

Top studies of 2022 relevant to primary care

From the PEER team

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Abstract

Objective To summarize 10 high-quality medical articles published in 2022 that are relevant to primary care physicians.

Selecting the evidence Routine surveillance of tables of contents in relevant medical journals and EvidenceAlerts was conducted by the PEER (Patients, Experience, Evidence, Research) team, a group of primary care health care professionals with an interest in evidence-based medicine. Articles were selected and ranked based on relevance to practice.

Main message Published articles from 2022 most likely to influence primary care practice examined the following subjects: reducing dietary sodium for heart failure; timing of blood pressure medications to reduce cardiovascular outcomes; adding as-needed corticosteroids to rescue puffers for asthma exacerbations; influenza vaccination after myocardial infarction; comparing various medications for diabetes management; tirzepatide for weight loss; low FODMAP diet for irritable bowel syndrome; prune juice for constipation; impact of regular acetaminophen use on patients with hypertension; and time required to care for patients in primary care. Two “honourable mention” studies are also summarized.

Conclusion Research published in 2022 yielded several high-quality articles on various conditions relevant to primary care, including hypertension, heart failure, asthma, and diabetes.

Every year, primary care physicians are inundated with a vast number of medical articles, increasing the complexity and time commitment of staying up to date. In this article we have summarized our choice of the top 10 medical articles published in 2022, along with 2 “honourable mentions,” that we believe are pertinent to physicians in comprehensive family practice.

Selecting the evidence

The PEER (Patients, Experience, Evidence, Research) team identified clinical trials, systematic reviews, and guidelines through scheduled searches of tables of contents from high-impact medical journals (eg, the *New England Journal of Medicine*, the *Lancet*, and *BMJ*). Further, we used EvidenceAlerts,¹ ACCESSSS,² and the American College of Physicians Journal Club³ to identify high-quality articles relevant to primary care practice. Identified articles were independently ranked by our team of primary care professionals. Owing to the timeline of our previous Top Studies publications, we searched publications from late 2021, and have consequently included 1 paper from this time frame. All results are statistically significant unless otherwise stated.

Editor's key points

► Staying up to date on the vast amount of new literature relevant to primary care presents a considerable challenge. The authors of this review summarize what they believe were the top 10 studies (and 2 honourable mentions) of 2022 that could have meaningful effects on comprehensive family medicine practice.

► Studies relate to a variety of conditions and topics commonly encountered in primary care, including cardiovascular health, asthma, diabetes, weight loss, irritable bowel syndrome, constipation, and time required to provide primary care.

► Honourable mentions include a study of whether providing nonspeculum and self-sampling options increases uptake of cervical cancer screening and another examining medication nonadherence.

Main message

Does reducing dietary sodium from low to very low levels improve heart failure outcomes?

Bottom line: Reducing dietary sodium from about 2100 to 1700 mg/day does not reduce cardiovascular-related hospital admissions or death in patients with chronic heart failure after 12 months.⁴ The average sodium intake of Canadians is 2760 mg/day.⁵

Methods: An open-label randomized controlled trial (RCT) (N=806) evaluated adults with chronic heart failure taking optimized therapy (median age 67, 67% male, 71% class II heart failure).⁴ Intervention participants received sample menus and counselling with a target of less than 1500 mg/day of dietary sodium, while control participants received general advice to restrict sodium.

Results: At 12 months, median sodium intake had decreased from 2286 to 1658 mg/day in the intervention group versus 2119 to 2073 mg/day in the control group. Rates of the primary outcome (composite of cardiovascular-related emergency visit or hospital admission or all-cause death) and of all-cause death alone were not statistically different between groups.

Does evening dosing of usual antihypertensive agents improve major cardiovascular outcomes compared with morning dosing?

Bottom line: The TIME (Treatment in Morning versus Evening) trial found that switching antihypertensive dosing from morning to evening had no impact on cardiovascular outcomes.⁶ These findings conflict with those of previous trials^{7,8}; however, additional trials are ongoing, including one involving some authors of this article (J.K. and G.M.A.).⁹

Methods: An open-label RCT (N=21,104; mean age 65 years; 43% female) randomized adults with hypertension to taking all their usual antihypertensive medications in the morning (6:00 AM to 10:00 AM) or evening (8:00 PM to midnight).⁶ The primary composite end point was vascular death or hospitalization for nonfatal myocardial infarction (MI) or nonfatal stroke.

Results: After 5.2 years, primary end point events had occurred in 3.4% of participants assigned to evening treatment and 3.7% assigned to morning treatment (not statistically different). Participants taking treatment in the evening reported fewer falls (21% vs 22%, number needed to treat [NNT]=86) and adverse events (dizziness, gastrointestinal symptoms, muscle aches; 69% vs 71%, NNT=77) but higher rates of "excessive" toilet visits (40% vs 36%, number needed to harm=28).

Does adding as-needed inhaled corticosteroids (ICSs) to rescue puffers improve outcomes in patients with moderate to severe asthma?

