EDITORIAL

2013 ACC/AHA Lipid Guidelines: Mind the Gaps

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ABSTRACT

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The recently published 2013 ACC/AHA guidelines for the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk seem to have various implementation problems and have already initiated an intense debate. These guidelines identify 4 high-risk groups who could benefit from statins, patients with pre-existing atherosclerotic cardiovascular disease (CVD); people with familial (heterozygous) hypercholesterolemia, as evidenced by an LDL-cholesterol (LDL-C) of >190 mg/dl; diabetic patients aged 40-75; and people aged 40-75 with at least a 7.5% risk of developing CVD in the next decade, according to a formula described in the guidelines. In contrast to all other guidelines for the management of dyslipidemia, the 2013 ACC/AHA guidelines do not recommend specific LDL-C targets. Instead, they propose a 30-50% reduction in LDL-C administering high- or moderate-intensity statin therapy depending on the CVD risk. The problems of adopting these new guidelines are herein discussed.

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Conflict of Interest: none declared

LIPID GUIDELINES

Elevated serum low-density lipoprotein cholesterol (LDL-C) levels are still a major risk factor for cardiovascular disease (CVD) morbidity and mortality; similarly the reduced levels of high-density lipoprotein cholesterol (HDL-C) play a role in the pathogenesis of CVD. The association between elevated triglyceride levels and CVD events is more controversial; however, they appear to play even a minor role in atherogenesis. Accordingly, the management of dyslipidemias is a major component of primary and secondary CVD prevention strategies. In this context, several medical organizations have formulated guidelines for the management of dyslipidemias. The first lipid guidelines were issued in November of 1985 from the National Cholesterol Education Program (NCEP), a branch of the National Heart, Lung, and Blood Institute (NHLBI) of US; Europe issued lipid guidelines much later (European Atherosclerosis Society 1989). At present time we follow in Greece the first Joint EAS/ESC lipid guidelines issued in 2011. These are very simple, because they have one primary target (LDL-C), and 3 levels of CVD risk with specific LDL-C targets of <115, <100, and <70 mg/dl. EAS/ESC guidelines have issued coloured charts showing the CVD risk, according to CVD risk factors; setting the cut of point (of the SCORE) at 5% risk of fatal CVD during the next 10 years (Figure 1). These guidelines encourage the European Countries to issue
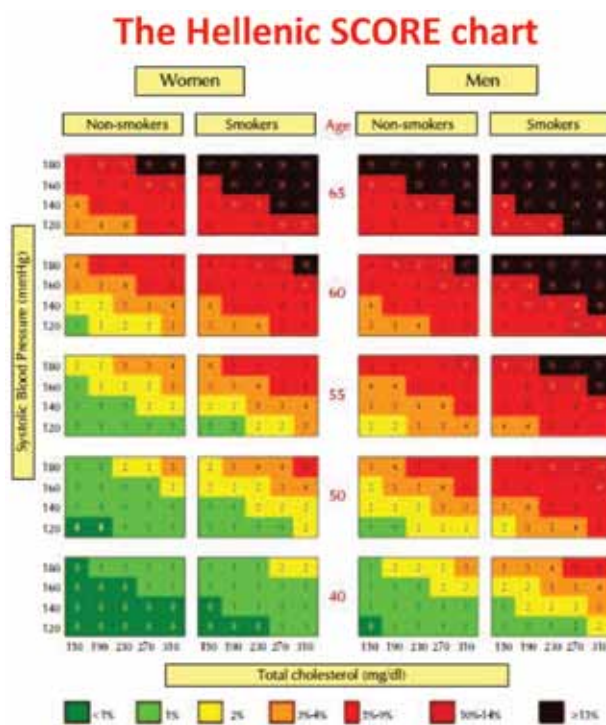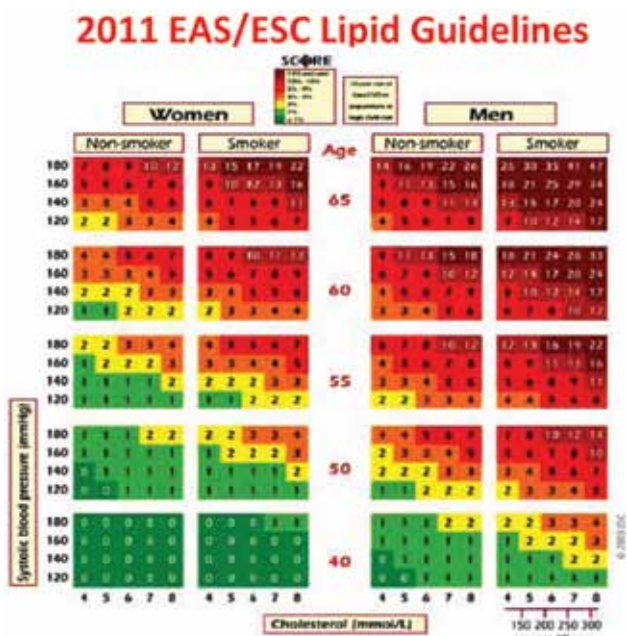
2011 EAS/ESC Lipid Guidelines

