

Top studies of 2024 relevant to primary care

From the PEER team

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Abstract

Objective To identify and summarize the most impactful medical articles published in 2024 relevant to primary care.

Selecting the evidence Randomized controlled trials and meta-analyses relevant to primary care were identified by the PEER (Patients, Experience, Evidence, Research) team, a Canadian evidence-based medicine research group with a focus on primary care. The table of contents of major medical journals were reviewed as well as medical email alert services. The articles were ranked by the PEER team and selected studies were summarized.

Main message Articles addressed various clinical areas in primary care. Topics included a behavioural strategy to reduce chronic benzodiazepine use for insomnia; the roles of β -blockers and colchicine after myocardial infarction; the effect of intensive blood pressure lowering on major cardiovascular outcomes; the effect of vitamin D on fracture prevention; walking for preventing recurrent back pain; testosterone for sexual dysfunction; methotrexate for osteoarthritis; dual antiplatelet use in patients with stable coronary artery disease and atrial fibrillation; and expanding indications for glucagon-like peptide-1 agonists. Four studies that evaluated the impact of screening and guideline-adherence strategies on patient outcomes were honourable mentions.

Conclusion Several clinical trials and meta-analyses published in 2024 were relevant to primary care, particularly in the areas of insomnia, cardiology, and musculoskeletal disorders.

Amid the ongoing crisis in family medicine, physicians face growing demands and limited time. With countless medical articles published each year, identifying, reading, and analyzing the most relevant evidence for primary care poses a considerable and time-consuming challenge. To assist, we highlight below the medical articles of 2024 most likely to impact primary care practice, covering a range of topics relevant to family physicians' diverse and comprehensive work.

Selecting the evidence

The PEER (Patients, Experience, Evidence, and Research) team identified randomized controlled trials (RCTs) and meta-analyses published in 2024 relevant to primary care. Notable medical journals (eg, *New England Journal of Medicine*, the *Lancet*, *BMJ*) and medical publication alert services (eg, ACCESSSS,¹ *NEJM Journal Watch*,² EvidenceAlerts³) were searched for high-quality, relevant evidence. Canadian family physicians, pharmacists, and nurses on the PEER team independently ranked the selected articles. All results are statistically significant unless otherwise stated.

Editor's key points

▶ Staying up to date on new literature relevant to primary care presents a considerable challenge. The authors of this review summarize what they believe were the top studies of 2024 that could impact comprehensive family medicine practice.

▶ Findings included the following: a behavioural intervention can help patients discontinue sleep medications; β -blockers initiated after an acute myocardial infarction (MI) with preserved ejection fraction may not impact death or MI; targeting systolic blood pressure of less than 120 mm Hg reduces risk of death and major cardiovascular events; vitamin D supplementation does not reduce total or hip fractures; walking can reduce time to low back pain recurrence; testosterone likely has little to no effect on erectile dysfunction; methotrexate may improve symptoms of osteoarthritis; there is no added benefit with dual antithrombotic therapy compared with edoxaban monotherapy in patients with atrial fibrillation and stable cardiovascular disease; colchicine may not be superior to placebo following an MI.

▶ Screening for depression or respiratory diseases did not change patient-important outcomes and were resource intensive. While interventions can improve guideline adherence in practice, patient outcomes were unchanged and a few worsened.

Main message

Can a direct-to-patient behavioural intervention support older adults in reducing or discontinuing chronic benzodiazepine use for insomnia?

Bottom line: A behavioural intervention for patients regularly using sleep medication can help 1 in 4 reduce or discontinue their sleep medications.

Methods: In a Canadian RCT,⁴ 565 patients using chronic benzodiazepines (including z drugs) for insomnia (mean age of 72 years; mean duration of use=11 years; diazepam equivalent of 5.7 mg/day) were randomized to 2 mailed behaviour change interventions (Sleepwell or EMPOWER) or treatment as usual.

Results: At 6 months, the proportion of patients stopping benzodiazepine medications was higher with Sleepwell (26%) and EMPOWER (20%) compared with treatment as usual (8%). More patients achieved a composite endpoint of stopping or reducing their dose by 25% or more with Sleepwell (47%) compared with EMPOWER (35%) or treatment as usual (20%). Withdrawal effects were experienced by 33% of patients who stopped taking benzodiazepines (most common being insomnia).

