR, Jacobson TA. Managing dyslipidemia in chronic kidney disease. *J Am Coll Cardiol* 2008;**51**:2375–2384.
- K/DOQI clinical practice guidelines for managing dyslipidemia in chronic kidney disease. *Am J Kidney Dis* 2003;**41**:S1–S237.
- Tonelli M, Isles C, Craven T, Tonkin A, Pfeffer MA, Shepherd J, Sacks FM, Furberg C, Cobbe SM, Simes J, West M, Packard C, Curhan GC. Effect of pravastatin on rate of kidney function loss in people with or at risk for coronary disease. *Circulation* 2005;**112**:171–178.
- Shepherd J, Kastelein JJP, Bittner V, Deedwania P, Breazna A, Dobson S, Wilson DJ, Zuckerman A, Wenger NK. Effect of intensive lipid lowering with atorvastatin on renal function in patients with coronary heart disease: the treating to new targets (TNT) study. *Clin J Am Soc Nephrol* 2007;**2**:1131–1139.
- Lal SM, Hewett JE, Petroski GF, Van Stone JC, Ross G Jr. Effects of nicotinic acid and lovastatin in renal transplant patients: a prospective, randomized, open-labeled crossover trial. *Am J Kidney Dis* 1995;**25**:616–622.
- Le VV, Racine N, Pelletier GB, Carrier M, Cossette M, White M. Impact of ezetimibe on cholesterol subfractions in dyslipidemic cardiac transplant recipients receiving statin therapy. *Clin Transplant* 2009;**2**:249–255.
- Crespo-Leiro MG, Paniagua MJ, Marzoa R, Grille Z, Naya C, Flores X, Rodriguez JA, Mosquera V, Franco R, Castro-Beiras A. The efficacy and safety of ezetimibe for treatment of dyslipidemia after heart transplantation. *Transplant Proc* 2008;**40**:3060–3062.
- Jardine AG, Fellström B, Logan JO, Cole E, Nyberg G, Grönhagen-Riska C, Madsen S, Neumayer HH, Maes B, Ambühl P, Olsson AG, Pedersen T, Holdaas H. Cardiovascular risk and renal transplantation: post hoc analyses of

- the Assessment of Lescol in Renal Transplantation (ALERT) Study. *Am J Kidney Dis* 2005;**46**:529–536.
- Lisik W, Schoenberg L, Lasky RE, Kahan BD. Statins benefit outcomes of renal transplant recipients on a sirolimus–cyclosporine regimen. *Transplant Proc* 2007;**39**:3086–3092.
  - Ridker PM, Stampfer MJ, Rifai N. Novel risk factors for systemic atherosclerosis: a comparison of C-reactive protein, fibrinogen, homocysteine, lipoprotein(a), and standard cholesterol screening as predictors of peripheral arterial disease. *JAMA* 2001;**285**:2481–2485.
  - Kapoor AS, Kanji H, Buckingham J, Devereaux PJ, McAlister FA *et al*. Strength of evidence for perioperative use of statins to reduce cardiovascular risk: systematic review of controlled studies. *BMJ* 2006;**333**:1149–1152.
  - Cannon CP, Braunwald E, McCabe CH, Rader DJ, Rouleau JL, Belder R, Joyal SV, Hill KA, Pfeffer MA, Skene AM; Pravastatin or Atorvastatin Evaluation Infection Therapy-Thrombolysis in Myocardial Infarction 22 Investigators. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med* 2004;**350**:1495–1504.
  - Vergouwen MDI, de Haan RJ, Vermeulen M, Roos YBWEM. Statin treatment and the occurrence of hemorrhagic stroke in patients with a history of cerebrovascular disease. *Stroke* 2008;**39**:497–502.
  - Escaut L, Monsuez JJ, Chironi G, Merad M, Teicher E, Smadja D, Simon A, Vittecoq D. Coronary artery disease in HIV infected patients. *Intensive Care Med* 2003;**29**:969–973.
  - Barbaro G, Di Lorenzo G, Cirelli A, Grisorio B, Lucchini A, Hazra C, Barbarini G. An open-label, prospective, observational study of the incidence of coronary artery disease in patients with HIV infection receiving highly active antiretroviral therapy. *Clin Ther* 2003;**25**:2405–2418.
