Acute Limb Ischemia: Systematic Review with ☸SAIMSARA.

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Abstract: This paper aims to systematically review and synthesize findings from recent scientific literature on acute limb ischemia, utilizing a multilayer AI research agent for keyword normalization, retrieval, structuring, and paper synthesis. The review utilises 2322 studies with 2528510 total participants (naïve ΣN). The 30-day mortality rate for acute limb ischemia patients ranged from 3% to 35.1%, with a median of 9.1% across various studies reporting this metric. This wide range underscores the critical nature of ALI and the variability in outcomes. Generalizability is limited by the heterogeneity of study designs and populations, with the reliance on retrospective data being the most significant limitation affecting certainty. Clinicians should prioritize early diagnosis and individualized treatment, recognizing the high risks in vulnerable populations, while future research focuses on large-scale comparative effectiveness trials and biomarker-guided personalized medicine.

Keywords: Acute Limb Ischemia; Revascularization; Limb Salvage; Amputation; Thrombolysis; Thrombectomy; Aortic Dissection; Compartment Syndrome; Prognostic Factors; Endovascular Therapy

Review Stats

- Generated: 2026-02-13 22:18:30 CET
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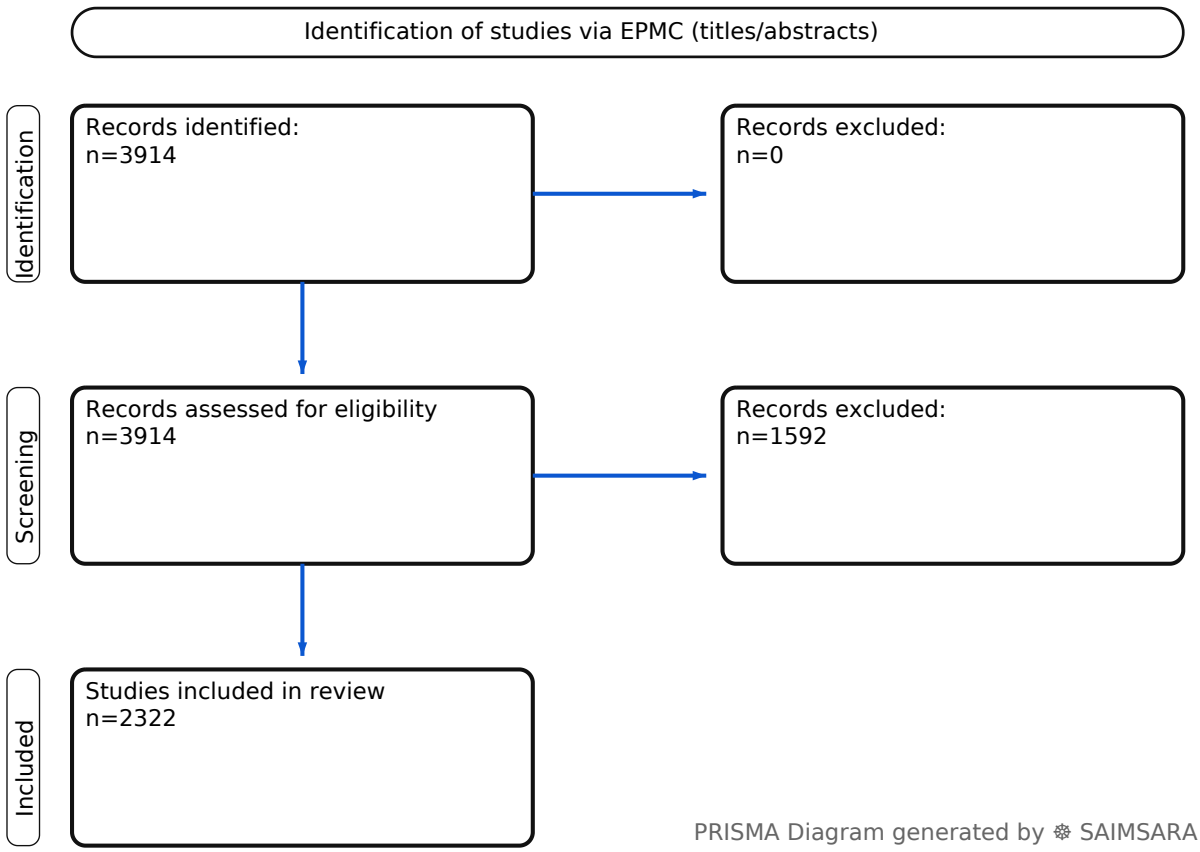
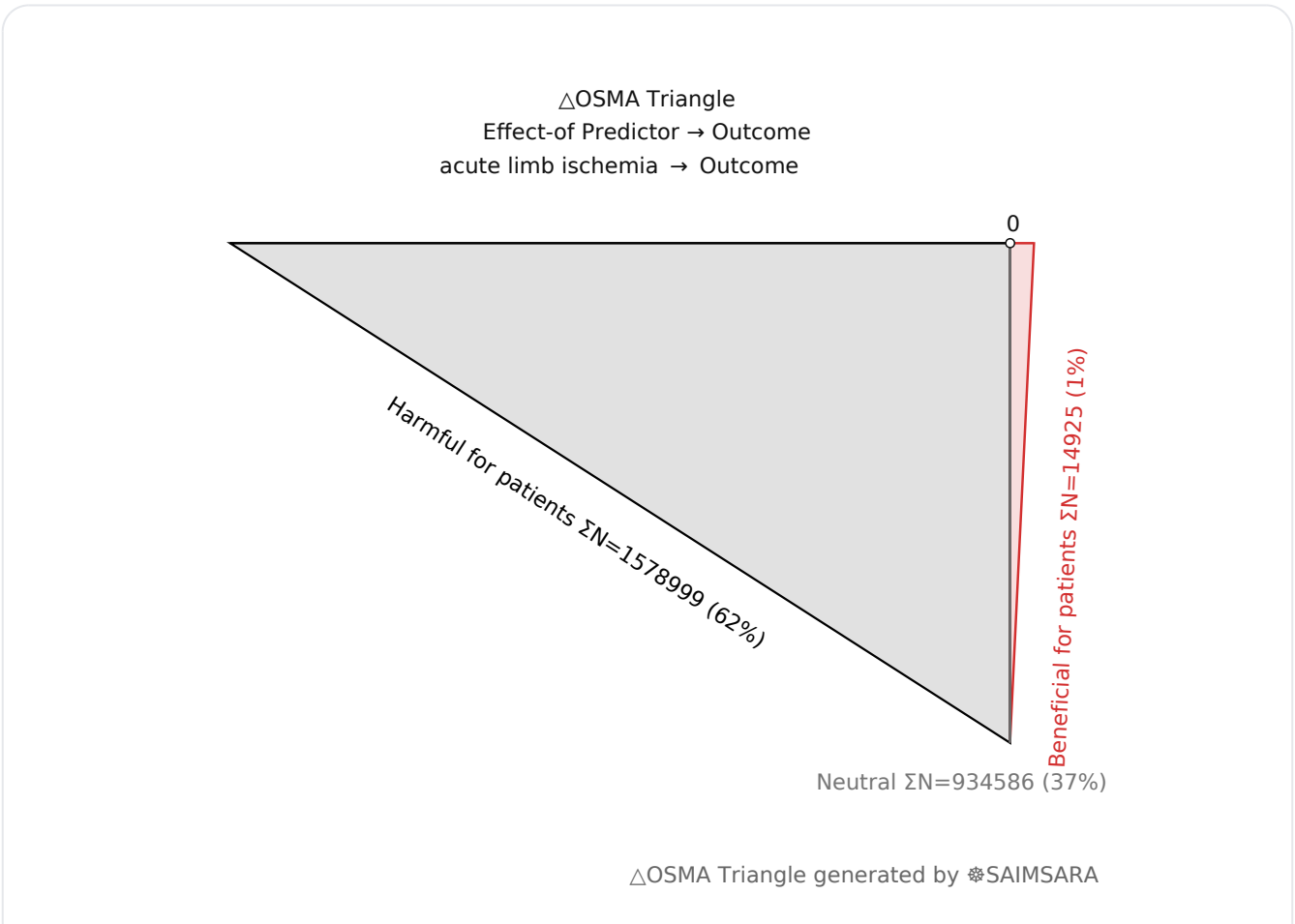
- Source: Europe PMC
- Scope: Titles/Abstracts (tiab)
- Keyword Gate: Fuzzy (≥60% of required terms, minimum 2 terms matched in title/abstract)
- Total Abstracts/Papers: 3914
- Downloaded Abstracts/Papers: 3914
- Included original Abstracts/Papers: 2322
- Total study participants (naïve ΣN): 2528510


Identification of studies via EPMC (titles/abstracts)
Identification
Records identified:
n=3914
Records excluded:
n=0
Screening
Records assessed for eligibility
n=3914
Records excluded:
n=1592
Included
Studies included in review
n=2322
PRISMA Diagram generated by ☸ SAIMSARA


△OSMA Triangle
Effect-of Predictor → Outcome
acute limb ischemia → Outcome
0
Harmful for patients ΣN=1578999 (62%)
Beneficial for patients ΣN=14925 (1%)
Neutral ΣN=934586 (37%)
△OSMA Triangle generated by ☸SAIMSARA

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

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

Outcome: Outcome Typical timepoints: 30-day, peri/post-op. Reported metrics: %, CI, p.

