Lipid Guidelines and Recommendations 2014 and Beyond

Reconciling the 2013 AHA/ACC Guidelines with other Guidelines, Recommendations and Statements by Creation of a ***US Expert Consensus Statement***

Eliot A. Brinton, MD, FAHA, FNLA
Director of Atherometabolic Research,
Utah Foundation for Biomedical Research
President, Utah Lipid Center
Salt Lake City, UT
eliot.brinton@utah.edu

The Case *Against* the New ACC/AHA Cholesterol Guidelines

2013 ACC/AHA Guidelines In Perspective

- *Not* the "official US guidelines" (!)
- *Not* NCEP/ATP-IV
- Are "orphan" guidelines (not "NHLBI", no NCEP consortium, ACC & AHA review was rushed and superficial)
- "Odd man out" in deleting lipid goals, contrast with ATP-I to III, ADA, AACE, European, Canadian and IAS guidelines
- Deletion of goals rejected by NLA, AACE, Europeans & Canadians

Evidence Levels for Guidelines

Evidence Level	2013 ACC/AHA Cholest. Guidelines	All other Lipid Guidelines
Multiple HQ RCTs*	Yes	Yes
Meta-analyses of RCTs*	Yes	Yes
Single HQ RCT**	No	Yes
Lower-quality (& earlier) RCTs***	No	Yes
Observational Data***	No	Yes
Biological MoA (animals, cells, etc)***	No	Yes
Expert Opinion***	No	Yes

Yes, let's give stronger emphasis to stronger evidence
No, don't exclude weaker evidence (prepond. of evidence)
Yes, use statins first and aggressively
No, don't exclude non-statins

Certainty of Evidence: *Level A; **Level B, ***Level C.

Why *Not* Continue to Treat to Target?

***Major difficulties with targets*:**

1. Current RCT data do not indicate what the target should be.
2. Unknown magnitude of additional ASCVD risk reduction with one target compared to another.
3. Unknown rate of additional adverse effects from multidrug therapy used to achieve a specific goal.
4. Therefore, unknown net benefit from treat-to-target approach.

Stone, NJ, et al. J Amer Coll Card, 2014;63:2889-2934

Why Not *Continue* to Treat to Target?