  - Dube MP, Stein JH, Aberg JA, Fichtenbaum CJ, Gerber JG, Tashima KT, Henry WK, Currier JS, Sprecher D, Glesby MJ; Adult AIDS Clinical Trials Group Cardiovascular Subcommittee; HIV Medical Association of the Infectious Disease Society of America. Guidelines for the evaluation and management of dyslipidaemia therapy: recommendations of the HIV Medical Association of the Infectious Disease Society of America and the Adult AIDS Clinical Trials Group. *Clin Infect Dis* 2003;**37**:613–627.
  - Boccarda F, Simon T, Lacombe K, Cohen A, Laloux B, Bozec E, Durand S, Girard PM, Laurent S, Boutouyrie P. Influence of pravastatin on carotid artery structure and function in dyslipidemic HIV-infected patients receiving antiretroviral therapy. *AIDS* 2006;**20**:2395–2398.
  - Tedeschi-Reiner E, Reiner Ž, Sonicki Z. Atherosclerosis and retinal arteries in men: role of serum lipoproteins and apoproteins. *Croat Med J* 2004;**45**:333–337.
  - Gree ML. Evaluation and management of dyslipidaemia in patients with HIV infection. *J Gen Intern Med* 2002;**17**:797–810.
  - Palacios R, Santos J, García A, Castells E, González M, Ruiz J, Márquez M. Impact of highly active antiretroviral therapy on blood pressure in HIV-infected patients. A prospective study in a cohort of naive patients. *HIV Med* 2006;**7**:10.
  - Naukkarinen J, Ehnholm C, Peltonen L. Genetics of familial combined hyperlipidemia. *Curr Opin Lipidol* 2006;**17**:285–290.
  - Plaisier CL, Horvath S, Huertas-Vazquez A, Cruz-Bautista I, Herrera MF, Tusie-Luna T, Aguilar-Salinas C, Pajukanta P. A systems genetics approach implicates USF1, FADS3 and other causal candidate genes for familial combined hyperlipidemia. *PLoS Genet* 2009;**5**:e1000642.
  - Petersen LK, Christensen K, Kragstrup J. Lipid-lowering treatment to the end? A review of observational studies and RCT's on cholesterol and mortality in 80+ year olds. *Age Ageing* 2010;**39**:674–680.
11. Monitoring of lipids and enzymes in patients on lipid lowering drug therapy
- Smellie WSA. Testing pitfalls and summary of guidance in lipid management. *BMJ* 2006;**333**:83–86.
  - Grover SA, Coupal L, Hu XP. Identifying adults at increased risk of coronary disease. How well do the current cholesterol guidelines work? *JAMA* 1995;**274**:801–806.
  - Nam BH, Kannel WB, D'Agostino RB. Search for an optimal atherogenic lipid risk profile: from the Framingham Study. *Am J Cardiol* 2006;**97**:372–375.
  - Glaziosi PP, Irwig L, Heritier S, Simes J, Tonkin A. Monitoring cholesterol levels: measurement error or true change? *Ann Intern Med* 2008;**148**:656–661.
12. How to improve adherence to lifestyle changes and compliance with drug therapy.
- Atella V, Brady A, Catapano AL, Critchley J, Graham IM, Hobbs FD, Leal J, Lindgren P, Vanuzzo D, Volpe M, Wood D, Paoletti R. Bridging science and health policy in cardiovascular disease: focus on lipid management. *Atherosclerosis Suppl* 2009;**10**:3–21.
  - Tsevat J, Kuntz KM, Orav EJ, Weinstein MC, Goldman L; International Society of Technology Assessment in Health Care. Meeting. Cost-effectiveness and the Cholesterol and Recurrent Events (CARE) study. *Annu Meet Int Soc Technol Assess Health Care* 1997;**13**:102.
  - Reiner Z. How to improve cardiovascular diseases prevention in Europe? *Nutr Metab Cardiovasc Dis* 2009;**19**:451–454.
  - World Health Organization. *Needs and Priorities in Cardiac Rehabilitation and Secondary Prevention in Patients with Coronary Heart Disease*. WHO Technical Report Series 831. Geneva: WHO; 1993.