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

Predictor: acute limb ischemia — exposure/predictor. Doses/units seen: 70 mg, 60 ml, 4000 iu. Routes seen: oral, intravenous, intramuscular, subcutaneous…. Typical comparator: endovascular revascularization, conventional treatment, 2-year outcomes, rural centers for patients….

- **1) Beneficial for patients** — Outcome with acute limb ischemia — [1006], [1700] — ΣN=14925
- **2) Harmful for patients** — Outcome with acute limb ischemia — [1], [2], [3], [4], [5], [6], [7], [8], [9], [10], [11], [13], [15], [16], [17], [19], [20], [21], [23], [24], [25], [26], [27], [28], [29], [30], [31], [32], [38], [42], [46], [61], [62], [66], [75], [79], [89], [94], [99], [100], [102], [103], [104], [108], [114], [115], [123], [127], [129], [133], [138], [154], [163], [174], [183], [191], [194], [200], [206], [213], [214], [219], [256], [262], [271], [272], [273], [274], [275], [276], [277], [278], [279], [280], [281], [282], [283], [284], [285], [287], [288], [289], [290], [292], [293], [294], [295], [296], [297], [298], [299], [300], [302], [304], [305], [314], [329], [331], [332], [334], [335], [338], [340], [341], [342], [343], [344], [345], [346], [348], [349], [350], [352], [353], [355], [356], [357], [358], [361], [363], [364], [366], [367], [369], [370], [372], [373], [376], [378], [379], [383], [384], [387], [388], [391], [392], [393], [397], [398], [400], [402], [404], [405], [406], [407], [409], [410], [413], [417], [419], [420], [429], [434], [452], [453], [454], [458], [461], [462], [463], [464], [471], [474], [477], [478], [480], [490], [491], [504], [508], [510], [513], [516], [520], [523], [525], [531], [544], [548], [562], [565], [567], [572], [578], [579], [581], [585], [586], [587], [588], [589], [590], [591], [595], [596], [597], [598], [601], [602], [606], [608], [613], [614], [620], [622], [629], [633], [635], [636], [640], [641], [645], [647], [655], [656], [661], [662], [663], [666], [667], [668], [670], [674], [677], [683], [688], [690], [693], [694], [699], [702], [703], [704], [708], [709], [710], [711], [714], [721], [722], [723], [724], [726], [727], [728], [729], [731], [733], [735], [736], [740], [741], [745], [746], [747], [748], [749], [750], [751], [752], [753], [754], [756], [757], [759], [760], [761], [762], [763], [766], [767], [768], [770], [779], [811], [812], [815], [818], [819], [822], [825], [829], [833], [834], [837], [842], [845], [849], [851], [858], [859], [863], [864], [865], [867], [868], [870], [877], [880], [881], [882], [886], [894], [899], [932], [936], [937], [947], [949], [952], [957], [969], [977], [985], [991], [1030], [1033], [1040], [1042], [1047], [1064], [1081], [1085], [1088], [1090], [1092], [1095], [1096], [1097], [1100], [1101], [1103], [1104],

[1105], [1106], [1113], [1116], [1120], [1123], [1125], [1126], [1128], [1131], [1138], [1139], [1156], [1162], [1172], [1173], [1174], [1175], [1176], [1177], [1178], [1179], [1180], [1181], [1183], [1185], [1186], [1188], [1190], [1191], [1194], [1196], [1198], [1199], [1201], [1208], [1216], [1217], [1232], [1233], [1234], [1235], [1237], [1240], [1242], [1243], [1245], [1246], [1247], [1249], [1250], [1254], [1258], [1259], [1260], [1261], [1264], [1265], [1267], [1282], [1284], [1286], [1288], [1292], [1294], [1295], [1296], [1297], [1299], [1300], [1305], [1306], [1307], [1313], [1314], [1316], [1317], [1322], [1331], [1340], [1349], [1354], [1355], [1359], [1363], [1365], [1368], [1369], [1370], [1371], [1373], [1375], [1381], [1382], [1384], [1410], [1411], [1412], [1413], [1418], [1426], [1431], [1435], [1437], [1441], [1442], [1444], [1445], [1446], [1447], [1448], [1450], [1451], [1452], [1454], [1455], [1456], [1457], [1458], [1459], [1460], [1461], [1463], [1469], [1502], [1509], [1510], [1512], [1515], [1517], [1524], [1526], [1529], [1533], [1534], [1535], [1538], [1544], [1545], [1548], [1549], [1550], [1551], [1552], [1553], [1554], [1559], [1560], [1563], [1566], [1580], [1584], [1585], [1590], [1595], [1599], [1601], [1604], [1606], [1612], [1613], [1614], [1622], [1624], [1627], [1628], [1629], [1630], [1635], [1636], [1637], [1638], [1639], [1641], [1642], [1646], [1647], [1648], [1649], [1650], [1682], [1684], [1685], [1696], [1697], [1699], [1705], [1708], [1709], [1711], [1732], [1735], [1738], [1740], [1742], [1743], [1745], [1746], [1752], [1758], [1761], [1762], [1763], [1765], [1766], [1769], [1771], [1773], [1777], [1783], [1786], [1792], [1795], [1796], [1799], [1801], [1802], [1803], [1804], [1805], [1808], [1810], [1814], [1815], [1816], [1817], [1820], [1822], [1823], [1824], [1825], [1829], [1830], [1839], [1847], [1851], [1856], [1861], [1863], [1866], [1869], [1870], [1871], [1872], [1874], [1875], [1877], [1879], [1880], [1883], [1884], [1885], [1886], [1888], [1890], [1892], [1903], [1910], [1912], [1917], [1922], [1923], [1924], [1926], [1927], [1929], [1937], [1938], [1939], [1940], [1941], [1942], [1943], [1944], [1945], [1947], [1948], [1949], [1950], [1954], [1955], [1958], [1961], [1962], [1966], [1968], [1969], [1970], [1974], [1975], [1976], [1977], [1979], [1982], [2016], [2022], [2024], [2026], [2032], [2034], [2035], [2038], [2044], [2068], [2070], [2072], [2074], [2078], [2089], [2092], [2093], [2095], [2097], [2099], [2100], [2101], [2104], [2115], [2117], [2120], [2121], [2124], [2125], [2130], [2132], [2133], [2135], [2136], [2137], [2138], [2140], [2143], [2145], [2146], [2149], [2150], [2152], [2153], [2154], [2155], [2156], [2157], [2158], [2159], [2160], [2161], [2163], [2165], [2166], [2169], [2170], [2172], [2176], [2179], [2180], [2182], [2185], [2186], [2187], [2191], [2192], [2193], [2194], [2195], [2197], [2199], [2200], [2201], [2202], [2203], [2204], [2205], [2206], [2208], [2209], [2212], [2213], [2218], [2219], [2220], [2221], [2230], [2232], [2236], [2240], [2244], [2246], [2250], [2252], [2260], [2261], [2263], [2265], [2266], [2272], [2275], [2277], [2296], [2299], [2305], [2311], [2312], [2313], [2314], [2315], [2316], [2317], [2318], [2319], [2320], [2322] — ΣN=1578999

- **3) No clear effect** — Outcome with acute limb ischemia — [12], [14], [18], [22], [33], [34], [35], [36], [37], [39], [40], [41], [43], [44], [45], [47], [48], [49], [50], [51], [52], [53], [54], [55], [56], [57], [58], [59], [60], [63], [64], [65], [67], [68], [69], [70], [71], [72], [73], [74], [76], [77], [78], [80], [81], [82], [83], [84], [85], [86], [87], [88], [90], [91], [92], [93], [95], [96], [97], [98], [101], [105], [106], [107], [109], [110], [111], [112], [113], [116], [117], [118], [119], [120], [121], [122], [124], [125], [126], [128], [130], [131], [132], [134], [135], [136], [137], [139], [140], [141], [142], [143], [144], [145], [146], [147], [148], [149], [150], [151], [152], [153], [155], [156], [157], [158], [159], [160], [161], [162], [164], [165], [166], [167], [168], [169], [170], [171], [172], [173], [175], [176], [177], [178], [179], [180], [181], [182], [184], [185], [186], [187], [188], [189], [190], [192], [193], [195], [196], [197], [198], [199], [201], [202], [203], [204], [205], [207], [208], [209], [210], [211], [212], [215], [216], [217], [218], [220], [221], [222], [223], [224], [225], [226], [227], [228], [229], [230], [231], [232], [233], [234], [235], [236], [237], [238], [239], [240], [241], [242], [243], [244], [245], [246], [247], [248], [249], [250], [251], [252], [253], [254], [255], [257], [258], [259], [260], [261], [263], [264], [265], [266], [267], [268], [269], [270], [286], [291], [301], [303], [306], [307], [308], [309], [310], [311], [312], [313], [315], [316], [317], [318], [319], [320], [321], [322], [323], [324], [325], [326], [327], [328], [330], [333], [336], [337], [339], [347], [351], [354], [359], [360], [362], [365], [368], [371], [374], [375], [377], [380], [381], [382], [385], [386], [389], [390], [394], [395], [396], [399], [401], [403], [408], [411], [412], [414], [415], [416], [418], [421], [422], [423], [424], [425], [426], [427], [428], [430], [431], [432], [433], [435], [436], [437], [438], [439], [440], [441], [442], [443], [444], [445], [446], [447], [448], [449], [450], [451], [455], [456], [457], [459], [460], [465], [466], [467], [468], [469], [470], [472], [473], [475], [476], [479], [481], [482], [483], [484], [485], [486], [487], [488], [489], [492], [493], [494], [495], [496], [497], [498], [499], [500], [501], [502], [503], [505], [506], [507], [509], [511], [512], [514], [515], [517], [518], [519], [521], [522], [524], [526], [527], [528], [529], [530], [532], [533], [534], [535], [536], [537], [538], [539], [540], [541], [542], [543], [545], [546], [547], [549], [550], [551], [552], [553], [554], [555], [556], [557], [558], [559], [560], [561], [563], [564], [566], [568], [569], [570], [571], [573], [574], [575], [576], [577], [580], [582], [583], [584], [592], [593], [594], [599], [600], [603], [604], [605], [607], [609], [610], [611], [612], [615], [616], [617], [618], [619], [621], [623], [624], [625], [626], [627], [628], [630], [631], [632], [634], [637], [638], [639], [642], [643], [644], [646], [648], [649], [650], [651], [652], [653], [654], [657], [658], [659], [660], [664], [665], [669], [671], [672], [673], [675], [676], [678], [679], [680], [681], [682], [684], [685], [686], [687], [689], [691], [692], [695], [696], [697], [698], [700], [701], [705], [706], [707], [712], [713], [715], [716], [717], [718], [719], [720], [725], [730], [732], [734], [737], [738], [739], [742], [743], [744], [755], [758], [764], [765],

