Cardiovascular Glossary of Terms for Media

atherosclerosis: Cholesterol-lipid-calcium deposits in the walls of arteries that can restrict blood flow. Atherosclerosis is a progressive disease. If left untreated, lesions may thicken and form fibrous plaques, nearly completely blocking blood flow and causing ischemia. If a plaque ruptures, the affected blood vessel may close, and organs or tissues may infarct.[1]

blood lipids (or blood fats): Blood lipids are mainly fatty acids and cholesterol. The presence of elevated or abnormal levels of lipids in the blood is a major risk factor for cardiovascular disease.[2]

cardiovascular disease (CVD): Cardiovascular disease generally refers to conditions that involve narrowed or blocked blood vessels that can lead to a heart attack, chest pain (angina) or stroke. Cardiovascular disease is the #1 killer in the United States (one death every 38 seconds).[3,4]

cardiovascular outcome trial (CVOT): Clinical trials that assess the effects of a new medication on cardiovascular events such as heart attack and stroke. Typically, these are large-scale and long-term trials that are randomized, double-blinded, and placebo-controlled.[5]

cardiovascular risk factors: Conditions or habits that are associated with a greater likelihood of developing a cardiovascular disease. Risk factors for cardiovascular disease include high blood pressure, high LDL ("bad") cholesterol, elevated triglycerides (TG), low HDL ("good") cholesterol, diabetes and prediabetes, smoking, being overweight or obese, physical inactivity, family history of early heart disease, history of preeclampsia during pregnancy, unhealthy diet, being 45 years or older in men and 55 years of age or older in women.[1]

coronary revascularization: In medical and surgical therapy, revascularization is the restoration of perfusion to the heart. Coronary stents, vascular bypass and angioplasty are examples of coronary revascularization.[6]

diabetes: Diabetes is a disease in which the body's ability to produce or respond to the hormone insulin is impaired, resulting in abnormal metabolism of carbohydrates and elevated levels of glucose in the blood and urine.[7]

dietary supplements: Dietary supplements are products classified as food used for nutritional purposes but not intended to treat or prevent any medical condition. Dietary supplements do not require advanced FDA approval of efficacy, safety, labeling, manufacturing or marketing claims. They are available on retail shelves without a prescription.[8]

established cardiovascular disease: Established cardiovascular disease means a diagnosis of cardiovascular disease, which is the name for the group of disorders of heart and blood vessels, and include: hypertension (high blood pressure), coronary heart disease (heart attack), cerebrovascular disease (stroke), and peripheral vascular disease.[9]

HDL cholesterol (HDL-C): High-density lipoprotein cholesterol, commonly referred to as "good cholesterol." HDL-C is composed of a high proportion of protein with little triglyceride and cholesterol and that is correlated with reduced risk of atherosclerosis.[10]

LDL cholesterol (LDL-C): Low-density lipoprotein cholesterol, commonly referred to as 'bad' cholesterol. Elevated LDL-C levels are associated with an increased risk of heart disease. Lipoproteins, which are combinations of fats (lipids) and proteins, are the form in which lipids are transported in the blood.[9]

major adverse cardiovascular events (MACE): Major adverse cardiovascular events that, in cardiovascular outcomes trials, may be measured as a composite endpoint and can include adverse events such as cardiovascular death, non-fatal myocardial infarction, non-fatal stroke and coronary revascularization.[11] Two common composites of MACE used in studies include: the three-point major adverse CV event (3P-MACE) composite which includes CV death, nonfatal myocardial infarction and nonfatal stroke; and the five-point major adverse CV event (5P-MACE) composite which additionally includes coronary revascularization and hospitalization for unstable angina.[12]

myocardial Infarction: Myocardial infarction is another term for heart attack.[13]

maximum-tolerated statin therapy: The highest dose of a statin that a patient can tolerate without experiencing adverse events that may lead to treatment discontinuation.[14] Statin therapy can he high, moderate, or low intensity, with higher intensity levels corresponding to greater reductions in LDL-cholesterol (LDL-C).[15]

over-the-counter-drugs (OTC): Previous prescription drugs or active ingredients which the FDA deems after years of use to be safe for use without prescription and without medical supervision. While OTC is a term used by some people to refer to dietary supplements because they often are presented near each other in retail stores, OTC drugs and dietary supplements are very different. Dietary supplements are not and have never been classified as drugs or reviewed by the FDA for safety or efficacy like drugs or reviewed for manufacturing quality and consistency like drugs.[16] Dietary supplements also should not be used to treat serious medical conditions such as cardiovascular disease.

