# CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

## Prevention of Stroke Evidence Tables

## *Acetylsalicylic acid (ASA)*

## *For Prevention of Vascular Events*

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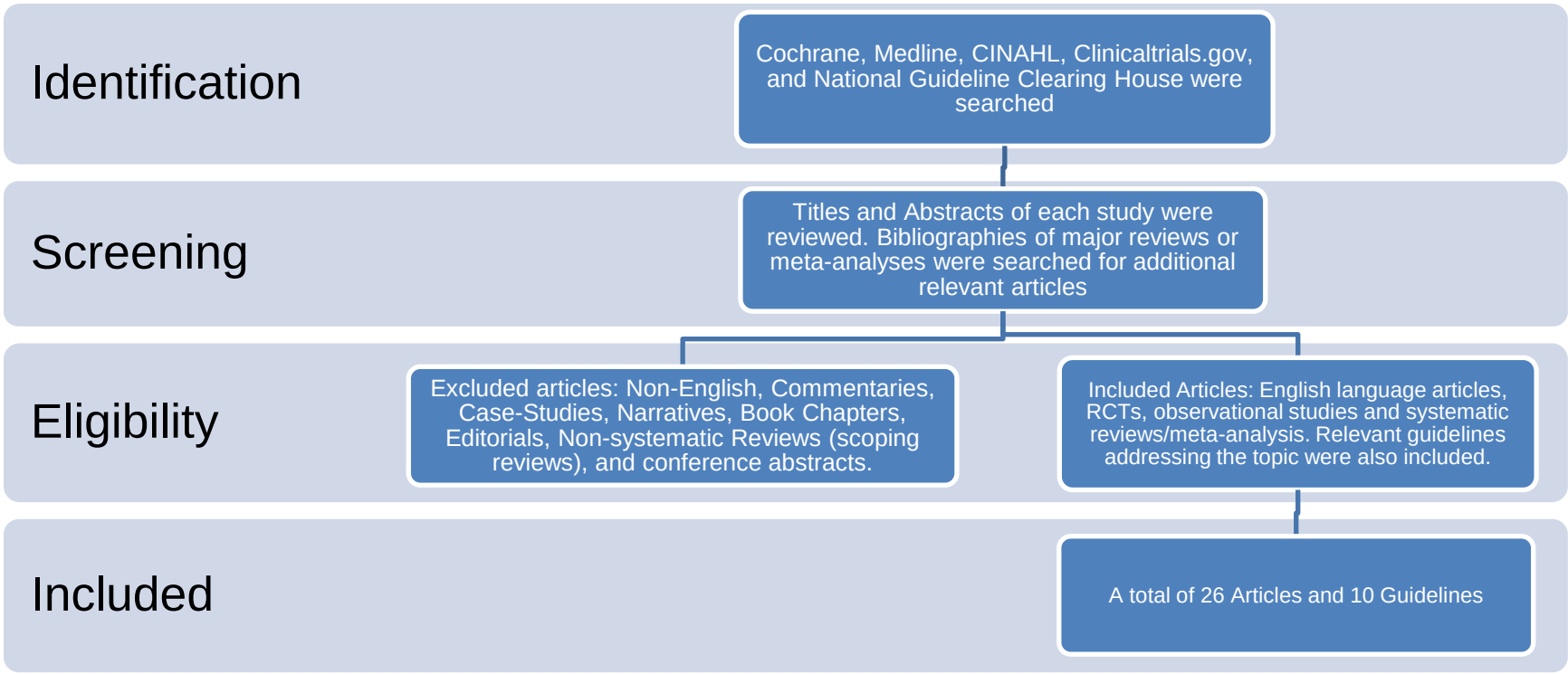
# Table of Contents

# Search Strategy




Cochrane, Medline, and CINAHL databases were search using the terms (“aspirin” OR “acetylsalicylic acid”) AND “cardiovascular disease” OR “cerebrovascular disease”. Articles were included if the focus was primary prevention and the treatment arms included aspirin monotherapy (any dose) and a placebo or no treatment control group. A separate search was conducted to identify articles regarding shared decision making in the context of vascular risk reduction. Bibliographies were reviewed to find additional relevant articles. Additional searches for relevant best practice guidelines were completed and included separately.

# Published Guidelines

| Guideline | Recommendations |
|---|---|
| **Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, Himmelfarb CD, Khera A, Lloyd-Jones D, McEvoy JW, Michos ED, Miedema MD, Muñoz D, Smith SC Jr, Virani SS, Williams KA Sr, Yeboah J, Ziaeian B.**<br><br>**2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines.**<br><br>***Circulation*. 2019;140:e596–e646** | 1. Low-dose aspirin (75-100 mg orally daily) might be considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk. COE IIb Harm; LOE A<br><br>2. Low-dose aspirin (75-100 mg orally daily) should not be administered on a routine basis for the primary prevention of ASCVD among adults >70 years of age. COE III Harm: LOE B-R<br><br>3. Low-dose aspirin (75-100 mg orally daily) should not be administered for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding. COE III Harm; LOE C-LD |
| **Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, Prescott E, Storey RF, Deaton C, Cuisset T, Agewall S.**<br><br>**2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes.**<br><br>***Eur Heart J*. 2019 Aug 3. pii: ehz425. doi: 10.1093/eurheartj/ehz425. [Epub ahead of print]** | Aspirin 75100 mg daily may be considered in patients without a history of MI or revascularization, but with definitive evidence of CAD on imaging. Class IIb; LOE C |
| **American Diabetes Association.**<br><br>**10. Cardiovascular disease and risk management: Standards of medical care in diabetes.**<br><br>**Diabetes Care 2019;42 (Suppl. 1): S103–S123.** | Aspirin therapy (75–162mg daily) may be considered as a primary prevention strategy in those with diabetes who are at increased risk of CVD after a discussion with the patient on the benefits versus increased risk of bleeding. Evidence level C |
| **Gerhard-Herman MD, Gornik HL, Barrett C, Barshes NR, Corriere MA, Drachman DE, Fleisher LA, Fowkes FG, Hamburg NM,** | Antiplatelet therapy with aspirin alone (range, 75–325 mg per day) or clopidogrel alone (75 mg per day) is recommended to reduce MI [myocardial infarction], stroke and vascular death in patients with symptomatic PAD Class 1; LOE A. |