[769], [771], [772], [773], [774], [775], [776], [777], [778], [780], [781], [782], [783], [784], [785], [786], [787], [788], [789], [790], [791], [792], [793], [794], [795], [796], [797], [798], [799], [800], [801], [802], [803], [804], [805], [806], [807], [808], [809], [810], [813], [814], [816], [817], [820], [821], [823], [824], [826], [827], [828], [830], [831], [832], [835], [836], [838], [839], [840], [841], [843], [844], [846], [847], [848], [850], [852], [853], [854], [855], [856], [857], [860], [861], [862], [866], [869], [871], [872], [873], [874], [875], [876], [878], [879], [883], [884], [885], [887], [888], [889], [890], [891], [892], [893], [895], [896], [897], [898], [900], [901], [902], [903], [904], [905], [906], [907], [908], [909], [910], [911], [912], [913], [914], [915], [916], [917], [918], [919], [920], [921], [922], [923], [924], [925], [926], [927], [928], [929], [930], [931], [933], [934], [935], [938], [939], [940], [941], [942], [943], [944], [945], [946], [948], [950], [951], [953], [954], [955], [956], [958], [959], [960], [961], [962], [963], [964], [965], [966], [967], [968], [970], [971], [972], [973], [974], [975], [976], [978], [979], [980], [981], [982], [983], [984], [986], [987], [988], [989], [990], [992], [993], [994], [995], [996], [997], [998], [999], [1000], [1001], [1002], [1003], [1004], [1005], [1007], [1008], [1009], [1010], [1011], [1012], [1013], [1014], [1015], [1016], [1017], [1018], [1019], [1020], [1021], [1022], [1023], [1024], [1025], [1026], [1027], [1028], [1029], [1031], [1032], [1034], [1035], [1036], [1037], [1038], [1039], [1041], [1043], [1044], [1045], [1046], [1048], [1049], [1050], [1051], [1052], [1053], [1054], [1055], [1056], [1057], [1058], [1059], [1060], [1061], [1062], [1063], [1065], [1066], [1067], [1068], [1069], [1070], [1071], [1072], [1073], [1074], [1075], [1076], [1077], [1078], [1079], [1080], [1082], [1083], [1084], [1086], [1087], [1089], [1091], [1093], [1094], [1098], [1099], [1102], [1107], [1108], [1109], [1110], [1111], [1112], [1114], [1115], [1117], [1118], [1119], [1121], [1122], [1124], [1127], [1129], [1130], [1132], [1133], [1134], [1135], [1136], [1137], [1140], [1141], [1142], [1143], [1144], [1145], [1146], [1147], [1148], [1149], [1150], [1151], [1152], [1153], [1154], [1155], [1157], [1158], [1159], [1160], [1161], [1163], [1164], [1165], [1166], [1167], [1168], [1169], [1170], [1171], [1182], [1184], [1187], [1189], [1192], [1193], [1195], [1197], [1200], [1202], [1203], [1204], [1205], [1206], [1207], [1209], [1210], [1211], [1212], [1213], [1214], [1215], [1218], [1219], [1220], [1221], [1222], [1223], [1224], [1225], [1226], [1227], [1228], [1229], [1230], [1231], [1236], [1238], [1239], [1241], [1244], [1248], [1251], [1252], [1253], [1255], [1256], [1257], [1262], [1263], [1266], [1268], [1269], [1270], [1271], [1272], [1273], [1274], [1275], [1276], [1277], [1278], [1279], [1280], [1281], [1283], [1285], [1287], [1289], [1290], [1291], [1293], [1298], [1301], [1302], [1303], [1304], [1308], [1309], [1310], [1311], [1312], [1315], [1318], [1319], [1320], [1321], [1323], [1324], [1325], [1326], [1327], [1328], [1329], [1330], [1332], [1333], [1334], [1335], [1336], [1337], [1338], [1339], [1341], [1342], [1343], [1344], [1345], [1346], [1347], [1348], [1350], [1351], [1352], [1353], [1356], [1357], [1358], [1360], [1361],

[1362], [1364], [1366], [1367], [1372], [1374], [1376], [1377], [1378], [1379], [1380], [1383], [1385], [1386], [1387], [1388], [1389], [1390], [1391], [1392], [1393], [1394], [1395], [1396], [1397], [1398], [1399], [1400], [1401], [1402], [1403], [1404], [1405], [1406], [1407], [1408], [1409], [1414], [1415], [1416], [1417], [1419], [1420], [1421], [1422], [1423], [1424], [1425], [1427], [1428], [1429], [1430], [1432], [1433], [1434], [1436], [1438], [1439], [1440], [1443], [1449], [1453], [1462], [1464], [1465], [1466], [1467], [1468], [1470], [1471], [1472], [1473], [1474], [1475], [1476], [1477], [1478], [1479], [1480], [1481], [1482], [1483], [1484], [1485], [1486], [1487], [1488], [1489], [1490], [1491], [1492], [1493], [1494], [1495], [1496], [1497], [1498], [1499], [1500], [1501], [1503], [1504], [1505], [1506], [1507], [1508], [1511], [1513], [1514], [1516], [1518], [1519], [1520], [1521], [1522], [1523], [1525], [1527], [1528], [1530], [1531], [1532], [1536], [1537], [1539], [1540], [1541], [1542], [1543], [1546], [1547], [1555], [1556], [1557], [1558], [1561], [1562], [1564], [1565], [1567], [1568], [1569], [1570], [1571], [1572], [1573], [1574], [1575], [1576], [1577], [1578], [1579], [1581], [1582], [1583], [1586], [1587], [1588], [1589], [1591], [1592], [1593], [1594], [1596], [1597], [1598], [1600], [1602], [1603], [1605], [1607], [1608], [1609], [1610], [1611], [1615], [1616], [1617], [1618], [1619], [1620], [1621], [1623], [1625], [1626], [1631], [1632], [1633], [1634], [1640], [1643], [1644], [1645], [1651], [1652], [1653], [1654], [1655], [1656], [1657], [1658], [1659], [1660], [1661], [1662], [1663], [1664], [1665], [1666], [1667], [1668], [1669], [1670], [1671], [1672], [1673], [1674], [1675], [1676], [1677], [1678], [1679], [1680], [1681], [1683], [1686], [1687], [1688], [1689], [1690], [1691], [1692], [1693], [1694], [1695], [1698], [1701], [1702], [1703], [1704], [1706], [1707], [1710], [1712], [1713], [1714], [1715], [1716], [1717], [1718], [1719], [1720], [1721], [1722], [1723], [1724], [1725], [1726], [1727], [1728], [1729], [1730], [1731], [1733], [1734], [1736], [1737], [1739], [1741], [1744], [1747], [1748], [1749], [1750], [1751], [1753], [1754], [1755], [1756], [1757], [1759], [1760], [1764], [1767], [1768], [1770], [1772], [1774], [1775], [1776], [1778], [1779], [1780], [1781], [1782], [1784], [1785], [1787], [1788], [1789], [1790], [1791], [1793], [1794], [1797], [1798], [1800], [1806], [1807], [1809], [1811], [1812], [1813], [1818], [1819], [1821], [1826], [1827], [1828], [1831], [1832], [1833], [1834], [1835], [1836], [1837], [1838], [1840], [1841], [1842], [1843], [1844], [1845], [1846], [1848], [1849], [1850], [1852], [1853], [1854], [1855], [1857], [1858], [1859], [1860], [1862], [1864], [1865], [1867], [1868], [1873], [1876], [1878], [1881], [1882], [1887], [1889], [1891], [1893], [1894], [1895], [1896], [1897], [1898], [1899], [1900], [1901], [1902], [1904], [1905], [1906], [1907], [1908], [1909], [1911], [1913], [1914], [1915], [1916], [1918], [1919], [1920], [1921], [1925], [1928], [1930], [1931], [1932], [1933], [1934], [1935], [1936], [1946], [1951], [1952], [1953], [1956], [1957], [1959], [1960], [1963], [1964], [1965], [1967], [1971], [1972], [1973], [1978], [1980], [1981], [1983], [1984], [1985], [1986], [1987], [1988], [1989], [1990],

