Appendix 4. Overall Results

Table 1. Primary Outcome: Major Adverse Cardiac Events (MACE)

Treatment	Primary Prevention or Mixed (Primary + Secondary)	MACE Definition	Systematic Review (Author, Year)	RCTs included	Sample Size (n)	Outcome Measured at (weeks)	Point Estimate (OR, RR, HR)	95% CI	Random or fixed effects analysis?	I^2
Bile acid sequestrants (BAS)										
BAS	Primary	"definite coronary heart disease death and/or nonfatal myocardial infarction"	RCT: Lipid Research Clinics Program, 1984	1	3806	386	RR 0.83*	0.67-1.01	N/A	N/A
BAS	Secondary	"death, myocardial infarction, coronary artery disease progression or both MI and progression"	RCT: Brensike, 1984	1	143	261	OR 0.60	0.30-1.21	N/A	N/A
BAS	Mixed	"total cardiac events- deaths, non, fatal MI, coronary surgery, angioplasty, and stroke"	RCT: Watts, 1992	1	53	170	RR 0.35*	0.04-3.12	N/A	N/A
Ezetimibe										

Ezetimibe	Mixed	"Varied between studies, with coronary revascularization included in most studies"	Hong, 2018	6	18921	48-288	RR 0.93	0.89-0.99	Random	0.9%
Ezetimibe	Mixed	composite of coronary heart death, nonfatal MI, stroke or coronary revascularization	Toyota, 2019	4	20688	NR	OR 0.90	0.85-0.96	Random	35%
Ezetimibe	Mixed	CV death non-fatal MI, non-fatal stroke, hospitalization for unstable angina or coronary revascularisation	Zhan, 2018	10	21727	52-312	RR 0.94	0.90-0.98	Fixed	0%
Fibrates										
Fibrates	Primary	"Combined CVD death, non-fatal MI, non-fatal stroke"	Jakob, 2016	6	16135	104-261	RR 0.84	0.74-0.96	Fixed	0%
Fibrates	Secondary	"Composite outcome of non-fatal stroke, non-fatal MI and vascular death"	Wang, 2015	12	16064	271	RR 0.88	0.81-0.97	Random	45%
Niacin										

Niacin	Mixed	"Overall deaths from coronary heart disease, nonfatal myocardial infarction, hospitalization for angina, stroke, revascularization procedures"	D'Andrea, 2019	17	10295	NR	RR 0.88	0.76- 1.01	Random	45%
Niacin	Mixed	"Total CVD"	Jenkins 2021	4	29254	NR	RR 0.97	0.91-1.03	Random	55%
Omega 3s (EPA+DHA)										
Omega 3s	Mixed	"Major vascular events (first occurrence nonfatal MI, death caused by CHD, nonfatal or fatal stroke, any revascularization procedure"	Aung, 2018	9	59195	NR	RR 0.98	0.94-1.02	NR	NR
Omega 3s	Mixed	NR	Casula, 2020	13	54011	NR	OR 0.96	0.88-1.04	NR	NR
Omega 3s	Mixed	NR	Khan, 2021	13	107714	NR	RR 0.99	0.95-1.02	Random	NR
EPA only										
EPA	Mixed	NR	Khan, 2021	4	27305	NR	RR 0.78	0.72-0.85	Random	NR
PCSK9 inhibitors										
PCSK9 Inhibitors	Mixed	"CV death, nonfatal MI, and nonfatal stroke"	AlTurki, 2019	22	NR	NR	OR 0.82	0.77-0.87	Random	0%
PCSK9 Inhibitors	Mixed	"CV Events"	Bai, 2018	11	38226	NR	RR 0.86	0.81-0.92	Fixed	0%