FIGURE 1. SCORE chart: 10 year risk of fatal cardiovascular disease (CVD) in populations at high CVD risk based on the following risk factors: age, gender, smoking, systolic blood pressure, and total cholesterol. To convert the risk of fatal CVD to risk of total (fatal + non-fatal) hard CVD, multiply by 3 in men and 4 in women, and slightly less in old people. Note: the SCORE chart is for use in people without overt CVD, diabetes, chronic kidney disease, or very high levels of individual risk factors because such people are already at high risk and need intensive risk factor advice.

The Hellenic SCORE chart

FIGURE 2

their own guidelines according to local data, and Greece was the second European Country to do that (HellenicSCORE - a Calibration of the ESC SCORE Project, by the group of Profs Stefanadis C, Pitsavos C, and Panagiotakos D – Figure 2). All the above made the EUROSCORE very easy to implement. Its only disadvantage is that it is based on the risk of CVD mortality only and does not take into consideration CVD morbidity, as it leaves out of the CVD risk calculation non-fatal myocardial infarction and non-fatal stroke.

NEW GUIDELINES

In antithesis, the recently published (12 Nov 2013) ACC/AHA "Guidelines on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults" presented at the American Heart Association's Scientific Sessions in Dallas, Texas, USA, seem to have various implementation problems and have already sparked an intense debate.

The guidelines identify **four high-risk groups** who could benefit from statins:

- Patients with pre-existing atherosclerotic CVD
- People with familial (heterozygous) hypercholesterolaemia, as evidenced by an LDL-C of 190 mg/dl or higher;
- Those ages 40 to 75 who have diabetes mellitus;
- People 40 to 75 with at least a 7.5% risk of developing CVD in the next decade, according to a formula described in the guidelines (please see below).

In contrast to all other guidelines for the management of dyslipidemia, the **2013 ACC/AHA guidelines do not recommend specific LDL-C targets**. Instead, they propose a 30-50% reduction in LDL-C administering high- or moderate-intensity statin therapy depending on the CVD risk (Figures 3 & 4).

- **High-intensity statin therapy includes atorvastatin 40-80 mg/day and rosuvastatin 20-40 mg/day.**
- Moderate-intensity statin therapy includes atorvastatin 10-20 mg/day, rosuvastatin 5-10 mg/day, simvastatin 20-40 mg/day, pravastatin 40-80 mg/day, fluvastatin 40-80 mg/day and pitavastatin 2-4 mg/day.
- According to the ACC/AHA guidelines, patients aged ≤75 **years with established atherosclerotic CVD** [coronary heart disease (CHD), stroke or peripheral arterial disease] and subjects with LDL-C levels > 190 mg/dl should be treated with **high-intensity statin therapy**.
- Patients aged 40-75 years **with type 2 diabetes mellitus (T2DM) and LDL-C 70-189 mg/dl but without CVD** should be treated **with high-intensity statin therapy only if their estimated 10-year risk for CVD (including CHD death,**

FIGURE 3. Algorithms for ACC/AHA guidelines.

FIGURE 4. Algorithms for ACC/AHA guidelines.

nonfatal myocardial infarction, fatal and nonfatal stroke) is ≥7.5% and with **moderate-intensity statin therapy** if their estimated **10-year CVD risk is <7.5%.**

- Finally, **patients aged 40-75 years with LDL-C 70-189 mg/dl but without T2DM or CVD** should be treated **with high- to moderate-intensity statin therapy if their estimated 10-year CVD risk is ≥7.5%**, whereas it is reasonable to administer **moderate-intensity statin therapy if their estimated 10-year CVD risk is 5% to <7.5%.**

- **In other patient groups** (i.e. those older than 75 years with or without CVD or T2DM and those without CVD or T2DM and with 10-year CVD risk < 5%), the **use of statins should be individualized** based on perceived benefits and risks of statin treatment, potential for drug-drug interactions, and patient's preferences.

To estimate 10-year CVD risk, a new equation is proposed, the **Pooled Cohort Equation**, derived from data from 5 large epidemiological studies (n = 24,626) conducted in US (Atherosclerosis Risk in Communities, Cardiovascular Health Study, Coronary Artery Risk Development in Young Adults, and the Framingham and Framingham Offspring studies). **chttp:// my.americanheart.org/professional/StatementsGuidelines/ PreventionGuidelines/ Prevention-Guidelines_UCM_457698_ SubHomePage.jsp**

PROBLEMS WITH THE IMPLEMENTATION OF 2013 ACC/AHA LIPID GUIDELINES

1. The guidelines for treatment of dyslipidemia are based solely on epidemiological data and not on the results of prospective, randomized, controlled, interventional, survival trials. We are long past from defining CVD (main) risk factors; at present we are at difficulty to implement previous simple treatment guidelines.