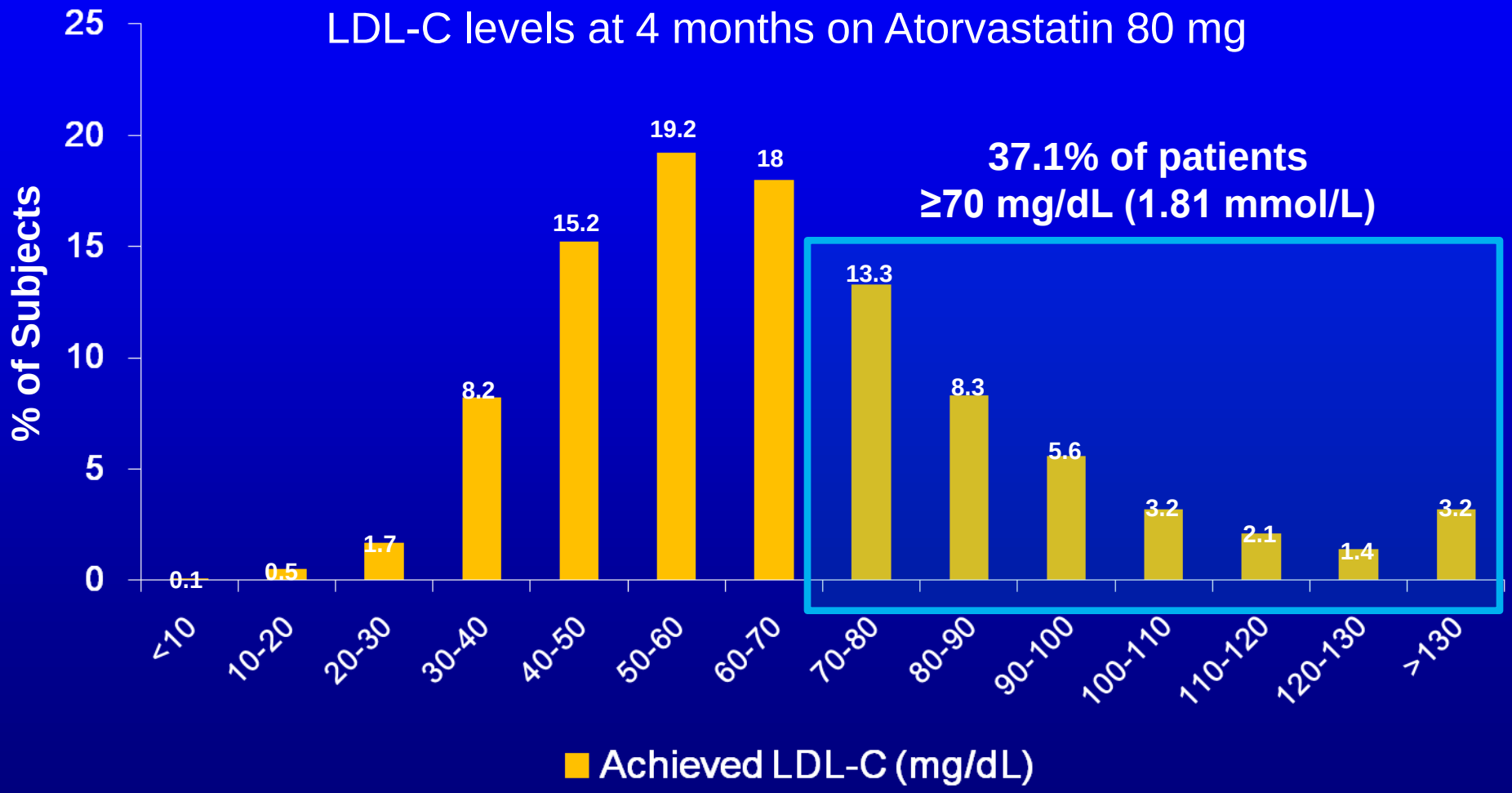
Counterpoint:

1. LDL and other apo-B-containing particles are universally acknowledged* as 1º cause of ASCVD.
2. ACC/AHA panel excluded evidence* used by others** for specific LDL-C & Non-HDL-C goals
3. LDL-C & Non-HDL-C goals main lipid focus for 25 y
4. RCT data all indicate: **lower LDL-C is better****
5. Therefore, deletion of LDL-C and Non-HDL-C goals is ***not*** **necessary and *not* helpful*****

Don't let the perfect be the enemy of the good!

*Stone, NJ, et al. J Amer Coll Card, 2014;63:2889-2934.
** Wiviott SD et al. *JACC.* 2005;46:1411-1416.
***Ray, KK, et al. Eur Heart J (2014) 35:960-968. Anderson TJ, et al. Can J Card e-pub 1/14/14. Jacobson, TA, et al. J Clin Lipidology, 2014;8:473-488.