| Guideline | Recommendations |
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| **Kinlay S, Lookstein R, Misra S, Mureebe L, Olin JW, Patel RA, Regensteiner JG, Schanzer A, Shishehbor MH, Stewart KJ, Treat-Jacobson D, Walsh ME.**<br><br>**2016 AHA/ACC guideline on the management of patients with lower extremity peripheral artery disease: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines.**<br><br>***Circulation.* 2017;135:e726–e779** | |
| **American Academy of Family Physicians (AAFP). Summary of recommendations for clinical preventive services. Leawood (KS), 2017** | Aspirin Prevention, Adults Younger than Age 50 Years<br>The AAFP concludes that the current evidence is insufficient to assess the balance of benefits and harms of initiating aspirin use for the primary prevention of CVD and CRC in adults younger than 50 years. (2016) (Grade: I recommendation)<br><br>Aspirin Prevention, Adults 50 to 59 Years<br>The AAFP recommends initiating low-dose aspirin use for the primary prevention of cardiovascular disease (CVD) and colorectal cancer (CRC) in adults aged 50 to 59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take lowdose aspirin daily for at least 10 years. (2016) (Grade: B recommendation)<br><br>Aspirin Prevention, Adults 60 to 69 Years<br>The decision to initiate low-dose aspirin use for the primary prevention of CVD and CRC in adults aged 60 to 69 years who have a 10% or greater 10-year CVD risk should be an individual one. Persons who are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years are more likely to benefit. Persons who place a higher value on the potential benefits than the potential harms may choose to initiate low-dose aspirin. (2016) (Grade: C recommendation)<br><br>Aspirin Prevention, Adults 70 Years and Older. The AAFP concludes that the current evidence is insufficient to assess the balance of benefits and harms of initiating aspirin use for the primary prevention of CVD and CRC in adults aged 70 years or older. (2016) (Grade: I recommendation) |
| **Bibbins-Domingo K.**<br><br>**Aspirin Use for the Primary Prevention of Cardiovascular Disease and Colorectal Cancer: U.S. Preventive Services Task Force Recommendation Statement.**<br><br>***Ann Intern Med*. 2016;164(12):836-45.** | The USPSTF recommends initiating low-dose aspirin use for the primary prevention of cardiovascular disease (CVD) and colorectal cancer (CRC) in adults aged 50 to 59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years. (B recommendation)<br><br>The decision to initiate low-dose aspirin use for the primary prevention of CVD and CRC in adults aged 60 to 69 years who have a 10% or greater 10-year CVD risk should be an individual one. Persons who are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years are more likely to benefit. Persons who place a higher value on the potential benefits than the potential harms may choose to initiate |

| Guideline | Recommendations |
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| | low-dose aspirin. (C recommendation)<br><br>The current evidence is insufficient to assess the balance of benefits and harms of initiating aspirin use for the primary prevention of CVD and CRC in adults younger than 50 years. (I statement)<br><br>The current evidence is insufficient to assess the balance of benefits and harms of initiating aspirin use for the primary prevention of CVD and CRC in adults aged 70 years or older. (I statement) |
| **Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, Cooney MT, Corra U, Cosyns B, Deaton C, Graham I.**<br><br>**2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR).**<br><br>***Eur Heart J.*** **2016 May 23;37(29):2315-81.**<br><br>**(selected)** | **Antiplatelet therapy in individuals with cardiovascular or cerebrovascular disease**<br>In patients with non-cardioembolic ischaemic stroke or TIA, prevention with aspirin only, or dipyridamole plus aspirin or clopidogrel alone is recommended. Class 1; Level A<br><br>**Antiplatelet therapy in individuals without cardiovascular disease**<br>Antiplatelet therapy is not recommended in individuals without CVD due to the increased risk of major bleeding. Class III; Level B |
| **Meschia JF, Bushnell C, Boden-Albala B, Braun LT, Bravata DM, Chaturvedi S, Creager MA, Eckel RH, Elkind MSV, Fornage M, Goldstein LB, Greenberg SM, Horvath SE, Iadecola C, Jauch EC, Moore WS, Wilson JA; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, Council on Functional Genomics and Translational Biology, and Council on Hypertension.**<br><br>**Guidelines for the primary prevention of stroke: a statement for healthcare** | 1. The use of aspirin for cardiovascular (including but not specific to stroke) prophylaxis is reasonable for people whose risk is sufficiently high (10-year risk >10%) for the benefits to outweigh the risks associated with treatment. (Class IIa; Level of Evidence A).<br><br>2. Aspirin (81 mg daily or 100 mg every other day) can be useful for the prevention of a first stroke among women, including those with diabetes mellitus, whose risk is sufficiently high for the benefits to outweigh the risks associated with treatment (Class IIa; Level of Evidence B).<br><br>3. Aspirin might be considered for the prevention of a first stroke in people with chronic kidney disease (ie, estimated glomerular filtration rate <45 mL/min/1.73 $m^2$) (Class IIb; Level of Evidence C). This recommendation does not apply to severe kidney disease (stage 4 or 5; estimated glomerular filtration rate <30 mL/min/1.73 $m^2$).<br><br>4. Cilostazol may be reasonable for the prevention of a first stroke in people with peripheral arterial disease (Class IIb; Level of Evidence B). |

