ESC/EAS GUIDELINES ON MANAGEMENT OF DYSLIPIDEMIAS IN CLINICAL PRACTICE

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Guidelines - do we need them?
Do we read them?

- Over 20,000 biomedical journals, and growing.
- 99% may be irrelevant rubbish hiding 1% with important information which should influence the care of your patients.
- GP would need to read 20 journals a day, 365 days a year to keep up to date.
- Median reading time for hospital doctors 0-60 min/week (self reported). Up to 75% read nothing in the last week.
- Up to date knowledge and clinical performance deteriorate with time.
Recent developments in CVD prevention in Europe

1994
- First Joint Task Force Recommendations

1994
- Joint European Societies Implementation Group on Coronary Prevention

1995-96
- EUROASPIRE I

1998
- Second Joint Task Force Recommendations

1999-2000
- EUROASPIRE II

2000
- Joint European Societies CVD Prevention Committee

2003
- Third Joint Task Force Recommendations

2006-2007
- EUROASPIRE III

2007
- Fourth Joint Task Force Recommendations
European guidelines on cardiovascular disease prevention in clinical practice: full text

Fourth Joint Task Force of the European Society of Cardiology and other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts)

Ian Graham (Chairperson)*a, Dan Atara, Knut Borch-Johnsenb,c, Gudrun Boysend, Gunilla Burellc, Renata Cifkova†, Jean Dallongevillea, Guy De Backera, Shah Ebrahim, Bjørn Gjelsvikg, Christoph Herrmann-Lingen, Arno Hoesg, Steve Humphries, Mike Knapton, Joep Perka, Silvia G. Prioria, Kalevi Pyorala, Zeljko Reinerl, Luis Ruilopea, Susana Sans-Menendez, Wilma Scholte Op Reimera, Peter Weissbergh, David Wooda, John Yarnell, Jose Luis Zamoranoa

European Journal of Cardiovascular Prevention and Rehabilitation 2007, 14(Suppl 2):S1–S113
In ALL cases, look for and manage all risk factors. Those with established CVD, diabetes type 2 or type 1 with microalbuminuria, or with severe hyperlipidaemia are already at high risk. For all other people, the SCORE charts can be used to estimate total risk.

- Dietary and exercise advice together with attention to all risk factors comes first.
- Aim to reduce total cholesterol to <4.5 mmol/L (~175 mg/dL) or <4 mmol/L (~155 mg/dL) if feasible, and LDL-cholesterol to <2.5 mmol/L (~100 mg/dL) or <2 mmol/L (~80 mg/dL) if feasible.
- This will require statin treatment in many. Some recommend statins for all CVD and most diabetic patients regardless of baseline levels.

Treatment goals are not defined for HDL cholesterol and triglycerides, but HDL-cholesterol <1.0 mmol/L (~40 mg/dL) for men and <1.2 mmol/L (~45 mg/dL) for women and fasting triglycerides of >1.7 mmol/L (~150 mg/dL) are markers of increased cardiovascular risk.
Primary focus of treatment guidelines is to reduce LDL-Cholesterol

NCEP ATP III Guidelines

• Lower risk:
  LDL-C <4,1 mmol/L

• Moderate risk:
  LDL-C <3,4 mmol/L for individuals with ≥2 risk factors

• High risk:
  LDL-C <2,6 mmol/L for individuals with CHD or CHD equivalents

• Very high risk (optional):
  LDL-C <1,8 mmol/L for high-risk individuals (eg, those with CHD and diabetes)

Joint European Guidelines

• LDL-C <3 mmol/L in general

• <2,5 mmol/L for highest risk individuals with an option of <2 mmol/L (eg, those with diabetes, CHD)

• Triglycerides:
  1.7 mmol/l - marker of increased risk

• HDL-C:
  < 1 in men and < 1.2 mmol/L in women - marker of increased risk

Dyslipidemia guidelines - how should they look like?

- Simple, user-friendly guidelines with improved content and more details concerning lipids than Joint European guidelines
- Increase doctor’s (particularly GP’s) and patient awareness & education
- Evidence based upon independent research (credible, trustworthy)
Dyslipidemia guidelines - how should they look like?

