Lipid Management in 2020: A Glimpse into the Future

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CVD will still be a problem in 2020!
Why?

- **Public Health**
  - Lifestyle
  - Increased life expectancy
  - Awareness/Knowledge
  - Treating more advanced disease
  - Lack of Screening

- **Therapies**
  - Inadequate use of evidence based treatments
  - Side effects of current Tx
  - Treatment threshold has been reached
  - Cost
**CEPHEUS: about half of patients achieved LDL-C goals**

Patients on lipid-lowering drugs for >3 months (stable medication >6 weeks)

<table>
<thead>
<tr>
<th>Country</th>
<th>Europe JETF guidelines</th>
<th>Asia NCEP ATP III guidelines*</th>
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<tbody>
<tr>
<td>Belgium</td>
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<td>Vietnam</td>
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</table>

*Patients with ≥2 cardiovascular risk factors according to NCEP ATP III guidelines;

CEPHEUS, CEntralized Pan-European survey on tHE Under-treatment of hypercholeSterolaemia,
NCEP ATP, National Cholesterol Educational Program Adult Treatment Panel; JETF, Joint European Task Force

What will change?

• Revolution in the management of FH

• Screening and Earlier Treatment to Prevent CVD

• More widespread understanding and use of absolute risk scores to
Familial Hypercholesterolaemia

Estimated millions of individuals worldwide with FH by WHO regions and by income groups

Nordestgaard BG et al. Eur Heart J 2013;34:3478-3490
Estimated % of individuals diagnosed with FH in different countries/territories, as a fraction of those theoretically predicted based on a frequency of 1/500 in the general population.
Despite available treatment approaches, we still have a significant percentage of patients not at goal.

Familial Hypercholesterolaemia

LDL-C burden in individuals with or without FH as a function of the age of initiation of statin therapy

Nordestgaard BG et al. Eur Heart J 2013;34:3478-3490
Solutions

• Awareness/ Improve Knowledge

• Screening systematically

• Change Policy/ ICD codes

• Additional new therapies
The European Atherosclerosis Society

Advancing and exchanging knowledge of the causes, natural history, treatments and prevention of atherosclerotic disease.

Prestigious, inclusive and state-of-the-art
Be part of EAS 2015 Glasgow.

EAS membership entitles you to a range of benefits.

Latest updates
3/13/2015
EAS 2015 Glasgow :: Focus on Workshop Speakers Rob Hegele and Ian S. Young
Meet the key contributors in a programme that will excite, inspire and inform.

EAS 2015 Glasgow
Key dates:
• Feb 16 2015 - Regular registration deadline
• March 22-25 2015 - Congress

More detailed information about the Congress is given HERE.

EAS Advanced Courses
Applications are welcome for the EAS Advanced Course X in Clinical Lipidology and Cardiovascular Prevention, held in Prague 15-16 April. Follow this link for more information.

Presentations from the EAS Advanced Course VIII: Clinical Excellence in Cardiovascular Prevention and Lipidology are now available in the EAS Academy.

EAS Academy
The EAS Academy is the Society’s educational resource, where EAS members can access a wide range of presentations, webcasts, video-podcasts, quizzes and other self-learning tools.
Find out more HERE

www.eas-society.org
RUTHERFORD-2: LDL-C$^a$ goal achievement <70 mg/dL at Week 12

**Graph:**

- Placebo Q2W (N = 54)
- Placebo QM (N = 55)
- Evolocumab 140 mg Q2W (N = 110)
- Evolocumab 420 mg QM (N = 110)

- Proportion of patients (%): 2%, 68%, 61%, 63%

$^a$Determined by the Friedewald formula with reflexive testing via preparative ultracentrifugation when calculated LDL-C was < 40 mg/dL or triglyceride levels were >400 mg/dL; $^b$p<0.001; analyzed using CMH test, stratified by the stratification factors.

Evolocumab is an investigational drug under clinical development.