| Guideline | Recommendations |
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| **professionals from the American Heart Association/American Stroke Association.**<br><br>***Stroke.* 2014;45:3754–3832.** | 5. Aspirin is not useful for preventing a first stroke in low-risk individuals (Class III; Level of Evidence A).<br><br>6. Aspirin is not useful for preventing a first stroke in people with diabetes mellitus in the absence of other high-risk conditions (Class III; Level of Evidence A).<br><br>7. Aspirin is not useful for preventing a first stroke in people with diabetes mellitus and asymptomatic peripheral artery disease (defined as asymptomatic in the presence of an ankle brachial index ≤0.99) (Class III; Level of Evidence B).<br><br>8. The use of aspirin for other specific situations (eg, AF,carotid artery stenosis) is discussed in the relevant sections of this statement.<br><br>9. As a result of a lack of relevant clinical trials, antiplatelet regimens other than aspirin and cilostazol are not recommended for the prevention of a first stroke (Class III; Level of Evidence C). |
| **Vandvik PO, Lincoff AM, Gore JM, Gutterman DD, Sonnenberg FA, Alonso-Coello P, Akl EA, Lansberg MG, Guyatt GH, Spencer FA.**<br><br>**Primary and secondary prevention of cardiovascular disease: antithrombotic therapy and prevention of thrombosis: American College of Chest Physicians evidence-based clinical practice guidelines.**<br><br>***Chest*. 2012 Feb 1;141(2):e637S-68S. (selected)** | 2.1. For persons aged 50 years or older without symptomatic cardiovascular disease, we suggest low-dose aspirin 75 to 100 mg daily over no aspirin therapy (Grade 2B). |
| **Bell AD, Roussin A, Cartier R, Chan WS, Douketis JD, Gupta A, Kraw ME, Lindsay TF, Love MP, Pannu N, Rabasa-Lhoret R.**<br><br>**The use of antiplatelet therapy in the outpatient setting: Canadian Cardiovascular Society guidelines.**<br><br>***Can J Cardiol.* 2011 May 1;27(3):S1-59.**<br><br>**(selected)** | For men and women without evidence of manifest vascular disease, the use of ASA at any dose is not recommended for routine use to prevent ischemic vascular events (Class III, Level A).<br><br>For men and women without evidence of manifest vascular disease, the use of clopidogrel 75 mg daily plus ASA at any dose is not recommended to prevent ischemic vascular events (Class III, Level B).<br><br>In special circumstances in men and women without evidence of manifest vascular disease in whom vascular risk is considered high and bleeding risk is low, ASA 75-162 mg daily may be considered (Class IIb, Level C).<br><br>There is currently no evidence to recommend routine use of ASA at any dose for the primary prevention of vascular ischemic events in patients with diabetes (Class III, Level A).<br><br>For patients with diabetes aged > 40 years and at low risk for major bleeding, low-dose ASA (75-162 mg daily) may be considered for primary prevention in patients with other cardiovascular risk factors for which its benefits are established (Class IIb, Level B). |

| Guideline | Recommendations |
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| | Low-dose ASA therapy (75-162 mg daily) may be considered for secondary prevention in patients with diabetes and manifest vascular disease for which its benefits are established (Class I, Level A).<br><br>Clopidogrel 75 mg daily may be considered for secondary prevention in patients with diabetes who are unable to tolerate ASA (Class IIa, Level B). |

