

The New Lipid Targets: How Low To Go And How Can We Achieve Them?

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May 12, 2007

Disclosure of Conflicts of Interest

I have received travel grants and honoraria from sanofi-aventis, Pfizer, Servier, Merck, Procter & Gamble, Biovail, AstraZeneca, Novartis and Merck/Frosst/Schering

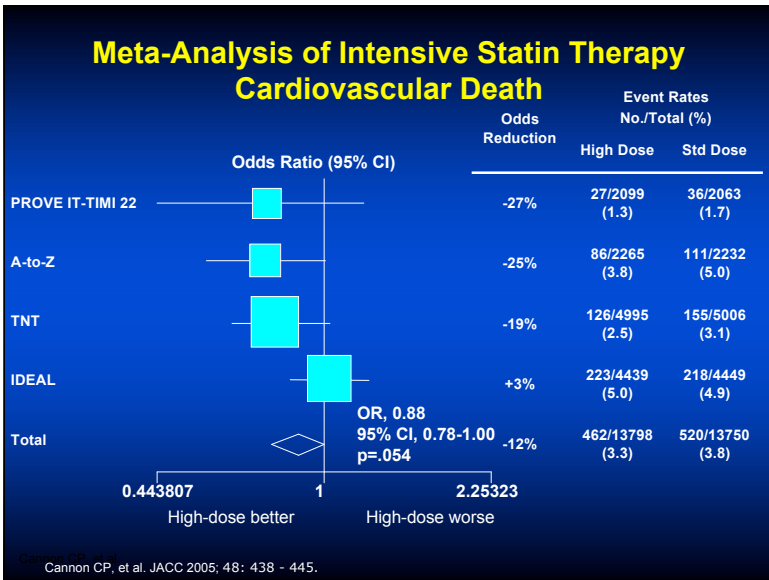
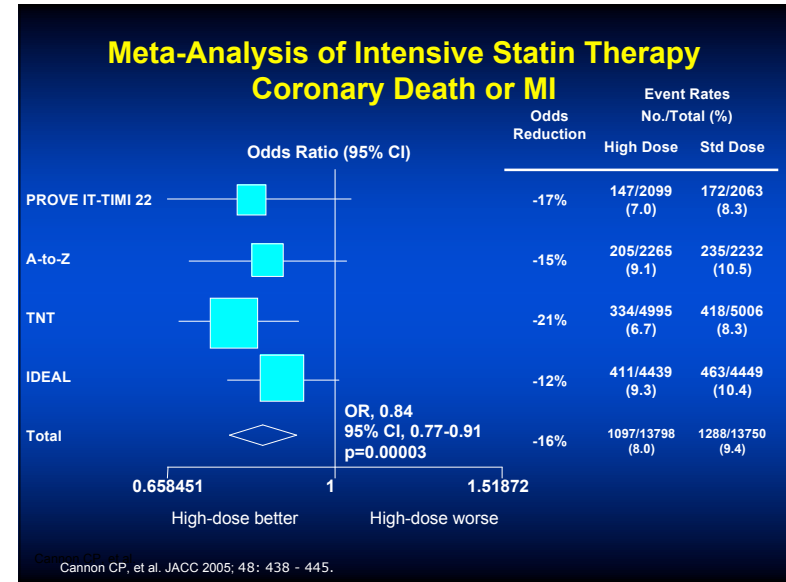
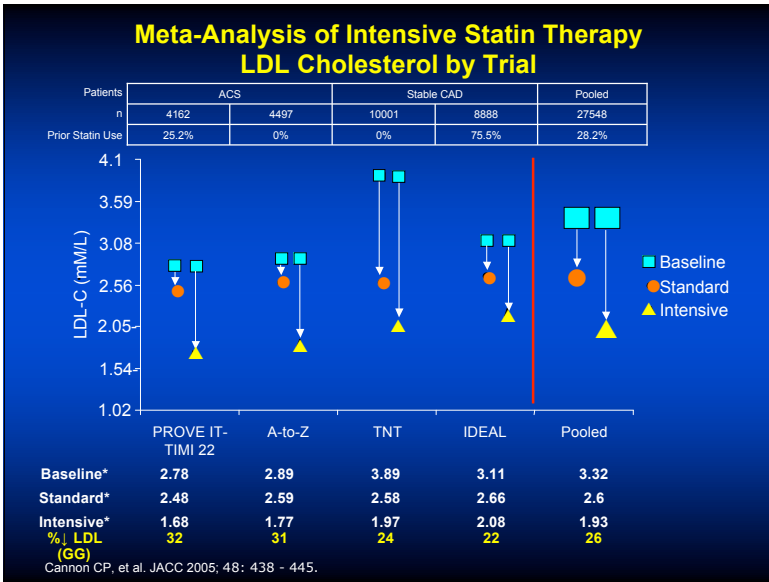
I am the local Primary Investigator of studies sponsored by Pfizer Boehringer-Ingelheim and sanofi-aventis

