What's New in Lipids

Medical Management

Nothing Comes Easy

Dave Kovacich MD FACC

Indiana Heart Physicians

What's New in Lipids

- Challenges Impacting our Ability to Provide Optimal Care In the Lipid Arena……

  1) Statin Intolerance

  2) Omega 3 Debacle

  3) Cost

  4) Payors

  5) Staffing

  6) Us

What's New in Lipids
Statin Intolerance

Compactin (ML-236B)

- Discovered in 1973 (Microbe/broth screening)
- Competitive inhibitor of HMG-CoA reductase
- Associated with hepatic crystals in mice
- Did not drop LDL levels in mice
- Associated with Lymphoma in dogs
- Temporarily halted development of lovastatin

What's New in Lipids
Statin Intolerance

SAMS=Statin Associated Muscle Symptoms

SAMS=Myalgia, fatigue, cramping (not arthralgia)

NOT a major concern with early landmark trials

Cancer and cataracts were closely monitored

What's New in Lipids
Statin Intolerance-Clinical Trials

SAMS=Very common in both arms of trials

SAMS=As common as you want to look!

In randomized, double blinded statin trials, the incidence of SAMS is 1.5-5%

HPS=SAMS simva group was 32.9%, 33.1% in placebo arm

How did we get from then to now?

What's New in Lipids

Statin Intolerance

Major Factors Contributing to Statin Intolerance

1)Social Media/Internet

2) The Lancet

3) Providers

What's New in Lipids

C	**1998 Google**							
I								
V		2004 Facebook						
I								
L			2006 Twitter					
I					2010 Instagram			
T							2011 SnapChat	
Y								2016 TikTok
			T	I	M	E		

What's New in Lipids
Statin Intolerance

Wakefield/Lancet Timeline

1) 1998; Case Study Published in Lancet (n=12), Connects MMR to Developmental Disorders
2) 1998-present; Epidemiologic Studies Conducted Refuting MMR Link to Autism
3) 2004; 10/12 Authors Retract Interpretation, Lancet Exonerates all from Charges of Ethical Violations and Scientific Misconduct Despite Proof of Funding by Lawyers Involved in Lawsuits Against Vaccine Producing Companies

What's New in Lipids

Statin Intolerance

"Research Integrity for our Time"

What's New in Lipids

Statin Intolerance

Wakefield/Lancet Timeline

4) 2010; Lancet Fully Retracts Paper, Citing Ethical and Scientific Concerns

5) 2010; BMJ Exposes Driving Force Behind Fraud-Financial Gain

6) 2008-present; Persistent Measles Outbreaks and Worldwide Vaccine Hesitancy, Growing Distrust in the Medical Field

What's New in Lipids
Statin Intolerance-Providers

We as Providers Can do a Better Job Framing the Statin Conversation…..

- Address SAMS head on
- Explain CV Event Reduction Associated with Statin Use
- Confirm Communication Channels

What's New in Lipids
Statin Intolerance

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Journal of Clinical Lipidology

Check for updates

NLA scientific statement on statin intolerance: a new definition and key considerations for ASCVD risk reduction in the statin intolerant patient

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KEYWORDS
Statin intolerance;
Statin;
Adherence;
Persistence;
Nocebo;
Non-statin;
Non-statin therapy;
Atherogenic lipoproteins

Abstract: Although statins are generally well tolerated, statin intolerance is reported in 5-30% of patients and contributes to reduced statin adherence and persistence, as well as higher risk for adverse cardiovascular outcomes. This Scientific Statement from the National Lipid Association was developed to provide an updated definition of statin intolerance and to inform clinicians and researchers about its identification and management. Statin intolerance is defined as one or more adverse effects associated with statin therapy which resolves or improves with dose reduction or discontinuation and can be classified as a complete inability to tolerate any dose of a statin or partial intolerance with inability to tolerate the dose necessary to achieve the patient-specific therapeutic objective. To classify a patient as having statin intolerance, a minimum of two statins should have been attempted, including at least one at the lowest approved daily dosage. This Statement acknowledges the importance of identifying modifiable risk factors for statin intolerance and recognizes the possibility of a "nocebo" effect (patient expectation of harm resulting in perceived side effects). To identify a tolerable statin regimen it is recommended that clinicians consider using several different strategies (e.g., different statin, dose, and/or dosing frequency).