# Evidence Tables

## ASA for the Primary Prevention of Cerebrovascular/Cardiovascular Disease

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| *Systematic reviews* | | | | | |
| **Abdelaziz et al. 2019**<br><br>**UK**<br><br>**Systematic review & meta-analysis** | 5 trials were deemed to be at low risk and 10 at intermediate risk. | 15 RCTs (n=165,502) that included persons without preexisting cardiovascular diseases. Mean age was 61.5 years. Percentage of men ranged from 0% to 100%.<br><br>Trials included ASPREE (2018), ARRIVE (2018), ASCEND (2018), AASER (2018), JPAD 2 (2017), JPPP (2014), AAA (2010), POPADAD (2008), WHS (2005), PPP (2001), HOT (1998), TPT (1998), ETDRS (1992), PHS (1989), BMD (1988)<br><br>(All trial abbreviations are defined below this table) | Trials compared aspirin (any dose) vs. control (no aspirin or placebo) for primary prevention with follow-up duration of ≥1 year.<br><br>Aspirin doses were 75 mg/day (n=2),100 mg/day (n=9), 100 mg every other day (n=1) and ≥325 mg/day (n=3). Duration of follow-up ranged from 3.6 to 10.3 years. | **Primary outcomes:**<br>All-cause death, cardiovascular (CV) death, MI, stroke, TIA, and major adverse cardiovascular events.<br><br>**Safety outcomes:**<br>Major bleeding, intracranial bleeding, fatal bleeding, and major GI bleeding | The risks of all-cause mortality and non-cardiovascular death were not reduced significantly with aspirin use (4.75% vs. 4.82%; RR= 0.97; 95% CI: 0.93 to 1.01; p= 0.13 and 3.3% vs. 3.3%; RR= 0.98; 95% CI: 0.92 to 1.05; p=0.53, respectively).<br><br>The risk of TIA was significantly lower in the aspirin group (1.06% vs. 1.33%; RR= 0.79; 95% CI: 0.71 to 0.89; p < 0.001), but not for total stroke (1.82% vs. 1.86%; RR= 0.97; 95% CI: 0.89 to 1.04; p=0.37). There was a significantly lower risk of ischemic stroke with aspirin (1.29% vs. 1.49%; RR= 0.87; 95% CI: 0.79 to 0.95; p=0.002), but a non-significantly higher risk of hemorrhagic stroke (0.29% vs. 0.23%; RR= 1.21; 95% CI: 0.99 to 1.47; p=0.059).<br><br>Aspirin use was associated with a lower risk of total MI (2.07% vs. 2.35%; RR= 0.85; 95% CI: 0.76 to 0.95; p=0.003). Aspirin was associated with a lower risk of MI in men, but not in women (RR= 0.69; 95% CI: 0.58 to 0.83; p < 0.001 vs. RR: 0.92; 95% CI: 0.78 to 1.1; p= 0.35; p for interaction= 0.03)<br><br>The risks of fatal MI (RR= 0.93; 95% CI: 0.79 to 1.11), angina pectoris (RR= 0.92; 95% CI: 0.79 to 1.08), coronary revascularization (RR= 0.96; 95% CI: 0.87 to 1.05), and symptomatic peripheral arterial disease (RR= 0.88; 95% CI: 0.70 to 1.09) were not reduced significantly with aspirin use.<br><br>The NNTs to prevent 1 event of MI, TIA, and ischemic stroke were 357, 370, and 500, respectively. |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
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| | | | | | Aspirin use for was associated with a significantly increased risk of major bleeding (1.47% vs. 1.02%; RR= 1.50; 95% CI: 1.33 to 1.69; p < 0.001), intracranial bleeding including hemorrhagic stroke (0.42% vs. 0.32%; RR= 1.32; 95% CI: 1.12 to 1.55; p= 0.001), and major GI bleeding (0.80% vs. 0.54%; RR= 1.52; 95% CI: 1.34 to 1.73; p < 0.001). |
| **Huang et al. 2019**<br><br>**Taiwan**<br><br>**Systematic review & meta-analysis** | In 3 trials, participants were not blinded to treatment group. 3 trials had attrition bias due to incomplete outcome data. | 13 RCTs (n= 134,446) that included persons without preexisting symptomatic cardiovascular diseases (eg, coronary heart disease, stroke, or peripheral artery disease). Mean age ranged from 42.9 to 74.0 years. Percentage of men ranged from 10% to 100%.<br><br>Trials included ASPREE (2018), ARRIVE (2018), ASCEND (2018), JPPP (2014), AAA (2010), JPAD (2008), POPADAD (2008), APLASA (2007), WHS (2005), ECLAP (2004), PPP (2001), TPT (1998), HOT (1998) | Trials compared low-dose aspirin (≤100 mg/day, for ≥6 months) vs. placebo, or no treatment. Daily doses in active treatment arm were 75 mg (n=2), 81 mg (n=1), 100 mg (n=8), 100 mg every other day (n=1) and 81 or 100 mg (n=1) | **Primary outcome:**<br>Any intracranial hemorrhage<br><br>**Secondary outcomes**:<br>Intracerebral hemorrhage, subdural or extradural hemorrhage, and subarachnoid hemorrhage (SAH) | Mean duration of follow-up ranged from 2.3 to 8.2 years.<br><br>Aspirin was associated with a significantly increased risk of any intracranial bleeding (RR=1.37, 95% CI, 1.13-1.66; n=8 trials; 2 additional intracranial hemorrhages in 1,000 people). In a sensitivity analysis, excluding the results from ASPREE, which included elderly people, the risk became non-significant (RR=1.28, 95% CI, 0.99-1.65).<br><br>Aspirin was not associated with a significantly increased risk of intracerebral hemorrhage (RR=1.23, 95% CI, 0.98- 1.54, n=10 trials) or SAH (RR= 1.13, 95% CI, 0.70-1.83, n=5 trials)<br><br>Aspirin was associated with a significantly increased risk of subdural or extradural hemorrhage (RR=1.53, 95% CI, 1.08-2.18, n=4 trials, 1 additional event in 1,000 people).<br><br>In subgroup analysis, Asians and persons with a BMI <25 taking aspirin were at significantly higher risk for intracerebral hemorrhage |
| **Mahmoud et al. 2019**<br><br>**USA**<br><br>**Systematic review & meta-analysis** | 1 trial had high risk of selection bias, 5 had high risk of performance bias, 3 had high risk of attrition bias | 11 RCTs (n=157,248) that included persons without prior history of atherosclerosis (including peripheral arterial disease, coronary artery disease, prior MI, prior stroke or TIA, prior percutaneous coronary intervention, prior coronary artery bypass | Trials compared aspirin vs. placebo, or no treatment | **Primary outcome:**<br>All-cause mortality<br><br>**Safety outcome:**<br>Major bleeding | Mean duration of follow-up was 6.6 years.<br><br>The use of aspirin was not associated with a lower incidence of all-cause mortality (4.6% vs. 4.7%; RR= 0.98, 95% CI 0.93–1.02; p = 0.30).<br><br>The risk of ischemic stroke was not reduced significantly with aspirin (1.7% vs. 1.8%; RR=0.94, 95% CI 0.86-1.04, p=0.24)<br><br>Aspirin was associated with an increased incidence |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
