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Original Contribution

An assessment by the Statin Diabetes Safety Task Force: 2014 update

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Abstract: Statin therapy reduces the risk of myocardial infarction, stroke, and cardiovascular death by 25% to 30% in primary as well as secondary prevention patients. Thus, statins are the pharmacologic therapy of choice for the management of high blood cholesterol levels. Prompted by examination of clinical trial data suggesting a modest, but statistically significant, increase in the incidence of new-onset type 2 diabetes mellitus with statin use, the US Food and Drug Administration in 2012 added a statement to the labels of statin medications indicating that increases in glycated hemoglobin (HbA_{1C}) and fasting glucose levels have been reported with statin use. This labeling change has raised questions among clinicians regarding the relative benefits and risks of statin use, both among patients with diabetes mellitus and among those with diabetes risk factors. This 2014 report from the Diabetes Subpanel of the National Lipid Association Expert Panel on Statin Safety reviews the published evidence relating statin use to the hazard for diabetes mellitus or worsening glycemia, examines potential mechanisms that may mediate the relationship between statin use and diabetes mellitus risk, and suggests future research efforts. Given the well-established benefits of statin therapy in the primary and secondary prevention of cardiovascular events among those with indications for treatment, no changes to clinical practice are recommended other than the measurement of HbA_{1C} or fasting glucose in those deemed to also be at elevated diabetes risk after initiating statin therapy, and potentially before initiation in selected patients considered to be at elevated risk of developing diabetes. The panel advocates following recommendations from the American Diabetes Association, or other relevant guidelines if outside the United States, for screening and diagnosis as well as lifestyle modification for prevention or delay of diabetes mellitus in those with prediabetes or other risk factors.

Disclosures: Dr Kevin Maki discloses that in the past 12 months he received consulting fees and/or research grants from Abbott Laboratories, Amarin, Omthera (now a subsidiary of AstraZeneca), Trygg Pharmaceuticals and that he was an employee of Biofortis Inc. Dr Ridker discloses that he has received research grants from Novartis, Amgen, Pfizer, and AstraZeneca, is a consultant for ISIS, Vascular Biogenics, Boston Heart, Genzyme, and Jannsen, and receives patent royalties from patents held by the Brigham and Women's Hospital that relate to the use of inflammatory biomarkers in cardiovascular disease and diabetes that have been licensed to AstraZeneca and Siemens. Dr Brown is editor of the Journal of Clinical Lipidology and further discloses that he has received consulting fees or honoraria from Amgen, Bristol-Myers Squibb, Genzyme, Sanofi, ISIS, Pfizer Inc., LipoScience Inc., Lilly, Merck and Co., Catabasis, GlaxoSmithKline, and Medtelligence, and has been a speaker for Merck and Vindico. Dr Scott Grundy discloses that he has received an honorarium as a consultant to Sanofi. Dr Naveed Sattar discloses that he has received consulting fees as a member of the Advisory Boards of AstraZeneca, Bristol Meyers Squibb, Amgen, and Sanofi, and he received an honorarium as a speaker for MSD–UK Subsidiary of Merck.

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Evidence grading: Strength of recommendation*

Grade	Strength of recommendation
A	**Strong recommendation** There is high certainty based on the evidence that the net benefit** is substantial
B	**Moderate recommendation** There is moderate certainty based on the evidence that the net benefit is moderate to substantial, or there is high certainty that the net benefit is moderate
C	**Weak recommendation** There is at least moderate certainty based on the evidence that there is a small net benefit
D	**Recommend against** There is at least moderate certainty based on the evidence that it has no net benefit or that the risks/harms outweigh benefits
E	**Expert opinion** There is insufficient evidence or evidence is unclear or conflicting, but this is what the expert panel recommends
N	**No recommendation for or against** There is insufficient evidence or evidence is unclear or conflicting

*The system was adapted as a hybrid of the National Heart Lung and Blood Institutes (NHLBI) rating system (NHLBI cardiovascular-based methodology) used in the new American Heart Association/American College of Cardiology cholesterol guidelines[1] and adapted from the original GRADE system of evidence rating.[2]

**Net benefit is defined as benefits minus risks/harms of the service/intervention.

Evidence grading: Quality of evidence

Type of evidence	Quality rating*
Well-designed, well-executed RCTs that adequately represent populations to which the results are applied and directly assess effects on health outcomes Well-conducted meta-analyses of such studies Highly certain about the estimate of effect; further research is unlikely to change our confidence in the estimate of effect	High
RCTs with minor limitations affecting confidence in, or applicability of, the results Well-designed, well-executed nonrandomized controlled studies and well-designed, well-executed observational studies Well-conducted meta-analyses of such studies Moderately certain about the estimate of effect; further research may have an impact on our confidence in the estimate of effect and may change the estimate	Moderate
RCTs with major limitations Nonrandomized controlled studies and observational studies with major limitations affecting confidence in, or applicability of, the results Uncontrolled clinical observations without an appropriate comparison group (eg, case series, case reports) Physiological studies in humans Meta-analyses of such studies Low certainty about the estimate of effect; further research is likely to have an impact on our confidence in the estimate of effect and is likely to change the estimate.	Low

RCT, randomized controlled trial.

This was the system used in the new American Heart Association/American College of Cardiology cholesterol guidelines[1] that were published in the 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults Report from the Panel members appointed to the Eighth Joint National Committee.[3]

Permission to reuse table granted from the American Medical Association.[3]

*The evidence quality rating system used in this guideline was developed by the National Heart, Lung, and Blood Institute's (NHLBI's) Evidence-Based Methodology Lead (with input from NHLBI staff, external methodology team, and guideline panels and work groups) for use by all the NHLBI cardiovascular disease guideline panels and work groups during this project. As a result, it includes the evidence quality rating for many types of studies, including studies that were not used in this guideline. Additional details regarding the evidence quality rating system are available in the online Supplement.