

Statin: Systematic Review with SAIMSARA.

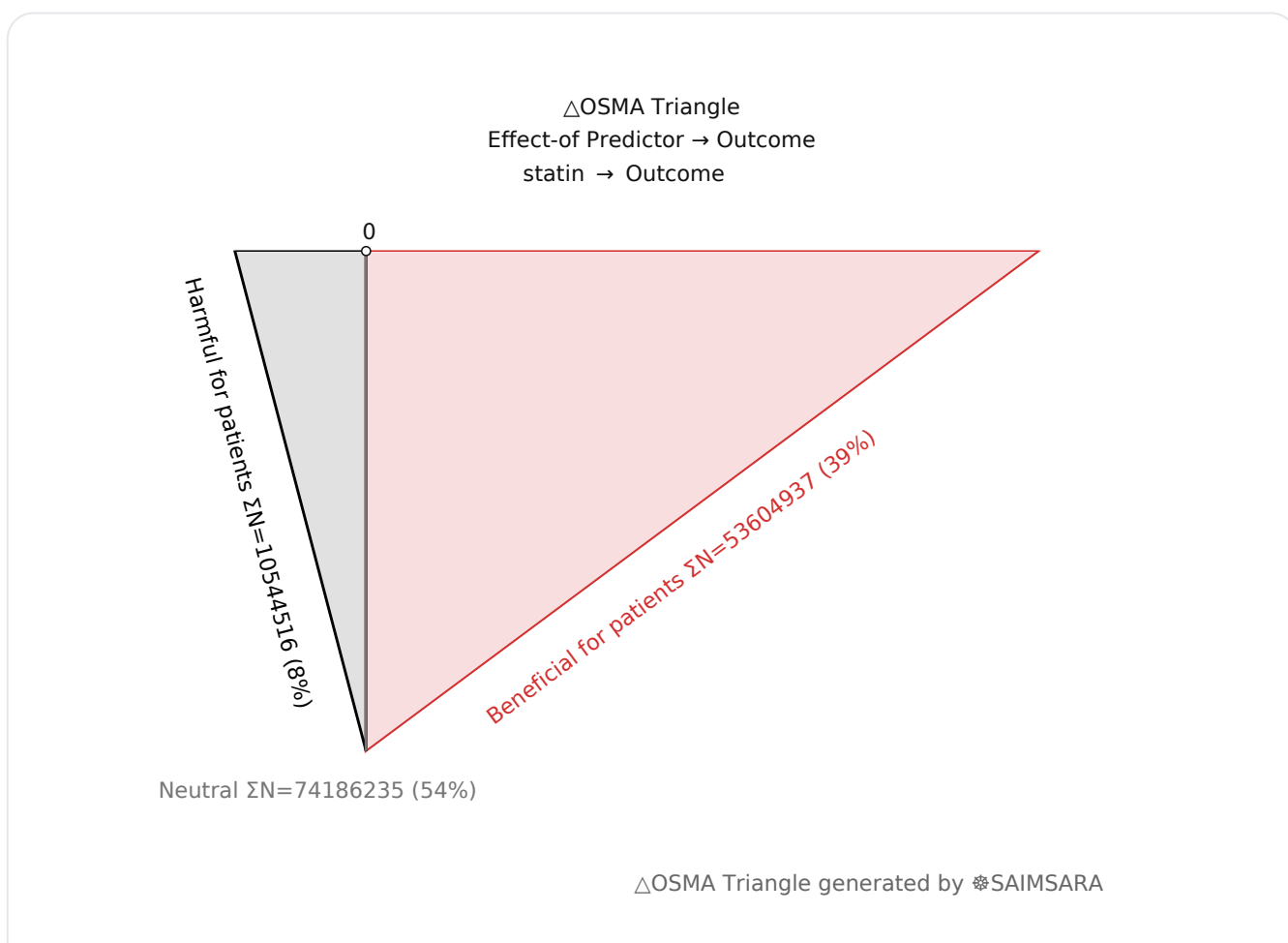
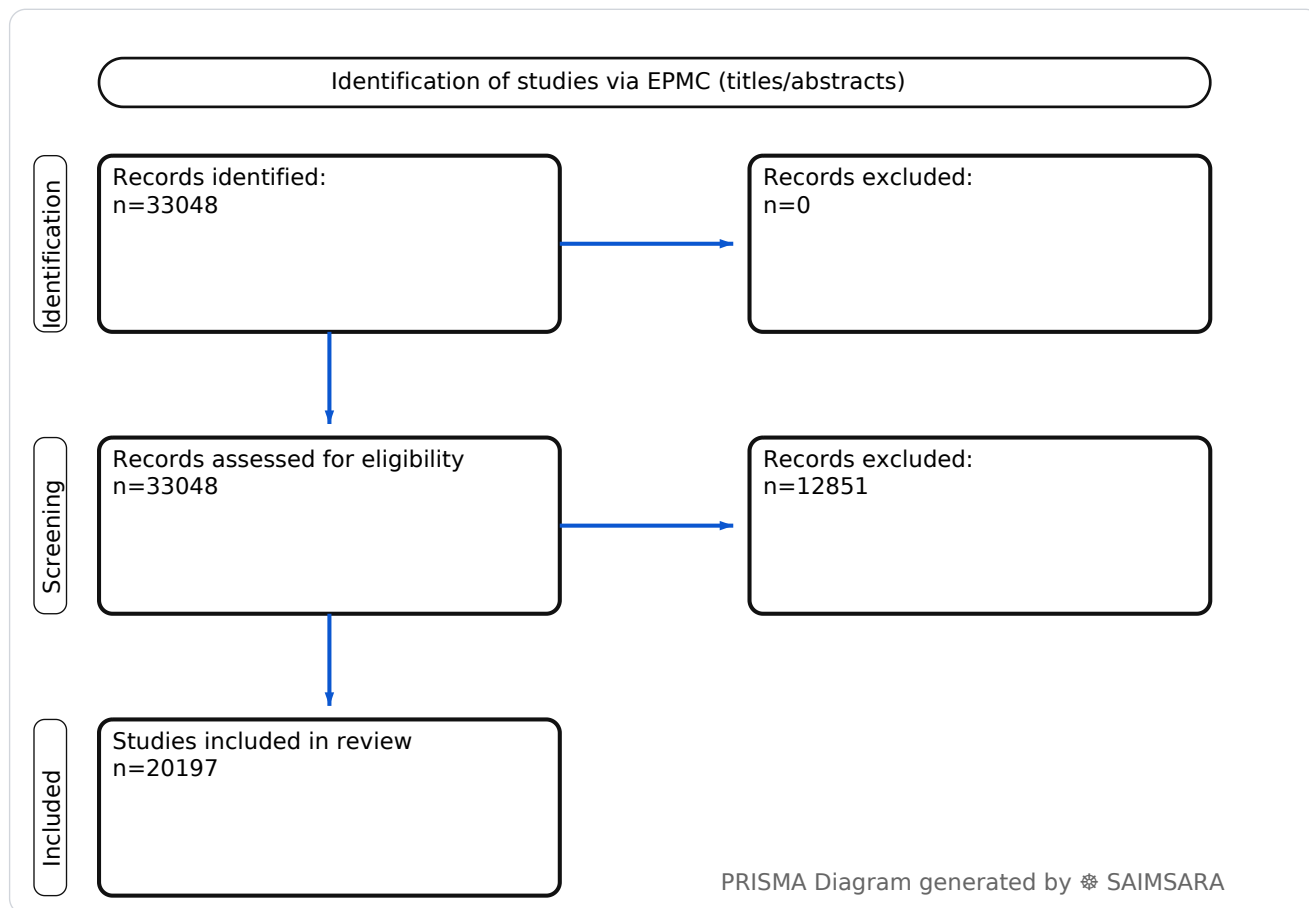
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Abstract: The aim of this paper is to systematically review and synthesize current scientific literature on statin therapy, focusing on its broad clinical impact, identified benefits, adverse effects, and future research directions. The review utilises 20197 studies with 138335688 total participants (naïve ΣN). This systematic review highlights the multifaceted impact of statin therapy, primarily driven by its potent LDL-C lowering capabilities, with a median reduction of 45.25%. Beyond cardiovascular protection, statins demonstrate promising effects in various cancers, neurological conditions, and inflammatory diseases, while also presenting challenges related to adherence and adverse effects. A notable limitation is the heterogeneity of study designs, which often precludes direct comparisons. Moving forward, a key research implication is the need for rigorous RCTs and real-world studies to optimize combination therapies and implement personalized, pharmacogenomic-guided prescribing strategies to maximize patient benefit and address existing gaps in care.

Keywords: Statin therapy; Lipid-lowering agents; Cardiovascular disease prevention; Statin-associated myopathy; Immune-mediated necrotizing myopathy; LDL cholesterol reduction; Cancer treatment; Metabolic dysfunction-associated steatotic liver disease; Neurodegenerative diseases; Statin adherence

Review Stats

- Generated: 2026-02-17 02:31:12 CET
- Plan: Pro (expanded craft tokens; source: Europe PMC)
- Source: Europe PMC
- Scope: Titles/Abstracts (tiab)
- Keyword Gate: Fuzzy ($\geq 60\%$ of required terms, minimum 2 terms matched in title/abstract)
- Total Abstracts/Papers: 33048
- Downloaded Abstracts/Papers: 33048
- Included original Abstracts/Papers: 20197
- Total study participants (naïve ΣN): 138335688



Outcome-Sentiment Meta-Analysis (OSMA): (LLM-only)

Frame: Effect-of Predictor → Outcome • *Source:* Europe PMC

Outcome: Outcome Typical timepoints: peri/post-op, 1-y. Reported metrics: %, CI, p.

Common endpoints: Common endpoints: mortality, complications, survival.

Predictor: statin — statin (lipid-lowering). Concentrations seen: 95%. Doses/units seen: 30 ml, 59 ml, 140 mg, 150 mg, 12.96 mg, 190 mg.... Routes seen: oral, topical, iv, intravenous....

Typical comparator: placebo, men, control, initiating statins after....

- **1) Beneficial for patients** — Outcome with statin — [8], [12], [14], [15], [16], [17], [20], [21], [25], [26], [29], [30], [38], [46], [48], [49], [55], [64], [65], [66], [67], [72], [77], [79], [82], [88], [91], [95], [98], [104], [113], [114], [127], [128], [133], [134], [136], [138], [139], [140], [142], [146], [147], [148], [150], [153], [154], [157], [158], [166], [167], [169], [170], [171], [173], [174], [180], [214], [218], [223], [225], [228], [235], [241], [251], [254], [255], [256], [257], [259], [263], [265], [266], [267], [271], [275], [284], [285], [289], [294], [297], [301], [303], [307], [308], [313], [319], [320], [341], [342], [344], [345], [348], [349], [351], [352], [353], [356], [357], [358], [367], [368], [377], [378], [380], [381], [383], [384], [385], [387], [390], [394], [396], [402], [405], [408], [414], [418], [426], [432], [433], [434], [435], [436], [437], [438], [442], [447], [448], [451], [460], [465], [466], [471], [473], [475], [479], [486], [500], [501], [508], [512], [513], [520], [521], [523], [524], [525], [526], [530], [532], [534], [541], [543], [544], [548], [550], [554], [557], [561], [564], [565], [569], [572], [576], [581], [582], [584], [591], [593], [595], [596], [597], [598], [599], [600], [608], [610], [611], [622], [624], [625], [626], [627], [631], [633], [636], [637], [639], [641], [643], [647], [653], [654], [655], [656], [657], [658], [659], [661], [663], [665], [667], [668], [672], [675], [683], [688], [691], [700], [703], [705], [711], [716], [720], [722], [726], [728], [729], [732], [734], [738], [742], [743], [747], [748], [756], [760], [762], [765], [767], [768], [769], [771], [773], [776], [777], [778], [779], [785], [789], [790], [796], [797], [803], [805], [807], [810], [811], [820], [827], [829], [834], [837], [838], [841], [842], [844], [851], [852], [857], [858], [860], [861], [862], [865], [867], [871], [875], [876], [879], [882], [883], [886], [889], [901], [903], [905], [906], [907], [916], [917], [921], [923], [928], [929], [930], [931], [939], [940], [941], [948], [950], [954], [960], [961], [967], [970], [973], [974], [977], [980], [982], [985], [986], [987], [989], [992], [1000], [1005], [1009], [1023], [1027], [1029], [1031], [1033], [1034], [1035], [1038], [1039], [1040], [1043], [1046], [1047], [1049], [1052], [1053], [1055], [1057], [1059], [1066], [1069], [1071], [1072], [1076], [1088], [1089], [1092], [1095], [1102], [1107], [1108], [1110], [1116], [1123], [1124], [1130], [1131], [1132], [1133], [1137], [1143], [1146], [1148], [1151], [1153], [1163], [1165], [1168], [1173], [1180], [1183], [1185], [1186],

[1187], [1190], [1193], [1195], [1198], [1205], [1210], [1213], [1214], [1220], [1232], [1235], [1241], [1242], [1243], [1246], [1247], [1251], [1252], [1256], [1257], [1258], [1259], [1260], [1261], [1262], [1264], [1271], [1276], [1277], [1281], [1284], [1287], [1288], [1289], [1292], [1303], [1306], [1307], [1308], [1309], [1310], [1313], [1315], [1319], [1320], [1353], [1358], [1360], [1362], [1367], [1372], [1376], [1382], [1384], [1386], [1387], [1388], [1401], [1404], [1421], [1423], [1430], [1432], [1440], [1441], [1443], [1444], [1446], [1447], [1449], [1452], [1453], [1459], [1461], [1462], [1466], [1467], [1468], [1470], [1475], [1479], [1480], [1485], [1488], [1493], [1497], [1502], [1512], [1515], [1522], [1523], [1524], [1525], [1527], [1528], [1532], [1535], [1536], [1537], [1541], [1543], [1547], [1553], [1554], [1559], [1560], [1564], [1565], [1568], [1569], [1571], [1572], [1574], [1581], [1586], [1587], [1589], [1591], [1593], [1595], [1598], [1599], [1602], [1604], [1605], [1609], [1613], [1615], [1620], [1622], [1623], [1626], [1628], [1630], [1631], [1632], [1634], [1637], [1638], [1639], [1642], [1645], [1646], [1648], [1649], [1651], [1665], [1667], [1673], [1677], [1678], [1680], [1681], [1682], [1683], [1685], [1687], [1696], [1704], [1706], [1707], [1709], [1712], [1715], [1722], [1734], [1742], [1761], [1763], [1766], [1767], [1768], [1769], [1775], [1779], [1783], [1790], [1794], [1798], [1801], [1803], [1804], [1805], [1807], [1808], [1809], [1812], [1813], [1816], [1817], [1818], [1819], [1820], [1822], [1823], [1825], [1829], [1836], [1837], [1838], [1839], [1844], [1846], [1847], [1852], [1853], [1854], [1858], [1859], [1860], [1861], [1867], [1868], [1873], [1874], [1879], [1880], [1881], [1889], [1896], [1897], [1898], [1910], [1912], [1914], [1915], [1919], [1920], [1923], [1929], [1933], [1934], [1936], [1937], [1945], [1946], [1947], [1952], [1954], [1955], [1959], [1965], [1967], [1970], [1971], [1984], [1988], [1989], [1994], [1995], [2000], [2001], [2003], [2005], [2006], [2009], [2011], [2014], [2017], [2018], [2019], [2021], [2025], [2026], [2028], [2030], [2036], [2037], [2039], [2041], [2047], [2054], [2055], [2057], [2064], [2065], [2067], [2070], [2071], [2072], [2075], [2077], [2078], [2081], [2085], [2088], [2089], [2092], [2094], [2095], [2096], [2097], [2098], [2100], [2101], [2102], [2103], [2105], [2106], [2115], [2120], [2121], [2128], [2133], [2135], [2140], [2141], [2143], [2147], [2150], [2151], [2152], [2153], [2154], [2161], [2163], [2167], [2169], [2174], [2175], [2181], [2188], [2200], [2203], [2206], [2214], [2222], [2223], [2229], [2231], [2233], [2234], [2236], [2237], [2240], [2246], [2247], [2249], [2250], [2251], [2257], [2259], [2265], [2267], [2268], [2269], [2271], [2273], [2281], [2286], [2299], [2300], [2302], [2307], [2311], [2313], [2317], [2319], [2321], [2326], [2331], [2338], [2341], [2344], [2345], [2346], [2348], [2349], [2351], [2355], [2358], [2364], [2366], [2368], [2369], [2372], [2375], [2377], [2380], [2383], [2387], [2389], [2395], [2399], [2401], [2408], [2411], [2412], [2414], [2415], [2416], [2418], [2425], [2436], [2439], [2443], [2446], [2448], [2452], [2454], [2455], [2456], [2457], [2466], [2469], [2477], [2481], [2482], [2484], [2485], [2492], [2494], [2495], [2496], [2501], [2510], [2511],

