

## Supplementary Online Content

D'Andrea E, Hey SP, Ramirez CL, Kesselheim AS. Assessment of the role of niacin in managing cardiovascular disease outcomes: a systematic review and meta-analysis. *JAMA Netw Open*. 2019;2(4):e192224. doi:10.1001/jamanetworkopen.2019.2224

**eTable 1.** List of all excluded studies after removing duplicates and reasons for exclusions

**eTable 2.** Definitions of cardiovascular outcomes evaluated in the meta-analyses and meta-regression analysis

**eTable 3.** Quality assessment and risk of bias of the studies included in the meta-analyses and meta-regression analysis

**eFigure 1.** Forest plot of meta-analyses on the effect of niacin therapy over time on coronary heart disease mortality, acute coronary syndrome, revascularization procedures, and MACE

**eFigure 2.** Forest plot of cumulative meta-analyses on the effect of niacin therapy over time on the CVD mortality, coronary heart disease mortality, acute coronary syndrome, revascularization procedures, and MACE

This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1. List of all excluded studies after removing duplicates and reasons for exclusions**

n.	References	Reason(s) for exclusion from qualitative and quantitative analysis
1	Ballantyne CM, Shah S, Kher U, Hunter JA, Gill GG, Cressman MD, Ashraf TB, Johnson-Levonas AO, Mitchel YB. Lipid-Modifying Efficacy and Tolerability of Anacetrapib Added to Ongoing Statin Therapy in Patients with Hypercholesterolemia or Low High-Density Lipoprotein Cholesterol. <i>Am J Cardiol.</i> 2017 Feb 1;119(3):388-396. PubMed PMID: 27956003. registered on ClinicalTrials.gov NCT01717300	No niacin
2	Silva de Paula E, Carneiro MF, Grotto D, Hernandez LC, Antunes LM, Barbosa F Jr. Protective effects of niacin against methylmercury-induced genotoxicity and alterations in antioxidant status in rats. <i>J Toxicol Environ Health A.</i> 2016;79(4):174-83. Epub 2016 Feb 25. PubMed PMID: 26914397.	No CT - no humans
3	El Khoury P, Waldmann E, Huby T, Gall J, Couvert P, Lacorte JM, Chapman J, Frisdal E, Lesnik P, Parhofer KG, Le Goff W, Guerin M. Extended-Release Niacin/Laropiprant Improves Overall Efficacy of Postprandial Reverse Cholesterol Transport. <i>Arterioscler Thromb Vasc Biol.</i> 2016 Feb;36(2):285-94. PubMed PMID: 26681758.	No CT - no humans
4	Ooi EM, Watts GF, Chan DC, Pang J, Tenneti VS, Hamilton SJ, McCormick SP, Marcovina SM, Barrett PH. Effects of extended-release niacin on the postprandial metabolism of Lp(a) and ApoB-100-containing lipoproteins in statin-treated men with type 2 diabetes mellitus. <i>Arterioscler Thromb Vasc Biol.</i> 2015Dec;35(12):2686-93. PubMed PMID: 26515419.	competing risk / special population
5	Croyal M, Ouguerram K, Passard M, Ferchaud-Roucher V, Chétiveaux M, Billon-Crossouard S, de Gouville AC, Lambert G, Krempf M, Nobécourt E. Effects of Extended-Release Nicotinic Acid on Apolipoprotein (a) Kinetics in Hypertriglyceridemic Patients. <i>Arterioscler Thromb Vasc Biol.</i> 2015 Sep;35(9):2042-7. PubMed PMID: 26160958.	No CVD outcomes and follow up shorter than 6 months
6	Gomaschi M, Ossoli A, Adorni MP, Damonte E, Niesor E, Veglia F, Franceschini G, Benghozi R, Calabresi L. Fenofibrate and extended-release niacin improve the endothelial protective effects of HDL in patients with metabolic syndrome. <i>Vascul Pharmacol.</i> 2015 Nov;74:80-86.	No CVD outcomes and follow up shorter than 6 months
7	Sprecher D, Maxwell M, Goodman J, White B, Tang CM, Boullay V, de Gouville AC. Discovery and characterization of GSK256073, a non-flushing hydroxy-carboxylic acid receptor 2 (HCA2) agonist. <i>Eur J Pharmacol.</i> 2015 Jun 5;756:1-7.	No CT
8	deGoma EM, Salavati A, Shinohara RT, Saboury B, Pollan L, Schoen M, Torigian DA, Mohler ER, Dunbar RL, Litt HI, Woo J, Rader DJ, Alavi A, Mehta NN. A pilot trial to examine the effect of high-dose niacin on arterial wall inflammation using fluorodeoxyglucose positron emission tomography. <i>Acad Radiol.</i> 2015 May;22(5):600-9.	No CVD outcomes and follow up shorter than 6 months
9	Khera AV, Qamar A, Reilly MP, Dunbar RL, Rader DJ. Effects of niacin, statin, and fenofibrate on circulating proprotein convertase subtilisin/kexin type 9 levels in patients with dyslipidemia. <i>Am J Cardiol.</i> 2015 Jan 15;115(2):178-82.	No CVD outcomes and follow up shorter than 6 months
10	Jiang RR, Zhao GP, Zhao JP, Chen JL, Zheng MQ, Liu RR, Wen J. Influence of dietary nicotinic acid supplementation on lipid metabolism and related gene expression in two distinct broiler breeds of female chickens. <i>J Anim Physiol Anim Nutr (Berl).</i> 2014 Oct;98(5):822-9. PubMed PMID: 25356484.	No CT - no humans
11	Hobbs T, Caso R, McMahon D, Nymark M. A novel, multi-ingredient supplement to manage elevated blood lipids in patients with no evidence of cardiovascular disease: a pilot study. <i>Altern Ther Health Med.</i> 2014 Sep-Oct;20(5):18-23.	No niacin - niacin as dietary supplement
12	HPS2-THRIVE Collaborative Group. HPS2-THRIVE randomized placebo-controlled trial in 25673 high-risk patients of ER niacin/laropiprant: trial design, pre-specified muscle and liver outcomes, and reasons for stopping study treatment. <i>Eur Heart J.</i> 2013 May;34(17):1279-91.	No CT
13	Nasser Figueiredo V, Vendrame F, Colontoni BA, Quinaglia T, Roberto Matos-Souza J, Azevedo Moura F, Coelho OR, de Faria EC, Sposito AC. Short-term effects of extended-release niacin with and without the addition of laropiprant on endothelial function in individuals with low HDL-C: a randomized, controlled crossover trial. <i>Clin Ther.</i> 2014 Jun 1;36(6):961-6.	No CVD outcomes and follow up shorter than 6 months
14	Aye MM, Kilpatrick ES, Afolabi P, Wootton SA, Rigby AS, Coady AM, Sandeman DD, Atkin SL. Postprandial effects of long-term niacin/laropiprant use on glucose and lipid metabolism and on cardiovascular risk in patients with polycystic ovary syndrome. <i>Diabetes Obes Metab.</i> 2014 Jun;16(6):545-52. ClinicalTrials.gov Identifier: NCT01118598	No CVD outcomes and follow up shorter than 6 months

n.	References	Reason(s) for exclusion from qualitative and quantitative analysis
15	27: Cenaarro A, Puzo J, Ferrando J, Mateo-Gallego R, Bea AM, Calmarza P, Jarauta E, Civeira F. Effect of Nicotinic acid/Laropiprant in the lipoprotein(a) concentration with regard to baseline lipoprotein(a) concentration and LPA genotype. <i>Metabolism</i> . 2014 Mar;63(3):365-71. doi: 10.1016/j.metabol.2013.10.014. Epub 2013 Nov 6. PubMed PMID: 24333007. ClinicalTrials.gov Identifier: NCT01321034	No CVD outcomes and follow up shorter than 6 months
16	31: Franceschini G, Favari E, Calabresi L, Simonelli S, Bondioli A, Adorni MP, Zimetti F, Gomasaschi M, Coutant K, Rossomanno S, Niesor EJ, Bernini F, Benghozi R. Differential effects of fenofibrate and extended-release niacin on high-density lipoprotein particle size distribution and cholesterol efflux capacity in dyslipidemic patients. <i>J Clin Lipidol</i> . 2013 Sep-Oct;7(5):414-22.	No CVD outcomes and follow up shorter than 6 months
17	32: Niesor EJ, Gauthamadasa K, Silva RA, Suchankova G, Kallend D, Gylling H, Asztalos B, Damonte E, Rossomanno S, Abt M, Davidson WS, Benghozi R. Xanthophylls, phytosterols and pre- $\beta$ 1-HDL are differentially affected by fenofibrate and niacin HDL-raising in a cross-over study. <i>Lipids</i> . 2013 Dec;48(12):1185-96.	No CT - no original data
18	40: Lin C, Grandinetti A, Shikuma C, Souza S, Parikh N, Nakamoto B, Kallianpur KJ, Chow D. The effects of extended release niacin on lipoprotein sub-particle concentrations in HIV-infected patients. <i>Hawaii J Med Public Health</i> . 2013 Apr;72(4):123-7.	competing risk / special population
19	42: Gillard BK, Raya JL, Ruiz-Esponda R, Iyer D, Coraza I, Balasubramanyam A, Pownall HJ. Impaired lipoprotein processing in HIV patients on antiretroviral therapy: aberrant high-density lipoprotein lipids, stability, and function. <i>Arterioscler Thromb Vasc Biol</i> . 2013 Jul;33(7):1714-21. ClinicalTrials.gov NCT00246376.	competing risk / special population
20	45: Williams PT, Zhao XQ, Marcovina SM, Brown BG, Krauss RM. Levels of cholesterol in small LDL particles predict atherosclerosis progression and incident CHD in the HDL-Atherosclerosis Treatment Study (HATS). <i>PLoS One</i> . 2013;8(2):e56782. doi: 10.1371/journal.pone.0056782. Epub 2013 Feb 27. ClinicalTrials.gov NCT00000553.	No CT - no original data
21	49: Phan BA, Muñoz L, Shadzi P, Isquith D, Triller M, Brown BG, Zhao XQ. Effects of niacin on glucose levels, coronary stenosis progression, and clinical events in subjects with normal baseline glucose levels (<100 mg/dl): a combined analysis of the Familial Atherosclerosis Treatment Study (FATS), HDL-Atherosclerosis Treatment Study (HATS), Armed Forces Regression Study (AFREGS), and Carotid Plaque Composition by MRI during lipid-lowering (CPC) study. <i>Am J Cardiol</i> . 2013 Feb 1;111(3):352-5.	No CT - no original data
22	47: Keenan JM. Wax-matrix extended-release niacin vs inositol hexanicotinate: a comparison of wax-matrix, extended-release niacin to inositol hexanicotinate "no-flush" niacin in persons with mild to moderate dyslipidemia. <i>J Clin Lipidol</i> . 2013 Jan-Feb;7(1):14-23.	No CVD outcomes and follow up shorter than 6 months
23	50: Dänschel W, Steinhagen-Thiessen E, Buffleben C, Pittrow D, Hildemann SK. Determinants of lipid goal achievement in patients on extended-release nicotinic acid/laropiprant in primary care clinical practice. <i>Curr Med Res Opin</i> . 2013 Jan;29(1):33-40.	No CT
24	51: Hamoud S, Kaplan M, Meilin E, Hassan A, Torgovicky R, Cohen R, Hayek T. Niacin administration significantly reduces oxidative stress in patients with hypercholesterolemia and low levels of high-density lipoprotein cholesterol. <i>Am J Med Sci</i> . 2013 Mar;345(3):195-9. Rambam Health Care Campus, Haifa, Israel (approval number 0258/09).	No outcome of interest - oxidative stress
25	52: Ahmadi F, Shamekhi F, Lessan-Pezeshki M, Khatami MR. Comparison of efficacy of the phosphate binders nicotinic acid and sevelamer hydrochloride in hemodialysis patients. <i>Saudi J Kidney Dis Transpl</i> . 2012 Sep;23(5):934-8. [to discuss]	competing risk / special population
26	56: Karl M, Rubenstein M, Rudnick C, Brejda J. A multicenter study of nutraceutical drinks for cholesterol (evaluating effectiveness and tolerability). <i>J Clin Lipidol</i> . 2012 Mar-Apr;6(2):150-8. ClinicalTrials.gov identifier: NCT01152073	No niacin - niacin as dietary supplement
27	58: Kim SH, Kim MK, Lee HY, Kang HJ, Kim YJ, Park BJ, Kim HS. Efficacy and tolerability of a new extended-release formulation of nicotinic acid in Korean adults with mixed dyslipidemia: an 8-week, multicenter, prospective, randomized, double-blind, and placebo-controlled trial. <i>Clin Ther</i> . 2011 Oct;33(10):1357-64.	No CVD outcomes and follow up shorter than 6 months
28	60: Aramwit P, Srisawadwong R, Supasynhd O. Effectiveness and safety of extended-release nicotinic acid for reducing serum phosphorus in hemodialysis patients. <i>J Nephrol</i> . 2012 May-Jun;25(3):354-62.	competing risk / special population
29	61: Safarova MS, Trukhacheva EP, Ezhov MV, Afanas'eva OI, Afanas'eva MI, Tripoten' MI, Liakishev AA, Pokrovskii SN. [Pleiotropic effects of nicotinic acid therapy in men with coronary heart disease and elevated lipoprotein(a) levels]. <i>Kardiologiia</i> . 2011;51(5):9-16. Russian.	No CVD outcomes