PCSK9 Inhibitors	Mixed	"Cardiovascular event incidence"	Casula, 2019	20	60878	NR	OR 0.83	0.78-0.87	Random	NR
PCSK9 Inhibitors	Mixed	"CV mortality, nonfatal MI, nonfatal stroke"	Dicembrini, 2019	27	84233	NR	OR 0.83	0.78-0.88	Random	0%
PCSK9 Inhibitors	Mixed	"CV death, non-fatal MI, and non-fatal stroke"	Du, 2019	31	92736	12-146	RR 0.84	0.79-0.89	Fixed	0%
PCSK9 Inhibitors	Mixed	NR	Ghadban, 2017	6	62776	NR	RR 0.81	0.70-0.93	Random	56%
PCSK9 Inhibitors	Mixed	NR	Khan, 2022	5	80732	26-146	RR 0.84	0.76-0.92	Random	NR
PCSK9 Inhibitors	Mixed	"CV death, stroke and MI"	Ma, 2021	20	86845	NR	RR 0.83	0.79-0.88	Fixed	9%
PCSK9 Inhibitors	Mixed	"CV death, nonfatal MI, nonfatal stroke"	Monami, 2019	3	47208	NR	OR 0.78	0.71-0.85	Random	37%
PCSK9 Inhibitors	Mixed	"Major CV Events"	Mu, 2020	15	NR	NR	RR 0.87	0.83-0.91	Random	NR
PCSK9 Inhibitors	Mixed	"Coronary heart death, non-fatal MI, stroke, or coronary revascularization"	Toyota, 2019	7	54677	NR	OR 0.81	0.73-0.90	Random	37%
PCSK9 Inhibitors	Mixed	Based on the individual trial definitions	Turgeon, 2018	21	59852	NR	RR 0.83	0.78-0.88	Fixed	2%
PCSK9 Inhibitors	Mixed	"CV Events"	Wang, 2021	13	24803	NR	RR 0.89	0.83-0.95	Fixed	0%
PCSK9 Inhibitors	Mixed	"Adjudicated CV events"	Zhao, 2020	8	49227	NR	RR 0.87	0.83-0.91	Fixed	0%
PCSK9 Inhibitors	Mixed	"CV Events"	Zhao, 2019	NR	62714	NR	OR 0.79	0.68-0.92	Random	NR

PCSK9 Inhibitors	Mixed	"Positively adjudicated CV events (composite of all-cause mortality, CV death, MI, stroke, revascularization, or hospitalization for unstable angina"	Zhu, 2019	15	35011	NR	RR 0.87	0.81-0.93	Random	0%
Statins										
Statins	Primary	"Any coronary heart events" (angina, MI, coronary revascularization, CHD death)	Li, 2019	8	37395	52-276	RR 0.73	0.68-0.78	Fixed	0%
Statins	Mixed	"Coronary Artery Disease"	Ponce, 2019	10	24728	NR	RR 0.71	0.63-0.80	Random	52%
Statins	Primary	"All CHD events" – 13 outcomes, see PDF (pg 3), excludes stroke	Sandwith, 2021	13	88876	NR	RR 0.78	0.71-0.85	Random	71%
Statins	Primary	Primary endpoint for each RCT (Appendix pg 21)	Singh, 2020	11	58504	NR	RR 0.71	0.62-0.82	Random	55%
Statins	Primary	"Fatal and non-fatal CVD"	Taylor, 2013	9	23805	NR	RR 0.75	0.70-0.81	Fixed	31%
Statins	Primary	"Non-fatal stroke, unstable angina,	Yebyo, 2013	23	NR	NR	RR 0.74	0.67-0.81	Random	49.5%

		non-fatal MI and CV death"								
Statins	Mixed	"CV events" (not defined in paper)	Zhao, 2019	NR	139233	NR	OR 0.80	0.76-0.85	Random	NR

BAS: Bile Acid Sequestrants; *Calculated by PEER team at https://www.medcalc.org/calc/relative_risk.php; RCT: Randomized Controlled Trial; n: Total sample size in meta-analysis; OR: Odds Ratio; RR: Risk Ratio; HR= Hazard Ratio; CI: Confidence Interval; I^2: indicates the level of heterogeneity; CVD: Cardiovascular Disease; NR: Not Reported; ACS: Acute coronary syndrome; US

Table 2. Secondary Outcome: Cardiovascular Mortality

Treatment	Primary Prevention or Mixed (Primary + Secondary)	Systematic Review (Author, Year)	RCTs included	Sample Size (n)	Outcome Measured at (weeks)	Point Estimate (OR, RR, HR)	95% CI	Random or fixed effects analysis?	I^2
Bile acid sequestrants (BAS)									
BAS	Primary	RCT: Lipids Research Clinics Program, 1984	1	3806	386	RR 0.79*	0.49-1.26	N/A	N/A
BAS	Mixed-MEN	RCT: Dorr, 1978	1	1094	52-157	RR 0.46*	0.23-0.92	N/A	N/A
BAS	Mixed-WOMEN	RCT: Dorr, 1978	1	1184	52-157	RR 1.08*	0.44-2.63	N/A	N/A
Ezetimibe									
Ezetimibe	Mixed	Toyota, 2019	3	18967	NR	OR 1.00	0.89-1.13	Random	0%
Ezetimibe	Mixed	Zhan, 2018	6	19457	52-312	RR 1.00	0.89-1.12	Fixed	0%
Fibrates									
Fibrates	Secondary	Wang, 2015	10	13653	282	RR 0.95	0.86-1.05	Fixed	11%
Niacin									
Niacin	Mixed	D'Andrea, 2019	16	35652	NR	RR 0.98	0.90-1.07	Random	0%
Niacin	Mixed	Garg, 2017	9	9236	NR	RR 0.91	0.81-1.02	Random	0.1%
Niacin	Mixed	Jenkins, 2021	2	3581	NR	RR 1.14	0.75-1.73	Random	0%
Niacin	Mixed	Riaz, 2019	4	32733	NR	RR 0.99	0.89-1.09	Random	NR
Niacin	Mixed	Schandelmaier, 2017	5	32966	52-260	RR 1.02	0.93-1.12	Random	0%
Omega 3s									
Omega 3s	Mixed	Cabiddu, 2020	11	100609	NR	RR 0.94	0.89-0.99	NR	0%
Omega 3s	Mixed	Hu, 2019	11	100599	NR	RR 0.93	0.88-0.99	Fixed	0.2%
Omega 3s	Mixed	Khan, 2021	22	116452	NR	RR 0.94	0.89-0.99	Random	NR