[2514], [2515], [2516], [2521], [2523], [2524], [2526], [2527], [2528], [2531], [2532], [2533], [2534], [2536], [2540], [2541], [2543], [2547], [2550], [2552], [2559], [2562], [2563], [2566], [2567], [2569], [2571], [2574], [2578], [2582], [2583], [2584], [2585], [2586], [2587], [2588], [2589], [2590], [2596], [2603], [2604], [2606], [2610], [2613], [2618], [2621], [2625], [2627], [2628], [2629], [2630], [2631], [2635], [2637], [2644], [2646], [2654], [2660], [2667], [2678], [2685], [2694], [2696], [2710], [2714], [2736], [2737], [2738], [2741], [2748], [2757], [2762], [2766], [2769], [2771], [2772], [2775], [2777], [2779], [2780], [2794], [2795], [2798], [2802], [2806], [2807], [2808], [2811], [2827], [2832], [2841], [2842], [2845], [2851], [2852], [2854], [2855], [2857], [2859], [2863], [2869], [2874], [2877], [2881], [2886], [2901], [2909], [2916], [2918], [2922], [2935], [2941], [2951], [2955], [2960], [2969], [2970], [2977], [2979], [2982], [2983], [2984], [2985], [2987], [2999], [3003], [3007], [3011], [3021], [3022], [3024], [3029], [3030], [3034], [3045], [3052], [3056], [3057], [3060], [3063], [3068], [3076], [3080], [3084], [3087], [3091], [3094], [3101], [3103], [3115], [3119], [3151], [3152], [3154], [3155], [3157], [3158], [3160], [3163], [3165], [3169], [3172], [3173], [3174], [3216], [3223], [3234], [3240], [3242], [3243], [3246], [3247], [3261], [3273], [3277], [3280], [3282], [3284], [3285], [3291], [3292], [3295], [3305], [3306], [3310], [3312], [3321], [3331], [3335], [3340], [3341], [3344], [3350], [3360], [3362], [3364], [3365], [3367], [3368], [3369], [3371], [3375], [3388], [3389], [3391], [3397], [3401], [3412], [3423], [3424], [3428], [3432], [3438], [3439], [3446], [3451], [3452], [3454], [3456], [3460], [3470], [3474], [3476], [3477], [3482], [3484], [3492], [3501], [3513], [3521], [3533], [3542], [3547], [3548], [3549], [3551], [3552], [3553], [3554], [3556], [3559], [3562], [3564], [3568], [3571], [3577], [3584], [3585], [3589], [3590], [3592], [3597], [3600], [3602], [3606], [3608], [3609], [3610], [3612], [3613], [3623], [3640], [3644], [3646], [3654], [3659], [3666], [3668], [3671], [3685], [3688], [3693], [3696], [3697], [3698], [3701], [3710], [3712], [3714], [3715], [3721], [3725], [3727], [3728], [3730], [3732], [3733], [3736], [3737], [3739], [3740], [3746], [3747], [3749], [3774], [3782], [3788], [3791], [3798], [3799], [3802], [3804], [3805], [3808], [3811], [3812], [3819], [3822], [3823], [3828], [3836], [3841], [3843], [3850], [3852], [3854], [3856], [3859], [3865], [3869], [3871], [3872], [3873], [3877], [3878], [3882], [3883], [3884], [3891], [3892], [3903], [3906], [3914], [3915], [3916], [3918], [3920], [3924], [3927], [3928], [3930], [3932], [3936], [3940], [3951], [3956], [3957], [3964], [3967], [3971], [3974], [3980], [3981], [3984], [3990], [3992], [3993], [4006], [4009], [4010], [4011], [4013], [4016], [4017], [4020], [4021], [4024], [4025], [4026], [4027], [4029], [4035], [4044], [4048], [4061], [4067], [4068], [4071], [4072], [4076], [4078], [4082], [4083], [4086], [4090], [4095], [4098], [4102], [4107], [4111], [4130], [4134], [4142], [4148], [4149], [4150], [4152], [4153], [4161], [4162], [4163], [4166], [4170], [4173], [4178], [4188], [4194], [4201], [4202], [4205], [4207], [4210], [4211], [4215], [4216], [4217], [4220], [4229],

[4232], [4235], [4236], [4242], [4246], [4251], [4254], [4260], [4261], [4263], [4264], [4266], [4268], [4270], [4276], [4281], [4288], [4289], [4295], [4298], [4301], [4305], [4307], [4310], [4315], [4317], [4321], [4325], [4326], [4332], [4333], [4336], [4338], [4340], [4341], [4342], [4343], [4346], [4350], [4356], [4357], [4358], [4360], [4361], [4362], [4378], [4380], [4382], [4385], [4387], [4393], [4406], [4417], [4420], [4424], [4425], [4429], [4432], [4433], [4434], [4440], [4441], [4444], [4447], [4448], [4449], [4451], [4453], [4454], [4461], [4465], [4466], [4470], [4471], [4474], [4475], [4476], [4477], [4478], [4479], [4480], [4481], [4487], [4488], [4491], [4493], [4499], [4505], [4507], [4510], [4512], [4519], [4520], [4523], [4526], [4529], [4538], [4539], [4541], [4545], [4549], [4550], [4553], [4555], [4556], [4557], [4560], [4564], [4565], [4570], [4571], [4572], [4575], [4576], [4577], [4578], [4579], [4581], [4585], [4586], [4587], [4591], [4594], [4595], [4596], [4598], [4599], [4600], [4604], [4609], [4611], [4612], [4613], [4617], [4619], [4621], [4624], [4626], [4630], [4631], [4632], [4633], [4634], [4639], [4640], [4642], [4644], [4645], [4649], [4651], [4652], [4653], [4654], [4655], [4658], [4661], [4665], [4676], [4680], [4682], [4688], [4691], [4697], [4701], [4705], [4711], [4717], [4721], [4722], [4723], [4725], [4727], [4728], [4729], [4732], [4734], [4744], [4745], [4752], [4753], [4755], [4760], [4764], [4766], [4767], [4772], [4776], [4782], [4785], [4792], [4793], [4794], [4795], [4796], [4797], [4798], [4801], [4802], [4803], [4814], [4820], [4821], [4825], [4827], [4830], [4831], [4837], [4838], [4842], [4848], [4850], [4851], [4852], [4855], [4861], [4862], [4867], [4870], [4874], [4875], [4876], [4881], [4888], [4893], [4895], [4908], [4916], [4930], [4932], [4934], [4938], [4939], [4952], [4956], [4958], [4961], [4962], [4966], [4967], [4968], [4969], [4976], [4978], [4981], [4982], [4987], [5006], [5010], [5011], [5012], [5020], [5023], [5026], [5027], [5029], [5030], [5035], [5036], [5039], [5041], [5050], [5052], [5058], [5059], [5071], [5075], [5079], [5080], [5086], [5087], [5091], [5092], [5097], [5098], [5103], [5115], [5116], [5118], [5121], [5123], [5128], [5129], [5132], [5136], [5143], [5145], [5152], [5153], [5157], [5161], [5166], [5172], [5173], [5174], [5177], [5179], [5180], [5187], [5191], [5194], [5195], [5196], [5197], [5198], [5201], [5203], [5205], [5223], [5232], [5233], [5235], [5236], [5237], [5238], [5243], [5247], [5249], [5251], [5253], [5254], [5255], [5256], [5257], [5258], [5268], [5269], [5270], [5273], [5281], [5284], [5286], [5287], [5288], [5289], [5290], [5295], [5311], [5312], [5315], [5317], [5325], [5332], [5337], [5340], [5345], [5346], [5347], [5348], [5349], [5357], [5358], [5359], [5372], [5379], [5386], [5388], [5389], [5390], [5394], [5405], [5410], [5411], [5412], [5416], [5422], [5430], [5435], [5436], [5437], [5438], [5440], [5441], [5445], [5446], [5447], [5449], [5453], [5457], [5460], [5462], [5464], [5467], [5469], [5471], [5476], [5478], [5479], [5482], [5491], [5493], [5501], [5505], [5508], [5509], [5511], [5512], [5515], [5519], [5523], [5529], [5531], [5532], [5547], [5549], [5550], [5553], [5558], [5559], [5561], [5572], [5577], [5584], [5585], [5594], [5616], [5625], [5626], [5627],

[5628], [5629], [5630], [5632], [5639], [5643], [5649], [5652], [5658], [5661], [5664], [5665], [5670], [5671], [5672], [5678], [5679], [5683], [5685], [5690], [5691], [5700], [5703], [5705], [5708], [5712], [5728], [5731], [5735], [5736], [5738], [5745], [5747], [5753], [5766], [5769], [5772], [5774], [5776], [5789], [5791], [5792], [5793], [5794], [5801], [5802], [5803], [5804], [5807], [5810], [5811], [5812], [5820], [5821], [5825], [5827], [5834], [5835], [5838], [5851], [5858], [5859], [5863], [5864], [5865], [5867], [5871], [5873], [5882], [5886], [5888], [5889], [5902], [5905], [5912], [5914], [5915], [5916], [5920], [5922], [5925], [5936], [5938], [5943], [5945], [5947], [5952], [5954], [5956], [5961], [5962], [5963], [5964], [5976], [5978], [5979], [5982], [5984], [5996], [6000], [6006], [6013], [6014], [6016], [6019], [6022], [6023], [6024], [6029], [6030], [6031], [6034], [6040], [6044], [6053], [6056], [6061], [6062], [6067], [6073], [6083], [6086], [6090], [6091], [6092], [6094], [6096], [6099], [6103], [6110], [6113], [6116], [6117], [6118], [6121], [6124], [6136], [6137], [6139], [6143], [6144], [6150], [6154], [6175], [6180], [6182], [6184], [6188], [6189], [6191], [6192], [6198], [6201], [6202], [6203], [6206], [6209], [6215], [6217], [6219], [6241], [6244], [6252], [6255], [6256], [6257], [6259], [6263], [6266], [6267], [6269], [6274], [6279], [6281], [6292], [6293], [6299], [6306], [6308], [6310], [6312], [6315], [6319], [6320], [6323], [6333], [6335], [6337], [6340], [6348], [6353], [6358], [6363], [6364], [6367], [6368], [6369], [6371], [6375], [6382], [6384], [6386], [6390], [6392], [6403], [6411], [6413], [6415], [6421], [6424], [6427], [6429], [6434], [6436], [6438], [6441], [6452], [6453], [6454], [6456], [6460], [6465], [6469], [6472], [6474], [6475], [6482], [6486], [6492], [6493], [6495], [6496], [6497], [6499], [6504], [6505], [6510], [6517], [6521], [6528], [6531], [6539], [6543], [6545], [6546], [6548], [6549], [6552], [6555], [6557], [6569], [6573], [6574], [6578], [6587], [6589], [6591], [6595], [6596], [6597], [6600], [6601], [6602], [6614], [6620], [6630], [6639], [6641], [6642], [6644], [6645], [6647], [6648], [6649], [6651], [6652], [6653], [6660], [6665], [6672], [6674], [6675], [6676], [6685], [6691], [6693], [6695], [6697], [6698], [6724], [6725], [6734], [6739], [6742], [6743], [6744], [6750], [6755], [6764], [6765], [6766], [6769], [6774], [6775], [6783], [6786], [6791], [6801], [6808], [6810], [6816], [6817], [6826], [6831], [6832], [6833], [6834], [6837], [6840], [6841], [6853], [6855], [6863], [6867], [6871], [6872], [6873], [6883], [6885], [6901], [6903], [6906], [6909], [6911], [6913], [6922], [6923], [6924], [6933], [6940], [6943], [6945], [6947], [6948], [6951], [6970], [6977], [6980], [6981], [6983], [6988], [6992], [6993], [6996], [7000], [7003], [7005], [7012], [7014], [7017], [7020], [7024], [7028], [7029], [7031], [7037], [7042], [7045], [7046], [7055], [7058], [7065], [7067], [7069], [7072], [7074], [7076], [7079], [7080], [7081], [7087], [7090], [7092], [7094], [7095], [7105], [7106], [7107], [7109], [7112], [7114], [7120], [7122], [7124], [7125], [7128], [7129], [7131], [7133], [7135], [7139], [7144], [7151], [7153], [7154], [7155], [7156], [7160], [7163], [7168], [7169], [7170], [7171], [7172], [7173], [7179], [7180], [7181],

[7185], [7186], [7195], [7204], [7206], [7208], [7209], [7211], [7212], [7214], [7219], [7222], [7226], [7229], [7232], [7235], [7237], [7239], [7246], [7248], [7250], [7252], [7254], [7257], [7258], [7263], [7265], [7266], [7267], [7269], [7270], [7272], [7273], [7274], [7278], [7279], [7281], [7283], [7288], [7292], [7293], [7294], [7297], [7303], [7305], [7307], [7309], [7313], [7319], [7320], [7322], [7323], [7327], [7328], [7335], [7336], [7337], [7340], [7342], [7343], [7348], [7351], [7352], [7354], [7363], [7365], [7366], [7375], [7376], [7378], [7379], [7382], [7385], [7386], [7388], [7392], [7396], [7400], [7404], [7409], [7416], [7417], [7418], [7426], [7430], [7433], [7434], [7436], [7439], [7441], [7442], [7446], [7451], [7455], [7459], [7460], [7461], [7464], [7466], [7467], [7470], [7471], [7478], [7481], [7482], [7485], [7489], [7492], [7495], [7499], [7501], [7502], [7505], [7509], [7512], [7519], [7527], [7530], [7532], [7536], [7538], [7549], [7552], [7556], [7560], [7574], [7576], [7577], [7581], [7585], [7591], [7596], [7601], [7602], [7603], [7604], [7606], [7612], [7613], [7615], [7621], [7625], [7634], [7639], [7645], [7648], [7651], [7652], [7654], [7668], [7675], [7677], [7680], [7684], [7686], [7691], [7693], [7695], [7699], [7706], [7708], [7709], [7710], [7713], [7715], [7720], [7724], [7729], [7735], [7740], [7741], [7742], [7750], [7752], [7757], [7758], [7762], [7772], [7773], [7781], [7786], [7789], [7797], [7801], [7805], [7806], [7810], [7812], [7815], [7816], [7817], [7818], [7820], [7837], [7839], [7841], [7842], [7848], [7852], [7853], [7855], [7858], [7861], [7864], [7865], [7868], [7875], [7876], [7877], [7878], [7879], [7880], [7890], [7892], [7893], [7895], [7896], [7898], [7904], [7908], [7915], [7921], [7927], [7937], [7950], [7952], [7955], [7956], [7959], [7962], [7965], [7967], [7971], [7973], [7978], [7979], [7980], [7981], [7985], [7987], [7988], [7989], [7992], [7993], [7998], [8001], [8002], [8003], [8004], [8011], [8016], [8020], [8024], [8026], [8027], [8028], [8034], [8035], [8036], [8038], [8039], [8040], [8041], [8048], [8050], [8059], [8063], [8071], [8073], [8074], [8078], [8085], [8091], [8092], [8094], [8099], [8103], [8106], [8110], [8111], [8113], [8118], [8136], [8137], [8138], [8139], [8143], [8155], [8159], [8160], [8161], [8162], [8164], [8167], [8169], [8174], [8176], [8177], [8179], [8182], [8186], [8187], [8188], [8191], [8192], [8193], [8196], [8199], [8204], [8206], [8215], [8218], [8219], [8220], [8222], [8226], [8227], [8228], [8233], [8235], [8237], [8238], [8239], [8240], [8243], [8247], [8254], [8255], [8256], [8259], [8262], [8263], [8266], [8270], [8277], [8281], [8282], [8291], [8297], [8308], [8310], [8312], [8316], [8317], [8325], [8338], [8339], [8341], [8342], [8343], [8352], [8355], [8356], [8360], [8362], [8363], [8368], [8373], [8377], [8379], [8383], [8389], [8390], [8393], [8398], [8399], [8400], [8403], [8405], [8406], [8407], [8418], [8424], [8433], [8436], [8438], [8441], [8446], [8453], [8454], [8455], [8457], [8463], [8480], [8481], [8482], [8483], [8484], [8487], [8493], [8494], [8495], [8499], [8500], [8504], [8510], [8516], [8521], [8523], [8528], [8537], [8538], [8539], [8543], [8544], [8545], [8549], [8554], [8559], [8562], [8569], [8573], [8575], [8585], [8586], [8587], [8588], [8593],

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[18330], [18331], [18336], [18342], [18343], [18344], [18348], [18349], [18350], [18351], [18352], [18353], [18354], [18355], [18362], [18369], [18375], [18378], [18380], [18381], [18388], [18389], [18392], [18394], [18397], [18400], [18401], [18403], [18407], [18408], [18416], [18422], [18423], [18429], [18431], [18439], [18451], [18458], [18459], [18464], [18473], [18476], [18478], [18482], [18487], [18497], [18498], [18499], [18502], [18505], [18506], [18510], [18511], [18513], [18516], [18520], [18528], [18531], [18532], [18541], [18542], [18545], [18547], [18548], [18549], [18552], [18553], [18561], [18563], [18568], [18569], [18578], [18587], [18591], [18593], [18603], [18604], [18606], [18610], [18611], [18613], [18614], [18615], [18619], [18620], [18621], [18623], [18625], [18627], [18628], [18629], [18630], [18661], [18662], [18663], [18665], [18678], [18679], [18692], [18693], [18694], [18695], [18696], [18697], [18701], [18706], [18707], [18710], [18711], [18712], [18713], [18714], [18716], [18717], [18725], [18727], [18730], [18734], [18735], [18743], [18746], [18766], [18768], [18777], [18783], [18786], [18792], [18795], [18797], [18798], [18804], [18810], [18811], [18812], [18815], [18816], [18818], [18819], [18823], [18828], [18829], [18830], [18832], [18833], [18835], [18836], [18840], [18842], [18847], [18850], [18851], [18856], [18859], [18867], [18870], [18871], [18873], [18875], [18882], [18883], [18890], [18893], [18896], [18903], [18907], [18914], [18920], [18921], [18923], [18925], [18931], [18936], [18937], [18938], [18940], [18943], [18946], [18951], [18955], [18959], [18961], [18970], [18976], [18984], [18989], [18991], [18995], [18998], [18999], [19003], [19009], [19019], [19021], [19022], [19030], [19031], [19035], [19037], [19039], [19040], [19046], [19048], [19051], [19058], [19061], [19067], [19072], [19078], [19085], [19106], [19108], [19116], [19119], [19123], [19124], [19132], [19133], [19134], [19135], [19136], [19138], [19139], [19142], [19143], [19144], [19145], [19147], [19149], [19157], [19158], [19161], [19162], [19164], [19166], [19172], [19189], [19195], [19197], [19199], [19202], [19209], [19211], [19215], [19220], [19224], [19225], [19226], [19232], [19245], [19246], [19247], [19258], [19260], [19261], [19262], [19263], [19268], [19272], [19273], [19276], [19279], [19285], [19286], [19294], [19297], [19301], [19305], [19306], [19308], [19310], [19312], [19316], [19323], [19338], [19339], [19342], [19348], [19352], [19356], [19357], [19362], [19366], [19368], [19371], [19376], [19380], [19390], [19392], [19398], [19405], [19413], [19416], [19417], [19428], [19430], [19431], [19439], [19440], [19442], [19443], [19455], [19460], [19479], [19484], [19487], [19488], [19491], [19493], [19494], [19497], [19504], [19505], [19517], [19523], [19527], [19530], [19539], [19542], [19549], [19564], [19565], [19570], [19574], [19583], [19585], [19592], [19595], [19597], [19604], [19609], [19610], [19613], [19615], [19619], [19620], [19624], [19633], [19636], [19660], [19663], [19672], [19676],

[19684], [19685], [19689], [19695], [19698], [19699], [19704], [19706], [19711], [19714], [19716], [19718], [19719], [19723], [19725], [19727], [19729], [19732], [19733], [19739], [19740], [19741], [19742], [19743], [19746], [19757], [19759], [19762], [19763], [19765], [19767], [19771], [19775], [19777], [19780], [19788], [19792], [19794], [19795], [19796], [19798], [19799], [19800], [19803], [19814], [19815], [19820], [19822], [19826], [19828], [19831], [19832], [19834], [19840], [19850], [19857], [19859], [19891], [19895], [19900], [19919], [19921], [19923], [19925], [19928], [19934], [19938], [19940], [19941], [19945], [19946], [19947], [19948], [19951], [19953], [19956], [19957], [19958], [19960], [19961], [19966], [19968], [19972], [19974], [19976], [19978], [19979], [19980], [19981], [19987], [20004], [20006], [20008], [20011], [20013], [20014], [20018], [20020], [20024], [20026], [20027], [20029], [20035], [20036], [20037], [20038], [20040], [20049], [20050], [20053], [20069], [20081], [20090], [20091], [20092], [20093], [20097], [20110], [20111], [20113], [20121], [20131], [20134], [20138], [20139], [20140], [20145], [20150], [20154], [20155], [20156], [20176], [20181], [20192], [20194], [20196] — $\Sigma N=53604937$