Raal et al Abstract No. 400-05, Featured Clinical Research, Oral Presentation, Saturday, March 29, 2:36 – 2:54 p.m. EDT
Most heFH Patients Receiving Alirocumab on Background Statin ± Other LLT Achieved LDL-C Goals

Proportion of patients reaching LDL-C goal† at Week 24

FH I

72.2%

FH II

81.4%

2.4%

11.3%

P<0.0001

†Very high-risk: <1.81 mmol/L (70 mg/dL); high-risk: <2.59 mmol/L (100 mg/dL). LLT = lipid-lowering therapy.
Preserve Health vs Treating Disease
Screen early, treat early, think about lifetime risk

54.5% relative risk reduction per 1 mM/L (38.7mg/dL) LDL-C lowering

22% relative risk reduction per 1 mmol/L (38.7mg/dL) LDL-C lowering

Solutions

• Systematic Screening

• Exemplar NHS Vascular Health Checks being offered in the UK to everyone aged 40-70
Problems

• Visualising absolute risk in an individual is poor

• Reluctance to use higher doses based on unfounded concerns

• Wait and watch approach
The Need for Absolute Risk Prediction for People on Statin Therapy
Relationship of LDL-C lowering and Risk Reduction with a statin

~ 20% reduction in RR per mmol LDL-C

Consistent effect on relative risk; diminishing effect on absolute risk

Log of Risk

8%

-20% = 1.6% abs RR

-20% = 1.3% abs RR

-20% = 1% abs RR

-20% = 0.8% abs RR

Consistent effect on relative risk; diminishing effect on absolute risk

As abs risk

NNT

LDL-C mmoles

0 1 2 3 4 5 6
Figure 3. Risk of Ischemic Events in the Subsequent 4 Years of Follow-up in Patients According to Baseline Risk Category

- **Prior ischemic events**
  - All: 21,890
    - Yes: 15,264
    - No: 6,626
  - Diabetes: 7,987
    - Yes: 5,686
    - No: 2,301
  - Polyvascular Disease: 5,158
    - Yes: 9,577
    - No: 1,581

- **Stable atherosclerosis without prior ischemic events**
  - All: 16,732
    - Yes: 13,233
    - No: 3,499
  - Diabetes: 13,903
    - Yes: 9,577
    - No: 4,326
  - Polyvascular Disease: 16,732
    - Yes: 13,233
    - No: 3,499

- **Risk factors only**
  - All: 8,073
    - Yes: 6,026
    - No: 2,045
  - Diabetes: Yes: 6,026
    - No: 2,045
Development and validation of a prediction rule for recurrent vascular events based on a cohort study of patients with arterial disease: the SMART risk score

Johannes A N Dorresteijn,¹ Frank L J Visseren,¹ Annemarie M J Wassink,¹ Martijn J A Gondrie,² Ewout W Steyerberg,³ Paul M Ridker,⁴ Nancy R Cook,⁴ Yolanda van der Graaf,² on behalf of the SMART Study Group
## Other Therapies

<table>
<thead>
<tr>
<th>CETP Inhibition</th>
<th>HDL pathways</th>
<th>Anti Inflammatory Tx</th>
<th>Other</th>
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<td>Anacetrapib</td>
<td>Apo A mimetics</td>
<td>IL-1B inhibition</td>
<td>Target Lp(a)</td>
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<td>Methotrexate</td>
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<td>PPAR alpha agonists</td>
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<td>High Dose fish oils</td>
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Overall rates of secondary prevention medication use for CVD is low worldwide

PURE study, 17 countries

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<th>Antiplatelet</th>
<th>Beta-blockers</th>
<th>ACEi or ARBs</th>
<th>Diuretics</th>
<th>BP-lowering</th>
<th>Ca-channel blockers</th>
<th>Statins</th>
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PURE, Prospective Urban Rural Epidemiology; ACEi, angiotensin-converting-enzyme inhibitor; ARB, angiotensin receptor blocker; BP, blood pressure

Conclusion

• All these emerging therapies will increase uptake of statins and other current Tx

• FH will be better detected (hope), better treated yes

• Screen and treat early

• Need to be more sophisticated about who we offer additional Tx to