Omega 3s	Mixed	Kim, 2020	13	NR	52-385	RR 0.93	0.88-0.99	Random	10%
Omega 3s	Mixed	Xie, 2021	8	49872	NR	RR 0.93	0.88-0.99	Fixed	0%
EPA only									
EPA	Mixed	Khan, 2021	3	27062	NR	RR 0.82	0.68-0.99	Random	NR
EPA	Mixed	Kim, 2020	1	8159	NR	RR 0.82	0.67-0.99	NR	NR
PCSK9 Inhibitors									
PCSK9 Inhibitors	Mixed	AlTurki, 2019	13	NR	NR	OR 0.95	0.84-1.07	Random	0%
PCSK9 Inhibitors	Mixed	Bai, 2018	7	36476	NR	RR 1.00	0.84-1.18	Fixed	5.2%
PCSK9 Inhibitors	Mixed	Casula, 2019	10	57306	NR	OR 0.94	0.83-1.07	Random	NR
PCSK9 Inhibitors	Mixed	Chaiyasothi, 2019	11	85021	NR	RR 0.97	0.86-1.08	Random	0%
PCSK9 Inhibitors	Mixed	Dicembrini, 2019	36	85521	NR	OR 0.97	0.86-1.09	Random	0%
PCSK9 Inhibitors	Mixed	Du, 2019	57	96709	12-146	RR 0.95	0.85-1.07	Random	0%
PCSK9 Inhibitors	Mixed	Ghadban, 2017	6	62776	NR	RR 0.98	0.78-1.22	Random	15%
PCSK9 Inhibitors	Mixed	Guedeney, 2019	NR	64707	8-208	RR 0.94	0.84-1.06	Random	0%
PCSK9 Inhibitors	Mixed	Karatasakis, 2017	34	44701	NR	OR 1.01	0.85-1.19	Random	0%
PCSK9 Inhibitors	Mixed	Khan, 2022	5	80732	26-146	RR 0.95	0.80-1.12	Random	NR
PCSK9 Inhibitors	Mixed	Khan, 2019	9	83318	NR	RR 0.95	0.85-1.07	Random	NR
PCSK9 Inhibitors	Mixed	Ma, 2021	13	84639	NR	RR 0.96	0.86-1.07	Fixed	0%
PCSK9 Inhibitors	Mixed	Mu, 2020	6	NR	NR	RR 0.93	0.79-1.11	Random	NR
PCSK9 Inhibitors	Mixed	Qin, 2021	7	57436	NR	RR 0.95	0.84-1.07	Fixed	2.5%
PCSK9 Inhibitors	Mixed	Toyota, 2019	6	53709	NR	OR 0.92	0.73-1.15	Random	47%
PCSK9 Inhibitors	Mixed	Turgeon, 2018	19	58021	NR	RR 0.95	0.84-1.07	Fixed	0%
PCSK9 Inhibitors	Mixed	Wang, 2021	4	20570	NR	RR 0.87	0.74-1.04	Fixed	0%
PCSK9 Inhibitors	Mixed	Zhao, 2020	6	48060	NR	RR 0.96	0.85-1.08	Fixed	0%
PCSK9 Inhibitors	Mixed	Zhao, 2019	NR	63501	NR	OR 0.99	0.87-1.13	Random	NR
PCSK9 Inhibitors	Mixed	Zhu, 2019	12	64323	NR	RR 1.01	0.87-1.18	Random	0%
Statins									
Statins	Mixed	Kim, 2020	27	97648	52-317	RR 0.86	0.80-0.92	Random	37.2%
Statins	Primary	Cai, 2021	22	95959	230	OR 0.83	0.76-0.91	Fixed	27%
Statins	Primary	Li, 2019	6	38935	NR	RR 0.85	0.74-0.99	Fixed	22%