- **2) Harmful for patients** — Outcome with statin — [1], [3], [5], [9], [11], [18], [27], [31], [40], [57], [86], [100], [106], [115], [119], [121], [122], [163], [177], [178], [179], [221], [238], [239], [281], [283], [290], [299], [322], [326], [328], [331], [332], [339], [340], [346], [361], [372], [376], [399], [412], [459], [462], [468], [498], [503], [505], [516], [522], [527], [545], [568], [616], [634], [669], [689], [696], [697], [706], [708], [715], [717], [724], [750], [754], [847], [848], [849], [884], [908], [912], [927], [932], [934], [938], [942], [962], [964], [976], [998], [1032], [1041], [1045], [1064], [1082], [1086], [1091], [1103], [1105], [1126], [1141], [1144], [1149], [1161], [1167], [1203], [1204], [1206], [1207], [1226], [1229], [1233], [1266], [1269], [1272], [1280], [1285], [1294], [1295], [1300], [1301], [1302], [1314], [1316], [1355], [1411], [1412], [1415], [1422], [1435], [1438], [1445], [1448], [1455], [1456], [1464], [1465], [1487], [1503], [1508], [1526], [1531], [1544], [1550], [1551], [1555], [1570], [1596], [1606], [1607], [1614], [1672], [1691], [1694], [1723], [1736], [1743], [1758], [1793], [1802], [1821], [1824], [1827], [1833], [1835], [1851], [1862], [1887], [1900], [1916], [1922], [1938], [1941], [1953], [1985], [1991], [1992], [2013], [2015], [2032], [2045], [2056], [2059], [2062], [2107], [2111], [2112], [2129], [2134], [2155], [2166], [2171], [2196], [2202], [2207], [2209], [2224], [2228], [2242], [2258], [2278], [2285], [2288], [2314], [2315], [2316], [2332], [2350], [2359], [2370], [2376], [2390], [2397], [2403], [2405], [2406], [2410], [2413], [2417], [2424], [2427], [2442], [2449], [2453], [2493], [2498], [2499], [2503], [2507], [2509], [2517], [2537], [2548], [2553], [2572], [2592], [2597], [2598], [2611], [2619], [2639], [2652], [2669], [2704], [2753], [2765], [2822], [2824], [2831], [2843], [2864], [2872], [2894], [2931], [2936], [2943], [2944], [2952], [2956], [2959],

[2971], [2975], [2988], [3002], [3043], [3049], [3066], [3074], [3086], [3120], [3153], [3156], [3178], [3233], [3235], [3241], [3244], [3248], [3251], [3254], [3278], [3286], [3297], [3303], [3356], [3357], [3370], [3372], [3376], [3378], [3394], [3398], [3422], [3431], [3433], [3440], [3442], [3466], [3490], [3495], [3504], [3507], [3520], [3527], [3532], [3544], [3624], [3632], [3639], [3642], [3653], [3655], [3656], [3665], [3674], [3687], [3695], [3699], [3700], [3705], [3716], [3745], [3752], [3760], [3790], [3846], [3857], [3881], [3897], [3902], [3933], [3947], [3953], [4052], [4054], [4080], [4091], [4092], [4112], [4118], [4157], [4159], [4160], [4193], [4198], [4204], [4213], [4222], [4306], [4330], [4351], [4363], [4365], [4372], [4373], [4395], [4402], [4405], [4452], [4456], [4463], [4473], [4513], [4516], [4521], [4542], [4558], [4559], [4561], [4583], [4597], [4629], [4638], [4646], [4648], [4650], [4693], [4699], [4714], [4758], [4763], [4784], [4791], [4800], [4828], [4829], [4846], [4849], [4853], [4857], [4860], [4899], [4904], [4907], [4911], [4915], [4935], [4940], [4947], [5038], [5040], [5047], [5094], [5106], [5110], [5112], [5126], [5138], [5168], [5192], [5206], [5209], [5216], [5217], [5229], [5239], [5242], [5245], [5246], [5266], [5274], [5279], [5280], [5294], [5309], [5318], [5328], [5343], [5351], [5353], [5361], [5365], [5382], [5385], [5397], [5400], [5406], [5443], [5448], [5474], [5481], [5483], [5492], [5495], [5510], [5536], [5574], [5595], [5641], [5644], [5654], [5675], [5687], [5715], [5720], [5724], [5732], [5741], [5742], [5744], [5748], [5868], [5884], [5890], [5893], [5931], [5942], [5950], [5951], [5966], [5983], [6039], [6046], [6058], [6064], [6066], [6100], [6122], [6128], [6130], [6135], [6169], [6204], [6218], [6220], [6228], [6240], [6304], [6316], [6321], [6328], [6329], [6365], [6385], [6423], [6428], [6440], [6442], [6447], [6458], [6477], [6540], [6610], [6615], [6618], [6629], [6650], [6664], [6681], [6688], [6689], [6704], [6714], [6723], [6740], [6746], [6767], [6770], [6792], [6796], [6822], [6823], [6935], [6939], [6941], [6955], [6960], [6991], [6995], [7001], [7023], [7038], [7044], [7062], [7070], [7089], [7096], [7103], [7108], [7145], [7189], [7202], [7220], [7225], [7268], [7282], [7291], [7317], [7338], [7355], [7390], [7407], [7412], [7420], [7474], [7476], [7508], [7511], [7523], [7547], [7554], [7565], [7567], [7607], [7643], [7647], [7674], [7701], [7714], [7719], [7730], [7745], [7755], [7768], [7795], [7796], [7809], [7813], [7828], [7840], [7869], [7872], [7913], [7914], [7925], [7926], [7934], [7936], [7944], [7954], [7968], [7972], [7974], [8010], [8013], [8043], [8065], [8107], [8131], [8140], [8163], [8178], [8181], [8202], [8221], [8234], [8268], [8319], [8326], [8344], [8347], [8365], [8366], [8371], [8375], [8391], [8412], [8427], [8431], [8432], [8437], [8452], [8469], [8471], [8474], [8498], [8506], [8514], [8520], [8522], [8535], [8540], [8558], [8566], [8568], [8574], [8578], [8630], [8645], [8656], [8659], [8690], [8698], [8704], [8710], [8763], [8772], [8793], [8812], [8845], [8849], [8900], [8901], [8910], [8954], [8978], [9001], [9029], [9089], [9093], [9106], [9125], [9131], [9132], [9146], [9152], [9156], [9159], [9168], [9169], [9170], [9178], [9180], [9205], [9216], [9237], [9272], [9283],

[9346], [9361], [9436], [9441], [9444], [9452], [9463], [9510], [9518], [9532], [9573], [9606], [9607], [9619], [9624], [9627], [9635], [9645], [9691], [9693], [9698], [9712], [9725], [9832], [9834], [9837], [9871], [9878], [9895], [9931], [9967], [9986], [10065], [10083], [10089], [10108], [10118], [10154], [10212], [10235], [10242], [10243], [10246], [10274], [10328], [10354], [10356], [10389], [10420], [10437], [10447], [10456], [10508], [10563], [10684], [10690], [10693], [10702], [10719], [10720], [10733], [10748], [10756], [10771], [10779], [10793], [10797], [10811], [10852], [10859], [10867], [10871], [10875], [10897], [10917], [10938], [10945], [10984], [10994], [11013], [11027], [11033], [11036], [11043], [11046], [11053], [11057], [11072], [11075], [11085], [11107], [11127], [11133], [11142], [11147], [11149], [11161], [11167], [11171], [11252], [11261], [11283], [11291], [11308], [11384], [11398], [11415], [11426], [11435], [11449], [11456], [11464], [11475], [11499], [11524], [11529], [11552], [11586], [11614], [11615], [11616], [11625], [11637], [11683], [11711], [11718], [11749], [11767], [11783], [11791], [11804], [11843], [11851], [11873], [11884], [11925], [11973], [11983], [11985], [11994], [11999], [12013], [12016], [12032], [12046], [12099], [12157], [12163], [12183], [12185], [12197], [12218], [12221], [12226], [12354], [12424], [12434], [12449], [12456], [12479], [12481], [12519], [12558], [12663], [12681], [12697], [12701], [12706], [12711], [12753], [12770], [12781], [12785], [12794], [12878], [12882], [12892], [12917], [12920], [12930], [12941], [12981], [12989], [13011], [13051], [13067], [13080], [13085], [13095], [13096], [13099], [13101], [13108], [13154], [13156], [13208], [13209], [13267], [13304], [13339], [13360], [13396], [13442], [13451], [13469], [13490], [13506], [13519], [13572], [13603], [13684], [13697], [13712], [13734], [13739], [13778], [13793], [13842], [13857], [13883], [13922], [13958], [13965], [13967], [13976], [13979], [13987], [13988], [14001], [14041], [14046], [14058], [14066], [14076], [14103], [14122], [14157], [14161], [14175], [14177], [14190], [14191], [14194], [14196], [14210], [14240], [14263], [14310], [14414], [14417], [14418], [14421], [14425], [14426], [14431], [14433], [14474], [14528], [14546], [14554], [14588], [14598], [14628], [14675], [14714], [14814], [14902], [14907], [14913], [14975], [15024], [15061], [15067], [15097], [15110], [15111], [15119], [15130], [15145], [15259], [15419], [15484], [15568], [15569], [15589], [15598], [15606], [15629], [15660], [15677], [15695], [15721], [15726], [15735], [15739], [15812], [15822], [15827], [15844], [15849], [15853], [15866], [15871], [15884], [15993], [15996], [16060], [16078], [16080], [16143], [16148], [16168], [16170], [16186], [16241], [16300], [16303], [16326], [16329], [16334], [16367], [16414], [16432], [16471], [16500], [16532], [16618], [16628], [16641], [16642], [16661], [16679], [16759], [16809], [16839], [16861], [16876], [16890], [16952], [16957], [16958], [17041], [17141], [17180], [17186], [17238], [17240], [17248],

[17285], [17287], [17292], [17313], [17318], [17348], [17372], [17403], [17409], [17417], [17422], [17424], [17443], [17470], [17479], [17481], [17498], [17520], [17548], [17554], [17583], [17589], [17633], [17655], [17657], [17661], [17680], [17681], [17694], [17695], [17704], [17738], [17744], [17757], [17767], [17811], [17813], [17836], [17865], [17866], [17982], [17997], [18002], [18013], [18034], [18035], [18089], [18117], [18201], [18206], [18218], [18252], [18306], [18325], [18364], [18370], [18404], [18418], [18455], [18471], [18491], [18500], [18527], [18540], [18557], [18559], [18608], [18755], [18761], [18762], [18779], [18876], [18902], [18908], [18926], [18964], [18974], [18985], [19045], [19109], [19126], [19150], [19176], [19192], [19203], [19269], [19281], [19518], [19534], [19553], [19575], [19589], [19600], [19608], [19658], [19715], [19722], [19750], [19774], [19781], [19901], [20034] — $\Sigma N=10544516$

- **3) No clear effect** — Outcome with statin — [2], [4], [6], [7], [10], [13], [19], [22], [23], [24], [28], [32], [33], [34], [35], [36], [37], [39], [41], [42], [43], [44], [45], [47], [50], [51], [52], [53], [54], [56], [58], [59], [60], [61], [62], [63], [68], [69], [70], [71], [73], [74], [75], [76], [78], [80], [81], [83], [84], [85], [87], [89], [90], [92], [93], [94], [96], [97], [99], [101], [102], [103], [105], [107], [108], [109], [110], [111], [112], [116], [117], [118], [120], [123], [124], [125], [126], [129], [130], [131], [132], [135], [137], [141], [143], [144], [145], [149], [151], [152], [155], [156], [159], [160], [161], [162], [164], [165], [168], [172], [175], [176], [181], [182], [183], [184], [185], [186], [187], [188], [189], [190], [191], [192], [193], [194], [195], [196], [197], [198], [199], [200], [201], [202], [203], [204], [205], [206], [207], [208], [209], [210], [211], [212], [213], [215], [216], [217], [219], [220], [222], [224], [226], [227], [229], [230], [231], [232], [233], [234], [236], [237], [240], [242], [243], [244], [245], [246], [247], [248], [249], [250], [252], [253], [258], [260], [261], [262], [264], [268], [269], [270], [272], [273], [274], [276], [277], [278], [279], [280], [282], [286], [287], [288], [291], [292], [293], [295], [296], [298], [300], [302], [304], [305], [306], [309], [310], [311], [312], [314], [315], [316], [317], [318], [321], [323], [324], [325], [327], [329], [330], [333], [334], [335], [336], [337], [338], [343], [347], [350], [354], [355], [359], [360], [362], [363], [364], [365], [366], [369], [370], [371], [373], [374], [375], [379], [382], [386], [388], [389], [391], [392], [393], [395], [397], [398], [400], [401], [403], [404], [406], [407], [409], [410], [411], [413], [415], [416], [417], [419], [420], [421], [422], [423], [424], [425], [427], [428], [429], [430], [431], [439], [440], [441], [443], [444], [445], [446], [449], [450], [452], [453], [454], [455], [456], [457], [458], [461], [463], [464], [467], [469], [470], [472], [474], [476], [477], [478], [480], [481], [482], [483], [484], [485], [487], [488], [489], [490], [491], [492], [493], [494], [495], [496], [497], [499], [502], [504], [506], [507], [509], [510], [511], [514], [515], [517], [518], [519], [528], [529], [531], [533], [535], [536], [537], [538], [539], [540], [542], [546], [547], [549],

[551], [552], [553], [555], [556], [558], [559], [560], [562], [563], [566], [567], [570], [571], [573], [574], [575], [577], [578], [579], [580], [583], [585], [586], [587], [588], [589], [590], [592], [594], [601], [602], [603], [604], [605], [606], [607], [609], [612], [613], [614], [615], [617], [618], [619], [620], [621], [623], [628], [629], [630], [632], [635], [638], [640], [642], [644], [645], [646], [648], [649], [650], [651], [652], [660], [662], [664], [666], [670], [671], [673], [674], [676], [677], [678], [679], [680], [681], [682], [684], [685], [686], [687], [690], [692], [693], [694], [695], [698], [699], [701], [702], [704], [707], [709], [710], [712], [713], [714], [718], [719], [721], [723], [725], [727], [730], [731], [733], [735], [736], [737], [739], [740], [741], [744], [745], [746], [749], [751], [752], [753], [755], [757], [758], [759], [761], [763], [764], [766], [770], [772], [774], [775], [780], [781], [782], [783], [784], [786], [787], [788], [791], [792], [793], [794], [795], [798], [799], [800], [801], [802], [804], [806], [808], [809], [812], [813], [814], [815], [816], [817], [818], [819], [821], [822], [823], [824], [825], [826], [828], [830], [831], [832], [833], [835], [836], [839], [840], [843], [845], [846], [850], [853], [854], [855], [856], [859], [863], [864], [866], [868], [869], [870], [872], [873], [874], [877], [878], [880], [881], [885], [887], [888], [890], [891], [892], [893], [894], [895], [896], [897], [898], [899], [900], [902], [904], [909], [910], [911], [913], [914], [915], [918], [919], [920], [922], [924], [925], [926], [933], [935], [936], [937], [943], [944], [945], [946], [947], [949], [951], [952], [953], [955], [956], [957], [958], [959], [963], [965], [966], [968], [969], [971], [972], [975], [978], [979], [981], [983], [984], [988], [990], [991], [993], [994], [995], [996], [997], [999], [1001], [1002], [1003], [1004], [1006], [1007], [1008], [1010], [1011], [1012], [1013], [1014], [1015], [1016], [1017], [1018], [1019], [1020], [1021], [1022], [1024], [1025], [1026], [1028], [1030], [1036], [1037], [1042], [1044], [1048], [1050], [1051], [1054], [1056], [1058], [1060], [1061], [1062], [1063], [1065], [1067], [1068], [1070], [1073], [1074], [1075], [1077], [1078], [1079], [1080], [1081], [1083], [1084], [1085], [1087], [1090], [1093], [1094], [1096], [1097], [1098], [1099], [1100], [1101], [1104], [1106], [1109], [1111], [1112], [1113], [1114], [1115], [1117], [1118], [1119], [1120], [1121], [1122], [1125], [1127], [1128], [1129], [1134], [1135], [1136], [1138], [1139], [1140], [1142], [1145], [1147], [1150], [1152], [1154], [1155], [1156], [1157], [1158], [1159], [1160], [1162], [1164], [1166], [1169], [1170], [1171], [1172], [1174], [1175], [1176], [1177], [1178], [1179], [1181], [1182], [1184], [1188], [1189], [1191], [1192], [1194], [1196], [1197], [1199], [1200], [1201], [1202], [1208], [1209], [1211], [1212], [1215], [1216], [1217], [1218], [1219], [1221], [1222], [1223], [1224], [1225], [1227], [1228], [1230], [1231], [1234], [1236], [1237], [1238], [1239], [1240], [1244], [1245], [1248], [1249], [1250], [1253], [1254], [1255], [1263], [1265], [1267], [1268], [1270], [1273], [1274], [1275], [1278], [1279], [1282], [1283], [1286], [1290], [1291], [1293], [1296], [1297], [1298], [1299], [1304], [1305], [1311], [1312], [1317], [1318], [1321], [1322], [1323], [1324], [1325],