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| | | grafting), and which enrolled ≥500 patients. Mean age was 61.3 years, 48% were men.<br><br>Trials included ASPREE (2018), ARRIVE (2018), ASCEND (2018), JPAD (2016), JPPP (2014), WHS (2005), PPP (2001), TPT (1998), HOT (1998), PHS (1989), BMD (1988) | | | of major bleeding (1.8% vs. 1.2%; RR=1.47, 95% CI 1.31–1.65; P < 0.0001) and intracranial haemorrhage (0.4% vs. 0.3%; RR= 1.33, 95% CI 1.13–1.58; P = 0.001). |
| **Zheng & Roddick 2019**<br><br>**UK**<br><br>**Systematic review &meta-analysis** | 4 open-label trials were deemed to be at high risk of bias. | 13 RCTs (n=164,225), which enrolled at least 1,000 participants with no known cardiovascular disease and a follow-up of at least 12 months.<br><br>Trials included ASPREE (2018), ARRIVE (2018), ASCEND (2018), JPPP (2014), AAA (2010), JPAD (2008), POPADAD (2008), WHS (2005), PPP (2001), TPT (1998), HOT (1998), PHS (1989), BMD (1988) | Trials compared aspirin vs. placebo, or no treatment. Doses ranged from 75 to 500 mg per day. 100 mg was the most common dose. | **Primary outcomes:**<br>*Cardiovascular outcome*<br>A composite of cardiovascular mortality, nonfatal MI, and nonfatal stroke,<br><br>**Bleeding outcomes:**<br>Major bleeding events, intracranial bleeding, GI bleeding | The use of aspirin was associated with a significant reduction in the cardiovascular outcome (HR=0.89 [95% CrI, 0.84-0.95]; ARR, 0.38% [95% CI, 0.20%-0.55%]; NNT= 265), and ischemic stroke (HR=0.81 [95% CrI, 0.76-0.87]; ARR, 0.16% [95% CI 0.06 to 0.30]; NNT=540).<br><br>The use of aspirin was associated with an increased rate of major bleeding (HR=1.43 [95% CrI, 1.30-1.56]; ARI, 0.47% [95% CI, 0.34%-0.62%]; NNH= 210), intracranial bleeding and GI bleeding.<br><br>The risk of the cardiovascular outcome was reduced significantly in persons at high and low cardiovascular risk, and those with diabetes. Bleeding risk was also significantly increased in these groups. |
| **Baigent et al. 2009**<br><br>***Antithrombotic Trialists' Collaborative (ATTC)***<br><br>**UK**<br><br>**Systematic review & meta-** | NA | 18 RCTs examining aspirin therapy for primary (n=6 with 95,456 subjects) and secondary (n=16) prevention of vascular events.<br><br>Primary prevention trials included: WHS (2005), PPP (2001), HOT (1998), TPT (1998), US Physicians' Health Study | Aspirin regimens (mg/day) in the primary prevention trials included 75 (n=2), 100 (n=1), 100 every other day (n=1), 325 every other day (n=1) and 500 (n=1) that was provided for at least 2 years. Persons in the control group received placebo in 3 trials. | **Primary outcome:**<br>Serious vascular event (MI, stroke or death from a vascular cause), major coronary event, any stroke, all-cause mortality, extracranial bleeding. | The mean duration of follow-up ranged from 3.7 to 10 years.<br><br>**Primary Prevention Trials**<br>There was a significant reduction in risk of any serious vascular event associated with aspirin therapy (RR=0.88, 95% CI 0.82-0.94, p=0.0001), including any major coronary event (RR= 0·82, 95% CI 0·75–0·90, p=0·00002).<br><br>There was no significant reduction in the risk of nonfatal MI (RR=0·77, 95% CI 0·67–0·89), death |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
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| **analysis (update to 2002)** | | (19888) and BDS (1988)<br><br>In the 3 of the primary prevention trials, participants were at higher risk for coronary heart disease. Trials recruited men only (n=3), women only (n=1) and included both sexes (n=2). | | | from coronary heart disease (RR=0·95, 95% CI 0·78–1·15), any stroke (RR=0.95, 95% CI 0.85-1.06, p=0.40), fatal stroke (RR=1.21, 95% CI 0.84-1.74) or nonfatal stroke (RR=0.92, 95% CI 0.79-1.07).<br><br>The risk of major gastrointestinal and other extracranial bleeds was significantly increased in persons taking aspirin (0·10% vs 0·07% per year, p<0·0001).<br><br>It has been estimated there would be 6 per 10,000 per year fewer serious vascular events with aspirin therapy and 3 per 10,000 extracranial events per year. |
| *Clinical Trials* | | | | | |
| **Gaziano et al. 2018**<br><br>**International**<br><br>**RCT**<br>***Aspirin to Reduce Risk of Initial Vascular Events (ARRIVE)*** | Concealed Allocation: ☑<br><br>Blinding:<br>Patient ☑<br>Assessor ☑<br><br>ITT: ☑ | 12,546 patients recruited primarily from primary care centres in 7 countries (Germany, Italy, Ireland, Poland, Spain, UK, and USA). Eligible men were ≥ 55 years and had 2-4 cardiovascular risk factors; eligible women were ≥60 years and had 3-5 risk factors. Persons with a significant cardiovascular history and those with a history of bleeding were excluded. Mean age was 63.9 years, 70.4% were men. Mean estimated ACC/AHA 10-year ASCVD risk score at baseline was 17.3% | Participants were randomized 1:1 to receive 100 mg aspirin or placebo daily for the duration of the trial | **Primary outcome:**<br>Composite of time to first occurrence of confirmed MI, stroke, cardiovascular death, unstable angina, or TIA<br><br>**Safety outcomes:**<br>Hemorrhagic events | Median duration of follow-up was 5.1 years.<br><br>29.6% of patients terminated the study early.<br><br>In the intention- to- treat analysis, the risk of the primary outcome and its component parts were not reduced significantly with aspirin therapy<br>Primary outcome: HR=0·96, 95% CI 0·81–1·13, p=0·6038<br>Fatal/nonfatal MI: HR=0·85, 95% CI 0·64–1·11, p=0·2325<br>Fatal/nonfatal stroke: HR=1.12, 95% CI 0·80–1·55, p=0·5072<br>Cardiovascular death: HR=0·97, 95% CI 0·62–1·52, p=0·9010<br>TIA: HR=0·93, 95% CI 0·61–1·42, p=0·7455<br><br>The risk of serious adverse events was similar between groups (20.19% vs. 20.89%).<br><br>The overall incidence of treatment-related adverse events was significantly higher in the aspirin group (16.75% vs. 13.54%, p<0·0001).<br><br>The authors suggested that the reason for the apparent lack of benefit of aspirin was due to the lower than expected event rate (1,500 expected, |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