Statins	Mixed	Ponce, 2019	12	35955	52-346	RR 0.85	0.76-0.96	Fixed	49.3%
Statins	Primary	Singh, 2020	8	54515	99-291	RR 0.90	0.78-1.04	Random	0%
Statins	Primary	Taylor, 2013	5	34012	NR	RR 0.83	0.72-0.96	Fixed	0%
Statins	Primary	Yebyo, 2019	15	NR	NR	RR 0.80	0.71-0.91	Random	35.3%
Statins	Mixed	Zhao, 2019	NR	134059	NR	OR 0.83	0.75-0.92	Random	NR

BAS: Bile Acid Sequestrants; *Calculated by PEER team at https://www.medcalc.org/calc/relative_risk.php; RCT: Randomized Controlled Trial; n: Total sample size in meta-analysis; OR: Odds Ratio; RR: Risk Ratio; CI: Confidence Interval; I^2: indicates the level of heterogeneity; NR= Not Reported

Table 3. Secondary Outcome: All-Cause Mortality

Treatment	Primary Prevention or Mixed (Primary + Secondary)	Systematic Review (Author, Year)	RCTs included	Sample Size (n)	Outcome Measured at (weeks)	Point Estimate (OR, RR, HR)	95% CI	Random or fixed effects analysis?	I^2
Bile acid sequestrants (BAS)									
BAS	Primary	RCT: Lipids Research Clinics Program, 1984	1	3806	386	RR 0.95*	0.69-1.32	N/A	N/A
BAS	Mixed-MEN	RCT: Dorr, 1978	1	1094	52-157	RR 0.63*	0.35-1.14	N/A	N/A
BAS	Mixed-WOMEN	RCT: Dorr, 1978	1	1184	52-157	RR 0.92*	0.50-1.69	N/A	N/A
BAS	Mixed	RCT: Watts, 1992	1	53	170	RR 0.35*	0.01-8.12	N/A	N/A
Ezetimibe									
Ezetimibe	Mixed	Toyota, 2019	3	19968	NR	OR 0.88	0.62-1.27	Random	54%
Ezetimibe	Mixed	Zhan, 2018	8	21222	52-312	RR 0.98	0.91-1.05	Fixed	0%
Fibrates									
Fibrates	Primary	Jakob, 2016	5	8471	52-261	RR 1.01	0.81-1.26	Fixed	0%
Fibrates	Mixed	Keene, 2014	19	45935	261	OR 0.98	0.89-1.08	Random	33%
Fibrates	Secondary	Wang, 2015	10	13653	282	RR 0.98	0.91-1.06	Fixed	23%
Niacin									
Niacin	Mixed	Garg, 2017	11	34810	NR	RR 0.99	0.88-1.12	Random	31%
Niacin	Mixed	Jenkins, 2021	4	29195	NR	RR 1.04	0.95-1.14	Random	16%
Niacin	Mixed	Riaz, 2019	5	33305	NR	RR 1.04	0.97-1.12	Random	NR
Niacin	Mixed	Schandelmaier, 2017	12	35543	26-260	RR 1.05	0.97-1.12	Random	0%
Omega 3s									
Omega 3s	Mixed	Khan, 2021	21	113921	NR	RR 0.98	0.93-1.03	Random	NR