[1326], [1327], [1328], [1329], [1330], [1331], [1332], [1333], [1334], [1335], [1336], [1337], [1338], [1339], [1340], [1341], [1342], [1343], [1344], [1345], [1346], [1347], [1348], [1349], [1350], [1351], [1352], [1354], [1356], [1357], [1359], [1361], [1363], [1364], [1365], [1366], [1368], [1369], [1370], [1371], [1373], [1374], [1375], [1377], [1378], [1379], [1380], [1381], [1383], [1385], [1389], [1390], [1391], [1392], [1393], [1394], [1395], [1396], [1397], [1398], [1399], [1400], [1402], [1403], [1405], [1406], [1407], [1408], [1409], [1410], [1413], [1414], [1416], [1417], [1418], [1419], [1420], [1424], [1425], [1426], [1427], [1428], [1429], [1431], [1433], [1434], [1436], [1437], [1439], [1442], [1450], [1451], [1454], [1457], [1458], [1460], [1463], [1469], [1471], [1472], [1473], [1474], [1476], [1477], [1478], [1481], [1482], [1483], [1484], [1486], [1489], [1490], [1491], [1492], [1494], [1495], [1496], [1498], [1499], [1500], [1501], [1504], [1505], [1506], [1507], [1509], [1510], [1511], [1513], [1514], [1516], [1517], [1518], [1519], [1520], [1521], [1529], [1530], [1533], [1534], [1538], [1539], [1540], [1542], [1545], [1546], [1548], [1549], [1552], [1556], [1557], [1558], [1561], [1562], [1563], [1566], [1567], [1573], [1575], [1576], [1577], [1578], [1579], [1580], [1582], [1583], [1584], [1585], [1588], [1590], [1592], [1594], [1597], [1600], [1601], [1603], [1608], [1610], [1611], [1612], [1616], [1617], [1618], [1619], [1621], [1624], [1625], [1627], [1629], [1633], [1635], [1636], [1640], [1641], [1643], [1644], [1647], [1650], [1652], [1653], [1654], [1655], [1656], [1657], [1658], [1659], [1660], [1661], [1662], [1663], [1664], [1666], [1668], [1669], [1670], [1671], [1674], [1675], [1676], [1679], [1684], [1686], [1688], [1689], [1690], [1692], [1693], [1695], [1697], [1698], [1699], [1700], [1701], [1702], [1703], [1705], [1708], [1710], [1711], [1713], [1714], [1716], [1717], [1718], [1719], [1720], [1721], [1724], [1725], [1726], [1727], [1728], [1729], [1730], [1731], [1732], [1733], [1735], [1737], [1738], [1739], [1740], [1741], [1744], [1745], [1746], [1747], [1748], [1749], [1750], [1751], [1752], [1753], [1754], [1755], [1756], [1757], [1759], [1760], [1762], [1764], [1765], [1770], [1771], [1772], [1773], [1774], [1776], [1777], [1778], [1780], [1781], [1782], [1784], [1785], [1786], [1787], [1788], [1789], [1791], [1792], [1795], [1796], [1797], [1799], [1800], [1806], [1810], [1811], [1814], [1815], [1826], [1828], [1830], [1831], [1832], [1834], [1840], [1841], [1842], [1843], [1845], [1848], [1849], [1850], [1855], [1856], [1857], [1863], [1864], [1865], [1866], [1869], [1870], [1871], [1872], [1875], [1876], [1877], [1878], [1882], [1883], [1884], [1885], [1886], [1888], [1890], [1891], [1892], [1893], [1894], [1895], [1899], [1901], [1902], [1903], [1904], [1905], [1906], [1907], [1908], [1909], [1911], [1913], [1917], [1918], [1921], [1924], [1925], [1926], [1927], [1928], [1930], [1931], [1932], [1935], [1939], [1940], [1942], [1943], [1944], [1948], [1949], [1950], [1951], [1956], [1957], [1958], [1960], [1961], [1962], [1963], [1964], [1966], [1968], [1969], [1972], [1973], [1974], [1975], [1976], [1977], [1978], [1979], [1980], [1981], [1982], [1983], [1986], [1987], [1990], [1993], [1996], [1997], [1998], [1999], [2002], [2004],

[2007], [2008], [2010], [2012], [2016], [2020], [2022], [2023], [2024], [2027], [2029], [2031], [2033], [2034], [2035], [2038], [2040], [2042], [2043], [2044], [2046], [2048], [2049], [2050], [2051], [2052], [2053], [2058], [2060], [2061], [2063], [2066], [2068], [2069], [2073], [2074], [2076], [2079], [2080], [2082], [2083], [2084], [2086], [2087], [2090], [2091], [2093], [2099], [2104], [2108], [2109], [2110], [2113], [2114], [2116], [2117], [2118], [2119], [2122], [2123], [2124], [2125], [2126], [2127], [2130], [2131], [2132], [2136], [2137], [2138], [2139], [2142], [2144], [2145], [2146], [2148], [2149], [2156], [2157], [2158], [2159], [2160], [2162], [2164], [2165], [2168], [2170], [2172], [2173], [2176], [2177], [2178], [2179], [2180], [2182], [2183], [2184], [2185], [2186], [2187], [2189], [2190], [2191], [2192], [2193], [2194], [2195], [2197], [2198], [2199], [2201], [2204], [2205], [2208], [2210], [2211], [2212], [2213], [2215], [2216], [2217], [2218], [2219], [2220], [2221], [2225], [2226], [2227], [2230], [2232], [2235], [2238], [2239], [2241], [2243], [2244], [2245], [2248], [2252], [2253], [2254], [2255], [2256], [2260], [2261], [2262], [2263], [2264], [2266], [2270], [2272], [2274], [2275], [2276], [2277], [2279], [2280], [2282], [2283], [2284], [2287], [2289], [2290], [2291], [2292], [2293], [2294], [2295], [2296], [2297], [2298], [2301], [2303], [2304], [2305], [2306], [2308], [2309], [2310], [2312], [2318], [2320], [2322], [2323], [2324], [2325], [2327], [2328], [2329], [2330], [2333], [2334], [2335], [2336], [2337], [2339], [2340], [2342], [2343], [2347], [2352], [2353], [2354], [2356], [2357], [2360], [2361], [2362], [2363], [2365], [2367], [2371], [2373], [2374], [2378], [2379], [2381], [2382], [2384], [2385], [2386], [2388], [2391], [2392], [2393], [2394], [2396], [2398], [2400], [2402], [2404], [2407], [2409], [2419], [2420], [2421], [2422], [2423], [2426], [2428], [2429], [2430], [2431], [2432], [2433], [2434], [2435], [2437], [2438], [2440], [2441], [2444], [2445], [2447], [2450], [2451], [2458], [2459], [2460], [2461], [2462], [2463], [2464], [2465], [2467], [2468], [2470], [2471], [2472], [2473], [2474], [2475], [2476], [2478], [2479], [2480], [2483], [2486], [2487], [2488], [2489], [2490], [2491], [2497], [2500], [2502], [2504], [2505], [2506], [2508], [2512], [2513], [2518], [2519], [2520], [2522], [2525], [2529], [2530], [2535], [2538], [2539], [2542], [2544], [2545], [2546], [2549], [2551], [2554], [2555], [2556], [2557], [2558], [2560], [2561], [2564], [2565], [2568], [2570], [2573], [2575], [2576], [2577], [2579], [2580], [2581], [2591], [2593], [2594], [2595], [2599], [2600], [2601], [2602], [2605], [2607], [2608], [2609], [2612], [2614], [2615], [2616], [2617], [2620], [2622], [2623], [2624], [2626], [2632], [2633], [2634], [2636], [2638], [2640], [2641], [2642], [2643], [2645], [2647], [2648], [2649], [2650], [2651], [2653], [2655], [2656], [2657], [2658], [2659], [2661], [2662], [2663], [2664], [2665], [2666], [2668], [2670], [2671], [2672], [2673], [2674], [2675], [2676], [2677], [2679], [2680], [2681], [2682], [2683], [2684], [2686], [2687], [2688], [2689], [2690], [2691], [2692], [2693], [2695], [2697], [2698], [2699], [2700], [2701], [2702], [2703], [2705], [2706], [2707], [2708], [2709], [2711], [2712], [2713], [2715], [2716], [2717], [2718],

[2719], [2720], [2721], [2722], [2723], [2724], [2725], [2726], [2727], [2728], [2729], [2730], [2731], [2732], [2733], [2734], [2735], [2739], [2740], [2742], [2743], [2744], [2745], [2746], [2747], [2749], [2750], [2751], [2752], [2754], [2755], [2756], [2758], [2759], [2760], [2761], [2763], [2764], [2767], [2768], [2770], [2773], [2774], [2776], [2778], [2781], [2782], [2783], [2784], [2785], [2786], [2787], [2788], [2789], [2790], [2791], [2792], [2793], [2796], [2797], [2799], [2800], [2801], [2803], [2804], [2805], [2809], [2810], [2812], [2813], [2814], [2815], [2816], [2817], [2818], [2819], [2820], [2821], [2823], [2825], [2826], [2828], [2829], [2830], [2833], [2834], [2835], [2836], [2837], [2838], [2839], [2840], [2844], [2846], [2847], [2848], [2849], [2850], [2853], [2856], [2858], [2860], [2861], [2862], [2865], [2866], [2867], [2868], [2870], [2871], [2873], [2875], [2876], [2878], [2879], [2880], [2882], [2883], [2884], [2885], [2887], [2888], [2889], [2890], [2891], [2892], [2893], [2895], [2896], [2897], [2898], [2899], [2900], [2902], [2903], [2904], [2905], [2906], [2907], [2908], [2910], [2911], [2912], [2913], [2914], [2915], [2917], [2919], [2920], [2921], [2923], [2924], [2925], [2926], [2927], [2928], [2929], [2930], [2932], [2933], [2934], [2937], [2938], [2939], [2940], [2942], [2945], [2946], [2947], [2948], [2949], [2950], [2953], [2954], [2957], [2958], [2961], [2962], [2963], [2964], [2965], [2966], [2967], [2968], [2972], [2973], [2974], [2976], [2978], [2980], [2981], [2986], [2989], [2990], [2991], [2992], [2993], [2994], [2995], [2996], [2997], [2998], [3000], [3001], [3004], [3005], [3006], [3008], [3009], [3010], [3012], [3013], [3014], [3015], [3016], [3017], [3018], [3019], [3020], [3023], [3025], [3026], [3027], [3028], [3031], [3032], [3033], [3035], [3036], [3037], [3038], [3039], [3040], [3041], [3042], [3044], [3046], [3047], [3048], [3050], [3051], [3053], [3054], [3055], [3058], [3059], [3061], [3062], [3064], [3065], [3067], [3069], [3070], [3071], [3072], [3073], [3075], [3077], [3078], [3079], [3081], [3082], [3083], [3085], [3088], [3089], [3090], [3092], [3093], [3095], [3096], [3097], [3098], [3099], [3100], [3102], [3104], [3105], [3106], [3107], [3108], [3109], [3110], [3111], [3112], [3113], [3114], [3116], [3117], [3118], [3121], [3122], [3123], [3124], [3125], [3126], [3127], [3128], [3129], [3130], [3131], [3132], [3133], [3134], [3135], [3136], [3137], [3138], [3139], [3140], [3141], [3142], [3143], [3144], [3145], [3146], [3147], [3148], [3149], [3150], [3159], [3161], [3162], [3164], [3166], [3167], [3168], [3170], [3171], [3175], [3176], [3177], [3179], [3180], [3181], [3182], [3183], [3184], [3185], [3186], [3187], [3188], [3189], [3190], [3191], [3192], [3193], [3194], [3195], [3196], [3197], [3198], [3199], [3200], [3201], [3202], [3203], [3204], [3205], [3206], [3207], [3208], [3209], [3210], [3211], [3212], [3213], [3214], [3215], [3217], [3218], [3219], [3220], [3221], [3222], [3224], [3225], [3226], [3227], [3228], [3229], [3230], [3231], [3232], [3236], [3237], [3238], [3239], [3245], [3249], [3250], [3252], [3253], [3255], [3256], [3257], [3258], [3259], [3260], [3262], [3263], [3264], [3265], [3266], [3267], [3268], [3269], [3270], [3271], [3272], [3274], [3275], [3276], [3279], [3281], [3283], [3287], [3288],

[3289], [3290], [3293], [3294], [3296], [3298], [3299], [3300], [3301], [3302], [3304], [3307], [3308], [3309], [3311], [3313], [3314], [3315], [3316], [3317], [3318], [3319], [3320], [3322], [3323], [3324], [3325], [3326], [3327], [3328], [3329], [3330], [3332], [3333], [3334], [3336], [3337], [3338], [3339], [3342], [3343], [3345], [3346], [3347], [3348], [3349], [3351], [3352], [3353], [3354], [3355], [3358], [3359], [3361], [3363], [3366], [3373], [3374], [3377], [3379], [3380], [3381], [3382], [3383], [3384], [3385], [3386], [3387], [3390], [3392], [3393], [3395], [3396], [3399], [3400], [3402], [3403], [3404], [3405], [3406], [3407], [3408], [3409], [3410], [3411], [3413], [3414], [3415], [3416], [3417], [3418], [3419], [3420], [3421], [3425], [3426], [3427], [3429], [3430], [3434], [3435], [3436], [3437], [3441], [3443], [3444], [3445], [3447], [3448], [3449], [3450], [3453], [3455], [3457], [3458], [3459], [3461], [3462], [3463], [3464], [3465], [3467], [3468], [3469], [3471], [3472], [3473], [3475], [3478], [3479], [3480], [3481], [3483], [3485], [3486], [3487], [3488], [3489], [3491], [3493], [3494], [3496], [3497], [3498], [3499], [3500], [3502], [3503], [3505], [3506], [3508], [3509], [3510], [3511], [3512], [3514], [3515], [3516], [3517], [3518], [3519], [3522], [3523], [3524], [3525], [3526], [3528], [3529], [3530], [3531], [3534], [3535], [3536], [3537], [3538], [3539], [3540], [3541], [3543], [3545], [3546], [3550], [3555], [3557], [3558], [3560], [3561], [3563], [3565], [3566], [3567], [3569], [3570], [3572], [3573], [3574], [3575], [3576], [3578], [3579], [3580], [3581], [3582], [3583], [3586], [3587], [3588], [3591], [3593], [3594], [3595], [3596], [3598], [3599], [3601], [3603], [3604], [3605], [3607], [3611], [3614], [3615], [3616], [3617], [3618], [3619], [3620], [3621], [3622], [3625], [3626], [3627], [3628], [3629], [3630], [3631], [3633], [3634], [3635], [3636], [3637], [3638], [3641], [3643], [3645], [3647], [3648], [3649], [3650], [3651], [3652], [3657], [3658], [3660], [3661], [3662], [3663], [3664], [3667], [3669], [3670], [3672], [3673], [3675], [3676], [3677], [3678], [3679], [3680], [3681], [3682], [3683], [3684], [3686], [3689], [3690], [3691], [3692], [3694], [3702], [3703], [3704], [3706], [3707], [3708], [3709], [3711], [3713], [3717], [3718], [3719], [3720], [3722], [3723], [3724], [3726], [3729], [3731], [3734], [3735], [3738], [3741], [3742], [3743], [3744], [3748], [3750], [3751], [3753], [3754], [3755], [3756], [3757], [3758], [3759], [3761], [3762], [3763], [3764], [3765], [3766], [3767], [3768], [3769], [3770], [3771], [3772], [3773], [3775], [3776], [3777], [3778], [3779], [3780], [3781], [3783], [3784], [3785], [3786], [3787], [3789], [3792], [3793], [3794], [3795], [3796], [3797], [3800], [3801], [3803], [3806], [3807], [3809], [3810], [3813], [3814], [3815], [3816], [3817], [3818], [3820], [3821], [3824], [3825], [3826], [3827], [3829], [3830], [3831], [3832], [3833], [3834], [3835], [3837], [3838], [3839], [3840], [3842], [3844], [3845], [3847], [3848], [3849], [3851], [3853], [3855], [3858], [3860], [3861], [3862], [3863], [3864], [3866], [3867], [3868], [3870], [3874], [3875], [3876], [3879], [3880], [3885], [3886], [3887], [3888], [3889], [3890], [3893], [3894], [3895], [3896], [3898], [3899], [3900], [3901], [3904], [3905], [3907],

[3908], [3909], [3910], [3911], [3912], [3913], [3917], [3919], [3921], [3922], [3923], [3925], [3926], [3929], [3931], [3934], [3935], [3937], [3938], [3939], [3941], [3942], [3943], [3944], [3945], [3946], [3948], [3949], [3950], [3952], [3954], [3955], [3958], [3959], [3960], [3961], [3962], [3963], [3965], [3966], [3968], [3969], [3970], [3972], [3973], [3975], [3976], [3977], [3978], [3979], [3982], [3983], [3985], [3986], [3987], [3988], [3989], [3991], [3994], [3995], [3996], [3997], [3998], [3999], [4000], [4001], [4002], [4003], [4004], [4005], [4007], [4008], [4012], [4014], [4015], [4018], [4019], [4022], [4023], [4028], [4030], [4031], [4032], [4033], [4034], [4036], [4037], [4038], [4039], [4040], [4041], [4042], [4043], [4045], [4046], [4047], [4049], [4050], [4051], [4053], [4055], [4056], [4057], [4058], [4059], [4060], [4062], [4063], [4064], [4065], [4066], [4069], [4070], [4073], [4074], [4075], [4077], [4079], [4081], [4084], [4085], [4087], [4088], [4089], [4093], [4094], [4096], [4097], [4099], [4100], [4101], [4103], [4104], [4105], [4106], [4108], [4109], [4110], [4113], [4114], [4115], [4116], [4117], [4119], [4120], [4121], [4122], [4123], [4124], [4125], [4126], [4127], [4128], [4129], [4131], [4132], [4133], [4135], [4136], [4137], [4138], [4139], [4140], [4141], [4143], [4144], [4145], [4146], [4147], [4151], [4154], [4155], [4156], [4158], [4164], [4165], [4167], [4168], [4169], [4171], [4172], [4174], [4175], [4176], [4177], [4179], [4180], [4181], [4182], [4183], [4184], [4185], [4186], [4187], [4189], [4190], [4191], [4192], [4195], [4196], [4197], [4199], [4200], [4203], [4206], [4208], [4209], [4212], [4214], [4218], [4219], [4221], [4223], [4224], [4225], [4226], [4227], [4228], [4230], [4231], [4233], [4234], [4237], [4238], [4239], [4240], [4241], [4243], [4244], [4245], [4247], [4248], [4249], [4250], [4252], [4253], [4255], [4256], [4257], [4258], [4259], [4262], [4265], [4267], [4269], [4271], [4272], [4273], [4274], [4275], [4277], [4278], [4279], [4280], [4282], [4283], [4284], [4285], [4286], [4287], [4290], [4291], [4292], [4293], [4294], [4296], [4297], [4299], [4300], [4302], [4303], [4304], [4308], [4309], [4311], [4312], [4313], [4314], [4316], [4318], [4319], [4320], [4322], [4323], [4324], [4327], [4328], [4329], [4331], [4334], [4335], [4337], [4339], [4344], [4345], [4347], [4348], [4349], [4352], [4353], [4354], [4355], [4359], [4364], [4366], [4367], [4368], [4369], [4370], [4371], [4374], [4375], [4376], [4377], [4379], [4381], [4383], [4384], [4386], [4388], [4389], [4390], [4391], [4392], [4394], [4396], [4397], [4398], [4399], [4400], [4401], [4403], [4404], [4407], [4408], [4409], [4410], [4411], [4412], [4413], [4414], [4415], [4416], [4418], [4419], [4421], [4422], [4423], [4426], [4427], [4428], [4430], [4431], [4435], [4436], [4437], [4438], [4439], [4442], [4443], [4445], [4446], [4450], [4455], [4457], [4458], [4459], [4460], [4462], [4464], [4467], [4468], [4469], [4472], [4482], [4483], [4484], [4485], [4486], [4489], [4490], [4492], [4494], [4495], [4496], [4497], [4498], [4500], [4501], [4502], [4503], [4504], [4506], [4508], [4509], [4511], [4514], [4515], [4517], [4518], [4522], [4524], [4525], [4527], [4528], [4530], [4531], [4532], [4533], [4534], [4535], [4536], [4537], [4540], [4543], [4544], [4546], [4547],