n.	References	Reason(s) for exclusion from qualitative and quantitative analysis
30	Balasubramanyam A, Coraza I, Smith EO, Scott LW, Patel P, Iyer D, Taylor AA, Giordano TP, Sekhar RV, Clark P, Cuevas-Sanchez E, Kamble S, Ballantyne CM, Pownall HJ. Combination of niacin and fenofibrate with lifestyle changes improves dyslipidemia and hypoadiponectinemia in HIV patients on antiretroviral therapy: results of "heart positive," a randomized, controlled trial. <i>J Clin Endocrinol Metab.</i> 2011 Jul;96(7):2236-47. <a href="https://clinicaltrials.gov/ct2/show/study/NCT00246376">ClinicalTrials.gov NCT00246376</a> .	competing risk / special population
31	Samson SL, Pownall HJ, Scott LW, Ballantyne CM, Smith EO, Sekhar RV, Balasubramanyam A. Heart positive: design of a randomized controlled clinical trial of intensive lifestyle intervention, niacin and fenofibrate for HIV lipodystrophy/dyslipidemia. <i>Contemp Clin Trials.</i> 2006 Dec;27(6):518-30. Epub 2006 Jul 21. <a href="https://clinicaltrials.gov/ct2/show/study/NCT00246376">ClinicalTrials.gov NCT00246376</a> .	No CT - no original data
32	Mal' GS. [Comparative efficiency of prolonged diet and drug therapies for hyperlipidemias in patients with ischemic heart disease]. <i>Klin Med (Mosk).</i> 2004;82(5):63-6. Russian. <a href="https://pubmed.ncbi.nlm.nih.gov/15230046/">PubMed PMID: 15230046</a> .	No CVD outcomes
33	Knab AM, Shanely RA, Henson DA, Jin F, Heinz SA, Austin MD, Nieman DC. Influence of quercetin supplementation on disease risk factors in community-dwelling adults. <i>J Am Diet Assoc.</i> 2011 Apr;111(4):542-9.	No niacin
34	Krasuski RA, Devendra GP, Cater G, Whitney EJ. The effect of gemfibrozil, niacin and cholestyramine combination therapy on metabolic syndrome in the Armed Forces Regression Study. <i>Am J Med Sci.</i> 2011 May;341(5):378-82.	No CT - no original data
35	Dobiášová M, Fröhlich J, Sedová M, Cheung MC, Brown BG. Cholesterol esterification and atherogenic index of plasma correlate with lipoprotein size and findings on coronary angiography. <i>J Lipid Res.</i> 2011 Mar;52(3):566-71. (HATS study)	No outcome of interest
36	Salgado BJ, Salgado JV, Dos Santos AM, Casulari LA. Effects of low-dose of niacin associated to simvastatin in the treatment of mixed dyslipidemia <i>Salgad. Minerva Cardioangiol.</i> 2010 Oct;58(5):531-42.	No CVD outcomes and follow up shorter than 6 months
37	Davidson MH, Donovan JM, Misir S, Jones MR. A 50-week extension study on the safety and efficacy of colesvelam in adults with primary hypercholesterolemia. <i>Am J Cardiovasc Drugs.</i> 2010;10(5):305-14.	No niacin
38	Howarth L, Petrisko Y, Furchner-Evanson A, Nemoseck T, Kern M. Snack selection influences nutrient intake, triglycerides, and bowel habits of adult women: a pilot study. <i>J Am Diet Assoc.</i> 2010 Sep;110(9):1322-7.	No CT - pilot study
39	Devendra GP, Whitney EJ, Krasuski RA. Impact of increases in high-density lipoprotein cholesterol on cardiovascular outcomes during the armed forces regression study. <i>J Cardiovasc Pharmacol Ther.</i> 2010 Dec;15(4):380-3.	No CT - no original data
40	Koh Y, Ben-Ezra V, Biggerstaff KD, Nichols DL. Responses of blood lipids and lipoproteins to extended-release niacin and exercise in sedentary postmenopausal women. <i>J Gerontol A Biol Sci Med Sci.</i> 2010 Sep;65(9):924-32.	No CVD outcomes and follow up shorter than 6 months
41	Devine PJ, Turco MA, Taylor AJ. Design and rationale of the ARBITER 6 trial (Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol)-6-HDL and LDL Treatment Strategies in Atherosclerosis (HALTS). <i>Cardiovasc Drugs Ther.</i> 2007 Jun;21(3):221-5. <a href="https://pubmed.ncbi.nlm.nih.gov/17404825/">PubMed PMID: 17404825</a> .	No CT
42	Stefanutti C, Mazza F, Vivencio A, Di Giacomo S, Perrone G, Serra M, Bucci A. Combined treatment with Dif1stat and diet reduce plasma lipid indicators of moderate hypercholesterolemia more effectively than diet alone: a randomized trial in parallel groups. <i>Lipids.</i> 2009 Dec;44(12):1141-8.	No niacin
43	Pan J, Shilian P, Ishida B, Wu X, Kane JP, Malloy MJ, Charles MA. Effect of niacin on pre $\beta$ -1 high-density lipoprotein levels in diabetes. <i>Metabolism.</i> 2011 Feb;60(2):292-7.	No CT - no original data
44	Chow DC, Stein JH, Seto TB, Mitchell C, Sriratanaviriyakul N, Grandinetti A, Gerschenson M, Shiramizu B, Souza S, Shikuma C. Short-term effects of extended-release niacin on endothelial function in HIV-infected patients on stable antiretroviral therapy. <i>AIDS.</i> 2010 Apr 24;24(7):1019-23.	competing risk / special population
45	Hiatt WR, Hirsch AT, Creager MA, Rajagopalan S, Mohler ER, Ballantyne CM, Regensteiner JG, Treat-Jacobson D, Dale RA, Rooke T. Effect of niacin ER/lovastatin on claudication symptoms in patients with peripheral artery disease. <i>Vasc Med.</i> 2010 Jun;15(3):171-9. doi: 10.1177/1358863X09360579. Mar 8. <a href="https://pubmed.ncbi.nlm.nih.gov/20212073/">PubMed PMID: 20212073</a> . <a href="https://clinicaltrials.gov/ct2/show/study/NCT00062556">ClinicalTrials.gov NCT00062556</a> .	No outcome of interest
47	Kaushik SV, Plaisance EP, Kim T, Huang EY, Mahurin AJ, Grandjean PW, Mathews ST. Extended-release niacin decreases serum fetuin-A concentrations in individuals with metabolic syndrome. <i>Diabetes Metab Res Rev.</i> 2009 Jul;25(5):427-34. doi: 10.1002/dmrr.967.	No outcome of interest