Omega 3s	Mixed	Kim, 2020	17	NR	52-385	RR 0.97	0.94-1.00	Random	2.2%
EPA Only									
EPA	Mixed	Khan, 2021	3	27062	NR	RR 0.96	0.85-1.10	NR	NR
EPA	Mixed	Kim, 2020	2	26804	NR	RR 0.98	0.81-1.18	NR	6%
PCSK9 Inhibitors									
PCSK9 Inhibitors	Mixed	AlTurki, 2019	17	NR	NR	OR 0.91	0.78-1.06	Random	21%
PCSK9 Inhibitors	Mixed	Bai, 2018	NR	NR	NR	RR 1.00	0.89-1.14	NR	NR
PCSK9 Inhibitors	Mixed	Casula, 2019	13	59504	NR	OR 0.93	0.85-1.03	Random	NR
PCSK9 Inhibitors	Mixed	Chaiyasothi, 2019	12	84092	NR	RR 0.94	0.82-1.06	Random	13.8%
PCSK9 Inhibitors	Mixed	Cordero, 2020	6	81696	NR	OR 0.95	0.86-1.04	NR	55.1%
PCSK9 Inhibitors	Mixed	Dicembrini, 2019	38	85230	NR	OR 0.94	0.84-1.04	Random	3%
PCSK9 Inhibitors	Mixed	Du, 2019	57	96427	12-146	RR 0.93	0.84-1.03	Random	3%
PCSK9 Inhibitors	Mixed	Ghadban, 2017	6	62776	NR	RR 1.01	0.86-1.20	Random	21%
PCSK9 Inhibitors	Mixed	Guedeney, 2019	NR	66478	8-208	RR 0.89	0.75-1.04	Random	13%
PCSK9 Inhibitors	Mixed	Karatasakis, 2017	35	45503	NR	OR 0.71	0.47-1.09	Random	18%
PCSK9 Inhibitors	Mixed	Khan, 2022	5	80732	26-146	RR 0.91	0.75-1.10	Random	NR
PCSK9 Inhibitors	Mixed	Khan, 2019	9	83318	NR	RR 0.94	0.81-1.09	Random	NR
PCSK9 Inhibitors	Mixed	Monami, 2019	3	1234	NR	OR 0.43	0.14-1.29	Random	0%
PCSK9 Inhibitors	Mixed	Mu, 2020	13	NR	NR	RR 0.88	0.72-1.07	Random	NR
PCSK9 Inhibitors	Mixed	Toyota, 2019	7	54677	NR	OR 0.87	0.69-1.10	Random	53%
PCSK9 Inhibitors	Mixed	Turgeon, 2018	23	60724	NR	RR 0.93	0.85-1.02	Fixed	19%
PCSK9 Inhibitors	Mixed	Wang, 2021	13	24773	NR	RR 0.80	0.66-0.96	Fixed	11%
PCSK9 Inhibitors	Mixed	Zhao, 2020	8	49227	NR	RR 0.95	0.86-1.05	Fixed	22%
PCSK9 Inhibitors	Mixed	Zhao, 2019	NR	60169	NR	OR 0.87	0.71-1.07	Random	NR
Statins									
Statins	Mixed	Byrne, 2022	19	132763	NR	RR 0.91	0.86-0.95	Random	52%
Statins	Mixed	Kim, 2020	30	138877	52-317	RR 0.90	0.86-0.94	Random	43.8%
Statins	Primary	Li, 2019	9	53656	52-276	RR 0.88	0.76-1.01	Random	58%
Statins	Mixed	Ponce, 2019	17	47083	52-346	RR 0.92	0.87-0.97	Random	20%
Statins	Primary	Sandwith, 2021	13	88876	NR	RR 0.93	0.89-0.97	Fixed	6%

Statins	Primary	Singh, 2020	11	58504	99-291	RR 0.92	0.83-1.02	Random	25%
Statins	Primary	Taylor, 2013	13	48060	260	OR 0.86	0.79-0.94	Fixed	0%
Statins	Primary	Yebyo, 2019	24	NR	NR	RR 0.89	0.85-0.93	Random	0%
Statins	Mixed	Zhao, 2019	NR	143995	NR	OR 0.91	0.86-0.96	Random	0%

BAS: Bile Acid Sequestrants; *Calculated by PEER team at https://www.medcalc.org/calc/relative_risk.php; RCT: Randomized Controlled Trial; n: Total sample size in meta-analysis; OR: Odds Ratio; RR: Risk Ratio; Cl: Confidence Interval; I^2: indicates the level of heterogeneity; NR= Not Reported

Table 4. Secondary Outcome: Myocardial Infarction

Treatment	Primary Prevention or Mixed (Primary + Secondary)	Systematic Review (Author, Year)	RCTs included	Sample Size (n)	Outcome Measured at (weeks)	Point Estimate (OR, RR, HR)	95% CI	Random or fixed effects analysis?	I^2
NON-FATAL MYOCARDIAL INFARCTION									
Bile acid sequestrants (BAS)									
BAS	Primary	RCT: Lipid Research Clinics Program, 1984	1	3806	386	RR 0.82*	0.66-1.03	N/A	N/A
BAS	Mixed	RCT: Watts, 1992	1	53	170	RR 1.04*	0.07-15.75	N/A	N/A
Ezetimibe									
Ezetimibe	Mixed	Zhan, 2018	6	21145	52-312	RR 0.88	0.81-0.95	Fixed	0%
Fibrates									
Fibrates	Mixed	Keene, 2014	18	45445	261	OR 0.80	0.74-0.87	Random	1%
Niacin									
Niacin	Mixed	Garg, 2017	9	34251	NR	RR 0.85	0.73-1.0	Random	29%
Niacin	Mixed	Schandelmaier, 2017	4	33164	NR	RR 0.91	0.77-1.07	Random	53%
Omega 3s									
Omega 3s	Mixed	Aung, 2018	9	59195	NR	RR 0.98	0.90-1.07	NR	NR
Omega 3s	Mixed	Khan, 2021	17	98549	NR	RR 0.92	0.85-1.00	Random	NR
EPA Only									
EPA	Mixed	Khan, 2021	3	27062	NR	RR 0.72	0.62-0.84	Random	NR
PCSK9 Inhibitors									
PCSK9 Inhibitors	Mixed	Chaiyasothi, 2019	12	83463	NR	RR 0.81	0.72-0.92	Random	28.4%
PCSK9 Inhibitors	Mixed	Dicembrini, 2019	34	80449	NR	OR 0.80	0.73-0.89	Random	9%