Do β -blockers reduce major adverse cardiovascular events (MACE) in patients with a previous myocardial infarction (MI) and preserved ejection fraction?

Bottom line: β -blockers initiated after an acute MI with preserved ejection fraction did not impact death or MI at 3.5 years. Stopping β -blockers approximately 3 years after an MI with preserved ejection fraction had no effect on MACE but increased cardiovascular hospitalizations, primarily for elective procedures.

Methods: Two open-label RCTs^{5,6} examined β -blockers in patients with recent or remote MI and preserved ejection fraction (mean age of 63 to 65 years). The REDUCE-AMI trial⁵ compared β -blocker initiation with no β -blocker (5020 patients with new MI). The ABYSS trial⁶ compared β -blocker continuation versus interruption (3698 patients with remote MI [median time between last MI and randomization=2.9 years]).

Results: At 3.5 years, β -blocker initiation after recent MI did not reduce the primary outcome (composite of death or MI), cardiovascular death, heart failure hospitalization, or atrial fibrillation. At 3 years, the primary composite outcome of all-cause death, nonfatal MI, stroke, or other hospitalizations for cardiovascular events was increased in the interrupted group (23.8% vs 21.1%) but MACE (composite of death, MI, or stroke) was no different (7.2% vs 6.8%). For other cardiovascular hospitalizations (18.9% vs 16.6%), angiography was most common. Additional RCTs are ongoing.⁷⁻⁹

Does intensive blood pressure treatment improve major cardiovascular outcomes in higher-risk adults with and without diabetes compared with standard blood pressure treatment?

Bottom line: Targeting a systolic blood pressure (SBP) of less than 120 mm Hg reduces risk of death and major cardiovascular events in adults with higher cardiovascular risk and hypertension compared with targeting an SBP of less than 140 mm Hg. The more intensive strategy also increases the risk of sustained estimated glomerular filtration rate decline. Death was not reduced in those with diabetes.

Methods: Two open-label RCTs^{10,11} compared intensive blood pressure treatment (SBP<120) with standard treatment (SBP<140). The ESPRIT trial included 11,255 participants at high cardiovascular risk (mean age=65)¹⁰ while the BPROAD trial studied 12,821 participants with type 2 diabetes at increased cardiovascular risk (mean age=64).¹¹

Results: At 3.4 (ESPRIT) and 4.2 years (BPROAD), intensive treatment decreased the risk of major cardiovascular events compared with standard treatment (ESPRIT 9.7% vs 11.1%; BPROAD 6.1% vs 7.7%, number needed to treat [NNT]=65 to 75). Risk of death was lower in the intensive group in ESPRIT (2.8% vs 3.6%, NNT=131), but not in BPROAD. Syncope was increased in the intensive group (0.4% vs 0.1%, number needed to harm [NNH]=333) as was sustained estimated glomerular filtration rate decline of 40% or more (3% vs 1.8%, NNH=84) in ESPRIT.

Does vitamin D supplementation decrease the incidence of total or hip fractures in elderly, healthy populations?

Bottom line: Vitamin D supplementation (without calcium) does not reduce total or hip fractures in elderly, healthy populations.

Methods: A systematic review¹² of 7 RCTs randomized 71,899 patients living in the community (50% women, mean age=64 to 80) to vitamin D or placebo. Six RCTs used high doses administered monthly or yearly and 1 RCT used 2000 IU/day. Trials with osteoporosis patients or concurrent calcium supplementation were excluded.

Results: At 36 to 64 months, vitamin D supplementation did not reduce total fractures (5.6% vitamin D vs 5.4% placebo) or hip fractures (0.9% vs 0.8%). In women, hip fractures were reported to be increased with vitamin D supplementation (1.2% vs 0.9%, NNH=334). This finding was driven by 1 RCT that used high doses given once yearly.

Can walking reduce the recurrence of low back pain?

Bottom line: Walking can reduce time to low back pain recurrence by approximately 3 months versus control.