- In concordance with the Joint European guidelines
- NO DIFFERENT GOALS!
- Fully include the concept of total risk (SCORE + ?)
Dyslipidemia guidelines - for whom do we write them?

- Primarily for GPs (but also for internists, cardiologists etc.)
- Information overload/ reading time mismatch
- GPs overwhelmed with different guidelines (PubMed guidelines-lipids 3612, guidelines-CVD 9260, guidelines 161 166 !)
ESC classes of recommendations

Class I: Evidence/general agreement that treatment is beneficial, useful and effective

Class II: Conflicting evidence-
    IIa: Weight of evidence in favour
    IIb: Usefulness/efficacy less well established

Class III: Not useful/effective or may be harmful
ESC levels of evidence

**A:** Multiple randomised clinical trials or meta-analyses

**B:** Single randomised clinical trial or large large, non-randomised studies

**C:** Consensus of experts and/or small studies, retrospective studies, registries
Grading the evidence

- While it, reasonably, gives the highest grading to RCTs, it inevitably favours drug treatments over lifestyle measures.
- The process is not transparent - is a numerical class or level evidence based, or just an opinion that has been given a number?
- All contributors have to be aware of the principles of EBM and the need to quote available systematic reviews.
- Differing types of evidence are needed when considering, for example, lifestyle measures, causality, screening and diagnostic techniques as opposed to therapeutic interventions.
The issue of low HDL-Cholesterol and high triglycerides

- New data?
- The residual risk
- How to increase HDL-cholesterol? - nothing in the Joint European guidelines
- Are all HDL particles beneficial?

Any hazard with very low LDL-Cholesterol?

- Almost nothing in the Joint European guidelines (particularly the issue of mental disorders and low but also high cholesterol etc.)
Children and lipids

• Nothing in Joint European guidelines (“normal” values, when to start with drugs, goals for treatment?)

Elderly and lipids

• Nothing in Joint European guidelines (“normal” values, goals for treatment, effects of diet, side effects of drugs, interactions of lipid lowering drugs with other drugs,?)
Drug combinations and side effects

- Still many doctors hesitate to prescribe combinations because of side effects - what is the reality?
- Not much about this issue in Joint European guidelines

Nutrition and “natural” substances for treating dyslipidemias

- Nothing in the Joint European guidelines (plant sterols, garlic, red rice, polycosanol, green tea, cocoa, etc.)
- The issue of red vine, alcohol
Kidney diseases, dialysis and lipids

- Not much about this issue in Joint European guidelines

Acute coronary syndrome and lipid-lowering drugs

- Not much about this issue in the Joint European guidelines
- When exactly to start, dosage etc.?
Women and lipids in CVD prevention

- AHA Evidence-Based Guidelines for Cardiovascular Disease Prevention in Women (Circulation 2004; 109: 672-93). Good but nothing on the role of women in prevention
- More in Joint European guidelines for CVD prevention but not to much
- WHY are 65% of medical students female yet <5% of consultants? Competence versus androgens?
- YET, in many medical cultures, the effective delivery of prevention is by women - physicians, nurse specialists, physiotherapists, nutritionists etc
- Women & the home - a major and undervalued resource
# Draft Timelines