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48	Kawata AK, Revicki DA, Thakkar R, Jiang P, Krause S, Davidson MH, Punzi HA, Padley RJ. Flushing ASsessment Tool (FAST): psychometric properties of a new measure assessing flushing symptoms and clinical impact of niacin therapy. <i>Clin Drug Investig.</i> 2009;29(4):215-29.	No outcome of interest
49	Loguercio C, Federico A, Masarone M, Torella R, Blanco Cdel V, Persico M. The impact of diet on liver fibrosis and on response to interferon therapy in patients with HCV-related chronic hepatitis. <i>Am J Gastroenterol.</i> 2008 Dec;103(12):3159-66.	No niacin - niacin as dietary supplement
50	Alves JD, Steinhagen-Thiessen E, Darioli R, Hostalek U, Vogt A. Influence of the timing of low-dose aspirin on tolerability of prolonged-release nicotinic acid in patients at elevated cardiovascular risk. <i>Curr Med Res Opin.</i> 2008 Oct;24(10):2815-20.	No CT - no original data
51	Westphal S, Luley C. Preferential increase in high-molecular weight adiponectin after niacin. <i>Atherosclerosis.</i> 2008 May;198(1):179-83. Epub 2007 Nov 8.	No CT - no original data
52	Ranga GS, Kalra OP, Tandon H, Gambhir JK, Mehrotra G. Effect of aspirin on lipoprotein(a) in patients with ischemic stroke. <i>J Stroke Cerebrovasc Dis.</i> 2007 Sep-Oct;16(5):220-4. PubMed PMID: 17845920.	No CT - no original data
53	Taylor AJ, Zhu D, Sullenberger LE, Lee HJ, Lee JK, Grace KA. Relationship between glycemic status and progression of carotid intima-media thickness during treatment with combined statin and extended-release niacin in ARBITER 2. <i>Vasc Health Risk Manag.</i> 2007;3(1):159-64. [ARBITER 2]	No CT - no original data
54	Norquist JM, Watson DJ, Yu Q, Paolini JF, McQuarrie K, Santanello NC. Validation of a questionnaire to assess niacin-induced cutaneous flushing. <i>Curr Med Res Opin.</i> 2007 Jul;23(7):1549-60. PubMed PMID: 17559750.	No CT - no original data
55	Sharma M, Sharma DR, Singh V, Panwar RB, Hira HS, Mohan B, Kumar N, Sharma SK, Gupta R. Evaluation of efficacy and safety of fixed dose lovastatin and niacin(ER) combination in asian Indian dyslipidemic patients: a multicentric study. <i>Vasc Health Risk Manag.</i> 2006;2(1):87-93.	No CVD outcomes and follow up shorter than 6 months
56	Dubé MP, Wu JW, Aberg JA, Deeg MA, Alston-Smith BL, McGovern ME, Lee D, Shriver SL, Martinez AI, Greenwald M, Stein JH; AIDS Clinical Trials Group A5148 Study Team. Safety and efficacy of extended-release niacin for the treatment of dyslipidaemia in patients with HIV infection: AIDS Clinical Trials Group Study A5148. <i>Antivir Ther.</i> 2006;11(8):1081-9.	No CT - no original data
57	Li XP, Duan J, Zhao SP, Tan MY, Xu ZM, Zhang DQ. [Efficacy and safety of extended-release niacin alone or with atorvastatin for lipid profile modification]. <i>Zhonghua Yi Xue Za Zhi.</i> 2006 Sep 12;86(34):2399-403. Chinese. PubMed PMID: 17156651.	No CVD outcomes and follow up shorter than 6 months
58	Singh U, Otvos J, Dasgupta A, de Lemos JA, Devaraj S, Jialal I. High-dose alpha-tocopherol therapy does not affect HDL subfractions in patients with coronary artery disease on statin therapy. <i>Clin Chem.</i> 2007 Mar;53(3):525-8. Epub 2007 Jan 18.	No niacin
59	Kuvin JT, Dave DM, Sliney KA, Mooney P, Patel AR, Kimmelstiel CD, Karas RH. Effects of extended-release niacin on lipoprotein particle size, distribution, and inflammatory markers in patients with coronary artery disease. <i>Am J Cardiol.</i> 2006 Sep 15;98(6):743-5.	No CT - no original data
60	Gerber MT, Mondy KE, Yarasheski KE, Drechsler H, Claxton S, Stoneman J, DeMarco D, Powderly WG, Tebas P. Niacin in HIV-infected individuals with hyperlipidemia receiving potent antiretroviral therapy. <i>Clin Infect Dis.</i> 2004 Aug 1;39(3):419-25. Epub 2004 Jul 16. PubMed PMID: 15307011.	competing risk / special population
61	Westphal S, Borucki K, Taneva E, Makarova R, Luley C. Extended-release niacin raises adiponectin and leptin. <i>Atherosclerosis.</i> 2007 Aug;193(2):361-5.	No CVD outcomes and follow up shorter than 6 months
62	Glueck CJ, Aregawi D, Agloria M, Khalil Q, Winiarska M, Munjal J, Gogineni S, Wang P. Rosuvastatin 5 and 10 mg/d: a pilot study of the effects in hypercholesterolemic adults unable to tolerate other statins and reach LDL cholesterol goals with nonstatin lipid-lowering therapies. <i>Clin Ther.</i> 2006 Jun;28(6):933-42.	No CT - no original data
63	Chang AM, Smith MJ, Galecki AT, Bloem CJ, Halter JB. Impaired beta-cell function in human aging: response to nicotinic acid-induced insulin resistance. <i>J Clin Endocrinol Metab.</i> 2006 Sep;91(9):3303-9. Epub 2006 Jun 6.	No outcome of interest
64	Zambon A, Brown BG, Hokanson JE, Motulsky AG, Brunzell JD. Genetically determined apo B levels and peak LDL density predict angiographic response to intensive lipid-lowering therapy. <i>J Intern Med.</i> 2006 Apr;259(4):401-9.	No CVD outcomes
65	Vogt A, Kassner U, Hostalek U, Steinhagen-Thiessen E; NAUTILUS Study Group. Evaluation of the safety and tolerability of prolonged-release nicotinic acid in a usual care setting: the NAUTILUS study. <i>Curr Med Res Opin.</i> 2006 Feb;22(2):417-25.	No outcome of interest
66	Canner PL, Furberg CD, McGovern ME. Benefits of niacin in patients with versus without the metabolic syndrome and healed myocardial infarction (from the Coronary Drug Project). <i>Am J Cardiol.</i> 2006 Feb 15;97(4):477-9. Epub 2005 Dec 21.	No CT - no original data

n.	References	Reason(s) for exclusion from qualitative and quantitative analysis
67	Benj3 AM, Maranh3o RC, Coimbra SR, Andrade AC, Favarato D, Molina MS, Brandizzi LI, da Luz PL. Accumulation of chylomicron remnants and impaired vascular reactivity occur in subjects with isolated low HDL cholesterol: effects of niacin treatment. <i>Atherosclerosis</i> . 2006 Jul;187(1):116-22. Epub 2006 Feb 3.	No outcome of interest
68	Cicero AF, Brancaleoni M, Laghi L, Donati F, Mino M. Antihyperlipidaemic effect of a <i>Monascus purpureus</i> brand dietary supplement on a large sample of subjects at low risk for cardiovascular disease: a pilot study. <i>Complement Ther Med</i> . 2005 Dec;13(4):273-8.	No niacin
69	Hughes TA, Stentz F, Gettys T, Smith SR. Combining beta-adrenergic and peroxisome proliferator-activated receptor gamma stimulation improves lipoprotein composition in healthy moderately obese subjects. <i>Metabolism</i> . 2006 Jan;55(1):26-34.	No niacin
70	Desai MY, Rodriguez A, Wasserman BA, Gerstenblith G, Agarwal S, Kennedy M, Bluemke DA, Lima JA. Association of cholesterol subfractions and carotid lipid core measured by MRI. <i>Arterioscler Thromb Vasc Biol</i> . 2005 Jun;25(6):e110-1	No CT - no original data
71	Burgess JW, Neville TA, Rouillard P, Harder Z, Beanlands DS, Sparks DL. Phosphatidylinositol increases HDL-C levels in humans. <i>J Lipid Res</i> . 2005 Feb;46(2):350-5.	No niacin
72	Preuss HG, Bagchi D, Bagchi M, Rao CV, Dey DK, Satyanarayana S. Effects of a natural extract of (-)-hydroxycitric acid (HCA-SX) and a combination of HCA-SX plus niacin-bound chromium and <i>Gymnema sylvestre</i> extract on weight loss. <i>Diabetes Obes Metab</i> . 2004 May;6(3):171-80.	No outcome of interest
73	Hecht HS, Harman SM. Relation of aggressiveness of lipid-lowering treatment to changes in calcified plaque burden by electron beam tomography. <i>Am J Cardiol</i> . 2003 Aug 1;92(3):334-6.	No CVD outcomes
74	See VY Jr, DeNofrio D, Goldberg L, Chang G, Sasseen B, Kolansky DM, Pickering F, Kao A, Loh E, Wilensky RL. Effect of atorvastatin on postcardiac transplant increase in low-density lipoprotein cholesterol reduces development of intimal hyperplasia and progression of endothelial dysfunction. <i>Am J Cardiol</i> . 2003 Jul 1;92(1):11-5.	competing risk / special population
75	Baskin F, Rosenberg RN, Fang X, Hynan LS, Moore CB, Weiner M, Vega GL. Correlation of statin-increased platelet APP ratios and reduced blood lipids in AD patients. <i>Neurology</i> . 2003 Jun 24;60(12):2006-7.	competing risk / special population
76	Vega GL, Weiner MF, Lipton AM, Von Bergmann K, Lutjohann D, Moore C, Svetlik D. Reduction in levels of 24S-hydroxycholesterol by statin treatment in patients with Alzheimer disease. <i>Arch Neurol</i> . 2003 Apr;60(4):510-5.	competing risk / special population
77	Matthan NR, Giovanni A, Schaefer EJ, Brown BG, Lichtenstein AH. Impact of simvastatin, niacin, and/or antioxidants on cholesterol metabolism in CAD patients with low HDL. <i>J Lipid Res</i> . 2003 Apr;44(4):800-6.	No CT - no original data
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247	Viswambharan H, Ming XF, Zhu S, Hubsch A, Lerch P, Vergères G, Rusconi S, Yang Z. Reconstituted high-density lipoprotein inhibits thrombin-induced endothelial tissue factor expression through inhibition of RhoA and stimulation of phosphatidylinositol 3-kinase but not Akt/endothelial nitric oxide synthase. <i>Circ Res</i> . 2004 Apr 16;94(7):918-25. Epub 2004 Feb 26. <a href="https://clinicaltrials.gov/ct2/show/study/NCT00508989">ClinicalTrials.gov identifier NCT00508989</a>	No niacin
248	Guyton JR, Fazio S, Adewale AJ, Jensen E, Tomassini JE, Shah A, Tershakovec AM. Effect of extended-release niacin on new-onset diabetes among hyperlipidemic patients treated with ezetimibe/simvastatin in a randomized controlled trial. <i>Diabetes Care</i> . 2012 Apr;35(4):857-60. doi: 10.2337/dc11-1369. Epub 2012 Feb 14. <a href="https://clinicaltrials.gov/ct2/show/study/NCT00271817">Clinicaltrials.gov Identifier: NCT00271817</a>	No CT - no original data
249	Guyton JR, Goldberg AC, Kreisberg RA, Sprecher DL, Superko HR, O'Connor CM. Effectiveness of once-nightly dosing of extended-release niacin alone and in combination for hypercholesterolemia. <i>Am J Cardiol</i> . 1998 Sep 15;82(6):737-43. <a href="https://clinicaltrials.gov/ct2/show/study/NCT00127218">ClinicalTrials.gov Identifier: NCT00127218</a>	No CT - no original data
250	Ballantyne CM, Herd JA, Ferlic LL, Dunn JK, Farmer JA, Jones PH, Schein JR, Gotto AM Jr. Influence of low HDL on progression of coronary artery disease and response to fluvastatin therapy. <i>Circulation</i> . 1999 Feb 16;99(6):736-43. <a href="https://clinicaltrials.gov/ct2/show/study/NCT00127218">ClinicalTrials.gov Identifier: NCT00127218</a>	No CT - no original data
251	Brown BG, Zhao XQ, Chait A, Fisher LD, Cheung MC, Morse JS, Dowdy AA, Marino EK, Bolson EL, Alaupovic P, Frohlich J, Albers JJ. Simvastatin and niacin, antioxidant vitamins, or the combination for the prevention of coronary disease. <i>N Engl J Med</i> . 2001 Nov 29;345(22):1583-92.	No CT - no original data
252	Cheung MC, Wolfbauer G, Brown BG, Albers JJ. Relationship between plasma phospholipid transfer protein activity and HDL subclasses among patients with low HDL and cardiovascular disease. <i>Atherosclerosis</i> . 1999 Jan;142(1):201-5. <a href="https://clinicaltrials.gov/ct2/show/study/NCT00000553">ClinicalTrials.gov NCT00000553</a> .	No niacin
253	Brown BG, Zhao XQ, Chait A, Frohlich J, Cheung M, Heise N, Dowdy A, DeAngelis D, Fisher LD, Albers J. Lipid altering or antioxidant vitamins for patients with coronary disease and very low HDL cholesterol? The HDL-Atherosclerosis Treatment Study Design. <i>Can J Cardiol</i> . 1998 Apr;14 Suppl A:6A-13A. Review. <a href="https://clinicaltrials.gov/ct2/show/study/NCT00000553">ClinicalTrials.gov NCT00000553</a> .	No CT - no original data
254	Brown G, Stewart BF, Zhao XQ, Hillger LA, Poulin D, Albers JJ. What benefit can be derived from treating normocholesterolemic patients with coronary artery disease? <i>Am J Cardiol</i> . 1995 Sep 28;76(9):93C-97C. Review. <a href="https://clinicaltrials.gov/ct2/show/study/NCT00000553">ClinicalTrials.gov NCT00000553</a> .	No CT - no original data
255	Morgan, J.M, Capuzzi, D.M, Guyton, J.R, Centor, R.M, Goldberg, R, Robbins, D.C, DiPette, D, Jenkins, S, and Marcovina, S. Treatment effect of Niaspan, a controlled-release niacin, in patients with hypercholesterolemia (a placebo-controlled trial) . <i>J Cardiovasc Pharmacol Therapeut</i> . 1996; 1: 195–202	No CVD outcomes and follow up shorter than 6 months



