SJHG Heartbeat

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Best Practical Cardiology Story of 2009

Many news articles have focused on the best cardiology advances of the past year. This *Heartbeat* will focus on the study that provided the most read, valuable and pertinent information we can use daily to improve outcomes—JUPITOR. **An analysis of the JUPITER study concluded that roughly four out of every five Americans older than 50 may be eligible for statin therapy.**

Results of the **J**ustification for the **U**se of Statins in **P**rimary **P**revention: An **I**ntervention **T**rial **E**valuating **R**osuvastatin (**JUPITER**) demonstrated that the statin rosuvastatin reduced the risk for cardiovascular (CV) events by almost half in patients with elevated high-sensitivity C-reactive protein (*hs*CRP) levels ≥2 mg/L) but with low density lipoprotein (LDL) levels below 130 mg/dL, which is more aggressive than the guideline indication for statin therapy.[1] JUPITER is the largest study to date to assess the role of statins in a demographically diverse patient population, including more than 7000 women and many older patients.

In a follow-up study, investigators performed an analysis to quantify the implications of the JUPITER results.[2] After reviewing NHANES data from 1999 to 2004, they estimated that nearly 60% of men aged ≥50 and women aged ≥60 (33.5 million Americans) would have an indication for statin therapy according to current LDL-based guidelines. Fewer than half of them are being treated. Using the JUPITER criteria, it was estimated that an additional 14% of the U.S. population (8.1 million people) would become eligible for statin treatment. Extending the JUPITER criteria to adults in the same age group with *hs*CRP levels ≥2 mg/L and LDL levels between 130 mg/dL to 160mg/dL would add another 3.1 million to this group.

These results confirm that many adults who are already eligible for statin treatment according to current guideline recommendations are not receiving them. Additionally, if the JUPITER criteria were to be incorporated into the future National Cholesterol Education Program Adult Treatment Panel (NCEP ATP) IV guideline recommendations—coming out later this year, millions more individuals — **80% of adults older than 50 — would become eligible for statin treatment.**

Compared with those who would continue to have no indication for statin therapy, the JUPITER group was more likely to be female, older, and to have obesity, hypertension, and the metabolic syndrome—i.e. a lot of these people had indications for statin treatment without an *hs*CRP level because they were at moderately high risk.[3] In JUPITER, rosuvastatin significantly reduced all-cause mortality by 20 % in individuals who do not currently qualify for statin therapy. But Framingham Risk Scores (FRS) for coronary heart disease risk stratification per NCEP/ATP-III Guidelines, non-HDL-C, apolipoprotein B (apoB) and LDL particle number/concentration (LDL-P via

LipoScience's NMR LipoProfile were not addressed.

The calculated mean **non-HDL**-C, total cholesterol minus HDL-C, from the baseline blood levels (median, interquartile range) in JUPITER was 137mg/dL. Therapy is warranted if it is > 130mg/dL (or > 100mg/dL in very-high-risk patients).[4] Newer data reveal that this calculation is always equal or better than LDL-C at predicting CVD risk.

It is essential to point out that the **JUPITER trial exposes** the **current LDL-C thresholds** for lipid-lowering therapy not only as arbitrary, but more importantly, **as a poor indicator of CV risk.** This should reinforce the need to calculate non-HDL-C and use apoB or LDL-P levels to more accurately assess CV risk as recommended in the recent American College of Cardiology/ American Diabetic Association Consensus Guidelines.[5] *LDL-P has emerged as a superb predictor of risk and also as a goal of therapy.*

Clinical Perspective

- JUPITER provides more evidence about the effectiveness of statin therapy in reducing CV risk, even among people who would not currently be considered for pharmacotherapy.

- Based on existing guidelines and the JUPITER study and subsequent analysis, 80% of the middle-aged to elderly population in the United States may now have an indication for statin therapy for primary prevention.

- Expanding recommendations for statin therapy to include individuals with at-goal LDL cholesterol (< 130mg.dL) but elevated *hs*CRP values and those moderate risk patients with a non-HDL-C > 130mg/dL will pose even greater challenges for us to get everyone to goal.

- Measure either apoB or an LDL-P via an NMR Lipoprofile to better assess CVD risk especially in those with triglyceride (high)/HDL-C (low) axis disorders.

- This is a definite opportunity to advance risk-reduction strategies and improve outcomes.

- Pravastatin 40 to 80mg is recommended as first-line therapy because of decreased cost if you can get to appropriate goals.

Please check the last page (after references) for our aggressive goals of therapy based on Framingham Offspring data.

Mario L Maiese DO, FACC, FACOI

Clinical Associate Professor of Medicine, UMDNJSOM
Email: maiese1@comcast.net

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[1] Ridker PM, Danielson E, Fonseca FA et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein (JUPITOR). *New Engl J Med* November 20 2008; 359: 2195-2207.

[2] Spatz ES et al. From here to JUPITER: Identifying new patients for statin therapy using data from the 1999–2004 National Health and Nutrition Examination Survey. *Circ Cardiovasc Qual Outcomes* January 2009; 2: 41-48.

[3] Maiese ML. The JUPITER trial: Should it change our practice? *Heartbeat* 131 December 2008; 131: 1-4. www.sjhg.org

[4] Dayspring T, Hembold D. You have a new job: Monitor the Lipid Profile. *OBG Management* December 2008; 20: 45-53.

[5] Brunzell JD, et al. Lipoprotein management in patients with cardiometabolic risk. *Diabetes Care* April 2008; 31: 811-822.

Goals of Therapy/Framingham Offspring Study

Many providers get various lipid concentrations and often do not understand how a given patient's lipid values relate to the rest of the population. Below are shown the population cut points from the Framingham Offspring Study. If a patient has an LDL-C of 100, he/she is in the 20th percentile of the population: i.e. 20% of people would have a better LDL-C and 80% would have a higher value. *Typically patients in the bottom 20th percentile have a lower risk than those with values in the higher percentiles.* **The 20th percentile is usually the goal of therapy for moderately high risk patients. The second percentile is the goal of therapy for very high risk patients.**

Although a patient with an LDL-C of < 70 mg/dL would seem to be at goal, if the non-HDL-C, apoB or LDL-P are also not at the second percentile then residual risk may be present. It is relatively easy to achieve an LDL-C of 70, it is much more difficult to reduce apoB < 60 or LDL-P < 750.

Moderately High-Risk Goal: 20th percentile.

Very High-Risk Goal: 2nd or 5th percentile.

Framingham Offspring Study Percentiles

n=3,367 (1,635 men; 1,732 women)

% tile	LDL-C (mg/dL)	Non-HDL-C (mg/dL)	LDL-P (nmol/L)	ApoB (mg/dL)
2	**70**	**83**	**720**	**54**
5	**78**	**94**	**850**	**62**
10	88	104	940	69
20	**100**	**119**	**1100**	**78**
30	111	132	1220	85
40	120	143	1330	91
50	130	153	1440	97
60	139	163	1540	103
70	149	175	1670	110
80	160	187	1820	118
90	176	205	2020	130
95	191	224	2210	140

Specimens were collected in 1988-1991 (exam cycle 4).

Analysis was restricted to subjects with TG <400 mg/dL.
Ethnic make-up was 99% Caucasian.

Freedman DS,et al. Sex and age differences in lipoprotein subclasses measured by nuclear magnetic resonance spectroscopy: the Framingham Study. *Clin Chem* 2004;50:1189 – 1200.

Contois JH, et al. Reference intervals for plasma apolipoprotein B determined with a standardized commercial immunoturbidometric assay: results from the Framingham Offspring Study. *Clin Chem* 1996;42:515–523.