[1991], [1992], [1993], [1994], [1995], [1996], [1997], [1998], [1999], [2000], [2001], [2002], [2003], [2004], [2005], [2006], [2007], [2008], [2009], [2010], [2011], [2012], [2013], [2014], [2015], [2017], [2018], [2019], [2020], [2021], [2023], [2025], [2027], [2028], [2029], [2030], [2031], [2033], [2036], [2037], [2039], [2040], [2041], [2042], [2043], [2045], [2046], [2047], [2048], [2049], [2050], [2051], [2052], [2053], [2054], [2055], [2056], [2057], [2058], [2059], [2060], [2061], [2062], [2063], [2064], [2065], [2066], [2067], [2069], [2071], [2073], [2075], [2076], [2077], [2079], [2080], [2081], [2082], [2083], [2084], [2085], [2086], [2087], [2088], [2090], [2091], [2094], [2096], [2098], [2102], [2103], [2105], [2106], [2107], [2108], [2109], [2110], [2111], [2112], [2113], [2114], [2116], [2118], [2119], [2122], [2123], [2126], [2127], [2128], [2129], [2131], [2134], [2139], [2141], [2142], [2144], [2147], [2148], [2151], [2162], [2164], [2167], [2168], [2171], [2173], [2174], [2175], [2177], [2178], [2181], [2183], [2184], [2188], [2189], [2190], [2196], [2198], [2207], [2210], [2211], [2214], [2215], [2216], [2217], [2222], [2223], [2224], [2225], [2226], [2227], [2228], [2229], [2231], [2233], [2234], [2235], [2237], [2238], [2239], [2241], [2242], [2243], [2245], [2247], [2248], [2249], [2251], [2253], [2254], [2255], [2256], [2257], [2258], [2259], [2262], [2264], [2267], [2268], [2269], [2270], [2271], [2273], [2274], [2276], [2278], [2279], [2280], [2281], [2282], [2283], [2284], [2285], [2286], [2287], [2288], [2289], [2290], [2291], [2292], [2293], [2294], [2295], [2297], [2298], [2300], [2301], [2302], [2303], [2304], [2306], [2307], [2308], [2309], [2310], [2321] — ΣN=934586

1) Introduction

Acute limb ischemia (ALI) represents a critical vascular emergency characterized by a sudden decrease in limb perfusion, threatening limb viability. Prompt diagnosis and revascularization are paramount to prevent irreversible tissue damage, amputation, and mortality. The etiology of ALI is diverse, ranging from arterial embolism and thrombosis to aortic dissection and iatrogenic injury. Despite advancements in diagnostic and therapeutic modalities, ALI continues to pose significant challenges, particularly in specific patient populations and clinical contexts. This paper synthesizes recent research to provide a comprehensive overview of current understanding, management strategies, outcomes, and prognostic factors associated with ALI.

2) Aim

This paper aims to systematically review and synthesize findings from recent scientific literature on acute limb ischemia, utilizing a multilayer AI research agent for keyword normalization, retrieval, structuring, and paper synthesis.

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. Retrospective cohort studies and case series, which constitute a significant portion of the evidence, are inherently susceptible to selection bias, confounding, and incomplete data reporting. The limited number of randomized controlled trials (RCTs) and prospective cohorts, along with the prevalence of single-center studies, further contributes to potential biases and limits generalizability.

4) Results

4.1 Study characteristics

The included studies predominantly comprised retrospective cohort studies and mixed-design studies, with a smaller number of case series and a few prospective randomized controlled trials or experimental animal models. Populations varied widely, from general ALI patients to specific subgroups such as those with complicated aortic dissection, COVID-19 infection, or undergoing particular interventions like endovascular therapy (EVT) or open surgical revascularization (OSR). Follow-up periods ranged from immediate post-procedure and 30-day assessments to long-term outcomes spanning several years, with some studies not specifying follow-up duration.

4.2 Main numerical result aligned to the query

The 30-day mortality rate for acute limb ischemia patients ranged from 3% [45] to 35.1% [17], with a median of 9.1% across various studies reporting this metric [2, 9, 17, 24, 30, 40, 45, 46, 66, 1761, 2100, 2257]. This wide range reflects heterogeneity in patient populations, disease severity, and treatment approaches.

4.3 Topic synthesis

- **Treatment Modalities & Efficacy:**
- Emergency thoracic endovascular aortic repair (TEVAR) for complicated type B aortic dissection achieved 90.0% successful limb revascularization [2] and 93.9% successful limb revascularization [9].
- Mechanical aspiration thrombectomy (MAT) resulted in significantly higher final TIMI flow grades and fewer minor complications compared to conventional treatment (CT) in lower extremity ALI (p=0.02) [4].
- Endovascular and open revascularization yielded comparable early outcomes, with endovascular treatment offering modest improvements in long-term survival, shorter hospital stays, and fewer infections, but an increased risk of intracranial hemorrhage [10].

- Catheter-directed arterial thrombolysis (CDT) with low-dose recombinant tissue plasminogen activator (rtPA) is recommended for acute lower limb ischemia (ALLI) patients with life expectancy >6 months, showing 82.3% amputation-free survival at 1 month [16]. CDT was effective for early-stage ALI (Rutherford I–IIa) with comparable limb salvage and survival, though open surgical revascularization (OSR) resulted in longer hospital stays (7.29 ± 4.58 vs. 6.08 ± 8.75 days, p=0.038) [27].
- Endovascular-first therapy showed increased 30-day reintervention (adjusted OR 2.29, p=0.03) and 3-year amputation in embolic etiology compared to open therapy, while CDT demonstrated decreased 3-year mortality (adjusted HR 0.41, p=0.033) compared to open therapy [25].
- Direct stent placement demonstrated comparable short- and long-term outcomes to percutaneous mechanical thrombectomy (PMT) in selected patients with ALLI (1-year primary patency: 90% vs. 78.6%, P = .789) [29].
- Mechanical thrombectomy (MT) for ALI achieved 91.0% freedom from major amputation at 30 days [40].
- A laser atherectomy-thrombectomy system showed 92% technical success and 5% major amputation rate as primary treatment for ALI [43].
- Percutaneous mechanical thrombectomy (PMT) showed a tendency towards higher technical success (96% vs. 80%) and lower amputation rates compared to CDT in acute thrombotic lower limb ischemia [44].
- Thrombo-aspiration (TA) had a lower amputation rate (0% vs. 8%) and higher technical success (57% technical success alone) than MT for ALI [45].
- Open surgical revascularization (OSR) remains predominant for ALLI, but endovascular therapy (EVT) is favored in specific cases despite higher reintervention (32.6% vs 8.9%) and bleeding rates (5.2% vs 1.0%) [54].
- Image-guided surgical thromboembolectomy with routine intraoperative angiography is safe and effective for ALLI, achieving 92.66% technical success and 3.67% 30-day amputation rates [86].
- Endovascular treatment (ET) showed significantly better amputation-free survival and lower mortality during follow-up compared with surgical treatment (ST) and hybrid treatment (HT) [95].
- Catheter-directed thrombolysis (CDT) is recommended for ALI patients with arterial thrombooclusion, with regression of lower-limb ischemia in 97% of patients [106].
- Endovascular and open revascularization for ALI due to femoro-popliteal in-stent occlusion showed similar early and 5-year outcomes [91].
- Endovascular revascularization (EVR) in ALI achieved 59.7% 1-year amputation-free survival [53].

- Rotarex mechanical thrombectomy (RMT) showed favorable short- and mid-term outcomes for ALI, with 3.3% major amputations at 1 year [73].
- The Indigo Aspiration System was successfully used to treat ALI in a super-elderly patient [63] and showed high limb salvage (98.2%) with few complications for lower extremity ALI [505].
- Endovascular revascularization options are expanding, with mechanical thrombectomy devices playing a significant role [90].
- Accelerated intraarterial thrombolysis is effective in treating acute and subacute limb ischemia with a low risk of major bleeding [621].
- Endovascular revascularization was associated with better in-hospital clinical outcomes, including lower mortality (2.8% vs 4.0%) and fasciotomy rates (1.9% vs 8.9%), compared to surgical revascularization [592].
- Catheter-based thrombectomy (CBT) for ALI showed higher technical success and shorter hospital stay compared to CDT alone [470].
- Intra-arterial thrombolysis (IAT) is effective for embolic ALI, particularly for clearing distal vessels, but contraindicated after abdominal surgery due to bleeding risk [2083].
- **Prognostic Factors & Risk Stratification:**
- Higher body weight (>83 kg, IRR 4.24), moderate to severe liver disease (IRR 14.41), low platelet count (IRR 2.38), and elevated CK levels (>510 U/L, IRR 3.17) are independent predictors of post-reperfusion compartment syndrome (CS) in ALI patients [5].
- Absence of atrial fibrillation (OR 3.3), functional dependency (OR 7.3), and neutrophil-to-lymphocyte ratio (NLR) >5.91 (OR 9.1) predict postoperative mortality in elderly ALI patients [17].
- A scoring scale was developed to predict amputation risk in ALI patients, showing prognostic ability with an AUC of 0.794 [22].
- Polyvascular disease significantly impacts ALI patients, with higher non-cardiovascular mortality rates [32].
- A nomogram incorporating diabetes, Rutherford grade, NLR, platelet-to-lymphocyte ratio (PLR), and low-density lipoprotein (LDL) showed good predictive performance for 30-day amputation rate after endovascular surgery for ALLI [33].
- Peripheral artery disease (PAD) is the strongest predictor of ALI as a complication of PCI for stable coronary artery disease, which is associated with 1.6 times greater risk of in-hospital mortality and 4.7 times greater risk of in-hospital major amputation [38].
- High neutrophil-to-lymphocyte ratio (NLR) is associated with a 3-fold higher risk of 30-day mortality or major amputation in ALLI [15].
- Advanced age, history of smoking, atrial fibrillation, and insufficient outflow were independent risk factors for amputation-free survival (AFS) in ALLI treated by EVT [100].