[4548], [4551], [4552], [4554], [4562], [4563], [4566], [4567], [4568], [4569], [4573], [4574], [4580], [4582], [4584], [4588], [4589], [4590], [4592], [4593], [4601], [4602], [4603], [4605], [4606], [4607], [4608], [4610], [4614], [4615], [4616], [4618], [4620], [4622], [4623], [4625], [4627], [4628], [4635], [4636], [4637], [4641], [4643], [4647], [4656], [4657], [4659], [4660], [4662], [4663], [4664], [4666], [4667], [4668], [4669], [4670], [4671], [4672], [4673], [4674], [4675], [4677], [4678], [4679], [4681], [4683], [4684], [4685], [4686], [4687], [4689], [4690], [4692], [4694], [4695], [4696], [4698], [4700], [4702], [4703], [4704], [4706], [4707], [4708], [4709], [4710], [4712], [4713], [4715], [4716], [4718], [4719], [4720], [4724], [4726], [4730], [4731], [4733], [4735], [4736], [4737], [4738], [4739], [4740], [4741], [4742], [4743], [4746], [4747], [4748], [4749], [4750], [4751], [4754], [4756], [4757], [4759], [4761], [4762], [4765], [4768], [4769], [4770], [4771], [4773], [4774], [4775], [4777], [4778], [4779], [4780], [4781], [4783], [4786], [4787], [4788], [4789], [4790], [4799], [4804], [4805], [4806], [4807], [4808], [4809], [4810], [4811], [4812], [4813], [4815], [4816], [4817], [4818], [4819], [4822], [4823], [4824], [4826], [4832], [4833], [4834], [4835], [4836], [4839], [4840], [4841], [4843], [4844], [4845], [4847], [4854], [4856], [4858], [4859], [4863], [4864], [4865], [4866], [4868], [4869], [4871], [4872], [4873], [4877], [4878], [4879], [4880], [4882], [4883], [4884], [4885], [4886], [4887], [4889], [4890], [4891], [4892], [4894], [4896], [4897], [4898], [4900], [4901], [4902], [4903], [4905], [4906], [4909], [4910], [4912], [4913], [4914], [4917], [4918], [4919], [4920], [4921], [4922], [4923], [4924], [4925], [4926], [4927], [4928], [4929], [4931], [4933], [4936], [4937], [4941], [4942], [4943], [4944], [4945], [4946], [4948], [4949], [4950], [4951], [4953], [4954], [4955], [4957], [4959], [4960], [4963], [4964], [4965], [4970], [4971], [4972], [4973], [4974], [4975], [4977], [4979], [4980], [4983], [4984], [4985], [4986], [4988], [4989], [4990], [4991], [4992], [4993], [4994], [4995], [4996], [4997], [4998], [4999], [5000], [5001], [5002], [5003], [5004], [5005], [5007], [5008], [5009], [5013], [5014], [5015], [5016], [5017], [5018], [5019], [5021], [5022], [5024], [5025], [5028], [5031], [5032], [5033], [5034], [5037], [5042], [5043], [5044], [5045], [5046], [5048], [5049], [5051], [5053], [5054], [5055], [5056], [5057], [5060], [5061], [5062], [5063], [5064], [5065], [5066], [5067], [5068], [5069], [5070], [5072], [5073], [5074], [5076], [5077], [5078], [5081], [5082], [5083], [5084], [5085], [5088], [5089], [5090], [5093], [5095], [5096], [5099], [5100], [5101], [5102], [5104], [5105], [5107], [5108], [5109], [5111], [5113], [5114], [5117], [5119], [5120], [5122], [5124], [5125], [5127], [5130], [5131], [5133], [5134], [5135], [5137], [5139], [5140], [5141], [5142], [5144], [5146], [5147], [5148], [5149], [5150], [5151], [5154], [5155], [5156], [5158], [5159], [5160], [5162], [5163], [5164], [5165], [5167], [5169], [5170], [5171], [5175], [5176], [5178], [5181], [5182], [5183], [5184], [5185], [5186], [5188], [5189], [5190], [5193], [5199], [5200], [5202], [5204], [5207], [5208], [5210], [5211], [5212], [5213], [5214], [5215], [5218], [5219], [5220],

[5221], [5222], [5224], [5225], [5226], [5227], [5228], [5230], [5231], [5234], [5240], [5241], [5244], [5248], [5250], [5252], [5259], [5260], [5261], [5262], [5263], [5264], [5265], [5267], [5271], [5272], [5275], [5276], [5277], [5278], [5282], [5283], [5285], [5291], [5292], [5293], [5296], [5297], [5298], [5299], [5300], [5301], [5302], [5303], [5304], [5305], [5306], [5307], [5308], [5310], [5313], [5314], [5316], [5319], [5320], [5321], [5322], [5323], [5324], [5326], [5327], [5329], [5330], [5331], [5333], [5334], [5335], [5336], [5338], [5339], [5341], [5342], [5344], [5350], [5352], [5354], [5355], [5356], [5360], [5362], [5363], [5364], [5366], [5367], [5368], [5369], [5370], [5371], [5373], [5374], [5375], [5376], [5377], [5378], [5380], [5381], [5383], [5384], [5387], [5391], [5392], [5393], [5395], [5396], [5398], [5399], [5401], [5402], [5403], [5404], [5407], [5408], [5409], [5413], [5414], [5415], [5417], [5418], [5419], [5420], [5421], [5423], [5424], [5425], [5426], [5427], [5428], [5429], [5431], [5432], [5433], [5434], [5439], [5442], [5444], [5450], [5451], [5452], [5454], [5455], [5456], [5458], [5459], [5461], [5463], [5465], [5466], [5468], [5470], [5472], [5473], [5475], [5477], [5480], [5484], [5485], [5486], [5487], [5488], [5489], [5490], [5494], [5496], [5497], [5498], [5499], [5500], [5502], [5503], [5504], [5506], [5507], [5513], [5514], [5516], [5517], [5518], [5520], [5521], [5522], [5524], [5525], [5526], [5527], [5528], [5530], [5533], [5534], [5535], [5537], [5538], [5539], [5540], [5541], [5542], [5543], [5544], [5545], [5546], [5548], [5551], [5552], [5554], [5555], [5556], [5557], [5560], [5562], [5563], [5564], [5565], [5566], [5567], [5568], [5569], [5570], [5571], [5573], [5575], [5576], [5578], [5579], [5580], [5581], [5582], [5583], [5586], [5587], [5588], [5589], [5590], [5591], [5592], [5593], [5596], [5597], [5598], [5599], [5600], [5601], [5602], [5603], [5604], [5605], [5606], [5607], [5608], [5609], [5610], [5611], [5612], [5613], [5614], [5615], [5617], [5618], [5619], [5620], [5621], [5622], [5623], [5624], [5631], [5633], [5634], [5635], [5636], [5637], [5638], [5640], [5642], [5645], [5646], [5647], [5648], [5650], [5651], [5653], [5655], [5656], [5657], [5659], [5660], [5662], [5663], [5666], [5667], [5668], [5669], [5673], [5674], [5676], [5677], [5680], [5681], [5682], [5684], [5686], [5688], [5689], [5692], [5693], [5694], [5695], [5696], [5697], [5698], [5699], [5701], [5702], [5704], [5706], [5707], [5709], [5710], [5711], [5713], [5714], [5716], [5717], [5718], [5719], [5721], [5722], [5723], [5725], [5726], [5727], [5729], [5730], [5733], [5734], [5737], [5739], [5740], [5743], [5746], [5749], [5750], [5751], [5752], [5754], [5755], [5756], [5757], [5758], [5759], [5760], [5761], [5762], [5763], [5764], [5765], [5767], [5768], [5770], [5771], [5773], [5775], [5777], [5778], [5779], [5780], [5781], [5782], [5783], [5784], [5785], [5786], [5787], [5788], [5790], [5795], [5796], [5797], [5798], [5799], [5800], [5805], [5806], [5808], [5809], [5813], [5814], [5815], [5816], [5817], [5818], [5819], [5822], [5823], [5824], [5826], [5828], [5829], [5830], [5831], [5832], [5833], [5836], [5837], [5839], [5840], [5841], [5842], [5843], [5844], [5845], [5846], [5847], [5848], [5849], [5850], [5852], [5853], [5854], [5855], [5856],

[5857], [5860], [5861], [5862], [5866], [5869], [5870], [5872], [5874], [5875], [5876], [5877], [5878], [5879], [5880], [5881], [5883], [5885], [5887], [5891], [5892], [5894], [5895], [5896], [5897], [5898], [5899], [5900], [5901], [5903], [5904], [5906], [5907], [5908], [5909], [5910], [5911], [5913], [5917], [5918], [5919], [5921], [5923], [5924], [5926], [5927], [5928], [5929], [5930], [5932], [5933], [5934], [5935], [5937], [5939], [5940], [5941], [5944], [5946], [5948], [5949], [5953], [5955], [5957], [5958], [5959], [5960], [5965], [5967], [5968], [5969], [5970], [5971], [5972], [5973], [5974], [5975], [5977], [5980], [5981], [5985], [5986], [5987], [5988], [5989], [5990], [5991], [5992], [5993], [5994], [5995], [5997], [5998], [5999], [6001], [6002], [6003], [6004], [6005], [6007], [6008], [6009], [6010], [6011], [6012], [6015], [6017], [6018], [6020], [6021], [6025], [6026], [6027], [6028], [6032], [6033], [6035], [6036], [6037], [6038], [6041], [6042], [6043], [6045], [6047], [6048], [6049], [6050], [6051], [6052], [6054], [6055], [6057], [6059], [6060], [6063], [6065], [6068], [6069], [6070], [6071], [6072], [6074], [6075], [6076], [6077], [6078], [6079], [6080], [6081], [6082], [6084], [6085], [6087], [6088], [6089], [6093], [6095], [6097], [6098], [6101], [6102], [6104], [6105], [6106], [6107], [6108], [6109], [6111], [6112], [6114], [6115], [6119], [6120], [6123], [6125], [6126], [6127], [6129], [6131], [6132], [6133], [6134], [6138], [6140], [6141], [6142], [6145], [6146], [6147], [6148], [6149], [6151], [6152], [6153], [6155], [6156], [6157], [6158], [6159], [6160], [6161], [6162], [6163], [6164], [6165], [6166], [6167], [6168], [6170], [6171], [6172], [6173], [6174], [6176], [6177], [6178], [6179], [6181], [6183], [6185], [6186], [6187], [6190], [6193], [6194], [6195], [6196], [6197], [6199], [6200], [6205], [6207], [6208], [6210], [6211], [6212], [6213], [6214], [6216], [6221], [6222], [6223], [6224], [6225], [6226], [6227], [6229], [6230], [6231], [6232], [6233], [6234], [6235], [6236], [6237], [6238], [6239], [6242], [6243], [6245], [6246], [6247], [6248], [6249], [6250], [6251], [6253], [6254], [6258], [6260], [6261], [6262], [6264], [6265], [6268], [6270], [6271], [6272], [6273], [6275], [6276], [6277], [6278], [6280], [6282], [6283], [6284], [6285], [6286], [6287], [6288], [6289], [6290], [6291], [6294], [6295], [6296], [6297], [6298], [6300], [6301], [6302], [6303], [6305], [6307], [6309], [6311], [6313], [6314], [6317], [6318], [6322], [6324], [6325], [6326], [6327], [6330], [6331], [6332], [6334], [6336], [6338], [6339], [6341], [6342], [6343], [6344], [6345], [6346], [6347], [6349], [6350], [6351], [6352], [6354], [6355], [6356], [6357], [6359], [6360], [6361], [6362], [6366], [6370], [6372], [6373], [6374], [6376], [6377], [6378], [6379], [6380], [6381], [6383], [6387], [6388], [6389], [6391], [6393], [6394], [6395], [6396], [6397], [6398], [6399], [6400], [6401], [6402], [6404], [6405], [6406], [6407], [6408], [6409], [6410], [6412], [6414], [6416], [6417], [6418], [6419], [6420], [6422], [6425], [6426], [6430], [6431], [6432], [6433], [6435], [6437], [6439], [6443], [6444], [6445], [6446], [6448], [6449], [6450], [6451], [6455], [6457], [6459], [6461], [6462], [6463], [6464], [6466], [6467], [6468], [6470], [6471], [6473], [6476], [6478], [6479], [6480],

[6481], [6483], [6484], [6485], [6487], [6488], [6489], [6490], [6491], [6494], [6498], [6500], [6501], [6502], [6503], [6506], [6507], [6508], [6509], [6511], [6512], [6513], [6514], [6515], [6516], [6518], [6519], [6520], [6522], [6523], [6524], [6525], [6526], [6527], [6529], [6530], [6532], [6533], [6534], [6535], [6536], [6537], [6538], [6541], [6542], [6544], [6547], [6550], [6551], [6553], [6554], [6556], [6558], [6559], [6560], [6561], [6562], [6563], [6564], [6565], [6566], [6567], [6568], [6570], [6571], [6572], [6575], [6576], [6577], [6579], [6580], [6581], [6582], [6583], [6584], [6585], [6586], [6588], [6590], [6592], [6593], [6594], [6598], [6599], [6603], [6604], [6605], [6606], [6607], [6608], [6609], [6611], [6612], [6613], [6616], [6617], [6619], [6621], [6622], [6623], [6624], [6625], [6626], [6627], [6628], [6631], [6632], [6633], [6634], [6635], [6636], [6637], [6638], [6640], [6643], [6646], [6654], [6655], [6656], [6657], [6658], [6659], [6661], [6662], [6663], [6666], [6667], [6668], [6669], [6670], [6671], [6673], [6677], [6678], [6679], [6680], [6682], [6683], [6684], [6686], [6687], [6690], [6692], [6694], [6696], [6699], [6700], [6701], [6702], [6703], [6705], [6706], [6707], [6708], [6709], [6710], [6711], [6712], [6713], [6715], [6716], [6717], [6718], [6719], [6720], [6721], [6722], [6726], [6727], [6728], [6729], [6730], [6731], [6732], [6733], [6735], [6736], [6737], [6738], [6741], [6745], [6747], [6748], [6749], [6751], [6752], [6753], [6754], [6756], [6757], [6758], [6759], [6760], [6761], [6762], [6763], [6768], [6771], [6772], [6773], [6776], [6777], [6778], [6779], [6780], [6781], [6782], [6784], [6785], [6787], [6788], [6789], [6790], [6793], [6794], [6795], [6797], [6798], [6799], [6800], [6802], [6803], [6804], [6805], [6806], [6807], [6809], [6811], [6812], [6813], [6814], [6815], [6818], [6819], [6820], [6821], [6824], [6825], [6827], [6828], [6829], [6830], [6835], [6836], [6838], [6839], [6842], [6843], [6844], [6845], [6846], [6847], [6848], [6849], [6850], [6851], [6852], [6854], [6856], [6857], [6858], [6859], [6860], [6861], [6862], [6864], [6865], [6866], [6868], [6869], [6870], [6874], [6875], [6876], [6877], [6878], [6879], [6880], [6881], [6882], [6884], [6886], [6887], [6888], [6889], [6890], [6891], [6892], [6893], [6894], [6895], [6896], [6897], [6898], [6899], [6900], [6902], [6904], [6905], [6907], [6908], [6910], [6912], [6914], [6915], [6916], [6917], [6918], [6919], [6920], [6921], [6925], [6926], [6927], [6928], [6929], [6930], [6931], [6932], [6934], [6936], [6937], [6938], [6942], [6944], [6946], [6949], [6950], [6952], [6953], [6954], [6956], [6957], [6958], [6959], [6961], [6962], [6963], [6964], [6965], [6966], [6967], [6968], [6969], [6971], [6972], [6973], [6974], [6975], [6976], [6978], [6979], [6982], [6984], [6985], [6986], [6987], [6989], [6990], [6994], [6997], [6998], [6999], [7002], [7004], [7006], [7007], [7008], [7009], [7010], [7011], [7013], [7015], [7016], [7018], [7019], [7021], [7022], [7025], [7026], [7027], [7030], [7032], [7033], [7034], [7035], [7036], [7039], [7040], [7041], [7043], [7047], [7048], [7049], [7050], [7051], [7052], [7053], [7054], [7056], [7057], [7059], [7060], [7061], [7063], [7064], [7066], [7068], [7071], [7073], [7075], [7077], [7078], [7082], [7083], [7084], [7085], [7086],