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What's New in Lipids
Statin Intolerance

NLA Scientific Statement on Statin Intolerance Purpose…

"To Provide an Updated Statin Intolerance Definition, with Accompanying Rationale to Inform Clinicians and Researchers in Identification, Management, and Investigation of the Syndrome of Statin Intolerance"

What's New in Lipids
Statin Intolerance

NLA Scientific Statement on Statin Intolerance Purpose…From a Clinician's Perspective

1) Confront the 5-30% Rate of Statin Intolerance
2) Navigate the Nocebo Effect
3) Improve Our Ability to Reach Target, and Thus Reduce CV Events

What's New in Lipids

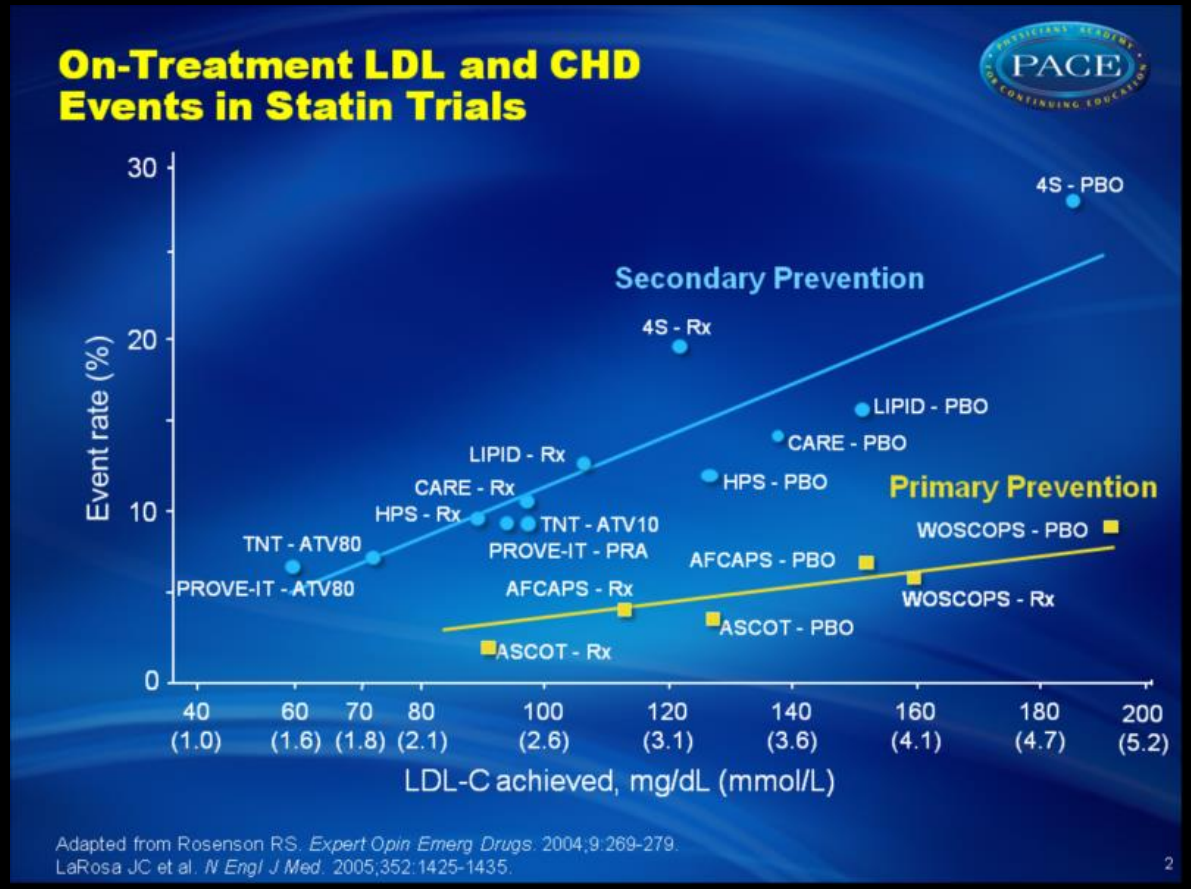
Statin Intolerance Definition

" One or More Adverse Effects Associated with Statin Therapy, which Resolves or Improves with Dose Reduction or Discontinuation, and can be Classified as Complete Inability to Tolerate any Dose of a Statin or Partial Intolerance, with Inability to Tolerate the Dose Necessary to Achieve the Patient Specific Therapeutic Objective.

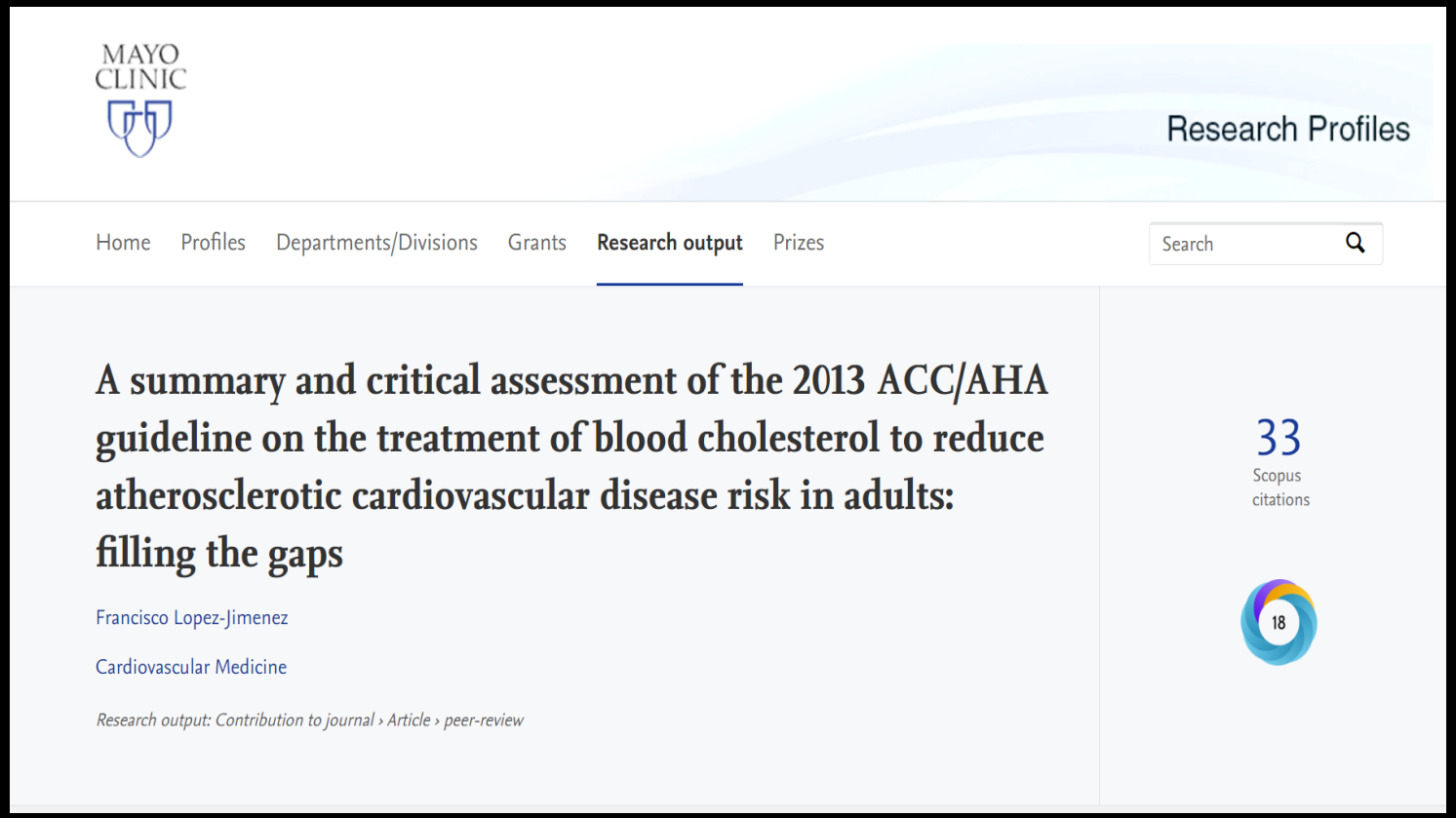
What's New in Lipids
Statin Intolerance Definition- Continued