- Skin speckle, myoglobin, and time-to-peak were independent risk factors for major amputation within 30 days post-revascularization in ALLI [102].
- Acute limb ischemia (ALI) in cardiogenic shock (CS) patients was significantly associated with mortality (adjusted OR 1.40), with peripheral vascular disease and multiple mechanical circulatory support devices increasing ALI risk [115].
- The BUN/creatinine ratio showed moderate predictive performance (AUC: 0.727) for amputation risk in ALI, and female gender was an independent predictor of amputation risk (OR 4.16) [129].
- Acute limb ischemia (ALI) after cardiovascular surgery is associated with high 1-year mortality (55.8%), with prolonged cardiopulmonary bypass (CPB) time (HR 3.067) and postoperative acute kidney injury (AKI) (HR 2.927) being significant risk factors [154].
- Frailty, modeled by the Risk Analysis Index (RAI), is associated with increased postoperative mortality and impacts discharge destination in patients undergoing open bypass revascularization for ALI [87].
- Unfavorable factors like prolonged onset time (>2.5 days, OR 1.4), absence of atrial fibrillation (OR 4.2), and collateral development (OR 9.0) predict failed endovascular therapy (EVT) in acute on chronic limb ischemia (AoCLI) [28].
- Acute limb ischemia (ALI) correlates with higher mortality (78.6% vs 47.4%) in patients receiving venoarterial extracorporeal membrane oxygenation (VA-ECMO) with femoral cannulation [661].
- Delayed diagnosis of Antiphospholipid Syndrome (APS) in ALI patients is associated with a high risk of amputation and mortality [256].
- Inadequate backflow, high serum creatine kinase levels, positive fluid balance, and advanced Rutherford category (IIB) were predictive factors for compartment syndrome following non-traumatic ALI [772].
- Age > 65 years, past history of symptomatic atherosclerosis, and treatment with low molecular weight heparin are risk factors for arterial thrombotic events (ATEs), including ALI, after unprovoked venous thromboembolism [896].
- Limb ischemia as a malperfusion syndrome in acute type A aortic dissection (TAAD) was associated with increased odds of in-hospital mortality after surgical repair [899].
- High neutrophil-to-lymphocyte ratio (NLR) was associated with significantly higher risks of 1-year all-cause and cardiac-related mortality and major adverse limb events (MALEs) in critical limb ischemia (CLI) patients, including those with ALI [931].
- Acute limb ischemia at diagnosis was significantly associated with major amputation (OR 5.95) in young patients with PAD [1040].
- Limb ischemia is an in-hospital complication associated with increased mortality in patients with acute type A aortic dissection [2140].

- Hypotension in patients with acute aortic dissection is associated with a higher rate of in-hospital adverse events, including limb ischemia [2016].
- Junctional bradycardia (JB) is potentially associated with ischemic stroke, and a composite of thromboembolic events including ALI was significantly higher in JB patients without a retrograde P wave [1752].
- **Special Populations & Etiologies:**
- Acute limb ischemia is a rare but serious complication of PCI for stable coronary artery disease [38].
- Conservative management with therapeutic anticoagulation achieved successful limb salvage in a premature neonate with ALI secondary to femoral artery thrombosis [14]. Intra-arterial thrombolysis was used for ALI in a newborn [141].
- Popliteal artery thrombosis leading to ALI is a rare but potentially fatal complication of total knee arthroplasty (TKA), with endovascular treatment preferred [75].
- Septic revision knee arthroplasty is associated with significantly higher rates of thromboembolic events, including limb ischemia and lower-limb amputation [79].
- Acute on chronic limb ischemia (AoCLI) presents with more complex lesions [28].
- Acute lower limb arterial occlusion due to fibrin-associated diffuse large B-cell lymphoma is a rare cause of ALI, emphasizing pathological evaluation of atypical thrombi [60].
- Patients with ALI during the COVID-19 pandemic experienced higher mortality (48.6% vs. 15.5% pre-COVID) and increased amputation rates [61]. COVID-19 significantly negatively impacts 30-day amputation-free survival in ALI patients undergoing urgent surgical revascularization, primarily due to increased mortality [287]. COVID-19 can lead to thrombotic complications necessitating surgical intervention, with ALI being common and a significant postoperative mortality rate [936].
- Acute limb ischemia can be caused by arterial tumor embolism secondary to renal cell carcinoma [52] or metastatic sarcoma [717], or gigantic left ventricular myxoma in pediatric patients [484].
- Cocaine use is associated with ALI, but endovascular treatment is underexplored [58]. A young cocaine user presented with ALI due to a floating thrombus in the non-atherosclerotic ascending aorta [168].
- Acute upper limb ischemia (AULI) can result from brachial embolectomy, with 76.4% technical success but high perioperative complication rates [66]. Paradoxical embolism is a rare cause of AULI [72, 568, 189].
- Systemic lupus erythematosus (SLE), antiphospholipid syndrome (APLS), and infective endocarditis (IE) can cause AULI [69].
- COVID-19-associated ALI is poorly understood, with hypercoagulability, vasospasm, hypoxia, and acidosis hypothesized as key mechanisms [57].

- Acute limb ischemia is an uncommon but serious complication of PCI for stable coronary artery disease [38].
- Atrial fibrillation (AF) was linked to a decreased risk of aorto-iliac and femoral-popliteal atherosclerosis in ALLI patients [39]. AF is a risk factor for embolism [387].
- Acute iliofemoral deep vein thrombosis (DVT) can be associated with ALI and May-Thurner syndrome [217]. Venous thromboembolism (VTE) commonly occurs with ALI [472].
- Acute limb ischemia (ALI) occurred in 5.6% of cardiogenic shock (CS) patients and was significantly associated with mortality [115]. ALI was more common in AMI-CS than HF-CS supported by Impella CP (14.4% vs 11.0%, p = 0.05) [138].
- Bilateral cystic adventitial disease presented as ALI in a healthy young patient [139].
- Acute limb ischemia can result from a saddle aortic embolus causing paraplegia [47], or concurrent ALI and pulmonary embolism in repaired tetralogy of Fallot [48].
- Recurrent ALI successfully treated with endovascular thrombectomy highlights the importance of medication adherence in atrial fibrillation [51].
- Acute on chronic left limb ischemia can be precipitated by amiodarone-induced thyroid dysfunction [486].
- Acute aortic occlusion (AAO) is a rare but serious condition often presenting with ALI [614].
- Acute limb ischemia can be a complication of peripheral VA-ECMO, associated with worsening outcomes [163]. Ipsilateral ALI occurred in 5.3% vs 10% of non-COVID and COVID patients, respectively, undergoing VA-ECMO [357].
- A rare case of acute limb ischemia caused by a thrombus formed in the left inferior pulmonary vein stump after left lower lobectomy [438, 536].
- Acute limb ischemia is a potential presentation of heparin-induced thrombocytopenia (HIT) [2031, 1341, 747, 449, 1217].
- Ulcerative colitis can present with acute limb ischemia and aortic mural thrombosis [428, 603].
- Acute limb ischemia due to bilateral persistent sciatic artery thrombosis is a rare vascular anomaly [236].
- Popliteal artery aneurysms (PAAs) can present with ALI, with seasonality and chronobiology potentially influencing symptom onset [552].
- Acute limb ischemia is a rare manifestation of PFO-mediated paradoxical embolism [392].
- Acute limb ischemia can occur after total hip arthroplasty, possibly related to tranexamic acid administration [1229].
- Acute limb ischemia is a common complication of severe diabetic hyperosmolarity (HHNS) [1801].
- Acute limb ischemia can be a complication of perigraft seroma after open AAA repair [1804].
- **Outcomes & Complications:**
- In-hospital mortality for complicated type B aortic dissection with critical ALI was 15.0% [2].