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| | | | | | 500 actual), which was attributed to aggressive prevention measures, particularly, the treatment of hypertension). |
| **Bowman et al. 2018**<br><br>**UK**<br><br>**RCT**<br>***A Study of Cardiovascular Events in Diabetes (ASCEND)*** | Concealed Allocation: ☑<br><br>Blinding:<br>Patient ☑<br>Assessor ☑<br><br>ITT: ☑ | 15,480 participants >40 years, with diabetes with no known CVD. Mean age was 63 years, 63% were men, 36% had taken aspirin previously. Median duration of diabetes was 7 years. 83% of participants had low or moderate vascular risk scores. | Participants were randomized 1:1 to receive 100 mg aspirin or placebo daily for the duration of the trial | **Primary outcome:**<br>First serious vascular event (MI, stroke, TIA or cardiovascular death)<br><br>**Secondary outcome:**<br>Gastrointestinal tract cancers<br><br>**Safety outcomes:**<br>Hemorrhagic events | Mean duration of follow-up was 7.4 years.<br><br>Estimated mean adherence was 70% in both groups.<br><br>The risk of the primary outcome was significantly lower in the aspirin group (8.5% vs, 9.6%, RR=0.88, 95% CI, 0.79 to 0.97; p=0.01).<br><br>The risk of any major bleeding was significantly increased in the aspirin group (4.1% vs. 3.2%, RR=1.29, 95% CI 1.09-1.52, p=0.003).<br><br>There was no significant difference between groups in the risk of GI cancer (2% vs. 2%, RR=0.99, 95% CI 0.80–1.24). |
| **McNeil et al. 2018**<br><br>**Australia**<br><br>**RCT**<br>***Aspirin in Reducing Events in the Elderly (ASPREE) trial*** | Concealed Allocation: ☑<br><br>Blinding:<br>Patient ☑<br>Assessor ☑<br><br>ITT: ☑ | 19,114 persons ≥70 years (or ≥65 years of age among blacks and Hispanics in the United States) without cardiovascular disease, dementia, or disability, recruited from Australia and the US between 2010 and 2014. Median age was 74 years, 44% were men. 14% had used NSAIDS regularly. | Participants were randomly assigned (1:1) to receive 100 mg of enteric-coated aspirin or placebo. | **Primary outcome:**<br>CVD (fatal coronary heart disease, nonfatal MI, fatal or nonfatal stroke, or hospitalization for heart failure).<br><br>**Safety outcomes:**<br>Major bleeding events | Median duration of follow-up was 4.7 years.<br><br>In the final 12 months of the trial, 62% of the participants in the aspirin group and 64% of those in the placebo group were still taking the assigned trial intervention.<br><br>The number of CVD events did not differ significantly between groups (10.7 vs. 11.3/1,000-person years, HR=0.95, 95% CI 0.83–1.08), nor did the number of ischemic strokes (3.5 vs. 3.9/1,000 person-years follow-up; HR=0.89, 95% CI 0.71–1.11).<br><br>The risk of major bleeding events was significantly increased in the aspirin group (8.6 vs. 6.2/1,000-person years; HR=1.38, 95% CI 1.18–1.62, p<0.001). The risk of fatal hemorrhagic stroke was not significantly increased with aspirin therapy (0.3 vs. 03/1,000-person years; HR=1.01, 95% CI 0.47–2.17). |
| *Atherosclerosis* | | | | | |
| **Fowkes et al.** | Concealed | 3,350 participants aged | Participants were | **Primary outcome:** | Mean duration of follow-up was 8.2 years. |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| **2010**<br><br>**UK**<br><br>**RCT**<br>***Aspirin for Asymptomatic Atherosclerosis (AAA) Trial*** | Allocation: ☑<br><br>Blinding:<br>Patient ☑<br>Assessor ☑<br><br>ITT: ☑ | 50 to 75 years at baseline with no history of vascular disease with an ankle brachial index (ABI) ≤ 0.95, recruited from the community. Mean age was 62 years, 29% were men. Mean ABI was 0.86 | randomized 1:1 to receive 100 mg aspirin daily or placebo for the duration of the trial. | A composite of initial fatal or nonfatal coronary event or stroke or revascularization.<br><br>**Secondary outcomes:**<br>All initial vascular events defined as a composite of a primary end point event or angina, intermittent claudication, or TIA and all-cause mortality. | There was no significant reduction in the risk of primary outcome in the aspirin group (aspirin, 13.7; 95% CI, 11.8-15.9 vs placebo, 13.3; 95% CI, 11.4-15.4, events per 1,000 person-years; HR=1.03; 95% CI, 0.84-1.27).<br><br>There was no significant reduction in the risk of the secondary outcome in the aspirin group (aspirin, 22.8; 95% CI, 20.2-25.6 vs placebo, 22.9; 95% CI, 20.3-25.7 events per 1,000 person-years; HR= 1.00; 95% CI, 0.85-1.17).<br><br>The risk of any of the individual components of either the primary or secondary outcomes were not reduced significantly with aspirin.<br><br>An initial major hemorrhage requiring admission to hospital occurred in 34 participants (2.5 per 1000 person-years) in the aspirin group and 20 (1.5 per 1000 person-years) in the placebo group (HR= 1.71; 95% CI, 0.99-2.97). |
| **Cote et al. 1995**<br><br>**Canada**<br><br>**RCT**<br>***Asymptomatic Cervical Bruit Study*** | Concealed Allocation: ☑<br><br>Blinding:<br>Patient ☑<br>Assessor ☑<br><br>ITT: ☑ | 372 neurologically asymptomatic patients with carotid stenosis of ≥50% in at least one artery. Sources of referred patients included family practices and internists and general practitioners from the community and hospital-based subspecialty clinics. Mean age was 66.7 years, 53% were women. | Participants were randomized 1:1 to receive 325 mg aspirin daily or placebo for the duration of the trial. | **Primary outcome:**<br>Composite of TIA, stroke, MI, unstable angina, or death.<br><br>**Secondary outcomes:**<br>Combinations of individual components of the primary outcome | Median duration of follow-up was 2.3 years.<br><br>The risk of the primary outcome was not significantly reduced with aspirin use (annual rate of 11% vs. 12.3%; HR= 0.988, 95% CI 0.667 to 1.464, p= 0.95).<br><br>Aspirin did not significantly reduce the risk of any of the secondary outcomes including 1) TIA, stroke, MI, unstable angina, and death from vascular causes; 2) stroke, MI, and death from vascular causes; 3) TIA and stroke; 4) stroke and death from vascular causes; and 5) MI, unstable angina, and death from vascular causes. |