"To Classify a Patient as Statin Intolerant, a Minimum of Two Statins Should have Been Attempted, Including at Least One at the Lowest Approved Daily Dose"

“Patient Specific Therapeutic Objective”



2013 ACC/AHA Guidelines



2013 ACC/AHA Guidelines

COMMENTARY

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New cholesterol guidelines: Worth the wait?

On November 12, 2013, a joint task force for the American College of Cardiology and American Heart Association released new guidelines for treating high blood cholesterol to reduce the risk of atherosclerotic cardiovascular disease (ASCVD) in adults.[1]

This document arrives after several years of intense deliberation, 12 years after the third Adult Treatment Panel (ATP III) guidelines,[2] and 8 years after an ATP III update recommending that low-density lipoprotein cholesterol (LDL-C) levels be lowered aggressively (to less than 70 mg/dL) as an option in patients at high risk.[3] It represents a major shift in the approach to and management of high blood cholesterol and has sparked considerable controversy.

In the following commentary, we summarize the new guidelines and the philosophy employed by the task force in generating them. We will also examine some advantages and what we believe to be several shortcomings of the new guidelines. These latter points are illustrated through case examples.

IN RANDOMIZED CONTROLLED TRIALS WE TRUST

In collaboration with the National Heart, Lung, and Blood Institute of the National Institutes of Health, the American College of Cardiology and American Heart Association formed an expert panel task force in 2008.

The task force elected to use only evidence from randomized controlled trials, systematic reviews, and meta-analyses of randomized controlled trials (and only predefined outcomes of the trials, not post hoc analyses) in formulating its recommendations, with the goal of providing the strongest possible evidence.

The authors state that "By using [randomized controlled trial] data to identify those *most likely to benefit* [emphasis in original] from cholesterol-lowering statin therapy, the recommendations will be of value to primary care clinicians as well as specialists concerned with ASCVD prevention. Importantly, the recommendations were designed to be easy to use in the clinical setting, facilitating the implementation of a strategy of risk assessment and treatment focused on the prevention of ASCVD."[3] They also state the guidelines are meant to "inform clinical judgment, not replace it" and that clinician judgment in addition to discussion with patients remains vital.

During the deliberations, the National Heart, Lung, and Blood Institute removed itself from participating, stating its mission no longer included drafting new guidelines. Additionally, other initial members of the task force removed themselves because of disagreement

The document is a major shift in treating cholesterol and has sparked considerable controversy

Drugs mentioned in this article

atorvastatin (Lipitor)	niacin (Niaspan)
ezetimibe (Zetia)	pitavastatin (Livalo)
fluvastatin (Lescol)	rosuvastatin (Crestor)
lovastatin (Mevacor)	simvastatin (Zocor)

[a] M.R. is a speaker for Abbott and Amarin.
[b] S.L.H. is named as co-inventor on pending and issued patents held by Cleveland Clinic relating to cardiovascular diagnostics and therapeutics. S.L.H. reports he has been paid as a consultant by the following companies: Cleveland Heart Lab, Esperion, Liposciences, Merck & Co., Pfizer, and Procter & Gamble. S.L.H. reports he has received research funds from Abbott, Astra Zeneca, Cleveland Heart Lab, Esperion, Liposciences, Procter & Gamble, and Takeda. S.L.H. has the right to receive royalty payments for inventions or discoveries related to cardiovascular diagnostics and therapeutics from Abbott Laboratories, Cleveland Heart Lab, Esperion, Frantz Biomarkers, and Liposciences.