n.	References	Reason(s) for exclusion from qualitative and quantitative analysis
256	Capuzzi DM, Morgan JM, Weiss RJ, Chitra RR, Hutchinson HG, Cressman MD. Beneficial effects of rosuvastatin alone and in combination with extended-release niacin in patients with a combined hyperlipidemia and low high-density lipoprotein cholesterol levels. <i>Am J Cardiol.</i> 2003 Jun 1;91(11):1304-10. Trial Number: 4522IL/0029	No CVD outcomes
257	Lauring B , Taggart AK , Tata JR , Dunbar R , Caro L , Cheng K , Chin J , Colletti SL , Cote J , Khalilieh S , Liu J , Luo WL , Maclean AA , Peterson LB , Polis AB , Sirah W , Wu TJ , Liu X , Jin L , Wu K , Boatman PD , Semple G , Behan DP , Connolly DT , Lai E , Wagner JA , Wright SD , Cuffie C , Mitchel YB , Rader DJ , Paolini JF , Waters MG and Plump A Niacin lipid efficacy is independent of both the niacin receptor GPR109A and free fatty acid suppression. <i>Science translational medicine</i> , 2012, 4(148), 148ra115	No outcome of interest
258	Usman MH , Qamar A , Gadi R , Lilly S , Goel H , Hampson J , Mucksavage ML , Nathanson GA , Rader DJ and Dunbar RL. Extended-release niacin acutely suppresses postprandial triglyceridemia. <i>The American journal of medicine</i> , 2012, 125(10), 1026	No outcome of interest
259	Sazonov V , Maccubbin D , Sisk CM and Canner PL. Effects of niacin on the incidence of new onset diabetes and cardiovascular events in patients with normoglycaemia and impaired fasting glucose. <i>International journal of clinical practice</i> , 2013, 67(4), 297	No CT - no original data
260	Paolini JF , Mitchel YB , Reyes R , Thompson-Bell S , Yu Q , Lai E , Watson DJ , Norquist JM , Sisk CM and Bays HE. Measuring flushing symptoms with extended-release niacin using the flushing symptom questionnaire: results from a randomised placebo-controlled clinical trial. <i>International journal of clinical practice</i> , 2008, 62(6), 896	No outcome of interest
261	Gleim G , Liu N , Thompson-Bell S , McCrary Sisk C , Pasternak RC , Mitchel Y , Paolini JF and Ballantyne CM. Efficacy and safety profile of co-administered ER niacin /laropirant and simvastatin in dyslipidaemia. <i>British journal of cardiology</i> , 2009, 16(2), 90. ClinicalTrials.gov Identifier: NCT00269217	No CVD outcomes and follow up shorter than 6 months
262	Karacaglar E , Atar I , Altin C , Yetis B , Cakmak A , Bayraktar N , Ozin B and Muderrisoglu H. The effects of niacin on HsCRP in patients with non ST elevated acute coronary syndrome. <i>International journal of cardiology</i> , 2010, 140, S25	competing risk / special population
263	Thachil R , Carson PS and Banka SS. Niaspirin: Combinations of niacin with aspirin to reduce niacin induced flush. <i>Cardiology (Switzerland)</i> , 2014, 128, 266	No outcome of interest
264	Karacaglar E , Atar I , Altin C , Yetis B , Cakmak A , Bayraktar N , Coner A , Ozin B and Muderrisoglu H. The effects of niacin on inflammation in patients with non-ST elevated acute coronary syndrome. <i>Acta Cardiologica Sinica</i> , 2015, 31(2), 120	No CVD outcomes and follow up shorter than 6 months
265	Asleh R , Farbstein D , Blum S , Vardi M , Shalom H , Saraf S , O'Brien K , Marcovina S , Roberts BH , Herrington D , Robinson JG and Levy AP. HDL-induced cholesterol efflux capacity from niacin therapy in diabetes is haptoglobin genotype-dependent. <i>Circulation</i> , 2014, 130	competing risk / special population
266	Rao M , Steffes M , Bostom A and Ix JH. Effect of niacin on FGF23 concentration in chronic kidney disease. <i>American journal of nephrology</i> , 2014, 39(6), 484	competing risk / special population
267	McBride R. The role of niacin in raising high-density lipoprotein cholesterol to reduce cardiovascular events in patients with atherosclerotic cardiovascular disease and optimally treated low-density lipoprotein cholesterol: Rationale and study design. the Atherothrombosis Intervention in Metabolic syndrome with low HDL/high triglycerides: Impact on Global Health outcomes (AIM-HIGH). <i>American heart journal</i> , 2011, 161(3), 471	No CT - no original data
268	Elbaz M , Lhermusier T , Bataille V , Bongard V , Roncalli J , Bura-Riviere A , Ferrieres J , Carrie D , Galinier M and Cambou J-P. Impact of Niacin therapy on endothelial vasomotricity in patients with low HDL shortly after an acute coronary syndrome. <i>Archives of Cardiovascular Diseases Supplements</i> , 2011, 3(1), 10	No CVD outcomes and follow up shorter than 6 months
269	Lin C , Grandinetti A , Shikuma C , Souza S , Parikh N , Nakamoto B , Kallianpur KJ and Chow D The effects of extended release niacin on lipoprotein sub-particle concentrations in HIV-infected patients. <i>Hawai'i journal of medicine &amp; public health : a journal of Asia Pacific Medicine &amp; Public Health</i> , 2013, 72(4), 123	competing risk / special population
270	Thakkar RB , Kashyap ML , Lewin AJ , Krause SL , Jiang P and Padley RJ. Acetylsalicylic acid reduces niacin extended-release-induced flushing in patients with dyslipidemia. <i>Am j card drugs</i> , 2009, 9(2), 69	No outcome of interest

n.	References	Reason(s) for exclusion from qualitative and quantitative analysis
271	Daniel Keene D , Price C , Shun-Shin M and Francis D. The observational HDL hypothesis: A useful therapeutic target? A meta-analysis of 117,411 patients in randomised controlled trials. <i>European Journal of Preventive Cardiology</i> , 2014, 21(1 SUPPL. 1), S121	No CT
272	Asghar J , Gill KU , Murad S , Asif S , Bashir A and Mahmood G. Biostatistical analysis of morbidity and Mortality due to myocardial infarction and its prevention by hypolipidemic drug regimen. <i>Pakistan Journal of Medical and Health Sciences</i> , 2011, 5(3), 445	No CT - no original data
273	Ferchaud-Roucher V , Croyal M , Krempf M and Ouguerram K. Plasma lipidome characterization using UHPLC-HRMS and ion mobility of hypertriglyceridemic patients on nicotinic acid. <i>Atherosclerosis</i> , 2015, 241(1), e123	No CVD outcomes and follow up shorter than 6 months
274	Benefit of Elevation of HDL-C on Cardiovascular Outcomes in Women. <i>ClinicalTrials.gov Identifier: NCT00590629</i>	No CVD outcomes and follow up shorter than 6 months
275	Influence of Combined Therapy of Niacin and Statins on Stem Cell Mobilization and Inflammatory Parameters in Patients Suffering From Coronary Artery Disease. Niacin As Secondary Prevention Of Coronary Artery Disease (NASPOCAD). <i>ClinicalTrials.gov Identifier: NCT00431145</i>	No results
276	A Study of AMR101 to Evaluate Its Ability to Reduce Cardiovascular Events in High Risk Patients With Hypertriglyceridemia and on Statin. The Primary Objective is to Evaluate the Effect of 4 g/Day AMR101 for Preventing the Occurrence of a First Major Cardiovascular Event. <i>ClinicalTrials.gov Identifier: NCT01492361</i>	No niacin
277	The Low HDL On Six Weeks Statin Therapy (LOW) Study. <i>ClinicalTrials.gov Identifier: NCT00238004</i>	No CVD outcomes and follow up shorter than 6 months
278	Retrospective Study of the Effectiveness and Safety of Niacin and Steroid Eye Drops for Retinal Vein Occlusions.	No outcome of interest
279	The Dose Response of Niacin ER/Lovastatin on Peak Walking Time (PWT) in Patients With Intermittent Claudication – TROPIC. <i>ClinicalTrials.gov Identifier: NCT00071266</i>	No results
281	Insull Jr W , Basile JN , Vo AN , Jiang P , Thakkar R and Padley RJ. Efficacy and safety of combination therapy with niacin extended-release and simvastatin versus atorvastatin in patients with dyslipidemia: The SUPREME Study. <i>Journal of clinical lipidology</i> , 2009, 3(2), 109	No CVD outcomes and follow up shorter than 6 months
282	Devasia T , Rao Y , Shenoy G , Razzak A and Rajaram P. Efficacy and safety of a combination therapy of statin and krill oil versus statin and niacin in dyslipidemia: A randomized, open, comparator study. <i>Indian heart journal</i> , 2013, 65, S85. <a href="http://www.ijbcp.com/index.php/ijbcp/article/viewFile/977/881">http://www.ijbcp.com/index.php/ijbcp/article/viewFile/977/881</a> .	No CVD outcomes and follow up shorter than 6 months
283	Merck Carotid Atherosclerosis Trial (MK-0000-111)(COMPLETED) (MCAT). <i>ClinicalTrials.gov Identifier: NCT00804843</i>	No CVD outcomes and follow up shorter than 6 months
284	Comparative Efficacy Evaluation of Lipids When Treated With Niaspan & Statin or Other Lipid-Modifying Therapies-COMPELL. <i>NCT00079638</i>	No CT - no original data
285	Evaluation of the Effect of NICOTinic Acid (Niacin) on Elevated Lipoprotein(a) Levels (NICOLa Study). <i>NCT00633698</i>	No results
316	Bregar U, Jug B, Keber I, Cevc M, Sebestjen M. Extended-release niacin/laropirant improves endothelial function in patients after myocardial infarction. <i>Heart Vessels</i> . 2014 May;29(3):313-9.	No CVD outcomes and follow up shorter than 6 months
354	Bays HE, McGovern ME. Once-daily niacin extended release/lovastatin combination suppsut has more favorable effects on lipoprotein particle size and subclass distribution than atorvastatin and simvastatin. <i>Prev Cardiol</i> . 2003;6:179- 88. [PMID: 14605511]	No CVD outcomes and follow up shorter than 6 months
363	Stein EA, Davidson MH, Dujovne CA, Hunninghake DB, Goldberg RB, Illingworth DR, et al. Efficacy and tolerability of low-dose simvastatin and niacin, alone and in combination, in patients with combined hyperlipidemia: a prospective trial. <i>J Cardiovasc Pharmacol Ther</i> . 1996;1:107-16. [PMID: 10684407]	No comparison of interest
373	Ballantyne CM, Davidson MH, McKenney J. Comparison of the safety and efficacy of a combination tablet of niacin extended release and simvastatin with simvastatin 80 mg monotherapy: the SEACOAST II (high-dose) study. <i>J Clin Lipidol</i> . 2008;2:79-90	No CT - no original data