**ASA Trial Abbreviations**

| | |
|---|---|
| AAA: Aspirin for Asymptomatic Atherosclerosis | AASER: Acido Acetil Salicilico en la Enfermedad |
| APLASA: The Antiphospholipid Antibody Acetylsalicylic Acid study | ARRIVE: Aspirin to Reduce Risk of Initial Vascular Events |

| | |
|---|---|
| ASCEND: A Study of Cardiovascular Events in Diabetes | ASPREE: Aspirin in Reducing Events in the Elderly |
| BMD: British Male Doctors Trial | ECLAP: The European Collaboration on Low-Dose Aspirin in Polycythemia Vera |
| ETDR: Early Treatment Diabetic Retinopathy | HOT: Hypertension Optimal Treatment |
| JPAD2: Japanese Primary Prevention of Atherosclerosis with Aspirin for Diabetes | JPPP: Japanese Primary Prevention Project |
| PHS: Physician's Health Study | POPADAD: Prevention of Progression of Arterial Disease and Diabetes |
| PPP: Primary Prevention Project | TPT: Thrombosis Prevention Trial |
| WHS: Woman Health Study | |

## Primary Prevention in Persons with Peripheral Artery Disease (PAD)

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| **Berger et al. 2009**<br><br>**USA**<br><br>**Systematic review & meta-analysis** | Jadad scores:<br>5 n=1<br>4 n=5<br>3 n=4<br>2 n=2<br>N/A n=6 | 18 RCTS (n=5,269) including participants with PAD. Participants with PAD included those with claudication, those undergoing percutaneous intervention or bypass surgery, and asymptomatic patients with an ankle brachial index of≤ 0.99. Two trials exclusively enrolled patients with both diabetes and PAD. Trials were published between 1975 and 2008. | 7 trials examined aspirin monotherapy vs. placebo or control, 7 trials examined combined aspirin and dipyridamole vs. placebo or control, and 4 trials had multiple arms (aspirin monotherapy, aspirin plus dipyridamole, and placebo). 3,019 participants were randomized to aspirin monotherapy therapy, of whom 1,516 received aspirin and 2,446 received placebo. Aspirin monotherapy doses ranged from 100 mg/d to 1500 mg/d. | **Primary outcomes:**<br>Cardiovascular events (nonfatal MI, nonfatal stroke, and cardiovascular death)<br><br>**Secondary outcomes:**<br>All-cause mortality, major bleeding, and the individual components of the primary outcome measures | The risk of the primary outcome was not reduced significantly with aspirin therapy (0.75; 95% CI, 0.48-1.18; results from 9 trials included).<br><br>The risk of nonfatal stroke was reduced significantly with aspirin monotherapy (RR=0.64, 95% CI, 0.42-0.99) but there was no significant reduction in the risk of all-cause or cardiovascular mortality or MI).<br><br>The risk of major bleeding was not increased significantly with aspirin monotherapy. |
| **Belch et al. 2008**<br><br>**UK**<br><br>**RCT (factorial)**<br>***POPADAD*** | Concealed Allocation: ☑<br><br>Blinding:<br>Patient ☑<br>Assessor ☑<br><br>ITT: ☑ | 1,276 participants aged ≥40 years with type 1 or type 2 diabetes and an ankle brachial pressure index of ≤0.99, but with no symptomatic cardiovascular disease. Mean age was 60 years, 54% were women. | Participants were randomized to receive 100 mg aspirin + antioxidant (n=320), aspirin + placebo (n=318), placebo + antioxidant (n=320), or placebo + placebo (n=318). | **Primary outcomes:**<br>i) Composite end points of death from coronary heart disease or stroke, non-fatal MI or stroke, or amputation above the ankle for critical limb ischemia; and ii) a composite of death from coronary heart disease or | Median duration of follow-up was 6.7 years.<br><br>**For the comparisons of aspirin vs placebo**<br>There were no significant differences between groups in the risk of the primary or secondary outcomes.<br><br>The percentage of persons who reached the first primary outcome was 18% in each group (HR= |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| | | | | stroke<br><br>**Secondary outcomes:**<br>All- cause mortality, non-fatal MI, and occurrence of other vascular events, including stroke, TIA, coronary or peripheral arterial bypass surgery, coronary or peripheral arterial angioplasty, development of angina, claudication, or critical limb ischemia. | 0.98, 95% CI 0.76 to 1.26). 6% of persons in the aspirin group achieved the second co-primary outcome vs. 5% in the placebo group (HR= 1.23, 95% CI 0.79 to 1.93).<br><br>2% of persons in the aspirin and placebo groups had an above ankle amputation for critical limb ischemia. 3% of persons in the aspirin and placebo groups developed critical limb ischemia.<br><br>18% of persons in the aspirin group developed claudication vs.15% of those in the placebo group. |
| **Catalano et al. 2007**<br><br>**Italy**<br><br>**RCT (factorial)**<br>***Critical Leg Ischaemia Prevention Study (Clips)*** | Concealed Allocation: ☑<br><br>Blinding: Patient ☑ Assessor ☑<br><br>ITT: ☑ | 366 outpatients with stage I-II PAD, with ankle/brachial index <0.6. Mean age was 66 years, 75% were men. 75% had diabetes. | Patients were randomized to receive i) 100 mg aspirin daily, ii) antioxidant vitamins (600 mg vitamin E, 250 mg vitamin C and 20 mg b-carotene daily), iii) both or iv) neither, given for 2 years. | **Primary outcome:**<br>Major vascular events (cardiovascular death, MI or stroke) and critical leg ischemia. | Mean duration of follow-up was 21 months.<br><br>**For the comparisons of aspirin vs placebo**<br>The risk of stroke (fatal and nonfatal) was not reduced significantly with aspirin use (4 vs. 7, HR= 0.54, 95% CI 0.16–1.85), nor did aspirin reduce the risks of pulmonary embolus or vascular death.<br><br>Aspirin use did reduce the risks of MI (fatal/nonfatal, HR=0.18 (0.04–0.83), a vascular event (HR=0.35, 95% CI 0.15–0.82) and a vascular event or critical limb ischaemic (HR=0.42, 95% CI 0.21–0.83). |

## Cognitive Decline

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| **Veronese et al. 2017**<br><br>**Italy**<br><br>**Systematic review & meta-analysis** | Look up after UWO access restored | 8 studies, 5 longitudinal and 3 RCTs (n=36,196), including participants without dementia or cognitive impairment at baseline. Mean age was 66 years, 63% were women. Of whom 8,484 (23.4%) received low-dose aspirin | The association between low-dose (<300 mg/d) aspirin and cognitive performance, was examined. | **Primary outcome:**<br>New onset dementia (longitudinal studies), changes in global cognition (RCTs) | In longitudinal studies, the use of low-dose aspirin did not significantly reduce the odds of dementia or cognitive impairment (OR = 0.82, 95% CI = 0.55–1.22, P = .33). Median duration of follow-up was 6 years.<br><br>In RCTs, the use of low-dose aspirin was not associated with better global cognitive test scores (SMD = 0.00, 95% CI = 0.04 to 0.05, p = .84). |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| | | | | | Median duration of follow-up was 5 years. |
| **Kelley et al. 2015**<br><br>**USA**<br><br>**Letter** | NA | 23,915 participants included in the REGARDS study who were cognitively normal at baseline. Mean age was 64 years, 43% were women | The association between regular aspirin use and cognitive decline was examined. | **Primary outcome:**<br>Change in mean 6-Item Screener (SIS) scores, Word List Learning (WLL) Word List Recall (WLR) Animal Fluency Test (AFT) and Letter Fluency (LF) | The odds of cognitive impairment (SIS <5) were not significantly higher among non-aspirin users, after adjustment for demographic factors (OR = 0.99, 95% CI = 0.89–1.09). Mean duration of follow-up was 5.9 years.<br><br>In fully adjusted models, there were no significant differences between groups (aspirin users vs, non-aspirin users) in mean change in memory or executive function tests. Mean duration of follow-up was 3.6 years. |
| **Price et al. 2008**<br><br>**UK**<br><br>**RCT**<br>***Aspirin for Asymptomatic Atherosclerosis (AAA) Trial*** | Concealed Allocation: ☑<br><br>Blinding: Patient ☑ Assessor ☑<br><br>ITT: ☑ | 3,350 participants aged 50 to 75 years at baseline with no history of vascular disease with an ankle brachial index (ABI) ≤ 0.95, recruited from the community. Mean age was 62 years, 29% were men. Mean ABI was 0.86<br><br>Of the enrolled participants, 1,004 underwent cognitive testing at baseline. | Participants were randomized 1:1 to receive 100 mg aspirin daily or placebo for the duration of the trial (5 years). | **Primary outcomes:**<br>Tests of memory, executive function, non-verbal reasoning, mental flexibility. Individual scores were also summed to create a summary cognitive score (general factor). | 1,025 participants were lost to cognitive follow-up.<br><br>32.7% (n=548) of participants in the aspirin group and 34.8% (n=583) in the placebo group achieved over the median general factor score. The odds of achieving ≥50% above the median score were not increased significantly in the aspirin group after adjustment for age, sex, ankle brachial index, social deprivation category, smoking status, and total plasma cholesterol (OR=0.93,95% CI 0.80 to 1.08, p=0.35).<br><br>There were no significant differences between groups in mean change scores over the trial period for any of the individual tests or for the general factor. |
| **Kang et al. 2007**<br><br>**USA**<br><br>**Cohort study within the Women's Health Study (factorial RCT)** | Concealed Allocation: ☑<br><br>Blinding: Patient ☑ Assessor ☑<br><br>ITT: ☑ | 6,377 women ≥65 years with no history of coronary heart disease, cerebrovascular, or other major chronic illnesses. Mean age was 66 years at randomization. | Participants were randomized to receive 100 mg aspirin every other day or placebo.<br><br>Cognitive assessments were carried out by telephone at baseline (5.6 years after initial randomization), and every two years (3 assessments in total). | **Primary outcome:**<br>Cognitive global score, calculated using the results of i) general cognition, ii) verbal memory, and iii) category fluency tests. | The average total duration of follow-up was 9.6 years.<br><br>79.5%of participants completed all cognitive assessments.<br><br>There was no significant difference between groups in mean decline in the global score over the study period (MD= 0.01, 95% CI−0.02 to 0.04, p=0.5).<br><br>There were no significant differences between groups in mean change scores for any of the individual tests of the global score from first to final assessment. |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| | | | | | In subgroup analysis, aspirin use was associated with better performance on global scores in those who were current smokers and those with raised chol.<br><br>The risk of substantial cognitive decline was not reduced significantly with aspirin use for any of the outcomes, except for verbal fluency (RR=0.80, 95% CI 0.67 to 0.97, p=0.02) |