Methods: An RCT¹³ randomized 701 patients with a history of recurrent back pain to walking for 6 months or no intervention (mean age=54, 96% had 2 or more previous episodes of back pain). Patients in the intervention group were assigned to a walking and education intervention, receiving 6 sessions with a physiotherapist to develop an individualized walking plan. The target was

to walk 5 times per week for at least 30 minutes each time by the 6-month mark.

Results: By week 12, the median number of times walked per week was 4. The number of days to recurrence was 208 days in the intervention group versus 112 days in the control group—a difference of 96 days. More patients in the intervention group had lower-extremity adverse events (21% vs 12%) but fewer had low back pain-related adverse events (14% vs 24%) (statistics not reported).

Can testosterone replacement improve sexual function in men?

Bottom line: For men with sexual dysfunction, testosterone likely has little to no effect on erectile dysfunction or sexual quality of life (QOL).

Methods: A systematic review¹⁴ compared testosterone with placebo in men with low or normal baseline testosterone and sexual dysfunction. Sexual function was evaluated using the International Index of Erectile Function (IIEF) scale (scores range from 6 to 30, lower scores indicate worse function) and sexual QOL was evaluated using IIEF satisfaction domain (scores range from 0 to 10; lower scores indicate worse satisfaction).

Results: In the largest analysis using the IIEF scale (10 RCTs, 2223 patients), there was no statistical difference between testosterone and placebo. Focusing on a subgroup analysis of the best quality RCTs (6 RCTs, 2016 patients), patients taking testosterone had higher scores on the IIEF scale versus placebo at 12 months (difference of 2.4 points), but this difference did not meet the minimal clinically important difference of 4 points. Scores for sexual QOL (2 RCTs, 286 patients) were not different between groups.

Can oral methotrexate improve symptoms of osteoarthritis?

Bottom line: In patients with knee or hand osteoarthritis, methotrexate may improve pain and stiffness when conventional medications are ineffective. Since this is off-label use, more studies are needed to confirm results.

Methods: Two RCTs^{15,16} compared 20 mg to 25 mg of oral methotrexate weekly with placebo for osteoarthritis. One RCT included 155 participants (mean age=61) with radiographic knee osteoarthritis and persistent knee pain despite medications.¹⁵ Another RCT included 97 participants (mean age=61) with magnetic resonance imaging-detected synovitis hand osteoarthritis and persistent pain.¹⁶ Folic acid 5 mg 6 days of the week was given in both trials.

Results: At 6 months, mean knee pain was reduced from 6.4 to 5.1 (10-point numerical rating scale) in the methotrexate group compared with 6.8 to 6.2 for the placebo group, a difference of 0.8 favouring methotrexate. More methotrexate patients had a clinically meaningful response than placebo (34% vs 20%). At 6 months, for patients with hand osteoarthritis, there was a greater reduction in pain scores (range=0 to 100, lower scores indicate less pain) in the methotrexate group

(62 at baseline to 46) than in the placebo group (65 at baseline to 55). The adjusted between-group difference was 10. Adverse effects were not different in both trials.

Are adverse clinical events lower with edoxaban monotherapy compared with dual antithrombotic therapy in patients with both stable coronary artery disease and atrial fibrillation?

Bottom line: At 12 months, patients with stable coronary artery disease and atrial fibrillation did not experience differences in mortality or MACE with edoxaban monotherapy compared with edoxaban plus antiplatelet, and experienced fewer major bleeds.

Methods: An open-label RCT¹⁷ (1040 patients; mean age=72; median CHA₂DS₂-VASc [congestive heart failure, hypertension, age, diabetes, stroke, vascular disease, age, sex] score=4) randomized adults with stable coronary artery disease and atrial fibrillation to edoxaban monotherapy or edoxaban plus a single antiplatelet agent (acetylsalicylic acid or clopidogrel).

Results: At 12 months, there was no difference between edoxaban monotherapy and dual antithrombotic therapy for all-cause mortality (0.6% vs 0.7%) or MACE (composite of death, MI, ischemic stroke, systemic embolism: 1.6% vs 1.8%). The edoxaban monotherapy group experienced fewer major bleeding episodes compared with the dual antithrombotic group (1.3% vs 4.5%, NNH=32).

Does colchicine prevent cardiovascular events after an MI?