New Canadian Guidelines 2006

- Low risk patient (Framingham risk score [FRS] <10%/10yr):
LDL-C < 5.0 (from 4.5) mM/L
- Medium risk patient (FRS: 10-20%/10 yr):
LDL < 3.5 mM/L
- High risk patient – i.e. one with ANY vascular disease or DM for over 10 yrs or with an FRS > 20%:
LDL < 2.0 (from 2.5) mM/L

Why Do We Need To Go Below An LDL 2.5 mmol/L

- The PROVE-IT Study
- The TNT Study
- HPS, A-Z, IDEAL and SPARCL
- 2 large meta-analyses of the above
- IVUS studies



- ### Meta-Analysis of 90,000 Patients In Lipid Lowering Trials
- 1 mmol/l LDL-C reduction corresponded to:
 - 12% reduction in all-cause mortality
 - 19% reduction in CHD mortality
 - NS re: in non-coronary vascular mortality and in non-vascular mortality
 - 23% reduction in MI or CHD death
 - 24% reduction in the need for coronary revasc.
 - 17% reduction in fatal or non-fatal stroke
 - 21% reduction in any such major vascular event in 5 years regardless of baseline LDL-levels!
- Cholesterol TT: Lancet 2005; 366: 1267-78.

What Options Did The Canadian Guidelines Have?

- They could have chosen:
 - The drug at the dose used in the studies – you can't endorse one drug
 - The LDL-difference between the arms (relative reduction) – you have to choose one approach
 - Other, better predictors like apoB levels or TC/HDL ratio – not practical
 - The average LDL-level achieved in the studies - not the approach in the studies, need for titration

What Is The Problem With The Chosen Recommendation?

- LDL < 2 was derived from the random results of the above studies – not a prespecified target, there was no titration to target in trials!
- What if the patient has an LDL of 2-2.5 on Lipitor 80?
- IVUS studies showed no reversal unless LDL < 1.8 mmol/L
- To achieve an LDL < 2 you need to add another drug, usually Ezetrol and although it is a low-risk intervention, no long-term outcome data exist

What Is The Evidence That An LDL < 2 is Good Enough?

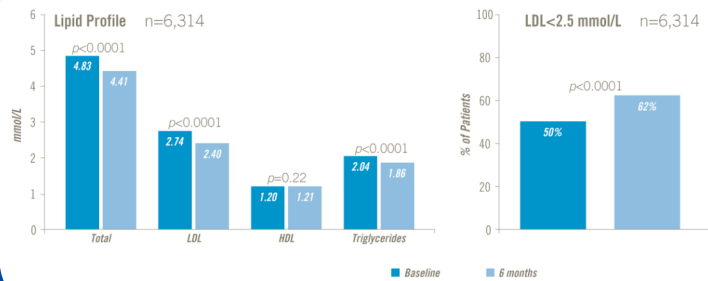
- Nothing, in fact, IVUS studies provide evidence that <1.8 is better than >1.8 and <1.6 induces more regression - ??Add EZE to the max. tolerated statin?? – ongoing studies address this issue
- The parallel design of REVERSAL and PROVE-IT suggests that plaque regression might be a meaningful outcome
- No documented risks of having an LDL < 1.0 mmol/L

Why Push This Agenda?