Bottom line: By adding ICSs to each use of short-acting β -agonist relievers, there is some improvement in asthma outcomes for those with moderate to severe asthma already taking regular preventive therapy.

Methods: Two randomized trials examined the impact of adding ICS puffer use with every use of short-acting β -agonist reliever versus usual care. Patients had moderate to severe asthma and were already taking daily ICSs.

- The PREPARE (Person Empowered Asthma Relief) trial¹⁰: open-label trial (N=1201 Black and Latinx participants, mean age 48, 84% female).
- The MANDALA trial¹¹: double-blind trial (N=3132, mean age 49, 65% female).

Results: Using different measures, both trials found improvements in asthma scores and exacerbations (in MANDALA, improvement was observed with a 160- μ g dose of budesonide but was seen less consistently with 80 μ g). Adding ICSs to the reliever medication reduced exacerbation rates by 15% to 25%.^{10,11} Overall, 47% of patients without added ICSs attained clinically meaningful improvement in their asthma scores compared with 52% with ICSs added to reliever medication.¹¹

What is the effect of influenza vaccination after acute MI?

Bottom line: Influenza vaccine administered within 72 hours after MI reduces the risk of cardiovascular death after 1 year.

Methods: In a double-blind RCT, 2532 participants (mean age 60, approximately 80% male) with MI (55% with ST-elevation MI) were randomized to receive influenza vaccine or placebo within 72 hours of angiography or percutaneous coronary intervention.¹²

Results: At 1 year, 5.3% of participants in the intervention group developed the primary composite outcome of all-cause death, MI, or stent thrombosis versus 7.2% in the placebo group (NNT=52). The rate of all-cause death was reduced from 4.9% to 2.9% with influenza vaccine (NNT=52), driven almost entirely by the reduction in cardiovascular death.

In patients with type 2 diabetes, how do different classes of antidiabetes medications compare when added to metformin?

Bottom line: In patients with type 2 diabetes, adding liraglutide or glargine to metformin resulted in more patients achieving an hemoglobin A_{1c} (HbA_{1c}) target below 7% compared with those taking sitagliptin or glimepiride. Liraglutide lowered the risk of cardiovascular events more than other drugs did. Microvascular outcomes were no different across groups.

Methods: An open-label RCT of 5047 patients with type 2 diabetes taking maximum-dose metformin (mean age 57 years, mean duration of diabetes of 4 years, mean HbA_{1c} 7.5%, cardiovascular disease in 7%) compared sitagliptin 100 mg, glimepiride 5 mg, liraglutide 1.6 mg, and glargine 50 units.^{13,14}

Results: After 5 years, more patients achieved a target HbA_{1c} below 7% with glargine (33%) or liraglutide (32%) compared with sitagliptin (23%) or glimepiride

(28%). Microvascular outcomes were not statistically different between groups. The risk of adverse cardiovascular outcomes was lowest with liraglutide (6.6% vs 9.0% to 9.6% for other treatments). Severe hypoglycemia was more common with glimepiride (2.2% vs 0.7% to 1.3% for other treatments), gastrointestinal effects with liraglutide (44% vs 34% to 36% for other treatments), and weight loss with liraglutide (3.5 kg) and sitagliptin (2.0 kg) versus others (0.6 to 0.7 kg).

Does tirzepatide help with weight loss?

Bottom line: Tirzepatide reduces weight by about 12 to 18 percentage points more than placebo in patients with obesity.

Methods: A double-blind RCT compared tirzepatide (5 to 15 mg subcutaneously once a week) with placebo in 2539 adult patients with obesity (mean age 45, 68% female, mean weight 105 kg).¹⁵

Results: At 72 weeks, the mean reductions in weight for placebo or 5, 10, or 15 mg of tirzepatide were 3%, 15%, 20%, and 21%, respectively, and the proportions of patients who lost at least 10% of their body weight were 19%, 69%, 78%, and 84%, respectively. Withdrawals owing to adverse effects were more common with tirzepatide (up to 7% for 10 mg of tirzepatide vs 3% for placebo). Gastrointestinal effects occurred commonly (eg, nausea up to 33% for 10 mg of tirzepatide vs 10% for placebo).¹⁵ Indirectly, relative to a recent RCT,¹⁶ weight loss in this RCT appears similar to that with semaglutide (mean percentage weight loss of 16%) and higher than that with liraglutide (6%).¹⁶

Does the low FODMAP diet reduce symptoms of irritable bowel syndrome (IBS) compared with otilonium bromide?

Bottom line: In patients with IBS, symptom severity was meaningfully reduced at 8 weeks in 71% of those treated with a low FODMAP diet compared with 61% of those treated with medication.

Methods: This RCT compared a low FODMAP (omitting short-chain carbohydrates that may cause digestive difficulty) diet with otilonium bromide (40 mg, 3 times daily) in 459 patients (mean age 41, 76% female) with IBS treated in primary care.¹⁷

Results: At 8 weeks, a higher proportion of patients responded (a 50-point or greater improvement in IBS symptom severity) to a FODMAP diet (71%) compared with medication (61%), NNT=10. No difference in response was found based on IBS subtype (IBS-diarrhea, IBS-constipation, or mixed). The FODMAP diet also improved symptom scores at 16 weeks compared with otilonium bromide but it was no longer statistically significantly better at 24 weeks. Rates of serious adverse events were not different between groups.