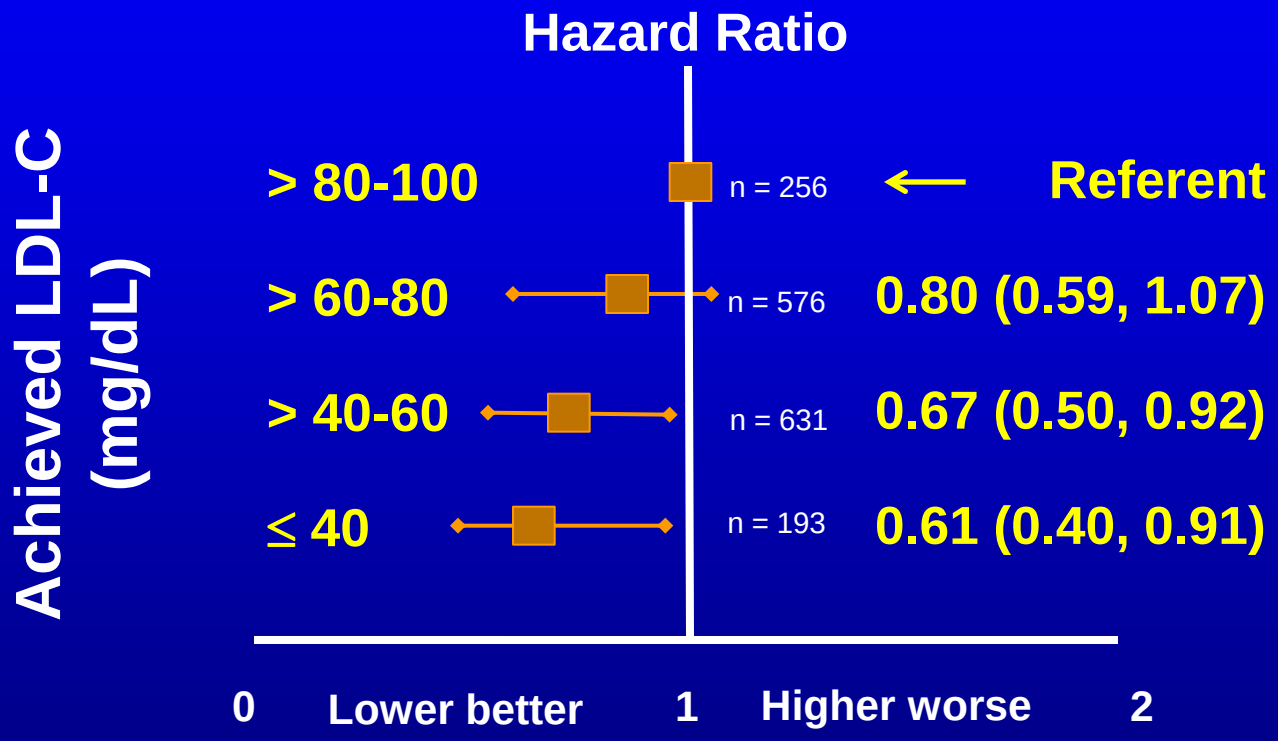
LDL-C Varies *Greatly* on High-Intensity Statin



Wiviott, SD, et al for the PROVE-IT TIMI-22 Investigators. *Am J Cardiol*. 2005;46(8):1411-16.

Lower On-Treatment LDL-C *IS* Better!

Atorvastatin 80 mg vs pravastatin 40 mg in 2099 ACS patients for 24 months



Endpoint: CHD death, nonfatal MI, CVA, recurrent ischemia, revascularization

*Adjusted for age, gender, baseline LDL-C, diabetes mellitus, and prior MI.

PROVE-IT/TIMI 22 Substudy. Wiviott SD et al. *JACC.* 2005;46:1411-1416.

Proposed Guideline Compromise

2013 ACC/AHA

ATP-III/NLA/IAS/AACE…

- Use 4 pt categories for stain Rx (w/ modif.)
  - Prior ASCVD (or bad subclinical athero?)
  - DM1 >40 y/o and DM2 all ages
  - Severe hypercholesterolemia (LDL-C > 190)
  - 10 y risk >7.5% (vs higher 10y; alt: lifelong >40%?)
- More aggressive statin use (but additionally retain low-dose statin option)
- Reinstate goals (simplified):
  - Non-HDL-C (<130/<100 mg/dL for high/v. high risk)
  - LDL-C (<70/<100 for high/v. high risk)
- Add/return RFs: FHx, MetSynd, HTG, CRF…?
- Consider non-statin adjuncts for
  - Residual dyslipidemia signalling
  - Residual ASCVD risk

Proposed *Inclusive* US Expert Consensus Lipid Management Statement

What should be included?