n.	References	Reason(s) for exclusion from qualitative and quantitative analysis
375	Jafri H, Alsheikh-Ali AA, Mooney P, Kimmelstiel CD, Karas RH, Kuvin JT. Extended-release niacin reduces LDL particle number without changing total LDL cholesterol in patients with stable CAD. <i>J Clin Lipidol</i> . 2009;3:45–50.	No CVD outcomes and follow up shorter than 6 months
379	Evaluation of the safety and efficacy of Advicor (a combination tablet of niacin extended-release/lovastatin immediate-release): a dose response study. FDA-Advicor (MA-14). Silver Spring, MD: U.S. Food and Drug Administration; 2008. (handsearch)	No CT
380	Evaluation of the safety and efficacy of Advicor (a combination tablet of niacin extended-release/lovastatin immediate-release): a dose ranging study. FDA- Advicor (M-06). Silver Spring, MD: U.S. Food and Drug Administration; 2008. (handsearch)	No outcome of interest
381	Maccubbin D, Bays HE, Olsson AG, Elinoff V, Elis A, Mitchel Y, et al. Lipid-modifying efficacy and tolerability of extended-release niacin/laropirant in patients with primary hypercholesterolaemia or mixed dyslipidaemia. <i>International Journal of Clinical Practice</i> 2008;62:1959–70. <a href="http://ClinicalTrials.gov">ClinicalTrials.gov</a> : NCT00269204	No CVD outcomes and follow up shorter than 6 months
382	Goldberg A, Alagona P Jr, Capuzzi DM, Guyton J, Morgan JM, Rodgers J, Sachson R, Samuel P. Multiple-dose efficacy and safety of an extended-release form of niacin in the management of hyperlipidemia. <i>Am J Cardiol</i> . 2000 May 1;85(9):1100-5. PubMed PMID: 10781759.	No CVD outcomes
383	Hunninghake DB, McGovern ME, Koren M, Brazg R, Murdock D, Weiss S, Pearson T. A dose-ranging study of a new, once-daily, dual-component drug product containing niacin extended-release and lovastatin. <i>Clin Cardiol</i> . 2003 Mar;26(3):112-8. PubMed PMID: 12685616.	No CVD outcomes
384	Thoenes M, Oguchi A, Nagamia S, Vaccari CS, Hammoud R, Umpierrez GE, Khan BV. The effects of extended-release niacin on carotid intimal media thickness, endothelial function and inflammatory markers in patients with the metabolic syndrome. <i>Int J Clin Pract</i> . 2007 Nov;61(11):1942-8.	No CVD outcomes
385	Santanu G, Suhrita P, Mookerjee S, Tania K, Mita S, Prमित G, Sharmila G, Miraj M, Debduitta M. Lipid modifying action of atorvastatin in comparison to combination of atorvastatin and nicotinic acid in patients with ischaemic heart disease. <i>Indian Heart J</i> . 2011 Sep-Oct;63(5):434-7.	No CVD outcomes
386	Ballantyne CM, Davidson MH, McKenney J, Keller LH, Bajorunas DR, Karas RH. Comparison of the safety and efficacy of a combination tablet of niacin extended release and simvastatin vs simvastatin monotherapy in patients with increased non-HDL cholesterol (from the SEACOAST I study). <i>Am J Cardiol</i> . 2008 May 15;101(10):1428-36. <a href="http://ClinicalTrials.gov">ClinicalTrials.gov</a> Identifier: NCT00082251	No CVD outcomes
387	Airan-Javia SL, Wolf RL, Wolfe ML, Tadesse M, Mohler E, Reilly MP. Atheroprotective lipoprotein effects of a niacin-simvastatin combination compared to low- and high-dose simvastatin monotherapy. <i>Am Heart J</i> . 2009 Apr;157(4):687.e1-8.	No CVD outcomes
388	Capuzzi DM, Morgan JM, Carey CM, Intenzo C, Tulenko T, Kearney D, Walker K, Cressman MD. Rosuvastatin alone or with extended-release niacin: a new therapeutic option for patients with combined hyperlipidemia. <i>Prev Cardiol</i> . 2004 Fall;7(4):176-81. Trial Number: 4522IL/0029	No CT - no original data
389	Nessim SA, Chin HP, Alaupovic P, Blankenhorn DH. Combined therapy of niacin, colestipol, and fat-controlled diet in men with coronary bypass. Effect on blood lipids and apolipoproteins. <i>Arteriosclerosis</i> . 1983 Nov-Dec;3(6):568-73.	No CVD outcomes
390	Lee JM, Robson MD, Yu LM, Shirodaria CC, Cunningham C, Kyllintireas I, Digby JE, Bannister T, Handa A, Wiesmann F, Durrington PN, Channon KM, Neubauer S, Choudhury RP. Effects of high-dose modified-release nicotinic acid on atherosclerosis and vascular function: a randomized, placebo-controlled, magnetic resonance imaging study. <i>J Am Coll Cardiol</i> . 2009 Nov 3;54(19):1787-94. Oxford Niaspan Study: Effects of Niaspan on Atherosclerosis and Endothelial Function; NCT00232531	No CVD outcomes
391	Harikrishnan S, Rajeev E, Tharakan JA, Titus T, Ajit Kumar VK, Sivasankaran S, Krishnamoorthy KM, Nair K. Efficacy and safety of combination of extended release niacin and atorvastatin in patients with low levels of high density lipoprotein cholesterol. <i>Indian Heart J</i> . 2008 May-Jun;60(3):215-22.	No CVD outcomes
392	Kashyap ML, McGovern ME, Berra K, Guyton JR, Kwiterovich PO, Harper WL, Toth PD, Favrot LK, Kerzner B, Nash SD, Bays HE, Simmons PD. Long-term safety and efficacy of a once-daily niacin/lovastatin formulation for patients with dyslipidemia. <i>Am J Cardiol</i> . 2002 Mar 15;89(6):672-8. PubMed PMID: 11897208.	No CVD outcomes

n.	References	Reason(s) for exclusion from qualitative and quantitative analysis
393	162. Elam MB, Hunninghake DB, Davis KB, Garg R, Johnson C, Egan D, Kostis JB, Sheps DS, Brinton EA. Effect of niacin on lipid and lipoprotein levels and glycemic control in patients with diabetes and peripheral arterial disease: the ADMIT study: A randomized trial. Arterial Disease Multiple Intervention Trial. JAMA. 2000 Sep 13;284(10):1263-70. ADMIT study – included only data on patients without diabetes – excluded measurement at 18-week	competing risk / special population
412	Brown BG, Bardsley J, Poulin D, et al. Moderate dose, three-drug therapy with niacin, lovastatin, and colestipol to reduce low-density lipoprotein cholesterol 100 mg/dl in patients with hyperlipidemia and coronary artery disease. Am J Cardiol 1997;80:111–5.	No CVD outcomes
413	Vega GL, Grundy SM. Lipoprotein responses to treatment with lovastatin, gemfibrozil, and nicotinic acid in normolipidemic patients with hypoalphalipoproteinemia. Arch Intern Med 1994;154:73– 82.	No CVD outcomes and follow up shorter than 6 months
414	Lavie CJ, Mailander L, Milani RV. Marked benefit with sustained- release niacin therapy in patients with "isolated" very low levels of high-density lipoprotein cholesterol and coronary artery disease. Am J Cardiol 1992;69:1083–5.	No CVD outcomes and follow up shorter than 6 months
415	Kuvin JT, Ramet ME, Patel AR, Pandian NG, Mendelsohn ME, Karas RH. A novel mechanism for the beneficial vascular effects of high-density lipoprotein cholesterol: enhanced vasorelaxation and increased endothelial nitric oxide synthase expression. Am Heart J 2002;144:165–72.	No CVD outcomes and follow up shorter than 6 months
416	Ball MJ, Vella M, Rechlass JP, et al. Acipimox in the treatment of patients with hyperlipidaemia: a double blind trial. Eur J Clin Pharmacol 1986;31:201– 4.	No CVD outcomes and follow up shorter than 6 months
417	Crepaldi G, Avogaro P, Descovich GC, et al. Plasma lipid lowering activity of acipimox in patients with type II and type IV hyperlipoproteinemia. Results of a multicenter trial. Atherosclerosis 1988;70: 115–21.	No CVD outcomes and follow up shorter than 6 months
418	Davoren PM, Kelly W, Gries FA, Hubinger A, Whately-Smith C, Alberti KG. Long-term effects of a sustained-release preparation of acipimox on dyslipidemia and glucose metabolism in non-insulin- dependent diabetes mellitus. Metabolism 1998;47:250–6.	competing risk / special population
419	Dean JD, McCarthy S, Betteridge DJ, Whately-Smith C, Powell J, Owens DR. The effect of acipimox in patients with type 2 diabetes and persistent hyperlipidaemia. Diabetes Med 1992;9:611–5.	competing risk / special population
420	Fulcher GR, Catalano C, Walker M, et al. A double blind study of the effect of acipimox on serum lipids, blood glucose control and insulin action in non-obese patients with type 2 diabetes mellitus. Diabetes Med 1992;9:908–14.	competing risk / special population
421	Koev D, Zlateva S, Susic M, et al. Improvement of lipoprotein lipid composition in type II diabetic patients with concomitant hyperlipoproteinemia by acipimox treatment. Results of a multicenter trial. Diabetes Care 1993;16:1285–90.	competing risk / special population
422	Otto C, Parhofer KG, Ritter MM, Richter WO, Schwandt P. Effects of acipimox on haemorrhology and plasma lipoproteins in patients with mixed hyperlipoproteinaemia. Br J Clin Pharmacol 1998;46: 473– 8.	No CVD outcomes and follow up shorter than 6 months
423	Taskinen MR, Nikkila EA. Effects of acipimox on serum lipids, lipoproteins and lipolytic enzymes in hypertriglyceridemia. Atherosclerosis 1988;69:249–55.	No CVD outcomes
424	Vaag AA, Beck-Nielsen H. Effects of prolonged Acipimox treatment on glucose and lipid metabolism and on in vivo insulin sensitivity in patients with non-insulin dependent diabetes mellitus. Acta Endocrinol (Copenh) 1992;127:344–50.	competing risk / special population
425	Carotid IMT (Intima Media Thickening) Study (0524A-041) (TERMINATED) (ACHIEVE). Merck Sharp & Dohme Corp. 2009. ClinicalTrials.gov (NCT00384293)	No results
426	Lee K, Ahn TH, Kang WC, Han SH, Choi IS, Shin EK. The effects of statin and niacin on plaque stability, plaque regression, inflammation and oxidative stress in patients with mild to moderate coronary artery stenosis. Korean Circulation Journal 2011;41:641–8.	No CVD outcomes
427	Moore A, Phan BA, Challender C, et al. Effects of adding extended-release niacin and colessevelam to statin therapy on lipid levels in subjects with atherosclerotic disease. J Clin Lipidol 2007;1:620–5.	No CVD outcomes
428	A Multicenter, Randomized, Double-Blind, "Crossover" Design Study to Evaluate the Lipid-Altering Efficacy and Safety of MK-0524B Combination Tablet Compared to MK-0524A + Simvastatin Coadministration in Patients With Primary Hypercholesterolemia and Mixed Dyslipidemia. Merck Sharp & Dohme Corp. 2016. ClinicalTrials.gov (NCT00479882)	No CVD outcomes and follow up shorter than 6 months