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What's New in Lipids

Statin Intolerance-Nocebo Effect

Nocebo Effect- Situation Where a Negative Outcome Occurs due to a Belief that the Intervention Will Cause Harm.

- Samson Trial
- StatinWISE Trial

Up to 90% of Statin Intolerance is Due to Nocebo Effect

What's New in Lipids
Statin Intolerance- NLA Key Points

- Statin intolerance is a continuum
- Look for Risk Factors: ETOH, Drug Interactions, Hypothyroidism, Low Vit D
- Do Not Delay Non Statin Therapy in High Risk Pts
- Nocebo Effect Does Not Make Symptoms Clinically Less Relevant or Reduce Need for Therapy

What's New in Lipids

Statin Intolerance-Lifestyle Modification

- Healthy Diet
- Weight Loss if Applicable
- Smoking Cessation if Applicable
- Regular Activity

  Minimum 150 Minutes Moderate Intensity, or
  Minimum 75 Minutes High Intensity, Plus
  2 Sessions of Resistance Training

What's New in Lipids
Statin Intolerance-Medications

Ezetimibe

Cholesterol Absorption Inhibitor

- 15-20% LDL Reduction Monotherapy, 20-25% with Statin
- Modest Event Reduction on Top of Statin in Improve-It Trial
- More Pronounced Event Reduction in Monotherapy in EWTOPIA Trial
- Enhance Trial-Doomed by Poor Design in More Ways Than One

What's New in Lipids
Statin Intolerance-Medications

PCSK9 Inhibitors

Alirocumab-Praluent

Evolocumab-Repatha

- Both Lower LDL by at Least 50-60%
- Both Have CV Outcomes Data Combined with Statin Therapy

What's New in Lipids

Statin Intolerance-Medications

PCSK9 Inhibitors/SiRNA

Inclisiran-Leqvio

What's New in Lipids
Statin Intolerance-Medications

ATP Citrate Lyase Inhibitor

Bempedoic Acid-Nexletol

What's New in Lipids
Statin Intolerance-Medications

Bile Acid Sequestrants

- Cholestyramine/Colestipol/Colesevelam
- LDL Reduction of 13-25%, Trig Rise of 5-20%
- Pre Statin Data: LRC-CPPT Trial, Modest Event Reduction
- Beware Binding Up Other Meds

What's New in Lipids
Statin Intolerance-Medications

PPAR Alpha Modulators-Fibrates

Fenofibric Acid, Fenofibrate, Gemfibrozil

- Lipid Effect Dependent on Phenotype
- Study Results Mixed

What's New in Lipids
Statin Intolerance-Medications

PPAR Alpha Modulators-Fibrates

Gemfibrozil-Helsinki Heart, VA- Hit

- CV Event Rates Reduced Modestly (No Statin)

Fenofibrate- Field, Accord Trials

- No Event Reduction
- Beware Using Gemfibrozil with Statins!

What's New in Lipids
Statin Intolerance-Medications

What's New in Lipids
Statin Intolerance-Medications

Omega 3s

- Pure EPA or EPA/DHA Combination
- Regulated or Supplement

What's New in Lipids Statin Intolerance-Medications

Clinical Trials

- Ascend-Lovaza-EPA and DHA- No Benefit in 15,000 Diabetic Patients
- Strength-Epanova-EPA and DHA- No Benefit in 13,000 High Risk CV Patients
- Reduce It-IPE-Significant CV Event Reduction
- IPE Incorporated into AHA, ADA, AACE,ESC, NLA Guidelines

What's New in Lipids Statin Intolerance-Medications

IPE

- Branded not Covered by Payors
- Generic Difficult to Find
- Toxic Mineral Oil Theory

What's New in Lipids
Statin Intolerance-Medications

Worldwide Supplements CEO

Questions?