- All evidence: no more "unprecedented" exclusion of valid evidence
- All doses of statins
- All non-statins
- All lipid disorders
- All major US ethnic groups (Hispanics/Native Americans, East & South Asians, Blacks)
- All good elements of all lipid guidelines = expert consensus of published guidelines

Who should be included in expert consensus process?

- Lipidologists: NLA
- Endocrinologists: Endo Society, AACE, ADA
- Cardiologists: AHA, ACC, ASPC, ABC, etc.
- Other Specialists & Generalists: ACP, AAFP, AAP, ACOG, NAMS, TOS, ASH, ASN…

(All interested professional societies invited as expert partners—***NCEP paradigm***)

How to create the Statement? Brief overview:

- Convene panel of experts selected and supported by respective societies
- NHLBI sponsorship (neutrality, "official US", clean $ source)
- Meetings mainly by webinar/teleconference to minimize cost (no Pharma $!)
- Consensus Statement finalized with society endorsements (as possible)

How to: Further Considerations—I

- The (failed) attempt to omit expert opinion from the 2013 ACC/AHA guidelines is one of its key failings and suggests that an expert consensus statement may be its best antidote.
- Involvement of international colleagues is welcome in many ways, but expert professional groups outside the US are already clearly and forcefully on-record rejecting the deletion of lipid goals form the 2013 ACC/AHA guidelines (its main defect).
- The US has a problem in that its federal lipid guidelines program changed into a non-federal program (ACC and AHA) which falls into the vacuum left with the exit of the NHLBI from the process
- AHA and ACC will NOT be willing to go officially against their recent guidelines, but every effort should be made to:
  - Invite them openly so they accept or their refusal is public
  - Invite people well-connected with the AHA to participate. Two past-presidents come to mind: Bob Eckel's recent defense of the guidelines at ADA may make it awkward or impossible for him, but he could be invited, and Virgil Brown must be invited.

How to: Further Considerations—II

- Success of this initiative may well hinge on the number of professional societies involved and endorsing.
- Is it feasible to ask organizations to fund their own liaison(s)? How should liaisons/panel members be chosen?
- Could NHLBI agree to help fund and direct this statement?
- Pharma support cannot be used!
- Do we need a “core committee” independent of society nominations? This would probably be useful but would require “core funding”. What source(s)? Last slide has poss. members.
- How to handle COI? The IOM suggests a policy similar to that of AHA. Probably best to ask for liaisons with the fewest possible conflicts and then have voting and non-voting panelists.
- IMPROVE-IT results will have impact on this process (and might lead to an addendum to 2013 ACC/AHA). This proposal will need to be re-evaluated in light of that report and its professional political fallout.

Suggested Process

1. Run these basics past the ILF faculty as a possible initial core group to review this draft process outline.
2. Seek appropriate core funding (how much? from whom—NHLBI? ILF? Other foundations?)
3. Write and send out invitations to the appropriate professional societies.
4. Work with all interested societies to maximize their participation and buy-in up front. In particular, a reasonably detailed set of rules for the process should be agreed upon by all parties.
5. Hold the first committee meeting
    a. Establish rapport among committee members and leaders.
    b. Review and finalize process rules, including time-frame.
    c. Divide tasks into subtopic “chapters”.
    d. Determine membership & leadership of subcommittees for each chapter.
6. Hold most subsequent subcommittee meetings (towards consensus chapter texts) by teleconference (or webinar) for cost-efficiency and time-efficiency.
7. Share the chapter texts with the entire committee to obtain further input and make needed modifications.
8. Re-convene the entire committee for final vetting and voting?
9. Confidential final draft sent to participating society leadership for vetting.
10. Incorporate society input into the document (how?).
11. Final document approval (by whom? how?) and publication (where?).