n.	References	Reason(s) for exclusion from qualitative and quantitative analysis
429	A Phase III Multicenter, Double-Blind, Crossover Design Study to Evaluate Lipid-Altering Efficacy and Safety of Extended-Release Niacin/Laropiprant/Simvastatin Combination Tablet in Patients With Primary Hypercholesterolemia or Mixed Dyslipidemia. Merck Sharp & Dohme Corp. 2016. ClinicalTrials.gov (NCT01294683)	No CVD outcomes and follow up shorter than 6 months
430	A Multicenter, Randomized, Double-Blind, Parallel Group, 12 Week Study to Evaluate the Efficacy and Safety of MK0524B Versus Atorvastatin in Patients With Mixed Hyperlipidemia. Merck Sharp & Dohme Corp. 2016. ClinicalTrials.gov (NCT00289900)	No CVD outcomes and follow up shorter than 6 months
CT, clinical trial; CVD, cardiovascular disease.		

**eTable 2. Definitions of cardiovascular outcomes evaluated in the meta-analyses and meta-regression analysis**

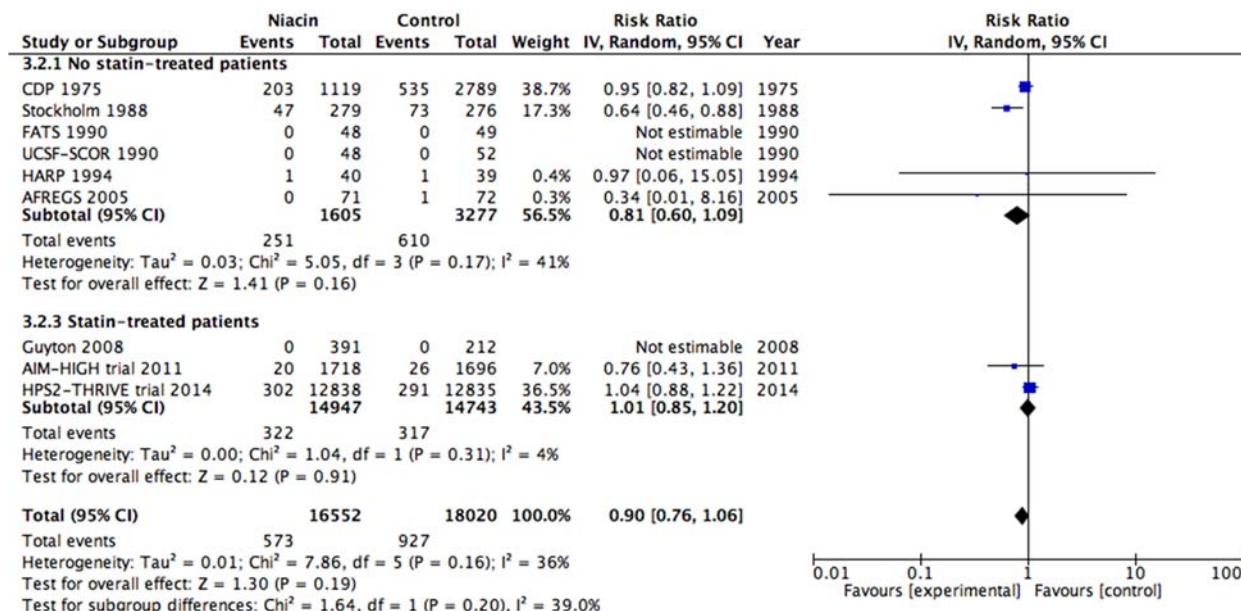
Endpoints	Definitions	No. studies that documented outcome events [Trial name or First Author]
Cardiovascular disease (CVD) mortality	Overall deaths from coronary heart disease ( <i>i.e.</i> , acute myocardial infarction, sudden death, or ischemic heart failure event), cerebrovascular events, or revascularization procedures.	17 [VA drug, CDP, CLAS I, STOCKHOLM, FATS, UCSF-SCOR, HARP, PAST, ARBITER-2, AFREGS, Guyton et al, SANG, ARBITER-6-HALTS, AIM-HIGH, NIA plaque, ELIMIT, HPS2-THRIVE]
Coronary heart disease mortality	Overall deaths from myocardial infarction, sudden death, or heart failure event.	9 [CDP, STOCKHOLM, FATS, UCSF-SCOR, HARP, AFREGS, Guyton et al, AIM-HIGH, HPS2-THRIVE]
Acute coronary syndrome	Fatal and non-fatal myocardial infarction, hospitalization for unstable angina.	16 [VA drug, CDP, CLAS I, STOCKHOLM, FATS, UCSF-SCOR, HARP, PAST, ARBITER-2, AFREGS, Guyton et al, SANG, ARBITER-6-HALTS, AIM-HIGH, ELIMIT, HPS2-THRIVE]
Stroke	Fatal and non-fatal stroke*	11 [CDP, STOCKHOLM, FATS, UCSF-SCOR, ARBITER - 2, AFREGS, Guyton et al, AIM-HIGH, NIA plaque, ELIMIT, HPS2-THRIVE]
Revascularization procedures	Coronary and non-coronary revascularization procedures.	13 [CDP, CLAS I, FATS, HARP, PAST, ARBITER - 2, AFREGS, SANG, ARBITER-6-HALTS, AIM-HIGH, NIA plaque, ELIMIT, HPS2-THRIVE]
Major Adverse events (MACE)	Overall deaths from coronary heart disease, nonfatal myocardial infarction, hospitalization for angina, stroke, revascularization procedures.	17 [VA drug, CDP, CLAS I, STOCKHOLM, FATS, UCSF-SCOR, HARP, PAST, ARBITER-2, AFREGS, Guyton et al, SANG, ARBITER-6-HALTS, AIM-HIGH, NIA plaque, ELIMIT, HPS2-THRIVE]
<p>CVD, cardiovascular disease; MACE, major adverse cardiovascular events; VA drug, Veterans Affairs drug study; CDP, Coronary Drug Project; CLAS I, Cholesterol-Lowering Atherosclerosis Study I; STOCKHOLM, Stockholm Ischaemic Heart Disease Secondary prevention study; FATS, Familial Atherosclerosis Treatment Study; UCSF-SCOR, University of California San Francisco - Arteriosclerosis Specialized Center of Research Intervention Trial; HARP, Heart and Renal Protection study; PAST, Prevenzione Aterosclerosi Studio Torino; ARBITER-2, Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol trial; AFREGS, Armed Forces Regression Study; ARBITER 6-HALTS, Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol 6-HDL and LDL Treatment Strategies in Atherosclerosis trial; AIM-HIGH, Atherothrombosis Intervention in Metabolic Syndrome With Low HDL/High Triglycerides trial; NIA plaque, The National Institute on Aging Plaque Study; ELIMIT, Effect of Lipid Modification on Peripheral Artery Disease after Endovascular Intervention Trial; HPS2-THRIVE, Heart Protection Study 2-Treatment of HDL to Reduce the Incidence of Vascular Events.</p> <p>* the Coronary Drug Project (CDP) study included also intermittent cerebral ischemic attacks.</p>		

**eTable 3. Quality assessment and risk of bias of the studies included in the meta-analyses and meta-regression analysis**

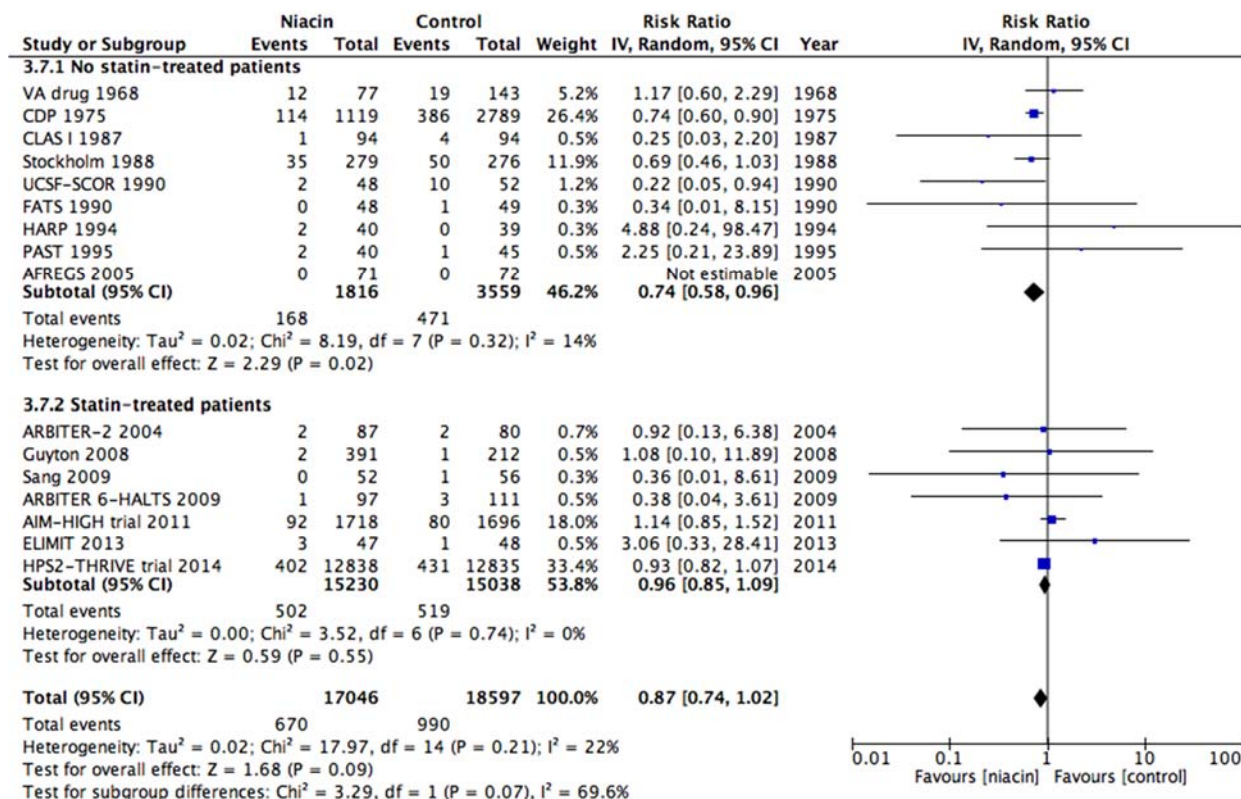
<b>Trials (Trial name or First Author)</b>	<b>random sequence generation (selection bias)</b>	<b>allocation concealment (selection bias)</b>	<b>blinding of participants and personnel (performance bias)</b>	<b>blinding of outcome assessors (performance bias)</b>	<b>incomplete outcome data (attrition bias)</b>	<b>selective outcome reporting (reporting bias)</b>	<b>other potential bias</b>	<b>overall assessment : risk of bias</b>
VA drug	?	?	+	?	+	+	+	unclear
CDP	+	+	+	?	+	+	+	low
CLAS I	?	?	+	+	-	-	+	unclear
STOCKHOLM	?	?	-	-	-	?	?	high
FATS	+	+	+	?	+	+	+	low
UCSF-SCOR	+	+	-	-	?	+	+	unclear
HARP	?	?	-	-	+	+	+	high
PAST	?	?	-	-	-	?	+	high
ARBITER - 2	+	+	+	+	-	+	+	low
AFREGS	+	+	+	?	+	+	+	low
Guyton et al	+	+	+	+	-		+	unclear
SANG	?	?	?	?	?	?	-	high
ARBITER-6-HALTS	+	+	-	+	?	-	+	unclear
AIM-HIGH	+	+	+	+	+	+	+	low
NIA plaque	+	+	+	?	-	-	+	unclear
ELIMIT	?	?	+	?	+	+	+	unclear
HPS2-THRIVE	+	+	+	+	+	+	+	low