PCSK9 Inhibitors	Mixed	Du, 2019	41	90605	12-146	RR 0.83	0.74-0.93	Random	12%
PCSK9 Inhibitors	Mixed	Zhao, 2020	4	20405	NR	RR 0.86	0.78-0.96	Fixed	0%
Statins									
Statins	Primary	Li, 2019	8	41191	NR	RR 0.60	0.51-0.69	Fixed	14%
Statins	Primary	Yebyo, 2019	16	NR	NR	RR 0.62	0.53-0.72	Random	31%
FATAL MYOCARDIAL INFARCTION									
Bile acid sequestrants (BAS)									
BAS	Mixed- MEN	RCT: Dorr, 1978	1	1094	52-157	RR 0.06*	0.00-1.01	N/A	N/A
Ezetimibe									
Ezetimibe	NR	NR	NR	NR	NR	NR	NR	NR	NR
Fibrates									
Fibrates	Mixed	Keene, 2014	17	45422	261	OR 0.92	0.81-1.04	Random	16%
Niacin									
Niacin	Mixed	Garg, 2017	4	33543	NR	RR 0.93	0.78-1.10	Random	55%
Niacin	Mixed	Jenkins, 2021	2	29087	NR	RR 1.04	0.90-1.21	Random	0%
Niacin	Mixed	Schandelmaier, 2017	6	33336	NR	RR 1.01	0.91-1.11	Random	0%
Omega-3s									
Omega-3s	NR	NR	NR	NR	NR	NR	NR	NR	NR
EPA only									
EPA	NR	NR	NR	NR	NR	NR	NR	NR	NR
Statins									
Statins	Mixed	Kim, 2020	8	NR	NR	RR 0.73	0.57-0.93	Random	17.6%
Statins	Primary	Li, 2019	3	10975	NR	RR 0.49	0.24-0.98	Fixed	0%
Statins	Primary	Yebyo, 2019	6	NR	NR	RR 0.72	0.50-1.03	Random	0%
MYOCARDIAL INFARCTION (ALL)									
Ezetimibe									
Ezetimibe	Mixed	Toyota, 2019	3	20585	NR	OR 0.86	0.79-0.95	Random	0%
Fibrates									
Fibrates	Primary	Jakob, 2016	6	16135	104-261	RR 0.79	0.68-0.92	Fixed	24%

Fibrates	Secondary	Wang, 2015	10	13942	277	RR 0.86	0.8-0.93	Fixed	24%
Niacin									
Niacin	Mixed	D'Andrea, 2019	16	35642	NR	RR 0.87	0.74-1.02	Random	22%
Niacin	Mixed	Jenkins, 2021	4	30196	NR	RR 0.96	0.85-1.08	Random	0%
Niacin	Mixed	Riaz, 2019	6	37175	NR	RR 0.89	0.74-1.07	Random	NR
Niacin	Mixed	Schandelmaier, 2017	9	34829	NR	RR 0.93	0.87-1.00	Random	0%
Omega 3s									
Omega 3s	Mixed	Casula, 2020	12	53711	NR	OR 0.88	0.74-1.04	NR	NR
EPA only									
EPA	NR	NR	NR	NR	NR	NR	NR	NR	NR
PCSK9 Inhibitors									
PCSK9 Inhibitors	Mixed	AlTurki, 2019	21	NR	NR	OR 0.80	0.65-0.91	Random	20%
PCSK9 Inhibitors	Mixed	Bai, 2018	8	36691	NR	RR 0.73	0.65-0.82	Fixed	3.9%
PCSK9 Inhibitors	Mixed	Casula, 2019	13	52899	NR	OR 0.78	0.72-0.84	Random	NR
PCSK9 Inhibitors	Mixed	Cordero, 2020	6	81696	NR	RR 0.81	0.76-0.87	NR	51.3%
PCSK9 Inhibitors	Mixed	Dicembrini, 2019	34	36734	NR	OR 0.55	0.49-0.61	Random	0%
PCSK9 Inhibitors	Mixed	Ghadban, 2017	6	62776	NR	RR 0.78	0.63-0.97	Random	54%
PCSK9 Inhibitors	Mixed	Guedeney, 2019	NR	61784	8-208	RR 0.80	0.74-0.86	Random	0%
PCSK9 Inhibitors	Mixed	Karatasakis, 2017	23	41932	NR	OR 0.72	0.64-0.81	Random	0%
PCSK9 Inhibitors	Mixed	Khan, 2022	5	80732	26-146	RR 0.80	0.69-0.93	Random	0%
PCSK9 Inhibitors	Mixed	Khan, 2019	9	83318	NR	RR 0.83	0.71-0.98	Random	NR
PCSK9 Inhibitors	Mixed	Ma, 2021	18	86020	NR	RR 0.81	0.76-0.87	Fixed	23%
PCSK9 Inhibitors	Mixed	Mu, 2020	10	NR	NR	RR 0.78	0.67-0.92	Random	NR
PCSK9 Inhibitors	Mixed	Toyota, 2019	7	54677	NR	OR 0.77	0.66-0.88	Random	29%
PCSK9 Inhibitors	Mixed	Turgeon, 2018	19	59059	NR	RR 0.80	0.74-0.86	Fixed	11%
PCSK9 Inhibitors	Mixed	Zhu, 2019	12	64368	NR	RR 0.78	0.71-0.86	Random	37.5%
Statins									
Statins	Mixed	Byrne, 2022	18	121190	NR	RR 0.71	0.66-0.78	Random	36%