[7088], [7091], [7093], [7097], [7098], [7099], [7100], [7101], [7102], [7104], [7110], [7111], [7113], [7115], [7116], [7117], [7118], [7119], [7121], [7123], [7126], [7127], [7130], [7132], [7134], [7136], [7137], [7138], [7140], [7141], [7142], [7143], [7146], [7147], [7148], [7149], [7150], [7152], [7157], [7158], [7159], [7161], [7162], [7164], [7165], [7166], [7167], [7174], [7175], [7176], [7177], [7178], [7182], [7183], [7184], [7187], [7188], [7190], [7191], [7192], [7193], [7194], [7196], [7197], [7198], [7199], [7200], [7201], [7203], [7205], [7207], [7210], [7213], [7215], [7216], [7217], [7218], [7221], [7223], [7224], [7227], [7228], [7230], [7231], [7233], [7234], [7236], [7238], [7240], [7241], [7242], [7243], [7244], [7245], [7247], [7249], [7251], [7253], [7255], [7256], [7259], [7260], [7261], [7262], [7264], [7271], [7275], [7276], [7277], [7280], [7284], [7285], [7286], [7287], [7289], [7290], [7295], [7296], [7298], [7299], [7300], [7301], [7302], [7304], [7306], [7308], [7310], [7311], [7312], [7314], [7315], [7316], [7318], [7321], [7324], [7325], [7326], [7329], [7330], [7331], [7332], [7333], [7334], [7339], [7341], [7344], [7345], [7346], [7347], [7349], [7350], [7353], [7356], [7357], [7358], [7359], [7360], [7361], [7362], [7364], [7367], [7368], [7369], [7370], [7371], [7372], [7373], [7374], [7377], [7380], [7381], [7383], [7384], [7387], [7389], [7391], [7393], [7394], [7395], [7397], [7398], [7399], [7401], [7402], [7403], [7405], [7406], [7408], [7410], [7411], [7413], [7414], [7415], [7419], [7421], [7422], [7423], [7424], [7425], [7427], [7428], [7429], [7431], [7432], [7435], [7437], [7438], [7440], [7443], [7444], [7445], [7447], [7448], [7449], [7450], [7452], [7453], [7454], [7456], [7457], [7458], [7462], [7463], [7465], [7468], [7469], [7472], [7473], [7475], [7477], [7479], [7480], [7483], [7484], [7486], [7487], [7488], [7490], [7491], [7493], [7494], [7496], [7497], [7498], [7500], [7503], [7504], [7506], [7507], [7510], [7513], [7514], [7515], [7516], [7517], [7518], [7520], [7521], [7522], [7524], [7525], [7526], [7528], [7529], [7531], [7533], [7534], [7535], [7537], [7539], [7540], [7541], [7542], [7543], [7544], [7545], [7546], [7548], [7550], [7551], [7553], [7555], [7557], [7558], [7559], [7561], [7562], [7563], [7564], [7566], [7568], [7569], [7570], [7571], [7572], [7573], [7575], [7578], [7579], [7580], [7582], [7583], [7584], [7586], [7587], [7588], [7589], [7590], [7592], [7593], [7594], [7595], [7597], [7598], [7599], [7600], [7605], [7608], [7609], [7610], [7611], [7614], [7616], [7617], [7618], [7619], [7620], [7622], [7623], [7624], [7626], [7627], [7628], [7629], [7630], [7631], [7632], [7633], [7635], [7636], [7637], [7638], [7640], [7641], [7642], [7644], [7646], [7649], [7650], [7653], [7655], [7656], [7657], [7658], [7659], [7660], [7661], [7662], [7663], [7664], [7665], [7666], [7667], [7669], [7670], [7671], [7672], [7673], [7676], [7678], [7679], [7681], [7682], [7683], [7685], [7687], [7688], [7689], [7690], [7692], [7694], [7696], [7697], [7698], [7700], [7702], [7703], [7704], [7705], [7707], [7711], [7712], [7716], [7717], [7718], [7721], [7722], [7723], [7725], [7726], [7727], [7728], [7731], [7732], [7733], [7734], [7736], [7737], [7738], [7739], [7743], [7744], [7746], [7747], [7748], [7749], [7751], [7753],

[7754], [7756], [7759], [7760], [7761], [7763], [7764], [7765], [7766], [7767], [7769], [7770], [7771], [7774], [7775], [7776], [7777], [7778], [7779], [7780], [7782], [7783], [7784], [7785], [7787], [7788], [7790], [7791], [7792], [7793], [7794], [7798], [7799], [7800], [7802], [7803], [7804], [7807], [7808], [7811], [7814], [7819], [7821], [7822], [7823], [7824], [7825], [7826], [7827], [7829], [7830], [7831], [7832], [7833], [7834], [7835], [7836], [7838], [7843], [7844], [7845], [7846], [7847], [7849], [7850], [7851], [7854], [7856], [7857], [7859], [7860], [7862], [7863], [7866], [7867], [7870], [7871], [7873], [7874], [7881], [7882], [7883], [7884], [7885], [7886], [7887], [7888], [7889], [7891], [7894], [7897], [7899], [7900], [7901], [7902], [7903], [7905], [7906], [7907], [7909], [7910], [7911], [7912], [7916], [7917], [7918], [7919], [7920], [7922], [7923], [7924], [7928], [7929], [7930], [7931], [7932], [7933], [7935], [7938], [7939], [7940], [7941], [7942], [7943], [7945], [7946], [7947], [7948], [7949], [7951], [7953], [7957], [7958], [7960], [7961], [7963], [7964], [7966], [7969], [7970], [7975], [7976], [7977], [7982], [7983], [7984], [7986], [7990], [7991], [7994], [7995], [7996], [7997], [7999], [8000], [8005], [8006], [8007], [8008], [8009], [8012], [8014], [8015], [8017], [8018], [8019], [8021], [8022], [8023], [8025], [8029], [8030], [8031], [8032], [8033], [8037], [8042], [8044], [8045], [8046], [8047], [8049], [8051], [8052], [8053], [8054], [8055], [8056], [8057], [8058], [8060], [8061], [8062], [8064], [8066], [8067], [8068], [8069], [8070], [8072], [8075], [8076], [8077], [8079], [8080], [8081], [8082], [8083], [8084], [8086], [8087], [8088], [8089], [8090], [8093], [8095], [8096], [8097], [8098], [8100], [8101], [8102], [8104], [8105], [8108], [8109], [8112], [8114], [8115], [8116], [8117], [8119], [8120], [8121], [8122], [8123], [8124], [8125], [8126], [8127], [8128], [8129], [8130], [8132], [8133], [8134], [8135], [8141], [8142], [8144], [8145], [8146], [8147], [8148], [8149], [8150], [8151], [8152], [8153], [8154], [8156], [8157], [8158], [8165], [8166], [8168], [8170], [8171], [8172], [8173], [8175], [8180], [8183], [8184], [8185], [8189], [8190], [8194], [8195], [8197], [8198], [8200], [8201], [8203], [8205], [8207], [8208], [8209], [8210], [8211], [8212], [8213], [8214], [8216], [8217], [8223], [8224], [8225], [8229], [8230], [8231], [8232], [8236], [8241], [8242], [8244], [8245], [8246], [8248], [8249], [8250], [8251], [8252], [8253], [8257], [8258], [8260], [8261], [8264], [8265], [8267], [8269], [8271], [8272], [8273], [8274], [8275], [8276], [8278], [8279], [8280], [8283], [8284], [8285], [8286], [8287], [8288], [8289], [8290], [8292], [8293], [8294], [8295], [8296], [8298], [8299], [8300], [8301], [8302], [8303], [8304], [8305], [8306], [8307], [8309], [8311], [8313], [8314], [8315], [8318], [8320], [8321], [8322], [8323], [8324], [8327], [8328], [8329], [8330], [8331], [8332], [8333], [8334], [8335], [8336], [8337], [8340], [8345], [8346], [8348], [8349], [8350], [8351], [8353], [8354], [8357], [8358], [8359], [8361], [8364], [8367], [8369], [8370], [8372], [8374], [8376], [8378], [8380], [8381], [8382], [8384], [8385], [8386], [8387], [8388], [8392], [8394], [8395], [8396], [8397], [8401], [8402], [8404], [8408], [8409], [8410], [8411], [8413],

[8414], [8415], [8416], [8417], [8419], [8420], [8421], [8422], [8423], [8425], [8426], [8428], [8429], [8430], [8434], [8435], [8439], [8440], [8442], [8443], [8444], [8445], [8447], [8448], [8449], [8450], [8451], [8456], [8458], [8459], [8460], [8461], [8462], [8464], [8465], [8466], [8467], [8468], [8470], [8472], [8473], [8475], [8476], [8477], [8478], [8479], [8485], [8486], [8488], [8489], [8490], [8491], [8492], [8496], [8497], [8501], [8502], [8503], [8505], [8507], [8508], [8509], [8511], [8512], [8513], [8515], [8517], [8518], [8519], [8524], [8525], [8526], [8527], [8529], [8530], [8531], [8532], [8533], [8534], [8536], [8541], [8542], [8546], [8547], [8548], [8550], [8551], [8552], [8553], [8555], [8556], [8557], [8560], [8561], [8563], [8564], [8565], [8567], [8570], [8571], [8572], [8576], [8577], [8579], [8580], [8581], [8582], [8583], [8584], [8589], [8590], [8591], [8592], [8594], [8595], [8596], [8597], [8599], [8600], [8601], [8602], [8603], [8604], [8606], [8609], [8611], [8612], [8613], [8614], [8615], [8616], [8617], [8619], [8620], [8621], [8622], [8623], [8624], [8625], [8626], [8627], [8628], [8629], [8631], [8632], [8633], [8635], [8638], [8639], [8640], [8642], [8643], [8644], [8646], [8647], [8648], [8649], [8650], [8651], [8652], [8653], [8657], [8658], [8662], [8663], [8664], [8665], [8666], [8668], [8669], [8670], [8672], [8673], [8675], [8676], [8677], [8678], [8682], [8683], [8684], [8685], [8686], [8688], [8689], [8691], [8692], [8693], [8694], [8696], [8697], [8699], [8700], [8701], [8702], [8703], [8708], [8709], [8711], [8712], [8713], [8714], [8715], [8717], [8719], [8720], [8721], [8723], [8724], [8725], [8726], [8727], [8730], [8737], [8739], [8740], [8743], [8744], [8746], [8747], [8750], [8751], [8753], [8754], [8755], [8756], [8759], [8760], [8761], [8762], [8764], [8766], [8768], [8769], [8770], [8771], [8773], [8774], [8775], [8776], [8777], [8779], [8780], [8781], [8782], [8785], [8786], [8787], [8788], [8789], [8790], [8792], [8794], [8795], [8800], [8802], [8806], [8807], [8808], [8810], [8811], [8813], [8814], [8815], [8816], [8820], [8821], [8823], [8824], [8825], [8826], [8828], [8829], [8830], [8831], [8832], [8833], [8834], [8835], [8836], [8837], [8838], [8839], [8840], [8841], [8843], [8844], [8846], [8848], [8850], [8852], [8854], [8855], [8856], [8857], [8859], [8862], [8863], [8864], [8865], [8866], [8867], [8869], [8871], [8874], [8875], [8877], [8881], [8882], [8883], [8884], [8885], [8888], [8889], [8892], [8893], [8894], [8895], [8896], [8897], [8902], [8903], [8906], [8907], [8909], [8911], [8912], [8913], [8914], [8915], [8917], [8919], [8920], [8921], [8923], [8924], [8926], [8929], [8931], [8932], [8933], [8935], [8936], [8937], [8938], [8939], [8942], [8943], [8944], [8946], [8947], [8948], [8950], [8951], [8952], [8953], [8955], [8957], [8958], [8959], [8960], [8962], [8963], [8965], [8966], [8967], [8968], [8969], [8970], [8973], [8974], [8975], [8976], [8977], [8979], [8980], [8982], [8983], [8984], [8985], [8986], [8987], [8988], [8989], [8990], [8993], [8994], [8995], [8996], [8997], [8998], [8999], [9000], [9002], [9003], [9004], [9005], [9008], [9009], [9010], [9012], [9013], [9014], [9016], [9017], [9018], [9019], [9020], [9021], [9022], [9024], [9025], [9026], [9027], [9028], [9030], [9033], [9035], [9037],

[9038], [9039], [9040], [9041], [9043], [9044], [9045], [9047], [9048], [9049], [9050], [9052], [9053], [9054], [9055], [9056], [9058], [9061], [9062], [9063], [9064], [9065], [9069], [9070], [9072], [9073], [9074], [9077], [9078], [9081], [9082], [9083], [9084], [9086], [9087], [9088], [9090], [9091], [9092], [9098], [9100], [9102], [9103], [9104], [9107], [9108], [9109], [9110], [9111], [9113], [9116], [9117], [9118], [9119], [9120], [9121], [9122], [9123], [9124], [9127], [9128], [9133], [9136], [9137], [9138], [9139], [9140], [9141], [9142], [9143], [9144], [9145], [9148], [9149], [9154], [9157], [9158], [9160], [9162], [9163], [9164], [9165], [9166], [9167], [9171], [9173], [9174], [9175], [9176], [9179], [9181], [9182], [9183], [9185], [9186], [9187], [9188], [9189], [9191], [9192], [9193], [9194], [9195], [9196], [9197], [9199], [9200], [9201], [9202], [9203], [9204], [9207], [9208], [9209], [9211], [9212], [9213], [9214], [9215], [9217], [9218], [9219], [9220], [9221], [9223], [9224], [9225], [9227], [9228], [9229], [9231], [9232], [9233], [9234], [9236], [9239], [9240], [9242], [9243], [9244], [9245], [9246], [9247], [9249], [9250], [9251], [9252], [9253], [9254], [9255], [9257], [9258], [9261], [9262], [9263], [9265], [9266], [9267], [9268], [9269], [9270], [9271], [9273], [9274], [9275], [9278], [9279], [9280], [9281], [9282], [9284], [9285], [9287], [9288], [9289], [9291], [9292], [9294], [9295], [9296], [9297], [9299], [9300], [9301], [9302], [9303], [9305], [9307], [9308], [9309], [9310], [9311], [9312], [9313], [9314], [9317], [9318], [9320], [9322], [9323], [9325], [9326], [9327], [9328], [9330], [9331], [9334], [9337], [9338], [9340], [9341], [9342], [9343], [9344], [9347], [9348], [9349], [9350], [9351], [9352], [9353], [9354], [9357], [9358], [9362], [9364], [9365], [9366], [9367], [9368], [9369], [9370], [9371], [9372], [9373], [9374], [9375], [9378], [9379], [9381], [9382], [9384], [9385], [9386], [9387], [9388], [9394], [9395], [9397], [9398], [9399], [9400], [9401], [9404], [9405], [9406], [9407], [9408], [9409], [9411], [9412], [9413], [9414], [9415], [9417], [9418], [9421], [9423], [9424], [9425], [9427], [9428], [9429], [9430], [9431], [9433], [9435], [9437], [9438], [9440], [9443], [9445], [9447], [9448], [9449], [9451], [9453], [9455], [9456], [9457], [9458], [9459], [9460], [9464], [9466], [9467], [9468], [9469], [9470], [9471], [9472], [9473], [9474], [9476], [9477], [9478], [9479], [9484], [9486], [9487], [9489], [9490], [9492], [9493], [9494], [9498], [9501], [9502], [9503], [9504], [9506], [9507], [9508], [9509], [9515], [9519], [9520], [9521], [9522], [9523], [9526], [9529], [9530], [9531], [9534], [9536], [9537], [9538], [9539], [9542], [9544], [9547], [9548], [9549], [9551], [9553], [9554], [9556], [9557], [9558], [9559], [9560], [9561], [9563], [9564], [9565], [9566], [9567], [9568], [9569], [9571], [9572], [9574], [9575], [9578], [9581], [9582], [9583], [9584], [9585], [9586], [9587], [9588], [9589], [9590], [9591], [9592], [9593], [9594], [9595], [9597], [9598], [9599], [9600], [9602], [9603], [9604], [9608], [9609], [9611], [9613], [9617], [9618], [9621], [9622], [9623], [9625], [9626], [9628], [9629], [9630], [9632], [9633], [9634], [9636], [9637], [9638], [9640], [9641], [9643], [9644], [9646], [9648], [9651], [9652], [9654], [9655], [9656],

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[19433], [19434], [19435], [19436], [19437], [19438], [19441], [19444], [19445], [19446], [19447], [19448], [19449], [19450], [19451], [19452], [19453], [19454], [19456], [19457], [19458], [19459], [19461], [19462], [19463], [19464], [19465], [19466], [19467], [19468], [19469], [19470], [19471], [19472], [19473], [19474], [19475], [19476], [19477], [19478], [19480], [19481], [19482], [19483], [19485], [19486], [19489], [19490], [19492], [19495], [19496], [19498], [19499], [19500], [19501], [19502], [19503], [19506], [19507], [19508], [19509], [19510], [19511], [19512], [19513], [19514], [19515], [19516], [19519], [19520], [19521], [19522], [19524], [19525], [19526], [19528], [19529], [19531], [19532], [19533], [19535], [19536], [19537], [19538], [19540], [19541], [19543], [19544], [19545], [19546], [19547], [19548], [19550], [19551], [19552], [19554], [19555], [19556], [19557], [19558], [19559], [19560], [19561], [19562], [19563], [19566], [19567], [19568], [19569], [19571], [19572], [19573], [19576], [19577], [19578], [19579], [19580], [19581], [19582], [19584], [19586], [19587], [19588], [19590], [19591], [19593], [19594], [19596], [19598], [19599], [19601], [19602], [19603], [19605], [19606], [19607], [19611], [19612], [19614], [19616], [19617], [19618], [19621], [19622], [19623], [19625], [19626], [19627], [19628], [19629], [19630], [19631], [19632], [19634], [19635], [19637], [19638], [19639], [19640], [19641], [19642], [19643], [19644], [19645], [19646], [19647], [19648], [19649], [19650], [19651], [19652], [19653], [19654], [19655], [19656], [19657], [19659], [19661], [19662], [19664], [19665], [19666], [19667], [19668], [19669], [19670], [19671], [19673], [19674], [19675], [19677], [19678], [19679], [19680], [19681], [19682], [19683], [19686], [19687], [19688], [19690], [19691], [19692], [19693], [19694], [19696], [19697], [19700], [19701], [19702], [19703], [19705], [19707], [19708], [19709], [19710], [19712], [19713], [19717], [19720], [19721], [19724], [19726], [19728], [19730], [19731], [19734], [19735], [19736], [19737], [19738], [19744], [19745], [19747], [19748], [19749], [19751], [19752], [19753], [19754], [19755], [19756], [19758], [19760], [19761], [19764], [19766], [19768], [19769], [19770], [19772], [19773], [19776], [19778], [19779], [19782], [19783], [19784], [19785], [19786], [19787], [19789], [19790], [19791], [19793], [19797], [19801], [19802], [19804], [19805], [19806], [19807], [19808], [19809], [19810], [19811], [19812], [19813], [19816], [19817], [19818], [19819], [19821], [19823], [19824], [19825], [19827], [19829], [19830], [19833], [19835], [19836], [19837], [19838], [19839], [19841], [19842], [19843], [19844], [19845], [19846], [19847], [19848], [19849], [19851], [19852], [19853], [19854], [19855], [19856], [19858], [19860], [19861], [19862], [19863], [19864], [19865], [19866], [19867], [19868], [19869], [19870], [19871], [19872], [19873], [19874], [19875], [19876], [19877], [19878], [19879], [19880], [19881], [19882], [19883], [19884], [19885], [19886], [19887], [19888], [19889], [19890],

[19892], [19893], [19894], [19896], [19897], [19898], [19899], [19902], [19903], [19904], [19905], [19906], [19907], [19908], [19909], [19910], [19911], [19912], [19913], [19914], [19915], [19916], [19917], [19918], [19920], [19922], [19924], [19926], [19927], [19929], [19930], [19931], [19932], [19933], [19935], [19936], [19937], [19939], [19942], [19943], [19944], [19949], [19950], [19952], [19954], [19955], [19959], [19962], [19963], [19964], [19965], [19967], [19969], [19970], [19971], [19973], [19975], [19977], [19982], [19983], [19984], [19985], [19986], [19988], [19989], [19990], [19991], [19992], [19993], [19994], [19995], [19996], [19997], [19998], [19999], [20000], [20001], [20002], [20003], [20005], [20007], [20009], [20010], [20012], [20015], [20016], [20017], [20019], [20021], [20022], [20023], [20025], [20028], [20030], [20031], [20032], [20033], [20039], [20041], [20042], [20043], [20044], [20045], [20046], [20047], [20048], [20051], [20052], [20054], [20055], [20056], [20057], [20058], [20059], [20060], [20061], [20062], [20063], [20064], [20065], [20066], [20067], [20068], [20070], [20071], [20072], [20073], [20074], [20075], [20076], [20077], [20078], [20079], [20080], [20082], [20083], [20084], [20085], [20086], [20087], [20088], [20089], [20094], [20095], [20096], [20098], [20099], [20100], [20101], [20102], [20103], [20104], [20105], [20106], [20107], [20108], [20109], [20112], [20114], [20115], [20116], [20117], [20118], [20119], [20120], [20122], [20123], [20124], [20125], [20126], [20127], [20128], [20129], [20130], [20132], [20133], [20135], [20136], [20137], [20141], [20142], [20143], [20144], [20146], [20147], [20148], [20149], [20151], [20152], [20153], [20157], [20158], [20159], [20160], [20161], [20162], [20163], [20164], [20165], [20166], [20167], [20168], [20169], [20170], [20171], [20172], [20173], [20174], [20175], [20177], [20178], [20179], [20180], [20182], [20183], [20184], [20185], [20186], [20187], [20188], [20189], [20190], [20191], [20193], [20195], [20197] — ΣN=74186235

1) Introduction

Statins, inhibitors of HMG-CoA reductase, are foundational in the management of hyperlipidemia and the prevention of atherosclerotic cardiovascular disease (ASCVD). Beyond their primary lipid-lowering effects, emerging research continues to explore their pleiotropic actions across diverse physiological systems, including potential roles in oncology, neurological health, and immune modulation. This paper synthesizes recent findings regarding statin efficacy, safety, adherence, and novel applications, highlighting both established benefits and areas requiring further investigation.