**eFigure 1. Forest plot of meta-analyses on the effect of niacin therapy over time on coronary heart disease mortality, acute coronary syndrome, revascularization procedures, and MACE**

**Coronary heart disease mortality**

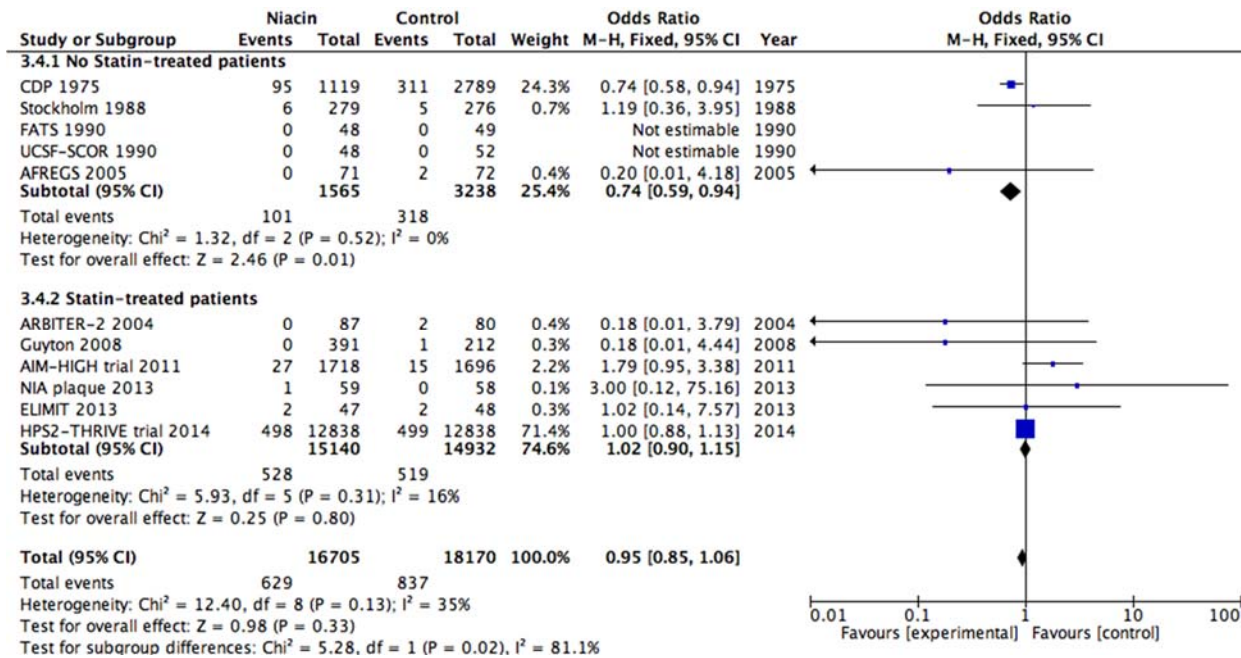


**Acute coronary syndrome**

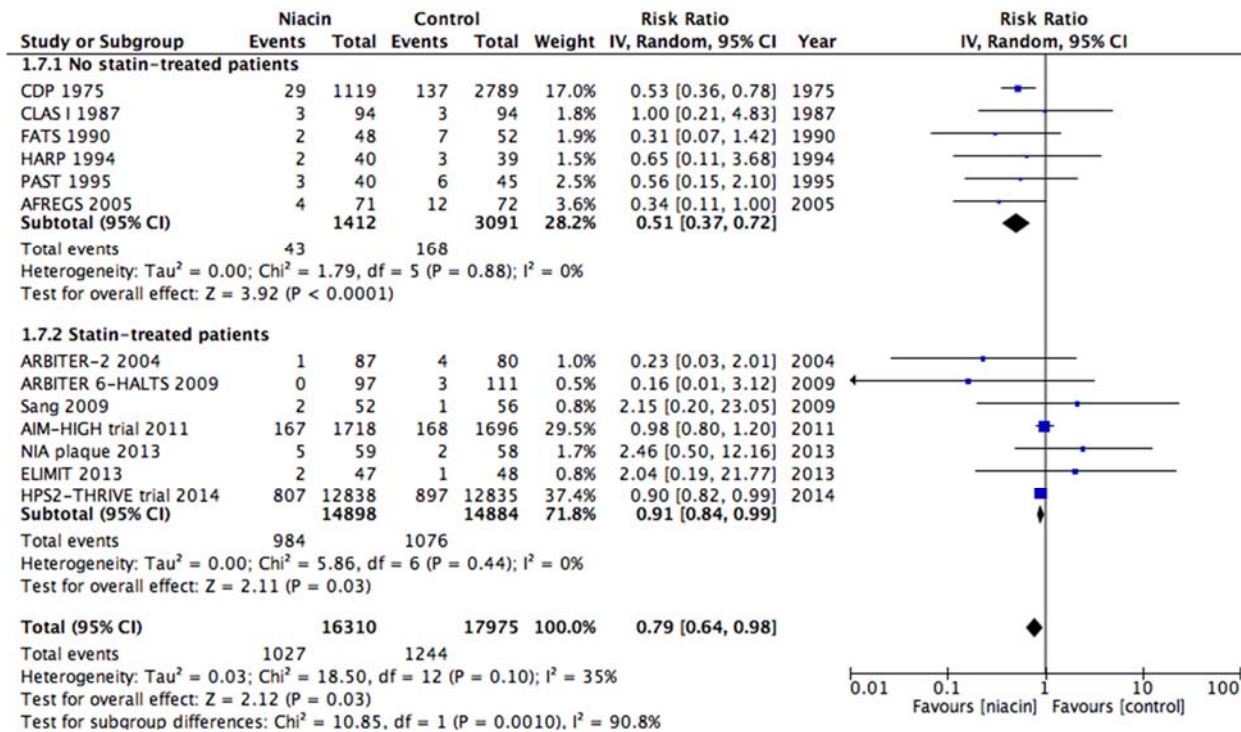




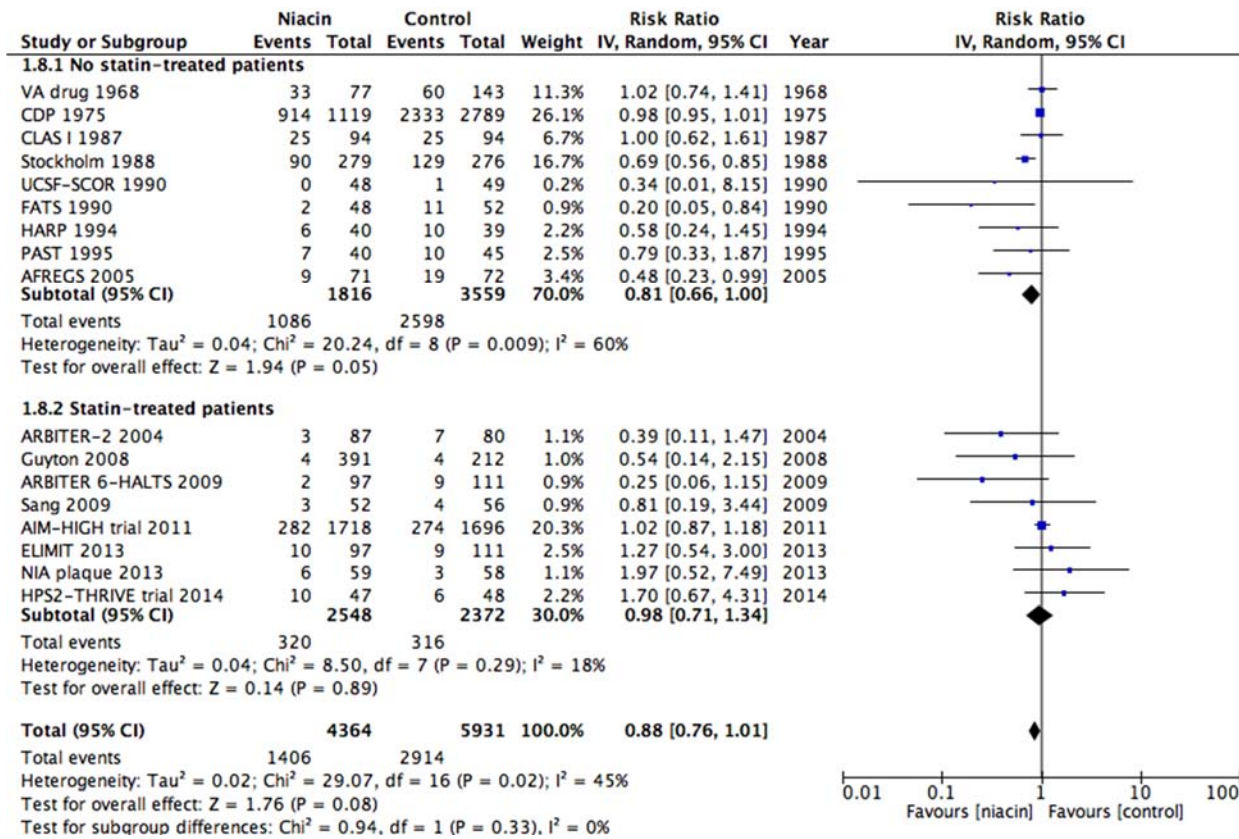
## Fatal and non-fatal stroke



## Revascularization procedures



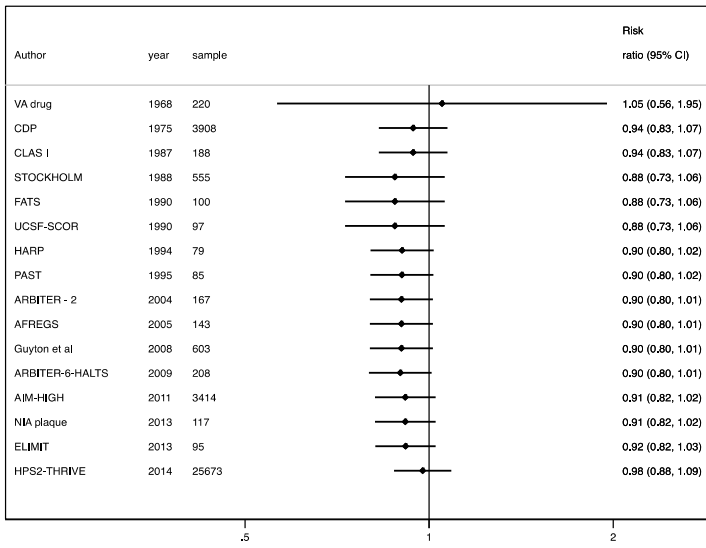
## Major adverse cardiac events (MACE)



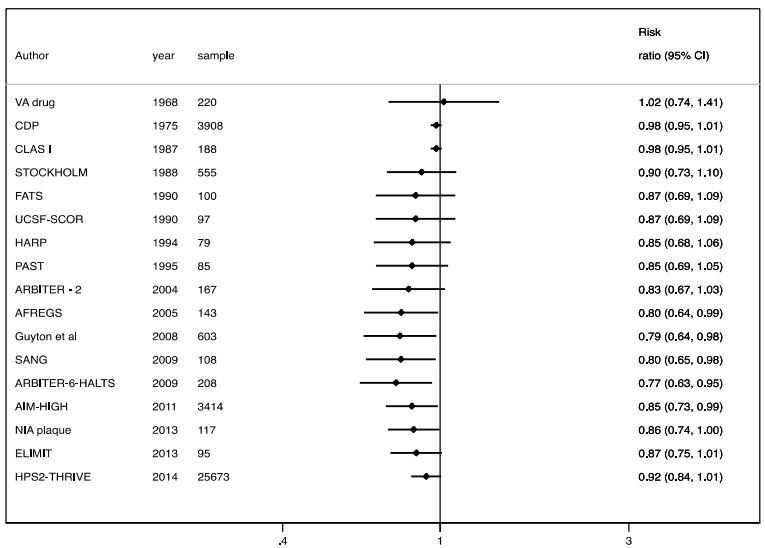
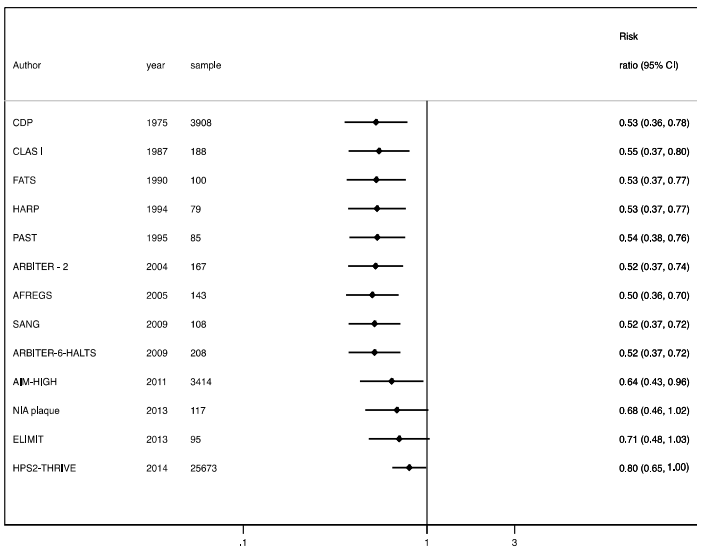
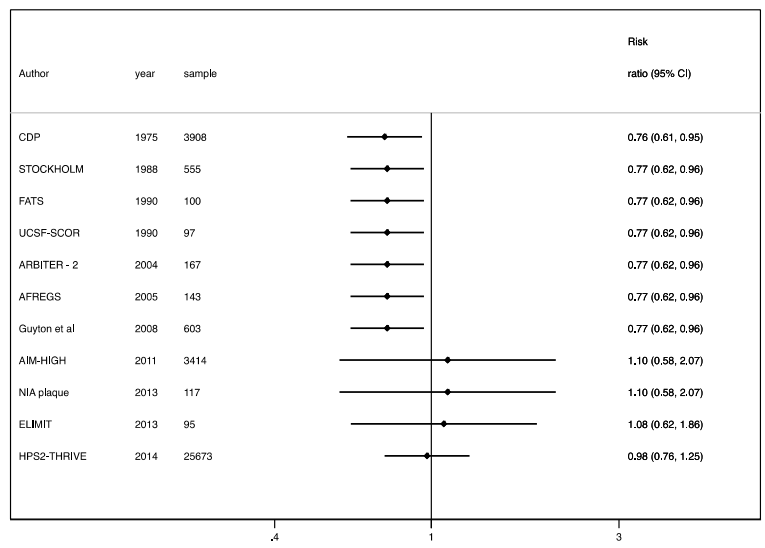
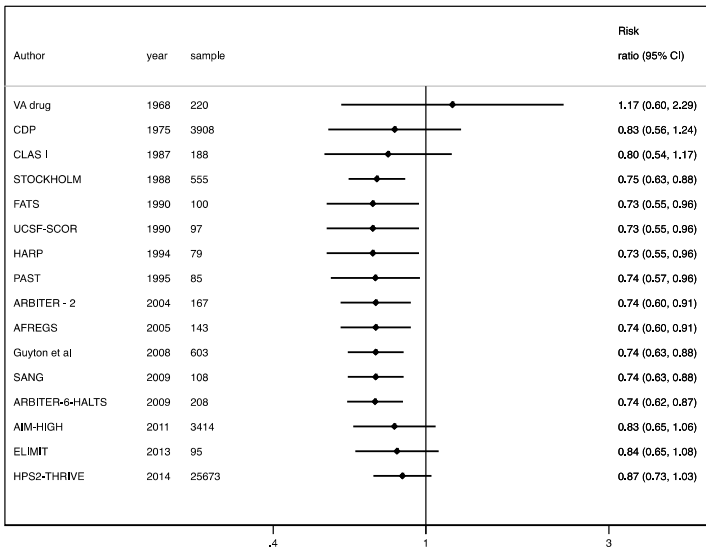
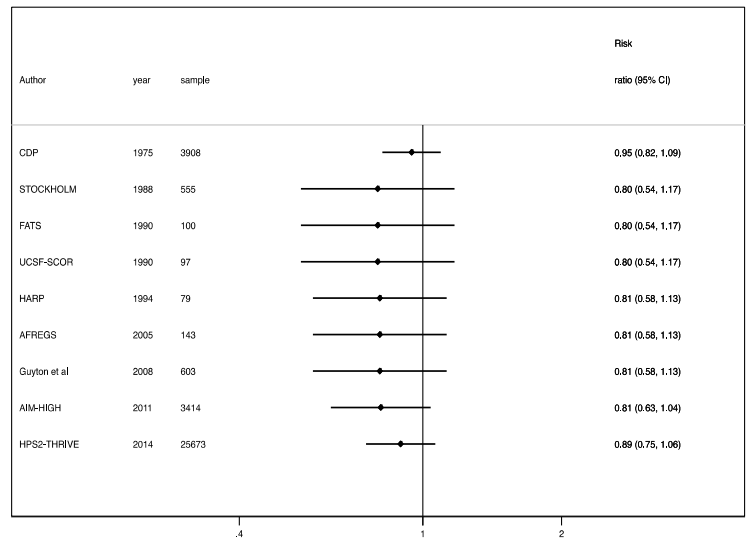
MACE, major adverse cardiovascular events; VA drug, Veterans Affairs drug study; CDP, Coronary Drug Project; CLAS I, Cholesterol-Lowering Atherosclerosis Study I; STOCKHOLM, Stockholm Ischaemic Heart Disease Secondary prevention study; FATS, Familial Atherosclerosis Treatment Study; UCSF-SCOR, University of California San Francisco - Arteriosclerosis Specialized Center of Research Intervention Trial; HARP, Heart and Renal Protection study; PAST, Prevenzione Aterosclerosi Studio Torino; ARBITER-2, Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol trial; AFREGS, Armed Forces Regression Study; ARBITER 6-HALTS, Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol 6-HDL and LDL Treatment Strategies in Atherosclerosis trial; AIM-HIGH, Atherothrombosis Intervention in Metabolic Syndrome With Low HDL/High Triglycerides trial; NIA plaque, The National Institute on Aging Plaque Study; ELIMIT, Effect of Lipid Modification on Peripheral Artery Disease after Endovascular Intervention Trial; HPS2-THRIVE, Heart Protection Study 2-Treatment of HDL to Reduce the Incidence of Vascular Events.