2. The studies used for the equation formula were conducted in the US only. Thus, these guidelines might be applicable in the US, but they are not probably applicable anywhere else in the world (Europe, Asia, Africa, and South America).

3. The guidelines suggest only statin treatment and practically ignore all other hypolipidaemic agents; thus, these are "statin" and not "lipid" guidelines.

4. The algorithms used to drive the choice of treatment are very complex and could not be remembered by all physicians that have to memorize and implement a number of algorithms for various other diseases, within their speciality.

5. There is no mention about coronary heart disease (CHD) equivalents, such as diabetes mellitus and chronic kidney disease (present in the Canadian, the EAS/ESC, and the Greek guidelines), as well as their combination (diabetic nephropathy has an annual mortality rate of 20%, similar to that of cancer). CHD equivalents are ignored at a time that other panels and task forces are considering to expand the concept of CHD equivalents including rheumatoid arthritis, non-alcoholic fatty liver disease or its advanced form, non alcoholic steatohepatitis, metabolic syndrome with 4-5 components, and others. The ACC/AHA guidelines deprive intensive statin treatment from all these high CVD patients.

6. On the other hand, the formula used to calculate risk in the ACC/AHA guidelines overestimates CVD risk in those without overt CVD of diabetes. There might be an increase by up to 150% of the number of primary CVD prevention individuals that need statin treatment. Patients on statins in US are at present 31.5 million and their number is estimated to rise up to 70 million, if these guidelines are fully implemented. It has also been projected that the application of the ACC/AHA guidelines worldwide will render more than 1 billion subjects eligible for statin treatment. The ACC/AHA panel is trying to protect US from the upcoming increase of CVD events due to the ever increasing prevalence of obesity, with cheep (generic atorvastatin costs less than 5$ a month) statins for everybody. Obesity, hypertension, dyslipidemia, type 2 diabetes mellitus, and metabolic syndrome are driving the CVD risk in US; CVD morbidity and mortality is expected to explode like a bomb in the next few years, if drastic measures are not taken. In terms of lifestyle changes the situation is disappointing. Despite the fact that 70% of US adults are overweight or obese, still diet quality continues to deteriorate, leading to the fact that at present time the majority of US adults display significant lipid abnormalities. However, statin for everybody without weighing the risk/benefit ratio is dangerous. Statins are known to cause new onset diabetes mellitus in up to 24% of people that take them, especially in obese people, those with metabolic syndrome, and those with prediabetes. Thus, this policy will probably cause a boost in the prevalence of diabetes, a major risk factor for CVD.

7. The lack of specific LDL-C targets is a great problem also. It is not rare to see in our practice a patient with heterozygous familial hypercholesterolemia and an LDL-C value 350-400 mg/dl. According to the ACC/AHA guidelines a 50% reduction is enough. However, is anybody accepting the value of 150-200 mg/dl of LDL-C of being at target? This suggests that some patients that need intensive hypolipidemic (mainly with combinations) drug treatment are deprived of it, while others that do not need it are considered eligible to receive it.

8. These guidelines will be an immense barrier that will at least delay the use of upcoming in the near future hypolipidemic drugs, such as antibodies against PCSK9 (evolocumab and alirocumab). These will be commercially available within the next two years and are expected to be expensive. These have an indication to be used in high CVD risk patients that can not reach the <70 mg/dl LDL-C goal with available treatments. How can one use these drugs if there is no specific LDL-C goal over which antibodies against PCSK9

should be administered?

9. Finally, the suggestion of these guidelines is that there is no need for follow-up visits and follow-up lab tests in patients on statins; the "fire and forget" dogma. This is another way to bring down the total cost of statin treatment.

All the above suggest that economic (cost) but not cost/effectiveness parameters were taken into consideration when preparing the ACC/AHA guidelines. This is probably the job of a politician rather than the job of a physician. With upcoming implementation of the Obamacare both US Administration and Legislature are taking into consideration the upcoming obesity-related boost in CVD incidence, and put pressure for a cheap solution for the treatment of dyslipidaemia, given that statins are the best selling drugs ever. However, other countries do not have this perspective and they do not need to adopt these guidelines. This is the reason that the Task Force of the European Atherosclerosis Society/European Society of Cardiology, the American Diabetes Association, the American Lipid Association, the American Society of Clinical Endocrinologists, and other smaller Societies from South America or Asia declined to endorse these new cholesterol (statin) guidelines and suggest to stick with previous guidelines. As a matter of fact no other Society adopted these guidelines.

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