- Urban centers reported higher mortality and cardiovascular events but lower rates of major amputation, fasciotomy, and major adverse limb events (MALE) compared to rural centers for ALI patients undergoing revascularization [23].
- Females had higher mortality (32% vs. 19% at 30 days) after surgical thromboembolectomy for ALLI, while males had higher rates of vascular patency loss and reintervention [24].
- Prophylactic fasciotomy in ALI patients did not improve amputation-free survival but was associated with increased mortality (HR 4.09, p=0.004 at 30 days) and higher fasciotomy wound infection rates (5.5% vs. 1.7%, p=0.017) [26].
- The ability to ambulate after ALLI, rather than amputation status, is a significant predictor of health-related quality of life [34].
- Misdiagnosis of ALI leads to delayed treatment, significantly reducing limb salvage rates (65% vs. 89%, p=0.02) and increasing reinterventions (65% vs. 18%, p<0.001) [42].
- Patients with ALLI continue to experience high mortality (9% at 30 days, 17% at 1 year) and limb loss rates (19% at 30 days, 34% at 1 year) despite treatment advancements [46].
- Intra-arterial thrombolysis had worse technical success in female patients (69.5% vs. 91%, P=0.01) with ALI, and amputation-free survival favored male patients (adjusted HR 0.21, P=0.046) [49].
- Female patients with ALI had higher mortality after revascularization and notably higher amputation rates after an endovascular-first approach compared to males (OR 2.6, Pinteraction = .01) [31].
- Compartment syndrome (CS) after CDT for ALLI is uncommon but associated with a higher risk of major amputation (OR 3.87, P=0.027) [276]. Patients developing acute compartment syndrome (ACS) during CDT for ALLI present with more severe ischemia, have a higher amputation rate (31% vs 17% at 1 year), and lower amputation-free survival (62% vs 73%) [279].
- Acute limb ischemia incidence and amputation rates are declining in the US, but mortality remains unchanged, with disparities noted based on gender and race [89].
- Frailty is common in ALI patients and predicts discharge site and nonambulation at follow-up, but not amputation or death [489].
- Patients with cancer who develop ALI have a significantly higher 1-year mortality rate (>50%) and are more likely to undergo major amputation if ALI occurs after cancer diagnosis [491].
- Acute limb ischemia (ALI) occurred in 1.4% of patients after cardiac surgery and was associated with reduced long-term survival (HR 3.72) [756].
- Urgent major lower extremity amputations, often for ALI, were associated with higher postoperative complications, inpatient mortality, and increased long-term mortality [587].
- Delayed fasciotomy was associated with a significantly higher risk of major amputation within 30 days (50% vs. 5.9%, P = 0.002) compared to prophylactic fasciotomy [591].

- Acute limb ischemia (ALI) was the most common vascular complication across all ECMO types (16.5%) and was associated with significantly lower in-hospital survival (32.5% vs 54%) [1138].
- Iliac limb occlusion (ILO) is a common EVAR failure mode, often presenting as ALI [332].
- **Diagnostic & Monitoring Tools:**
- Cooling to 15°C in a swine model of ALI reduced local tissue metabolites, while 5°C increased muscle damage [37].
- Severe foot poikilothermy, indicated by a temperature gradient (ΔTmax F-F ≥9.5°C), is associated with increased risk of amputation in ALI [62].
- MRI, specifically IVIM perfusion imaging, effectively quantifies microcirculatory impairment in ALI, with perfusion fraction values showing a strong negative correlation with ischemic duration [201].
- Near-infrared spectroscopy (NIRS) monitoring significantly reduced the incidence of rhabdomyolysis and ALI in peripheral VA ECMO, with ALI increasing 4-year mortality risk by 80% [99].
- 2D perfusion angiography with enhanced visual and quantitative analysis shows potential to evaluate endovascular intervention efficacy for ALI, providing a quantitative tool to assess post-endovascular limb perfusion [237].
- Emergency medicine-performed hand-held Doppler (HH) and spectral Doppler (SD) demonstrated high sensitivity in identifying abnormal posterior tibial (PT) or dorsalis pedis (DP) flow in patients with complete angiographic occlusion, suggesting their utility in evaluating ALI [487].
- The change trend of plasma D-dimer levels during CDT for ALI can predict CDT efficacy and guide therapeutic regimen adjustments [493].
- CT angiography imaging findings are crucial for radiologists to evaluate lower extremity vascular pathologies in ALI [547].
- 18F-sodium fluoride positron emission tomography shows promise in imaging atherosclerosis, which underlies ALI [530].
- Multispectral optoacoustic tomography (MSOT) can non-invasively image muscle hemodynamics and oxygenation, potentially aiding in ALI assessment [1323].
- **Prevention & Management Strategies:**
- A substantial decline in the incidence of hospital-admitted ALI and venous thromboembolism (VTE) was observed in Austria over 15 years, potentially due to improved cardiovascular risk management [35].
- Higher hospital volumes for endovascular therapy (EVT) were associated with better procedural outcomes for ALI, with low-volume hospitals showing a significantly higher rate of procedural failure (11.7% vs 8.0%, P=.008) [36].

- Low-dose rivaroxaban plus aspirin significantly reduces ALI after lower extremity revascularization (LER) in patients with peripheral artery disease (PAD), with early and sustained benefit [531, 574, 1116, 1128, 1006].
- Ticagrelor, in addition to aspirin, reduced limb events, including ALI (HR: 0.24; P = 0.009), in patients with type 2 diabetes mellitus (T2DM) and atherosclerosis, although it increased bleeding risk [513].
- The below-knee popliteal artery (BKPA) approach for surgical thrombectomy in ALI resulted in a lower reintervention rate (0% vs. 30.8%) and incidence of distal embolism (4.5% vs. 38.5%) compared to the common femoral artery (CFA) approach [59].
- Conservative management with therapeutic anticoagulation achieved successful limb salvage in a neonate with ALI secondary to femoral artery thrombosis [14].
- Universal application of novel anticoagulants like rivaroxaban to ALI patients could potentially reduce adverse cardiovascular events [323].
- Direct oral anticoagulants (DOACs) were associated with a reduction in ALI but at the expense of an increased risk of major bleeding events (RR = 1.43) [824].
- Cooling to 15°C in a swine model of ALI reduced local tissue metabolites [37].
- Endovascular repair of popliteal artery aneurysms (PAA) with ALI resulted in no major amputations at mid-term follow-up, with comparable outcomes to open repair [534].
- The MANTA® vascular closure device is safe and effective for VA-ECMO decannulation, with a low incidence of ALI (5.0%) [336].
- Supervised exercise therapy (SET) should be offered to all patients with symptomatic PAD who are not at risk of ALI [1022].
- A temporary extracorporeal femoral-femoral crossover bypass is a feasible, safe, and effective technique for treating ALI caused by Impella MLVAD [1067].
- Prompt diagnosis and treatment are crucial for ALI; endovascular approaches are considered for Rutherford Categories IIa and IIb, with time to restore blood flow being an important factor [346].
- Intraoperative urokinase lysis improves limb perfusion and causes low major and intracranial bleeding, and can be safely applied to patients with severe ischemia when surgical restoration of the outflow tract fails [369].
- Cross-limb vascular shunting (CLS) enables early reperfusion of the injured limb and is effective as a temporary vascular shunting method for traumatic popliteal artery injury (PAI) with severe ischemia [366].
- The quality of the initial bedside evaluation in ALI patients is crucial, as better clinical examinations are associated with favorable outcomes at 1 year [337].
- Covered stents (CS) were associated with a lower rate of ALI (17% vs. 34%) compared to bare metal stents (BMS) in femoropopliteal interventions [678].

- Optimizing the ECMO treatment regimen, including earlier initiation and lower-flow ECMO, improves survival rates in adult patients with acute fulminant myocarditis and reduces complications like lower limb ischemia [999].
- Percutaneous, antegrade superficial femoral artery (SFA) access can be safely used for complex endovascular interventions for infrainguinal occlusive disease, including in cases of ALI [966].
- Thrombolysis with urokinase is an effective sole or adjunctive treatment for ALI secondary to native artery occlusion, providing durable arterial patency and limb salvage [1576].
- Intra-arterial streptokinase therapy for ALLI resulted in limb salvage in 71% of patients, with low morbidity and mortality [1947].
- Early amputation of nonviable limbs and prompt operative revascularization for threatened but viable extremities minimizes morbidity and mortality rates and maximizes limb salvage in severe, acute lower limb ischemia [2133].
- **Pathophysiology & Biomarkers:**
- Inflammation is central to the pathophysiology and prognosis of ALLI, and high neutrophil-to-lymphocyte ratio (NLR) is associated with a 3-fold higher risk of 30-day mortality or major amputation [15].
- Th1 immune responses, indicated by elevated IL-12 and IFN-γ, are believed to play a role in the pathogenesis of ALI [67].
- Elevated lipoprotein A (Lp[a]) is associated with an increased risk of peripheral arterial disease (PAD), cardiovascular events, and worse outcomes, potentially increasing the risk of ALI [68].
- COVID-19-associated ALI involves hypercoagulability, vasospasm, hypoxia, and acidosis, involving pathways like ACE2, inflammation, and platelet activation [57].
- High systemic inflammatory biomarkers (MLR, NLR, PLR, SII, SIRI, AISI) and CT Severity Score values at admission strongly predict ALI risk, ICU admission, and mortality in COVID-19 patients [385].
- Galectin-9 is identified as a female-specific PAD biomarker that, combined with clinical features, accurately predicts major adverse limb events (MALE) [345].
- HIF-1α-mediated gene therapy using a PEI-β-CD vector demonstrated potential for treating limb ischemia by increasing blood perfusion and alleviating tissue damage in a murine model [364].
- Human iPS-derived extracellular vesicles enriched with miR-126 promoted angiogenesis, increased perfusion, and enhanced functional recovery in a murine model of ALI [584].
- The cyclooxygenase-2 (COX-2) pathway is essential in reducing ischemia caused by acute injury from snake venom [606].
- HMGB1 binding with RAGE promotes vascular inflammation and endothelial cell apoptosis, mediating vascular injury during acute limb ischemia/reperfusion (IR) [1180].