P-value: The probability of a finding occurring by random chance rather than as a result of the treatment being tested. The P-value can be thought of as a means of determining whether an observed effect is real or a chance occurrence. A P-value of 0.05 is a commonly used cutoff for statistical significance. In a clinical trial, a P-value of <0.05 often confirms a statistically significant difference in the treatment groups.[17]

persistent cardiovascular risk: The residual risk for a cardiovascular event (e.g., heart attack, stroke, or death) even after a patient is treated with current standard-of-care therapies, such as cholesterol management with statin therapy or treatments to manage blood pressure and diabetes.[18]

prescription drug or prescription medicine: Drug therapy approved by regulatory authorities (FDA in the United States) for treating medical conditions.[19]

primary prevention (1º): Preventing illness in a patient or healthy population unaffected by the targeted disease or condition. Primary prevention of cardiovascular disease aims to reduce the risk of heart attack, stroke, and other cardiovascular events in those who have not yet experienced a clinical manifestation of the disease. Some primary prevention patients are deemed to be higher risk (e.g., patients with diabetes) than others.[20]

REDUCE-IT: REDUCE-IT was a landmark global cardiovascular outcomes study that investigated the cardioprotective effects of 4 grams daily VASCEPA. The study commenced in late 2011 with results presented in November 2018. In REDUCE-IT, VASCEPA was studied as an add-on to statin therapy to reduce the risk of cardiovascular events in patients with bad (LDL) cholesterol between 41-100 mg/dL (median baseline LDL-C 75 mg/dL) who had other cardiovascular risk factors, including elevated triglyceride levels between 135-499 mg/dL (median baseline TG 216 mg/dL) as well as either an established history of MACE or diabetes mellitus and other cardiovascular risk factors. It was not designed to validate the effect of lowering triglyceride levels or any other lipid biomarker on a stand-alone basis.[21]

relative risk reduction (RRR): The amount of risk reduction relative to the baseline risk.[22]

secondary prevention (2º): Limiting the risk of recurrence or disease progression in patients who are already affected (who have established cardiovascular disease) by the targeted disease or condition. Secondary prevention in patients with established cardiovascular disease aims to lower the risk of future cardiovascular events.[23]

statins: Statins, also known as HMG-CoA reductase inhibitors, are a class of lipid-lowering medications. Statins have been found to reduce cardiovascular disease and mortality in those who are at high risk of cardiovascular disease. Statins lower LDL-cholesterol levels and have other pleiotropic effects (effects of a drug other than those for which the agent was specifically developed).[24,25]

statin intolerant: Patients with a clinical indication for statin therapy but who are unable to tolerate a suitable dose to reduce their cardiovascular risk due to some degree of intolerance, most typically due to muscle-related adverse events.[26,27] This may affect approximately 3.5 million patients in the United States.[28]

stroke: The sudden death of brain cells due to lack of oxygen, caused by blockage of blood flow or rupture of an artery to the brain. Sudden loss of speech, weakness, or paralysis of one side of the body can be symptoms.[29]

triglycerides: Triglycerides (TG) are the main constituents of natural fats and oils, and elevated concentrations in the blood indicate an increased risk of cardiovascular disease, with such risk beginning to increase at TG levels of less than 100 mg/dL.[30,31]

unstable angina: Unstable angina is a condition in which your heart doesn't get enough blood flow and oxygen. It may lead to a heart attack. Angina is a type of chest discomfort caused by poor blood flow through the blood vessels (coronary vessels) of the heart muscle (myocardium).[32]

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1 "Atherosclerosis." Heart.org, American Heart Association, www.heart.org/en/health-topics/cholesterol/about-cholesterol/atherosclerosis.