## Shared Decision Making

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| **Johnson et al. 2018**<br><br>**UK**<br><br>**Systematic review** | 3 RCTs were at low risk of bias in most domains. | 6 studies (5 RCTs) that included adults in primary care being treated for hypertension. Mean age range was 58.5-64.5 years, 32.5%-66.0% were women. | Studies evaluated the effects of shared decision-making interventions compared with any comparator, targeting either the patient or physician.<br><br>Interventions included: 1) Mailed booklet with information on hypertension including treatment options vs. unspecified control; 2) one-hour decision analysis session + video/leaflet vs. usual care; 3) training programme for GPs “to develop communication skills necessary to practice shared decision making” + regular consultations between trained | **Primary outcome:**<br>Shared decision making.<br><br>Scales used included the Shared Decision Making Questionnaire, Autonomy Preference Index, Decisional Conflict Scale, Physicians’ Participatory Decision-Making Style, Patients’ Perceived Involvement in Care Scale<br><br>**Secondary outcome:**<br>Effect of intervention on blood pressure | In only one study did the intervention increase shared decision making. Outcomes were assessed from 14 days to 18 months after the intervention.<br><br>4 studies reported blood pressure 6 months to 3 years after the intervention. There was no difference in blood pressure between intervention and control groups in any study. |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| | | | physicians and patients to make decisions on further treatment + hypertension education module for patients vs. education module for patients only; 4) coaching sessions for patients + communication skill training programme for physicians vs. minimal services for patients and physicians; 5) training programme for GPs vs. usual care; and short /extended versions of a decision aide vs. usual care. | | |
| **Bailey et al. 2016**<br><br>**USA**<br><br>**RCT** | Concealed Allocation: ☑<br><br>Blinding: Patient ☒ Assessor ☑<br><br>ITT: ☑ | 225 participants, recruited from 27 US primary care and endocrinology clinics with type 2 diabetes (T2DM) who were receiving metformin with persistent hyperglycemia who were recommended to consider medication intensification. Mean age was 52.3 years, 54.7% were women. Mean duration since T2DM diagnosis was 6.6 years. | Participants were randomized to receive either a patient decision aid (PDA) targeting decisions about treatment intensification via an email link or usual care. The PDA took approximately 30 minutes to complete. | **Primary outcome:** Knowledge, assessed using a study specific scale, based on 17 true/false/not sure statements at 4-6 weeks follow-up<br><br>**Secondary outcomes:** Decision Self Efficacy Scale (DSES), Decisional Conflict Scale (DCS). | Participants in the PDA group had significantly greater knowledge gains from baseline (35.0 % vs. 9.9 %, p < 0.0001) and larger improvements in DSES scores (3.7 vs.−3.9, p < 0.0001) and DCS scores (−22.2 vs. −7.5, p < 0.0001). |
| **Tinsel et al. 2013**<br><br>**Germany**<br><br>**Cluster RCT** | Concealed Allocation: ☑<br><br>Blinding: Patient ☑ Assessor ☑<br><br>ITT: ☑ | 1,120 adults with treated but uncontrolled hypertension recruited from 36 GP practices. Mean age of patients was 64 years, 45% were men. | GP practices were randomized to an intervention or a control arm. GPs of the intervention group took part in a 6-hour, multicomponent program of SDM training. GPs of | **Primary and secondary patient outcomes:** Change in perceived participation (SDM-Q-9), change in SBP, change in DBP, knowledge, Medication Adherence Report Scale (MARS-D), and cardiovascular risk score | Mean baseline SBP was 133.19 mmHg in the intervention group and 130.80 mmHg in the control group.<br><br>From baseline to 18 months, the mean difference between groups in SDM-Q-9 scores was 3.1182, 97.5% CI −2.3730; 8.6093, *P* = 0.2029 (not statistically significant at 2.5% level due to |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| | | | the control group treated their patients as usual. | (CVR). Assessments were conducted at 6, 12 and 18 months | Bonferroni correction for multiple outcome measures).<br><br>There were no significant differences between groups on any of the other outcome measures |
| **Krones et al. 2008**<br><br>**Germany**<br><br>**Cluster RCT** | Concealed Allocation: ☑<br><br>Blinding: Patient ☑ Assessor ☑<br><br>ITT: ☒ | 1,132 patients recruited from 14 continuing medical education (CME) groups (91 physicians). Mean age of patients was 59 years, 58% were men. Mean baseline CVD risk score was 10.5%. | Physicians were randomized to a CME intervention or control group. Physicians in the intervention group attended 2 interactive CME sessions that focused on CVD risk reduction. Physicians also received a booklet, a paper-based risk calculator, and individual summary sheets for each patient. Control physicians attended 1 CME-session on an alternative topic | **Primary patient outcomes:** Patient participation (Patient Participation Scale), assessed after the intervention<br><br>**Secondary outcomes:** Shared decision making- Q (SDM-Q) scale and an instrument on decisional regret, knowledge of CVD prevention, decision regret (assessed for those who remembered their decision 6 months previously) | Patients in the intervention group were significantly more satisfied with process and result (mean difference=0.80, p<0.001).<br><br>Decisional regret was significantly lower at follow-up (mean difference 3.39, p = 0.02).<br><br>There were no significant differences between groups in CVD prevention knowledge or mean change in CVD risk score. |

**Abbreviations**

| | | |
|---|---|---|
| ARR: absolute risk reduction | CI: confidence interval | HR: hazard ratio |
| ITT: intention-to-treat | MI: myocardial infarction | NA: not assessed |
| NNTB: number needed to benefit | OR: odds ratio | RR: relative risk |
| RRR: relative risk reduction | | |

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