- Macrophage IL-1β expression is required for pro-angiogenic VEGF-A expression and for VEGF-A-induced blood flow recovery in an ALI model [946].
- The prothrombotic fibrin clot phenotype has been reported to have a predictive value in terms of myocardial infarction, ischemic stroke, and ALI [1014].
- Five novel plasma protein biomarkers were identified as independent risk factors for major adverse cardiovascular events (MACE), including ALI, in patients with stable CAD [1030].
- Nonatherosclerotic medial arterial calcification (MAC) is a significant and distinct contributor to PAD, which can progress to critical limb ischemia and ALI [759].
- In skeletal muscles from patients with ALI, cDNA and protein levels of MMP-9, MMP-19, collagen type IV chains, TIMP-1 and TIMP-2 were high [1674].
- Thromboxane A2 plays a major role in the ischemia-reperfusion injury of acute compartmental syndrome [2125].
- Severe lower limb ischemia in acute arterial occlusion is associated with a significant increase in systemic fibrinolytic activity due to excessive t-PA release [2106].
- **Geographic & Socioeconomic Disparities:**
- Urban centers reported higher mortality and cardiovascular events but lower rates of major amputation, fasciotomy, and MALE compared to rural centers for ALI patients undergoing revascularization [23].
- Acute limb ischemia incidence and amputation rates are declining in the US, but mortality remains unchanged, with disparities noted based on gender and race [89].
- Acute limb ischemia in Ethiopia is associated with high morbidity and mortality, with patients often presenting late and with irreversible ischemia [334, 342].
- Socioeconomic status was not associated with the severity of ALI at patient presentation or with 30-day or 1-year limb loss and mortality, but was associated with increased 30-day readmission [241].
- Outcomes from PAD, including critical limb-threatening ischemia (CLTI), ALI amputation, and mortality, remain increased among specific racial and ethnic groups due to social determinants of health [331].
- Hospitalization for ALI was most frequent in Europe and North America compared to Asia and Central/South America [1095].
- Black patients with PAD had a higher incidence of MALE, which include acute or chronic limb ischemia, compared to White patients [812].
- In a hub-and-spoke health system model, 100% of patients with ALI received intervention within guideline-recommended time frames after transfer [876].
- Telemedicine provided safe and efficient vascular surgery services, with a small number of patients requiring emergency department visits for concerns like ALI [1031].
- The COVID-19 pandemic was associated with a significantly higher percentage of patients experiencing ALLI [745].

5) Discussion

5.1 Principal finding

The 30-day mortality rate for acute limb ischemia patients ranged from 3% [45] to 35.1% [17], with a median of 9.1% across various studies reporting this metric, indicating a persistent and significant risk associated with ALI despite diverse treatment modalities.

5.2 Clinical implications

- Early and accurate diagnosis of ALI is crucial, as misdiagnosis leads to significantly reduced limb salvage rates and increased reinterventions [42]. Prompt evaluation by a vascular specialist and staging of ischemic injury severity are emphasized [238].
- Treatment selection should be individualized, considering patient characteristics, etiology (embolic vs. thrombotic), and disease severity (Rutherford classification) [238, 346]. While open surgery remains predominant, endovascular techniques are increasingly effective, particularly for early-stage ischemia [54, 95, 437].
- Specific patient populations, such as females [24, 31, 49, 93, 129, 647, 773], the elderly [17, 61, 334, 342, 803], cancer patients [363, 410, 413, 491, 784, 952], and those with comorbidities like chronic kidney disease (CKD) [127, 633] or polyvascular disease [32], face higher risks of mortality and amputation, necessitating tailored management.
- Inflammatory biomarkers like NLR [15, 17, 33, 931] and elevated CK levels [5, 772] are valuable prognostic tools for predicting adverse outcomes and compartment syndrome, guiding clinical vigilance and intervention.
- Prophylactic fasciotomy does not consistently improve amputation-free survival and may increase mortality and infection rates [26, 297], suggesting a more selective approach based on ischemic severity (e.g., Rutherford 2B) [278, 279].

5.3 Research implications / key gaps

- **Optimal Antithrombotic Regimens:** Further research is needed to determine the optimal antithrombotic therapy for ALI patients, particularly balancing efficacy in reducing ALI and other vascular events with the risk of major bleeding [672, 513, 824, 1006, 1529].
- **Comparative Effectiveness of Revascularization:** Large-scale, prospective randomized controlled trials are needed to definitively compare long-term outcomes (e.g., amputation-free survival, quality of life) of endovascular versus open surgical approaches across different ALI etiologies and Rutherford classifications, especially for complex lesions and specific anatomical locations [10, 25, 54, 95, 258, 560, 573, 646].
- **Biomarkers for Personalized Risk Assessment:** Development and validation of novel biomarkers (e.g., specific inflammatory markers, genetic profiles) are needed to improve

personalized risk stratification for complications like post-reperfusion compartment syndrome, amputation, and mortality, particularly in vulnerable populations [5, 15, 17, 33, 62, 67, 102, 129, 385, 810, 1030].

- **Impact of Socioeconomic and Geographic Disparities:** Studies are required to understand the underlying mechanisms of observed disparities in ALI outcomes between urban/rural, racial, and socioeconomic groups, and to develop targeted interventions to mitigate these inequities [23, 89, 331, 812, 1095].
- **Management of COVID-19-Associated ALI:** Further investigation into the unique pathophysiology and optimal management strategies for COVID-19-associated ALI is crucial, given its high mortality and amputation rates, and the potential for atypical presentations and hypercoagulable states [57, 61, 287, 304, 372, 378, 640, 665, 718, 723, 745, 792, 793, 936, 947, 1294].

5.4 Limitations

- **Heterogeneous Study Designs** — The reliance on predominantly retrospective cohorts and case series limits the ability to establish causality and introduces potential biases.
- **Variability in Outcome Reporting** — Inconsistent definitions and reporting timepoints for key outcomes (e.g., amputation, mortality, limb salvage) hinder direct comparisons and meta-analysis.
- **Selection Bias in Treatment Comparisons** — Observed differences between endovascular and open surgical approaches may be influenced by selection bias, as treatment decisions are often based on patient and lesion characteristics.
- **Limited Long-Term Follow-up** — Many studies, particularly those on specific interventions, lack comprehensive long-term follow-up data, making it difficult to assess durability and sustained patient benefit.
- **Geographic and Setting Specificity** — A significant portion of the data originates from specific regions or single centers, potentially limiting the generalizability of findings to diverse healthcare systems and populations.

5.5 Future directions

- **Standardized Outcome Reporting** — Implement uniform definitions and reporting standards for ALI outcomes across studies.
- **Large-Scale RCTs** — Conduct multi-center, randomized controlled trials comparing modern endovascular and open surgical techniques.

- **Biomarker-Guided Treatment Trials** — Design studies to evaluate treatment strategies tailored by novel prognostic and predictive biomarkers.
- **Health Equity Research** — Investigate and address disparities in ALI care and outcomes through population-based studies and intervention trials.
- **AI-Enhanced Diagnostic Pathways** — Develop and validate AI tools for early and accurate diagnosis of ALI and its complications, such as compartment syndrome.

6) Conclusion

The 30-day mortality rate for acute limb ischemia patients ranged from 3% [45] to 35.1% [17], with a median of 9.1% across various studies reporting this metric. This wide range underscores the critical nature of ALI and the variability in outcomes. Generalizability is limited by the heterogeneity of study designs and populations, with the reliance on retrospective data being the most significant limitation affecting certainty. Clinicians should prioritize early diagnosis and individualized treatment, recognizing the high risks in vulnerable populations, while future research focuses on large-scale comparative effectiveness trials and biomarker-guided personalized medicine.

References

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Figure 1. Publication-year distribution of included originals