2 Sugerman DT. Blood Lipids. JAMA. 2013;310(16):1751. doi:https://doi.org/10.1001/jama.2013.280593

3 American Heart Association. Heart Disease and Stroke Statistics – 2019 Update: A Report from the American Heart Association. Published January 31, 2019.
4 American Heart Association. 2017. Cardiovascular disease: A costly burden for America projections through 2035.
5 Schnell, O., Rydén, L., Standl, E. et al. Current perspectives on cardiovascular outcome trials in diabetes. Cardiovasc Diabetol 15, 139 (2016) doi:10.1186/s12933-016-0456-8
6 King SB, Marshall JJ, Tummala PE, "Revascularization for coronary artery disease: stents versus bypass surgery." Annual Review Medical, 2010, https://www.ncbi.nlm.nih.gov/pubmed/19824825
7 "What Is Diabetes?" National Institute of Diabetes and Digestive and Kidney Diseases, U.S. Department of Health and Human Services, 1 Dec. 2016, www.niddk.nih.gov/health-information/diabetes/overview/what-is-diabetes.
8 "Questions and Answers on Dietary Supplements." U.S. Food and Drug Administration, FDA, 22 July 2019, www.fda.gov/food/information-consumers-using-dietary-supplements/questions-and-answers-dietary-supplements
9 World Health Organization. About Cardiovascular Diseases. https://www.who.int/cardiovascular_diseases/about_cvd/en/
10 "LDL & HDL: Good & Bad Cholesterol." Centers for Disease Control and Prevention, 31 Oct. 2017, www.cdc.gov/cholesterol/ldl_hdl.htm.
11 Goldfarb, Michael et al. "Outcome Reporting in Cardiac Surgery Trials: Systematic Review and Critical Appraisal." Journal of the American Heart Association vol. 4,8 e002204. 17 Aug. 2015, doi:10.1161/JAHA.115.002204
12 Rosenblit, P.D., "Extreme Atherosclerotic Cardiovascular Disease (ASCVD) Risk Recognition." Current Diabetes Report, 2019 Jul 22;19(8):61. doi: 10.1007/s11892-019-1178-6.
13 "About Heart Attacks." Heart.org, American Heart Association, www.heart.org/en/health-topics/heart-attack/about-heart-attacks.
14 Naidoo P, Mothilal R, Blom DJ. Therapeutic Management of Dyslipidemia Patients at Very High Cardiovascular Risk (CARDIO TRACK): Protocol for the Observational Registry Study. JMIR Res Protoc. 2018;7(6):e163.
15 American Heart Association. Cholesterol Management Guide for Healthcare Practitioners. Available at: https://www.heart.org/-/media/files/health-topics/cholesterol/chlstrmngmntgd_181110.pdf.
16 "Now Available Without a Prescription." U.S. Food and Drug Administration, FDA, May 2016, www.fda.gov/drugs/drug-information-consumers/now-available-without-prescription.
17 Panagiotakos, Demosthenes B. "Value of p-value in biomedical research." The open cardiovascular medicine journal vol. 2 (2008): 97-9. doi:10.2174/1874192400802010097
18 Wong, Nathan D et al. "Residual atherosclerotic cardiovascular disease risk in statin-treated adults: The Multi-Ethnic Study of Atherosclerosis." Journal of clinical lipidology vol. 11,5 (2017): 1223-1233. doi:10.1016/j.jacl.2017.06.015
19 "Prescriptions Q&A." Diversion Control Division, U.S, Department of Justice & Drug Enforcement Administration, www.deadiversion.usdoj.gov/faq/prescriptions.htm.
20 Stewart, Jack et al. "Primary prevention of cardiovascular disease: A review of contemporary guidance and literature." JRSM cardiovascular disease vol. 6 2048004016687211. 1 Jan. 2017, doi:10.1177/2048004016687211
21 Bhatt DL, Steg PG, Miller M, et al. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. N Engl J Med 2019;380:11-22.
22 Irwig L, Irwig J, Trevena L, et al. Smart Health Choices: Making Sense of Health Advice. London: Hammersmith Press; 2008. Chapter 18, Relative risk, relative and absolute risk reduction, number needed to treat and confidence intervals, https://www.ncbi.nlm.nih.gov/books/NBK63647/
23 Sachith Paramie Karunathilake and Gamage Upeksha Ganegoda, "Secondary Prevention of Cardiovascular Diseases and Application of Technology for Early Diagnosis," BioMed Research International, vol. 2018, Article ID 5767864, 9 pages, 2018. https://doi.org/10.1155/2018/5767864.
24 "Cholesterol Management Guide for Healthcare Practitioners." American Heart Association, https://www.heart.org/-/media/files/health-topics/cholesterol/chlstrmngmntgd_181110.pdf
25 Davignon, Jean. "Beneficial Cardiovascular Pleiotropic Effects of Statins." Circulation. 2004;109:III-39–III-43. https://doi.org/10.1161/01.CIR.0000131517.20177.5a
26 Saeed B, Wright E, Evans M, et al. PS1-45: Prevalence of Statin Intolerance in a High Risk Cohort and Management Strategies in Contemporary Cardiology. Clin Med Res. 2013;11(3):136.
27 Toth PP, Patti AM, Giglio RV, et al. Management of Statin Intolerance in 2018: Still More Questions Than Answers. Am J Cardiovasc Drugs. 2018;18(3):157-173.
28 Harvard Heart Letter, April 2019. https://www.health.harvard.edu/heart-health/muscle-aches-from-statins-real-but-sometimes-imagined.
29 Jr., William C. Shiel. "Definition of Stroke." MedicineNet, 25 Jan. 2017, www.medicinenet.com/script/main/art.asp?articlekey=9791.
30 "Can Triglycerides Affect My Heart Health?" Mayo Clinic, Mayo Foundation for Medical Education and Research, 13 Sept. 2018, www.mayoclinic.org/diseases-conditions/high-blood-cholesterol/in-depth/triglycerides/art-20048186.
31 Wong ND, Fan W, Philip S, et al. MDP414 - Many Statin Treated Persons With Borderline Triglyceride Levels are at Risk of ASCVD. American Heart Association 2019 Scientific Sessions. Available at: https://www.abstractsonline.com/pp8/#!/7891/presentation/33779.
32 Unstable Angina. American Heart Association, www.heart.org/en/health-topics/heart-attack/angina-chest-pain/unstable-angina.