THE CARE GAP:

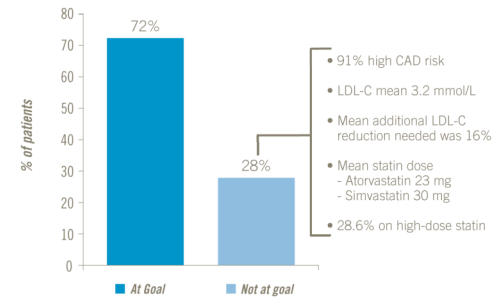
Current target LDL-C levels are not achieved in a high proportion of high-risk patients

Results From The Canadian GOALL Registry Of High-Risk Patients



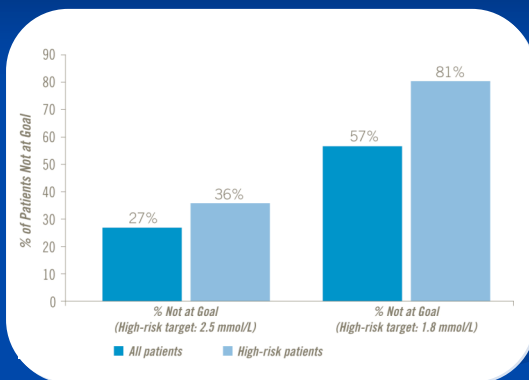
Yan A et al. Am J Med. 2006; 119:676-83.

PROPORTION OF PATIENTS ACHIEVING LDL-C GOALS



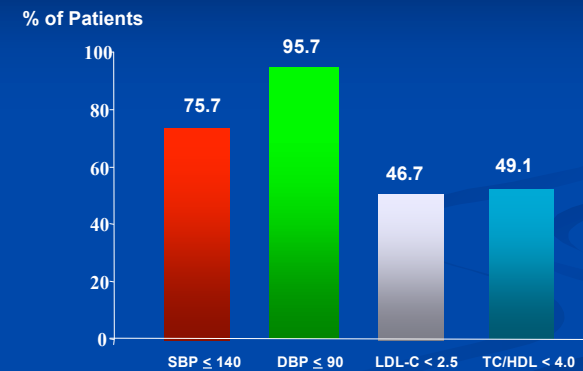
CALIPSO: Bourgault et al. Can J Cardiol 2005;21:1187-93.

CALIPSO FINDINGS: RESULTS BASED ON NCEP ATP III UPDATE

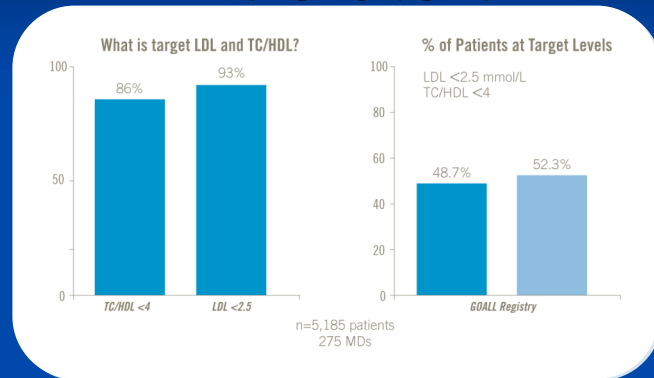


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VPEX Registry: Targets Achieved in Canada



GOALL Registry Chart Review: CARE GAP IS NOT A KNOWLEDGE GAP BUT AN ACTION GAP!



Yan A et al. Am J Med. 2006; 119:676-83.

This Is A Missed Opportunity!

So How Can We Achieve
These Aggressive Targets?

My Recommendations - 1

- Keep everyone (high-risk patients only!!!) on a high dose potent statin (Lipitor 80) for as long as possible
- Hold the drug in case of AE but re-challenge patients with the same dose – many perceived side-effects are non-statin related
- Most patients achieve the new targets on this dose

My Recommendations - 2

- If LDL-targets are not achieved, look at the TC/HDL ratio
- If <4 the patient is probably fine, especially if the LDL-reduction was 30% or over 1 mmol/L
- If neither LDL, nor ratio targets are achieved, add Ezetrol 10 mg od – no outcome studies yet
- Ezetrol is very well tolerated and usually reduces LDL by 1 mmol/L or 20% - can't be a bad thing
- Do NOT replace statin w/ Ezetrol for now unless AE on high dose only – not a typical case

My Recommendations - 3

- Fibrates and statins are NOT INTERCHANGEABLE!!
- Adding fibrates to a statin might increase HDL but also increases the risk of myopathy and no outcome data exist
- Fibrates are OK for $\uparrow\uparrow$ TG \pm \downarrow HDL (DM) but minimal outcome data
- Niacin is a very good alternative, its reputation is undeservedly bad – outcomes are reasonable - mainly in combo w/ statins

Thank You!

Q & A