  - Report on a Seminar, Noordwijk aan Zee. *The Rehabilitation of Patients with Cardiovascular Diseases*. Copenhagen: WHO, Regional Office for Europe, 1969.
  - Jolliffe JA, Rees K, Taylor RS, Thompson D, Oldridge N, Ebrahim S. Exercise-based rehabilitation for coronary heart disease. *Cochrane Database Syst Rev* 2001;**1**:CD001800.
  - Taylor R, Brown A, Ebrahim S, Jolliffe J, Noorani H, Rees K, Skidmore B, Stone JA, Thompson DR, Oldridge N. Exercise based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. *Am J Med* 2004;**116**:682–692.
  - McAlister FA, Lawson FME, Teo KK, Armstrong PW. Randomised trials of secondary prevention programmes in coronary heart disease: systematic review. *BMJ* 2001;**323**:957–962.
  - Clark AM, Hartling L, Vandermeer B, McAlister FA. Meta-analysis: secondary prevention programs for patients with coronary artery disease. *Ann Intern Med* 2005;**143**:659–672.
  - EUROASPIRE Study Group. Cardiovascular prevention guidelines in daily practice: a comparison of EUROASPIRE I, II and III surveys in 8 European countries. *Lancet* 2009;**373**:929–940.
  - Kotseva K, Wood D, De Bacquer D, Heidrich J, De Backer G; EUROASPIRE II Study Group. Cardiac rehabilitation for coronary patients: lifestyle, risk factor and therapeutic management. Results from the EUROASPIRE II survey. *Eur Heart J* 2004;**6**(suppl J):j17–j26.
  - De Sutter J, De Bacquer D, Kotseva K, Sans S, Pyörälä K, Wood D, De Backer G; EUROpean Action on Secondary Prevention through Intervention to Reduce Events II study group. Screening of family members of patients with premature coronary heart disease. Results from the EUROASPIRE II family survey. *Eur Heart J* 2003;**24**:249–257.
  - Ebrahim S, Davey Smith G. Systematic review of randomised controlled trials of multiple risk factor interventions for preventing coronary heart disease. *BMJ* 1997;**314**:1666–1674.
  - Ebrahim S, Beswick A, Burke M, Davey Smith G. Multiple risk factor interventions for primary prevention of coronary heart disease. *Cochrane Database Syst Rev* 2006;**4**:CD001561.
  - Goble A, Jackson B, Phillips P, Race E, Oliver RG, Worcester MC. The Family Atherosclerosis Risk Intervention Study (FARIS): risk factor profiles of patients and their relatives following an acute cardiac event. *Austr N Z J Med* 1997;**27**:568–577.
  - Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomised trials. *Lancet* 2003;**362**:1527–1545.
  - Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of different blood pressure-lowering regimens on major cardiovascular events in individuals with and without diabetes mellitus. *Arch Intern Med* 2005;**165**:1410–1419.
  - Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of different regimens to lower blood-pressure on major cardiovascular events in older and younger adults: meta-analysis of randomised trials. *BMJ* 2008;**336**:1121–1123.
  - Law MR, Wald NJ, Thompson SG. By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischaemic heart disease? *BMJ* 1994;**308**:367–372.
  - Wood DA, Kotseva K, Jennings C, Mead A, Jones J, Holden A, Connolly S, De Bacquer D *et al*. EUROACTION: a European Society of Cardiology demonstration project in preventive cardiology. A cluster randomised controlled trial of a multi-disciplinary preventive cardiology programme for coronary patients, asymptomatic high risk individuals and their families. Summary of design, methodology and outcomes. *Eur Heart J* 2004;**6**(Suppl J):j3–j15.
  - Reiner Z, Mihatov Š, Miličić D, Bergovec M, Planinc D, on behalf of the TASPIC-CRO Study Group Investigators. Treatment and secondary prevention of ischemic coronary events in Croatia (TASPIC-CRO study). *Eur J Cardiovasc Prevent Rehabil* 2006;**13**:646–654.
  - Wahl LM, Nowak MA. Adherence and drug resistance: predictions for therapy outcome. *Proc R Soc B: Biol Sci* 2000;**267**:835–843.