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Description</th>
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<tbody>
<tr>
<td>20 &amp; 21 January 2009</td>
<td>Kick-off meeting Chateau Mont Royal Paris</td>
<td>Presentation of processes, Agreement on table of contents, writing assignments, Timelines, Instructions (writers, circulation, web site, meetings)</td>
</tr>
<tr>
<td>End March 2009</td>
<td>Draft 1 finished by section lead authors and sent to their section co-authors for their comments/approval</td>
<td>End March 2009 Draft 1 finished by section lead authors and sent to their section co-authors for their comments/approval</td>
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<tr>
<td>End April 2009</td>
<td>Draft 1 due in to Chairs with all co-authors comments integrated</td>
<td>End April 2009 Draft 1 due in to Chairs with all co-authors comments integrated</td>
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<tr>
<td>13 May 2009</td>
<td>Meeting 2 Croatia</td>
<td>13 May 2009 Meeting 2 Croatia Whole group goes through entire draft and makes comments</td>
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<tr>
<td>14 June 2009</td>
<td>Draft 2 finished by section lead authors and sent to their section co-authors for their comments/approval</td>
<td>14 June 2009 Draft 2 finished by section lead authors and sent to their section co-authors for their comments/approval</td>
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<td>28 June 2009</td>
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<td>28 June 2009 Draft 2 due in to Chairs with all co-authors comments integrated</td>
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<tr>
<td>Beg July 2009</td>
<td>Chairs send new draft to all Task Force Members</td>
<td>Beg July 2009 Chairs send new draft to all Task Force Members</td>
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<tr>
<td>10-11 July 2009</td>
<td>Chateau Mont Royal Paris</td>
<td>10-11 July 2009 Chateau Mont Royal Paris Third meeting with the whole group, Whole group goes through entire draft and makes comments</td>
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<td>Barcelona 2009</td>
<td>No meeting</td>
<td>Barcelona 2009 No meeting</td>
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<td>End August 2009</td>
<td>Draft 3 finished by section lead authors and sent to their section co-authors for their comments/approval</td>
<td>End August 2009 Draft 3 finished by section lead authors and sent to their section co-authors for their comments/approval</td>
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<tr>
<td>20 September 2009</td>
<td>Draft 3 due in to Chairs with all co-authors comments integrated</td>
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<tr>
<td>11 October 2009</td>
<td>Chairs create first Master copy and homogenize/balance all sections</td>
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<tr>
<td>8 November 2009</td>
<td>Internal review of Master copy 1 by all the Task Force Members</td>
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<tr>
<td>30 November/1 December 2009</td>
<td>Fourth meeting to go through Master copy 1 with all TF members</td>
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<td><strong>Meeting 4?</strong></td>
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<tr>
<td>January 2010</td>
<td>Official CPG review process</td>
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<td>Comments from the ESC reviewers and CPG</td>
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<tr>
<td>February 2010</td>
<td>Task Force integrates review comments into the document and give feedback to the reviewers</td>
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<tr>
<td><strong>Meeting 5?</strong></td>
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<tr>
<td>March 2010</td>
<td>Document submitted to CPG for validation from reviewers</td>
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<tr>
<td>April 2010</td>
<td>Publication approval and submission to EHJ</td>
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<tr>
<td>May-June 2010</td>
<td>Proofreading and formatting of document for publication</td>
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<td>Summer 2010</td>
<td>Publication of document in EHJ &amp; Atherosclerosis</td>
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<tr>
<td>1. CPG Preamble</td>
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<td>2. Scope of the problem &amp; health economics</td>
<td>Clinical risk assessment (clinical variables that should be used to stratify cardiovascular risk)</td>
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<td>3. Total CV risk, symptomatic and asymptomatic patients etc (all clinical scenarios)</td>
<td>Concept of total risk (reference to joint guidelines)</td>
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<td>4. Evaluation of laboratory lipid and apoprotein parameters (when, how and for whom and by whom)</td>
<td>Lifestyle changes</td>
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<td>5. Efficacy and safety of management</td>
<td>Functional food &amp; „natural“ substances for treating of dyslipidemias</td>
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<td>Drugs for treatment of hypercholesterolemia (including apheresis)</td>
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<td>Drugs to raise HDL</td>
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<td>Drug combinations</td>
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### 6. Treatment of dyslipidemias in different clinical settings

- **Familial forms**
- **Children**
- **Women**
- **Elderly**

- **Metabolic risk factors**
  - Diabetes (type 1 and 2, glucose intolerance, obesity)
  - HF and valve disease
  - Renal dysfunction, dialysis
  - Transplantation patients
  - PAD
  - Stroke
  - HIV
  - Coronary Disease (including ACS)

### 7. Patient follow-up

### 8. How to improve compliance to lifestyle changes and therapy and implementation

### 9. Gaps in evidence and emerging data

### 10. Conflict of Interest Statements

### 11. References

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40 references per journal page, 2 to 4 tables per journal page.
Total number of words, including tables, figures and references, for the whole document: 35000 (35 journal pages maximum)
Guidelines are nothing without implementation

• Guidelines alone are good for the vanity of the authors and bad for rain forests; they are a waste of time without a defined implementation strategy

(Ian Graham)
Thank you!