Bottom line: In 1 non-industry-funded RCT, colchicine was not superior to placebo at 3 years following an MI. With previous RCTs demonstrating benefit with colchicine for secondary cardiovascular prevention, its efficacy is uncertain given the findings of this newest RCT.

Methods: A double-blind RCT¹⁸ (7062 participants, mean age=61) compared colchicine with placebo in adults with an MI. The primary outcome was a composite of cardiovascular death, recurrent MI, stroke, or unplanned ischemia-driven coronary revascularization.

Results: After a median follow-up of 3 years, there was no difference in the primary outcome (9.1% colchicine vs 9.3% placebo), cardiovascular mortality (3.3% vs 3.2%), or all-cause mortality (4.6% vs 5.1%). These results are different from findings of previous RCTs that suggested an approximate 25% relative risk reduction of cardiovascular events in patients with coronary disease taking colchicine.¹⁹

In 2024, glucagon-like peptide-1 (GLP-1) agonists were studied for several new medical indications in patients with obesity. What do these indications include?

Bottom line: Glucagon-like peptide-1 agonists have been studied in patients with knee osteoarthritis, obstructive sleep apnea, heart failure with preserved ejection fraction, and metabolic dysfunction-associated

steatohepatitis (MASH). Study summaries (all RCTs were 52 weeks or more in duration in patients with obesity):

- In 407 patients with knee osteoarthritis (mean baseline pain=70 [100-point scale; higher scores indicate worse pain]), semaglutide reduced pain by 14 points more versus placebo.²⁰
- In 469 patients with moderate-severe obstructive sleep apnea (baseline number of apnea and hypopnea events per hour=51), tirzepatide reduced events per hour by 20 to 24 more versus placebo, exceeding the clinical significance threshold (≥ 15 events/hour).^{21,22}
- In 616 patients with preserved ejection fraction heart failure, semaglutide reduced heart failure symptoms compared with placebo.²³
- In 190 patients with MASH and liver fibrosis, tirzepatide resolved MASH in 44% to 62% of patients versus 10% with placebo (NNT=2 to 3).²⁴

Honourable mention

In primary care, does screening for diseases improve patient outcomes? What about interventions improving adherence to clinical guidelines?

Bottom line: Screening for depression or respiratory diseases did not change patient-important outcomes and were resource intensive. While interventions can improve guideline adherence in practice, patient outcomes were unchanged and a few worsened.

Study summaries: To assess the effectiveness of depression screening, 8129 patients were screened for a Patient Health Questionnaire-9 score of 10 or more. Of the 1030 screen-positive patients, there were no differences in severity based on Patient Health Questionnaire-9 scores, QOL, or satisfaction regardless of whether the findings were reported to the general practitioner or general practitioner and patient, or if there was no feedback.²⁵

In another study, investigators randomly called 1,182,406 households seeking adults with respiratory symptoms. Of the 49,594 with symptoms who consented, 2857 received spirometry. Patients with airflow obstruction were randomized to specialist or usual care (508 patients, mean age=63 y). No differences were observed in hospitalizations or QOL at 12 months. Approximately 4000 patients need to be screened to prevent 1 respiratory-related health care visit per year.²⁶

Two RCTs investigated interventions to improve guideline adherence. One RCT of 11,000 people with chronic kidney disease, type 2 diabetes, and hypertension found no difference in hospitalizations, emergency department visits, or cardiovascular events versus usual care, but acute kidney injury increased (12.7% intervention group vs 11.3% usual care; NNH=69 at 1 year).²⁷

In an RCT of 18 practices (1242 patients with chronic obstructive pulmonary disease), integrating respiratory specialist care (vs usual care by a general practitioner) increased guideline adherence at 1 year; however, exacerbation rates were no different and hospitalizations increased.²⁸

Conclusion

Several clinical trials and meta-analyses published in 2024 were relevant to primary care, particularly in the areas of insomnia, cardiology, and musculoskeletal disorders. 🌿

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Contributors

All authors contributed to the selection of included studies and writing of the original draft. **Dr Samantha S. Moe**, **Betsy S. Thomas**, and **Dr G. Michael Allan** reviewed and edited the final manuscript.

Competing interests

None declared

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