2) Aim

The aim of this paper is to systematically review and synthesize current scientific literature on statin therapy, focusing on its broad clinical impact, identified benefits, adverse effects, and future research directions.

3) Methods

Systematic review with multilayer AI research agent: keyword normalization, retrieval & structuring, and paper synthesis (see SAIMSARA About section for details).

- **Bias:** Qualitatively inferred from study design fields.

4) Results

4.1 Study characteristics

The included studies comprise a diverse range of designs, primarily retrospective and prospective cohort studies, randomized controlled trials (RCTs), and case-control studies. Populations investigated include UK Biobank participants, patients with Parkinson's disease (PD), various cancer types, individuals with diabetes mellitus (DM), and those with statin intolerance, among others. Follow-up periods varied widely, from 30 days post-randomization in acute settings to lifetime horizons in cost-effectiveness analyses.

4.2 Main numerical result aligned to the query

Statin therapy, often in combination with other lipid-lowering agents, demonstrates significant efficacy in reducing low-density lipoprotein cholesterol (LDL-C) levels. Across studies reporting percentage LDL-C reduction, the median observed decrease was 45.25%, with a range from 33% to 56.2% [4925, 5326, 7473, 10613, 11098, 18927]. For instance, inclisiran combined with statin therapy showed a placebo-adjusted mean LDL-C reduction of 33.3% [4925] and 47.5% [10613], while lerodalcibep with statins achieved a 56.2% reduction [7473]. Atorvastatin monotherapy reduced LDL-C by 43% [11098].

4.3 Topic synthesis

- **Cardiovascular Disease Prevention and Outcomes:**
 - Reduced risk of all-cause mortality in Parkinson's disease (HR 0.600, 95% CI 0.521-0.691) [8].
 - Reduced risk of hospitalization for heart failure (OR=0.71, 95% CI: 0.60-0.83) and in-hospital mortality (OR=1.43, 95% CI: 1.10-1.86) in acute heart failure (AHF) patients [349].
 - Lower risk of incident stroke (adjusted HR, 0.80) regardless of air pollutant exposure [256].

- Reduced risk of major adverse cardiovascular events (MACE) in high-risk diabetic patients inadequately controlled with statins alone, with PCSK9 inhibitors (HR: 0.41; 95% CI: 0.17-0.98) [2381].
- Improved primary patency (87.3% vs. 75.8%) in femoropopliteal lesions with drug-eluting/coated stents [259].
- Reduced 90-day venous thromboembolism (VTE) events (0.43% vs. 1.13%) after total hip arthroplasty (THA) [297].
- Preoperative high-dose rosuvastatin conferred cardioprotection, reducing postoperative atrial fibrillation (AF) (8% vs. 24%) in chronic statin users undergoing off-pump coronary artery bypass grafting (OPCABG) [72].
- Statin use associated with a lower risk of acute limb ischemia (ALI) (HR 0.7, 95% CI 0.5-0.9) [14435].
- Statin therapy associated with lower 1-year and overall mortalities in patients with myocardial injury after noncardiac surgery (MINS) (1-year mortality: 6.1% vs 13.3%, HR 0.55) [2319].
- Statin use was protective against 30-day all-cause mortality (OR = 0.27, 95% CI [0.10-0.74]) in patients undergoing common vascular procedures [15621].
- Preoperative statin use was protective against 5-year mortality in patients undergoing carotid endarterectomy (CEA) for asymptomatic stenosis ($P < .001$) [11574].
- Statin use was associated with decreased risk of all-cause mortality ($P < .001$) in patients undergoing renal artery (RA) stent placement [16254].
- Statin therapy was associated with a reduction in all-cause mortality (HR = 0.78, 95% CI 0.68-0.89) following transcatheter aortic valve implantation (TAVI) [3155].
- Statin therapy was associated with reduced ischemic heart disease (IHD) risk in pre-dialysis chronic kidney disease (CKD) patients [3562].
- Statin use was associated with a lower risk of incident stroke among adults aged 60 years and older [256].
- Statin use was associated with significantly lower rates of non-fatal myocardial infarction (MI) and fewer revascularizations in ischemic heart disease (IHD) patients [954].
- Statin use was associated with a reduced risk of major adverse limb events (MALEs) (OR, 0.8; 95% CI, 0.62-0.99) in patients undergoing lower extremity revascularization for critical limb ischemia (CLI) [17237].
- Statin use was associated with decreased risk of long-term death after cephalad arteries percutaneous transluminal angioplasty with stent implantation [18697].
- Statin use was protective against cardiovascular mortality after thoracic endovascular aortic repair (TEVAR) for aortic arch disease (HR 0.11, 95% CI 0.02-0.66) [14265].
- Statin use was a negative independent determinant of the progression of coronary calcification in postmenopausal women ($p = 0.015$) [18280].

- A 10.2% 10-year cardiovascular (CV) risk threshold for statin prescription in Germany could avoid 271,739 to 581,363 CV events over 10 years, with net population savings of €15 billion [182].

- **Cancer Outcomes:**

- Post-diagnosis statin use appears to confer a 10% to 25% improvement in overall survival across gynecologic malignancies [48].
- Statin-dye conjugates selectively killed KRAS mutant pancreatic cancer cells [16].
- Statin use significantly improved survival and decreased liver-related outcomes (all-cause mortality reduction: 19%; liver-related mortality reduction: 37%) in metabolic dysfunction-associated steatotic liver disease (MASLD) patients [64].
- Statin therapy associated with improved overall (90.5 months vs. 59.9 months) and recurrence-free survival (77.3 vs. 48.1 months) in patients undergoing hepatectomy for intrahepatic cholangiocarcinoma (ICC) [140].
- Statin therapy may confer beneficial effects on clinical outcomes in female breast cancer patients, including reduced all-cause mortality (HR 0.8583), breast cancer-specific mortality (HR 0.8183), and recurrence (HR 0.7911) [1353].
- Statin use correlates with improved outcomes in lung adenocarcinoma (LUAD) brain metastasis (BM) patients [1634].
- Statin use was associated with decreased colorectal cancer (CRC) risk [2092].
- Statin use was associated with a reduced risk of hepatocellular carcinoma (HCC) (aHR 0.43) in patients with chronic hepatitis B [2096, 12570].
- Statin therapy was linked to a decreased risk of developing colonic polyps [2269].
- Statin use was associated with reduced liver growth in polycystic liver disease (PLD) patients [1859].
- Statin use was associated with a significantly lower incidence of esophageal adenocarcinoma (EAC) (OR 0.52, 95% CI 0.27-0.92) [6649].
- Statin users had significantly improved overall survival (HR 0.72, 95% CI 0.53-0.97) in gastric cancer treatment [8847].
- Statin use was associated with a complete response to neoadjuvant chemoradiation therapy in rectal cancer patients (OR 2.45, p=0.049) [8106].

- **Adverse Effects and Intolerance:**

- Continuous statin use was associated with a decline in muscle function and mass over time (baseline grip strength β = -0.68 kg; decline in grip strength β = -0.32 kg/year) [5].
- Statin use is associated with increased risks of ocular hypertension (aOR = 1.12, 95% CI, 1.09-1.15) and primary open-angle glaucoma (POAG) (aOR = 1.07, 95% CI, 1.04-1.11) [31].
- The HLA-DRB1*11 allele was strongly associated with anti-HMGCR immune-mediated necrotizing myopathy (IMNM) (OR = 13.5, 95% CI 1.73-15.3) [13].

- Statin-associated IMNM is significantly more common in Native Americans in the American Southwest [57].
- Coenzyme Q10 supplementation was associated with improved control of statin-associated muscle symptoms (SAMS) [32].
- Statin exposure was associated with an increased risk of skin cancer (adjusted OR 1.71, 95% CI 1.67-1.75) in Korea [106].
- Statin use was associated with a higher risk of low birth weight (OR 2.42) in pregnant women with familial hypercholesterolemia (FH) [243].
- A statistically significant disproportionality signal indicates a possible association between statin use and tubulointerstitial nephritis (TIN) [178].
- Atorvastatin had the strongest association with diabetes-related adverse events among different statin drugs (Reporting Odds Ratio (ROR) of 36.70) [186].
- Statin use was associated with greater cortical thickness in multiple brain regions across healthy controls, mild cognitive impairment (MCI), and Alzheimer's disease (AD) participants [208].
- Statin use may increase the risk of intracerebral hemorrhage (ICH) (HR = 1.18) in Chinese patients without a history of ICH [252].
- Statin use was associated with a higher likelihood of developing CKD stages 3-5 (44.3% for high intensity) in patients with type 2 diabetes mellitus (T2DM) [1326].
- Statin use was associated with an increased risk of hospitalization due to cardiovascular or cerebrovascular events among people with dementia (HR = 1.06) [40].
- Statin use was identified as a significant risk factor for developing diabetic retinopathy (DR) (AOR = 4.19, P < 0.001) in type 2 diabetes mellitus (T2DM) patients [1167].
- Statin treatment for hypercholesterolemia is potentially related to the development of lateral epicondylitis (LE) [5741].
- Statin therapy was the only significant risk factor for progression from normoglycemia to prediabetes or type 2 diabetes mellitus (DM II) in ischemic stroke patients [5353].
- Statin use was associated with increased graft rejection (OR 1.40, 95% CI [1.02-1.93]) in adult liver transplant (LT) recipients [712].
- **Adherence and Prescription Patterns:**
 - Adherence to statin therapy remains suboptimal (pooled prevalence of good adherence: 62.4%) and is significantly influenced by demographic and clinical factors [53].
 - A significant gap exists between guideline recommendations and real-world prescribing patterns for statin therapy in type 1 diabetes mellitus (T1DM) patients, particularly younger individuals with additional cardiovascular disease (CVD) risk factors [103].
 - LDL-C target attainment is low in patients with statin intolerance (15.8% in total cohort), especially among women (11.4%) [202].

- Adherence to statin therapy improves with subsequent treatment sequences and age, with younger patients showing lower adherence [211].
- Low utilization rate of statin therapy for primary prevention of CVD among patients prior to their first ST-segment elevation myocardial infarction (STEMI) (15.8%) [293].
- Suboptimal LDL-C control and low guideline adherence (only 5.6% meeting goals) in countries with high/very high CV risk [3649].
- Women with peripheral arterial disease (PAD) or ischemic cerebrovascular disease (ICVD) had lower odds of receiving any statins, high-intensity statins (HIS), or being statin adherent compared to men [2086].
- The overall use of high-intensity statins remained low among Korean individuals with type 2 diabetes mellitus and cardiovascular disease [4291].
- Statin use was common among practicing physicians in India (42.3%), but suboptimal adherence to preventive monitoring was evident [2930].
- Adherence to statin therapy was lower for individuals with opioid use disorder (OUD) (70.4%) compared with individuals without OUD (76.7%) [13129].
- Statin prescribing was initially 10-fold higher and later threefold higher than SGLT2 inhibitor prescribing in elderly T2DM patients [8475].
- Females with type 2 diabetes mellitus were less often prescribed statin treatment compared to males (19.7% vs. 24.7%) [8329].
- Statin intake was significantly lower in Ukraine (67.1%) compared to Switzerland (87.3%) and Poland for acute ischemic stroke patients [8688].
- **Novel and Adjunctive Therapies:**
 - Combination of moderate-intensity statin and ezetimibe is evaluated for long-term efficacy and safety compared with high-intensity statin monotherapy [56].
 - The combination of ezetimibe, inclisiran, and bempedoic acid may serve as a safe and effective therapeutic option in patients with severe statin intolerance [130].
 - Moderate-intensity statin plus ezetimibe may be a possible primary treatment to achieve LDL-C targets across several populations, offering considerable efficacy and better safety [469].
 - Adding evolocumab to statin + ezetimibe therapy in coronary artery bypass grafting (CABG) patients significantly reduced major cardiovascular events (HR 0.38) and improved lipid levels [1065].
 - Inclisiran is predicted to significantly reduce low-density lipoprotein cholesterol (49.7%) and major adverse cardiovascular events (25.2%) when used as an adjunct to high-intensity statin therapy [2226].
 - Ezetimibe was associated with lower stroke recurrence (6.3% vs. 17.9%) and statin side effects, and a higher rate of achieving recommended LDL-C levels (81.0% vs. 48.4%) compared to statins in acute ischemic stroke patients with SLCO1B1 variants [2242].

- PCSK9 inhibitors combined with statin therapy significantly decreased percent atheroma volume and total atheroma volume compared to statin therapy alone [2773].
- Evolocumab on a background of statin reduced LDL-C levels significantly and lowered the incidence of recurrent cerebrovascular events [3869].
- Lerodalcibep significantly reduced LDL-C (56.2%) in patients with CVD or at high risk of atherosclerotic cardiovascular disease [7473].
- PCSK9 inhibitors were associated with a significant reduction in all-cause death and a lower risk of hospitalization in eligible patients [5439].
- Early combination therapy with a high-intensity statin and ezetimibe achieved recommended LDL-C targets in most STEMI patients [8167].
- Inclisiran provided sustained reductions in LDL cholesterol (47.5%) and PCSK9 concentrations and was well tolerated over 4 years in patients with high cardiovascular risk and elevated LDL cholesterol [10613].
- Ezetimibe is an effective LDL cholesterol-lowering agent in the kidney transplant population, and it was more effective when used in combination with a statin [18927].
- **Pharmacogenetics and Biomarkers:**
 - SLCO1B1 variation did not significantly affect LDL-C reduction, statin-associated muscle symptom occurrence, or statin adherence [34].
 - 11% of the Indian population exhibit decreased or poor function of SLCO1B1, necessitating adjustments in statin doses to minimize the risk of statin-induced myopathy [245].
 - APOE ε4 genotype increases mortality risk, including in statin-treated patients [232].
 - Pharmacogenomic variants and demographic factors like ethnicity and gender influence statin-associated adverse effects, with increased risks of liver enzyme elevation for rosuvastatin users with ABCG2 variant and SAMS for atorvastatin users with SLCO1B1 variant [1019].
 - Risk-weighted apoB (RW-apoB) improved coronary heart disease (CHD) risk prediction, especially in statin-treated subjects [2230].
 - Lipoprotein(a) [Lp(a)] and LDL-C levels are independently and additively associated with ASCVD risk, and LDL-C lowering does not fully offset Lp(a)-mediated risk [1764].
 - The lipid-lowering efficacy of rosuvastatin is significantly affected by the polymorphisms of SLCO1B1, ApoE and ABCG2 genes [2099].
 - Lp(a) ordering is low in patients with or at risk for ASCVD, and non-Hispanic Black and Hispanic patients are less likely to have an Lp(a) order, despite higher median Lp(a) levels [5911].
- **Other Clinical Applications:**
 - Statin use was associated with a lower risk of developing inflammatory bowel disease (IBD) (aHR: 0.84) [67].

- Statin use was associated with a reduced risk of post-stroke dementia (PSD) (HR 0.86, CI = 0.79-0.92) [5812].
- Statin use was associated with beneficial bone health effects, specifically a slower decline in vertebral bone mineral density [637].
- Statin use was associated with a lower depression risk (Pooled OR: 0.84, 95% CI: 0.74-0.96) [142].
- Statin use was a protective factor against primary arteriovenous access failure in hemodialysis patients [1165].
- Statin use was associated with decreased aneurysm wall enhancement (AWE) of fusiform intracranial aneurysms (FIAs) [4099].
- Statin use was associated with a significantly lower hazard ratio for developing exophthalmos (HR = 0.559) and reduced hazards for diplopia and optic nerve surgery in Graves' disease patients [977].
- Statin use was associated with lower odds of worse hearing (odds ratio = 0.46) in Meniere's disease patients [2054].
- Statin use was associated with lower in-hospital mortality in sepsis patients [1241].
- Statin use was associated with a reduced risk of 60-day mortality (HR 0.54) in patients with severe influenza [6150, 6182].
- Statin use was found to be protective for tricuspid regurgitation (TR) progression [9733].
- Statin use was associated with a lower rate of brain-heart interaction (BHI) in patients with acute severe stroke [15372].
- Statin use was associated with a decrease in intracerebral hemorrhage (ICH) volume in primary infratentorial ICH [16202].
- Statin use was associated with reduced venous thrombosis (OR 0.45, 95% CI 0.36-0.56) [19116].
- **Healthcare Utilization and Cost-Effectiveness:**
- Statin treatment reduces individual rates of hospital inpatient services and medication prescriptions but increases overall healthcare use driven by increased longevity and ageing [52].
- AI-based clinical decision support (CDS) improved cardiovascular risk assessment and statin prescription by general practitioners in resource-constrained settings [2198].
- A 10.2% 10-year CV risk threshold for statin prescription in Germany could generate substantial cost savings [182].
- Pharmacist referrals were associated with a substantial increase in statin prescriptions [201].
- Full implementation of guideline-recommended therapies, including statins, would be cost-saving or highly cost-effective for acute ischemic stroke (AIS) prevention in T2D [1160].