**eFigure 2. Forest plot of cumulative meta-analyses on the effect of niacin therapy over time on the CVD mortality, coronary heart disease mortality, acute coronary syndrome, revascularization procedures, and MACE**

**CVD mortality**



**Coronary heart disease mortality**



CVD, cardiovascular disease; MACE, major adverse cardiovascular events; VA drug, Veterans Affairs drug study; CDP, Coronary Drug Project; CLAS I, Cholesterol-Lowering Atherosclerosis Study I; STOCKHOLM, Stockholm Ischaemic Heart Disease Secondary prevention study; FATS, Familial Atherosclerosis Treatment Study; UCSF-SCOR, University of California San Francisco - Arteriosclerosis Specialized Center of Research Intervention Trial; HARP, Heart and Renal Protection study; PAST, Prevenzione Aterosclerosi Studio Torino; ARBITER-2, Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol trial; AFREGS, Armed Forces Regression Study; ARBITER 6-HALTS, Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol 6-HDL and LDL Treatment Strategies in Atherosclerosis trial; AIM-HIGH, Atherothrombosis Intervention in Metabolic Syndrome With Low HDL/High Triglycerides trial; NIA plaque, The National Institute on Aging Plaque Study; ELIMIT, Effect of Lipid Modification on Peripheral Artery Disease after Endovascular Intervention Trial; HPS2-THRIVE, Heart Protection Study 2–Treatment of HDL to Reduce the Incidence of Vascular Events.