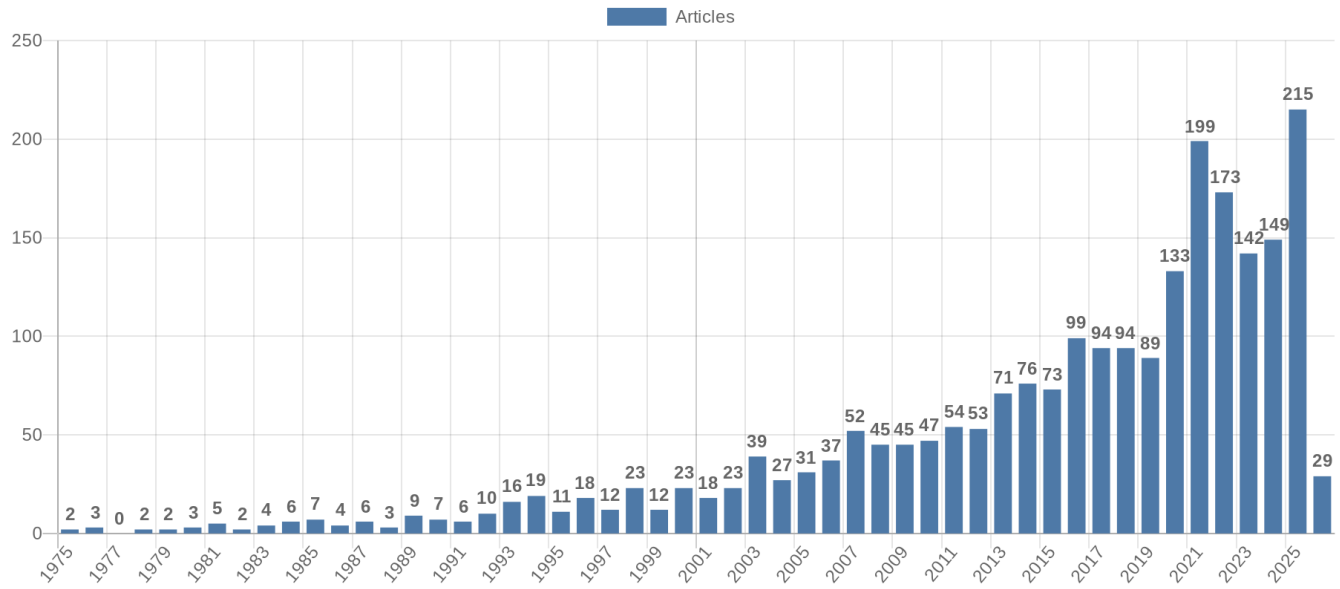

Figure 2. Study-design distribution of included originals

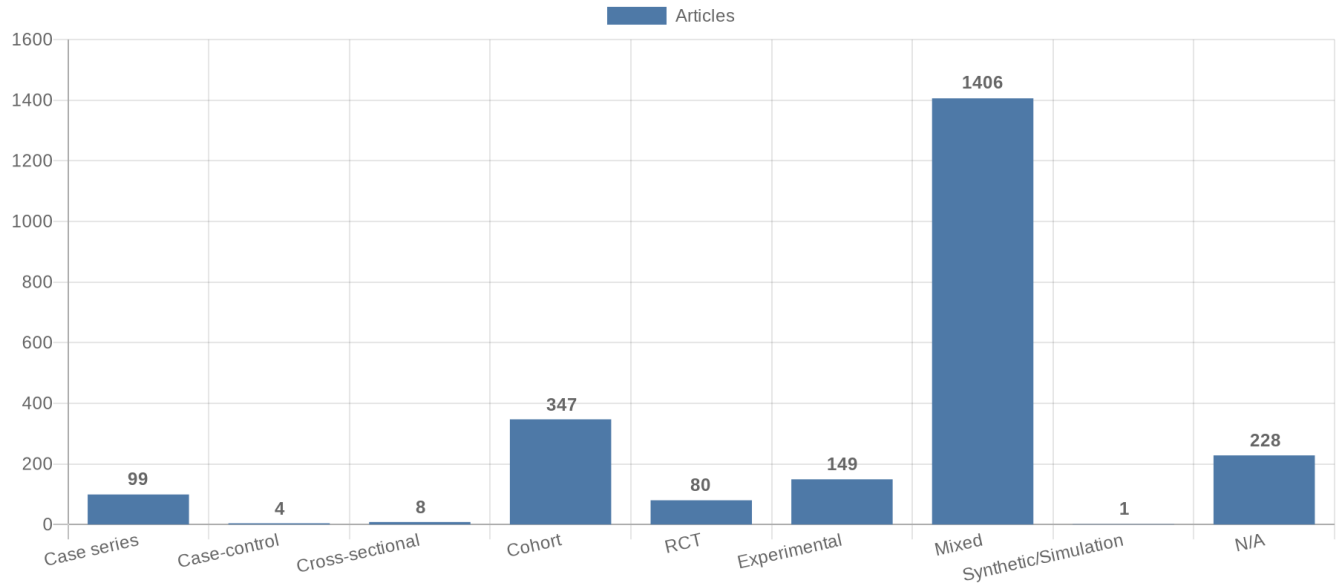

Figure 3. Study-type (directionality) distribution of included originals

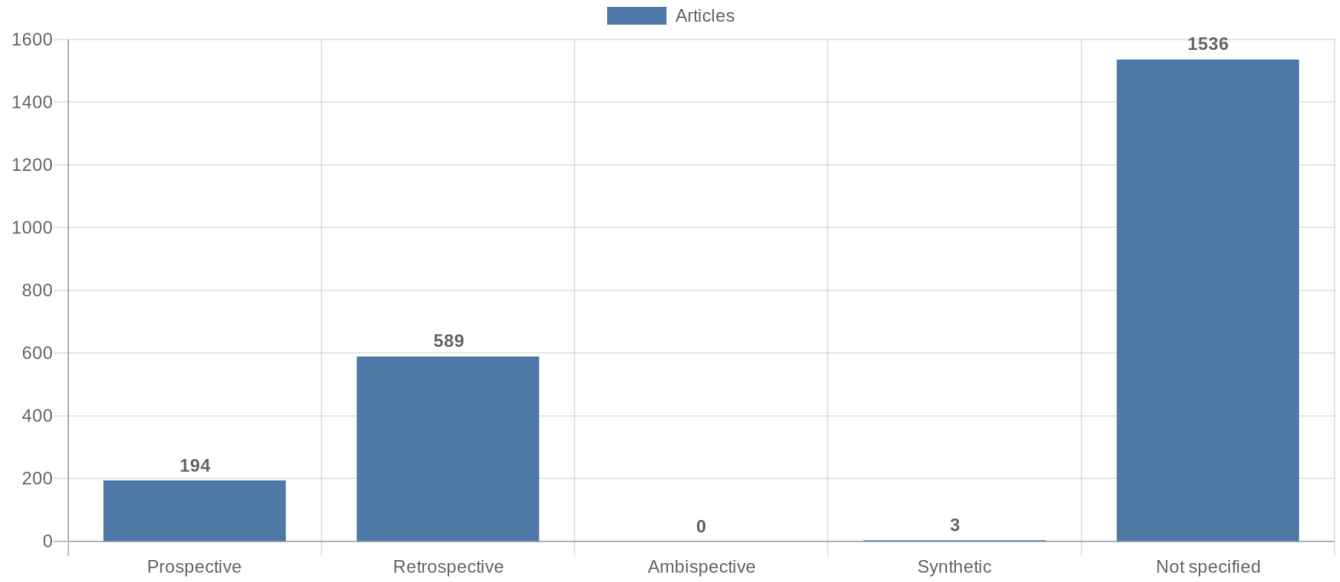

Figure 4. Main extracted research topics

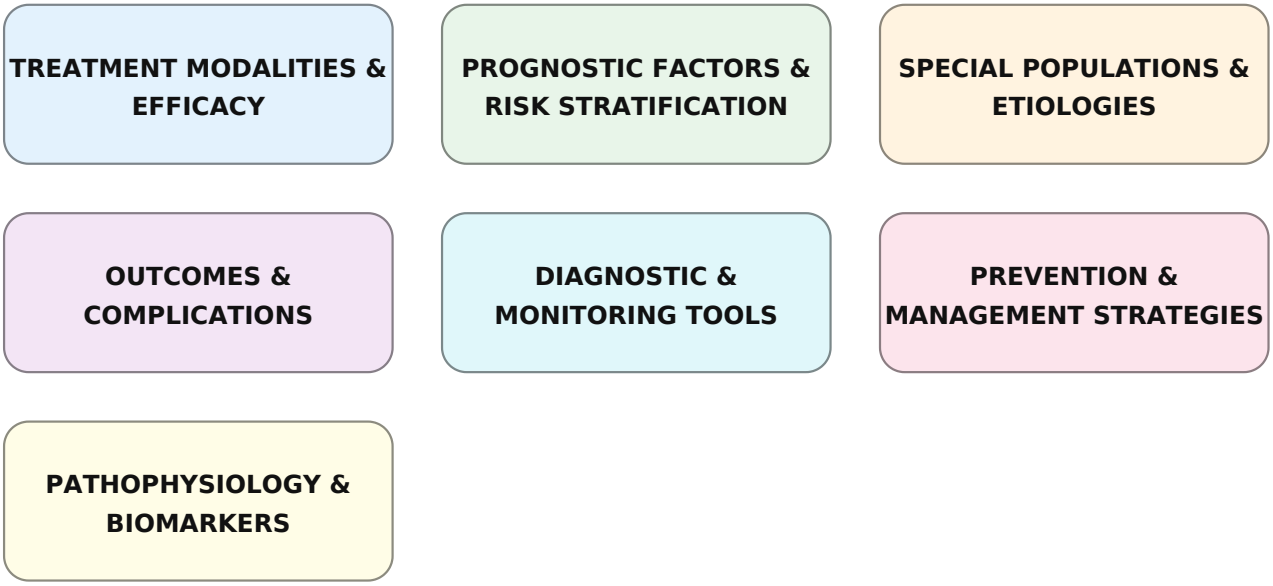

Figure 5. Limitations of current studies (topics)

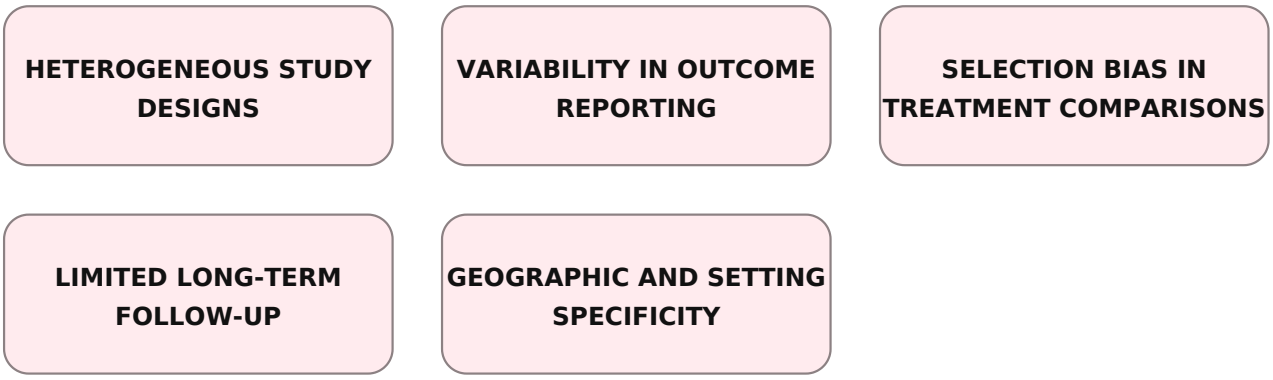

Figure 6. Future research directions (topics)