- A pharmacist-led intervention to increase adherence to statin and antihypertensives medications was estimated to prevent 170,000 CVD DALYs by 2040 [7693].

5) Discussion

5.1 Principal finding

The central finding of this review is the consistent efficacy of statin therapy, often in combination with other lipid-lowering agents, in achieving substantial reductions in LDL-C levels, with a median reduction of 45.25% across various studies [4925, 5326, 7473, 10613, 11098, 18927]. This underscores their critical role in lipid management and cardiovascular risk reduction.

5.2 Clinical implications

- **Enhanced LDL-C Reduction:** For many patients, especially those at high or very high cardiovascular risk, combination therapy with statins and agents like ezetimibe or PCSK9 inhibitors is crucial to achieve recommended LDL-C targets [469, 1065, 2226, 2381, 3266, 3869, 7030, 7473, 8167, 10613, 18927].
- **Personalized Risk Assessment:** Genetic factors (e.g., APOE ε4, SLCO1B1, ABCG2) and biomarkers (e.g., Lp(a), OxPL-apoB, RW-apoB) should be increasingly considered to refine ASCVD risk estimation and tailor statin therapy, particularly in statin-intolerant or high-risk populations [232, 245, 1019, 1764, 2091, 2099, 2230, 2441, 5100, 5598, 5911, 6778, 9738].
- **Addressing Adherence Gaps:** Suboptimal statin adherence remains a significant challenge, particularly in primary prevention, younger patients, women, and specific ethnic groups, necessitating targeted interventions like pharmacist-led programs and AI-based decision support to improve prescription and persistence [53, 103, 201, 202, 211, 2085, 2086, 2930, 3690, 4271, 4285, 507, 5503, 6113, 6305, 6668, 7693, 8190, 8329, 8688, 11919, 12259, 12336, 12425, 12782, 13129, 13583, 16390, 16600, 16738, 18230, 19198].
- **Broader Therapeutic Potential:** Statins demonstrate protective effects beyond lipid lowering, including reduced mortality in Parkinson's disease [8], improved cancer outcomes [48, 140, 1353, 1634, 2096, 2269, 8106, 8847], decreased risk of inflammatory bowel disease [67], and reduced post-stroke dementia [5812], suggesting diverse clinical utility.
- **Managing Adverse Effects:** Awareness of potential adverse effects such as muscle symptoms (IMNM, SAMS) [5, 13, 32, 57, 1019, 1203, 2040, 2045, 2441, 4919, 5074], ocular hypertension/glaucoma [31], and increased risk of diabetes [186, 11683, 5353] is crucial for patient monitoring and personalized treatment strategies.

5.3 Research implications / key gaps

- **Long-Term Outcomes in Specific Cancers:** Further prospective studies are needed to confirm the long-term survival benefits of statins across various gynecologic malignancies [48], intrahepatic cholangiocarcinoma [140], and breast cancer [1353, 2076, 2220], and to elucidate underlying mechanisms.
- **Mechanisms of Adverse Effects:** Research is warranted to fully understand the mechanisms of statin-associated muscle decline [5, 2045], ocular risks [31], and the increased risk of type 2 diabetes [186, 11683, 5353], including the role of genetic predispositions [13, 57, 1019, 245, 2099].
- **Optimal Combination Therapies:** RCTs are needed to define optimal combination strategies for statins with novel lipid-lowering agents (e.g., ezetimibe, PCSK9 inhibitors, bempedoic acid) across diverse patient populations and risk profiles, focusing on both efficacy and long-term safety [56, 130, 469, 1065, 2226, 2381, 2773, 3212, 3486, 3869, 4368, 7030, 7473, 8167, 9651, 10105, 10613, 1292, 16353].
- **Impact on Neurological and Cognitive Health:** More research is required to clarify the complex relationship between statin use and cognitive function, including its impact on cortical thickness [208], dementia risk [2071, 5812, 1220], and intracerebral hemorrhage [252, 10859, 16202], especially in vulnerable populations.
- **Real-World Effectiveness and Implementation:** Studies focusing on real-world adherence and the effectiveness of implementation strategies (e.g., AI-based tools, pharmacist interventions) are needed to translate guideline recommendations into improved patient outcomes across diverse healthcare settings and demographic groups [201, 2198, 2085, 6113, 6305, 7693, 11919, 12259, 16317].

5.4 Limitations

- **Heterogeneity of Study Designs** — The diverse study designs (cohort, RCT, case-control, mixed) limit direct comparability and meta-analysis of outcomes.
- **Variability in Statin Regimens** — Differences in statin type, intensity, and concomitant therapies make it challenging to isolate the specific effects of statin monotherapy.
- **Diverse Patient Populations** — Studies span a wide range of ages, comorbidities, and ethnicities, which may affect generalizability of findings to specific patient groups.
- **Reliance on Observational Data** — Many reported associations are from observational studies, which cannot establish causality and are prone to confounding.
- **Inconsistent Follow-up Durations** — Follow-up periods vary significantly, impacting the assessment of long-term effects and rare adverse events.

5.5 Future directions

- **RCTs for Combination Therapies** — Conduct large-scale RCTs comparing novel statin-based combination therapies against high-intensity statin monotherapy for long-term cardiovascular and non-cardiovascular outcomes.
- **Pharmacogenomic-Guided Prescribing** — Implement prospective studies evaluating the efficacy and safety of statin therapy guided by pharmacogenomic testing (e.g., SLCO1B1, ABCG2, APOE) in diverse populations to personalize dosing and minimize adverse effects.
- **Real-World Adherence Interventions** — Develop and test scalable interventions (e.g., digital health tools, pharmacist-led programs) to improve long-term statin adherence and persistence in underserved and high-risk populations.
- **Mechanistic Studies on Pleiotropic Effects** — Investigate the molecular mechanisms underlying statins' non-lipid-lowering effects in cancer, neurological health, and inflammation through preclinical and translational research.
- **Cost-Effectiveness in Diverse Settings** — Perform comprehensive cost-effectiveness analyses of statin-based therapies, including combination regimens, across different healthcare systems and income levels to inform policy decisions.

6) Conclusion

This systematic review highlights the multifaceted impact of statin therapy, primarily driven by its potent LDL-C lowering capabilities, with a median reduction of 45.25%. Beyond cardiovascular protection, statins demonstrate promising effects in various cancers, neurological conditions, and inflammatory diseases, while also presenting challenges related to adherence and adverse effects. A notable limitation is the heterogeneity of study designs, which often precludes direct comparisons. Moving forward, a key research implication is the need for rigorous RCTs and real-world studies to optimize combination therapies and implement personalized, pharmacogenomic-guided prescribing strategies to maximize patient benefit and address existing gaps in care.

References

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Figure 1. Publication-year distribution of included originals

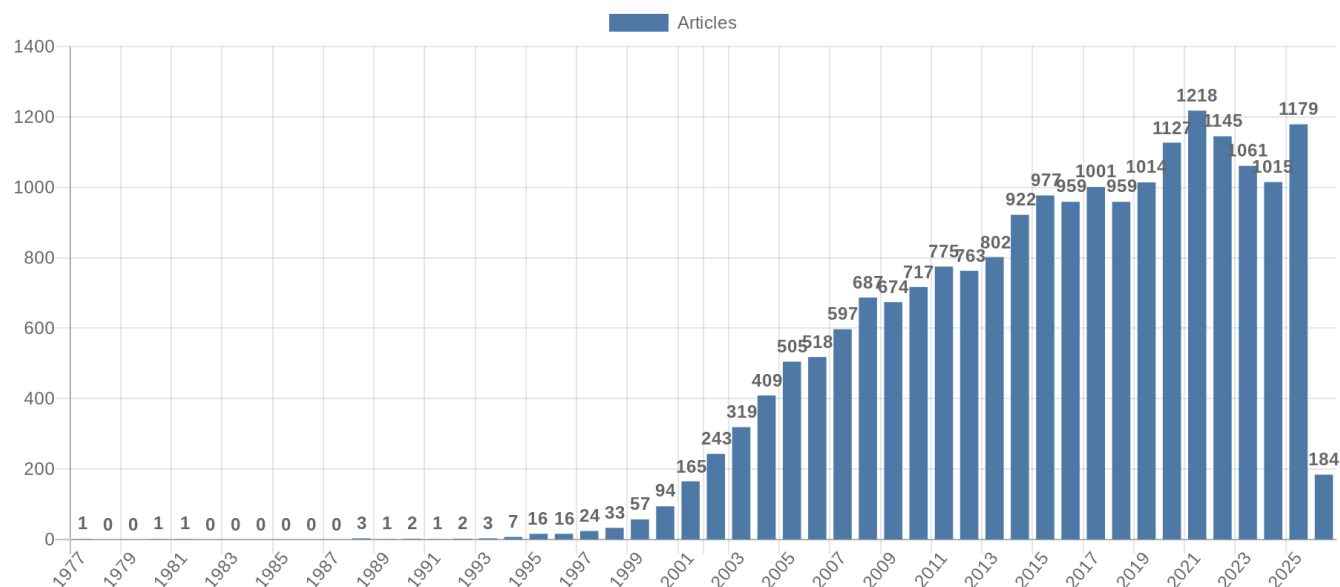


Figure 2. Study-design distribution of included originals

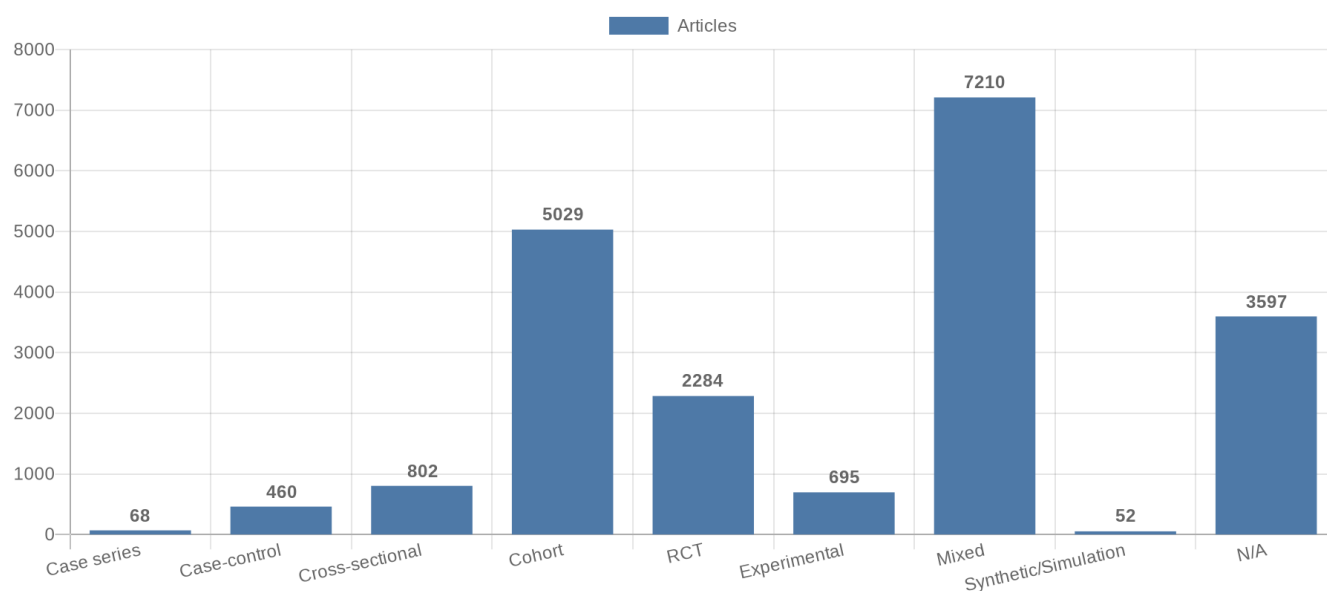


Figure 3. Study-type (directionality) distribution of included originals

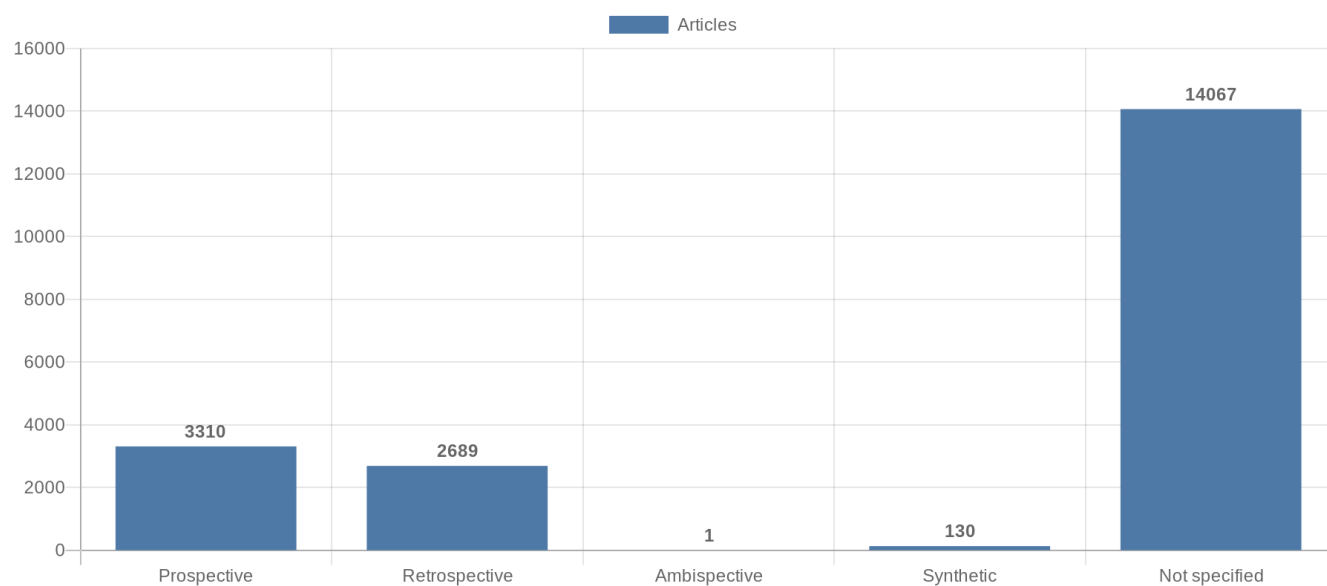


Figure 4. Main extracted research topics

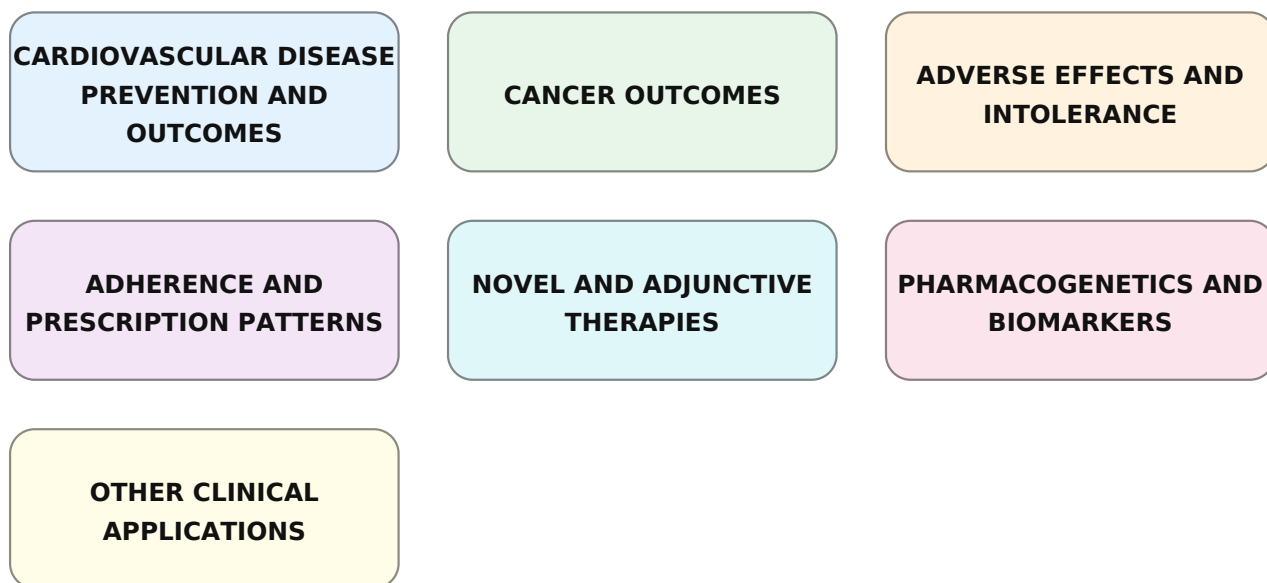


Figure 5. Limitations of current studies (topics)

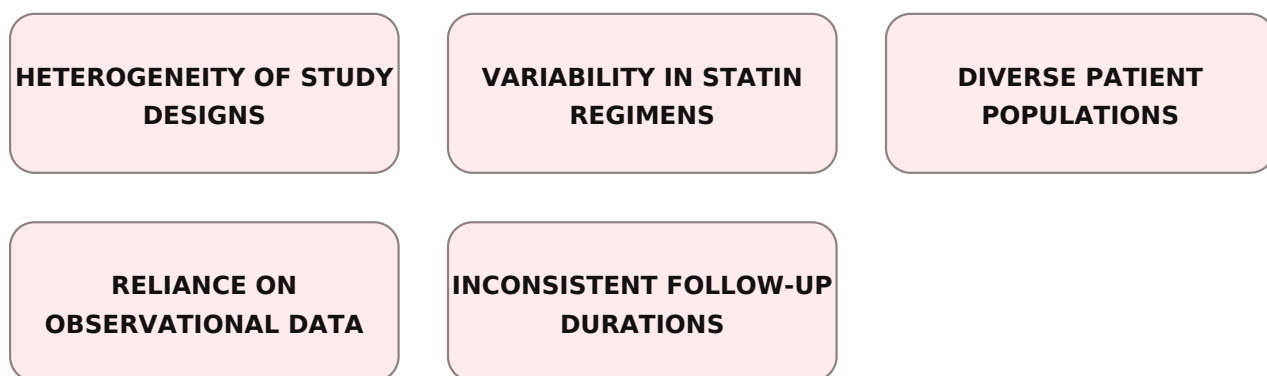


Figure 6. Future research directions (topics)