Is prune juice effective for constipation?

Bottom line: Prune juice may be effective for functional constipation.

Methods: In a single industry-sponsored RCT, 84 patients (mean age 51, approximately 75% female) with functional constipation (fewer than 3 bowel movements per week or Bristol Stool Form Scale [BSFS] scores of 1 to 2 for the past 3 months) were given 54 g of prune juice or matching placebo daily.¹⁸

Results: At 8 weeks, the number of patients with normal bowel movements (BSFS=4) was 50% for prune juice versus 25% for placebo (NNT=4). There was no difference in the rate of loose or watery stools (BSFS=5 to 7). Flatulence scores were not different between groups.

Does regular acetaminophen use increase blood pressure (BP) in patients with hypertension?

Bottom line: One 2-week trial found that regular daily intake of 4 g of acetaminophen increased mean daytime systolic BP in individuals with hypertension by about 5 mm Hg. Longer-term effects have yet to be studied.

Methods: A double-blind trial randomized 110 adults with pre-existing controlled hypertension to receive 1 g of acetaminophen or placebo 4 times daily for a 2-week period.¹⁹ Patients crossed over to the alternate treatment arm after a 2-week washout. Blood pressure was measured by 24-hour ambulatory pressures taken at the beginning and end of each treatment arm.

Results: In 103 patients completing the study, regular acetaminophen intake showed a statistically significant 4.7 mm Hg increase in mean daytime systolic BP versus placebo. Mean daytime diastolic BP also showed an increase of 1.6 mm Hg versus placebo.

How much time do family doctors need to provide patient care?

Bottom line: A family physician would need approximately 27 hours per day to provide preventive, chronic, and acute care to a patient panel. Team-based practices can reduce this time to about 9 hours. Guideline authors need to consider the time requirements of recommendations.

Methods: A simulation study applied preventive, chronic (10 most prevalent conditions), and acute care to hypothetical adult patient panels.²⁰ Preventive care was based on recommendations from the United States Preventive Services Task Force. Time for each service was calculated based on assessment of guidelines, literature searches, and data collected on the number of required visits.

Results: For an average 2500-patient panel, a family physician would need approximately 27 hours per day to provide care. Approximately 14 hours were needed for preventive care, including counselling (eg, obesity, cardiovascular disease prevention). Chronic disease management (eg, hypertension, mood disorders) took

about 7 hours per day, while acute care and administrative tasks each took about 2 to 3 hours per day. In team-based practice, the total time decreased by 65% to approximately 9 hours per day, mainly owing to counselling referrals.

Honourable mentions

Does offering nonspeculum clinician-taken or self-sampling options increase rates of cervical cancer screening?

Bottom line: In women not being regularly screened, providing nonspeculum and self-sampling options significantly increases uptake of cervical cancer screening at 4 and 12 months versus usual care. Canadian health care system changes would be required to implement home-based human papillomavirus screening.

Methods: A 12-month RCT (N=784) in England compared a “choice” recommendation (clinician nonspeculum, speculum, or self-sample) with usual care (reminder letter sent to women every 5 years).²¹ Participants were 50 to 64 years of age and had last been screened 6 to 15 years prior. To improve access, text or online booking options and evening clinics were made available.

Results: Uptake of cervical cancer screening was improved at both 4 (20% vs 5%) and 12 months (31% vs 14%) among women offered a choice, compared with usual care. When given a choice, at 12 months 42%, 36%, and 23% of participants chose speculum, self-sampling, and clinician nonspeculum sampling, respectively. Choice differed based on ethnicity, with 51% of White women choosing self-sampling and 53% to 71% of women from Black, Asian, and other ethnic backgrounds choosing traditional speculum sampling. Of 70 samples taken, 4 were positive for human papillomavirus, all of which had normal results on cytology or biopsy.

What are the rates of medication nonadherence among Canadian patients?

Bottom line: Failure to fill a new prescription occurs anywhere from 14% to 30% of the time and is more common with asymptomatic conditions.

Methods: A retrospective observational study included 91,660 new primary care prescriptions from more than 200,000 adult patients in Manitoba and linked prescriptions to pharmacy dispensing data.²²

Results: Overall, rates of primary medication nonadherence (initial prescription not filled within 90 days of prescription date) ranged from 14% (antidepressants) to 30% (antihypertensives). For symptomatic conditions (eg, infections, anxiety), rates of nonadherence ranged from 14% to 18%, while for asymptomatic conditions (eg, hypertension, osteoporosis), rates ranged from 21% to 30%. Lipid-lowering agents had a relatively low nonadherence rate at 15%.

Conclusion

Research conducted in 2022 yielded several high-quality articles about various conditions relevant to primary care, including hypertension, heart failure, asthma, and diabetes.

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All authors contributed to the literature review and interpretation, and to preparing the manuscript for submission.

Competing interests

None declared

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