Statins	Primary	Cai, 2021	22	95148	229	OR 0.72	0.66-0.78	Fixed	33%
Statins	Mixed	Ponce, 2019	10	17856	226-346	RR 0.66	0.56-0.78	Random	37%
Statins	Primary	Singh, 2020	6	50784	NR	RR 0.56	0.47-0.67	Random	0%

BAS: Bile Acid Sequestrants; *Calculated by PEER team at https://www.medcalc.org/calc/relative_risk.php; RCT: Randomized Controlled Trial; n: Total sample size in meta-analysis; OR: Odds Ratio; RR: Risk Ratio; Cl: Confidence Interval; I^2: indicates the level of heterogeneity; NR= Not Reported

Table 5. Secondary Outcome: Stroke

Treatment	Primary Prevention or Mixed (Primary + Secondary)	Systematic Review (Author, Year)	RCTs included	Sample Size (n)	Outcome Measured at (weeks)	Point Estimate (OR, RR, HR)	95% CI	Random or fixed effects analysis?	I^2
NON-FATAL STROKE									
BAS									
BAS	NR	NR	NR	NR	NR	NR	NR	NR	NR
Ezetimibe									
Ezetimibe	Mixed	Zhan, 2018	6	21205	52-312	RR 0.83	0.71-0.97	Fixed	0%
Fibrates									
Fibrates	NR	NR	NR	NR	NR	NR	NR	NR	NR
Niacin									
Niacin	NR	NR	NR	NR	NR	NR	NR	NR	NR
Omega 3s									
Omega 3s	Mixed	Khan, 2021	6	56987	NR	RR 1.16	1.00-1.34	Random	NR
EPA only									
EPA	Mixed	Khan, 2021	2	8417	NR	RR 0.71	0.54-0.94	Random	N/A
PCSK9 Inhibitors									
PCSK9 Inhibitors	Mixed	Dicembrini, 2019	33	80487	NR	OR 0.73	0.63-0.84	Random	0%
Statins									
Statins	Primary	Taylor, 2013	5	28097	NR	RR 0.69	0.58-0.83	Fixed	0%
Statins	Primary	Yebyo, 2019	16	NR	NR	RR 0.84	0.76-0.92	Random	0%
FATAL STROKE									
BAS									
BAS	NR	NR	NR	NR	NR	NR	NR	NR	NR
Ezetimibe									

Ezetimibe	NR	NR	NR	NR	NR	NR	NR	NR	NR
Fibrates									
Fibrates	NR	NR	NR	NR	NR	NR	NR	NR	NR
Niacin									
Niacin	NR	NR	NR	NR	NR	NR	NR	NR	NR
Omega 3s									
Omega 3s	NR	NR	NR	NR	NR	NR	NR	NR	NR
EPA only									
EPA	NR	NR	NR	NR	NR	NR	NR	NR	NR
PCSK9 Inhibitors									
PCSK9 Inhibitors	NR	NR	NR	NR	NR	NR	NR	NR	NR
Statins									
Statins	Mixed	Kim, 2020	12	NR	NR	RR 1.11	0.87-1.41	Random	40.1%
Statins	Primary	Taylor, 2013	3	27238	NR	RR 0.63	0.18-2.23	Random	68%
Statins	Primary	Yebyo, 2019	6	NR	NR	RR 0.79	0.53-1.18	Random	0%
STROKE (ALL)									
Bile acid sequetrants (BAS)									
BAS	Primary	RCT: Lipid Research Clinics Program, 1984	1	3086	386	RR 1.21	0.60-2.45	NA	NA
BAS	Mixed	RCT: Watts, 1992	1	53	170	RR 1.04	0.02-50.43	NA	NA
Ezetimibe									
Ezetimibe	Mixed	Toyota, 2019	3	20585	NR	OR 0.86	0.74-1.00	Random	0%
Fibrates									
Fibrates	Mixed	Keene, 2014	13	43188	261	OR 1.01	0.90-1.13	Random	1%
Fibrates	Secondary	Wang, 2015	6	11719	282	RR 1.03	0.91-1.16	Fixed	11%
Niacin									
Niacin	Mixed	D'Andrea, 2019	11	34875	NR	OR 0.95	0.85-1.06	Fixed	35%

Niacin	Mixed	Garg, 2017	5	30428	NR	RR 0.89	0.72-1.10	Random	34%
Niacin	Mixed	Jenkins, 2021	4	30196	NR	RR 1.01	0.90-1.14	Random	37%
Niacin	Mixed	Riaz, 2019	5	34104	NR	RR 0.92	0.70-1.21	Random	NR
Niacin	Mixed	Schandelmaier, 2017	7	33661	NR	RR 0.95	0.74-1.22	Random	42%
Omega-3s									
Omega-3s	NR	NR	NR	NR	NR	NR	NR	NR	NR
EPA only									
EPA	NR	NR	NR	NR	NR	NR	NR	NR	NR
PSCK9 Inhibitors									
PCSK9 Inhibitors	Mixed	AlTurki, 2019	12	NR	NR	OR 0.75	0.65-0.85	Random	0%
PCSK9 Inhibitors	Mixed	Bai, 2018	7	36476	NR	RR 0.81	0.68-0.96	Fixed	0%
PCSK9 Inhibitors	Mixed	Bajaj, 2018	11	37613	NR	RR 0.77	0.64-0.93	Random	NR
PCSK9 Inhibitors	Mixed	Casula, 2019	7	50792	NR	OR 0.77	0.67-0.89	Random	NR
PCSK9 Inhibitors	Mixed	Chaiyasothi, 2019	11	87605	NR	RR 0.74	0.65-0.85	Random	0%
PCSK9 Inhibitors	Mixed	Cordero, 2020	6	80764	NR	RR 0.77	0.67-0.88	NR	10%
PCSK9 Inhibitors	Mixed	Dicembrini, 2019	34	34793	NR	OR 0.80	0.67-0.96	Random	0%
PCSK9 Inhibitors	Mixed	Du, 2019	35	94408	12-146	RR 0.75	0.65-0.85	Random	0%
PCSK9 Inhibitors	Mixed	Ghadban, 2017	6	62776	NR	RR 0.74	0.64-0.87	Random	0%
PCSK9 Inhibitors	Mixed	Guedeney, 2019	NR	60328	8-208	RR 0.78	0.67-0.89	Random	0%

PCSK9 Inhibitors	Mixed	Karatasakis, 2017	23	42748	NR	OR 0.80	0.67-0.96	Random	0%
PCSK9 Inhibitors	Mixed	Khan, 2022	3	48829	NR	RR 0.75	0.64-0.88	Random	NR
PCSK9 Inhibitors	Mixed	Khan, 2019	9	82417	NR	RR 0.75	0.66-0.86	Random	NR
PCSK9 Inhibitors	Mixed	Ma, 2021	12	83406	NR	RR 0.75	0.66-0.86	Fixed	0%
PCSK9 Inhibitors	Mixed	Mu, 2020	7	NR	NR	RR 0.77	0.67-0.89	Random	NR
PCSK9 Inhibitors	Mixed	Qin, 2021	6	55095	NR	RR 0.77	0.67-0.88	Fixed	0%
PCSK9 Inhibitors	Mixed	Toyota, 2019	6	54461	NR	OR 0.77	0.67-0.89	Random	0%
PCSK9 Inhibitors	Mixed	Turgeon, 2018	17	57355	NR	RR 0.78	0.67-0.90	Fixed	0%
PCSK9 Inhibitors	Mixed	Zhao, 2020	4	47001	NR	RR 0.75	0.64-0.87	Fixed	0%
PCSK9 Inhibitors	Mixed	Zhu, 2019	9	63745	NR	RR 0.76	0.65-0.89	Random	0%
Statins									
Statins	Mixed	Byrne, 2022	18	131086	NR	RR 0.86	0.78-0.95	Random	49%
Statins	Primary	Cai, 2021	17	78473	244	OR 0.80	0.72-0.89	Fixed	20%
Statins	Mixed	Milionis, 2020	4	35622	104-276	RR 0.70	0.60-0.82	Fixed	20%
Statins	Mixed	Ponce, 2019	12	39918	168-288	RR 0.80	0.70-0.91	Random	41.4%
Statins	Primary	Singh, 2020	9	57754	NR	RR 0.78	0.63-0.96	Random	47%
Statins	Primary	Taylor, 2013	10	40295	NR	RR 0.78	0.68-0.89	Fixed	26%

BAS: Bile Acid Sequestrants; *Calculated by PEER team at https://www.medcalc.org/calc/relative_risk.php; RCT: Randomized Controlled Trial; n: Total sample size in meta-analysis; OR: Odds Ratio; RR: Risk Ratio; Cl: Confidence Interval; I^2: indicates the level of heterogeneity; NR= Not Reported